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International Agency for Research on Cancer



2. CANCER IN HUMANS

Since the previous evaluation of the carcinogenicity of firefighting by the IARC Monographs programme in 2007, published in Volume 98 (IARC, 2010), numerous studies have been published on cancer incidence and mortality in firefighters. A systematic search was conducted of the PubMed, Web of Science, and Embase databases to identify epidemiological studies evaluating the association between the agent – occupational exposure as a firefighter - and the occurrence (reported as incidence or mortality) of cancer in humans (Clarivate, 2022; Elsevier, 2022; NLM, 2022). The search terms used and the results of the literature search are available online at: https://hawcproject.iarc.who.int/lit/ assessment/666/. The search (conducted without restriction as to start date and concluded on 13 June 2022) led to the identification of 643 studies considered for inclusion in the review of evidence on cancer in humans, Section 2 of the present monograph.

A study was excluded from the review if: (i) the occurrence of cancer as an outcome was not reported (n = 444); (ii) a cross-sectional or ecological study design (n = 3) was used; (iii) it was reported as a conference abstract or was a duplicate of an existing study (n = 15); (iv) no primary estimates of association between the agent and cancer (n = 41) were presented; (v) it was a "letter to the editor" or commentary about an included study (n = 21); or (vi) it was an occupational surveillance study that did not investigate cancer in firefighters a priori (n = 37). The exclusion of such general occupational surveillance studies was carried out to reduce the potential for publication bias in the studies included for review, given that these studies tended to only highlight occupations associated with increased risk. Some studies of this type were previously included in the evaluation of firefighting by the IARC Monographs programme in 2007 (IARC, 2010) but were excluded from the present evaluation. One study that was published with analytical errors was considered to be uninformative and was excluded from the evaluation (Colbeth et al., 2020b; [personal communication with the authors]).

All other studies (n = 83) were considered eligible for inclusion in the evaluation of the evidence on cancer in humans. Where study populations had been updated with additional follow-up or participants, only the most recent or most informative publication was reviewed in detail. A total of 71 studies were therefore reviewed in detail. This included 41 cohort studies, 10 case–control studies, 1 mortality surveillance study, 7 meta-analyses, and 12 case reports.

Owing to the large number of studies included in the evaluation, studies were grouped according to cancer site, type of exposure assessment, and study design. Studies were grouped into sections numbered first by cancer site (2.x)and then by type of exposure assessment (2.x.1 or 2.x.2). For the studies grouped in Section 2.x.1, "Studies reporting occupational characteristics of firefighters", the design or analysis of the study contained an assessment of the employment or exposure characteristics of firefighters, such as the number or type of emergency responses, working in a fire combat role, or duration of employment. The studies grouped in Section 2.x.2, "Studies only reporting having ever worked as a firefighter", only provided information on having ever worked in the occupation. The latter group (Section 2.x.2) was further subdivided into: (a) occupational cohort studies; and (b) population-based studies. Within each section, studies were described in order of geographical continent (Asia, Europe, North America, Oceania) then publication year, from most to least recent. To reduce repetition in study description and appraisal, studies were described in detail at first mention (primarily in Section 2.1), and in less detail in subsequent sections.

The Working Group conducted a metaanalysis of cohort studies, the results of which are described in Section 2.8.2. A synthesis of the evidence regarding cancer in humans is presented in Section 2.9.

2.1 Cancers of the lung and respiratory system, including mesothelioma

2.1.1 Studies reporting occupational characteristics of firefighters

See <u>Table 2.1</u>.

The Working Group identified 26 occupational and population-based cohort studies and one pooled international case–control study that had investigated the relation between occupational exposure as a firefighter and risk of cancer of the lung and respiratory system (including the larynx, lung, trachea, and bronchus) and mesothelioma (Feuer & Rosenman, 1986; Vena & Fiedler, 1987; Demers et al., 1992a, 1994; Guidotti, 1993; Aronson et al., 1994; Tornling et al., 1994; Bates et al., 2001; Zeig-Owens et al., 2011; Ahn et al., 2012; Daniels et al., 2014, 2015; Ahn & Jeong, 2015; Glass et al., 2016a, b, 2017, 2019; Bigert et al., 2016; Petersen et al., 2018a, b; Kullberg et al., 2018; Bigert et al., 2020; Pinkerton et al., 2020; Webber et al., 2021; Marjerrison et al., 2022a, b). Some studies reported results for all cancers of the respiratory system combined (defined variously by individual studies). Studies described in this section assessed employment or exposure characteristics of firefighters in the design or analysis of the study, for example, the number or type of emergency responses, working in a fire combat role, or duration of employment.

Two studies reporting on cancer incidence and cancer mortality, respectively, originated from Asia (Ahn et al., 2012; Ahn & Jeong, 2015). Of the seven European studies, all of which were carried out in Scandinavia, five investigated cancer incidence (Tornling et al., 1994; Kullberg et al., 2018; Petersen et al., 2018a; Bigert et al., 2020; Marjerrison et al., 2022a, b), whereas four examined cancer mortality (Tornling et al., 1994; Petersen et al., 2018b; Marjerrison et al., 2022a, b). Of 13 studies from the USA, 2 reported on cancer incidence (Zeig-Owens et al., 2011; Webber et al., 2021) among firefighters working at the World Trade Center (WTC) disaster site. Five of the remaining studies comprised analyses in a pooled cohort of firefighters from San Francisco, Chicago, and Philadelphia with varying follow-up periods, exposure metrics, and types of outcome data (Daniels et al., 2014, 2015; Pinkerton et al., 2020) or analyses of the individual cohorts (Beaumont et al., 1991; Baris et al., 2001), whereas four presented incidence or mortality data based on analyses of pooled or individual cohorts from Seattle and Tacoma, in Washington, and Portland, Oregon (Heyer et al., 1990; Demers et al., 1992a, b, 1994). Three of

Table 2.1 Cohort and case-control studies reporting occupational characteristics of firefighters and cancers of the lung and respiratory system, including mesothelioma

Reference, location, enrolment/ follow-up period, study design	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments
Ahn & Jeong (2015) Republic of Korea Enrolment, 1980– 2007/follow-up, 1992–2007 Cohort	33 442 men employed as emergency responders for ≥ 1 mo between 1980 and 2007, with (29 453) and without (3989) firefighting experience and not deceased in 1991 Exposure assessment method: ever employed and categorical duration of employment (years) as first- or second- line firefighter and non-firefighters from employment records	Lung and bronchus, mortality Lung and bronchus, mortality	Duration of firefig (SMR): 1 mo to < 10 yr 10 to < 20 yr \ge 20 yr Total Duration of firefig (RR): < 10 yr (including non-firefighters) 10 to < 20 yr \ge 20 yr	6 7 13 26	0.69 (0.25–1.48) 0.53 (0.21–1.10) 0.56 (0.30–0.96) 0.58 (0.38–0.84)	Age, calendar period	<i>Exposure assessment</i> <i>critique</i> : Satisfactory quality. Heterogeneity of direct firefighter exposure within job title. May include municipal and rural firefighters. <i>Strengths</i> : employment duration and internal comparison limits healthy-worker bias; only professional [career] firefighters were included in the cohort. <i>Limitations</i> : small number of cases of lung cancer; no information on personal characteristics or confounders; follow-up time was reasonably short; cohort members were fairly young; no direct measure

of exposure.

Table 2.1 (continued)

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Reference, location, enrolment/ follow-up period, study design	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments
Ahn et al. (2012) Republic of Korea Enrolment, 1980– 2007/follow-up, 1996–2007 Cohort	33 416 men employed as emergency responders for ≥ 1 mo between 1980 and 2007, with (29 438) and without (3978) firefighting experience and not deceased in 1995 Exposure assessment method: ever employed and categorical duration of employment (years) as first- or second- line firefighter and non-firefighters from employment records	Larynx, incidence Lung and bronchus, incidence Lung and bronchus, incidence	Duration of firefig (SIR): 1 mo to < 10 yr ≥ 10 yr Total Duration of firefig (SIR): 1 mo to < 10 yr ≥ 10 yr Total SRR: Non-firefighters Ever employed as a firefighter	0 3 3	0 (NR) 0.72 (0.15–2.11) 0.57 (0.11–1.67)	Age, calendar period	<i>Exposure assessment</i> <i>critique</i> : Satisfactory quality. Heterogeneity of direct firefighter exposure within job title. May include municipal and rural firefighters. <i>Strengths</i> : employment duration and internal comparison limits healthy-worker bias; only professional [career] firefighters were included in the cohort. <i>Limitations</i> : small numbe of cases of lung cancer; no information on personal characteristics or confounders (except the firefighter cohort had a lower BMI and smoked less than the comparison population for the SIR analysis); follow-up time was reasonably short; cohort members were fair young; no direct measure of exposure.

Reference, location, enrolment/ follow-up period, study design	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments
Marjerrison et al.	3881 male professional	Larynx, incidence	SIR:			Age, calendar	Exposure assessment
<u>(2022a)</u> Norway	[career] firefighters employed (most were		Firefighters	12	1.77 (0.91–3.08)	year	<i>critique</i> : Satisfactory quality. Included
Enrolment,	full-time) in positions	Larynx, incidence	Year of first emplo				firefighters with current or
1950–2019/follow-	entailing active		Pre-1950	6	2.34 (0.86–5.09)		previous positions entailing
up, 1960–2018	firefighting at any of		1950-1969	5	2.02 (0.65-4.71)		active firefighting duties
Cohort 15 fire departments between 1950 and 2019 Exposure assessment method: employment history from personnel records	.	1970 or after	1	0.57 (0.01–3.18)		but no assessment of length of time in active firefightin positions, may include municipal and rural	
	Larynx, incidence	Time since first en					
		< 20 yr	0	0 (0.00-7.04)			
			20–39 yr	2	0.59 (0.07–2.14)		firefighters.
	history from	T	$\geq 40 \text{ yr}$	10	3.33 (1.60-6.13)		Strengths: long length
	personnel records	Larynx, incidence	Duration of emplo < 10 yr	0): 0 (0.00–5.55)		of follow-up (mean,
			< 10 yr 10–19 yr	0	0 (0.00-5.55) 2.7 (0.33-9.75)		28 yr), near complete
			20–29 yr	2	0.51 (0.01–2.85)		ascertainment of both cancer incidence and mortality; analyses by duration and timing of
			$\geq 30 \text{ yr}$	9	2.53 (1.16-4.80)		
		Lung, incidence	SIR:	,	2.35 (1.10-4.00)		
		Dung, meldenee	Firefighters	81	0.98 (0.78-1.22)		employment.
		Lung, incidence	Year of first emplo				<i>Limitations</i> : probable healthy-worker effect;
		241.9, 1101401100	Pre-1950	40	1.37 (0.98–1.87)		low number of cases for
			1950-1969	28	0.87 (0.58–1.26)		laryngeal cancer and
			1970 or after	13	0.61 (0.33–1.04)		mesothelioma; no data on
		Lung, incidence	Time since first en	nployment (potential confounders apar
		0.	< 20 yr	4	1.07 (0.29-2.74)		from age, sex, and calendar
			20-39 yr	22	0.64 (0.40-0.98)		time.
			$\geq 40 \text{ yr}$	55	1.23 (0.93-1.60)		
		Lung, incidence	Duration of emplo	yment (SIR):		
			< 10 yr	4	0.62 (0.17-1.59)		
			10–19 yr	7	0.86 (0.34-1.76)		
			20–29 yr	18	0.81 (0.48–1.29)		
			≥ 30 yr	52	1.14 (0.85-1.49)		

Reference, location, enrolment/ follow-up period, study design	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments
Marjerrison et al.		Mesothelioma,	SIR:			Age, calendar	
<u>(2022a)</u>		incidence	Firefighters	7	2.46 (0.99-5.06)	year	
(cont.)		Mesothelioma,	Year of first emplo	yment (SIR)	:		
		incidence	Pre-1950	3	3.74 (0.77–10.9)		
			1950-1969	2	1.52 (0.18-5.49)		
			1970 or after	2	2.74 (0.33-9.90)		
		Mesothelioma, incidence	Time since first en	nployment (SIR):		
			< 20 yr	0	0 (0.00-30.4)		
			20–39 yr	1	0.98 (0.02-5.46)		
			\geq 40 yr	6	3.47 (1.27–7.55)		
		Mesothelioma,	Duration of emplo	yment (SIR)):		
		incidence	< 10 yr	1	4.21 (0.11-23.4)		
			10–19 yr	0	0 (0.00–11.4)		
			20–29 yr	1	1.38 (0.03-7.66)		
			≥ 30 yr	5	3.09 (1.00-7.20)		
<u>Marjerrison et al.</u>	3881 male professional	Larynx, mortality	SMR:			Age, calendar	Exposure assessment
<u>(2022b)</u>	[career] firefighters		Firefighters	< 5	1.92 (0.52-4.91)	year	critique: Satisfactory
Norway	employed (most were	Larynx, incidence	Period of follow-u	p (SIR):			quality. Included
Enrolment, 1950–2019/follow-	full-time) in positions entailing active		1984 or before	0	0 (0.00–1.77)		firefighters with current of previous positions entaili
up, 1960–2019/10110w-	firefighting at any of		1985–1994	5	3.57 (1.16-8.33)		active firefighting duties,
Cohort	15 fire departments		1995 or after	7	1.89 (0.76-3.90)		may include municipal ar
	between 1950 and	Larynx, mortality	Period of follow-u	p (SMR):			rural firefighters.
	2019		1984 or before	0	0 (0.00-5.58)		Strengths: long length
	Exposure assessment		1985–1994	< 5	2.37 (0.06–13.2)		of follow-up (mean,
	method: employment history from personnel records		1995 or after	< 5	2.66 (0.55–7.77)		28 yr); near complete ascertainment of both cancer incidence and mortality; analyses by duration and timing of employment.

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Reference, location, enrolment/ follow-up period, study design	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments
Marjerrison et al.		Larynx, incidence	Age at diagnosis (S	SIR):		Age, calendar	Limitations: probable
(<u>2022b)</u>			≤ 49 yr	0	0 (0.00-6.12)	year	healthy-worker effect;
(cont.)			50-69 yr	< 5	0.74 (0.15-2.16)		low number of cases for
			≥ 70 yr	9	3.99 (1.82-7.57)		laryngeal cancer and mesothelioma; no data on potential confounders apar from age, sex, and calendar time.
		Larynx, mortality	Age at diagnosis (S	SMR):			
			≤ 49 yr	0	0 (0.00-34.9)		
			50-69 yr	< 5	1.00 (0.03-5.56)		
			≥ 70 yr	< 5	3.00 (0.62-8.77)		
		Lung, mortality	SMR:				
		0, 1	Firefighters	61	0.91 (0.69–1.16)		
		Lung, incidence	Period of follow-u				
		0,	1984 or before	17	1.12 (0.65-1.79)		
			1985-1994	17	1.11 (0.64–1.77)		
			1995 or after	47	0.90 (0.66–1.20)		
		Lung, mortality	Period of follow-u		, ,		
		Dang, mortanty	1984 or before	14	1.09 (0.59-1.82)		
			1985-1994	15	1.11 (0.62–1.83)		
			1995 or after	32	0.78 (0.53-1.10)		
		Lung, incidence	Age at diagnosis (S	SIR):			
		0,	$\leq 49 \text{ yr}$	< 5	1.00 (0.27-2.56)		
			50–69 yr	29	0.68 (0.46-0.98)		
			\geq 70 yr	48	1.33 (0.98–1.77)		
		Lung, mortality	Age at diagnosis (S				
		8, 11, 17	$\leq 49 \text{ yr}$	< 5	0.73 (0.09-2.63)		
			50-69 yr	20	0.61 (0.37-0.94)		
			\geq 70 yr	39	1.23 (0.88–1.68)		
		Mesothelioma,	SMR:				
		mortality	Firefighters	< 5	2.40 (0.65-6.15)		
		Mesothelioma,	Period of follow-u				
		incidence	1984 or before	< 5	4.23 (0.11-23.56)		
			1985–1994	0	0 (0.00-6.16)		
			1995 or after	6	2.82 (1.04–6.14)		

Reference, location, enrolment/ follow-up period, study design	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments
Marjerrison et al.		Mesothelioma,	Period of follow-u	p (SMR):		Age, calendar	
<u>(2022b)</u>		mortality	1984 or before	< 5	0 (NR)	year	
(cont.)			1985–1994	0	0 (NR)		
			1995 or after	< 5	1.08 (0.37-5.27)		
		Mesothelioma,	Age at diagnosis (S	SIR):			
		incidence	≤ 49 yr	0	0 (0.00-30.5)		
			50–69 yr	< 5	2.33 (0.48-6.80)		
			≥ 70 yr	< 5	2.74 (0.75-7.01)		
		Mesothelioma,	Age at diagnosis (S	SMR):			
		mortality	\leq 49 yr	0	0 (0.00–159)		
			50–69 yr	< 5	3.16 (0.38-11.41)		
			≥ 70 yr	< 5	1.98 (0.24–7.14)		
Bigert et al. (2020) Sweden Enrolment, 1960–	8136 male firefighters identified from national censuses in	Larynx, incidence	SIR: Firefighters SIR:	12	0.92 (0.48–1.61)	Age, calendar period	<i>Exposure assessment</i> <i>critique</i> : Satisfactory quality. Unclear if
1990/follow-up, 1961–2009	1960, 1970, 1980, and 1990		Firefighters	110	0.87 (0.72-1.05)		individuals were active
Cohort	Exposure	Lung, incidence	Histological type	(SIR):			firefighters for whole employment. May include
Conort	assessment method:		Adenocarcinoma	31	1.01 (0.69–1.43)		full-time, part-time,
	questionnaire;		Small cell	10	0.72 (0.34-1.32)		municipal, and rural
	ever employed and		Squamous cell	38	0.93 (0.66-1.28)		firefighters.
	categorical duration of		Other	31	0.77 (0.52-1.09)		Strengths: near complete
	employment (years) as firefighter from census	Lung, incidence	Duration of emplo	yment (SIR)):		ascertainment of cancer incidence; long length
	surveys		1–9 yr	3	1.03 (0.21-3.01)		of follow-up (mean,
			10–19 yr	33	1.06 (0.73–1.48)		28 yr); analyses stratified
			20–29 yr	34	0.85 (0.59–1.18)		by calendar period of
			≥ 30 yr	40	0.78 (0.56-1.06)		employment.
			Trend-test P value	, 0.10			

Reference, location, enrolment/ follow-up period, study design	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments
<u>Bigert et al. (2020)</u>		Lung, incidence	Time period (SIR)	:		Age, calendar	Limitations: no data on job
(cont.)		-	1961–1975	11	0.94 (0.47-1.68)	period	duties, employment type,
			1976-1990	32	0.84 (0.58-1.19)		or potential confounders
			1991-2009	67	0.88 (0.68-1.12)		(aside from age, sex, and calendar year); probable healthy-worker hire bias;
		Lung	Duration of emplo	yment (SIR)):		
	(adenocarcinoma), incidence	1–9 yr	1	2.59 (0.07-14.4)		potential non-differential misclassification of	
		10–19 yr	8	1.32 (0.57-2.60)			
			20–29 yr	6	0.65 (0.24-1.41)		employment duration
			\geq 30 yr	16	1.06 (0.61–1.72)		
			Trend-test P value	, 0.94			
		Lung	Time period (SIR)	:			
		(adenocarcinoma),	1961–1975	2	1.50 (0.18-5.40)		
		incidence	1976-1990	6	0.87 (0.32-1.90)		
			1991-2009	23	1.02 (0.65-1.53)		
		Mesothelioma,	SIR:		, , , , , , , , , , , , , , , , , , ,		
		incidence	Firefighters	7	1.11 (0.45-2.29)		
		Mesothelioma,	Duration of emplo	wment (SIR)			
		incidence	1–9 yr	1	13.68 (0.35–76.2)		
			10–19 yr	0	0 (0.00-2.80)		
			20–29 yr	3	1.46 (0.30-4.28)		
			≥ 30 yr	3	1.04 (0.21–3.04)		
			Trend-test <i>P</i> value	, 0.85	(,		
		Mesothelioma,	Time period (SIR)	·			
		incidence	1961–1975	0	0 (0.00-19.0)		
			1976–1990	2	1.29 (0.16-4.67)		
			1991-2009	5	1.10 (0.36–2.56)		

Reference, location, enrolment/ follow-up period, study design	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments
Kullberg et al.	1080 men who worked	Bronchus and	Follow-up period	(SIR):		Birth year,	Exposure assessment
<u>(2018)</u>	\geq 1 yr as a firefighter	lung, incidence	Full, 1958–2012	27	0.79 (0.52–1.15)	calendar	critique: Satisfactory
Stockholm, Sweden	in Stockholm between 1931 and 1983		Former, 1958–1986	17	0.96 (0.56–1.55)	period	quality. Unclear if individuals were active
Enrolment, 1931–1983/follow-	Exposure assessment method: ever		Extended, 1987–2012	10	0.61 (0.29–1.12)		firefighters for whole employment. Municipal
up, 1958–2012 Cohort	employed and categorical duration of	Pleura, incidence	Follow-up period	(SIR):			firefighters. Strengths: long follow-up
Conort	employment (years) as		Full, 1958–2012	2	2.41 (0.29-8.71)		period, near complete
	an urban [municipal] firefighter from		Former, 1958–1986	1	5.24 (0.13-29.19)		ascertainment of cancer incidence; analyses of
	annual enrolment records		Extended, 1987–2012	1	1.57 (0.04–8.73)		duration and era of employment. <i>Limitations</i> : no data on potential confounders

(aside from age, sex, and calendar year), lack of exposure assessment based on job tasks or fire responses.

Table 2.1 (con	tinued)						
Reference, location, enrolment/ follow-up period, study design	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments
Tornling et al. (1994) Stockholm, Sweden Enrolment, 1931–1983/follow- up, 1951–1986 (mortality), 1958– 1986 (incidence) Cohort	1116 for mortality/1091 for incidence; male firefighters employed for ≥ 1 yr by the city of Stockholm between 1931 and 1983, identified from annual enrolment records Exposure assessment method: ever firefighter and duration (years) of firefighting employment from annual enrolment records; number of fires fought ascertained from exposure index developed from fire reports	Bronchus and lung, mortality Bronchus and lung, incidence	SMR: Firefighters SIR: Firefighters	18 16	0.90 (0.53–1.42) 0.89 (0.51–1.45)	Age, calendar period	<i>Exposure assessment</i> <i>critique:</i> Satisfactory/good quality. Enhanced exposure assessment (but based on 10% sample of reports) to differentiate exposure based on number of fires fought accounting for job position, station, and year of exposure. Municipal firefighters. <i>Strengths:</i> long follow-up period; near complete ascertainment of cancer incidence and mortality; assessed exposure to fire responses for some outcomes. <i>Limitations:</i> no data on potential confounders (aside from age, sex, and calendar year).

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Reference, location, enrolment/ follow-up period, study design	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments
Petersen et al.	9061 male firefighters	Larynx, incidence	Reference group (S	SIR):		Age, calendar	Exposure assessment
<u>(2018a)</u> Denmark Enrolment 1964–	(full-time, part- time, and volunteer) identified from		Firefighters vs general population	16	0.92 (0.56–1.50)	period	<i>critique</i> : Satisfactory quality. Includes part-time and full-time firefighters.
2004/follow-up, 1968–2014 Cohort	employer, trade union, and Danish Civil Registration System		Firefighters vs sample of employees	16	0.92 (0.57–1.51)		Excluded those who did not actually fight fires. Ma include municipal and
or later, employe before age 60 yr 31 December 20 no cancer diagn before employm as a firefighter, a a job title/functi indicating actua	records, born in 1928 or later, employed		Firefighters vs military	16	1.01 (0.62–1.66)		rural firefighters. Strengths: long period of follow-up, near-complete ascertainment of cancer incidence, use of three reference groups to evaluate healthy-worker bias; analyses by proxies of exposure including job task. Limitations: little information on potential confounders; results for mesothelioma based on large proportion of part-
		Lung, incidence	Reference group (S	SIR):			
	no cancer diagnosis before employment		Firefighters vs general population	132	0.91 (0.76–1.07)		
	a job title/function indicating actual firefighting exposure		Firefighters vs sample of employees	132	0.95 (0.80–1.13)		
	Exposure assessment method: ever		Firefighters vs military	132	1.06 (0.90–1.26)		
	employed and	Lung, incidence	Employment type	(SIR):			
	categorical duration of employment (years),		Full-time	82	0.87 (0.70-1.08)		
	as well as employment type, job title/		Part-time or volunteer	50	0.97 (0.73-1.27)		time/volunteer firefighter
	function, and work	Lung, incidence	Era of first employ	ment (SIR):			
	history, ascertained		Pre-1970	77	0.99 (0.79–1.24)		
	from civil registration,		1970-1994	48	0.80 (0.60-1.06)		
	pension, employer		1995 or after	7	0.88 (0.42-1.85)		
	personnel, and trade union membership records	Lung, incidence	Job function (SIR)	:			
		C C	Regular	125	0.92 (0.77-1.09)		
			Specialized	7	0.73 (0.35–1.54)		
		Lung, incidence	Age at first employ	yment (SIR):	:		
		- <	< 25 yr	70	0.95 (0.75-1.20)		
			25-34 yr	31	0.78 (0.55-1.10)		
			≥ 35 yr	31	0.97 (0.68–1.38)		

Reference, location, enrolment/ follow-up period, study design	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments
Petersen et al.		Lung, incidence	Duration of emplo	yment (SIR):	Age, calendar	
<u>(2018a)</u>			< 1yr	50	1.13 (0.85–1.49)	period	
(cont.)			$\geq 1 \text{ yr}$	82	0.81 (0.65-1.00)		
			≥ 10 yr	65	0.73 (0.57-0.93)		
			≥ 20 yr	49	0.70 (0.53-0.93)		
		Mesothelioma,	Reference group (S	SIR):			
		incidence	Firefighters vs general population	4	0.65 (0.24–1.73)		
			Firefighters vs sample of employees	4	0.68 (0.26-1.82)		
			Firefighters vs military	4	0.71 (0.27–1.89)		

Table 2.1 (contin **പ**)

Reference, location, enrolment/ follow-up period, study design	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments
Petersen et al. (2018b) Denmark Enrolment, 1964–2014/follow- up, 1970–2014 Cohort	11 775 male firefighters (full- time, part-time, and volunteer) identified from employer, trade union, and Danish Civil Registration System records, born in 1928 or later, employed before age 60 yr and 31 December 2004, and a job title/ function indicating actual firefighting exposure Exposure assessment method: ever employed and categorical duration of employment (years) as a firefighter ascertained from civil registration, pension, employer personnel, and trade union membership records	Larynx, trachea, and lung (ICD-10, C32–C34), mortality Larynx, trachea, and lung (ICD-10, C32–C34), mortality	Employment type (SMR): Full-time Part-time/ volunteer Duration of emplo group) (SMR): Full-time firefighters: < 1 yr ≥ 1 yr ≥ 10 yr ≥ 20 yr	76 42	1.13 (0.91–1.42) 1.16 (0.86–1.57)	Age, calendar period	Exposure assessment critique: Satisfactory quality. Includes part-time and full-time firefighters. Excluded those who did not actually fight fires. May include municipal and rural firefighters. Strengths: long period of follow-up, use of military reference group to evaluate healthy-worker bias; analyses by duration of employment. Limitations: little information on potential confounders.

Reference, location, enrolment/ follow-up period, study design	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments
Webber et al.	10 786 FDNY,	Lung, incidence	Group (SIR, US re	ference rate	s)	Age, calendar	Exposure assessment
(2021) 8813 CFHS male		CFHS firefighters	83	0.71 (0.57–0.89)	year, race/	critique: Satisfactory	
USA 2001–2016	01–2016 were active on 11		FDNY WTC firefighters	44	0.53 (0.39-0.72)	ethnicity	quality. Intensity of exposure at WTC captured but did not consider
Cohort	September 2001; FDNY cohort included men who	Lung, incidence	SIR (2-yr adjustme bias):	IR (2-yr adjustment for potential surveillance ias):			previous firefighter work. Oualitative assessment
worked	worked at the WTC site any time between		FDNY WTC firefighters	NR	0.47 (0.34–0.65)		based on presence at the WTC site, exposures
	11 September 2001	Lung, incidence	Group (RR):			Age on 11 September	complex and probably unique to 9/11 disaster. Municipal firefighters. <i>Strengths</i> : ascertainment of cancer incidence, comparison of two
	and 25 July 2002;		CFHS firefighters	83	1		
	CFHS cohort included men who were actively		FDNY WTC firefighters	44	0.87 (0.57–1.33)	2001, race/ ethnicity	
	employed on 11 September 2001 and	Lung, incidence	Group RR (2-yr ad surveillance bias):	justment fo	r potential		
	assumed not to be		CFHS firefighters	NR	1		firefighter cohorts to
	working at the WTC site Exposure assessment method: presence at WTC site from employment records and duty rosters		FDNY WTC firefighters	NR	0.77 (0.50–1.19)		evaluate bias; adjustment for smoking. <i>Limitations</i> : medical surveillance bias; young ag of cohort; relatively short length of follow-up.

Table 2.1 (continued) Cancer type Reference, Population size, Exposure Exposed location. description, exposure (histopathology), category or level cases or enrolment/ assessment method incidence or deaths follow-up period, mortality study design 9853 male FDNY Zeig-Owens et al. Lung, incidence WTC-exposure status (SIR): (2011) firefighters who were Non-exposed 8 New York City, employed for ≥ 18 mo, Exposed 9 USA were active firefighters SIR ratio NR Enrolment, on 1 January 1996, (exposed vs non-1996; followwith no prior cancer, exposed) up/1996-2008 and, if alive on 12 WTC-exposure status (2-yr adjustment for Lung, incidence Cohort September 2001, also potential surveillance bias) (SIR): had known WTC Non-exposed 8 exposure status Exposure assessment Exposed 6 method: WTC SIR ratio NR exposed and (exposed vs nonunexposed firefighters exposed) from employment

							information on potential confounders.
Pinkerton et al. (2020) San Francisco, Chicago, and Philadelphia, USA Enrolment, 1950– 2009/follow-up, 1950–2016 Cohort	29 992 municipal career firefighters in the CFHS cohort employed by the fire departments of San Francisco, Chicago, or Philadelphia for ≥ 1 day between 1950 and 2009; exposure– response analyses limited to 19 287 male firefighters of known race hired in 1950 or later and employed for	Lung, mortality	Fire department San Francisco Chicago Philadelphia Overall Heterogeneity P	154 638 405 1197	0.71 (0.60-0.83) 1.2 (1.11-1.30) 1.14 (1.03-1.26) 1.08 (1.02-1.15)	Gender, race, age, calendar period	Exposure assessment critique: Good quality. Minimal bias in exposure assessment in internal analyses. Municipal firefighters. Strengths: long period of follow-up, exposure- response modelling for three metrics of exposure assessed using job-exposure matrices, adjustment for HWSE.

Risk estimate

0.52 (0.26-1.05)

0.42(0.20-0.86)

0.80 (0.29-2.18)

0.52 (0.26-1.05)

0.28 (0.13-0.62)

0.53(0.18 - 1.54)

(95% CI)

Covariates

controlled

Age, race,

calendar year

Comments

ethnic origin, *critique*: Satisfactory

Exposure assessment

quality. Intensity of

but did not consider

previous firefighter

methods. WTC site

disaster.

work. WTC exposure

self-reported using three

exposures complex and

probably unique to 9/11

Strengths: evaluation of

medical surveillance bias.

hire bias; short length of follow-up; young age at

end of follow-up; little

Limitations: healthy-worker

exposure at WTC captured

 $\geq 1 \text{ yr}$

records and

questionnaires

Reference, location, enrolment/ follow-up period, study design	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments
<u>Pinkerton et al.</u> (2020)	Exposure assessment method: ever	Lung, mortality	Exposed-days mod 2500 exposed-days		700 exposed-days vs	Age, race, birthdate	<i>Limitations</i> : healthy-worker selection bias in external comparison analyses, little information on potential confounders.
(cont.) employed as a firefighter, and number of expose	firefighter, and number of exposed		Loglinear without HWSE adjustment	556	0.97 (0.81–1.16)	(within 5 yr), fire department	
	days, fire-runs, fire- hours reconstructed using job-exposure		RCS without HWSE adjustment	556	1.01 (0.81–1.27)		
	matrix based on job titles and assignments and departmental		Fully adjusted loglinear	556	1.38 (1.08–1.78)		
	work history records and historical fire-run		Fully adjusted RCS	556	1.45 (1.06–2.01)		
	and fire-hour data	Lung, mortality	Fire-runs (Chicago (HR at 8800 runs		lelphia only) model 5, 10-yr lag):		
			Loglinear without HWSE adjustment	516	1.06 (0.93–1.19)		
			RCS without HWSE adjustment	516	0.95 (0.82–1.11)		
			Fully adjusted loglinear	516	1.21 (1.05–1.38)		
			Fully adjusted RCS	516	1.12 (0.95–1.33)		

Reference, location, enrolment/ follow-up period, study design	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments
<u>Pinkerton et al.</u> (2020)		Lung, mortality	Fire-hours (Chicag 600 h, 10-yr lag):	go only) mo	del (HR at 2300 h vs	Age, race, birthdate	
(cont.)			Loglinear without HWSE adjustment	348	1.27 (1.06–1.52)	(within 5 yr), fire department	
			RCS without HWSE adjustment	348	1.20 (0.95–1.51)		
			Fully adjusted loglinear	348	1.48 (1.21–1.80)		
			Fully adjusted RCS	348	1.46 (1.13–1.88)		
		Lung, mortality	Time since first ex and Philadelphia o model (HR for 880	only) fully a	Age, race, birthdate (within		
			Lag to < 20 yr	NR	1.53 (1.04–2.21)	5 yr), fire	
			20 to < 30 yr	NR	1.28 (0.94-1.73)	department,	
			≥ 30 yr	NR	1.04 (0.82-1.30)	employment duration	
			LRT P value, 0.16			duration	
		Lung, mortality	Age at exposure in Philadelphia only) (HR for 8800 runs	fully adjust	ed loglinear model		
			< 40 yr	NR	1.05 (0.83-1.31)		
			\geq 40 yr	NR	1.37 (1.11–1.69)		
			LRT P value, 0.13				
		Lung, mortality	Period of exposure Philadelphia only) (HR for 8800 runs	fully adjust	ed loglinear model		
			Pre-1970	NR	1.24 (0.95–1.61)		
			1970 or after LRT <i>P</i> value, 0.79	NR	1.19 (1.00–1.41)		

Reference, location, enrolment/ follow-up period, study design	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments		
Pinkerton et al.		Mesothelioma,	Fire department (S	SMR):		Gender, race,			
<u>(2020)</u>		mortality	San Francisco	< 5	2.00 (0.54-5.12)	age, calendar			
(cont.)			Chicago	10	2.14 (1.03-3.93)	period			
			Philadelphia	< 5	1.33 (0.36-3.40)				
			Overall	18	1.86 (1.10-2.94)				
			Heterogeneity P v	alue, 0.71					
<u>Daniels et al.</u> (<u>2015)</u> San Francisco, Chicago,	19 309; all male career firefighters in the CFHS cohort of known race who	Lung, incidence	Exposed-days mod 10-yr lag): 8700 days vs 2500 days	del (HR, log 382	linear model, 1.05 (0.84–1.33)	Age, race, fire department, birth cohort	<i>Exposure assessment</i> <i>critique</i> : Good quality. Minimal bias in exposure assessment in internal		
Chicago, bit Kilowii race with Philadelphia, USA were on active duty Enrolment, 1950– ≥ 1 day from 1950 through 2009 in the	were on active duty ≥ 1 day from 1950 through 2009 in the	Lung, incidence	'		lelphia only) model g): 1.10 (0.94–1.28)	Age, race, fire department, birth cohort	analyses. Municipal firefighters. <i>Strengths</i> : long period		
1950–2009 (mortality), 1985– 2009 (incidence) Cohort	fire departments of Chicago, Philadelphia, or San Francisco with ≥ 1 yr of employment	Lung, incidence	2100 runs Fire-hours (Chica model, 10-yr lag):	go only) mo	del (HR, loglinear	Age, race, birth cohort	of follow-up, exposure- response modelling for three metrics of exposur assessed using job-		
	Exposure assessment method: number of exposed days, fire-runs, fire-hours	Lung, incidence	2300 h vs 600 h2431.39 (1.10–1.74)Time since first exposure in piecewise loglinearfire-runs (Chicago and Philadelphia only) model(HR at 4600 runs, 10-yr lag):			Age, race, fire department, birth cohort	exposure matrices. <i>Limitations</i> : little information on potential confounders.		
	reconstructed using		10–20 yr	NR	1.06 (0.80-1.37)				
	job-exposure matrix		20-30 yr	NR	1.08 (0.86-1.34)				
	based on job titles		> 30 yr	NR	1.08 (0.88-1.32)				
	and assignments and departmental work history records and historical fire-run and fire-hour data		LRT <i>P</i> value, 0.987	7					
		story records and Lung, incidence storical fire-run and	(Chicago and Phil	Age at exposure in piecewise loglinear fire-runs (Chicago and Philadelphia only) model (HR at 4600 runs, 10-yr lag):		Age, race, fire department, birth cohort			
			< 40 yr	NR	0.97 (0.81-1.16)				
			\geq 40 yr	NR	1.17 (0.99–1.37)				
			LRT <i>P</i> value, 0.194	1					

Reference, location, enrolment/ follow-up period, study design	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments
Daniels et al. (2015) (cont.)		Lung, incidence	Exposure period i (Chicago and Phil 4600 runs, 10-yr l Pre-1970	ladelphia on	loglinear fire-runs ly) model (HR at 1.06 (0.86–1.29)	Age, race, fire department, birth cohort	
			1970 or after	NR	1.08 (0.94–1.24)		
			LRT P value, 0.92				
<u>Daniels et al.</u>	29 993 (24 453 for	Larynx, incidence	SIR:			Gender, race,	Exposure assessment
<u>(2014)</u>	incidence analyses)	·	All cancers	84	1.50 (1.19–1.85)	age, calendar	<i>critique</i> : Satisfactory quality. Minimum
Chicago, San	male and female	Larynx, incidence	Fire department (SIR, all canc	ers):	period	
Francisco, and Philadelphia, USA	career firefighters in the CFHS cohort		San Francisco	10	1.02 (0.49–1.88)		exposure is 1 day of work a municipal firefighter.
Enrolment, 1950–	1950– employed for		Chicago	42	1.51 (1.08–2.03)		<i>Strengths</i> : long period of
2009/follow-up,			Philadelphia	32	1.73 (1.18–2.44)		follow-up, ascertained
1950–2009	San Francisco, or	Lung, incidence	SIR:				incidence outcomes,
(mortality), 1985–	Philadelphia fire		All cancers	716	1.12 (1.04–1.21)		included female firefighte <i>Limitations</i> : healthy- worker hire bias in
2009 (incidence) Cohort	departments between 1950 and 2009		First primary	602	1.13 (1.04–1.22)		
Collort	Exposure assessment		cancer				worker hire bias in external comparisons, littl
	method: ever	Lung, incidence	Fire department (information on potential
	employed and		San Francisco	81	0.70 (0.56–0.87)		confounders.
	categorical duration		Chicago	409	1.30 (1.17–1.43)		
	of employment (years)		Philadelphia	226	1.09 (0.96–1.25)		
	from employment records	T · · 1	Heterogeneity P v				
	1000103	Lung, incidence	Race (SIR, all can		1.15 (1.05, 1.24)	Age, calendar period	
			Among men: Caucasian [White]	689	1.15 (1.07–1.24)	period	
			Other	24	0.67 (0.43-1.00)		
		Lung, incidence	Age (SIR, all canc	ers):		Gender, race,	
			17–64 yr	222	1.12 (0.98–1.28)	age, calendar	
			65 to \geq 85 yr	494	1.13 (1.03–1.23)	period	
			Heterogeneity P v	alue, 1.00			

Reference, location, enrolment/ follow-up period, study design	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments
Daniels et al.		Mesothelioma,	SIR:			Gender, race,	
<u>(2014)</u>		incidence	All cancers	35	2.29 (1.60-3.19)	age, calendar	
(cont.)			First primary cancer	26	2.00 (1.31-2.93)	period	
		Mesothelioma,	Fire department (S	SIR, all canc	ers):		
		incidence	San Francisco	6	2.05 (0.75-4.47)		
			Chicago	20	2.71 (1.65-4.18)		
			Philadelphia	9	1.82 (0.83-3.46)		
<u>Demers et al.</u>	2447 male firefighters employed for \geq 1 yr between 1944 and 1979, alive as of	Larynx, incidence	SIR (local county i	rates):		Age, calendar	Exposure assessment
		Larynx, incidence Lung, incidence	Firefighters	5	1.0 (0.3–2.3)	period	critique: Satisfactory
Seattle and Tacoma, USA			IDR:				quality. Duration of years involved in direct firefighting (surrogate for fire smoke) was not measured equally in the
Enrolment,	1 January 1974 and		Local police	4	1		
1944-1979/follow-	known to be a resident		Firefighters	5	0.8 (0.2–3.5)		
up, 1974–1989	of one of 13 counties		SIR (local county i				
Cohort	in the catchment area		Firefighters	45	1.0 (0.7–1.3)		two study populations.
	of the tumour registry for ≥ 1 mo; reference	Lung, incidence	Histological type (Municipal firefighters. <i>Strengths</i> : use of two
	group included 1878		Adenocarcinoma	14	1.1 (NR)		comparison groups,
	local male police		Squamous cell Small cell	10	0.7 (NR)		including comparison
	officers			7 5	1.0 (NR)		with police officers to limit
	Exposure assessment method: ever employed for ≥ 1 yr, and categorical duration of employment (years) in direct firefighting positions from employment records	ever for ≥ 1 yr, orical of ent (years) Grefighting from	Large cell	5	1.3 (NR)		healthy-worker bias. <i>Limitations</i> : little information on potential confounders, including smoking.

Reference, location, enrolment/ follow-up period, study design	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments
<u>Demers et al.</u> (1994)		Lung, incidence	Duration of expos county rates):	ed employm	ent (SIR, local	Age, calendar period	
(cont.)			< 10 yr	8	1.4 (0.6-2.7)	-	
			10–19 yr	9	1.4 (0.7-2.7)		
			20–29 yr	26	0.9 (0.6-1.3)		
			≥ 30 yr	2	0.4 (0.1–1.5)		
		Lung, incidence	Years since first er rates):	nployment (SIR, local county		
			< 20 yr	0	0 (0.0-2.5)		
			20–29 yr	11	1.5 (0.7–2.6)		
			≥ 30 yr	34	0.9 (0.6–1.3)		
		Lung, incidence	IDR:				
			Local police	20	1		
			Firefighters	45	1.1 (0.6–1.9)		
Demers et al.	4401 male firefighters	Larynx, mortality	SMR:			Age, calendar	Exposure assessment
(1992a) Seattle and	employed for ≥ 1 yr between 1944 and	Lung, mortality	Firefighters SMR:	2	0.47 (0.06–1.70)	period	<i>critique</i> : Satisfactory/good quality. Duration of years
Tacoma, Washington; Portland, Oregon,	1979 in Seattle, Tacoma, or Portland, USA; reference group	Lung, mortality	Firefighters IDR:	95	0.96 (0.77–1.17)		involved in fire combat (surrogate for fire smoke) was not measured equally
USA	included 3676 local		Local police	55	1		in the three municipal
1944–1979/follow- Expc up, 1945–1989 meth Cohort ever for ≥ categ (year	police officers Exposure assessment method: records; ever employed for ≥ 1 yr, and categorical duration (years) of exposure to fire combat from		Firefighters	95	0.95 (0.67–1.33)		firefighter populations. Strengths: use of two comparison groups, including comparison with police officers to limit healthy-worker bias. Limitations: little information on potential

Reference, location, enrolment/ follow-up period, study design	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments
Vena & Fiedler (1987) Buffalo, New York, USA 1950–1979 Cohort	1867 White male career firefighters employed by the City of Buffalo for ≥ 5 yr, with ≥ 1 yr as a firefighter Exposure assessment method: ever- employment, timing, and duration of employment from employment records	Respiratory system, mortality	Years worked as a 1-9 yr 10-19 yr 20-29 yr 30-39 yr ≥ 40 yr Total	firefighter (8 0 3 11 9 5 28	SMR): 0 [0.91 (0.2–2.5)] [1.20 (0.6–2.1)] [0.76 (0.4–1.4)] [1.22 (0.4–2.7)] 0.94 (0.62–1.36)	Age, calendar period	<i>Exposure assessment</i> <i>critique</i> : Minimal quality. Only assessed ever- employment and duration of employment as a municipal firefighter. <i>Strengths</i> : long length of follow-up. <i>Limitations</i> : healthy-worker hire bias; little information on potential confounders or exposure to firefighting activities.
Feuer & Rosenman (1986) New Jersey (NJ), USA 1974–1980 Cohort	263 deceased White male firefighters in the New Jersey Police and Firemen Retirement System (firefighters vested with ≥ 10 yr of service, or firefighters who died while on payroll regardless of employment duration); one reference group included 567 White male police deaths Exposure assessment method: ever employed, and categorical duration of employment (years), as a career firefighter from retirement system records	Respiratory system, mortality Respiratory system, mortality	Reference populat Firefighters vs US White men Firefighters vs NJ White men Firefighters vs White male NJ police Duration of emplo ≤ 20 yr 20–25 yr > 25 yr	23 23 23	[0.98 (0.64–1.45)] [0.92 (0.60–1.35)] [1.02 (0.66–1.50)] R): [0.72 (0.23–1.74)] [0.96 (0.42–1.90)] [0.98 (0.53–1.67)]	Age	Exposure assessment critique: Satisfactory quality. Assessment provides duration of employment categories. May include municipal and rural firefighters. Strengths: comparison with other uniformed service occupation. Limitations: PMR study design lacks event-free follow-up time, short observation period; little information on potential confounders.

Reference, location, enrolment/ follow-up period, study design	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments
Aronson et al. (1994) Toronto, Canada 1950–1989 Cohort	5414 male firefighters employed for ≥ 6 mo at one of six fire departments in Metropolitan Toronto any time between 1950 and 1989 Exposure assessment method: ever employed and categorical duration of employment (years) as municipal firefighter from employment records	Larynx, mortality Lung, mortality Lung, mortality Lung, mortality	SMR: Any employment SMR: Any employment Years since first en < 20 yr 20-29 yr $\ge 30 \text{ yr}$ Years of employme < 15 yr 15-29 yr $\ge 30 \text{ yr}$ Age (SMR): < 60 yr	54 nployment (1 13 40 ent (SMR): 8 16 27 22	0.23 (0.01–1.29) 1.03 (0.55–1.76) 1.00 (0.71–1.36) 1.30 (0.56–2.57) 0.85 (0.49–1.38) 0.85 (0.56–1.24) 0.91 (0.57–1.39)	Age, calendar period	<i>Exposure assessment</i> <i>critique</i> : Satisfactory quality. Unclear if individuals were active firefighters for whole employment. Likely municipal firefighters. <i>Strengths</i> : long period of follow-up, analysis of employment duration. <i>Limitations</i> : healthy-worker hire bias; little information on confounders or exposure; ascertained mortality outcomes only.
Guidotti (1993) Edmonton and Calgary, Canada 1927–1987 Cohort	3328; all firefighters employed between 1927 and 1987 by either of the fire departments of Edmonton or Calgary Exposure assessment method: ever employed and categorical duration of employment (years) from employment records; exposure index of years of employment weighted by time spent in proximity to fires based on job classification	Lung, mortality Lung, mortality	≥ 60 yr SMR Any employment Year of cohort entr Pre-1920 1920–1929 1930–1939 1940–1949 1950–1959 1960–1969 1970–1979		0.97 (0.66–1.37) 1.42 (0.91–2.11) [2.23 (0.90–4.63)] [0.95 (0.05–4.68)] 0 [1.55 (0.68–3.06)] [1.18 (0.48–2.44)] [1.69 (0.28–5.57)] [2.61 (0.13–12.8)]	Age, calendar period	<i>Exposure assessment</i> <i>critique</i> : Good quality. Good approach to differentiate exposure between ranks. Municipal firefighters. <i>Strengths</i> : long length of follow-up; analyses by duration of employment and exposure index. <i>Limitations</i> : little information on potential confounders; ascertained mortality outcomes only; low number of cases for stratified analyses.

Reference, location, enrolment/ follow-up period, study design	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments
<u>Guidotti (1993)</u>		Lung, mortality	Latency (SMR):			Age, calendar	
(cont.)			< 20 yr	4	[1.92 (0.61-4.64)]	period	
			20–29 yr	4	[0.95 (0.30-2.29)]		
			30–39 yr	10	[1.73 (0.88-3.08)]		
			40-49 yr	3	[0.97 (0.25-2.63)]		
			≥ 50 yr	3	[1.75 (0.44-4.75)]		
		Lung, mortality	Duration of emplo	yment (SMI	R):		
			< 1 yr	2	[2.83 (0.47-9.35)]		
			1–9 yr	4	[1.97 (0.63-4.75)]		
			10–19 yr	3	[1.49 (0.38-4.06)]		
			20–29 yr	6	[1.31 (0.53-2.73)]		
			30–39 yr	7	[1.07 (0.47-2.12)]		
			≥ 40 yr	2	[2.02 (0.34-6.67)]		
		Lung, mortality	Exposure index (y	ear × weight	t) (SMR):		
			0	2	[1.76 (0.30-5.82)]		
			> 0, < 1	1	[1.69 (0.08-8.33)]		
			1-4	1	[1.14 (0.06-5.62)]		
			5–9	4	[2.58 (0.82-6.23)]		
			10-14	2	[1.90 (0.32-6.28)]		
			15-19	2	[1.39 (0.23-4.59)]		
			20-24	1	[0.32 (0.02-1.58)]		
			25-29	4	[1.11 (0.35-2.68)]		
			30-35	3	[1.21 (0.31-3.29)]		
			> 35	4	[4.08 (1.30-9.85)]		

location, enrolment/ follow-up period, study design	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments
<u>Glass et al. (2019)</u>	39 644 female	Respiratory	SIR:			Age, calendar	Exposure assessment
Australia Enrolment, varied	firefighters, both paid [career] (1682) and	system, incidence	All volunteer firefighters	66	0.90 (0.70–1.15)	period	<i>critique</i> : Good quality. Enhanced exposure
by agency/follow-	volunteer (37 962),		Volunteers	34	1.23 (0.85-1.72)		assessment to differentiate
up, 1980–2011 (mortality); 1982–	from nine fire agencies in Australia		who attended		`		exposure based on number of incidents for volunteer
2010 (incidence)	Exposure assessment	Respiratory system, incidence	incidents	ll voluntoor	s (RIR) [equivalent		firefighters. Included
Cohort	method: ever career or		to rate ratios]:	II volunteers	(KIK) [equivalent		specific incident types but
	volunteer firefighter, ever attended an		Zero incidents	28	1		early exposure extrapolated from more recent data. Volunteers mainly rural.
	incident, tertiles of		Tertile 1	10	1.25 (0.61–2.57)		
	cumulative number		Tertile 2	11	1.17 (0.58–2.35)		Strengths: study of female
	of incidents and type		Tertile 3	13	1.60 (0.83-3.09)		firefighters, includes
	of incidents attended from personnel records		Trend-test P value				predominantly rural firefighters, ascertained exposure to number and type of incidents. <i>Limitations</i> : short length of follow-up, young age at end of follow-up, probable healthy-worker
		Respiratory	No. of fire inciden				
		system, incidence	Zero incidents	30	1		
			Tertile 1	10	1.27 (0.62–2.60)		
			Tertile 2 Tertile 3	9 13	1.11 (0.53–2.34)		
			Trend-test <i>P</i> value		1.69 (0.88–3.23)		
		Respiratory			all volunteers (RIR):		bias; little information on
		system, incidence	Zero incidents	52	1		confounders.
			Tertile 1	0	0 (NR)		
			Tertile 2	6	1.21 (0.52–2.82)		
			Tertile 3	4	0.84 (0.30-2.33)		
			Trend-test P value	, 0.17			
		Respiratory system, incidence	No. of landscape fr (RIR):	re incidents	s, all volunteers		
			Zero incidents	33	1		
			Tertile 1	10	1.52 (0.75-3.09)		
			Tertile 2	5	0.64 (0.25-1.63)		
			Tertile 3	14	1.82 (0.97–3.40)		
			Trend-test P value	, 0.56			

Reference, location, enrolment/ follow-up period, study design	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments
<u>Glass et al. (2019)</u>		Respiratory	No. of vehicle fire	incidents, al	l volunteers (RIR):	Age, calendar	
(cont.)		system, incidence	Zero incidents	53	1	period	
			Tertile 1	1	0.38 (0.05-2.59)		
			Tertile 2	3	0.90 (0.28-2.86)		
			Tertile 3	5	1.50 (0.60-3.76)		
			Trend-test P value	, 0.18			
		Lung, incidence	SIR:				
			All volunteer firefighters	65	0.93 (0.72–1.18)		
			Volunteers who attended incidents	34	1.30 (0.90–1.82)		
		Lung, incidence	No. of incidents, a	ll volunteers			
			Zero incidents	27	1		
			Tertile 1	10	1.29 (0.63-2.67)		
			Tertile 2	11	1.21 (0.60-2.45)		
			Tertile 3	13	1.66 (0.86-3.22)		
			Trend-test P value	, 0.51			
		Lung, incidence	No. of fire inciden	ts, all volunt	teers (RIR):		
		C	Zero incidents	29	1		
			Tertile 1	10	1.31 (0.64-2.70)		
			Tertile 2	9	1.15 (0.54-2.43)		
			Tertile 3	13	1.74 (0.90-3.35)		
			Trend-test P value	, 0.46			
		Lung, incidence	No. of structure fir	re incidents,	all volunteers (RIR):		
			Zero incidents	51	1		
			Tertile 1	0	0 (NR)		
			Tertile 2	6	1.23 (0.53-2.88)		
			Tertile 3	4	0.86 (0.31-2.37)		
			Trend-test P value	, 0.17			

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Reference, location, enrolment/ follow-up period, study design	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments
<u>Glass et al. (2019)</u> (cont.)		Lung, incidence	No. of landscape fr (RIR):	ire incidents	, all volunteers	Age, calendar period	
			Zero incidents	32	1		
			Tertile 1	10	1.57 (0.78-3.19)		
			Tertile 2	5	0.66 (0.26-1.69)		
			Tertile 3	14	1.87 (1.00-3.51)		
			Trend-test P value	, 0.56			
		Lung, incidence	No. of vehicle fire	incidents, al	l volunteers (RIR):		
			Zero incidents	52	1		
			Tertile 1	1	0.36 (0.05-2.64)		
			Tertile 2	3	0.91 (0.29–2.93)		
			Tertile 3	5	1.53 (0.61–3.83)		
			Trend-test P value	, 0.18			
		Mesothelioma,	SIR:				
		incidence	All volunteer firefighters	3	1.47 (0.30-4.29)		
			Volunteers who attended incidents	1	1.29 (0.03–7.19)		

Reference, location, enrolment/ follow-up period, study design	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments		
Glass et al. (2017) Australia Enrolment, date varied by agency (1998–2000)/	163 094 male volunteer firefighters from five fire agencies enrolled on or after the date on which	Respiratory system, incidence	SIR: All volunteers Volunteers who attended incidents	429 263	0.49 (0.45–0.54) 0.48 (0.42–0.54)	Age, calendar period	<i>Exposure assessment</i> <i>critique</i> : Good quality. Enhanced exposure assessment to differentiate exposure based on number		
follow-up to	the agency's roll was	Respiratory	Era of first service	(SIR):			of incidents. Included		
30 November 2011 (mortality) and	complete and who had ever held an active	system, incidence	Pre-1970	118	0.41 (0.34-0.49)		specific incident types but early exposure extrapolated from more recent data. Firefighters from rural or peri-urban areas. <i>Strengths</i> : includes predominantly rural firefighters, ascertained exposure to number and type of incidents. <i>Limitations</i> : short length of follow-up, young age at end of follow-up,		
31 December 2010	firefighting role		1970-1994	163	0.50 (0.43-0.59)				
(cancer incidence)	Exposure assessment		1995 or after	148	0.58 (0.49-0.68)				
Cohort	method: ever volunteer firefighter,	nethod: ever Respiratory olunteer firefighter, system, incidence ategorical volunteer uration (years) and	Duration of servic [equivalent to rate		eers (RIR)				
			> 3 mo to < 10 yr	136	1				
	duration (years) and era from service		10–20 yr	101	1.18 (0.91–1.53)				
	records; ever volunteer		≥ 20 yr	187	0.76 (0.61-0.96)				
	firefighter who		Trend-test P value	, < 0.01					
	attended an incident, tertiles of cumulative	Respiratory system, incidence	Duration of servic incidents (RIR):	e, volunteer	s who attended				
	emergency incidents		> 3 mo to < 10 yr	62	1		probable healthy-worker		
	from contemporary		10–20 yr	67	1.35 (0.96–1.92)		bias; little information on confounders.		
	incident data		≥ 20 yr	133	0.70 (0.51-0.95)		confounders.		
			Trend-test P value	, < 0.01					
	Respiratory	No. of incidents at	tended by v	olunteers (RIR):					
		system, incidence	Baseline	247	1				
			Group 2	9	0.79 (0.41-1.54)				
			Group 3	7	1.27 (0.60-2.69)				
		Respiratory	No. of fire incident	ts attended l	by volunteers (RIR):				
		system, incidence	Baseline	246	1				
			Group 2	12	1.01 (0.57–1.81)				
		Group 3	5	1.03 (0.42-2.49)					

Reference, location, enrolment/ follow-up period, study design	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments
<u>Glass et al. (2017)</u> (cont.)		Respiratory system, incidence	No. of structure five volunteers (RIR):	re incidents	attended by	Age, calendar period	
			Baseline	252	1	-	
			Group 2	7	1.01 (0.48-2.14)		
			Group 3	4	1.09 (0.41-2.93)		
		Respiratory system, incidence	No. of landscape f volunteers (RIR):	ire incidents	attended by		
			Baseline	218	1		
			Group 2	29	0.74 (0.50-1.09)		
			Group 3	16	1.08 (0.65–1.80)		
		Respiratory system, incidence	No. of vehicle fire (RIR):	incidents att	ended by volunteers		
			Baseline	248	1		
			Group 2	9	0.76 (0.39-1.47)		
			Group 3	6	1.31 (0.58–2.95)		
		Larynx, incidence	SIR:				
			All volunteers	36	0.45 (0.31-0.62)		
			Volunteers who attended incidents	22	0.42 (0.26-0.63)		
		Lung, incidence	SIR:				
			All volunteers	371	0.48 (0.44-0.54)		
			Volunteers who attended incidents	228	0.47 (0.41–0.54)		
		Lung, incidence	Era of first service	(SIR):			
		-	Pre-1970	109	0.42 (0.34-0.50)		
			1970-1994	141	0.50 (0.42-0.59)		
			1995 or after	121	0.55 (0.45-0.65)		

Reference, location, enrolment/ follow-up period, study design	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments
<u>Glass et al. (2017)</u>		Lung, incidence	Duration of servic	e, all volunt	eers (RIR):	Age, calendar	
(cont.)			> 3 mo to < 10 yr	114	1	period	
			10–20 yr	86	1.19 (0.90-1.57)		
			$\geq 20 \text{ yr}$	168	0.79 (0.62-1.01)		
			Trend-test P value	, 0.03			
		Lung, incidence	Duration of servic incidents (RIR):	e, volunteer	s who attended		
			> 3 mo to < 10 yr	52	1		
			10–20 yr	57	1.36 (0.93–1.98)		
			≥ 20 yr	119	0.72 (0.51-1.00)		
			Trend-test P value	, 0.01			
		Lung, incidence	No. of incidents at	tended by v	olunteers (RIR):		
			Baseline	214	1		
			Group 2	8	0.81 (0.40-1.65)		
			Group 3	6	1.26 (0.56-2.84)		
		Lung, incidence	No. of fire inciden	ts attended l	by volunteers (RIR):		
			Baseline	213	1		
			Group 2	11	1.07 (0.58-1.96)		
			Group 3	4	0.95 (0.35-2.56)		
		Lung, incidence	No. of structure fin volunteers (RIR):	re incidents	attended by		
			Baseline	218	1		
			Group 2	7	1.17 (0.55–2.49)		
			Group 3	3	0.95 (0.30-2.95)		
		Lung, incidence	No. of landscape five volunteers (RIR):	re incidents	attended by		
			Baseline	186	1		
			Group 2	27	0.81 (0.54-1.21)		
			Group 3	15	1.18 (0.70-2.00)		

Reference, location, enrolment/ follow-up period, study design	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments
<u>Glass et al. (2017)</u> (cont.)		Lung, incidence	No. of vehicle fire (RIR):	incidents at	tended by volunteers	Age, calendar period	
			Baseline	215	1		
			Group 2	9	0.88 (0.45-1.71)		
			Group 3	4	1.01 (0.38-2.73)		
		Mesothelioma,	SIR:				
		incidence	All volunteers	42	0.64 (0.46-0.87)		
			Volunteers who attended incidents	22	0.54 (0.34–0.81)		
		Mesothelioma,	Era of first service	e (SIR):			
		incidence	Pre-1970	7	0.30 (0.12-0.63)		
			1970-1994	17	0.72 (0.42-1.15)		
			1995 or after	18	0.98 (0.58-1.55)		

Reference, location, enrolment/ follow-up period, study design	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments
<u>Glass et al.</u>	30 057 full- (17 394)	· · · · · · · · · · · · · · · · · · ·	Firefighter status ((SIR):		Age, calendar	critique: Good quality. Enhanced exposure assessment to differentiate exposure based on number of incidents, including specific incident types. Included specific incident types but early exposure extrapolated from more recent data. Municipal firefighters. <i>Strengths</i> : internal analysis by exposure to number and type of incidents, ascertained cancer incidence. <i>Limitations</i> : healthy-worker
<u>(2016a)</u>	or part-time (12 663)	nale firefighters	Full-time	100	0.81 (0.66–0.99)	period	
Australia	paid male firefighters		Part-time	17	0.41 (0.24–0.65)		
Enrolment, 1976–2003/follow-	employed at one of eight Australian		All	117	0.71 (0.59-0.85)		
up, 1976–2011 (mortality), 1982–	fire agencies for \geq 3 mo from	Respiratory system, incidence	Duration of emplo (RIR) [equivalent				
2010 (incidence,	start of personnel		> 3 mo to 10 yr	9	1		
except two states,	records (1976–2003,	ords (1976–2003, ending on agency) oosure assessment chod: employed as urt-time or full- system incidence	10–20 yr	15	1.28 (0.55–2.96)		
2009)	depending on agency)		≥ 20 yr	75	0.99 (0.45-2.18)		
Cohort			Trend-test P value	, 0.75			
	a part-time or full- time firefighter for		Duration of emplo (RIR):	oyment, part	t-time firefighters		
	\geq 3 mo, categorical		> 3 mo to 10 yr	5	1		
	employment duration		10–20 yr	2	0.48 (0.08-2.72)		
	(years) and era		≥ 20 yr	10	1.13 (0.28-4.58)		
	from employment		Trend-test P value	, 0.71			
	records; tertiles of	Respiratory	Duration of emplo	yment (RIR	k):		hire bias; short length of
	cumulative emergency incidents and type of incident attended from contemporary incident data	system, incidence	> 3 mo to 10 yr	14	1		follow-up, young age at end of follow-up; little
			10–20 yr	17	1.15 (0.55–2.39)		information on potential
			≥ 20 yr	85	1.15 (0.59–2.27)		confounders.
			Trend-test P value				
		Respiratory system, incidence	No. of incidents at (RIR):	tended by fu	all-time firefighters		
			Tertile 1	6	1		
			Tertile 2	4	0.72 (0.20-2.55)		
			Tertile 3	12	1.58 (0.59-4.28)		
			Trend-test P value	, 0.31			

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Reference, location, enrolment/ follow-up period, study design	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments
<u>Glass et al.</u> (2016a)		Respiratory system, incidence	No. of fire inciden firefighters (RIR):	ts attended b	by full-time	Age, calendar period	
(cont.)		system, merdenee	Tertile 1	6	1	period	
			Tertile 2	5	0.97 (0.30-3.21)		
			Tertile 3	11	1.37 (0.50–3.76)		
			Trend-test P value	, 0.52	(,		
		Respiratory system, incidence	No. of structure fit time firefighters (I	re incidents	attended by full-		
			Tertile 1	6	1		
			Tertile 2	6	1.19 (0.38-3.70)		
			Tertile 3	10	1.23 (0.44-3.42)		
			Trend-test P value	, 0.70			
		Respiratory system, incidence	No. of landscape fi time firefighters (H		attended by full-		
			Tertile 1	8	1		
			Tertile 2	6	0.83 (0.29-2.40)		
			Tertile 3	8	0.79 (0.29–2.13)		
			Trend-test P value				
		Respiratory system, incidence	No. of vehicle fire firefighters (RIR):	incidents att	tended by full-time		
			Tertile 1	5	1		
			Tertile 2	5	1.21 (0.35-4.23)		
			Tertile 3	12	1.97 (0.69–5.64)		
			Trend-test P value	, 0.19			
		Respiratory system, incidence	Duration of emplo (SIR):	yment, full-	time firefighters		
			> 3 mo to 10 yr	9	1.05 (0.48–1.99)		
			10–20 yr	15	0.95 (0.53-1.56)		
			≥ 20 yr	75	0.77 (0.60-0.96)		

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Reference, location, enrolment/ follow-up period, study design	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments
<u>Glass et al.</u>		Respiratory	Duration of emplo	oyment, part	-time firefighters	Age, calendar	
(2016a)		system, incidence	(SIR):	_	(period	
(cont.)			> 3 mo to 10 yr	5	0.57 (0.18–1.33)		
			10–20 yr	2	0.22 (0.03-0.80)		
			≥ 20 yr	10	0.42 (0.20-0.78)		
		Respiratory	· ·		ime firefighters (SIR):	•	
		system, incidence	Pre-1970	61	0.83 (0.63–1.06)	age groups	
			1970–1994	34	0.78 (0.54–1.08)		
			1995 or after	5	0.93 (0.30-2.16)		
		Respiratory		ment, part-ti	ime firefighters (SIR):	5-yr-interval	
		system, incidence	Pre-1970	1	0.09 (0.00-0.49)	age groups	
			1970–1994	15	0.60 (0.34-1.00)		
			1995 or after	1	0.18 (0.00-1.02)		
		Larynx, incidence	Firefighter status ((SIR):		Age, calendar	
			Full-time	11	0.86 (0.43-1.54)	period	
			Part-time	1	0.23 (0.01-1.26)		
			All	12	0.70 (0.36-1.22)		
		Larynx, incidence	Duration of emplo (SIR):	oyment, full-	time firefighters		
			> 3 mo to 10 yr	1	1.05 (0.03-5.85)		
			10–20 yr	3	1.65 (0.34-4.81)		
			$\geq 20 \text{ yr}$	7	0.71 (0.28–1.46)		
		Larynx	Duration of emplo	oyment, part			
			> 3 mo to 10 yr	0	0 (NR)		
			10–20 yr	0	0 (NR)		
			$\geq 20 \text{ yr}$	1	0.43 (0.01-2.38)		
		Larynx, incidence	•	ment, full-ti	ime firefighters (SIR):		
			Pre-1970	5	0.72 (0.23–1.67)		
			1970-1994	5	0.97 (0.31-2.26)		
			1995 or after	1	1.71 (0.04–9.53)		

Reference, location, enrolment/ follow-up period, study design	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments	
Glass et al.		Larynx, incidence	Era of first employ	ment, part-ti	ime firefighters (SIR):	Age, calendar		
<u>(2016a)</u>			Pre-1970	0	0 (NR)	period		
(cont.)			1970–1994	1	0.36 (0.01-2.00)			
			1995 or after	0	0 (NR)			
		Lung, incidence	Firefighter status	(SIR):				
			Full-time	86	0.81 (0.65-1.00)			
			Part-time	15	0.42 (0.23-0.69)			
			All	101	0.71 (0.58-0.86)			
		Lung, incidence	Duration of emplo (RIR):	oyment, full-	-time firefighters			
			> 3 mo to 10 yr	8	1			
			10–20 yr	11	1.01 (0.40-2.56)			
			≥ 20 yr	66	0.84 (0.36-1.96)			
			Trend-test P value	, 0.60				
		Lung, incidence	Duration of employment, part-time firefighters (RIR):					
			> 3 mo to 10 yr	4	1			
			10–20 yr	2	0.70 (0.11-4.37)			
			≥ 20 yr	9	1.62 (0.33-7.90)			
			Trend-test P value	, 0.46				
		Lung, incidence	Duration of emplo	oyment (RIR	k):			
			> 3 mo to 10 yr	12	1			
			10–20 yr	13	0.99 (0.44-2.23)			
			≥ 20 yr	75	1.06 (0.51-2.21)			
			Trend-test P value	, 0.84				
		Lung, incidence	No. of incidents at (RIR):	ttended by fu	all-time firefighters			
			Tertile 1	5	1			
			Tertile 2	4	0.88 (0.24-3.31)			
			Tertile 3	7	1.07 (0.34-3.43)			
			Trend-test P value	, 0.90				

Reference, location, enrolment/ follow-up period, study design	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments		
<u>Glass et al.</u> (2016a)		Lung, incidence	No. of fire inciden firefighters (RIR):	ts attended l	oy full-time	Age, calendar period			
cont.)			Tertile 1	5	1	1			
		Tertile 2	4	0.98 (0.26-3.70)					
			Tertile 3	7	0.99 (0.31-3.18)				
			Trend-test P value	, 0.99					
		Lung, incidence	No. of structure fi full-time firefighte		attended by				
			Tertile 1	5	1				
			Tertile 2	5	1.23 (0.35-4.28)				
			Tertile 3	6	0.84 (0.25-2.76)				
			Trend-test P value, 0.75						
		Lung, incidence	No. of landscape fi full-time firefighte						
			Tertile 1	7	1				
			Tertile 2	4	0.65 (0.19-2.24)				
			Tertile 3	5	0.55 (0.17-1.76)				
			Trend-test P value	, 0.31					
		Lung, incidence	No. of vehicle fire firefighters (RIR):	incidents at	tended by full-time				
			Tertile 1	4	1				
			Tertile 2	4	0.28 (0.32-5.16)				
			Tertile 3	8	1.59 (0.47-5.30)				
			Trend-test P value	, 0.45					
		Lung, incidence	Duration of emplo (SIR):	oyment, full-	time firefighters				
			> 3 mo to 10 yr	8	1.14 (0.49–2.25)				
			10–20 yr	11	0.83 (0.42-1.49)				
			$\geq 20 \text{ yr}$	66	0.77 (0.60-0.98)				

Reference, location, enrolment/ follow-up period, study design	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments		
Glass et al.		Lung, incidence	Duration of emplo	yment, part	-time firefighters	Age, calendar			
<u>(2016a)</u>			(SIR):			period			
(cont.)			> 3 mo to 10 yr	4	0.56 (0.15–1.44)				
			10–20 yr	2	0.26 (0.03-0.94)				
			≥ 20 yr	9	0.43 (0.20-0.82)				
		Lung, incidence	· ·	ment, full-ti	me firefighters (SIR):				
			Pre-1970	54	0.83 (0.62–1.08)				
			1970–1994	28	0.76 (0.51-1.10)				
			1995 or after	4	0.91 (0.25-2.32)				
		Lung, incidence	Era of first employ	ment, part-ti	me firefighters (SIR):				
			Pre-1970	1	0.10 (0.00-0.55)				
			1970–1994	13	0.61 (0.33–1.05)				
		1995 or after	1	0.23 (0.01-1.27)					
		Mesothelioma,	Firefighter status (SIR):						
		incidence	Full-time	11	1.33 (0.66–2.37)				
			Part-time	4	1.38 (0.37-3.52)				
			All	15	1.34 (0.75–2.21)				
		Mesothelioma, incidence	Duration of emplo (SIR):	oyment, full-	time firefighters				
			> 3 mo to 10 yr	3	5.82 (1.20-17.00)				
			10–20 yr	2	2.01 (0.24-7.25)				
			≥ 20 yr	6	0.89 (0.33-1.94)				
		Mesothelioma, incidence	Duration of emplo (SIR):	oyment, part	-time firefighters				
			> 3 mo to 10 yr	1	2.00 (0.05-11.12)				
			10–20 yr	1	1.62 (0.04–9.04)				
			$\geq 20 \text{ yr}$	2	1.12 (0.14-4.05)				
		Mesothelioma,			me firefighters (SIR):				
		incidence	Pre-1970	3	0.59 (0.12–1.71)				
			1970–1994	6	2.08 (0.76-4.53)				
			1995 or after	2	6.65 (0.81–24.02)				

Table 2.1 (con	tinued)						
Reference, location, enrolment/ follow-up period, study design	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments
<u>Glass et al.</u> (2016a) (cont.)		Mesothelioma, incidence	Era of first employ Pre-1970 1970–1994 1995 or after	ment, part-ti 1 2 1	ime firefighters (SIR): 1.14 (0.03–6.37) 1.15 (0.14–4.14) 3.49 (0.09–19.46)	Age, calendar period	
Glass et al. (2016b) Victoria, Australia Enrolment, 1971–1999/follow- up, 1980–2011 (mortality), 1982– 2012 (incidence) Cohort	614 male (611) and female (3) employed and volunteer Country Fire Authority trainers and a group of paid [career] Country Fire Authority firefighters who trained at the Fiskville site between 1971 and 1999; all analyses limited to men as no deaths or cancers were observed among women Exposure assessment method: employed or volunteer firefighter trainers and paid [career] firefighters who trained at training facility for any period of time from human resource records, categorized into risk of low, medium, and high chronic exposure to smoke and other agents based on job assignment	Respiratory system, incidence	Risk of chronic ex Low Medium High	posure (SIR 0 3 1): 0 0.84 (0.17-2.46) 0.68 (0.02-3.77)	Age, calendar period	Exposure assessment critique: Satisfactory quality. Incorporated categorical level of exposure into assessment for each type of firefighter. Volunteers mainly rural, paid [career] firefighters were municipal. Strengths: included firefighter instructors with high potential exposure to smoke and other hazardous agents, assessed exposure based on job assignment. Limitations: low number of cases, young age at end of follow-up.

Reference, location, enrolment/ follow-up period, study design	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments
<u>Bates et al. (2001)</u> New Zealand	4305; the cohort comprised all male	Lung, incidence	Follow-up period		1.14 (0.5.1.0)	Age, calendar period	<i>Exposure assessment</i> <i>critique</i> : Satisfactory
Enrolment, 1977	(4221) and female		1977-1996	17	1.14 (0.7–1.8)	period	quality. Heterogeneity of
through June	(84) firefighters	T · · 1	1990–1996	7	0.82 (0.3–1.7)		direct firefighter exposure within job classification. May include urban [municipal] and rural firefighters. <i>Strengths</i> : ascertained both
1995/follow-	(paid [career] and	Lung, incidence	Duration of paid s				
up, 1977–1995	volunteer) employed		0–10 yr	3	0.93 (0.2–2.7)		
(mortality), 1977-	as a career firefighter		11–20 yr	4	1.45 (0.4–3.7)		
1996 (incidence)	for ≥ 1 yr and who		> 20 yr	8	1.52 (0.7–3.0)		
Cohort	also worked as a		Trend-test P value	, 0.48			
	career firefighter for	Lung, incidence	Duration of paid and volunteer service (SIR):				incidence and mortality
	≥ 1 day between 1977 and 1995; all analyses		0–10 yr	1	0.66 (0.0-3.7)		outcomes. <i>Limitations</i> : little information on
	limited to men due		11–20 yr	4	2.04 (0.6-5.2)		
	to small numbers of		> 20 yr	10	1.25 (0.6–2.3)		confounders; significant
	women		Trend-test P value	, 0.85			loss to follow-up.
	Exposure assessment method: ever employed and categorical duration of employment (years) from employment records	Lung, mortality	SMR:				
			Firefighters vs male New Zealand population	10	0.86 (0.4–1.6)		

Reference, location, enrolment/ follow-up period, study design	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments
Bigert et al. (2016) Cases: 14 748 adult	Lung, incidence	Firefighter status (OR):		Age, study	Exposure assessment	
Europe, Canada,	male lung cancer cases		Never	14 662	1	site	<i>critique</i> : Satisfactory quality. Possible recall bias
New Zealand, and	with information		Ever	86	1.03 (0.77-1.38)		
China on smoking or work 1985–2010 history extracted from	history extracted from	Lung, incidence	Duration of firefig	hter employ	ment (OR):		May be heterogeneity of exposure, includes urban
Case-control	the SYNERGY-studies		Never	14 662	1		[municipal] and rural
Sube control	database of pooled case-control studies		< 6 yr	32	1.56 (0.91-2.67)		firefighters, from several
			6–21 yr	22	1.13 (0.64-2.00)		countries, differing time
Controls: 17 543; control selection varied between			22–32 yr	14	0.69 (0.36-1.33)		periods and categories of
			≥ 33 yr	18	0.84 (0.46-1.53)		firefighter.
	varied between individual studies and		Trend-test P value	, 0.46			Strengths: large study size smoking information is
	were drawn from the	Lung, incidence	Firefighter status (OR):		Age, study site, pack- years, and time since quitting smoking	available. <i>Limitations</i> : potential for recall bias; lacking information on exposure; hospital controls were used for some studies, which
	general population or		Never	14 662	1		
	hospitals		Ever	86	0.95 (0.68-1.32)		
	Exposure	Lung, incidence	Duration of firefig	hter employ	ment (OR):		
	assessment method:	-	Never	14 662	1		
	questionnaire; ever		< 6 yr	32	1.19 (0.65-2.15)		
	employed, and categorical duration of		6–21 yr	22	0.99 (0.52-1.86)		may be a poor referent for healthy individuals select
	employment (years),		22–32 yr	14	0.70 (0.32-1.50)		into firefighting.
	from self-reports		≥ 33 yr	18	0.91 (0.47-1.77)		
	coded from interviews		Trend-test P value	, 0.58			
		Lung, incidence	Firefighter status (OR):		Age, study	
			Never	14 662	1	site, pack-	
		Ever	86	0.95 (0.68–1.32)	years, and time since quitting smoking, employed in other exposed job (ever/never)		

Reference, location, enrolment/ follow-up period, study design	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments	
<u> 3 3 3 3 3 3 3 3 3 3 3 3 3 3 3 3 3 3 3</u>		Lung, incidence	Duration of firefig	hter employ	ment (OR):	Age, study		
(cont.)			Never	14 662	1	site, pack-		
			< 6 yr	32	1.21 (0.67-2.19)	years, and		
			6–21 yr	22	0.97 (0.51-1.84)	time since		
			22–32 yr	14	0.69 (0.32-1.49)	quitting smoking,		
			≥ 33 yr	18	0.92 (0.48-1.78)	employed		
			Trend-test <i>P</i> value	, 0.58		in other exposed job		
						(ever/never)		
		Lung, incidence	Firefighter status,	never smoke	ers (OR):	Age, study		
			Never	457	1	site		
	Lung, inc		Ever	2	0.60 (0.14-2.58)			
		Lung, incidence	Firefighter status,	former smol	Age, study			
			Never 4922 1			site, pack-		
			Ever	25	0.75 (0.45–1.26)	years, and time since quitting smoking		
		Lung, incidence	Firefighter status,	current smo	kers (OR):	Age, study		
		5	Never	9278	1	site, smoking		
			Ever	59	1.18 (0.73-1.90)	pack-years		
		Lung	Firefighter status (OR):	. ,	Age, study		
	(adenocare incidence	(adenocarcinoma),	Never	3832	1	site, pack-		
			Ever	24	1.03 (0.64-1.67)	years, and		
		Lung (squamous cell carcinoma),	Firefighter status (OR):			time since		
			Never	5938	1	quitting		
			Ever	34	1.03 (0.66–1.60)	smoking		

Table 2.1	(continued)
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Reference, location, enrolment/ follow-up period, study design	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments		
<u>Bigert et al. (2016)</u>		Lung (small cell/	Firefighter status (OR):		Age, study			
(cont.)		oat cell), incidence	Never	2263	1	site, pack-			
			Ever	15	1.03 (0.57–1.87)	years, and time since			
		Other (specify): lung (other/ unspecified histological type), incidence	Firefighter status (OR):		quitting			
			Never	2629	1	smoking			
			Ever	13	0.84 (0.46–1.55)				

9/11, World Trade Center disaster, 11 September 2001; BMI, body mass index; CFHS, Career Firefighter Health Study; CI, confidence interval; FDNY, Fire Department of the City of New York; HR, hazard ratio; HWSE, healthy-worker survivor effect; ICD-10, International Classification of Diseases, 10th revision; IDR, incidence density ratio; LRT, likelihood ratio test; mo, month; NJ, New Jersey; NR, not reported; OR, odds ratio; PMR, proportionate mortality ratio; RCS, restricted cubic splines; RIR, relative incidence ratio; RR, rate ratio; SIR, standardized incidence ratio; SMR, standardized mortality ratio; vs, versus; SRR, standardized rate ratio; vs, versus; WTC, World Trade Center; yr, year.

these studies were excluded because they largely represented earlier follow-up of other included studies (Heyer et al., 1990; Beaumont et al., 1991; Baris et al., 2001). The remaining two studies from the USA presented results from mortality analyses in cohorts from the State of New Jersey, and from Buffalo, New York, respectively (Feuer & Rosenman, 1986; Vena & Fiedler, 1987). Two cohort studies from Canada reported on cancer mortality among firefighters in Edmonton and Calgary, and in Toronto, respectively (Guidotti, 1993; Aronson et al., 1994). In Oceania, cancer incidence among firefighters has been reported in five occupational and population-based studies, of which four were from Australia (Glass et al., 2016a, b, 2017, 2019) and one from New Zealand (Bates et al., 2001).

In addition to ever-employment in the occupation, exposure was typically defined as duration of employment or firefighting activity, ever-employment in a fire combat role, time since first or last employment, age at exposure, or exposure calendar period. In some instances, the authors had developed quantitative metrics on the basis of work history records or job-exposure matrices to assign exposure to the number and type of incidents, the number of fire-runs, fire-hours (i.e. the time spent at fires), or exposure days. [Since these studies included exposure contrasts, they were generally more informative than studies relying on classification on the basis of job title only. Although long follow-up periods were generally a strength of many of these studies, long follow-up can also prove to be a challenge for exposure assessment, because exposures are likely to change over time, employment records may not capture time spent firefighting, and exposures were assessed retrospectively in the cohort studies] (see Section 1.8.1 for more detail).

A cohort mortality study of 33 442 male professional [career] emergency responders (of whom 29 453, or 88%, were firefighters) in the Republic of Korea, who had been employed for \geq 1 month between 1980 and 2007 and followed

up from 1992 through 2007, provided information on the risk of cancer of the lung and bronchus (Ahn & Jeong, 2015). Firefighters were identified from a national database of emergency responders using work history and job title information, and were defined as any individual with first-line (e.g. pump, ladder, and operation chief) or second-line (e.g. drivers and division chief) firefighting duties in their work history. Mortality information was ascertained through a national database with near complete follow-up. The male population of the Republic of Korea was used as the reference population for the standardized mortality ratio (SMR), which was adjusted for age and calendar year, with a 1-year lag. An internal analysis using Poisson regression models that adjusted for age and calendar year was also performed. Twenty-six deaths from lung cancer were identified among the firefighters. The overall SMR for lung cancer was decreased for firefighters compared with the population of the Republic of Korea (SMR, 0.58; 95% confidence interval, CI, 0.38-0.84), and SMRs in three categories of employment duration $(< 10, 10 \text{ to } < 20, \text{ and } \ge 20 \text{ years})$ were all less than one. The internal analyses suggested an increased risk [estimated using adjusted rate ratios] of lung cancer for firefighters with ≥ 20 years of employment (adjusted relative risk, ARR, 1.21; 95% CI, 0.46-3.18; 13 deaths) and a decreased risk for firefighters with 10 to < 20 years of employment (ARR, 0.71; 95% CI, 0.26-1.96; 7 deaths) compared with firefighters with < 10 years of employment and non-firefighters within the cohort, but the results were statistically imprecise. [The Working Group noted that this study was limited by little adjustment for confounding (no adjustment for smoking), a relatively short length of follow-up (mean follow-up, 11.3 years), the relatively young age of the cohort (mean age at the end of follow-up, 41.3 years), and the low number of cases. The consideration of employment duration and job title was a strength of the exposure assessment, although there was no analysis of tasks performed. The study population included firefighting activity across the country, various work shifts (e.g. full-time and part-time work), and probably included both municipal and rural firefighters. Analyses by duration of employment and the use of internal analyses comparing firefighters with emergency responders and firefighters with < 10 years of experience was a strength and limited the influence of healthy-worker hire bias.]

An earlier study of the same cohort of 33 416 male professional [career] emergency responders (of whom 29 438, or 88%, were firefighters) in the Republic of Korea investigated incidence of rather than mortality from cancers of the respiratory system (Ahn et al., 2012). Follow-up for cancer incidence was conducted from 1996 through 2007 using data from a national cancer registry that had near complete follow-up. Stratified standardized incidence ratios (SIRs) were calculated for firefighters who had worked for \geq 10 years and those who had worked for < 10 years, using the male population of the Republic of Korea as the referent. An internal analysis was also performed using age- and calendar year-adjusted standardized rate ratios (SRR) estimated through Poisson regression in which the incidence of cancer of the lung and bronchus among firefighters was compared with that among non-firefighters. In the external comparison, an apparent decreased risk was observed in the incidence of cancer of the lung and bronchus (SIR, 0.78; 95% CI, 0.55-1.09; 36 cases) and cancer of the larynx (SIR, 0.57; 95% CI, 0.11–1.67; 3 cases). The risk was not found to be increased among workers with an employment duration of > 10 years. There was also little evidence from the internal analysis for an increased risk of cancer of the lung in firefighters (SRR, 0.69; 95% CI, 0.21–2.26; 36 cases) compared with non-firefighter emergency responders, although the estimate was imprecise. [The Working Group noted that the SIR analysis in this study was limited by probable healthy-worker hire bias, limited adjustment for

confounding (with no adjustment for smoking; the firefighter cohort reportedly smoked a little less and had less obesity than the comparison population), a relatively short length of follow-up (maximum follow-up, 12 years), the relatively young age of the cohort (mean age at the end of follow-up, 41.3 years), and the low number of cases. The analyses by employment duration and internal analyses comparing firefighters with non-firefighter emergency responders were strengths; however, most cohort members were classified as firefighters even though many were primarily medical/rescue technicians who only rotated temporarily through firefighter duties, potentially leading to non-differential exposure misclassification that would tend to bias the results towards the null. The study did not distinguish between typical exposure scenes (e.g. structure or wildland firefighting, and municipal or rural settings.]

An incidence and mortality study in a cohort of 3881 male professional [career] firefighters in Norway provided information on the risk of cancers of the respiratory system (larynx, lung, and mesothelioma) (Marjerrison et al., 2022a, b). Participants were firefighters employed in any of 15 fire departments covering 50% of the Norwegian population, with a geographical spread that was representative of the general population. The firefighters had worked in one of the departments at some time between 1950 and 2019, and most (92%) were engaged fulltime throughout their employment. The cohort included firefighters with past or present positions entailing active firefighting duties; individuals who had worked exclusively as chimney sweeps, fire inspectors, or office personnel were excluded. [Results were also presented for the broader cohort that included never-active firefighting personnel, but the Working Group considered the results for active firefighters to be more informative.] Incidence data came from the Cancer Registry of Norway, for which there is mandatory reporting of cancers. Mortality

data came from the Norwegian Cause of Death Registry. The follow-up period for both the cancer incidence and mortality analyses was from 1960 through 2018 (mean follow-up length for cancer incidence, 28 years). The general male population of Norway was the reference population for SIRs and SMRs, which were standardized by age and calendar year. The results of analyses conducted by year of first employment, time since first employment, and duration of employment were reported in Marjerrison et al. (2022a), whereas results stratified by follow-up period and age at diagnosis were reported for both incidence and mortality in Marjerrison et al. (2022b). The estimated risk of cancer of the larynx among firefighters was higher than that in the general population, but the result was imprecise (SIR, 1.77; 95% CI, 0.91-3.08; 12 cases); the SMR point estimate was similar but had even less precision (SMR, 1.92; 95% CI, 0.52–4.91; < 5 deaths). There was little evidence to suggest that the risk of cancer of the lung was raised in firefighters compared with the general population, whether based on incidence (SIR, 0.98; 95% CI, 0.78-1.22; 81 cases) or mortality (SMR, 0.91; 95% CI, 0.69-1.16; 61 deaths). The risk of mesothelioma appeared to be considerably elevated compared with that in the general population, although the number of cases was small (SIR, 2.46; 95% CI, 0.99-5.06; 7 cases; and SMR, 2.40; 95% CI, 0.65–6.15; < 5 deaths). Separate stratified analyses were also conducted. Most of these were too imprecise to be informative for cancer of the larynx or for mesothelioma, but risk for cancer of the larynx in firefighters did appear to be elevated compared with that in the general population \geq 40 years after first employment, after \geq 30 years of employment, for follow-up from 1985 through 1994, and for cases diagnosed in firefighters aged \geq 70 years. For mesothelioma, elevated risk was found for \geq 40 years after first employment, after \geq 30 years of employment, and for follow-up from 1995 onwards. The precision was better for analyses of cancer of the lung because of the

larger number of cases, but there was no strong evidence of an increase in risk for any of the stratified analyses. [The Working Group noted that this study was limited by probable healthyworker hire bias, the low number of cases of laryngeal cancer and mesothelioma, and the lack of data on potential confounders apart from age, calendar year, and sex. Although the analyses excluded individuals who had never performed active firefighting duties, the main limitations regarding the exposure assessment were that job changes over time were not accounted for, and that the proportion of rural to municipal firefighters was unknown. Healthy-worker hire bias may have influenced results because of the lack of internal analyses by specific job tasks and the use of an external reference group. The ascertainment of cancer incidence, the long length of follow-up, and the stratification of analyses on the basis of duration and time of employment were strengths. The presentation of both incidence and mortality data for the same sites and strata allowed for direct comparisons of the potential for surveillance bias.]

A study of cancer incidence in a cohort of 8136 male firefighters that used an extended follow-up of the Nordic Occupational Cancer (NOCCA) cohort in Sweden provided information on risk of cancers of the respiratory system (larynx, lung, and mesothelioma). Employment information was ascertained from national decennial censuses, starting in 1960 and ending in 1990 (eligible firefighters had to be aged between 30 and 64 years at the time of the relevant census and have worked as a firefighter for more than half of regular working hours that year). Cancer incidence data were ascertained from the Swedish Cancer Registry with follow-up from 1961 through 2009 (mean follow-up length, 28 years) (Bigert et al., 2020). The extent of any increased risk was assessed by external comparisons, including analyses of work duration as a proxy for exposure, and stratified by calendar period of follow-up. The male general population

of Sweden was the referent for all external comparisons. For external comparison estimates stratified by duration of employment categories, tests for a linear trend were conducted using a generalized linear model. There were no findings of elevated risk for cancer of the larynx or lung. The SIR for laryngeal cancer was 0.92 (95% CI, 0.48–1.61; 12 cases). For lung cancer, the overall SIR was 0.87 (95% CI, 0.72–1.05; 110 cases), with no elevated risk observed for analyses based on histological subtype, or after stratification by duration of employment (P = 0.10) or period of follow-up. Similar analyses specific to the incidence of adenocarcinoma were too imprecise to be informative. The incidence of mesothelioma was modestly elevated with an SIR of 1.11 (95% CI, 0.45-2.29; 7 cases). A separate analysis of mesothelioma stratified by duration of employment was too imprecise to be informative. The Working Group noted that this study was limited by probable healthy-worker hire bias given the use of a single external general population referent, the lack of work history data from employment records, and the absence of data on potential confounders apart from age, sex, and calendar time. There was likely to have been error (non-differential misclassification) in the measurement of duration of employment as a firefighter given that data were collected from the decennial census. It was unclear whether individuals were active firefighters for the whole of their employment, and the cohort probably included a combination of full-time, part-time, municipal, and rural firefighters. Strengths of this study included the long follow-up period, the ascertainment of cancer incidence, and analyses stratified by calendar period of employment.]

A study of cancer incidence in a cohort of 1080 male firefighters in Stockholm, Sweden, provided information on the risk of cancer of the bronchus and lung combined, and cancer of the pleura (Kullberg et al., 2018). Firefighters were identified through annual enrolment records from 15 fire stations in Stockholm and had worked for \geq 1 year between 1931 and 1983. This was an update to a previous study (Tornling et al., 1994) and added 26 years of follow-up for cancer incidence (from 1958 through 2012) from the Swedish Cancer Registry. For the incidence results, only those from the more recent study are discussed here. External comparisons were made with reference rates for the male general population of Stockholm County. Analyses were also stratified by age, employment duration, and starting year of employment for some cancer outcomes. The overall SIR for bronchus and lung cancer combined was less than one (SIR, 0.79; 95% CI, 0.52-1.15; 27 cases). There were only two cases of cancer of the pleura although 0.8 cases were expected. [The Working Group noted that this study was limited by probable healthyworker hire bias, because of the reliance on an external reference population, and by a lack of data on important potential confounders, particularly smoking. Strengths of this study included the ascertainment of cancer incidence, the long follow-up period, and analyses stratified by duration and era of employment, although stratified results were not reported for cancers of the respiratory system. Although the long follow-up period was a strength, it could also lead to misclassification of exposure because job activities and exposures probably changed over the study period and no results were reported for an association with job tasks or number of fires attended. It was unclear to what extent individuals had undertaken active firefighting duties during their employment.]

The earlier study of the same cohort also investigated mortality outcomes in a slightly larger population of 1116 male firefighters and provided information on risk of lung cancer mortality (<u>Tornling et al., 1994</u>). Vital status was determined through linkage with the census, death register, and emigration register. The cause of death was obtained from official death certificates. Mortality follow-up was from 1951 to the end of 1986. Exposure to fire events was assessed using reports of fires fought by the Stockholm fire brigade between 1933 and 1983, although associations were not reported for cancers of the respiratory tract. With male regional mortality as the referent, the overall SMR for lung cancer (SMR, 0.90; 95% CI, 0.53–1.42; 18 deaths) was not elevated. [The Working Group noted that this study was limited by probable healthy-worker hire bias and a lack of data on important potential confounders, particularly smoking. A strength of the exposure assessment was the differentiation of exposure on the basis of number of fires fought accounting for job position, station, and year of exposure, although associations were reported for few outcomes.]

A cancer incidence study in a cohort of 9061 male full-time, part-time, and volunteer firefighters in Denmark provided information on risk of cancers of the larynx and lung, and mesothelioma (Petersen et al., 2018a). Firefighters were identified using employer, trade union, and Danish Civil Registration System records that contained information on work history. Firefighters from all municipal districts in Denmark were represented in the cohort. Cohort members had been employed as firefighters at some time between 1964 and 2004, and cancer incidence follow-up was conducted in the Danish Cancer Registry from 1968 through 2014. Several proxy measures of exposure were used, including duration of employment, era of first employment, employment type (e.g. full-time, other), and job function (e.g. regular, specialized). The subpopulation of firefighters identified as "specialized" were smoke divers, who were considered to have a heavier exposure to smoke than the other firefighters. Three populations served as reference populations in external SIR analyses: the national male general population of Denmark, a random sample of Danish male employees, and Danish military personnel. Internal comparisons were also conducted, but results contributed little new information and were not reported. A total of 132 cases of lung cancer were identified, with overall SIRs of close to one using all three comparison populations (estimates ranging from 0.91 to 1.06). The SIRs were also less than, but generally close to, the null for analyses based on all proxy measures of exposure, including full-time versus other employment types. The exception was employment duration, for which the SIR estimate was modestly raised (SIR, 1.13; 95% CI, 0.85-1.49; 50 cases) for < 1 year of employment, but less than one for longer durations of employment, including ≥ 1 year (SIR, 0.81; 95%) CI, 0.65–1.00; 82 cases), ≥ 10 years (SIR, 0.73; 95%) CI, 0.57-0.93; 65 cases), and ≥ 20 years (SIR, 0.70; 95% CI, 0.53-0.93; 49 cases). For cancer of the larynx (SIRs ranging from 0.92 to 1.01; 16 cases) and mesothelioma (SIRs ranging from 0.65 to 0.71; 4 cases), point estimates were below or close to one. For mesothelioma, results were imprecise and were not stratified by full-time versus part-time employment status or other proxies of exposure. [The Working Group noted that this study was limited by a lack of adjustment for confounders, particularly smoking. Also, more than half of the cohort consisted of parttime/volunteer firefighters, which could have biased the result for mesothelioma towards the null. Strengths of this study included the use of working and military reference populations to reduce the influence of healthy-worker hire bias, the long period of follow-up, the ascertainment of cancer incidence outcomes, and the analyses by various proxies of exposure, such as job task. The study population excluded those without actual firefighting exposure based on job title/ function.]

Cancer mortality was investigated in the same cohort of Danish firefighters over a similar calendar period (<u>Petersen et al., 2018b</u>). An expanded study population of 11 775 male firefighters was identified using the same methods as described in <u>Petersen et al. (2018a</u>). Firefighters were followed for mortality and cause of death in the Danish national death registry from 1970 through 2014. The mean length of follow-up was

28 years for full-time firefighters and 17 years for part-time and volunteer firefighters. Two reference populations were used for external comparison analyses – a random sample of the Danish working male population and a sample of Danish military personnel. Seventy-six deaths from cancers of the larynx, trachea, and lung were identified, with a modest excess of deaths from this cause (SMR, 1.13; 95% CI, 0.91–1.42), in the subsample of full-time firefighters (n = 4659) compared with the military reference population. The SMR among part-time and volunteer firefighters was also modestly elevated (SMR, 1.16; 95% CI, 0.86-1.57; 42 deaths) compared with the military referent. For full-time firefighters, the SMRs based on duration of employment were imprecise but close to one, apart from that for firefighters who had worked for < 1 year (SMR, 1.30; 95% CI, 0.96–1.77; 41 deaths). There was no test for trend in risk across employment duration categories. [The Working Group noted that this study was largely subject to the same strengths and limitations as the cancer incidence study by Petersen et al. (2018a). The reliance on mortality outcomes in this study may have contributed to a survival bias, in the sense that occupational exposure as a firefighter may have conferred survival advantage because of earlier detection or better treatment availability than that for non-firefighters.]

A series of studies in the USA evaluated the cancer experience of firefighters from the Fire Department of New York (FDNY) who were involved in the WTC disaster response in 2001 (Zeig-Owens et al., 2011; Moir et al., 2016; Webber et al., 2021). These studies reported various lengths of follow-up for certain cancer sites, in addition to an assessment of exposure at the disaster site and evaluation of medical surveillance bias. Comparisons were also made with a separate cohort study of United States (US) municipal firefighters in which an assessment of exposure to firefighting activities was conducted (Daniels et al., 2014, 2015; Pinkerton et al., 2020).

The most recent study was of cancer incidence in a cohort of 10 786 male firefighters from the FDNY and 8813 male firefighters from the Career Firefighter Health Study (CFHS), which included firefighters from Philadelphia, Chicago, and San Francisco fire departments, USA, and provided information on the risk of lung cancer (Webber et al., 2021) [a previous study by Moir et al. (2016) was not reviewed here since it did not report the latest follow-up for lung cancer]. Firefighters were included if they had been employed on 11 September 2001, and the FDNY firefighters had to have worked at the WTC disaster site for \geq 1 day between 11 September 2001 and 25 July 2002. Cancer incidence follow-up was conducted using several state cancer registries selected on the basis of residential history information, beginning on 11 September 2001 and ending in 2016. Exposure for FDNY firefighters was categorized into one of five groups on the basis of the time of arrival and first day of work at the WTC site. All CFHS firefighters were considered to be unexposed using this exposure metric. External comparisons were made using the US male general population as the referent. In addition, internal comparisons were made comparing incidence rates in the FDNY to rates in the CFHS using Poisson regression, controlling for age and race or ethnicity. Several secondary and sensitivity analyses were performed. These included attempting to take into account increased medical surveillance of the FDNY cohort by adding a 2-year and 5-year lag to external comparison analyses for lung cancers diagnosed within 6 months of a routine computerized tomography (CT) scan of the chest, adjusting for smoking in internal regression analyses among the subset of firefighters for whom smoking data were available (FDNY, 10723; CFHS, 2856), and examining a dose-response relation in regression analyses between WTC exposure category and cancer in the FDNY cohort only. [The Working Group noted the low proportions of (self-reported) smokers in both cohorts (FDNY, 3.5%

current smokers, 30.2% former smokers; CFHS, 6.6% current, 37.0% former) compared with the general population of the USA, suggesting that negative confounding by smoking might have been present in many of the studies considered, unless smoking was explicitly adjusted for in the analyses.]

SIRs for lung cancer were decreased in both the FDNY (SIR, 0.53; 95% CI, 0.39-0.72; 44 cases) and CFHS (SIR, 0.71; 95% CI, 0.57–0.89; 83 cases) cohorts using the general population reference rates. After adjustment for medical surveillance bias, the SIR for lung cancer for the FDNY cohort was even lower (SIR, 0.47; 95% CI, 0.34-0.65). In internal analyses, the risk of lung cancer appeared to be lower in FDNY firefighters than in CFHS firefighters, but the estimate was imprecise (relative rate, RR [rate ratio], 0.87; 95% CI, 0.57-1.33). This was also the case after adjustment for surveillance bias (RR, 0.77; 95% CI, 0.50-1.19). [The Working Group noted that this study was limited by a possible incompletely controlled effect of greater medical surveillance bias in FDNY firefighters than in CFHS firefighters or the US general population, although this bias may be less influential for lung cancer than for other cancer sites. Limitations also included the relatively young age of the cohort, and the relatively short follow-up period (15 years). Further, the exposure being assessed was WTC disaster response, rather than all firefighting activity up to 2001, which limited the applicability of these studies to an assessment of the cancer hazard arising from all firefighting activities. Strengths of this study included the ascertainment of cancer incidence outcomes, the comparison of two firefighter cohorts to evaluate the impact of surveillance bias in this specialized cohort, and the adjustment for smoking in sensitivity analyses.]

Cancer incidence associated with exposure at the WTC disaster site was also investigated in an earlier study of an overlapping cohort of 9853 FDNY male firefighters (Zeig-Owens et al., 2011). The firefighters included had been employed for \geq 18 months, were active on 1 January 1996 with no previous history of cancer, and aged < 60 years on 11 September 2001 ("9/11"). Follow-up time was classified as "unexposed" before 9/11 for all firefighters and after 9/11 for firefighters who did not attend the WTC site (n = 926), and as "exposed" from 9/11 for firefighters who did attend the WTC site for \geq 1 day (*n* = 8927). Separate results were available for these "exposed" and "unexposed" periods of person-time. [A later methods study by Zeig-Owens et al. (2016) did not provide additional information that was informative to the deliberations of the Working Group.] Cancer incidence follow-up was conducted in state cancer registries from 1996 through 2008. SIRs, adjusted for age, race, ethnic origin, and calendar year, were calculated using the US male general population reference rates. In addition, "SIR ratios" were calculated using the unexposed person-time as the reference group. [The Working Group noted that "SIR ratio" is not a standard epidemiological effect measure. It was presumed to be interpretable as the ratio of an SIR for an exposed period to an SIR for an unexposed period, although the SIRs were not standardized to the same population. The SIR ratios in the study were subject to confounding by age, race, and ethnic origin, and were considered to be of limited informativeness.] SIR ratios for some cancers were presented with and without correction for medical surveillance bias. The "corrected" SIR ratios lagged the diagnosis date by 2 years for three cases of lung cancer. For lung cancer incidence, the corrected SIR restricted to exposed person-time was less than one (SIR, 0.28; 95% CI, 0.13-0.62; 6 cases), as was the corrected SIR ratio (SIR ratio, 0.53; 95% CI, 0.18-1.54; 14 cases, 6 exposed versus 8 unexposed), although the former estimate was imprecise. [The Working Group noted that this study was limited by probable healthy-worker hire bias, young age at end of follow-up of the cohort, and short follow-up period after exposure at the WTC disaster site (mean duration, 12.7 years). The analysis was probably subject to residual medical surveillance bias, although this bias may be less influential for lung cancer than for other sites.]

The CFHS is a separate cohort study conducted by the National Institute for Occupational Safety and Health (NIOSH) of cancer incidence and mortality among 29 992 municipal career firefighters from San Francisco, Chicago, and Philadelphia, USA (Pinkerton et al., 2020). The firefighters included were men and women who had worked for ≥ 1 day between 1950 and 2009. Firefighters were identified through personnel records and data from a previous study (Beaumont et al., 1991; Baris et al., 2001). The most recent mortality follow-up study by Pinkerton et al. (2020) included an additional 7 years of follow-up relative to the previous studies (Daniels et al., 2014, 2015). Mortality follow-up was conducted through national death registry, state vital records, and retirement board data sources from 1950 through 2016. The US general population was the referent in external comparison analyses using the SMR, which was standardized by gender, race, age, and calendar year. Sensitivity analyses were also conducted using state mortality reference rates. Three measures of exposure to firefighting activities were available for a subset of 19 287 male firefighters: exposeddays, fire-runs (Chicago and Philadelphia cohorts only), and fire-hours (Chicago cohort only). Exposure was defined as exposure to the combustion by-products of fire and assessed by linking detailed work histories with job-exposure matrices based on job, location, and firefighting apparatus assignments (<u>Dahm et al., 2015</u>). With the US general population referent, the overall SMR for lung cancer among firefighters was 1.08 (95% CI, 1.02-1.15; 1197 deaths), with considerable heterogeneity (P < 0.01) between results for the three included cohorts: San Francisco SMR, 0.71 (95% CI, 0.60–0.83); Chicago SMR, 1.20 (95% CI, 1.11-1.30); Philadelphia SMR, 1.14 (95%

CI, 1.03–1.26). This heterogeneity diminished but was still significant (P < 0.01) when state reference rates were used. For mesothelioma mortality, the overall SMR was considerably elevated at 1.86 (95% CI, 1.10-2.94; 18 deaths), with little heterogeneity (P = 0.71). Internal regression analyses were conducted to estimate associations with the three exposure metrics and applying a 10-year lag. Models were adjusted for age, race, birthdate, and fire department, with partial adjustment for the healthy-worker survivor effect in some models by including a variable on employment duration. For internal analyses, the hazard rate at the 75th percentile of the exposure distribution was compared with that at the 25th percentile. For lung cancer mortality, there was a positive association with number of exposed days (hazard ratio, HR for 8700 days versus 2500 days, 1.38; 95% CI, 1.08–1.78), fire-runs (HR for 8800 versus 2100 runs, 1.21; 95% CI, 1.05-1.38) and firehours (HR for 2300 versus 600 hours, 1.48; 95% CI, 1.21–1.80). In analyses of fire-runs, there was little evidence of differences in risk according to time since exposure, age at exposure, or exposure period. [The Working Group noted that some external comparison results were limited by probably healthy-worker hire bias. Internal analyses were not subject to this bias, and regression modelling attempted to control for a healthy-worker survivor effect through covariate adjustment of employment duration. There was a lack of data on important potential confounders, including smoking. However, confounding by smoking was considered less likely in the internal regression analyses. Strengths of this study included the long follow-up period, and the use of quantitative exposure metrics in internal analyses.]

An earlier study of a subset of firefighters from the same CFHS cohort examined internal exposure–response associations for both cancer mortality and incidence with follow-up to the end of 2009 (<u>Daniels et al., 2015</u>). The study included 19 309 firefighters of known race hired in 1950 or later and employed for ≥ 1 year. Methods were similar to those used in Pinkerton et al. (2020); however, results in the present study were not adjusted for employment duration. Mortality results in the two studies were similar. For lung cancer incidence, a positive exposure-response association was observed for number of firehours (HR for 2300 hours versus 600 hours, 1.39; 95% CI, 1.10-1.74), but not exposed days (HR for 8700 versus 2500 days, 1.05; 95% CI, 0.84-1.33) or fire-runs (HR for 8800 versus 2100 runs, 1.10; 95% CI, 0.94-1.28). Consistent with Pinkerton et al. (2020), there were no important differences in lung cancer mortality according to time since exposure, age at exposure, or exposure period. [The Working Group noted that an important difference between the models in **Daniels et al**. (2015) and Pinkerton et al. (2020) was that the earlier study did not adjust for employment duration. Confounding by employment duration appeared to be strong for lung cancer mortality in Pinkerton et al. (2020).]

An additional study of the CFHS cohort investigated both cancer mortality and incidence in 29 993 municipal career firefighters and reported external and internal comparison analyses with follow-up to the end of 2009 (Daniels et al., 2014). The methods were similar to those in the updated mortality study by Pinkerton et al. (2020), and only the incidence results are reviewed here. Cancer incidence follow-up was conducted in state cancer registries relevant to each fire department to the end of 2009, with start years varying between 1985 and 1988. Residential history information was used to select state registries for follow-up. US general population reference rates were used in external comparison analyses with SIRs standardized by gender, race, age, and calendar year. Separate analyses were conducted for two end-points, first primary cancer diagnosis and all primary cancer diagnoses, although results were similar for each [only results for all primary cancers were reported]. With the US general population as the referent, the SIR among firefighters was raised for laryngeal cancer (SIR, 1.50; 95% CI, 1.19-1.85; 84 cases). For lung cancer, the overall SIR was modestly raised (SIR, 1.12; 95% CI, 1.04-1.21; 716 cases). The excess was observed among Caucasian [White] men (SIR, 1.15; 95% CI, 1.07–1.24; 689 cases) but not among men of other racial groups (SIR, 0.67; 95% CI, 0.43-1.00; 24 cases). There was evidence of heterogeneity in the lung cancer SIRs between the three fire departments (P < 0.001). For mesothelioma, the overall SIR for firefighters was considerably raised (SIR, 2.29; 95% CI, 1.60-3.19; 35 cases). The Working Group noted that evidence of risk heterogeneity by department suggested that differences in exposures or other risk factors (e.g. smoking habits) across departments may not have been adequately addressed. Limitations included the lack of data on important potential confounders, particularly smoking. Strengths included the long period of follow-up, the ascertainment of incidence outcomes, and the inclusion of female firefighters.]

A cohort study of 2447 male municipal firefighters from Seattle and Tacoma, USA, reported on incidence of lung and laryngeal cancer compared with that in the local male general population and in a cohort of male police officers from Washington state (Demers et al., 1994). Firefighters had been employed for ≥ 1 year between 1944 and 1979, and cancer incidence follow-up was conducted from 1974 through 1989 in the regional Surveillance, Epidemiology, and End Results (SEER) cancer registry. Residential history information from pension and other sources was used to reduce loss to follow-up attributable to migration outside of the catchment area of the cancer registry. Information on exposure duration was available for the subcohort of Seattle firefighters, for whom exposure was assessed on the basis of information from employment records about the duration (in years) of active-duty employment in direct firefighting positions (i.e. administrative or support positions excluded). SIRs and incidence density

ratios (IDR) [the IDR can be interpreted as a rate ratio] were adjusted for age and calendar year. There were 45 cases of cancer of the lung, trachea, and bronchus, and 5 cases of cancer of the larynx, with estimates of effect close to or equal to one regardless of whether comparison was made with the local general population (SIR for lung, 1.0; 95% CI, 0.7–1.3; and SIR for larynx, 1.0; 95% CI, 0.3–2.3) or with police officers (IDR for lung, 1.1; 95% CI, 0.6–1.9; and IDR for larynx, 0.8; 95% CI, 0.2–3.5). When considering lung cancer by histological type, SIRs for adenocarcinoma, squamous cell carcinoma (SCC), small cell carcinoma, and large cell carcinoma did not differ from expected estimates. For lung cancer overall, SIR estimates using the general population referent appeared to decrease with increasing duration of employment and with time since first employment, although no formal test for trend was performed. [The Working Group noted that this study was limited by little adjustment for confounding, and no adjustment for smoking. The assessment of the duration of years involved in direct firefighting (intended as a surrogate for cumulative fire-smoke exposure) was a strength, although it was not measured equally in the Seattle and Tacoma study populations. The use of police officers as a comparison group was a strength that limited healthy-worker hire bias.]

An earlier study of 4401 municipal firefighters, which included the Portland, Seattle, and Tacoma firefighters described above, reported findings for risk of mortality for cancers of the respiratory system (Demers et al., 1992a). Firefighters had been employed between 1944 and 1979, and mortality follow-up was conducted in national and state sources from 1945 through 1989. An earlier publication of the mortality findings of the Seattle portion of the cohort was published with shorter follow-up (Heyer et al., 1990), as was a study of both cancer incidence and mortality including only Seattle and Tacoma (Demers et al., 1992b). [Since the results of these previous studies were subsumed

by those of the later studies, the results from these publications were not given a full review by the Working Group.] Fire department records were used to assign years of active duty in positions involving fire combat (in the Seattle and Portland firefighters) or employment as a firefighter (in Tacoma firefighters). Mortality rates were compared to those in the US White male general population and in a cohort of local male police officers. There were 95 deaths from cancer of the trachea, bronchus, and lung among firefighters, with estimates of close to one using both comparison groups (compared with the general population, SMR, 0.96; 95% CI, 0.77-1.17; and compared with police officers, IDR, 0.95; 95% CI, 0.67–1.33). Two deaths from cancer of the larynx provided a very imprecise estimate indicating no excess risk. There were no results for cancers of the respiratory system stratified by any employment, age, or exposure characteristics, including duration of employment in active firefighting positions. [Although this study evaluated mortality outcomes only, it had similar limitations and strengths to those of the later study by <u>Demers et al. (1994)</u>.]

A mortality study in a cohort of 1867 White male municipal firefighters who worked for the City of Buffalo, USA, provided information on the risk of cancers of the respiratory system (Vena & Fiedler, 1987). Firefighters had been employed for \geq 1 year between 1950 and 1979, and mortality follow-up was from 1950 through 1979. The US White male general population was the reference population in external comparison analyses. Stratification by year of hire, year of death, duration of firefighter employment, and latency was used for some cancer sites, but an analysis stratified only by duration of employment was performed for cancers of the respiratory system (International Classification of Diseases, ICD-8, 160–163). The observed number of deaths from cancer of the respiratory system was close to that expected (SMR, 0.94; 95% CI, 0.62-1.36; 28 deaths), with no apparent relation

to duration of employment as a firefighter. [The Working Group noted that this study was limited by probable healthy-worker hire bias and a lack of data on important potential confounders (particularly smoking). The number of deaths was low for analyses by duration of employment. No formal tests for trend were conducted. It was unclear whether individuals were active firefighters for the whole of their employment. The long follow-up period was a strength. Confidence intervals for stratified analyses were calculated by the Working Group.]

A proportionate mortality study of deceased police and firefighters was conducted in New Jersey, USA (Feuer & Rosenman, 1986). Analyses were based on 263 deaths in White male firefighters reported to the state comprehensive retirement system for police officers and firefighters in 1974-1980. Three reference populations were used to compare mortality proportions among firefighters, including the US general population, the New Jersey general population, and police officers identified in the same data source. No excesses of mortality from cancer of the respiratory system were observed among firefighters compared with any reference group, and there was no association with duration of employment. [A strength of this study was the comparison with another uniformed service occupation. The proportionate mortality study design, lack of information on potential confounders, and short observation period limited the informativeness of this study. Confidence intervals were calculated by the Working Group.]

A mortality study in a cohort of 5414 male municipal firefighters in Toronto, Canada, who worked for \geq 6 months between 1950 and 1989 provided information on the risk of cancers of the respiratory system (Aronson et al., 1994). Mortality follow-up was conducted in a national mortality database from 1950 through 1989. The male general population of Ontario was the reference population for external comparison analyses using the SMR. Analyses were also stratified by years since first employment, duration of employment, and age (analysis by duration of employment was restricted to 5373 firefighters). Employment information was ascertained from fire-department employment records. The overall SMR for cancers of the trachea, bronchus, and lung was close to one (SMR, 0.95; 95% CI, 0.71-1.24; 54 deaths). There was no evidence of increasing risk of lung cancer with increasing employment duration or time since first employment. There was little difference in the results when the analysis was stratified by age. There was only one death from cancer of the larynx. [The Working Group noted that this study was limited by probable healthyworker hire bias, a lack of data on important potential confounders such as smoking, and the ascertainment of mortality outcomes only, which may contribute to survival bias. Also, the extent of active firefighting duties and exposure in the cohort over the employment period of 39 calendar years was unclear. Strengths of this study included the long follow-up period and the analysis by duration of employment.]

A mortality study of 3328 municipal firefighters in two cohorts from Calgary and Edmonton, Canada, who worked at some time between 1927 and 1987 provided information on risk of cancers of the respiratory system (Guidotti, 1993). Mortality follow-up was conducted in both provincial and national sources from 1927 through 1987. The male general population of Alberta was the reference population for external comparison analyses. [The number of female firefighters in the cohort was described as "negligible" by the study author.] Analyses were also stratified by year of cohort entry, latency, duration of employment, and an exposure index. The exposure index was based on years of firefighter service weighted by an estimate of the relative time spent in proximity to fires according to job classification. Interviews with Edmonton firefighters were used to generate the weighted estimates for all job types. With the general

population of Alberta as the referent, the overall SMR among firefighters for cancer of the trachea, bronchus, and lung was elevated (SMR, 1.42; 95%) CI, 0.91–2.11; 24 deaths). However, the excess was confined to the Edmonton cohort, and the authors raised the possibility that the lung cancer results were confounded by smoking. There was no apparent relation with year of cohort entry, latency, duration of employment, or the exposure index. No deaths from cancer of the larynx were identified. [The Working Group noted that this study was limited by probable healthy-worker hire bias and a lack of data on important potential confounders, particularly smoking. The considerable follow-up during the middle and later part of the last century suggested that the availability and use of effective personal protective equipment (PPE) may have been lower than for firefighters included in studies in more recent decades. The long follow-up period and use of the exposure index based on duration of employment and job classification were strengths.]

Four studies investigated cancer risk among diverse types of firefighter in Australia (Glass et al., 2016a, b, 2017, 2019). These studies involved male and female volunteer, career, full-time, part-time, and instructor firefighters in urban and rural environments. Each study also assessed exposure to specific events involved in firefighting. The methods used to enumerate and analyse the cohorts in each study were broadly similar.

The most recent of the four studies was on cancer incidence in an entirely female cohort of 37 962 volunteer firefighters in Australia, which provided information on risk of cancers of the respiratory system (Glass et al., 2019). The cohort included firefighters from fire agencies representing all except two states of Australia. Firefighters entered the cohort at various calendar periods depending on the fire agency. Work history information describing the number and type of incidents attended was ascertained from fire agency personnel records. Cancer incidence follow-up was conducted in a national cancer registry from 1982 through 2010. [Mortality results and results for 1682 career firefighters were not reported for specific cancer sites.] In external comparison analyses, the female general population of Australia was the referent. Internal regression analyses were also conducted according to duration of service, whether fire incidents were attended, the number of incidents attended, and incident type. Among volunteer firefighters who attended incidents (n = 16320), an excess of lung cancer cases was observed with the general population as the referent (SIR, 1.30; 95% CI, 0.90-1.82; 34 cases). There was no excess of lung cancer among all volunteer firefighters $(n = 37 \ 097)$. For mesothelioma, SIR estimates were statistically imprecise but suggested excess risk. There were three cases of mesothelioma diagnosed among all volunteer firefighters and one case diagnosed among volunteers who attended incidents. In internal analyses, the relative incidence ratios (RIRs) [equivalent to rate ratios] for the association between the number of incidents attended and lung cancer were statistically imprecise but indicated elevated rates among volunteers who had ever attended incidents versus never attended incidents. Trend tests using tertile categories did not suggest a relation between risk of lung cancer and the total number of incidents attended overall (P = 0.51), or all fire incidents (P = 0.46), structure fire incidents (P = 0.17), landscape [wildland] fire incidents (P = 0.56), or vehicle fire incidents (P = 0.18). [The Working Group noted that this study was limited by probable healthy-worker hire bias, the young age of the volunteer cohort at the end of follow-up (mean, 46 years), a lack of information on important potential confounders such as smoking, and a short follow-up period (approximate mean, 7 years). Strengths of this study included the internal comparison analyses and the exposure assessment involving the number and type of attended incidents, including landscape fires. This study was also based on a large population

of female firefighters and included many firefighters working in rural environments.]

Using the same methods as those in the study of female firefighters, cancer incidence was also investigated in a parallel cohort of 163 094 male volunteer firefighters in Australia (Glass et al., 2017). The data collection, follow-up period, and analysis were similar to those described in the cohort study in female firefighters (Glass et al., 2019), although the cohort of male firefighters was drawn from five fire agencies, and analyses were additionally reported by duration of service. With the male general population of Australia as the referent, SIRs among all volunteer firefighters (n = 157931) were decreased for all cancers of the respiratory system combined (SIR, 0.49; 95% CI, 0.45-0.54; 429 cases) and for lung cancer (SIR, 0.48; 95% CI, 0.44 to 0.54; 371 cases), cancer of the larynx (SIR, 0.45; 95% CI, 0.31-0.62; 36 cases), and mesothelioma (SIR, 0.64; 95% CI, 0.64-0.87; 42 cases). Results were similar for volunteer firefighters who had attended incidents $(n = 100 \ 126)$. In internal regression analyses, the RIR [equivalent to rate ratio] for all volunteer firefighters was decreased in the longest duration of service category (≥ 20 years) compared with the shortest (> 3 months to 10 years) for incidence of cancers of the respiratory system combined (P < 0.01) and for incidence of lung cancer (P = 0.03). Results were similar for firefighters who had attended incidents. In internal regression analyses, the RIRs did not suggest a positive relation between the tertile of number of incidents attended (overall or by incident type) and the risk of cancers of the respiratory system combined or lung cancer, although the estimates were imprecise. [The Working Group noted that this study exhibited the same strengths and limitations as the study of female volunteer firefighters in Australia. This study was similarly limited by a short follow-up period (mean follow-up, 9.4 years) and the young age of the cohort (mean age at end of follow-up, 48.7 years). It was also noted that the exposure tertiles

were based on exposure in a separate cohort of career firefighters and the distribution of cases was unequal, with very few cases in the highest tertiles for all cancer sites in this cohort of volunteer firefighters. This may indicate that volunteers participated in fewer fire incidents.]

A cancer incidence study in a cohort of 30 057 paid full-time and part-time male firefighters in Australia provided information on the risk of cancers of the respiratory system (Glass et al., 2016a). The methods used to enumerate and analyse the cohort were similar to those previously described for the studies of volunteer firefighters (Glass et al., 2017, 2019), although 8 out of 10 fire agencies supplied records to identify the study population, and the study included firefighters who were employed full-time (n = 17 394) or part-time (n = 12 663) and had worked for \geq 3 months between 1976 and 2003. The cohort consisted primarily of municipal and semi-metropolitan firefighters. Cancer incidence follow-up was conducted in a national registry to the end of 2010. With the male general population of Australia as the referent, overall SIRs for firefighters were decreased for cancers of the respiratory system combined (SIR, 0.71; 95% CI, 0.59-0.85; 117 cases), lung cancer (SIR, 0.71; 95% CI, 0.58 to 0.86; 101 cases), and laryngeal cancer (SIR, 0.70; 95% CI, 0.36-1.22; 12 cases). There was an excess risk of mesothelioma (SIR, 1.34; 95% CI, 0.75-2.21; 15 cases). In internal regression analyses adjusted for age and calendar year, there was no evidence of a positive trend in lung cancer risk with increasing employment duration in all firefighters (P = 0.84) or in strata of full-time (P = 0.60) or part-time firefighters (P = 0.46). There was also no evidence of a positive trend in lung cancer risk with increasing number of incidents (overall or by incident type) in full-time firefighters who had ever attended incidents. [The Working Group noted that this study was limited by probable healthy-worker hire bias, a lack of data on potential confounders (particularly smoking), the short follow-up period, and

the relatively young age of the cohort at the end of follow-up (mean age, 49.9 and 44.5 years, for fulltime and part-time firefighters, respectively). The study benefited from an enhanced assessment to differentiate exposure based on the number and type of incidents attended, but early exposure was extrapolated from more recent data. The internal analyses comparing risk across exposure categories within the cohort reduced the influence of biases related to using an external reference group.]

A study of cancer incidence was conducted in a cohort of 614 firefighters and trainers who attended a firefighter-training facility in Australia (Glass et al., 2016b). Three female firefighters were excluded from the analysis. Cancer incidence follow-up was conducted from 1982 through 2012. The study assessed exposure to hazardous substances at the training facility rather than to typical firefighter work. The male general population of Victoria was the reference group in external comparison analyses. Participants were grouped into risk categories of low, medium, and high chronic exposure (to smoke and other hazardous agents) on the basis of job assignment. The "high risk of chronic exposure" group comprised paid [career] instructors and operators, the medium-risk group comprised career and volunteer regional instructors, and the low-risk group comprised career practical firefighting trainees. There were only four cases of cancer of the respiratory system (expected, 6.17 cases) and the SIRs across three categories of exposure were based on too few cases to be informative. [The Working Group noted that this was the only study reviewed that specifically investigated firefighter instructors, a group assumed to have greater potential for high exposure. This study was limited by the small number of cases and the young age of the participants. Strengths of this study included the long follow-up period and the internal comparison analysis by exposure level.]

A study of mortality and cancer incidence in a cohort of 4305 paid [career] and volunteer firefighters in New Zealand provided information on risk of cancers of the respiratory system (Bates et al., 2001). The cohort included 84 female firefighters who were excluded from the analysis. The included firefighters had worked for ≥ 1 year as a career firefighter and been employed for \geq 1 day between 1977 and 1995. Follow-up for cancer mortality and incidence was conducted in a national data source to the end of 1995 (for mortality) or 1996 (for incidence). The male general population of New Zealand was the reference population in external comparison analyses. Analyses were stratified by calendar year, years of service, and employment type (e.g. career, volunteer service). With the general population as the referent, overall mortality from lung cancer among firefighters was decreased (SMR, 0.86; 95% CI, 0.4-1.6; 10 cases) and incidence was increased (SIR, 1.14; 95% CI, 0.7-1.8; 17 cases). There was some evidence of a positive relation between lung cancer incidence and duration of career service (P = 0.48), although estimates were based on few cases and were imprecise. [The Working Group noted that this study was limited by probable healthy-worker hire bias and a lack of data on potential confounders, particularly smoking. A significant proportion of the cohort was lost to follow-up. It was unclear the extent to which the study population included municipal versus rural firefighters.]

Bigert et al. (2016) analysed pooled information from the IARC SYNERGY study that included 14 case-control studies conducted in Canada, China, Europe, and New Zealand. The SYNERGY study was designed to evaluate confounding and effect modification in the assessment of occupational lung carcinogens and risk of lung cancer. Study information was collected by questionnaire between 1985 and 2010. The average response proportion among individual studies was 78% (range, 41–100%). Selection of controls varied by study and included hospital patients, general populations, or both. Participants were restricted to working males with detailed "lifetime" work histories and smoking information, resulting in a study group comprising 14 748 incident cases of lung cancer and 17 543 controls. Firefighters (n = 190; 86 cases of lung cancer, 104 controls) were identified from self-reported lifetime work histories. Age- and smoking-adjusted logistic regression models were fitted to calculate odds ratios (ORs), with firefighting as the exposure of interest. The adjustment for smoking comprised cumulative cigarette smoking (pack-years), and time since quitting smoking cigarettes. Models were also fit including adjustment for employment in a job known to present an excess risk of lung cancer (e.g. mining industry, asbestos production, metals industry, construction industry, and shipbuilding). Outcomes included lung cancer overall and stratified by histology. Analyses for all lung cancers were repeated after stratification by smoking status (never, former, current) and work duration (< 6, 6–21, 22–32, and > 32 years). Meta-analysis was used to examine heterogeneity across the studies. There was no evidence of increased lung cancer risk in models either with (OR, 0.95; 95% CI, 0.68-1.32) or without (OR, 1.03; 95% CI, 0.77–1.38) adjustment for smoking. Further adjustment for high-risk employment did not substantively change the estimate (OR, 0.95; 95% CI, 0.68-1.32). There was no evidence of increasing lung cancer risk with employment duration (P = 0.58). There was also no evidence of differences in lung cancer risk across categories of smoking status, although there were only two lung cancers among firefighters classified as never smokers. In analyses for major histological types of lung cancer, there was no evidence of increased risk of adenocarcinoma, SCC, small cell carcinoma, or other/unspecified types in firefighters compared with other occupations. There was no evidence of study heterogeneity $(I^2 = 0.0\%, P = 0.738)$. [The Working Group noted that control for smoking was a strength of this

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study, as was the detailed occupational history collected for every participant. Limitations included the small number of cases in stratified analyses, a lack of information on exposures and other risk factors, and the use of hospital controls in some individual studies.]

2.1.2 Studies only reporting having ever worked as a firefighter

(a) Occupational cohort studies

See Table S2.2 (Annex 2, Supplementary material for Section 2, Cancer in Humans, online only, available from: <u>https://publications.iarc.</u> <u>fr/615</u>).

Between 1978 and 2021, there were eight studies examining the risk of cancers of the respiratory system in firefighters compared with non-firefighter populations (Musk et al., 1978; Eliopulos et al., 1984; Grimes et al., 1991; Giles et al., 1993; Deschamps et al., 1995; Ma et al., 2005, 2006; Amadeo et al., 2015). Of these studies, three had an exposure assessment of satisfactory quality (Musk et al., 1978; Eliopulos et al., 1984; Deschamps et al., 1995), whereas the remaining studies were found to have exposure assessments of minimal quality (see Table 1.8.1). Exposures probably stemmed mostly from structure fires in urban settings. Cancer sites considered included the trachea, lung and bronchus, larynx, and mesothelioma. All studies conducted external comparisons that did not examine exposureresponse associations using direct measures or proxies for exposure. Most studies had longitudinal cohort designs that included information on the firefighter population at risk; however, one study conducted only a proportionate mortality ratio (PMR) analysis (Grimes et al., 1991). In all the studies, only career firefighters were specifically identified, and most were probably assigned to tasks common to fighting structure fires. Most studies examined cancers observed in career firefighters employed at a single municipal department (Musk et al., 1978; Eliopulos

et al., 1984; Grimes et al., 1991; Giles et al., 1993; Deschamps et al., 1995); however, multidepartment cohorts were also evaluated (Ma et al., 2005, 2006; Amadeo et al., 2015). [The Working Group noted that the reliance on external reference populations for occupational cohorts, leading to potential downward bias from healthy-worker effects, was a shared limitation among all studies reviewed. In general, informativeness was considered to be superior in studies on cancer incidence compared with studies on cancer mortality; the latter having a greater potential for information and selection biases. Among other limitations, studies lacked individual information on occupational exposures and important risk factors other than demographic characteristics such as age and sex. Also, this group of studies covered a long time period, such that fire environments in earlier studies (e.g. Musk et al., 1978; Eliopulos et al., 1984) probably differed greatly from those experienced in later studies. The Working Group noted that, in the absence of information on the population of interest, risk estimates from PMR studies relied heavily on strong assumptions that may not be valid for firefighter cohorts. The Working Group also noted the sparse information available on the risk of mesothelioma because of its long latency, rarity, and lack of a widely available disease classification before the late 1990s.]

Amadeo et al. (2015) examined mortality among civilian male career firefighters in France (n = 10 829), actively employed in 1979 and followed to the end of 2008 (308 089 personyears). Firefighter status was determined by employment records covering 93% of all French municipal fire departments. Vital status and causes of death were determined from linkage to national vital records. Cause-specific cancer risk was assessed in age- and calendar year-adjusted SMRs using the general male population of France as the referent. The mean age at entry was 30 years (range, 17–64 years). About 15% of the cohort was deceased at the end of follow-up. Mortality from cancers of the lung and bronchus was lower than expected (SMR, 0.86; 95% CI, 0.74–0.99; 187 deaths). There was no evidence of excess mortality from cancers of the larynx and trachea (SMR, 1.10; 95% CI, 0.73-1.59; 28 deaths). There were six deaths from mesothelioma, which was reported to be near the expected number, although the specific SMR was not reported. [The large study size, firefighter identification, and long follow-up period were notable strengths. The Working Group also noted that all-cause mortality was significantly below that expected in the cohort. The SMRs tended to be low among young firefighters and to increase with age. These findings suggested relatively strong downward bias from healthy-worker selection.]

Deschamps et al. (1995) examined mortality in male career firefighters (n = 830) (with specialized military status) who were employed by the Brigade des sapeurs-pompiers de Paris (Paris Fire Brigade) for a minimum of 5 years by 1977 and were followed to the end of 1990 (11 414 person-years). Occupation was determined by employment records. Vital status was ascertained from pension records, and the underlying cause of death was determined via linkage with the national mortality registry. Age- and calendar-year adjusted cause-specific SMRs were calculated using the male general population of France as the referent. The duration of fire combat was assessed among decedents; however, this information was not used when estimating cancer rate ratios. By the end of the study, less than 4% (n = 32) of the participants were deceased, which was about half that expected. Mortality from cancers of the respiratory system was close to that expected, with wide confidence intervals (SMR, 1.12; 95% CI, 0.45–2.30; 7 deaths). [The Working Group noted that the small study size and young cohort led to few deaths during observation, and necessitated analysis restricted to a heterogenous group of all cancers of the respiratory system combined. There was also a strong potential for downward

bias from healthy-worker effects, given the short mortality follow-up and use of a specialized group of firefighters who had been selected for good physical and psychological health, received annual medical examinations, and were required to meet high standards of physical training.]

Ma et al. (2006) examined cancer incidence in a cohort of 36 813 career firefighters employed in Florida, USA, beginning in 1972, who were followed from 1981 through 1999 (431 865 person-years). Employment was determined by state firefighter certification records. The cohort was mostly White (90.1%) and relatively young, with an average age of < 60 years at the end of the study. The median follow-up time was 13 years. Follow-up time was shorter for female firefighters (5.5% of the cohort) than for males. Incident cases were identified by linkage with the state cancer registry. Age- and calendar year-adjusted SIRs were determined separately for men and women, with state cancer rates as the referent. The incidence rate of cancers of bronchus and lung combined was greater than expected among female firefighters (SIR, 1.51; 95% CI, 0.30-4.40), although there were only three cases, and the confidence interval was wide. The incidence rate of cancers of the bronchus and lung was lower than expected among male firefighters (SIR, 0.65; 95% CI, 0.54–0.78; 128 cases).

Ma et al. (2005) also examined cancer mortality between 1972 and 1999 in the same cohort of Florida career firefighters described above. The cause of death was ascertained via linkage with state vital records. Age- and calendar year-adjusted SMRs were calculated separately for male (n = 34796) and female (n = 2017) firefighters. Comparisons were made with state general-population rates as the referent. The patterns of mortality from cancers of the bronchus and lung in men (SMR, 0.93; 95% CI, 0.79–1.09; 155 deaths) and women (SMR, 2.22; 95% CI, 0.45–6.49; 3 deaths) were compatible with the incidence results. [The Working Group noted the large study size and sex-specific risk estimates as strengths of the Florida cohort studies, although risk estimates for women were limited by small numbers. The follow-up period may have been insufficient to observe excess incidence or mortality for cancers of the respiratory system, and the Florida firefighter cohort was still relatively young at the end of follow-up. The significant deficit in all-cause mortality among males in the Florida firefighter cohort suggests the potential for strong downward bias from healthy-worker effects.]

Grimes et al. (1991) examined proportionate mortality in male firefighters with ≥ 1 year of service in the fire department of the City of Honolulu, USA, and followed from 1969 through 1988. Information on the cause of death was abstracted from death certificates obtained from state vital records. Analyses were stratified by ethnic group ("Caucasian" [White] and "Hawaiian"). The expected numbers were based on all deaths among males aged > 20 years in the state population. There were 205 deaths observed. The PMR for deaths from cancer of the respiratory system in the full cohort was 1.28 (95% CI, 0.82–2.00; [18] deaths). There was no indication of effect modification by ethnic group (Caucasian [White] versus Hawaiian). [Reporting estimates stratified by ethnicity was a notable strength. However, in addition to the general limitations of study designs without denominator data, the Working Group noted that the PMRs were not standardized by age or calendar period.]

Musk et al. (1978) examined mortality patterns among 5655 male career firefighters with \geq 3 years of service in the Boston Fire Department, Massachusetts, USA, who were followed for mortality from 1915 through 1975 (142 975 person-years). Occupation as a firefighter was determined by employment records. Causes of death were ascertained from death certificates obtained from state vital records. Death certificates were not available for nearly 8% of known decedents. Relative risk associated with employment as a firefighter was estimated from

age- and calendar period-adjusted cause-specific SMRs using mainly Massachusetts state rates as the referent. The number of expected deaths was determined from rates for the state (all men) and national (White men) population. Nearly all participants (99.7%) were White and 246 people (4.4%) were lost to follow-up. A total of 2470 deaths were observed (43.7%), which was 91% of that expected. Observed deaths from cancers of the respiratory system were fewer than expected (SMR, 0.88; 95% CI, [0.69–1.10]; 70 deaths). [The long observation period was a notable study strength that also lessened the potential for strong bias from healthy-worker effects. The Working Group also noted that, given the relatively few cancer deaths, the analysis was restricted to all cancers of the respiratory system combined rather than to specific types. Confidence intervals were calculated by the Working Group.]

Giles et al. (1993) examined cancer incidence among 2865 male firefighters from Melbourne, Australia, who were first employed between 1917 and 1989 and followed from 1980 through 1989 (20 853 person-years). Information on cancer incidence was obtained via linkage with the Victorian Cancer Registry. Age- and calendar year-adjusted cause-specific SIRs were calculated using the male population of Victoria as the referent. The incidence of cancers of the trachea, bronchus, and lung was lower than expected among the firefighters (SIR, 0.77; 95%) CI, 0.28–1.68; 6 cases). [The Working Group noted that the long period between first employment and observation would result in potential selection bias from survivor effects caused by the exclusion of firefighters who may have died before the start of follow-up in 1980, and whose deaths would therefore not have been observed. The study also had limited power given the small study size and short observation period.]

Eliopulos et al. (1984) examined mortality among 990 Australian men first employed as full-time firefighters between 1939 and 1978 and followed through 1978 (16 876 person-years). More than half (64.5%) were still employed at the end of follow-up, with about 3% lost to follow-up after accounting for emigration. Vital status was obtained from a variety of information sources, and the underlying cause of death was abstracted from death certificates. Age- and calendar period-adjusted SMRs were calculated using the adult male population of Western Australia as the reference group. [The Working Group noted that PMRs were also calculated but did not consider them informative for the evaluation, given the availability of SMRs for cancer of the respiratory system.] A total of 116 deaths (11.7%) were observed in the cohort, which was 80% of that expected. There were fewer than expected deaths from cancers of the respiratory system (SMR, 0.84; 95% CI, 0.33-1.71; 7 deaths). [The Working Group noted that the observed trends in all-cause mortality were consistent with strong healthy-worker effects and that this study had limited power, given the small study size.]

(b) Population-based studies

See Table S2.2 (Annex 2, Supplementary material for Section 2, Cancer in Humans, online only, available from: <u>https://publications.iarc.</u> <u>fr/615</u>).

Between 1989 and 2021, five population-based cohort studies were published that included findings on the risk of cancers of the respiratory system among firefighters (Hansen, 1990; Pukkala et al., 2014; Harris et al., 2018; Zhao et al., 2020; Sritharan et al., 2022), and ten case-control or mortality surveillance studies reporting risk estimates for cancers of the respiratory system from employment as a firefighter (Sama et al., 1990; Burnett et al., 1994; Ma et al., 1998; Bates, 2007; Kang et al., 2008; Tsai et al., 2015; Muegge et al., 2018; Langevin et al., 2020; Lee et al., 2020; McClure et al., 2021). Of all the studies in this section, only the study by Langevin et al. (2020) was found to have an exposure assessment of satisfactory quality. Exposure assessments in the remaining studies were considered to be

of minimal quality (see Table S1.28, Annex 1, Supplementary material for Section 1, Exposure Characterization, online only, available from: <u>https://publications.iarc.fr/615</u>).

The cohort studies compared incidence or mortality of cancer in firefighters to that expected in the general population overall or in a non-firefighting reference population. Four cohort studies used national census data to enumerate the cohort (Hansen, 1990; Pukkala et al., 2014; Harris et al., 2018; Zhao et al., 2020), whereas one study examined a cohort formed using an occupational injury and disease claims database and linkage to person and cancer registries (Sritharan et al., 2022). All cohort studies determined firefighter employment status from self- or proxy-reported information gathered at the time of census or death.

Six case-control studies had event-only designs using cancer registry information to identify individuals with cancers of the respiratory system as cases and other cancers as controls (Sama et al., 1990; Bates, 2007; Kang et al., 2008; Tsai et al., 2015; Lee et al., 2020; McClure et al., 2021). Two case-control studies used death certificate information in similar event-only designs (Ma et al., 1998; Muegge et al., 2018). The remaining case-control study was a multicentre population-based case-control study of laryngeal cancer incidence among residents in a large metropolitan area (Langevin et al., 2020). An additional study used information from death certificates obtained from a national occupational mortality surveillance database to calculate PMRs specifically focused on firefighters (Burnett et al., 1994).

In general, cancer incidence was considered more informative than mortality, although exceptions may apply on the basis of other considerations, such as the potential for cancer screening bias. The Working Group noted that the reliance on external reference populations, leading to probable healthy-worker selection bias, was a shared limitation among the cohort studies, given the strong potential for bias in a highly selected population of interest. Another limitation of all studies in this section was the reliance on a one-time qualitative measure of exposure, employment as a firefighter, from censuses, claims data, or death certificates. Occupational information abstracted from death certificates was subject to additional errors. Most studies lacked individual information on important risk factors (e.g. tobacco use) other than demographic characteristics such as age and sex, although the case-control study by Langevin et al. (2020) was a notable exception. Finally, long latency, rarity of occurrence, and lack of disease classification before the late 1990s limited the informativeness of studies on mesothelioma risk. The Working Group noted that a shared strength of the eventonly case-control studies was the availability of large case numbers, resulting in improved statistical power. There were also important shared limitations. First, event-only designs used other incident cancers, cancer deaths, or non-cancer deaths as controls. As such, the effect measure is a valid measure of relative risk only if the rate of control events among the exposed is the same as that among the unexposed. In the absence of this condition, a serious bias in either direction can occur. Second, cancer registries and death certificates contain only limited information on occupation, which can result in considerable exposure misclassification. This misclassification can be differential with respect to case status, leading to potential bias in either direction.]

Zhao et al. (2020) examined mortality patterns by occupation in a longitudinal study of the male population of Spain as reported in the 2001 census and followed to the end of 2011. At baseline, the study included nearly 10 million working men aged 20–64 years, of whom 27 365 were firefighters (266 562 person-years among firefighters and 93 752 897 person-years among other occupations). Occupation was determined from census report at baseline. The underlying cause of death was ascertained by linkage with

the national mortality registry. Age-adjusted mortality rate ratios (MRRs) were calculated to compare rates for firefighters to rates for men in all other occupations. The rate ratio for laryngeal cancer mortality was increased (MRR, 1.77; 95% CI, 1.01-3.09; 14 deaths). There was no evidence of increased lung cancer risk among firefighters (MRR, 0.94; 95% CI, 0.77-1.15; 104 deaths). With only one death observed, there was also no evidence of excess mortality from mesothelioma. [The large sample size and use of a working population as the reference group were notable strengths; however, the short follow-up period and young age of the cohort resulted in limited informativeness, especially for cancers with a long latency such as lung cancer and mesothelioma.]

Pukkala et al. (2014) examined cancer incidence in the NOCCA cohort, a large cohort of male career firefighters (n = 16422), using data from five Nordic countries for the period 1961-2005 (412 991 person-years). Firefighter status was determined by national census questionnaire. Cancer incidence was determined by linkage with national cancer registries. In the full cohort, lung cancer incidence (310 cases) did not differ meaningfully from the expected number, with the national population as the referent; however, an excess of lung cancer was observed in Danish firefighters (SIR, 1.37; 95% CI, 1.03-1.77; 56 cases), which was consistent with the results of an earlier census-based mortality study of Danish male firefighters followed from 1970 through 1980 (<u>Hansen, 1990</u>). [The earlier study (<u>Hansen</u>, 1990) will not be further discussed here because of its overlap with <u>Pukkala et al. (2014)</u>.] The authors attributed this excess to increased relative risk of adenocarcinoma of the lung among older Danish firefighters. The incidence of lung adenocarcinoma was greater than expected in the full cohort (SIR, 1.29; 95% CI, 1.02-1.60; 80 cases), which was largely attributable to the findings among Danish firefighters, although tests of heterogeneity among countries were not reported.

The SIR for adenocarcinoma was greatest for attained age \geq 70 years compared with that for younger firefighters. The SIR was also greatest in the most recent observation period (1991–2005) compared with earlier periods, although differences were much less pronounced. There was no evidence of an increased risk of SCC or small cell carcinoma. Pukkala et al. (2014) also reported that the incidence of mesothelioma was greater than expected, although this was based on small numbers of cases (SIR, 1.55; 95% CI, 0.90-2.48; 17 cases). The SIR for mesothelioma was substantially elevated among those aged \geq 70 years (SIR, 2.59; 95% CI, 1.24-4.77; 10 cases). [The Working Group noted that this finding was consistent with the long latency between asbestos exposure and occurrence of mesothelioma observed in other studies.] The mesothelioma risk appeared largely attributable to a substantial excess in Norwegian firefighters (SIR, 2.78; 95% CI, 1.02-6.06; 6 cases). [Strengths of the study included the use of cancer incidence as the end-point; increased statistical power resulting from the pooling of information from multiple countries; the long follow-up period and the large number of firefighters; and the examination of risk by attained age, period of follow-up, histological type, and country. The Working Group noted as limitations the likelihood of healthyworker selection bias, the infrequent ascertainment of firefighting status through use of the decennial census, and the lack of information on potential confounders.]

Sritharan et al. (2022) investigated cancer incidence in a cohort of 13 642 firefighters employed in Ontario, Canada. The study group was enumerated using information from an occupational injury and disease claims database and linkage to person registries. Information was abstracted for claimants (n = 2 368 226) between 1983 and 2019 who were aged \geq 15 years and had complete information on sex, birthdate, claim date, and occupation and industry information. The cohort was then linked to the Ontario Cancer Registry to obtain information on site-specific cancer incidence. People with a cancer diagnosis recorded before 1983 or who entered the cohort for an occupational cancer claim were excluded. Workers were followed from first claim date to date of first cancer diagnosis, emigration out of Ontario, attained age 85 years, death, or study end (2020), whichever was earliest. Site-specific cancer risk was assessed using Cox proportional hazards regression, controlling for age at start of follow-up, birth year, and sex. Models compared cancer incidence in firefighters to that in all other occupations and in police. There was no evidence of an increased incidence of cancers of the lung or larynx among firefighters compared with either reference group. The incidence rate of mesothelioma among firefighters was three times that among police (HR, 3.21; 95% CI, 1.10-10.20; 11 cases). This excess was greatly attenuated in comparisons using all workers as the reference group (HR, 1.56; 95% CI, 0.86-2.84). [The Working Group noted that the large study size and access to tumour information were important strengths. Another study strength was the inclusion of female firefighters. Among limitations, exposure information consisted only of the job title available at the time of the worker compensation claim. The type of compensation claims used to identify the cohort may have differed by occupation, which could also introduce bias. Additional information would be needed to determine whether exposure misclassification was differentially distributed, which could result in a bias in either direction.]

Harris et al. (2018) examined cancer incidence by occupation in the Canadian Census Health and Environment Cohort (CanCHEC) (1991–2010). The cohort was created from the 1991 national census that collected data on about 20% of Canadian households. Occupation was determined from self-report of the longest-held job in the previous year. The study roster was probabilistically matched to the national cancer registry to ascertain cancer cases. Cox proportional hazards regression models adjusting for age, region, and education level were fitted to estimate the cancer risk associated with work as a firefighter compared with that for other occupations. The analyses were restricted to working adult men aged 25-74 years at baseline and included 1 108 410 people (of whom 4535 were firefighters). The average follow-up length among firefighters was 17.9 years. With other workers as the referent, firefighters in this study did not have an increased risk of lung cancer (HR, 0.90; 95% CI, 0.71–1.15; 65 cases). [A notable strength was the use of a large population-based cohort that supported several comparisons of firefighters with a working population, thereby reducing the potential for strong bias from healthy-worker effects. The Working Group also noted that analyses were restricted to outcomes with more than five events. Therefore, size restrictions precluded information on rare events, such as mesothelioma and laryngeal cancer. The lack of accounting for race or ethnicity in fitted models was considered to be a minor limitation.]

Lee et al. (2020) examined site-specific cancer incidence in a registry-based case-control study using data from Florida, USA. Employment records for people certified as firefighters in 1972–2012 ($n = 109\ 009$) were linked with state cancer registry data (1981-2014) to identify 3760 male and 168 female firefighters aged \geq 20 years at diagnosis of their first primary cancer. Logistic regression was used to calculate age- and calendar year-adjusted ORs separately for men and women, with firefighting as the exposure of interest. Results stratified by tumour stage and age (< 50 years, \geq 50 years) were also reported for men. The controls in primary analyses comprised all cancer cases identified in the state registry except for cases of the cancer of interest. In post hoc analyses, ORs for men were calculated using controls excluding smoking-related cancers (lung, larynx, oesophagus, bladder, oral/ pharynx) because the smoking rate among firefighters was assumed to be lower than that in

the general population. Most firefighters were non-Hispanic (95.1%) or White (93.6%) and diagnosed between age 45 and 64 years. There was no evidence of increased lung cancer risk among male (OR, 0.79; 95% CI, 0.72-0.87; 466 cases) or female (OR, 0.54; 95% CI, 0.28-1.02; 10 cases) firefighters compared with other occupations. Among men, lung cancer ORs were higher in the older age group and the late-stage tumour group than in the younger group and the earlystage tumour group, respectively; however, all ORs were below one. The OR for mesothelioma was increased among male firefighters but had wide confidence intervals (OR, 1.26; 95% CI, 0.70-2.29; 11 cases). There were no mesothelioma cases among women. Laryngeal cancer was less likely to occur in male firefighters than in non-firefighters (OR, 0.48; 95% CI, 0.34-0.67; 35 cases), with no cases observed among female firefighters. Excluding smoking-related cancers from the control group only slightly attenuated ORs, suggesting little potential for a strong bias from smoking. [A strength of the study was the linkage to the Florida state firefighter certification database, which was a superior source of information on firefighter status when compared with the cancer registry. The Working Group noted overlap with the previous cohort study of Florida firefighters by Ma et al. (2006), which had follow-up through 1999. That study used a standard longitudinal cohort design rather than the event-only case-control design of Lee et al. (2020). Comparing estimates from Ma et al. (2006) with those from Lee et al. (2020) revealed notable inconsistencies between findings, which might have stemmed from differences in analytical methods, follow-up, or both. These differences could have been more thoroughly explored by replicating the previous cohort study methods using the extended follow-up for comparison with current findings.]

<u>McClure et al. (2021)</u> extended the Florida cancer registry-based case–control study to assess whether results differed according to the method by which firefighter status was identified, either by cancer registry data alone (n = 1831) or by linkage between the registry and the state firefighter certification records, as reported by Lee et al. (2020). The OR for cancers of the respiratory system in male firefighters identified from certification records (OR, 0.73; 95% CI, 0.67–0.81; 505 cases) was lower than that obtained from data restricted to registry information (OR, 0.99; 95% CI, 0.87–1.11; 311 cases). The study confirmed that occupational data were frequently missing from registry records, and that the absence of these data was not random but was differentially distributed by sociodemographic and diagnostic characteristics. Female firefighters, less-recent diagnoses, and older-aged patients were less likely to have information on firefighter occupation listed in the cancer registry (McClure et al., 2019). [The Working Group noted that differentially distributed exposure misclassification could result in bias in either direction and concluded that all studies relying on cancer registry information for occupation merited cautious interpretation.]

Langevin et al. (2020) conducted a population-based case-control study of head and neck cancers among men in the Boston area, Massachusetts, USA. Cases (718 people, of whom 11 were firefighters) were ascertained from records in major area hospitals and verified through linkage with the state cancer registry. Controls (905 people, of whom 13 were firefighters) were identified through municipal and state records as living within the catchment area and having no history of head and neck cancer. Controls were frequency-matched to cases on age, sex, and location of residence. Enrolment occurred in two phases: December 1999 to December 2003 (phase I) and October 2006 and June 2011 (phase II). Self-reported information on occupational histories, sociodemographic factors, alcohol consumption, and tobacco use were collected using questionnaires. Firefighters were defined as those reporting a current or former job as a career firefighter with job duties that involved

firefighting. The classification excluded volunteer firefighters, fire inspectors, and fire administration staff. Participation rates were 78% and 47% for cases and controls, respectively. The odds of laryngeal SCC were increased among firefighters compared with non-firefighters (OR, 1.70; 95% CI, 0.45-6.41); however, there were only three cases in firefighters. In analyses stratified by smoking status, there was a strong association between firefighting and SCCs of the hypopharynx and larynx combined in people with a history of smoking of < 18.4 pack-years (OR, 8.06; 95% CI, 1.74–37.41; 3 cases in firefighters). The exposure-response relation per decade firefighting was also substantially elevated (OR, 2.10; 95% CI, 1.06-4.14). These associations were not found among heavy smokers (> 18.4 pack-years). [Analysis adjusting for several important risk factors, such as age, race, education, smoking, and alcohol consumption, was a notable strength. However, the Working Group also noted that few firefighters participated in the study, and that stratified analyses were adversely affected by small numbers. The Working Group also noted a potential for bias because of reliance on self-report, although the contribution of information on occupation to this bias was expected to be small, given that self-reported firefighter status is likely to be more accurately reported than for some other occupations. There was also a potential upward selection bias given that firefighters were less likely to participate as controls.]

Muegge et al. (2018) examined firefighter mortality in a registry-based case–control study using death certificate information obtained from the vital records system in Indiana, USA (1985–2013). Decedents aged \geq 18 years at death and of known race and ethnicity were identified as either firefighters or non-firefighters using industry and occupation information recorded at time of death. Each firefighter death record (n = 2818) was matched to four randomly selected non-firefighter deaths (n = 11272) without replacement. Matching variables were exact on attained age, sex, race, ethnicity, and year of death. Conditional logistic regression was used to calculate site-specific cancer mortality ORs. There were 318 deaths from cancers of the respiratory system among firefighters. The authors stated that there was no evidence of increased odds of death attributable to cancers of the respiratory system among firefighters, although point estimates were not shown. Post hoc calculation of PMRs and standardized mortality odds ratios (SMORs) was said to have provided similar findings (excluding deaths attributable to assault and homicide), although results were not shown. [The Working Group noted the use of a non-standard analysis approach applied to event-only data as a limitation. Reporting of results from analysis of alternative approaches (e.g. PMRs and SMORs) would have better supported study findings. Among other limitations, the Working Group noted the lack of a risk measure for cancers of the respiratory system and the reliance on death certificates for exposure status.]

Tsai et al. (2015) examined site-specific cancer incidence in a registry-based event-only case-control study of firefighters in California, USA, in 1988-2007. Researchers obtained data from the state cancer registry, including demographic information, cancer characteristics, and information on industry and occupation for the longest held job by each study participant. Keyword searches of occupation and industry fields were used to identify firefighters using codes related to firefighting from the 1990 revision of the US Census Bureau. The study was restricted to first malignant primary tumours among male participants aged 18-97 years at diagnosis for whom information on occupation and industry was available (n = 678 132). About 44% of records meeting all other eligibility criteria were excluded because of missing occupation. The control group comprised cancers of the pharynx, stomach, liver, and pancreas, which were selected on the basis of review of the literature suggesting that

cancers at these sites were not associated with firefighting. These cancers were removed from the control group when selected as the cancer of interest. Logistic regression models were fitted to calculate ORs adjusted for age at diagnosis, year of diagnosis, and race. The study included 3996 male firefighters, most of whom (90.2%) were White. Among cancers of the respiratory system, the risk of non-specific, non-small cell lung cancer (International Classification of Diseases for Oncology, ICD-O, 8046) was substantially increased (OR, 2.01; 95% CI, 1.38-2.93; 42 cases). There was no evidence of increased risk of other lung cancer histological types or of all lung cancers combined. The OR for mesothelioma was elevated (OR, 1.40; 95% CI, 0.89-2.21; 21 cases). In contrast, the risk of laryngeal cancer was decreased in firefighters (OR, 0.59; 95% CI, 0.39-0.89; 25 cases) compared with other occupations. Bates (2007) conducted a similar study with the California Cancer Registry, USA, in 1988–2003, but these data were included in the study conducted by Tsai et al. (2015). [The Working Group noted that study strengths included the large number of incident cancers with histological confirmation of diagnosis and analyses by lung cancer histological type. Several limitations were also noted, including largely incomplete information on occupation, and lack of information on exposure and potential confounding factors (e.g. smoking).]

Kang et al. (2008) extended a previous cancer registry-based case–control study of White male firefighters in Massachusetts, USA (Sama et al., 1990). Study data (1987–2003) were obtained from the registry and included age, sex, smoking status, detailed tumour information, and self-reported information on occupation and industry. Occupational information was available for 62.5% of all cancer cases listed in the registry. Among eligible cases (n = 161 778), the occupational fields were searched by keyword to identify firefighting as the exposure of interest (n = 2125). Two unexposed reference groups (police, all other occupations) were used, with police preferred in most analyses. Smoking information, which was available for 84.5% of firefighters, 85.4% of police, and 82.2% of other occupations, was used to define smoking status as never, past, current, or unknown. Standardized morbidity odds ratios (SMBORs), adjusted for age and smoking, were calculated for 25 cancer types of concern (lip, buccal cavity, nasopharynx, pharynx, oesophagus, stomach, colon, rectum, liver, pancreas, larynx, lung, cutaneous melanoma (hereafter referred to as "melanoma"), soft tissue sarcoma, breast, prostate, testis, kidney, bladder, brain, thyroid, leukaemia, non-Hodgkin lymphoma (NHL), Hodgkin lymphoma, multiple myeloma), with each site compared individually to the group of control [comparison] cancers (i.e. cancer sites other than those of concern) among each of the two unexposed reference groups. SMBORs were also calculated for age groups 18–54, 55–74, and \geq 75 years. The numbers of lung and larynx cancers among firefighters were 379 and 38, respectively. There was no evidence of increased risk of cancers of the lung or larynx among firefighters in analyses using either reference group or within any age group. [The Working Group noted that the availability of information on smoking and control for smoking in estimating ORs were important strengths. However, the methods used for control for smoking (including the handling of missing data) were not clear. The Working Group noted differences in ORs by reference group. There was not an obvious pattern of differences by reference group across all outcomes; therefore, the choice of referent appeared inconsequential. Another notable limitation was the largely incomplete information on occupation. The effect of the missing information was unclear given some evidence that missingness may be differentially distributed by important sociodemographic variables (McClure et al., 2021).]

Sama et al. (1990) conducted a registry-based cancer incidence study using information from the cancer registry in Massachusetts, USA, for the 4 years (1982-1986) before the start of the study by Kang et al. (2008). The study examined nine cancer types, including cancers of the trachea, bronchus, and lung combined. The cancer cases included White men aged \geq 18 years at diagnosis, with confirmed primary tumours coded in accordance with ICD-O. Occupational information was available for only about half of all registry cases. Information on occupation was coded according to the US Census Bureau on the basis of the self-reported longest job held, as identified at the time of cancer diagnosis. Firefighters (n = 315) were identified as those with jobs listed as firefighter or fire chief. SMBORs, adjusted for age, were calculated using two groups as referent: (i) registry cases with any occupational information other than firefighter; and (ii) cases among protective services, identified as police, police chief, sheriff, and correctional officers. For each cancer of a priori interest, control cancers included all other cancers except those of the organ systems of concern, namely cancers of the digestive and respiratory systems, and lymphatic and haematopoietic tissues. Smoking status included information on cigarettes, and participants were categorized as current, former, or never smokers; this information was available for 89% of firefighters, 85% of police controls, and 86% of state controls. Analyses were not adjusted for smoking, although the prevalence of current smoking among firefighters was 46.3% compared with 40.1% and 41.6% for police and state cases, respectively. Incident lung cancer was more likely among firefighters compared with either reference group - SMBOR for all occupations other than firefighter referent, 1.22 (95% CI, 0.87–1.69); and SMBOR for police referent, 1.30 (95% CI, 0.84–2.03) – although confidence intervals were wide. [The Working Group noted that information on occupation was substantially incomplete. This is a common limitation of cancer registries.

The effect of incomplete information on risk estimates was not clear, given evidence that data gaps might not be random (McClure et al., 2021). Other limitations included the lack of control for smoking, as well as limitations inherent to the study design restricted to cancer event data.]

Using the occupational mortality surveillance system in the PMR study by Burnett et al. (1994) (described below), Ma et al. (1998) examined race-specific cancer risk among male firefighters in a case-control study of decedents from 24 states in the USA. The database contained information on causes of death and occupation that was abstracted from death certificates obtained from 24 US states between 1984 and 1993. Racespecific cancer mortality odds ratios (MORs) were calculated with all non-cancer deaths as referent and adjusting for year and age at death. There were 6607 deaths and 1883 cancer deaths among firefighters. Among firefighter cancer deaths, 96.5% and 3.5% were observed in White and Black firefighters, respectively. Lung cancer risk was marginally increased among White firefighters (MOR, 1.1; 95% CI, 1.0-1.2; 633 deaths) but not among Black firefighters (MOR, 0.8; 95% CI, 0.5-1.3; 15 deaths). There was no evidence of increased risk of laryngeal cancer for either racial group. Mesothelioma was not directly investigated; however, the MOR for cancers of the pleura among White firefighters was elevated (MOR, 1.8; 4 deaths). There were no pleural cancers observed among Black firefighters. [The use of a large and geographically diverse national occupational mortality database was a notable strength. The Working Group noted that analyses of certain outcomes and of Black firefighters were limited by small numbers.]

In a mortality surveillance study, <u>Burnett et al.</u> (1994) calculated PMRs using death certificate data collected from 27 US states in 1984–1990 that were coded into a national occupational surveillance database. Firefighter status was determined from death certificate information about the usual occupation and industry over the

decedent's lifetime that was provided by a proxy (e.g. next of kin) at the time of death. Age-adjusted PMRs compared the proportion of deaths from specific causes in White male firefighters to the proportion of deaths from the same causes for all White male decedents. Separate analyses were conducted for all deaths and for deaths occurring before age 65 years. The lung cancer PMR was as expected for all firefighter deaths (PMR, 1.02; 95% CI, 0.94-1.11; 562 deaths) and for deaths before age 65 years (PMR, 0.98; 95% CI, 0.86–1.12; 236 deaths). Other cancers of the respiratory system were not investigated. The authors acknowledged the potential for error in the information on occupation from death certificates because of a tendency among firefighters to retire early and seek other employment. Information on the duration of employment or occupational exposure was not available. [The use of information from a national occupational surveillance database spanning several states was a notable strength. Among the substantial limitations of this study was that the potential for incomplete or erroneous information on occupation from death certificates may have resulted in downward bias from differential misclassification based on occupation status. The Working Group also noted that a PMR analysis may overestimate risk for specific causes of death among firefighters, given the relatively low overall death rate among this occupational group.]

2.2 Cancers of the urogenital system

2.2.1 Studies reporting occupational characteristics of firefighters

See <u>Table 2.3</u>.

Studies first described in Section 2.1.1 are described in less detail in the present section.

The Working Group identified 23 occupational and population-based cohort studies on the relation between occupational exposure as a firefighter and risk of cancers of the genitourinary system, including the prostate, testis, bladder, and kidney (Vena & Fiedler, 1987; Demers et al., 1992a, 1994; Guidotti, 1993; Aronson et al., 1994; Tornlingetal., 1994; Bates et al., 2001; Zeig-Owens et al., 2011; Ahn et al., 2012; Daniels et al., 2014, 2015; Glass et al., 2016a, b, 2017, 2019; Petersen et al., 2018a, b; Kullberg et al., 2018; Bigert et al., 2020; Pinkerton et al., 2020; Webber et al., 2021; Marjerrison et al., 2022a, b). Of these studies, one was from Asia, seven from Europe, fourteen from North America, and five from Oceania. Four of these studies were excluded because they largely represented earlier follow-up of included studies (Heyer et al., 1990; Beaumont et al., 1991; Baris et al., 2001) or covered similar data to that in an included study (Demers et al., 1992b). [The Working Group noted that the study strengths and limitations pertaining to design that were previously described for cancers of the respiratory system in Section 2.1.2(b) also apply to outcomes in the present section.]

A cohort study of cancer incidence in 33 416 male professional [career] emergency responders (29 438, or 88%, were firefighters) in the Republic of Korea provided information on the risk of cancers of the genitourinary system (Ahn et al., 2012). Emergency responders were employed between 1980 and 2007, and cancer incidence follow-up was carried out from 1996 through 2007. With the male population of the Republic of Korea as the referent, the SIRs for firefighters were raised for cancers of the kidney (SIR, 1.56; 95% CI, 1.01–2.41; 20 cases), urinary bladder (SIR, 1.60; 95% CI, 1.01-2.56; 17 cases), and prostate (SIR, 1.32; 95% CI, 0.60-2.51; 9 cases), but the evidence was less clear for prostate cancer because of the wide confidence interval. The age- and calendar year-adjusted SRRs from internal analyses (with non-firefighter emergency responders as the referent) were not elevated for cancers of the prostate, kidney, or bladder.

An incidence and mortality study in a cohort of 3881 male professional [career] firefighters from several departments in Norway provided

Table 2.3 Cohort studies reporting occupational characteristics of firefighters and cancers of the urogenital system

Reference, location enrolment/follow- up period, study design	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments
up period, study		incidence or	level Duration of fir (SIR): 1 mo to < 10 yr ≥ 10 yr Total SRR: Non- firefighters Ever employed as a firefighter Duration of fir (SIR): 1 mo to < 10 yr ≥ 10 yr Total SRR: Non- firefighters Ever employed as a firefighters Ever employed as a firefighters Ever	deaths refighting en 1 8 9 2 9 efighting en 6 14 20 2 20 2 20 efighting en	(95% CI) aployment, 1-yr lag 0.75 (0.01–4.16) 1.47 (0.63–2.89) 1.32 (0.60–2.51) 1 0.22 (0.05–1.05) aployment, 1-yr lag 1.62 (0.59–3.52) 1.54 (0.84–2.58) 1.56 (1.01–2.41) 1 0.69 (0.16–2.99) aployment, 1-yr lag 0.39 (0.01–2.18) 1.98 (1.13–3.22) 1.60 (1.01–2.56)	Age, calendar period	Exposure assessment critique: Satisfactory quality. Heterogeneity of direct firefighter exposure within job title. May include rural and municipal firefighters. Strengths: employment duration and internal comparison limits healthy- worker bias; only professional [career] firefighters were included in the cohort. Limitations: no information on personal characteristics or confounders (except the firefighter cohort had a lower BMI and smoked less than the comparison population for the SIR analysis); follow- up time was reasonably short; cohort members were fairly young; no direct measure of exposure.
		Urinary bladder, incidence	SRR: Non- firefighters Ever employed as a firefighter	3 17	1 0.40 (0.12–1.40)		

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Reference, location enrolment/follow- up period, study design	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments
Marjerrison et al.	3881 male professional	Kidney,	SIR:			Age,	<i>Exposure assessment</i> <i>critique</i> : Satisfactory quality. Included firefighters with current or previous positions entailing active firefighting
(<u>2022a)</u>	[career] firefighters	incidence	Firefighters	29	1.28 (0.86–1.84)	calendar	
Norway Enrolment,	(most were full-time) employed in positions	Kidney,	Year of first en	nployment (SIR):	year	
.950–2019/follow-	entailing active	incidence	Pre-1950	10	1.61 (0.77–2.96)		
ip, 1960–2018	firefighting at any of		1950-1969	9	1.24 (0.57–2.35)		duties but no assessment
Cohort 15 fire departments between 1950 and 2019		1970 or after	10	1.09 (0.52–2.01)		of length of time in active firefighting positions, may	
	Kidney,	Time since firs	st employme	ent (SIR):			
	Exposure assessment	incidence	< 20 yr	1	0.47 (0.01-2.64)		include municipal and rura
	method: employment		20–39 yr	15	1.41 (0.79-2.32)		firefighters.
history from personne records	7 I		$\geq 40 \text{ yr}$	13	1.32 (0.70-2.26)		<i>Strengths</i> : long length of follow-up (mean, 28 yr);
	records	Kidney,	Duration of er	nployment (SIR):		near complete ascertainme
		incidence	< 10 yr	3	1.32 (0.27-3.85)		of both cancer incidence
			10–19 yr	3	1.07 (0.22-3.14)		and mortality; analyses
			20–29 yr	6	0.95 (0.35-2.06)		by duration and timing of employment. <i>Limitations</i> : probable healthy-worker effect; no dat on potential confounders apart from age, sex, and calendar time.
			≥ 30 yr	17	1.51 (0.88-2.42)		
		Urinary tract	SIR:				
		(ICD-10, C65– C68), incidence	Firefighters	69	1.25 (0.97–1.58)		
		Urinary tract	Year of first en	nployment (SIR):		
		(ICD-10, C65-	Pre-1950	35	1.71 (1.19–2.38)		
		C68), incidence	1950-1969	22	1.04 (0.65-1.58)		
			1970 or after	12	0.88 (0.45-1.54)		
		Urinary tract	Time since firs	st employme	ent (SIR):		
		(ICD-10, C65-	< 20 yr	3	1.13 (0.23-3.30)		
		C68), incidence	20–39 yr	17	0.86 (0.50-1.38)		
			≥ 40 yr	49	1.49 (1.10–1.97)		
		Urinary tract	Duration of er	nployment (SIR):		
		(ICD-10, C65–	< 10 yr	8	1.82 (0.79-3.60)		
		C68), incidence	10–19 yr	3	0.55 (0.11–1.60)		
			20–29 yr	22	1.54 (0.97–2.34)		
			$\geq 30 \text{ yr}$	36	1.16 (0.81-1.60)		

enrolment/follow- description, exposure (hist up period, study assessment method incid	ncer type stopathology), idence or rtality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments
designmorMarjerrison et al. (2022b)3881 male professional [career] firefighters (most were full-time) employed in positions entailing active firefighting at any of 15 fire departments between 1950 and 2019 Exposure assessment method: employment history from personnel recordsPros incid Pros incidPros incidPros firefighting at any of 15 fire departments between 1950 and 2019 Exposure assessment method: employment history from personnel recordsPros morPros incidPros firefighting at any of 15 fire departments between 1950 and 2019 Exposure assessment method: employment 	rtality state, idence state, rtality state, idence state, rtality state, idence state, idence state, idence state, idence state, idence	SIR: Firefighters SMR: Firefighters Period of follo 1984 or before 1985–1994 1995 or after Period of follo 1984 or before 1985–1994 1995 or after Age at diagnos ≤ 49 yr 50–69 yr ≥ 70 yr Age at diagnos ≤ 49 yr 50–69 yr ≥ 70 yr SIR: Firefighters SMR: Firefighters	214 54 w-up (SIR): 14 32 168 w-up (SMR) 6 7 41 sis (SIR): < 5 109 101 sis (SMR): 0 7 47 17 0	1.18 (1.03–1.35) 1.07 (0.80–1.39) 0.83 (0.45–1.39) 1.33 (0.91–1.88) 1.20 (1.02–1.39) : 0.91 (0.33–1.97) 0.70 (0.28–1.44) 1.21 (0.87–1.64) 2.65 (0.72–6.79) 1.22 (1.01–1.48) 1.11 (0.91–1.35) 0 (0.00–22.03) 0.72 (0.29–1.48) 1.16 (0.85–1.54) 1.39 (0.81–2.22) 0 (0.00–3.07)	Age, calendar year	Exposure assessment critique: Satisfactory quality. Included firefighters with current or previous positions entailing active firefighting duties but no assessment of length of time in active firefighting positions, may include municipal and rural firefighters. Strengths: long length of follow-up (mean, 28 yr); near complete ascertainment of both cancer incidence and mortality; analyses by duration and timing of employment. Limitations: probable healthy-worker effect; no data on potential confounders apart from age, sex, and calendar time.
Test	tis, incidence	Period of follo 1984 or before 1985–1994 1995 or after	w-up (SIR): < 5 0 13	1.64 (0.45–4.21) 0 (0.00–1.34) 1.72 (0.91–2.93)		

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Table 2.3	(continued)
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Reference, location enrolment/follow- up period, study design	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments
Marjerrison et al.		Testis, mortality	Period of follo	w-up (SMR)	:	Age,	
<u>2022b)</u> cont.)			1984 or before	0	0 (0.00-5.24)	calendar year	
			1985-1994	0	0 (0.00-25.3)		
			1995 or after	0	0 (0.00–10.5)		
		Testis, incidence	Age at diagno				
			$\leq 49 \text{ yr}$	15	1.47 (0.82-2.43)		
			50-69 yr	< 5	1.10 (0.13-3.97)		
			≥ 70 yr	0	0 (0.00-12.7)		
		Testis, mortality	Age at diagno	sis (SMR):			
		,	≤ 49 yr	0	0 (0.00-4.86)		
			50-69 yr	0	0 (0.00-12.3)		
			≥ 70 yr	0	0 (0.00-25.8)		
		Kidney,	SMR:				
		mortality	Firefighters	10	0.97 (0.46-1.78)		
	Kidney,	Period of follo	w-up (SIR):				
		incidence	1984 or before	< 5	1.07 (0.29–2.74)		
			1985-1994	8	2.40 (1.04-4.74)		
			1995 or after	17	1.09 (0.64-1.75)		
		Kidney,	Period of follo	w-up (SMR)	:		
		mortality	1984 or before	< 5	0.43 (0.01–2.37)		
			1985-1994	< 5	2.00 (0.54-5.11)		
			1995 or after	5	0.83 (0.27-1.95)		
		Kidney,	Age at diagno	sis (SIR):			
		incidence	≤ 49 yr	< 5	0.78 (0.09-2.80)		
			50-69 yr	12	0.97 (0.50-1.69)		
			≥ 70 yr	15	1.96 (1.10-3.23)		
		Kidney,	Age at diagno	sis (SMR):			
		mortality	≤ 49 yr	< 5	3.01 (0.36-10.9)		
			50-69 yr	< 5	0.83 (0.23-2.13)		
			≥ 70 yr	< 5	0.82 (0.22-2.11)		

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NO	
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Reference, location enrolment/follow- up period, study design	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments
Marjerrison et al. (2022b) (cont.)		Urinary tract (ICD-10, C65– C68), mortality	SMR: Firefighters	15	1.14 (0.64–1.88)	Age, calendar year	
		Urinary tract (ICD-10, C65– C68), incidence	Period of follo 1984 or before	w-up (SIR): 13	1.42 (0.76–2.43)		
			1985–1994 1995 or after	15 41	1.47 (0.82–2.43) 1.14 (0.82–1.55)		
		Urinary tract (ICD-10, C65– C68), mortality	Period of follo 1984 or before	w-up (SMR) < 5	: 1.20 (0.25–3.51)		
			1985–1994 1995 or after	< 5 8	1.58 (0.43–4.05) 0.99 (0.43–1.94)		
		Urinary tract (ICD-10, C65– C68), incidence	Age at diagnos $\leq 49 \text{ yr}$ 50-69 yr $\geq 70 \text{ yr}$	< 5 23	1.05 (0.22–3.06) 0.96 (0.61–1.44)		
		Urinary tract (ICD-10, C65– C68), mortality	≥ 70 yr Age at diagnos ≤ 49 yr 50-69 yr ≥ 70 yr	43 sis (SMR): 0 < 5 12	1.52 (1.10–2.04) 0 (0.00–12.0) 0.79 (0.16–2.30) 1.32 (0.68–2.31)		
			- / 0 y1	12	1.52 (0.00-2.51)		

Reference, location enrolment/follow- up period, study design	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments
Bigert et al. (2020) Sweden Enrolment, 1960–1990/follow- up, 1961–2009 Cohort	8136 male firefighters identified from national censuses in 1960, 1970, 1980, and 1990 Exposure assessment method: questionnaire; ever employed and categorical duration of employment (years) as firefighter from census surveys	Prostate, incidence Prostate, incidence Prostate, incidence Prostate, incidence Testis, incidence Kidney, incidence Urinary bladder and ureter, incidence	SIR: Firefighters Duration of er 1–9 yr 10–19 yr 20–29 yr ≥ 30 yr Trend-test P w Time period (1961–1975 1976–1990 1991–2009 SIR: Firefighters SIR: Firefighters SIR: Firefighters	2 76 114 252 ralue, 0.13	1.06 (0.96–1.16) SIR): 0.50 (0.06–1.81) 0.94 (0.74–1.18) 0.98 (0.81–1.17) 1.14 (1.01–1.29) 0.68 (0.29–1.34) 1.09 (0.86–1.36) 1.06 (0.95–1.18) 0.39 (0.11–1.01) 0.84 (0.61–1.14) 1.08 (0.89–1.31)	Age, calendar period	<i>Exposure assessment</i> <i>critique</i> : Satisfactory quality Unclear if individuals were active firefighters for whole employment. May include full-time, part- time, municipal, and rural firefighters. <i>Strengths</i> : precise linkage to high-quality outcome data; near complete ascertainmen of cancer incidence, long length of follow-up (mean, 28 yr); analyses stratified by calendar period of employment. <i>Limitations</i> : no data on job duties, employment type, or potential confounders (aside from age, sex, and calendar year); probable healthy-worker hire bias; potential non-differential misclassification of employment duration.

Reference, location enrolment/follow- up period, study design	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments
Kullberg et al. (2018)	1080 men who worked	Prostate,	Follow-up per	iod (SIR):		Birth year,	Exposure assessment critique:
Stockholm, Sweden Enrolment,	≥ 1 year as a firefighter in Stockholm in	ter incidence	Full: 1958–2012	60	0.68 (0.52–0.87)	calendar period	Satisfactory quality. Unclear if individuals were active
1931–1983/follow- up, 1958–2012	1931–1983 Exposure assessment		Former: 1958–1986	29	1.19 (0.80–1.72)		firefighters for whole of employment. Municipal
Cohort	ort method: ever employed and categorical duration of employment (years) as an urban [municipal] firefighter from annual enrolment records		Extended: 1958–2012	31	0.48 (0.33-0.69)		firefighters. <i>Strengths</i> : long follow-up period; near complete ascertainment of cancer incidence; analyses of duration and era of employment.
		[municipal] Prostate, om annual incidence	Age at risk (SI	R):			
			< 50 yr	1	4.24 (0.11-23.6)		
			50-64 yr	10	0.50 (0.24-0.92)		
			≥ 65 yr	49	0.72 (0.53-0.95)		
			Trend-test <i>P</i> value, 0.52				<i>Limitations</i> : no data on
		Prostate,	Duration of employment (SIR):			potential confounders (aside from age, sex, and calendar	
		incidence	1–9 yr	7	0.64 (0.30-1.33)		year); lack of exposure
			10–19 yr	3	0.41 (0.13-1.26)		assessment based on job tasks
			20–29 yr	17	1.06 (0.66–1.70)		or fire responses.
			≥ 30 yr	33	0.61 (0.43-0.86)		
			Trend-test P v	alue, 0.75			
		Prostate,	Period of first	employmen	t (SIR):		
		incidence	1902-1939	24	0.87 (0.59–1.31)		
			1940-1959	31	0.87 (0.61–1.23)		
			1960–1986	5	0.20 (0.08-0.47)		
			Trend-test P v	alue, < 0.01			

Reference, location enrolment/follow- up period, study design	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments
Kullberg et al. (2018)		Kidney,	Follow-up peri	iod (SIR):		Birth year,	
(cont.)		incidence	Full: 1958–2012	6	0.57 (0.21–1.23)	calendar period	
			Former: 1958–1986	2	0.37 (0.04–1.33)		
			Extended: 1987–2012	4	0.78 (0.21–1.99)		
		Urinary organs	Follow-up peri	iod (SIR):			
		(ICD-7 181), incidence	Full: 1958–2012	16	0.72 (0.41–1.17)		
			Former: 1958–1986	8	0.95 (0.41–1.88)		
			Extended: 1987–2012	8	0.58 (0.25-1.14)		
<u>Tornling et al.</u> (1994) Stockholm, Sweden	1116 for mortality/1091 for incidence; male firefighters employed for ≥ 1 yr by the City of Stockholm between 1931 and 1983, identified from annual enrolment recordsProstate, incidenceKidney, identified from annual enrolment recordsKidney, mortalityExposure assessment method: ever firefighter and duration (years) of firefighting employment from annual enrolment records; number of fires fought ascertained from exposure index developed from fire reportsProstate, mortality Prostate, incidence	mortality Prostate, incidence Kidney, mortality	SMR: Firefighters SIR:	14	1.21 (0.66-2.02)	Age, calendar period	Exposure assessment critique: Satisfactory/good quality. Enhanced exposure assessment (but based on 10% sample of reports) to differentiate exposure based on number of fires fought accounting for job position, station, and year of exposure. Municipal firefighters. Strengths: long follow-up period; near complete ascertainment of cancer incidence and mortality; assessed exposure to fire responses for some outcomes Limitations: no data on potential confounders (aside from age, sex, and calendar year).
Enrolment, 1931–1983/follow-			Firefighters SMR:	28	1.14 (0.76–1.65)		
up, 1951–1986 (mortality), 1958– 1986 (incidence)			Firefighters SIR:	4	1.10 (0.30–2.81)		
Cohort		incidence	Firefighters	2	0.36 (0.04–1.29)		

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Reference, location enrolment/follow- up period, study design	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments
<u>Petersen et al. (2018a)</u> Denmark Enrolment,	9061 male firefighters (full-time, part-time, and volunteer) identified from employer, trade	Prostate, incidence	Reference grou Firefighters vs general population	ıp (SIR): 202	1.10 (0.95–1.26)	Age, calendar period	<i>Exposure assessment critique</i> Satisfactory quality. Includes part-time and full-time firefighters. Excluded those
1964–2004/follow- up, 1968–2014 Cohort	union, and Danish Civil Registration System records, born 2 April 1928 or later, employed		Firefighters vs sample of employees	202	1.15 (1.00–1.32)		who did not actually fight fires. May include municipal and rural firefighters. <i>Strengths</i> : long period of follow-up; near-complete ascertainment of cancer incidence; use of three reference groups to evaluate healthy-worker bias; analyses by proxies of exposure
	before age 60 yr and 31 December 2004,		Firefighters vs military	202	1.02 (0.88–1.17)		
	no cancer diagnosis	Prostate, incidence	Employment t	ype (SIR):			
	before employment as a firefighter, and a job title/function indicating		Full-time	130	1.12 (0.95-1.33)		
			Part-time or volunteer	72	1.05 (0.83–1.32)		
	actual firefighting	Prostate,	Era of first em	ployment (S	including job task.		
	exposure	incidence	Pre-1970	108	1.16 (0.96–1.40)		<i>Limitations</i> : little information on potential confounders.
	Exposure assessment method: ever employed		1970-1994	85	1.05 (0.85-1.30)		
	and categorical duration		1995 or after	9	0.90 (0.47-1.73)		
	of employment (years),	Prostate,	Job function (SIR):			
	as well as employment	incidence	Regular	188	1.09 (0.95–1.26)		
	type, job title/function,		Specialized	14	1.15 (0.68–1.94)		
	and work history,	Prostate,	Age at first em	ployment (S	SIR):		
	ascertained from civil registration, pension,	incidence	< 25 yr	100	1.12 (0.92–1.36)		
employer pe and trade ur	employer personnel,		25–34 yr	56	1.08 (0.83-1.41)		
	and trade union membership records		≥ 35 yr	46	1.06 (0.80–1.42)		
		Prostate,	Duration of er	nployment ((SIR):		
		incidence	< 1 yr	59	1.12 (0.87–1.45)		
			$\geq 1 \text{ yr}$	143	1.09 (0.92–1.28)		
			≥ 10 yr	125	1.09 (0.91–1.29)		
			≥ 20 yr	101	1.12 (0.92–1.36)		

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Reference, location enrolment/follow- up period, study design	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments
Petersen et al.		Testis, incidence	Reference gro	up (SIR):		Age,	
<u>(2018a)</u> (cont.)			Firefighters vs general population	47	1.30 (0.97–1.73)	calendar period	
			Firefighters vs sample of employees	47	1.04 (0.78–1.39)		
			Firefighters vs military	47	0.98 (0.73-1.30)		
		Testis, incidence	Employment t	ype (SIR):			
			Full-time	23	1.23 (0.82-1.86)		
			Part-time or volunteer	24	1.36 (0.91–2.04)		
		Testis, incidence	Era of first em	ployment (S	IR):		
			Pre-1970	8	1.55 (0.77-3.09)		
			1970-1994	28	1.32 (0.91–1.91)		
			1995 or after	11	1.12 (0.62–2.02)		
		Testis, incidence	Job function (SIR):			
			Regular	43	1.27 (0.94–1.71)		
			Specialized	4	1.65 (0.62-4.39)		
		Testis, incidence	Age at first em	ployment (S	IR):		
			< 25 yr	25	1.33 (0.90–1.97)		
			25–34 yr	17	1.21 (0.75–1.94)		
			≥ 35 yr	5	1.48 (0.62–3.56)		
		Testis, incidence	Duration of en	nployment (SIR):		
			< 1 yr	10	1.72 (0.92–3.19)		
			$\geq 1 \text{ yr}$	37	1.22 (0.88–1.68)		
			$\geq 10 \text{ yr}$	25	1.07 (0.73–1.59)		
			≥ 20 yr	14	0.99 (0.58-1.67)		

Table 2.3 (conti	nued)						
Reference, location enrolment/follow- up period, study design	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments
Petersen et al.		Other genitals	Reference grou	up (SIR):		Age,	
(2018a) (cont.)		(ICD-10, C60, C63), incidence	Firefighters vs general population	3	0.78 (0.25–2.41)	calendar period	
			Firefighters vs sample of employees	3	0.82 (0.26-2.54)		
			Firefighters vs military	3	0.70 (0.23–2.18)		
		Kidney,	Reference grou	up (SIR):			
		incidence	Firefighters vs general population	32	1.04 (0.74–1.47)		
			Firefighters vs sample of employees	32	1.02 (0.72–1.44)		
			Firefighters vs military	32	1.04 (0.74–1.48)		
		Kidney (urinary	Reference grou	up (SIR):			
		pelvis/upper urinary tract), incidence	Firefighters vs general population	10	1.46 (0.79–2.72)		
			Firefighters vs sample of employees	10	1.59 (0.85–2.95)		
			Firefighters vs military	10	1.35 (0.73–2.51)		

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	er Firefighters			controlled	
ven et al. Urinary bladd a) (ICD-10, C67, D09.0, D30.3,	vs general population	88	1.09 (0.89–1.35)	Age, calendar period	
D41.4), incide:		88	1.11 (0.90–1.37)	I	
	Firefighters vs military	88	1.05 (0.86–1.30)		
Urinary bladd		type (SIR):			
(ICD-10, C67,	Full-time	59	1.14 (0.89–1.48)		
D09.0, D30 D41.4), inc	Part-time of volunteer	29	1.01 (0.70–1.45)		
Urinary bladd	er Era of first en	nployment (S	IR):		
(ICD-10, C67,	Pre-1970	51	1.21 (0.92–1.59)		
D09.0, D30.3,	1970-1994	35	1.05 (0.75-1.46)		
D41.4), incide	1995 or after	2	0.41 (0.10–1.66)		
Urinary bladd		(SIR):			
(ICD-10, C67,	Regular	83	1.10 (0.89–1.37)		
D09.0, D30.3, D41.4), incide		5	0.95 (0.39–2.28)		
Urinary bladd	0	nployment (S			
(ICD-10, C67,	< 25 yr	54	1.32 (1.01–1.73)		
D09.0, D30.3, D41.4), incide:	25–34 yr	17	0.76 (0.47–1.22)		
	≥ 35 yr	17	0.98 (0.61–1.58)		
Urinary bladd					
(ICD-10, C67, D00 0, D30 3	< 1 yr	31	1.28 (0.90–1.82)		
D09.0, D30.3, D41.4), incide:	$\geq 1 \text{ yr}$	57	1.01 (0.78–1.32)		
D 11.1, include	≥ 10 yr	51	1.04 (0.79–1.37)		
	≥ 20 yr	37	0.97 (0.70-1.34)		

Reference, location enrolment/follow- up period, study design	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments
Petersen et al. (2018b) Denmark Enrolment, 1964–2014/follow- up, 1970–2014 Cohort	11 775 male firefighters (full-time, part-time, and volunteer) identified from employer, trade union, and Danish Civil Registration System records, born in 1928 or later, employed before age 60 yr and 31 December 2004, and a job title/function indicating actual firefighting exposure Exposure assessment method: ever employed and categorical duration of employment (years) as a firefighter ascertained from civil registration, pension, employer personnel, and trade union membership records	Prostate, mortality Prostate, mortality	group): Full-time Part-time/ volunteer	16 20 mployment (military reference 0.66 (0.40–1.07) 1.89 (1.22–2.93) (SMR, military e firefighters: 0.56 (0.27–1.17) 0.77 (0.40–1.47) 0.75 (0.37–1.50) 0.74 (0.35–1.56)	Age, calendar period	<i>Exposure assessment critique:</i> Satisfactory quality. Includes part-time and full-time firefighters. Excluded those who did not actually fight fires. May include municipal and rural firefighters. <i>Strengths</i> : long period of follow-up; use of military reference group to evaluate healthy-worker bias; analyses by duration of employment. <i>Limitations</i> : little information on potential confounders.

Reference, location enrolment/follow- up period, study design	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments
Webber et al. (2021)	10 786 FDNY, 8813	Prostate,	Group (SIR, U			Age,	Exposure assessment critique:
USA 2001–2016	CFHS; FDNY and CFHS cohorts; male	incidence	CFHS firefighters	358	1.22 (1.11–1.35)	calendar year, race/	Satisfactory quality. Intensity of exposure at WTC captured
Cohort	firefighters who were active on 11 September		FDNY WTC firefighters	332	1.70 (1.53–1.88)	ethnicity	but did not consider previous firefighter work. Qualitative
	2001; FDNY cohort included men who worked at the WTC site any time between 11 September 2001 and 25	Prostate, incidence	SIR (2-yr adjus bias):	stment for p	otential surveillance		assessment based on presence at the WTC site, exposures complex and probably unique to 9/11 disaster. Municipal firefighters.
			FDNY WTC firefighters	NR	1.55 (1.39–1.73)		
	July 2002; CFHS cohort	Prostate, incidence	Group (RR):	259		Age on 11 September	Strengths: ascertainment of
	included men who were actively employed	mendence	CFHS firefighters	358	1	2001, race/ ethnicity	cancer incidence; comparison of two firefighter cohorts to evaluate bias. <i>Limitations</i> : medical
	on 11 September 2001 and assumed not to be		FDNY WTC firefighters	332	1.39 (1.19–1.63)		
	working at the WTC site Exposure assessment	Prostate,	Group RR (2-yr adjustment for potential				surveillance bias; young age of cohort; relatively short
	method: presence	incidence	surveillance bi CFHS	as): NR	1		length of follow-up.
	at WTC site from employment records		firefighters				
	and duty rosters		FDNY WTC firefighters	NR	1.28 (1.09–1.51)		
		Kidney,	Group (SIR, U	S reference i	rates):	Age,	
		incidence	CFHS firefighters	55	1.19 (0.90–1.56)	calendar year, race/	
			FDNY WTC firefighters	39	0.93 (0.67–1.28)	ethnicity	
		Kidney, incidence	SIR (2-yr adjustment for potential surveillance bias):				
			FDNY WTC firefighters	NR	0.85 (0.61–1.19)		

Reference, location enrolment/follow- up period, study design	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments
<u>Webber et al. (2021)</u> (cont.)		Kidney, incidence	Group (RR): CFHS	55	1	Age on 11 September	
(00111)			firefighters	55	1	2001, race/	
			FDNY WTC firefighters	39	0.82 (0.52–1.30)	ethnicity	
		Kidney, incidence	Group RR (2-y surveillance bi		t for potential		
			CFHS firefighters	NR	1		
			FDNY WTC firefighters	NR	0.75 (0.47–1.20)		
<u>Zeig-Owens et al.</u> (<u>2011)</u>	$\begin{array}{llllllllllllllllllllllllllllllllllll$	Prostate, incidence	WTC exposure status (SIR, 2-yr adjustment for potential surveillance bias):			Age, race, ethnic	<i>Exposure assessment critique</i> Satisfactory quality. Intensit
New York City, USA			Non-exposed	45	1.35 (1.01–1.81)	origin,	of exposure at WTC capture
Enrolment, 1996/ follow-up, 1996–	were active firefighters on 1 January 1996, with		Exposed	73	1.21 (0.96–1.52)	calendar year	but did not consider previou firefighter work. WTC
2008	no prior cancer, and, if		SIR ratio	NR	0.90 (0.62–1.30)	, ea.	exposure self-reported using three methods. WTC site exposures complex and
Cohort	alive on 12 September 2001, also had known		(exposed vs non-				
			exposed)				
	WTC exposure status Exposure assessment	Testis, incidence	WTC exposure status (SIR):				probably unique to 9/11 disaster.
	method: WTC-exposed		Non-exposed	11	1.54 (0.85-2.78)		Strengths: evaluation of
	and non-exposed		Exposed	≤ 5	0.86 (0.36-2.06)		medical surveillance bias.
	firefighter from		SIR ratio	NR	0.56 (0.19–1.60)		Limitations: healthy-worker
	employment records		(exposed				hire bias; short length of
	and questionnaires		vs non- exposed)				follow-up; young age at end follow-up; little information
		Kidney,	WTC exposure	e status (SIR	.).		on potential confounders.
		incidence	Non-exposed	5	0.30 (0.07–1.18)		-
			Exposed	10	0.86 (0.46–1.60)		
			SIR ratio	NR	2.91 (0.64–13.30)		
			(exposed		. ,		
			vs non-				

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Reference, location enrolment/follow- up period, study design	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments
Zeig-Owens et al. (2011) (cont.)		Urinary bladder, incidence	WTC exposure Non-exposed Exposed SIR ratio (exposed vs non- exposed)		R): 0.79 (0.36–1.76) 1.01 (0.56–1.83) 1.28 (0.47–3.46)	Age, race, ethnic origin, calendar year	
Pinkerton et al. (2020) San Francisco, Chicago and Philadelphia, USA Enrolment, 1950–2009/follow- up, 1950–2016	29 992 municipal career firefighters in the CFHS cohort employed by the fire departments of San Francisco, Chicago, or Philadelphia for \geq 1 day between 1950 and 2009; exposure-response	Prostate, mortality	Fire departmer San Francisco Chicago Philadelphia Overall Heterogeneity	60 176 98 334	0.89 (0.68–1.15) 1.23 (1.05–1.42) 0.99 (0.81–1.21) 1.08 (0.97–1.20) 6	Gender, race, age, calendar period	<i>Exposure assessment critique</i> : Good quality. Minimal bias in exposure assessment in internal analyses. Municipal firefighters. <i>Strengths</i> : long period of follow-up; exposure-response modelling for three metrics
Cohort	analyses limited to 19 287 male firefighters of known race hired in 1950 or later and employed for ≥ 1 yr Exposure assessment method: ever employed	Prostate, mortality	Exposed-days days vs 2500 ex Loglinear without HWSE adjustment RCS without		at 8700 exposed- s, 10-yr lag): 0.88 (0.62–1.25) 0.80 (0.52–1.27)	Age, race, birthdate (within 5 yr), fire department	of exposure assessed using job-exposure matrices; adjustment for HWSE. <i>Limitations</i> : healthy-worker selection bias in external comparison analyses; little information on potential
	as a firefighter, and number of exposed days, fire-runs, fire- hours reconstructed using job-exposure matrix based on job titles and assignments and departmental work history records and		HWSE adjustment Fully adjusted loglinear Fully adjusted RCS	126 126	1.04 (0.65–1.71) 0.85 (0.47–1.62)		confounders.

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Table 2.3 (conti	nued)						
Reference, location enrolment/follow- up period, study design	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments
<u>Pinkerton et al.</u> (2020) (cont.)		Prostate, mortality	Fire-runs (Chio model (HR at 8 10-yr lag):		ladelphia only) 2100 runs,	Age, race, birthdate (within	
			Loglinear without HWSE adjustment	104	0.87 (0.66–1.14)	5 yr), fire department	
			RCS without HWSE adjustment	104	0.81 (0.58–1.13)		
			Fully adjusted loglinear	104	0.92 (0.67–1.25)		
			Fully adjusted RCS	104	0.86 (0.58–1.27)		
		Prostate, mortality	Fire-hours (Ch 2300 h vs 600 ł		nodel (HR at		
			Loglinear without HWSE adjustment	76	0.78 (0.53–1.14)		
			RCS without HWSE adjustment	76	0.63 (0.40–1.01)		
			Fully adjusted loglinear	76	0.82 (0.52–1.27)		
			Fully adjusted RCS	76	0.66 (0.39–1.12)		

Reference, location enrolment/follow- up period, study design	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments
Pinkerton et al.		Other male	Fire departme	nt (SMR):		Gender,	
(2020) (cont.)		genital (ICD-10, C60, C62–C63),	San Francisco	< 5	0.52 (0.01-2.90)	race, age, calendar	
		mortality	Chicago	0	0 (NR)	period	
			Philadelphia	< 5	0.85 (0.18-2.49)		
			Overall	< 5	0.39 (0.11-1.00)		
			Heterogeneity	<i>P</i> value, 0.1	5		
		Kidney, mortality	Fire departme	nt (SMR):			
			San Francisco	15	0.85 (0.48-1.40)		
			Chicago	66	1.57 (1.22-2.00)		
			Philadelphia	27	0.93 (0.61-1.36)		
			Overall	108	1.22 (1.00-1.47)		
			Heterogeneity	P value, 0.02	2		
		Kidney, mortality		Exposed-days model (HR at 8700 exposed- days vs 2500 exposed-days, 10-yr lag):			
			Loglinear without HWSE adjustment	62	1.15 (0.64–2.13)	(within 5 yr), fire department	
			RCS without HWSE adjustment	62	1.23 (0.64–2.52)		
			Fully adjusted loglinear	62	1.03 (0.50–2.24)		
			Fully adjusted RCS	62	1.16 (0.50–2.92)		

Reference, location	Population size,	Cancer type	Exposure	Exposed	Risk estimate	Covariates	Comments
enrolment/follow- up period, study design	description, exposure assessment method	(histopathology), incidence or mortality	category or level	cases or deaths	(95% CI)	controlled	connicitts
Pinkerton et al. (2020) (cont.)	Let al.Kidney, mortalityFire-runs (Chicago and Philadelphia only) model (HR at 8800 runs vs 2100 runs, 10-yr lag):				Age, race, birthdate (within		
			Loglinear without HWSE adjustment	55	1.03 (0.67–1.53)	5 yr), fire department	
			RCS without HWSE adjustment	55	1.15 (0.69–1.94)		
			Fully adjusted loglinear	55	0.94 (0.59–1.46)		
			Fully adjusted RCS	55	1.08 (0.61–1.96)		
		Kidney, mortality	Fire-hours (Cl 2300 h vs 600				
		·	Loglinear without HWSE adjustment	42	1.26 (0.72–2.14)		
			RCS without HWSE adjustment	42	1.55 (0.78–3.22)		

1.15 (0.63-2.08)

1.56 (0.72-3.58)

Fully adjusted

loglinear Fully adjusted RCS 42

42

276

Reference, location enrolment/follow- up period, study design	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments
<u>Pinkerton et al.</u>		Urinary bladder,	Fire departme	nt (SMR):		Gender,	
(2020) (cont.)		mortality	San Francisco	23	1.01 (0.64–1.52)	race, age, calendar	
			Chicago	48	0.98 (0.72-1.30)	period	
			Philadelphia	33	0.96 (0.66-1.34)		
			Overall	104	0.98 (0.80-1.18)		
			Trend-test P va	alue, 0.98			
		Urinary bladder, mortality	Exposed-days model (HR at 8700 exposed- days vs 2500 exposed-days, 10-yr lag):			Age, race, birthdate	
			Loglinear without HWSE adjustment	37	0.71 (0.37–1.38)	(within 5 yr), fire department	
			RCS without HWSE adjustment	37	0.71 (0.33–1.67)		
			Fully adjusted loglinear	37	1.23 (0.50-3.41)		
			Fully adjusted RCS	37	2.66 (0.67–14.7)		

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Reference, location enrolment/follow- up period, study design	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments
Daniels et al. (2015) San Francisco, Chicago, Philadelphia, USA	19 309, all male careerProstate,firefighters in the CFHSincidencecohort of known racewho were on active duty		Exposed-days 10-yr lag): 8700 days vs 2500 days	model (HR, 832	RCS model, 0.90 (0.77–1.05)	Age, race, fire department, birth cohort	<i>Exposure assessment critique</i> : Good quality. Minimal bias in exposure assessment in internal analyses. Municipal firefighters. <i>Strengths</i> : long period of follow-up; exposure-response modelling for three metrics of exposure assessed using
Enrolment, 1950–2009/follow-	\geq 1 day in 1950–2009 in the fire departments of	Prostate, incidence	'		iladelphia only) del 10-yr lag):		
up, 1950–2009 (mortality), 1985–	Chicago, Philadelphia, or San Francisco, with	mendence	8800 runs vs 2100 runs	678	1.02 (0.91–1.14)		
2009 (incidence) Cohort	≥ 1 yr of employment Exposure assessment method: number of	Prostate, incidence	Fire-hours (Chicago only) model (HR, power model, 10-yr lag):			Age, race, birth cohort	job-exposure matrices. <i>Limitations</i> : little information
exposed days, fire-runs, fire-hours reconstructed		2300 h vs 600 h	419	0.98 (0.90-1.09)		on potential confounders.	
	using job-exposure matrix based on job titles and assignments	Prostate, incidence	Time since exposure in fire-runs (Chicago and Philadelphia only) loglinear model (HR at 4600 runs, 10-yr lag):			Age, race, fire department,	
	and departmental work history records and		Lag to lag + 10 yr	NR	0.60 (0.21–1.53)	birth cohort	
	historical fire-run and fire-hour data		Lag + 10 to lag + 20 yr	NR	0.68 (0.35–1.23)		
			> lag + 20 yr LRT <i>P</i> value, 0	NR .807	0.80 (0.52–1.18)		
		Prostate, incidence		nly) loglinea	ns (Chicago and ar model (HR at		
			< 40 yr	NR	0.72 (0.42-1.16)		
			≥ 40 yr	NR	0.73 (0.50-1.04)		
			LRT <i>P</i> value, 0	.953			
		Prostate, incidence			ns (Chicago and ar model (HR at		
			Pre-1970	NR	0.91 (0.55-1.44)		
			1970 or after LRT <i>P</i> value, 0	NR	0.63 (0.43-0.91)		

Reference, location enrolment/follow- up period, study design	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments
<u>Daniels et al. (2015)</u> (cont.)		Urinary bladder, incidence			power model,	Age, race, fire	
			8700 days vs 2500 days	174	1.01 (0.89–1.19)	department, birth cohort	
		Urinary bladder, incidence	Fire-runs (Chi model (HR, po	0	niladelphia only) 10-yr lag):		
		TT · 11 11	8800 runs vs 2100 runs	144	1.05 (0.89–1.27)		
		Urinary bladder, incidence	Fire-hours (Ch model, 10-yr la		model (HR, power	Age, race, birth cohort	
			2300 h vs 600 h	95	0.98 (0.79–1.27)		
Chicago, San inc		FHS	Fire departme San Francisco	nt (SIR, all o 278	cancers): 1.21 (1.07–1.36)	Race, age, calendar period	<i>Exposure assessment</i> <i>critique</i> : Satisfactory quality. Minimum exposure
Philadelphia, USA	firefighters in the CFHS		Chicago	602	0.98 (0.91-1.07)	I	was 1 day of work as a municipal firefighter. <i>Strengths</i> : long period of follow-up; ascertained
Enrolment, 1950–2009/follow- up, 1950–2009	cohort employed for ≥ 1 day in Chicago, San Francisco, or	Prostate,	Philadelphia SIR:	398	0.98 (0.89–1.09)		
(mortality), 1985–	Philadelphia fire	incidence	All cancers	1261	1.03 (0.98–1.09)		incidence outcomes; included
2009 (incidence) Cohort	departments between 1950 and 2009		First primary cancer	1176	1.03 (0.97–1.09)		female firefighters. <i>Limitations</i> : healthy-
	Exposure assessment	Prostate,	Fire departme				worker hire bias in
	method: ever employed and categorical duration	incidence	San Francisco	276	1.22 (1.08–1.37)		external comparisons; little information on potential
	of employment (years) from employment		Chicago	592	0.99 (0.91-1.07)		confounders.
	records		Philadelphia	393	0.99 (0.90-1.10)		
			Heterogeneity <i>P</i> value, 0.078				
		Prostate,	Race (SIR, all o			Age,	
		incidence	Caucasian [White]	1167	1.02 (0.96–1.08)	calendar period	
			Other	94	1.26 (1.02–1.54)		

Reference, location enrolment/follow- up period, study design	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments
Daniels et al. (2014)		Prostate,	Age (SIR, all c	ancers):		Race, age,	
(cont.)		incidence	17–64 yr	426	1.21 (1.10-1.33)	calendar	
			65 to ≥ 85 yr	835	0.96 (0.90-1.03)	period	
			Heterogeneity	P value, < 0	.001		
		Other male	SIR:				
		genital (ICD-10,	All cancers	17	0.62 (0.36-0.99)		
		C60, C62–C63),	First primary	17	0.67 (0.39-1.07)		
		incidence	cancer				
		Other and	Fire departme	nt (SIR, all c	cancers):		
		unspecified male	San	0	0 (NR)		
		genital (ICD-	Francisco				
		10, C60, C63), incidence	Chicago	< 5	0.53 (0.06–1.92)		
		Incluence	Philadelphia	0	0 (NR)		
		Other male	Race (SIR, all cancers):			Age,	
		genital (ICD-10, C60, C62–C63),	Caucasian [White]	16	0.64 (0.37–1.04)	calendar period	
		incidence	Other	< 5	0.38 (0.01-2.13)		
		Testis, incidence	SIR:			Race, age,	
			All cancers	15	0.75 (0.42–1.24)	calendar	
		First primary cancer	15	0.79 (0.44–1.30)	period		
		Testis, incidence	Fire departme	nt (SIR, all c	cancers):	Gender,	
			San	< 5	0.74 (0.09–2.67)	race, age,	
			Francisco			calendar period	
			Chicago	8	0.76 (0.33–1.50)	period	
			Philadelphia	5	0.75 (0.24–1.75)		
	Urinary organs (ICD-10, C64– C68), incidence	1 0	Fire departme				
			San Francisco	89	1.15 (0.93–1.42)		
			Chicago	234	1.17 (1.02–1.32)		
			Philadelphia	159	1.17 (1.00-1.37)		

Reference, location enrolment/follow- up period, study design	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments
<u>Daniels et al. (2014)</u>		Kidney,	SIR:			Gender,	
(cont.)		incidence	All cancers	166	1.27 (1.09–1.48)	race, age,	
			First primary cancer	129	1.24 (1.04–1.48)	calendar period	
		Kidney,	Fire department	nt (SIR, all c	ancers):		
		incidence	San Francisco	26	1.10 (0.72–1.61)		
			Chicago	83	1.30 (1.04-1.61)		
			Philadelphia	57	1.33 (1.00–1.72)		
			Heterogeneity	P value, 1.0	0		
	Kidney, incidence		Race (SIR, all cancers):			Age,	
		Among men: Caucasian [White]	151	1.26 (1.06–1.47)	calendar period		
		Kidney,	Other	14	1.46 (0.80-2.45)		
			Age (SIR, all ca	ancers):		Gender,	
	incidence	17–64 yr	79	1.41 (1.12–1.76)	race, age,		
			65 to ≥ 85 yr Heterogeneity	87 P value, 1.0	1.17 (0.94–1.44) 0	calendar period	
		Urinary bladder,	SIR:	1 (4140, 110	•		
		incidence	All cancers	316	1.12 (1.00-1.25)		
			First primary cancer	272	1.18 (1.05–1.33)		
		Urinary bladder,	Fire department	nt (SIR, all c	cancers):		
	incidence	San Francisco	63	1.18 (0.91–1.51)			
			Chicago	151	1.10 (0.93–1.29)		
			Philadelphia	102	1.10 (0.90–1.33)		
			Heterogeneity	P value, 1.0	0		

Reference, location enrolment/follow- up period, study design	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments		
<u>Daniels et al. (2014)</u> (cont.)		Urinary bladder, incidence	Race (SIR, all o Among men: Caucasian [White]	cancers): 305	1.11 (0.99–1.24)	Age, calendar period			
			Other	7	0.92 (0.37-1.91)				
		Urinary bladder, incidence	Age (SIR, all ca	ancers):	(,	Gender,			
			17–64 yr	133	1.33 (1.08-1.62)	race, age,			
			65 to ≥ 85 yr	219	1.04 (0.91–1.19)	calendar			
			Heterogeneity	P value, 0.0	02	period			
Seattle and Tacoma, emple USA betwee Enrolment, alive	2447 male firefighters			Prostate,	SIR (local cour	nty rates):		Age,	Exposure assessment critique
	employed for ≥ 1 yr	incidence	Firefighters	66	1.4 (1.1–1.7)	calendar period	Satisfactory quality. Duration		
	between 1944 and 1979, alive as of 1 January	Prostate, incidence	Duration of ex county rates):				(years) involved in direct firefighting (surrogate for fire smoke) was not measured		
1944–1979/follow- up, 1974–1989	1974 and known to be a resident of one of		< 10 yr	7	1.4 (0.6-2.8)		smoke) was not measured equally in the two study populations. Municipal firefighters. Strengths: use of two		
Cohort	thirteen counties in		10–19 yr	6	1.2 (0.4-2.6)				
Conort	the catchment area of the tumour registry for		20–29 yr	47	1.5 (1.1–2.0)				
			≥ 30 yr	6	0.9 (0.3-1.9)				
	≥ 1 mo; reference group included 1878 male	Prostate, incidence	Years since first employment (SIR, local county rates):				comparison groups; including comparison		
	local police officers		< 20 yr	1	7.4 (0.2–41)		with police officers to limit		
	Exposure assessment method: ever employed		20–29 yr	5	1.8 (0.6-4.3)		healthy-worker bias. <i>Limitations</i> : little information		
	for ≥ 1 yr, and		≥ 30 yr	60	1.3 (1.0–1.7)		on potential confounders.		
	categorical duration	Prostate,	IDR:						
	of employment (years)	incidence	Local police	28	1				
	in direct firefighting		Firefighters	66	1.1 (0.7–1.8)				
	positions from	Kidney,	SIR (local cour	nty rates):					
	employment records	incidence	Firefighters	3	0.5 (0.1–1.6)				
		Kidney,	IDR:						
		incidence	Local police	4	1				
			Firefighters	3	0.4 (0.1-2.1)				

Reference, location enrolment/follow- up period, study design	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments
Demers et al. (1994)		Urinary bladder,	SIR (local cou	nty rates):		Age,	
(cont.)		incidence	Firefighters	18	1.2 (0.7–1.9)	calendar period	
		Urinary bladder, incidence	Duration of excounty rates):		oyment (SIR, local		
			< 10 yr	4	2.2 (0.6-5.6)		
			10–19 yr	2	0.9 (0.1-3.4)		
			20–29 yr	9	1.0 (0.4–1.8)		
			\geq 30 yr	3	1.6 (0.3-4.8)		
		Urinary bladder, incidence	Years since first employment (SIR, local county rates):				
			< 20 yr	1	1.4 (0.0-7.5)		
			20–29 yr	4	2.0 (0.5-5.1)		
			\geq 30 yr	13	1.0 (0.6–1.8)		
		Urinary bladder,	IDR:				
		incidence	Local police	6	1		
			Firefighters	18	1.7 (0.7-4.3)		
<u>Demers et al.</u>	4401 male firefighters	Prostate,	SMR:			Age,	<i>Exposure assessment critique</i> : Satisfactory/good quality.
<u>1992a)</u>	employed for ≥ 1 yr	mortality	Firefighters	30	1.34 (0.90–1.91)	calendar	
eattle and Tacoma,	between 1944 and	Prostate,	Duration of exposed employment (SMR):			period	Duration (years) involved
Vashington; ortland, Oregon,	1979 in Seattle, Tacoma, or Portland,	mortality	< 10 yr				in fire combat (surrogate for fire smoke) was not
JSA	USA; reference group		10–19 yr	2	1.12 (0.1-4.1)		measured equally in the
Enrolment,	included 3676 local		20–29 yr	14	1.23 (0.7–2.1)		three municipal firefighter
944–1979/follow-	police officers		\geq 30 yr	11	1.36 (0.7–2.4)		populations.
ip, 1945–1989	Exposure assessment	Prostate,	Years since fir	st employme	ent (SMR):		Strengths: use of two
Cohort	method: ever employed for > 1 we and	mortality	< 20 yr	0	0 (0.0–26.6)		comparison groups,
	for \geq 1 yr, and categorical duration		20–29 yr	0	0 (0.0–3.1)		including comparison with police officers to limit
	(years) of exposure		≥ 30 yr	30	1.42 (1.0–2.0)		healthy-worker bias.
	to fire combat from	Prostate,	Age at risk (SI	MR):			Limitations: little information
	employment records	mortality	18–39 yr	0	0 (0.0–178)		on potential confounders; ascertained mortality
			40-64 yr	4	0.86 (0.2–2.2)		
			≥ 65 yr	26	1.46 (1.0-2.1)		outcomes only.

Reference, location enrolment/follow- up period, study design	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments
Demers et al.		Prostate,	IDR:			Age,	
<u>(1992a)</u>		mortality	Local police	11	1	calendar	
(cont.)			Firefighters	30	1.43 (0.71–2.85)	period	
		Kidney,	SMR:				
		mortality	Firefighters	2	0.27 (0.03-0.97)		
		Bladder and	SMR:				
		other urinary cancers (ICD-9, 188, 189.3–189.9), mortality	Firefighters	2	0.23 (0.03–0.83)		
		Bladder and	IDR:				
		other urinary	Local police	4	1		
		cancers (ICD-9, 188, 189.3–189.9), mortality	Firefighters	2	0.16 (0.02–1.24)		
Vena & Fiedler	1867 White male career	Prostate,	SMR:			Age,	Exposure assessment critique:
(<u>1987)</u>	firefighters employed by	mortality	Overall	5	0.71 (0.23-1.65)	calendar	Minimal quality. Only assessed ever-employment
Buffalo, New York, USA	the City of Buffalo for ≥ 5 yr, with ≥ 1 yr as a	Kidney,	SMR:			period	
1950–1979	\geq 5 yr, with \geq 1 yr as a firefighter	mortality	Overall	3	1.30 (0.26-3.80)		and duration of employment as a municipal firefighter.
Cohort	Exposure assessment	Urinary bladder,	Years worked	as a firefight			<i>Strengths</i> : long length of
	method: ever-	mortality	1–9 yr	1	[5.00 (0.3-24.7)]		follow-up.
	employment, timing,		10–19 yr	0	0 (NR)		Limitations: healthy-worker
	and duration of		20–29 yr	1	[1.25 (0.1-6.2)]		hire bias; little information
	employment from employment records		30–39 yr	3	[2.14 (0.5-5.8)]		on potential confounders or exposure to firefighting
	employment records		\geq 40 yr	4	[5.71 (1.8–13.8)]		activities.
			Overall	9	2.86 (1.3-5.4)		
		Urinary bladder,	Calendar year	of death (SN			
		mortality	1950–1959	1	[1.56 (0.1-8.2)]		
			1960–1969	7	[6.36 (2.8–12.6)]		
			1970-1979	1	[0.67 (0.0-3.3)]		

Reference, location enrolment/follow- up period, study design	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments
Vena & Fiedler		Urinary bladder,	Year of hire (S	MR):	Age,		
<u>(1987)</u>		mortality	Prior to 1930	9	[4.74 (2.3-8.7)]	calendar	
(cont.)			1930-1939	0	0 (NR)	period	
			1940-1949	0	0 (NR)		
			1950 or after	0	0 (NR)		
		Urinary bladder,	Years of latenc	cy (SMR):			
		mortality	< 20 yr	0	0 (NR)		
			20–29 yr	0	0 (NR)		
			30–39 yr	1	[1.04 (0.1-5.5)]		
			40-49 yr	5	[4.53 (1.7-10.3)]		
			≥ 50 yr	3	[6.38 (1.5-16.3)]		
<u>(1994)</u>	5414 male firefighters employed for ≥ 6 mo at one of six fire	Prostate, mortality	SMR: Any employment	16	1.32 (0.76–2.15)	Age, calendar period	<i>Exposure assessment</i> <i>critique</i> : Satisfactory quality Unclear if individuals were
1950–1989	departments in	Prostate,	Years since first employment (SMR):				active firefighters for whole
Cohort	Metropolitan Toronto	mortality	< 20 yr	0	0 (0-16.04)		employment. Probably municipal firefighters. <i>Strengths</i> : long period
	any time between 1950 and 1989		20–29 yr	2	2.44 (0.30-8.81)		
	Exposure assessment		≥ 30 yr	14	1.27 (0.69–2.13)		of follow-up; analysis of
	method: ever employed	Prostate,	Years of emplo	oyment (SMI	R):		employment duration.
	and categorical duration	mortality	< 15 yr	1	1.61 (0.04-8.99)		Limitations: healthy-worker
	of employment (years)		15–29 yr	5	2.43 (0.79-5.66)		hire bias; little information
	as municipal firefighter from employment records	Prostate,	≥ 30 yr Age (SMR):	9	0.97 (0.44–1.84)		on confounders or exposure ascertained mortality
		mortality	< 60 yr	2	1.53 (0.19-5.52)		outcomes only.
		Testis, mortality	≥ 60 yr SMR:	14	1.30 (0.71–2.18)		
			Any employment	3	2.52 (0.52-7.37)		

Reference, location enrolment/follow- up period, study design	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments
Aronson et al.		Testis, mortality	Years since firs	st employme	ent (SMR):	Age,	
<u>(1994)</u>			< 20 yr	3	3.26 (0.67-9.53)	calendar	
(cont.)			20–29 yr	0	0 (0-24.59)	period	
			≥ 30 yr	0	0 (0-30.74)		
		Testis, mortality	Years of emplo	yment (SMI	R):		
			< 15 yr	3	3.66 (0.75-10.69)		
			15–29 yr	0	0 (0-14.19)		
			≥ 30 yr	0	0 (0-36.89)		
		Testis, mortality	Age (SMR):				
			< 60 yr	3	2.75 (0.57-8.04)		
			≥ 60 yr	0	0 (0-40.99)		
		Kidney and	SMR:				
		ureter (ICD-9,	Any	2	0.43 (0.05-1.56)		
		189), mortality	employment				
		Urinary bladder,	SMR:				
		mortality	Any	7	1.28 (0.51–2.63)		
G : 1: (1000)		D	employment				
<u>Guidotti (1993)</u> Edmonton and	3328, all firefighters employed between	Prostate, mortality	SMR:	0	1 46 (0 62 2 99)	Age, calendar	<i>Exposure assessment critique:</i> Good quality. Good approach
Calgary, Canada	1927–1987 by either of	mortanty	Any employment	8	1.46 (0.63–2.88)	period	to differentiate exposure
1927–1987	the fire departments of	Prostate,	Latency (SMR)).		Pulloa	between ranks. Municipal
Cohort	Edmonton or Calgary	mortality	< 20 yr	0	0		firefighters.
	Exposure assessment		< 20 yr 20–29 yr	1	[2.86 (0.13–12.7)]		Strengths: long length of
	method: ever employed and categorical duration		30–39 yr	2	[1.65 (0.28 - 5.46)]		follow-up; analyses by
	of employment (years)		40–49 yr	2	[1.2(0.20-3.96)]		duration of employment and exposure index.
	from employment		$\geq 50 \text{ yr}$	3	[1.45 (0.37–3.96)]		<i>Limitations</i> : little informatio
	records; exposure index	Kidney and	SMR:	~	[1.10 (0.07 0.70)]		on potential confounders;
	of years of employment weighted by time spent in proximity to fires based on job	ureter (ICD-9, 189), mortality	Any employment	7	4.14 (1.66-8.53)		ascertained mortality outcomes only; low numbe of cases for stratified analyses.

Reference, location enrolment/follow- up period, study design	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments
<u>Guidotti (1993)</u>		Kidney and	Year of cohor	t entry (SMR):	Age,	
(cont.)		ureter (ICD-9,	Pre-1920	4	[17.28 (5.50-41.8)]	calendar	
		189), mortality	1920-1929	0	0	period	
			1930-1939	0	0		
			1940-1949	0	0		
			1950-1959	2	[3.34 (0.56-11.0)]		
			1960-1969	1	[5.16 (0.26-25.4)]		
			1970-1979	0	0		
		Kidney and	Latency (SMR	t):			
		ureter (ICD-9,	< 20 yr	1	[4.08 (0.20-19.7)]		
		189), mortality	20–29 yr	2	[3.92 (0.66-13.0)]		
			30–39 yr	0	0		
			40-49 yr	4	[21.29 (6.69-50.8)]		
			≥ 50 yr	0	0		
		Kidney and	Duration of e	mployment (SMR):		
		ureter (ICD-9, 189), mortality	< 1 yr	0	0		
			1–9 yr	0	0		
			10–19 yr	1	[4.3 (0.21-21.2)]		
			20–29 yr	2	[3.84 (0.64–12.7)]		
			30-39 yr	2	[3.38 (0.57-11.2)]		
			≥ 40 yr	2	[36.12 (6.10-120)]		
		Kidney and	Exposure opp	ortunity (yea	ar × weight) (SMR):		
		ureter (ICD-9,	0	1	[8.9 (0.45-44.0)]		
		189), mortality	> 0, < 1	0	0		
			1-4	0	0		
			5-9	0	0		
			10-14	1	[8.54 (0.43-42.2)]		
			15-19	1	[6.54 (0.33-32.2)]		
			20-24	0	0		
			25-29	2	[5.22 (0.88-17.3)]		
			30-35	0	0		
			≥ 35	2	[35.42 (5.99–118)]		

Reference, location enrolment/follow- up period, study design	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments
<u>Guidotti (1993)</u> (cont.)		Urinary bladder, mortality	SMR: Any employment	4	3.16 (0.86-8.08)	Age, calendar period	
		Urinary bladder,	Year of cohort	entry (SMR):		
	mortality	mortality	Pre-1920	3	[7.10 (1.80–19.3)]		
			1920-1929	0	0		
			1930-1939	0	0		
			1940-1949	1	[3.44 (0.17-17.0)]		
			1950-1959	0	0		
			1960-1969	0	0		
			1970-1979	0	0		
		Urinary bladder,	Latency (SMR)):		Age and	
		mortality	< 20 yr	0	0	time period	
			20–29 yr	0	0	-	
			30–39 yr	1	[2.78 (0.14-13.7)]		
			40-49 yr	3	[13.93 (3.47–37.1)]		
			≥ 50 yr	0	0		

Table 2.3 (conti	inued)						
Reference, location enrolment/follow- up period, study design	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments
design Glass et al. (2019) Australia Enrolment, varied by agency/follow- up, 1980–2011 (mortality); 1982– 2010 (incidence) Cohort	39 644 female firefighters, both paid [career] (1682) and volunteer (37 962), from nine fire agencies in Australia Exposure assessment method: ever career or volunteer firefighter, ever attended an incident, tertiles of cumulative number of incidents and type of incidents attended from personnel records	mortalityFemale reproductive cancer (ICD- 10, C51-C58), incidenceFemale reproductive cancer (ICD- 10, C51-C58), incidenceFemale reproductive cancer (ICD- 10, C51-C58), incidenceFemale reproductive cancer (ICD- 10, C51-C58), incidenceFemale reproductive cancer (ICD- 10, C51-C58), incidence	Zero incidents Tertile 1 Tertile 2 Tertile 3 Trend-test <i>P</i> va	rate ratios]: 32 9 11 15 alue, 0.16 dents, all vo 35 8 9 15 alue, 0.09	0.80 (0.64–0.98) 0.81 (0.57–1.11) teers (RIR) 1 0.97 (0.46–2.05) 1.04 (0.53–2.08) 1.70 (0.91–3.16) dunteers (RIR): 1 0.87 (0.40–1.89) 0.96 (0.46–2.01) 1.74 (0.94–3.21) ents, all volunteers 1	Age, calendar period	<i>Exposure assessment critique</i> : Good quality. Enhanced exposure assessment to differentiate exposure based on number of incidents for volunteer firefighters. Included specific incident types, but early exposure was extrapolated from more recent data. Volunteers mainly rural. <i>Strengths</i> : study of female firefighters; includes predominantly rural firefighters; ascertained exposure to number and type of incidents. <i>Limitations</i> : short length of follow-up; young age at end of follow-up; probable healthy-worker bias; little information on confounders.
	i	incidence	Tertile 1 Tertile 2 Tertile 3 Trend-test <i>P</i> va	0 6 6	0 (NR) 1.16 (0.50–2.70) 1.22 (0.52–2.85)		

Occupational exposure as a firefighter

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Reference, location enrolment/follow- up period, study design	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments
<u>Glass et al. (2019)</u>		Female		pe fire incid	ents, all volunteers	Age,	
(cont.)		reproductive cancer (ICD- 10, C51–C58),	(RIR): Zero	35	1	calendar period	
		incidence	incidents Tertile 1	0	1 15 (0 52 - 2 40)		
			Tertile 1 Tertile 2	8	1.15 (0.53–2.49)		
				9	1.09 (0.52–2.27)		
			Tertile 3	15	1.92 (1.05–3.54)		
		T	Trend-test P va		11 1		
		Female reproductive	No. of vehicle f (RIR):	ire incident	s, all volunteers		
	cancer (ICD- 10, C51–C58),	10, C51–C58),	Zero incidents	56	1		
		incidence	Tertile 1	2	0.66 (0.16-2.72)		
			Tertile 2	3	0.86 (0.27-2.76)		
			Tertile 3	6	1.76 (0.75-4.10)		
			Trend-test P va	lue, 0.18			
		Cervix/uterine	SIR:				
		cervix, incidence	All volunteer firefighters	12	0.53 (0.28-0.93)		
			Volunteers who attended incidents	5	0.48 (0.16–1.13)		
		Urinary tract	SIR:				
		(ICD-10, C64– C68), incidence	All volunteer firefighters	23	0.78 (0.49–1.17)		
			Volunteers who attended incidents	7	0.62 (0.25–1.28)		

Reference, location enrolment/follow- up period, study design	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments
<u>Glass et al. (2019)</u>		Urinary tract	No. of incider	nts, all volunt	teers (RIR):	Age,	
(cont.)		(ICD-10, C64– C68), incidence	Zero incidents	12	1	calendar period	
			Tertile 1	0	0 (NR)		
			Tertile 2	3	0.74 (0.21-2.61)		
			Tertile 3	4	1.12 (0.36-3.48)		
			Trend-test P	value, 0.09			
		Urinary tract	No. of fire inc	idents, all vo	lunteers (RIR):		
		(ICD-10, C64– C68), incidence	Zero incidents	12	1		
			Tertile 1	0	0 (NR)		
			Tertile 2	3	0.92 (0.26-3.25)		
			Tertile 3	4	1.26 (0.41-3.93)		
			Trend-test P	value, 0.09			
		Urinary tract (ICD-10, C64– C68), incidence	No. of structure fire incidents, all volunteers (RIR):				
			Zero incidents	14	1		
			Tertile 1	0	0 (NR)		
		Urinary tract (ICD-10, C64–	Tertile 2	1	0.74 (0.10-5.60)		
			Tertile 3	4	3.04 (1.00-9.27)		
			Trend-test P	value, 0.08			
			No. of landsc (RIR):	ape fire incid	ents, all volunteers		
		C68), incidence	Zero incidents	13	1		
			Tertile 1	0	0 (NR)		
			Tertile 2	2	0.64 (0.14-2.85)		
			Tertile 3	4	1.29 (0.42-3.97)		
			Trend-test P	value, 0.09			

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Reference, location enrolment/follow- up period, study design	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments
Glass et al. (2019) (cont.)		Urinary tract (ICD-10, C64–	No. of vehicle f (RIR):	ire incidents	s, all volunteers	Age, calendar	
``´		C68), incidence	Zero incidents	15	1	period	
			Tertile 1	0	0 (NR)		
			Tertile 2	2	2.06 (0.47–9.02)		
			Tertile 3	2	2.06 (0.47–9.03)		
			Trend-test <i>P</i> va		,		
		Kidney,	SIR:				
		incidence		19	0.98 (0.59–1.53)		
			Volunteers who attended incidents	6	0.77 (0.28–1.69)		
		Kidney,	No. of incident	s, all volunt	eers (RIR):		
		incidence	Zero incidents	10	1		
			Tertile 1	0	0 (NR)		
			Tertile 2	3	0.87 (0.24-3.18)		
			Tertile 3	3	0.99 (0.27-3.60)		
			Trend-test P va	lue, 0.16			
		Kidney,	No. of fire incid	dents, all vol	unteers (RIR):		
		incidence	Zero incidents	10	1		
			Tertile 1	0	0 (NR)		
			Tertile 2	3	1.09 (0.30-3.95)		
			Tertile 3	3	1.12 (0.31-4.09)		
			Trend-test P va	lue, 0.16			

Reference, location enrolment/follow- up period, study design	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments
<u>Glass et al. (2019)</u> (cont.)		Kidney, incidence	No. of structure fire incidents, all volunteers (RIR):			Age, calendar	
(cont.)		meldence	Zero incidents	12	1	period	
			Tertile 1	0	0 (NR)		
			Tertile 2	1	0.85 (0.11-6.51)		
			Tertile 3	3	2.61 (0.73-9.31)		
			Trend-test P	value, 0.13			
		Kidney, incidence	No. of landsc (RIR):	ape fire incid	ents, all volunteers		
			Zero incidents	11	1		
			Tertile 1	0	0 (NR)		
			Tertile 2	2	0.75 (0.17-3.40)		
			Tertile 3	3	1.14 (0.32-4.08)		
			Trend-test P	value, 0.16			
		Kidney, incidence	No. of vehicle (RIR):	fire incident	s, all volunteers		
			Zero incidents	13	1		
			Tertile 1	0	0 (NR)		
			Tertile 2	1	1.17 (0.15-8.96)		
			Tertile 3	2	2.33 (0.52-10.39)		
			Trend-test P	value, 0.24			

Reference, location enrolment/follow- up period, study design	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments
<u>Glass et al. (2017)</u>	al. (2017) 163 094, all male	Male reproductive	SIR:			Age,	Exposure assessment critiq
Australia	volunteer firefighters		All	2763	1.08 (1.04–1.12)	calendar	Good quality. Enhanced
Enrolment, date	from five fire agencies enrolled on or after	(ICD-10, C60-	volunteers			period	exposure assessment to differentiate exposure based on number of incidents. Included specific incident types but early exposure
varied by agency (1998–2000)/	the date on which	C63), incidence	Volunteers	1777	1.09 (1.04–1.14)		
follow-up through	the agency's roll was		who attended incidents				
30 November 2011	complete and who had	Male		rias (CID).			
(mortality) and 31	ever held an active	reproductive	Era of first service (SIR):				extrapolated from more
December 2010	firefighting role	(ICD-10, C60– C63), incidence	Pre-1970	860 1073	1.13 (1.06–1.21)		recent data. Firefighters fr rural or peri-urban areas. <i>Strengths</i> : includes
(cancer incidence) Cohort	Exposure assessment		1970–1994 1995 or after	1075 830	1.11 (1.05–1.18) 0.99 (0.92–1.06)		
Conort	method: ever volunteer firefighter, categorical volunteer duration	Male				predominantly rural	
		reproductive	Duration of service, all volunteers (RIR) [equivalent to rate ratios]:				firefighters; ascertained
	(years) and era from	(ICD-10, C60– C63), incidence	> 3 mo to	752	1		exposure to number and typ of incidents. <i>Limitations:</i> short length of follow-up; young age at end of follow-up; probable healthy-worker bias; little information on confounders
	service records; ever volunteer firefighter who attended an incident, tertiles of cumulative emergency incidents from contemporary incident data		< 10 yr	, 52	1		
			10–20 yr	497	1.07 (0.96-1.20)		
			$\geq 20 \text{ yr}$	1480	1.13 (1.04–1.24)		
			Trend-test P va	alue, 0.01			
		Male reproductive (ICD-10, C60– C63), incidence	Duration of ser incidents (RIR		teers who attended		
			> 3 mo to	347	1		
			< 10 yr				
			10–20 yr	293	1.12 (0.96–1.31)		
			≥ 20 yr	1148	1.18 (1.04–1.34)		
			Trend-test P va	alue, 0.01			
		Male reproductive (ICD-10, C60– C63), incidence	No. of incident	ts attended			
			Baseline	1659	1		
			Group 2	80	1.04 (0.83–1.30)		
			Group 3	38	1.00 (0.73-1.38)		

Reference, location enrolment/follow- up period, study design	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments
<u>Glass et al. (2017)</u> (cont.)		Male reproductive	No. of fire incidents attended by volunteers (RIR):			Age, calendar	
		(ICD-10, C60–	Baseline	1664	1	period	
		Male reproductive (ICD-10, C60– C63), incidence Male reproductive (ICD-10, C60– C63), incidence Male reproductive (ICD-10, C60–	Group 2	77	0.95 (0.75-1.19)		
			Group 3	36	1.06 (0.77-1.48)		
			No. of structure fire incidents attended by volunteers (RIR):				
			Baseline	1699	1		
			Group 2	52	1.10 (0.83-1.45)		
			Group 3	26	1.03 (0.70-1.51)		
			No. of landscape fire incidents attended by volunteers (RIR):				
			Baseline	1408	1		
			Group 2	276	1.08 (0.94-1.22)		
			Group 3	93	0.95 (0.77-1.17)		
			No. of vehicle fire incidents attended by volunteers (RIR):				
			Baseline	1657	1		
			Group 2	87	1.08 (0.87-1.34)		
		Prostate,	Group 3 SIR:	33	1.05 (0.74–1.48)		
		incidence	All volunteers	2655	1.12 (1.08–1.16)		
		Volunteers who attended incidents	1692	1.13 (1.08–1.19)			
		Prostate,	Era of first serv	vice (SIR):			
	incidence	Pre-1970	851	1.18 (1.10–1.26)			
		1970-1994	1022	1.15 (1.08-1.22)			
			1995 or after	782	1.03 (0.96-1.11)		

Reference, location enrolment/follow- up period, study design	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments
<u>Glass et al. (2017)</u>		Prostate, I	Duration of se	ervice, all vol	lunteers (RIR):	Age,	
(cont.)		incidence	> 3 mo to < 10 yr	701	1	calendar period	
			10–20 yr	470	1.06 (0.95-1.19)		
			$\geq 20 \text{ yr}$	1452	1.12 (1.02-1.23)		
			Trend-test P v	alue, 0.02			
		Prostate, incidence	Duration of se incidents (RII		teers who attended		
			> 3 mo to < 10 yr	315	1		
			10–20 yr	266	1.07 (0.91–1.26)		
			≥ 20 yr	1123	1.15 (1.01–1.31)		
			Trend-test P v	value, 0.03			
		Prostate,	No. of incider	nts attended b	by volunteers (RIR):		
		incidence	Baseline	1578	1		
			Group 2	77	1.04 (0.83-1.31)		
			Group 3	38	1.04 (0.75-1.43)		
		Prostate, incidence	No. of fire inc (RIR):	idents attend	led by volunteers		
			Baseline	1581	1		
			Group 2	76	0.97 (0.77-1.23)		
			Group 3	36	1.10 (0.79–1.53)		
		Prostate, incidence	No. of structu volunteers (R		ents attended by		
			Baseline	1615	1		
			Group 2	52	1.15 (0.87–1.52)		
			Group 3	26	1.06 (0.72–1.57)		
		Prostate, incidence	No. of landsca volunteers (R		ents attended by		
			Baseline	1337	1		
			Group 2	264	1.07 (0.94–1.22)		
			Group 3	92	0.97 (0.78-1.19)		

Reference, location enrolment/follow- up period, study design	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments
<u>Glass et al. (2017)</u> (cont.)		Prostate, incidence	No. of vehicle t volunteers (RI		s attended by	Age, calendar	
(cont.)		Incluence	Baseline	к): 1577	1	period	
			Group 2	83	1 1.08 (0.87–1.35)	period	
			Group 3	33	1.08 (0.37 - 1.53) 1.09 (0.77 - 1.54)		
		Testis, incidence	SIR:	55	1.09 (0.77-1.34)		
		restis, mendence	All volunteers	99	0.92 (0.75-1.13)		
			Volunteers who attended incidents	81	1.10 (0.88–1.37)		
		Testis, incidence	Era of first serv	vice (SIR):			
			Pre-1970	7	1.99 (0.80-4.10)		
			1970-1994	47	1.07 (0.79–1.43)		
			1995 or after	45	0.75 (0.55-1.01)		
		Testis, incidence	Duration of se	rvice, all vol	unteers (RIR):		
			> 3 mo to < 10 yr	48	1		
			10–20 yr	25	1.36 (0.83-2.21)		
			≥ 20 yr	25	1.76 (1.00-3.08)		
		Trend-test P va	alue, 0.04				
		Testis, incidence	Duration of set incidents (RIR		teers who attended		
			> 3 mo to < 10 yr	32	1		
			10–20 yr	25	1.66 (0.98-2.81)		
			$\geq 20 \text{ yr}$	23	1.62 (0.86-3.02)		
		Trend-test P va	alue, 0.08				
		Testis, incidence	No. of incident	ts attended b	by volunteers (RIR):		
			Baseline	78	1		
			Group 2	3	0.94 (0.30-2.97)		
			Group 3	0	0 (NR)		

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Reference, location enrolment/follow- up period, study design	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Co
<u>Glass et al. (2017)</u> (cont.)		Testis, incidence	No. of fire inci (RIR):	idents attend	led by volunteers	Age, calendar	
			Baseline	80	1	period	
			Group 2	1	0.33 (0.05-2.35)		
			Group 3	0	0 (NR)		
		Testis, incidence	No. of structur volunteers (RI		ents attended by		
			Baseline	81	1		
			Group 2	0	0 (NR)		
			Group 3	0	0 (NR)		
		Testis, incidence	No. of landsca volunteers (RI		lents attended by		
			Baseline	69	1		
			Group 2	11	1.16 (0.61-2.21)		
			Group 3	1	0.41 (0.06-2.99)		
		Testis, incidence	No. of vehicle volunteers (RI		ts attended by		
			Baseline	77	1		
			Group 2	4	1.13 (0.42-3.10)		
			Group 3	0	0 (NR)		
		Urinary tract	SIR:				
		(ICD-10, C64– C68), incidence	All volunteers	334	0.72 (0.65–0.81)		
			Volunteers who attended incidents	205	0.70 (0.60-0.80)		
		Urinary tract	Era of first ser	vice (SIR):			
		(ICD-10, C64-	Pre-1970	101	0.72 (0.59-0.88)		

1970-1994

1995 or after 110

C68), incidence

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0.69 (0.57-0.82)

0.77 (0.63-0.93)

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Reference, location enrolment/follow- up period, study design	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments
<u>Glass et al. (2017)</u>		(ICD-10, C64–	Duration of se	ervice, all vol	lunteers (RIR):	Age,	
(cont.)			> 3 mo to < 10 yr	105	1	calendar period	
			10–20 yr	56	0.86 (0.62-1.19)		
		Urinary tract	≥ 20 yr	169	0.94 (0.73-1.22)		
			Trend-test P v	alue, 0.72			
			Duration of se incidents (RII		teers who attended		
		C68), incidence	> 3 mo to < 10 yr	46	1		
			10–20 yr	31	0.90 (0.57-1.42)		
			≥ 20 yr	133	1.15 (0.80-1.64)		
			Trend-test P v	alue, 0.35			
		Urinary tract (ICD-10, C64– C68), incidence Urinary tract (ICD-10, C64– C68), incidence	No. of incider	its attended l	oy volunteers (RIR):		
			Baseline	187	1		
			Group 2	12	1.40 (0.78–2.52)		
			Group 3	6	1.47 (0.65–3.31)		
			No. of fire incidents attended by volunteers (RIR):				
			Baseline	184	1		
			Group 2	17	1.95 (1.18–3.20)		
			Group 3	4	1.13 (0.42–3.06)		
		Urinary tract (ICD-10, C64–	No. of structu volunteers (R		ents attended by		
		C68), incidence	Baseline	188	1		
			Group 2	10	1.94 (1.03-3.66)		
			Group 3	7	2.63 (1.24-5.59)		
		Urinary tract (ICD-10, C64–	No. of landsca volunteers (R		ents attended by		
		C68), incidence	Baseline	154	1		
			Group 2	35	1.27 (0.88–1.84)		
			Group 3	16	1.59 (0.95-2.67)		

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Reference, location enrolment/follow- up period, study design	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments	
<u>Glass et al. (2017)</u> (cont.)		Urinary tract (ICD-10, C64–	No. of vehicle f volunteers (RII		s attended by	Age, calendar		
			Baseline	187	1	period		
			Group 2	15	1.68 (0.99-2.84)			
			Group 3	3	0.88 (0.28-2.74)			
		Kidney,	SIR:					
		incidence	All volunteers	196	0.82 (0.71–0.94)			
			Volunteers who attended incidents	130	0.83 (0.70-0.99)			
		Kidney, incidence	Era of first serv	vice (SIR):				
			Pre-1970	56	0.93 (0.70-1.21)			
			1970-1994	74	0.75 (0.59-0.94)			
			1995 or after	66	0.81 (0.63-1.04)			
		Kidney,	Duration of service, all volunteers (RIR):					
		incidence	> 3 mo to < 10 yr	65	1			
			10–20 yr	32	0.81 (0.53-1.24)			
	Kidney, incidence		$\geq 20 \text{ yr}$	98	1.00 (0.72-1.40)			
		Trend-test P va	lue, 0.92					
		Kidney, incidence	Duration of ser incidents (RIR		teers who attended			
			> 3 mo to < 10 yr	31	1			
			10–20 yr	18	0.78 (0.43-1.40)			
			≥ 20 yr	84	1.19 (0.77–1.84)			
			Trend-test P va	lue, 0.31				
		Kidney,	No. of incident	s attended b	by volunteers (RIR):			
		incidence	Baseline	115	1			
			Group 2	9	1.70 (0.86-3.34)			
			Group 3	6	2.37 (1.04-5.38)			

Table 2.3	(continued)
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Reference, location enrolment/follow- up period, study design	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments
<u>Glass et al. (2017)</u> (cont.)		Kidney, incidence	No. of fire inci (RIR):	dents attend	led by volunteers	Age, calendar	
()			Baseline	114	1	period	
			Group 2	12	2.22 (1.22-4.02)	-	
			Group 3	4	1.84 (0.68-4.99)		
		Kidney, incidence	-		ents attended by		
			Baseline	116	1		
			Group 2	7	2.15 (1.00-4.62)		
			Group 3	7	4.23 (1.97-9.08)		
		Kidney, incidence	No. of landsca volunteers (RI		ents attended by		
			Baseline	91	1		
			Group 2	26	1.58 (1.02-2.45)		
			Group 3	13	2.24 (1.25-4.01)		
		Kidney, incidence	No. of vehicle volunteers (RI		s attended by		
			Baseline	114	1		
			Group 2	13	2.34 (1.32-4.16)		
			Group 3	3	1.41 (0.45-4.44)		
		Urinary bladder,	SIR:				
		incidence	All volunteers	117	0.60 (0.50-0.72)		
			Volunteers who attended incidents	67	0.55 (0.43–0.7)		

Reference, locationPopulation size, description, exposure assessment method design	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments
Glass et al. (2016a) $30\ 057;\ full-(17\ 394)$ Australiaor part-time (12\ 663)Enrolment,paid male firefighters1976-2003/follow-employed at one of eightUp, 1976-2011Australian fire agencies(mortality), 1982-for $\geq 3\ mo\ from\ start$ 2010 (incidence,except two states,2009)CohortCohortExposure assessmentmethod: employed asa part- or full-timefirefighter for $\geq 3\ mo$,categorical employmentduration (years) andera from employmentrecords; tertiles ofcumulative emergencyincident attended fromcontemporary incidentdatadata	Male reproductive (ICD-10, C60– C63), incidence Male reproductive (ICD-10, C60– C63), incidence Male reproductive (ICD-10, C60– C63), incidence Male reproductive (ICD-10, C60– C63), incidence	(RIR) [equival > 3 mo to 10 yr 10-20 yr \ge 20 yr Trend-test <i>P</i> va Duration of er firefighters (RI > 3 mo to 10 yr 10-20 yr \ge 20 yr Trend-test <i>P</i> va Duration of er > 3 mo to 10 yr 10-20 yr \ge 20 yr Trend-test <i>P</i> va No. of inciden firefighters (RI Tertile 1 Tertile 2 Tertile 3	357 167 524 nployment, ent to rate r 40 37 277 alue, 0.14 nployment, (R): 32 47 86 alue, 0.99 nployment (72 84 363 alue, 0.26 ts attended 1 (R): 20 37 58	1 0.82 (0.53–1.30) 1.23 (0.83–1.81) part-time 1 1.52 (0.94–2.46) 1.10 (0.68–1.80) RIR): 1 1.21 (0.88–1.68) 1.21 (0.90–1.64)	Age, calendar period	<i>Exposure assessment critique</i> : Good quality. Enhanced exposure assessment to differentiate exposure based on number of incidents, including specific incident types. Included specific incident types, but early exposure was extrapolated from more recent data. Municipal firefighters. <i>Strengths</i> : internal analysis by exposure to number and type of incidents; ascertained cancer incidence. <i>Limitations</i> : healthy-worker hire bias; short length of follow-up; young age at end of follow-up; little information on potential confounders.
		Trend-test P va	100, 0.02			

Reference, location enrolment/follow- up period, study design	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments
<u>Glass et al. (2016a)</u> (cont.)		Male reproductive	No. of fire inci firefighters (RI		led by full-time	Age, calendar	
		(ICD-10, C60–	Tertile 1	23	1	period	
		C63), incidence	Tertile 2	26	1.42 (0.81–2.49)	-	
			Tertile 3	66	1.91 (1.21–3.09)		
			Trend-test P va				
		Male reproductive		re fire incide	ents attended by full-		
		(ICD-10, C60– C63), incidence	Tertile 1	23	1		
			Tertile 2	27	1.41 (0.81-2.47)		
		Tertile 3	65	1.96 (1.21-3.17)			
			Trend-test P va	alue, 0.01	· · · ·		
		Male reproductive	No. of landsca full-time firefi		ents attended by		
		(ICD-10, C60–	Tertile 1	25	1		
		C63), incidence	Tertile 2	36	1.64 (0.99-2.74)		
			Tertile 3	54	1.49 (0.92-2.40)		
			Trend-test P va	alue, 0.14	. ,		
		Male reproductive	No. of vehicle time firefighter		s attended by full-		
		(ICD-10, C60–	Tertile 1	22	1		
		C63), incidence	Tertile 2	30	1.80 (1.03-3.13)		
			Tertile 3	63	2.13 (1.31-3.48)		
			Trend-test P va	alue, < 0.01			
		Male reproductive	Duration of en (SIR):	nployment,	full-time firefighters		
		(ICD-10, C60–	> 3 mo to 10 yr	40	1.36 (0.98-1.86)		
		C63), incidence	10–20 yr	37	0.98 (0.69-1.35)		
			$\geq 20 \text{ yr}$	277	1.21 (1.07-1.36)		

Reference, location enrolment/follow- up period, study design	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments
Glass et al. (2016a) (cont.)		Male reproductive	Duration of en firefighters (SI		part-time	Age, calendar	
(cont.)		(ICD-10, C60–	e		1 11 (0 76 1 57)	period	
		C63), incidence	> 3 mo to 10 yr	32 47	1.11(0.76-1.57)	period	
			10−20 yr		1.85 (1.36–2.46)		
		N 1	$\geq 20 \text{ yr}$	86	1.34 (1.07–1.66)		
		Male reproductive	(SIR):	ployment, fi	Ill-time firefighters		
		(ICD-10, C60–	Pre-1970	17	1.12 (0.96–1.3)		
		C63), incidence	1970-1994	161	1.27 (1.08-1.48)		
		1995 or after	26	1.29 (0.84–1.89)			
		Male reproductive	Era of first emp (SIR):	ployment, p	art-time firefighters		
		(ICD-10, C60–	Pre-1970	37	1.33 (0.93-1.83)		
		C63), incidence	1970-1994	101	1.42 (1.16-1.73)		
			1995 or after	29	1.47 (0.98-2.11)		
		Male reproductive	No. of incident firefighters (RI		by part-time		
		(ICD-10, C60–	Tertile 1	10	1		
		C63), incidence	Tertile 2	25	1.51 (0.72-3.18)		
			Tertile 3	33	0.83 (0.40-1.73)		
			Trend-test P va	alue, 0.24	, ,		
		Male			led by part-time		
		reproductive	No. of fire incidents attended by part-time firefighters (RIR):				
		(ICD-10, C60–	Tertile 1	14	1		
		C63), incidence	Tertile 2	21	0.90 (0.46-1.79)		
			Tertile 3	33	0.61 (0.32-1.18)		
			Trend-test P va	alue, 0.10			

Reference, location enrolment/follow- up period, study design	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments
<u>Glass et al. (2016a)</u>		Male reproductive (ICD-10, C60–			ents attended by	Age,	
(cont.)			part-time firef	-		calendar period	
		C63), incidence	Tertile 1 Tertile 2	12	1	period	
		000), 110140100		20	1.12 (0.55–2.31)		
			Tertile 3	36	0.75 (0.38–1.48)		
			Trend-test P va	· ·	1 11		
		Male reproductive	No. of landsca part-time firef		ents attended by .):		
		(ICD-10, C60–	Tertile 1	13	1		
	C63), incidence	Tertile 2	22	1.11 (0.56-2.21)			
			Tertile 3	33	0.75 (0.39-1.45)		
			Trend-test P va	alue, 0.26			
		Male reproductive	No. of vehicle time firefighter		s attended by part-		
		(ICD-10, C60–	Tertile 1	19	1		
		C63), incidence	Tertile 2	21	0.95 (0.51-1.78)		
			Tertile 3	28	0.50 (0.28-0.91)		
			Trend-test P va	alue, 0.01			
		Prostate,	Firefighter stat	us (SIR):			
		incidence	Full-time	325	1.23 (1.10-1.37)		
			Part-time	153	1.51 (1.28–1.77)		
			All	478	1.31 (1.19–1.43)		
		Prostate, incidence	Duration of en (RIR):	nployment,	full-time firefighters		
			> 3 mo to 10 yr	23	1		
			10–20 yr	30	1.05 (0.61-1.82)		
			≥ 20 yr	270	1.56 (0.98-2.51)		
			Trend-test P va	alue, 0.02			

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Reference, location enrolment/follow- up period, study design	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments
<u>Glass et al. (2016a)</u> (cont.)		Prostate, incidence	Duration of en firefighters (RI		part-time	Age, calendar	
			> 3 mo to 10 yr		1	period	
			10–20 yr	41	1.51 (0.90-2.54)		
			$\geq 20 \text{ yr}$	86	1.16 (0.70-1.95)		
			Trend-test P va	alue, 0.86			
		Prostate,	Duration of en	nployment ((RIR):		
		incidence	> 3 mo to 10 yr	49	1		
			10–20 yr	71	1.29 (0.89–1.88)		
			≥ 20 yr	356	1.32 (0.94–1.85)		
			Trend-test P va	alue, 0.15			
		Prostate, incidence	No. of incident firefighters (RI		by full-time		
			Tertile 1	14	1		
			Tertile 2	29	2.49 (1.32-4.72)		
			Tertile 3	54	2.45 (1.35-4.41)		
			Trend-test P va	alue, 0.01			
		Prostate, incidence	No. of fire inci- firefighters (RI		led by full-time		
			Tertile 1	15	1		
			Tertile 2	20	1.78 (0.91-3.48)		
			Tertile 3	62	2.55 (1.45-4.50)		
			Trend-test P va	alue, < 0.01			
		Prostate, incidence	No. of structur time firefighter		ents attended by full-		
			Tertile 1	16	1		
			Tertile 2	20	1.57 (0.81-3.04)		
			Tertile 3	61	2.45 (1.40-4.26)		
			Trend-test P va	alue, < 0.01			

Reference, location enrolment/follow- up period, study design	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments
<u>Glass et al. (2016a)</u> (cont.)		Prostate, incidence	No. of landsca firefighters (RI		ents by full-time	Age, calendar	
			Tertile 1	18	1	period	
			Tertile 2	27	1.78 (0.98-3.24)		
			Tertile 3	52	1.88 (1.09-3.22)		
			Trend-test P va	alue, 0.03			
		Prostate, incidence	No. of vehicle t time firefighter		s attended by full-		
			Tertile 1	16	1		
			Tertile 2	22	1.95 (1.02-3.73)		
			Tertile 3	59	2.60 (1.50-4.54)		
			Trend-test P va	alue, < 0.01			
		Prostate, incidence	Duration of en (SIR):	nployment,	full-time firefighters		
			> 3 mo to 10 yr	23	1.26 (0.8–1.89)		
			10–20 yr	30	1.01 (0.68–1.44)		
			≥ 20 yr	269	1.26 (1.11–1.42)		
		Prostate, incidence	Duration of en firefighters (SI		part-time		
			> 3 mo to 10 yr	26	1.42 (0.93–2.08)		
			10–20 yr	41	1.84 (1.32–2.49)		
			≥ 20 yr	85	1.41 (1.13–1.75)		
		Prostate, incidence	Era of first emp (SIR):	ployment, fu	ll-time firefighters		
			Pre-1970	16	1.19 (1.02–1.39)		
			1970–1994	141	1.29 (1.09–1.52)		
			1995 or after	15	1.14 (0.64–1.88)		
		Prostate, incidence	Era of first emp (SIR):	ployment, p	art-time firefighters		
			Pre-1970	37	1.43 (1.01–1.97)		
			1970-1994	95	1.50 (1.22–1.84)		
			1995 or after	21	1.76 (1.09-2.68)		

Reference, location enrolment/follow- up period, study design	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments
<u>Glass et al. (2016a)</u> cont.)		Prostate, incidence	No. of incider firefighters (R		by part-time	Age, calendar	
(001111)			Tertile 1	7	1	period	
			Tertile 2	24	2.30 (0.99–5.36)	-	
			Tertile 3	31	1.37 (0.60–3.14)		
			Trend-test P v		,		
		Prostate, incidence		idents attend	led by part-time		
			Tertile 1	11	1		
			Tertile 2	20	1.21 (0.58-2.54)		
			Tertile 3	31	0.90 (0.44-1.80)		
			Trend-test P v	value, 0.55			
		Prostate, incidence	No. of structu part-time fire:		ents attended by A):		
			Tertile 1	9	1		
			Tertile 2	19	1.54 (0.70-3.42)		
			Tertile 3	34	1.17 (0.56-2.48)		
			Trend-test P v	value, 0.95			
		Prostate, incidence	No. of landsca part-time fire		ents attended by		
			Tertile 1	10	1		
			Tertile 2	21	1.41 (0.66-3.00)		
			Tertile 3	31	1.05 (0.51-2.16)		
			Trend-test P v	value, 0.83			
		Prostate, incidence	No. of vehicle time firefighte		s attended by part-		
			Tertile 1	16	1		
			Tertile 2	20	1.08 (0.56-2.09)		
			Tertile 3	26	0.66 (0.35-1.23)		
			Trend-test P v	value, 0.13			

Reference, location enrolment/follow- up period, study design	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments
<u>Glass et al. (2016a)</u>		Testis, incidence	Firefighter stat	us (SIR):		Age,	
(cont.)			Full-time	31	1.44 (0.98-2.05)	calendar	
			Part-time	12	0.93 (0.48-1.63)	period	
			All	43	1.25 (0.91-1.69)		
		Testis, incidence	Duration of en (RIR):	nployment,	full-time firefighters		
			> 3 mo to 10 yr	17	1		
			10–20 yr	7	0.60 (0.24-1.52)		
			≥ 20 yr	7	0.67 (0.20-2.31)		
			Trend-test P va	alue, 0.39			
		Testis, incidence	Duration of en firefighters: (R		part-time		
			> 3 mo to 10 yr	6	NR		
			10–20 yr	5	NR		
			$\geq 20 \text{ yr}$	0	0 (NR)		
		Testis, incidence	Duration of en	nployment (RIR):		
			> 3 mo to 10 yr		1		
			10–20 yr	12	1.18 (0.57-2.48)		
			$\geq 20 \text{ yr}$	7	0.93 (0.31-2.75)		
			Trend-test P va	alue, 0.96			
		Testis, incidence	No. of incident firefighters (RI		oy full-time		
			Tertile 1	6	1		
			Tertile 2	8	1.27 (0.44-3.66)		
			Tertile 3	4	0.62 (0.17-2.25)		
			Trend-test P va	alue, 0.51			

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Reference, location enrolment/follow- up period, study design	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments
<u>Glass et al. (2016a)</u> (cont.)		Testis, incidence	No. of fire inci firefighters (RI		led by full-time	Age, calendar	
			Tertile 1	8	1	period	
			Tertile 2	6	0.71 (0.25-2.04)		
			Tertile 3	4	0.46 (0.13-1.60)		
			Trend-test P va	alue, 0.21			
		Testis, incidence	No. of structur time firefighter		ents attended by full-		
			Tertile 1	7	1		
			Tertile 2	7	0.97 (0.34-2.78)		
			Tertile 3	4	0.54 (0.15-1.89)		
			Trend-test P va	alue, 0.35			
		Testis, incidence	No. of landsca full-time firefi		ents attended by):		
			Tertile 1	7	1		
			Tertile 2	9	1.21 (0.45-3.26)		
			Tertile 3	2	0.26 (0.05-1.28)		
			Trend-test P va	alue, 0.13			
		Testis, incidence	No. of vehicle time firefighter		s attended by full-		
			Tertile 1	6	1		
			Tertile 2	8	1.26 (0.44-3.65)		
			Tertile 3	4	0.62 (0.17-2.26)		
			Trend-test P va	alue, 0.51			
		Testis, incidence	Duration of en (SIR):	nployment,	full-time firefighters		
			> 3 mo to 10 yr	17	1.65 (0.96-2.63)		
			10–20 yr	7	0.99 (0.40-2.05)		
			≥ 20 yr	7	1.85 (0.74-3.81)		

Reference, location enrolment/follow- up period, study design	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments
<u>Glass et al. (2016a)</u> (cont.)		Testis, incidence	Duration of en firefighters (SI		part-time	Age, calendar	
			> 3 mo to 10 yr	6	0.61 (0.22-1.33)	period	
			10–20 yr	5	2.32 (0.75-5.41)		
			≥ 20 yr	0	0 (NR):		
		Testis, incidence	Era of first emp (SIR):	ployment, fu	all-time firefighters		
			Pre-1970	0	0 (NR):		
			1970-1994	20	1.46 (0.89-2.25)		
			1995 or after	11	1.66 (0.83-2.98)		
	Testis, i	Testis, incidence	Era of first emp (SIR):	ployment, p	art-time firefighters		
			Pre-1970	0	0 (NR):		
			1970-1994	4	0.74 (0.20-1.91)		
			1995 or after	8	1.09 (0.47-2.14)		
		Urinary tract	Firefighter stat	us (SIR):			
		(ICD-10, C64–	Full-time	59	0.91 (0.69–1.17)		
		C68), incidence	Part-time	25	1.04 (0.67–1.53)		
			All	84	0.94 (0.75-1.17)		
		Urinary tract (ICD-10, C64–	Duration of en (RIR):	nployment, i	full-time firefighters		
		C68), incidence	> 3 mo to 10 yr	2	1		
			10–20 yr	12	5.63 (1.25-25.30)		
			≥ 20 yr	45	5.92 (1.33-23.30)		
			Trend-test P va	lue, 0.03			
		Urinary tract (ICD-10, C64–	Duration of en firefighters (RI		part-time		
		C68), incidence	> 3 mo to 10 yr	4	1		
			10–20 yr	9	4.42 (1.26–15.44)		
			≥ 20 yr	12	4.32 (1.12–16.72)		
			Trend-test P va	lue, 0.05			

Reference, location enrolment/follow- up period, study design	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments
<u>Glass et al. (2016a)</u>		Urinary tract	Duration of en	nployment (RIR):	Age,	
(cont.)		(ICD-10, C64–	> 3 mo to 10 yr	6	1	calendar	
		C68), incidence	10–20 yr	21	4.29 (1.71–10.78)	period	
			≥ 20 yr	57	4.32 (1.71–10.89)		
			Trend-test P va	alue, 0.01			
		Urinary tract (ICD-10, C64–	No. of incident firefighters (RI		oy full-time		
		C68), incidence	Tertile 1	5	1		
			Tertile 2	7	1.57 (0.50-4.95)		
			Tertile 3	8	0.99 (0.32-3.06)		
			Trend-test P va	alue, 0.91			
		Urinary tract (ICD-10, C64– C68), incidence	No. of fire inci- firefighters (RI		led by full-time		
			Tertile 1	4	1		
			Tertile 2	6	1.80 (0.51-6.39)		
			Tertile 3	10	1.51 (0.47-4.86)		
			Trend-test P va	alue, 0.55			
		Urinary tract (ICD-10, C64–	No. of structure fire incidents attended by full- time firefighters (RIR):				
		C68), incidence	Tertile 1	5	1		
			Tertile 2	7	1.58 (0.50-4.99)		
			Tertile 3	8	1.00 (0.32-3.09)		
			Trend-test P va	alue, 0.92			
		Urinary tract (ICD-10, C64–	No. of landscap full-time firefig		ents attended by):		
		C68), incidence	Tertile 1	3	1		
			Tertile 2	6	2.18 (0.54-8.72)		
			Tertile 3	11	2.37 (0.66-8.57)		
			Trend-test P va	alue, 0.21	. , ,		

Table 2.3	(continued)
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Reference, location enrolment/follow- up period, study design	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments
<u>Glass et al. (2016a)</u> (cont.)		Urinary tract (ICD-10, C64–	No. of vehicle time firefighter		s attended by full-	Age, calendar	
		C68), incidence	Tertile 1	4	1	period	
			Tertile 2	4	1.23 (0.31-4.96)		
			Tertile 3	12	2.01 (0.66-6.46)		
			Trend-test P va	alue, 0.19			
		Urinary tract (ICD-10, C64–	Duration of en firefighters (SI		ttended by full-time		
		C68), incidence	> 3 mo to 10 yr	2	0.32 (0.04-1.14)		
			10–20 yr	12	1.14 (0.59–1.99)		
		≥ 20 yr	45	0.95 (0.69-1.27)			
	(ICD-10, C	Urinary tract (ICD-10, C64–	Duration of en firefighters (SI		part-time		
		C68), incidence	> 3 mo to 10 yr	4	0.58 (0.16-1.49)		
			10–20 yr	9	1.60 (0.73-3.04)		
			≥ 20 yr	12	1.05 (0.54-1.83)		
	(ICD-10	Urinary tract (ICD-10, C64–	Era of first emp (SIR):	ployment, fu	all-time firefighters		
		C68), incidence	Pre-1970	30	0.92 (0.62-1.31)		
			1970-1994	28	1.00 (0.66-1.45)		
			1995 or after	1	0.23 (0.01-1.30)		
		Urinary tract (ICD-10, C64–	Era of first emp (SIR):	ployment, p	art-time firefighters		
		C68), incidence	Pre-1970	7	1.37 (0.55-2.83)		
			1970-1994	16	1.11 (0.63–1.80)		
			1995 or after	2	0.44 (0.05-1.60)		
		Kidney,	Firefighter stat	us (SIR):			
		incidence	Full-time	33	0.97 (0.67-1.36)		
			Part-time	19	1.34 (0.81–2.10)		
			All	52	1.08 (0.81-1.41)		

Reference, location enrolment/follow- up period, study design	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments
<u>Glass et al. (2016a)</u> (cont.)		Kidney, incidence	Duration of en (RIR):	nployment,	full-time firefighters	Age, calendar	
			> 3 mo to 10 yr	1	1	period	
			10–20 yr	7	6.95 (0.85-56.81)		
			$\geq 20 \text{ yr}$	25	8.19 (1.01-66.62)		
			Trend-test P va	alue, 0.05			
		Kidney, incidence	Duration of en firefighters (RI		part-time		
			> 3 mo to 10 yr		1		
			10–20 yr	8	5.34 (1.31-21.76)		
			$\geq 20 \text{ yr}$	8	3.97 (0.83-19.02)		
			Trend-test P va	alue, 0.13			
		Kidney,	Duration of en	nployment (RIR):		
		incidence	> 3 mo to 10 yr		1		
			10–20 yr	15	4.81 (1.57-14.72)		
			$\geq 20 \text{ yr}$	33	4.29 (1.37-13.50)		
			Trend-test P va	alue, 0.03			
		Kidney, incidence	No. of incident firefighters (RI		oy full-time		
			Tertile 1	2	1		
			Tertile 2	5	2.73 (0.53-14.11)		
			Tertile 3	5	1.68 (0.32-8.75)		
			Trend-test P va	alue, 0.65			
	Kidney, incidence	Kidney, incidence	No. of fire inci firefighters (RI		led by full-time		
			Tertile 1	2	1		
			Tertile 2	4	2.3 (0.42-12.61)		
			Tertile 3	6	1.96 (0.39–9.87)		
			Trend-test P va	alue, 0.47	. ,		

Table 2.3	(continued)
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Reference, location nrolment/follow- p period, study lesign	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments
<u>Glass et al. (2016a)</u> cont.)		Kidney, incidence	No. of structur time firefighter		ents attended by full-	Age, calendar	
			Tertile 1	3	1	period	
			Tertile 2	6	2.23 (0.56-8.94)		
			Tertile 3	3	0.65 (0.13-3.26)		
			Trend-test P va	alue, 0.55			
		Kidney, incidence	No. of landscap full-time firefig		ents attended by):		
			Tertile 1	2	1		
			Tertile 2	3	1.60 (0.27-9.60)		
			Tertile 3	7	2.47 (0.51-12.03)		
			Trend-test P va	alue, 0.24			
		Kidney, incidence	No. of vehicle fire incidents attended by full- time firefighters (RIR):				
			Tertile 1	2	1		
			Tertile 2	2	1.17 (0.16-8.34)		
			Tertile 3	8	2.97 (0.62-14.15)		
			Trend-test P va	alue, 0.13			
		Kidney, incidence	Duration of en (SIR):	nployment,	full-time firefighters		
			> 3 mo to 10 yr	1	0.24 (0.01-1.35)		
			10–20 yr	7	1.07 (0.43-2.21)		
			≥ 20 yr	25	1.08 (0.70-1.60)		
		Kidney, incidence	Duration of employment, part-time firefighters (SIR):				
			> 3 mo to 10 yr	3	0.63 (0.13-1.83)		
			10–20 yr	8	2.28 (0.98-4.49)		
			≥ 20 yr	8	1.39 (0.60-2.73)		

Reference, location enrolment/follow- up period, study design	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments
<u>Glass et al. (2016a)</u> (cont.)		Kidney, incidence	Era of first emp (SIR):	ployment, fu	all-time firefighters	Age, calendar	
			Pre-1970	17	1.26 (0.73-2.01)	period	
			1970-1994	15	0.86 (0.48-1.41)		
			1995 or after	1	0.33 (0.01-1.82)		
		Kidney, incidence	Era of first emp (SIR):	ployment, p	art-time firefighters		
			Pre-1970	4	1.77 (0.48-4.52)		
			1970-1994	13	1.51 (0.81-2.59)		
			1995 or after	2	0.61 (0.07-2.21)		
		Urinary bladder,	Firefighter stat	us (SIR):			
		incidence	Full-time	23	0.85 (0.54-1.27)		
			Part-time	5	0.57 (0.19-1.34)		
			All	28	0.78 (0.52-1.13)		
		Urinary bladder, incidence	Duration of en (SIR):	nployment,	full-time firefighters		
			> 3 mo to 10 yr	1	0.52 (0.01-2.88)		
			10–20 yr	4	1.14 (0.31–2.91)		
			≥ 20 yr	18	0.84 (0.50-1.32)		
		Urinary bladder, incidence	Duration of en firefighters (SI		part-time		
			> 3 mo to 10 yr	1	0.55 (0.01-3.07)		
			10–20 yr	1	0.54 (0.01-3.02)		
			≥ 20 yr	3	0.60 (0.12-1.75)		
		Urinary bladder, incidence	Era of first emp firefighters(SIF		ıll-time		
			Pre-1970	11	0.65 (0.33-1.17)		
			1970-1994	12	1.31 (0.67–2.28)		
			1995 or after	0	0		

Reference, location enrolment/follow- up period, study design	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments
<u>Glass et al. (2016a)</u> (cont.)		Urinary bladder, incidence	Era of first em (SIR):	ployment, p	art-time firefighters	Age, calendar	
			Pre-1970	2	0.81 (0.10-2.91)	period	
			1970-1994	3	0.58 (0.12-1.71)		
			1995 or after	0	0 (NR)		
<u>Glass et al. (2016b)</u>	614, all male (611) and	Male	Risk of chroni	c exposure (SIR):	Age,	Exposure assessment
Victoria, Australia	female (3) employed and	reproductive	Low	2	0.52 (0.06-1.87)	calendar	critique: Satisfactory quality.
Enrolment,	volunteer Country Fire	(ICD-10, C60-	Medium	7	0.71 (0.29-1.47)	period	Incorporated categorical level of exposure into assessment for each type of firefighter.
1971–1999/follow- up, 1980–2011	Authority trainers and a group of paid [career]	C63), incidence	High	7	1.77 (0.71–3.65)		
(mortality), 1982–	Country Fire Authority	Prostate,	Risk of chronic exposure (SIR):				Volunteers mainly rural,
2012 (incidence)	firefighters who trained	incidence	Low	2	0.63 (0.08-2.28)		paid [career] firefighters were municipal. <i>Strengths</i> : included firefighter
Cohort	at the Fiskville site		Medium	7	0.79 (0.32-1.62)		
	between 1971 and 1999;		High	5	1.43 (0.46–3.34)		
	all analyses limited to	Testis, incidence	Risk of chronic exposure (SIR):				instructors with high
	men since no deaths or cancers were observed		Low	0	0 (NR)		potential exposure to smoke and other hazardous agents; assessed exposure based on job assignment.
	among women		Medium	0	0 (NR)		
	Exposure assessment		High	2	11.9 (1.44-42.9)		
	method: employed or	Urinary tract	Risk of chronic exposure (SIR):				<i>Limitations</i> : low number of
	volunteer firefighter	(ICD-10, C64–	Low	0	0 (NR)		cases; young age at end of
	trainers and paid	C68), incidence	Medium	1	0.50 (0.01-2.81)		follow-up.
[career] firefighters who trained at training facility for any period of time from human resources records, categorized into risk of low, medium, and high chronic exposure to smoke and other agents based on job assignment.		High	1	1.27 (0.03-7.07)			

Reference, location enrolment/follow- up period, study design	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments
Bates et al. (2001) New Zealand Enrolment, 1977 through June 1995/ follow-up, 1977– 1995 (mortality), 1977–1996 (incidence) Cohort	4305; the cohort comprises all male (4221) and female (84) firefighters (paid [career] and volunteer) employed as a career firefighter for ≥ 1 yr and who also worked as a career firefighter for ≥ 1 day between 1977 and 1995; all analyses limited to men due to small numbers of women Exposure assessment method: ever employed and categorical duration of employment (years) from employment records	Prostate, incidence Prostate, incidence Prostate, incidence Testis, incidence Testis, incidence Testis, incidence	0-10 yr 11-20 yr > 20 yr Trend-test <i>P</i> v. Follow-up per 1977-1996 1990-1996 Duration of pa 0-10 yr 11-20 yr > 20 yr Trend-test <i>P</i> v. Duration of pa 0-10 yr 11-20 yr > 20 yr Trend-test <i>P</i> v. Follow-up per	11 9 aid service (S 3 1 1 alue, 0.12 aid and volue 1 2 2 alue, 0.21 iod (SIR): 11 8 aid service (S 3 4 2 alue, 0.21 aid and volue 2 5 2 alue, 0.44 iod (SIR):	1.46 (0.3–4.3) 0.60 (0.0–3.3) 0.29 (0.0–1.6) nteer service (SIR): 1.09 (0.0–6.1) 1.90 (0.2–6.9) 0.38 (0.0–1.4) 1.55 (0.8–2.8) 2.97 (1.3–5.9) SIR): 1.55 (0.3–4.5) 3.51 (1.0–9.0) 4.14 (0.5–14.9) nteer service (SIR): 1.39 (0.2–5.0) 4.03 (1.3–9.4) 2.65 (0.3–9.6)	Age, calendar period	Exposure assessment critique: Satisfactory quality. Heterogeneity of direct firefighter exposure within job classification. May include urban [municipal] and rural firefighters. Strengths: ascertained both incidence and mortality outcomes. Limitations: little information on confounders; significant loss to follow-up.
		menuence	1977-1996	2	0.57 (0.1–2.1)		

Reference, location enrolment/follow- up period, study design	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments
Bates et al. (2001)		Urinary bladder,	Follow-up per	iod (SIR):		Age,	
(cont.)		incidence	1977-1996	5	1.14 (0.4–2.7)	calendar	
			1990-1996	2	0.74 (0.1-2.7)	period	
		Urinary bladder,	SMR:				
		incidence	Firefighters	2	2.73 (0.3-9.8)		
			vs male New				
			Zealand				
			population				

9/11, World Trade Center disaster, 11 September 2001; BMI, body mass index; CFHS, Career Firefighter Health Study; CI, confidence interval; FDNY, Fire Department of the City of New York; HR, hazard ratio; HWSE, healthy-worker survivor effect; ICD, International Classification of Diseases; IDR, incidence density ratio; JEM, job-exposure matrix; LRT, likelihood ratio test; mo, month; NR, not reported; RCS, restricted cubic splines; RIR, relative incidence ratio; SIR, standardized incidence ratio; SMR, standardized mortality ratio; SRR, standardized rate ratio; US, United States; vs, versus; WTC, World Trade Center; yr, year.

information on the risk of cancers of the genitourinary system (prostate, testis, and kidney, excluding the renal pelvis) and cancers of the urinary tract (urinary bladder and renal pelvis) (Marjerrison et al., 2022a, b). The cohort included mostly full-time firefighters employed between 1950 and 2019 with past or present employment in positions entailing active firefighting duties. The follow-up period for both cancer incidence and mortality analyses was from 1960 through 2018. With the general male population of Norway as the referent, the SIR for prostate cancer was moderately elevated (SIR, 1.18; 95% CI, 1.03–1.35; 214 cases), but the SMR (SMR, 1.07; 95% CI, 0.80-1.39; 54 deaths) was not. The SIR for cancer of the testis was elevated (SIR, 1.39; 95% CI, 0.81-2.22; 17 cases), as was the SIR for kidney cancer (SIR, 1.28; 95% CI, 0.86-1.84; 29 cases); however, the kidney cancer mortality rate was not elevated (SMR, 0.97; 95% CI, 0.46-1.78; 10 deaths). Incidence (SIR, 1.25; 95% CI, 0.97–1.58; 69 cases) and mortality (SMR, 1.14; 95% CI, 0.64-1.88; 15 deaths) for cancer of the urinary tract appeared to be moderately elevated compared with that in the general population. The only findings of note in analyses stratified by employment characteristics were: a raised SIR for prostate cancer for follow-up from 1995 onwards and for cases diagnosed in firefighters aged 50–69 years; a raised SIR for kidney cancer for follow-up between 1985 and 1994 and for cases diagnosed in firefighters aged \geq 70 years; and a raised SIR for urinary tract cancer in firefighters first employed before 1950, in firefighters \geq 40 years after first employment, and for cases diagnosed in firefighters aged \geq 70 years.

A cancer incidence study in a cohort of 8136 male firefighters in Sweden provided information on the risk of cancers of the urogenital system (cancers of the prostate, testis, kidney, and urinary bladder) (<u>Bigert et al., 2020</u>). Employment information was ascertained from national decennial censuses from 1960 through 1990, and cancer incidence was ascertained from the national cancer registry with follow-up from 1961 through 2009. The SIRs for cancers of the prostate (SIR, 1.06; 95% CI, 0.96–1.16; 444 cases), kidney (SIR, 0.84; 95% CI, 0.61–1.14; 41 cases), and bladder (SIR, 1.08; 95% CI, 0.89–1.31; 109 cases) were all close to the null, whereas the SIR for testicular cancer was less than expected (SIR, 0.39; 95% CI, 0.11–1.01; 4 cases) but based on few cases. For prostate cancer, there was no apparent relation with duration of employment (P = 0.13) or period of follow-up (no results from test of linear trend were provided). Results for duration of employment were not reported for other urogenital cancers.

A cancer incidence study in a cohort of 1080 male firefighters in Stockholm, Sweden, provided information on the risk of cancers of the urogenital system (Kullberg et al., 2018). Firefighters were identified through annual enrolment records from 15 fire stations and worked for ≥ 1 year between 1931 and 1983. This was an update to a previous study (<u>Tornling et al., 1994</u>) and added 26 years of cancer incidence follow-up from 1958 through 2012 in the Swedish Cancer Registry. For cancer incidence, only the more recent study is discussed here. With the male general population of Stockholm County as the referent, the overall SIR was less than one for cancer of the prostate (SIR, 0.68; 95% CI, 0.52–0.87; 60 cases). The overall SIR also appeared to be decreased for cancer of the kidney (SIR, 0.57; 95% CI, 0.21–1.23; 6 cases) and cancer of the urinary organs (SIR, 0.72; 95% CI, 0.41–1.17; 16 cases), but results were imprecise. The SIR for prostate cancer did not increase with age or employment duration and showed a significant but inconsistent decreasing trend with starting year of employment (P < 0.01).

The earlier study in the same cohort also investigated mortality in a slightly larger population of 1116 male firefighters (with follow-up from 1951 through 1986) and provided information on the risk of cancers of the prostate and kidney (<u>Tornling et al., 1994</u>). The overall SMRs for prostate cancer (SMR, 1.21; 95% CI, 0.66–2.02; 14 deaths) and kidney cancer (SMR, 1.10; 95% CI, 0.30–2.81; 4 cases) suggested modest elevations, although confidence intervals were wide.

A cancer incidence study in a cohort of 9061 male full-time, part-time, and volunteer firefighters provided information on the risk of cancers of the urogenital system (Petersen et al., 2018a). Cohort members were employed as firefighters at some time between 1964 and 2004, and cancer incidence follow-up was conducted in the Danish Cancer Registry from 1968 through 2014. The SIR for prostate cancer was slightly raised when the referent used was a random sample of Danish employees (SIR, 1.15; 95% CI, 1.00–1.32; 202 cases) or the general population (SIR, 1.10; 95% CI, 0.95-1.26; 202 cases), but not when the referent was the Danish military (SIR, 1.02; 95% CI, 0.88–1.17; 202 cases). The SIRs for cancer of the renal pelvis (10 cases) were 1.46, 1.59, and 1.35 with the general population, employed, and military population, respectively, as referent, whereas the SIR for cancer of the testis (47 cases) was raised only with the general population as referent (SIR, 1.30; 95% CI, 0.97-1.73). The SIRs for urinary bladder cancer (88 cases) were similar regardless of the comparison group: 1.09 (95%) CI, 0.89–1.35) with the general population; 1.11 (95% CI, 0.90–1.37) with a sample of employees; and 1.05 (95% CI, 0.86-1.30) with the military population. For incidence of cancers of the prostate, testis, and urinary bladder, there was no association with employment type, era of first employment, job function (e.g. regular, specialized), age at first employment, or employment duration, apart from a raised SIR for cancer of the urinary bladder when the age at first employment was < 25 years.

Cancer mortality was investigated in the same cohort of Danish firefighters as described above (<u>Petersen et al., 2018b</u>). An expanded study population of 11 775 male firefighters was followed for mortality in the Danish national death registry from 1970 through 2014. With the military as the referent, the SMR for prostate cancer was raised for part-time and volunteer firefighters (SMR, 1.89; 95% CI, 1.22–2.93; 20 deaths), but not for full-time firefighters (SMR, 0.66; 95% CI, 0.40–1.07; 16 deaths), and there was no relation between prostate cancer mortality and duration of employment for full-time firefighters. [The Working Group noted that the relatively strong association in part-time and volunteer firefighters, but not full-time firefighters, suggested the possibility of medical surveillance bias.]

A cancer incidence study in a cohort of 10 786 male firefighters from the FDNY exposed to the WTC disaster site and 8813 firefighters in the CFHS (which included firefighters from fire departments in Philadelphia, Chicago, and San Francisco) provided information on the risk of cancers of the prostate and kidney (Webber et al., 2021). Cancer incidence follow-up was conducted in several state cancer registries selected on the basis of residential history information and began on 11 September 2001 and ended in 2016. With the US male general population as the referent, overall SIRs for prostate cancer were increased in both the FDNY (SIR, 1.70; 95% CI, 1.53–1.88; 332 cases) and CFHS (SIR, 1.22; 95% CI, 1.11-1.35; 358 cases) cohorts. Because WTC-exposed FDNY firefighters undergo free and routine health-monitoring examinations, the authors noted concern about medical surveillance bias attributable to earlier detection since such screening is not widely available to the general population. After adjusting for potential medical surveillance bias by adding a 2-year lag to diagnosis dates for cases diagnosed within 6 months of a routine blood test, the SIR for prostate cancer in the FDNY cohort remained elevated (SIR, 1.55; 95% CI, 1.39–1.73). In internal comparison analyses, the risk of prostate cancer was increased in FDNY firefighters compared with CFHS firefighters (RR, 1.39; 95% CI, 1.19–1.63). This was also the case after adjustment for surveillance bias (RR, 1.28; 95% CI, 1.09–1.51). For kidney cancer, SIRs were close to one for the FDNY cohort (SIR, 0.93; 95% CI, 0.67-1.28; 39 cases) and slightly raised in the

CFHS cohort (SIR, 1.19; 95% CI, 0.90-1.56; 55 cases). After the adjustment for medical surveillance bias (for cases diagnosed within 6 months of a chest CT scan), the estimated SIR for kidney cancer for the FDNY cohort remained below one (SIR, 0.85; 95% CI, 0.61-1.19). The risk of kidney cancer appeared decreased in FDNY firefighters compared with CFHS firefighters in internal comparison analyses (RR, 0.82; 95% CI, 0.52–1.30). This was also the case after the adjustment for medical surveillance bias (RR, 0.75; 95% CI, 0.47-1.20). [The Working Group noted that this study was limited by a possible incompletely controlled effect of greater medical surveillance bias in FDNY firefighters than in CFHS firefighters or the US general population. This bias may be particularly influential for prostate cancer.]

An earlier study of cancer incidence in an overlapping cohort of 9853 FDNY male firefighters investigated the risk of cancers of the prostate, testis, kidney, and urinary bladder associated with exposure to the WTC disaster site. (Zeig-Owens et al., 2011). Cancer incidence follow-up was conducted in state cancer registries from 1996 through 2008. With the US male general population as the referent, the SIR for prostate cancer (adjusted for increased cancer surveillance) was raised when restricted to exposed person-time in firefighters (SIR, 1.21; 95% CI, 0.96-1.52; 73 cases) and was also raised when restricted to unexposed persontime in firefighters (SIR, 1.35; 95% CI, 1.01-1.81; 45 cases). The SIR restricted to exposed persontime was not raised for testicular cancer, kidney cancer, or bladder cancer. The equivalent SIR for unexposed person-time was 1.54 (95% CI, 0.85-2.78; 11 cases) for testicular cancer, 0.30 (95% CI, 0.07–1.18; \leq 5 cases) for kidney cancer, and 0.79 (95% CI, 0.36-1.76; 6 cases) for bladder cancer. The estimated SIR ratios (SIR for exposed person-time divided by the SIR for unexposed person-time) for kidney cancer and for bladder cancer were raised but imprecise. The estimated SIR ratios for prostate cancer (SIR ratio, 0.90; 95% CI, 0.62–1.30) and testicular cancer (SIR ratio, 0.56; 95% CI, 0.19–1.60) were less than one but also imprecise. [The Working Group noted that the SIR ratio is not a standard epidemiolog-ical effect measure. The results for prostate cancer may be influenced by medical surveillance bias in this cohort.]

A mortality study was conducted in a cohort of 29 992 male and female municipal career firefighters in the USA. The CFHS from San Francisco, Chicago, and Philadelphia provided information on the risk of cancers of the prostate, kidney, and bladder (Pinkerton et al., 2020). Mortality follow-up was conducted from 1950 through 2016. With the US general population as the referent, the SMR for prostate cancer was raised for the Chicago subcohort (SMR, 1.23; 95% CI, 1.05-1.42; 176 deaths), but not for the other subcohorts or the cohort overall. Also, the SMR for kidney cancer was raised for the whole cohort (SMR, 1.22; 95% CI, 1.00-1.47; 108 deaths) and for the Chicago subcohort (SMR, 1.57; 95% CI, 1.22-2.00; 66 deaths), but not for the other subcohorts. However, in internal regression analyses using fully adjusted models, there was no evidence of a positive association between number of exposed days, fire-runs, or fire-hours and kidney cancer or prostate cancer. However, for bladder cancer, the hazard ratio estimate for number of exposed days was elevated (HR, 1.23; 95% CI, 0.50-3.41) and crossed the null after adjustment for employment duration. [The Working Group noted that this may reflect healthy-worker survivor bias in the unadjusted point estimates for the number of exposed days.] In external comparison analyses, the SMRs for bladder cancer were not raised, either overall (SMR, 0.98; 95% CI, 0.80-1.18; 104 deaths) or for any of the municipal subcohorts. There were too few cases of cancer of other male genital organs to provide informative information for this cancer type.

An earlier study of a subset of 19 309 firefighters from the same CFHS cohort examined internal exposure-response associations for both mortality and incidence of cancer, with follow-up to the end of 2009 (Daniels et al., 2015). The methods were similar to those used in Pinkerton et al. (2020); however, the results of the present study were not adjusted for employment duration. There was no evidence of increasing incidence of bladder or prostate cancer with measures of exposure in any regression model, nor was there evidence of prostate cancer risk heterogeneity by time since exposure, age at exposure, or exposure period. [The Working Group noted that confounding by employment duration was evident for bladder cancer mortality in <u>Pinkerton et al. (2020)</u>, shifting the association from negative to positive when controlling for duration.]

An additional study in the CFHS cohort investigated cancer incidence in 29 993 municipal career firefighters and reported external and internal comparison analyses with follow-up to the end of 2009 (Daniels et al., 2014). The methods were similar to those used in the study by <u>Pinkerton et al. (2020)</u>. Cancer incidence follow-up was conducted in state cancer registries relevant to each fire department to the end of 2009, with start years varying between 1985 and 1988. Residential history information was used to select state registries for follow-up. With the US general population as the referent, the SIR for prostate cancer (including all primary cancers) among firefighters was not elevated (SIR, 1.03; 95% CI, 0.98-1.09; 1261 cases), and this was consistent for Caucasian [White] firefighters (SIR, 1.02; 95% CI, 0.96-1.08; 1167 cases), but not for "Other" race groups (SIR, 1.26; 95% CI, 1.02–1.54; 94 cases). For kidney cancer, the overall SIR was elevated (SIR, 1.27; 95% CI, 1.09-1.48; 166 cases). For bladder cancer, the overall SIR was modestly elevated (SIR, 1.12; 95% CI, 1.00-1.25; 316 cases). There was no excess incidence of testicular or other male genital cancers.

There was no strong evidence of heterogeneity among the elevated SIRs for the three fire departments for any of the cancers of the urogenital system (prostate cancer, P = 0.078; kidney cancer, P = 1.00; bladder cancer, P = 1.00). However, there was evidence of heterogeneity among results in different age groups for prostate cancer (P < 0.001) and bladder cancer (P = 0.002). The excess prostate and bladder cancer incidence was mostly among firefighters in younger age groups (17–64 years). The authors noted that the excess in prostate cancer incidence was limited to those aged 45-59 years, whereas for bladder cancer the pattern was less clear. [The Working Group noted that some evidence of risk heterogeneity by fire department suggested that differences in exposures or other risk factors (e.g. smoking habits) across departments may not have been adequately addressed. There was also a lack of data on many important potential confounders, particularly smoking. Heterogeneity by age at onset of prostate cancer may indicate a medical surveillance bias related to screening.]

A cancer incidence study in a cohort of 2447 male municipal firefighters from Seattle and Tacoma, USA, provided information on the risk of cancer of the prostate, bladder and kidney in comparison with the local male general population or with a cohort of male police officers from Washington state (Demers et al., 1994). Firefighters were employed for ≥ 1 year between 1944 and 1979, and cancer incidence follow-up was conducted from 1974 through 1989 in the regional SEER cancer registry using residential history information to reduce loss to follow-up. Duration of active-duty employment in direct firefighting positions was ascertained from employment records in the Seattle subcohort. With the general population as the referent, the SIR was raised for prostate cancer (SIR, 1.4; 95% CI, 1.1-1.7; 66 cases) and, more moderately, for bladder cancer (SIR, 1.2; 95% CI, 0.7-1.9; 18 cases), but not for kidney cancer (SIR, 0.5; 95% CI, 0.1–1.6; 3 cases). The SIR for prostate cancer

was raised among firefighters with 20-29 years of employment (SIR, 1.5; 95% CI, 1.1-2.0; 47 cases), but not for those with a shorter or longer duration of employment, although the number of cases in the other groups was small (all less than 10). The SIR for prostate cancer was also increased for the longest time since first employment group (SIR for \geq 30 years since first employment, 1.3; 95% CI, 1.0-1.7; 60 cases). The SIR for bladder cancer was not related to years of exposure or time since first employment. In internal comparisons using the police officers as the reference group, the IDR was not increased for prostate cancer or kidney cancer, but was increased for bladder cancer (IDR, 1.7; 95% CI, 0.7-4.3; 18 cases), although the result was imprecise.

An earlier study of 4401 male municipal firefighters, including firefighters from Portland, Oregon, and Seattle and Tacoma, Washington, reported findings for the risk of mortality from cancers of the prostate, kidney, bladder, and other organs of the urinary tract (Demers et al., 1992a). The mortality follow-up period was from 1945 to the end of 1989. Comparison of mortality rates was made with US White males in the general population and with a cohort of local male police officers. With the general population as the referent, the SMR for cancer of the prostate was elevated (SMR, 1.34; 95% CI; 0.90–1.91; 30 deaths). There were only two cases each of cancers of the kidney, bladder, and other urinary organs. Similar results were found when using police officers as the referent. There was no apparent relation between mortality risk and duration of exposed employment for prostate cancer; however, the SMR for prostate cancer was raised in firefighters with \geq 30 years since first employment (SMR, 1.42; 95% CI, 1.0-2.0; 30 deaths) and in those aged \geq 65 years (SMR, 1.46; 95% CI, 1.0-2.1; 26 deaths).

A mortality study in a cohort of 1867 White male municipal firefighters who worked for the City of Buffalo, USA, provided information on the risk of cancers of the prostate, kidney, and urinary bladder (Vena & Fiedler, 1987). Firefighters had been employed for ≥ 1 year between 1950 and 1979, and mortality follow-up was from 1950 through 1979. With the US White male general population as the referent, the mortality rate for bladder cancer was raised (SMR, 2.86; 95% CI, 1.30–5.40; 9 deaths), as was the mortality rate for kidney cancer (SMR, 1.30; 95% CI, 0.26-3.80; 3 deaths), although both estimates were imprecise. The mortality rate for prostate cancer (SMR, 0.71; 95% CI, 0.23-1.65; 5 deaths) was not raised. The SMR for bladder cancer was particularly elevated in firefighters with a long duration of employment (SMR for \geq 40 years duration, 5.71; 95% CI, [1.8-13.8]; 4 deaths) and latency period (SMR for 40-49 years latency, 4.53; 95% CI, [1.7-10.3]; 5 deaths; and SMR for \geq 50 years latency, 6.38; 95% CI, [1.5–16.3]; 3 deaths).

A mortality study in a cohort of 5414 male career firefighters in Toronto, Canada, who had worked for \geq 6 months between 1950 and 1989 provided information on the risk of cancers of the prostate, testis, kidney and ureter, and bladder (Aronson et al., 1994). Mortality follow-up was conducted in a national mortality database from 1950 through 1989. Compared with the male general population of Ontario, the cohort exhibited an excess of cancers of the prostate (SMR, 1.32; 95% CI, 0.76-2.15; 16 cases), testis (SMR, 2.52; 95% CI, 0.52-7.37; 3 cases), and bladder (SMR, 1.28; 95% CI, 0.51-2.63; 7 cases), although estimates were somewhat imprecise. There was a deficit in mortality from cancer of the kidney and ureter, but this result was based on only two cases. There was little evidence of a relation between the SMR and duration of employment, time since first employment, or age for cancers of the prostate and testis.

A mortality study of 3328 municipal firefighters in two cohorts from Calgary and Edmonton, Canada, provided information on the risk of cancers of the prostate, kidney and ureter, and urinary bladder (<u>Guidotti, 1993</u>). Firefighters were employed between 1927 and

1987, and mortality follow-up was conducted in both provincial and national sources from 1927 through 1987. Compared with the male general population of Alberta, firefighters had elevations in overall SMR for cancers of the kidney and ureter (SMR, 4.14; 95% CI, 1.66-8.53), prostate (SMR, 1.46; 95% CI, 0.63-2.88), and bladder (SMR, 3.16; 95% CI, 0.86-8.08), but estimates were based on few cases and were imprecise. The SMR for cancer of the kidney and ureter was raised for firefighters who entered the cohort before 1920 and for latencies of 40-49 years, but not for other years of entry or other latencies. The SMR for bladder cancer was raised for firefighters who entered the cohort before 1920 and for latencies of 40–49 years, although results were based on few cases. Other SMRs for cancer of the bladder and for cancer of the kidney and ureter for different cohort entry years and different latencies were not raised. [The Working Group noted that this study was limited by the low number of deaths for genitourinary system cancers, and confidence intervals were wide.]

A cancer incidence study in an entirely female cohort of 37 962 volunteer firefighters in Australia provided information on the risk of cancer of the kidney, urinary tract, cervix/uterus, and reproductive system (Glass et al., 2019). Cancer incidence follow-up was conducted in a national cancer registry from 1982 through 2010. Work history information describing the number and type of incidents attended was ascertained from fire agency personnel records. With the female general population of Australia as the referent, SIRs for all volunteer firefighters were equal to or below one for cancers of the urinary tract (SIR, 0.78; 95% CI, 0.49-1.17; 23 cases), kidney (SIR, 0.98; 95% CI, 0.59-1.53; 19 cases), and reproductive system, including cervix (SIR, 0.80; 95% CI, 0.64–0.98). Results were similar for volunteers who had attended incidents. Results from internal regression analyses were statistically imprecise for cancers of the urinary tract and kidney but indicated elevated rates of reproductive system

cancers among firefighters in the highest tertile of number of incidents attended compared with those who had never attended incidents. Trend tests across tertile categories did not suggest a relation between risk of any of these cancers and the total number of incidents attended overall, or all fire incidents, structure fire incidents, landscape fire incidents, or vehicle fire incidents.

Using the same methods as in the study of female firefighters, cancer incidence was also investigated in a parallel cohort of 163 094 male volunteer firefighters in Australia (Glass et al., 2017). With the male general population of Australia as the referent, SIRs among all volunteer firefighters were increased for male reproductive cancers combined (SIR, 1.08; 95% CI, 1.04–1.12; 2763 cases) and for prostate cancer (SIR, 1.12; 95% CI, 1.08-1.16; 2655 cases). In contrast, SIRs for urinary tract cancers combined, kidney cancer, and bladder cancer were all decreased (SIR for urinary tract cancers combined, 0.72; 95% CI, 0.65–0.81; 334 cases; SIR for kidney cancer, 0.82; 95% CI, 0.71-0.94, 196 cases; and SIR for bladder cancer, 0.60; 95% CI, 0.50-0.72, 117 cases). The results for volunteers who had attended incidents were similar to those for all volunteers. The SIRs for male reproductive cancers combined, prostate cancer, and testicular cancer decreased with period of first employment from before 1970 to more recent years, but there was no formal test for trend. In internal regression analyses, there was a trend of increasing incidence of male reproductive cancers combined and increasing duration of service among both volunteer firefighters (P = 0.01) and volunteer firefighters who attended incidents (P = 0.01). This trend was also observed for prostate and testicular cancers, but not for cancers of the urinary tract or kidney. The RIRs [equivalent to rate ratios] from the analysis of number and type of incidents attended indicated positive associations for cancers of the urinary tract and exposure to structure fire incidents, including kidney cancer and exposure to several incident types, although estimates were

imprecise. For prostate and testicular cancers, there was no apparent association between the number and type of incidents attended and risk.

Using similar methods as those in the two studies of volunteer firefighters, a cancer incidence study in a cohort of 30 057 paid full-time and part-time male firefighters in Australia provided information on the risk of cancers of the reproductive system, prostate, testis, kidney, urinary bladder, and urinary tract (Glass et al., 2016a). Included firefighters had worked between 1976 and 2003 and were primarily municipal or semi-metropolitan firefighters. Cancer incidence follow-up was conducted in a national registry to the end of 2010. With the Australian male general population as the referent, SIRs were increased for male reproductive cancers combined and prostate cancer in all firefighters (SIR for male reproductive cancers combined, 1.26; 95% CI, 1.15-1.37; 524 cases; and SIR for prostate cancer, 1.31; 95% CI, 1.19-1.43; 478 cases). The excess persisted with stratification among both full-time (SIR for male reproductive cancers combined, 1.20; 95% CI, 1.08-1.33; 357 cases; and SIR for prostate cancer, 1.23; 95% CI, 1.10-1.37; 325 cases) and part-time firefighters (SIR for male reproductive cancers combined, 1.41; 95% CI, 1.20-1.64; 167 cases; and SIR for prostate cancer, 1.51; 95% CI, 1.28-1.77; 153 cases). The SIR for cancer of the testis among full-time firefighters was also increased (SIR, 1.44; 95% CI, 0.98-2.05; 31 cases), but otherwise there was no increase in SIRs for cancers of the testis, urinary tract, kidney, or urinary bladder. In internal regression analyses, there was evidence of increasing risk of prostate cancer with increasing duration of employment. Duration results for cancer of the urinary tract and kidney cancer were too imprecise to make inferences. As for the duration of employment results, there was evidence of increasing risk of prostate cancer with an increasing number of total incidents attended among full-time firefighters. This association persisted for all types of attended incidents (all fire, structure fire,

landscape fire, and vehicle fire). There was little evidence of positive associations for cancers of the testis, urinary tract, or kidney, although the analyses were based on few cases. [The apparent increased risk of prostate cancer could be partly because of increased medical surveillance of firefighters, although the authors reported that the fire agencies employing the firefighters did not offer screening for prostate cancer.]

A study of cancer incidence was conducted in a cohort of 614 firefighters and trainers who attended a firefighter-training facility in Australia (Glass et al., 2016b). Three female firefighters were excluded from the analysis. Cancer incidence follow-up was conducted from 1982 through 2012. Participants were grouped into risk categories of low, medium, and high chronic exposure (to smoke and other hazardous agents) on the basis of job assignment. The male general population of Victoria was the reference group in external comparison analyses. None of the SIRs for male reproductive cancers, prostate cancer, or cancer of the urinary tract were raised for any of the assessed exposure categories (low, medium, and high chronic exposure risk based on job assignment), although estimates were imprecise because of low numbers of cases. The SIR for testicular cancer was raised among those with high chronic exposure risk, although the estimate was based on only two cases.

A mortality and cancer incidence study in a cohort of 4305 paid [career] and volunteer firefighters in New Zealand provided information on the risk of cancer of the prostate, testis, kidney, and urinary bladder (Bates et al., 2001). The cohort included 84 female firefighters who were excluded from the analysis. Included firefighters had worked for ≥ 1 year as a career firefighter and were employed for ≥ 1 day between 1977 and 1995. Follow-up for cancer mortality and incidence was conducted in a national data source to the end of 1995 (for mortality) or 1996 (for incidence). With the male general population of New Zealand as the referent, none of the SIRs for

cancer of the prostate (SIR, 1.08; 95% CI, 0.5–1.9; 11 cases), testis (SIR, 1.55; 95% CI, 0.8-2.8; 11 cases), kidney (SIR, 0.57; 95% CI, 0.1–2.1; 2 cases) or bladder (SIR, 1.14; 95% CI, 0.4-2.7; 5 cases) appeared raised, but results were generally based on few cases and were imprecise. Results were similar when restricted to recent calendar years (1990–1996) of diagnosis, except for testicular cancer, for which the SIR was raised (SIR, 2.97; 95% CI, 1.3-5.9; 8 cases). There was little evidence of a positive relation between the incidence of prostate or testicular cancer and either duration of career service or duration of total (career and volunteer) service, and estimates were based on few cases. Overall excess risk of bladder cancer incidence and mortality was suggested, but results were similarly imprecise.

2.2.2 Studies only reporting having ever worked as a firefighter

(a) Occupational cohort studies

Studies first described in Section 2.1.2(a) are described in less detail in the present section.

See Table S2.4 (Annex 2, Supplementary material for Section 2, Cancer in Humans, online only, available from: <u>https://publications.iarc.</u> <u>fr/615</u>).

Between 1978 and 2021, eight occupational cohort studies were published that reported on the risk of cancers of the urogenital system among firefighters compared with non-firefighting populations, using employment status as proxy for exposure (Musk et al., 1978; Eliopulos et al., 1984; Grimes et al., 1991; Giles et al., 1993; Deschamps et al., 1995; Ma et al., 2005, 2006; Amadeo et al., 2015). This section includes a description of the relevant findings of these studies on cancers of the reproductive and urinary systems. Most studies were longitudinal (cohort) designs reporting SMRs or SIRs; however, two early studies reported PMRs (Eliopulos et al., 1984; Grimes et al., 1991). [The Working Group noted that many of the strengths

and limitations described in Section 2.1.2(a) also apply to outcomes in the present section. In addition, cancers of the urogenital system as a group have favourable survival; therefore, mortality studies may largely underestimate cancer risk. The Working Group also noted a potential for upward bias in prostate cancer incidence studies (and downward bias in mortality studies) because of increased cancer screening among firefighters compared with the general population (e.g. Sritharan et al., 2018; Jakobsen et al., 2021). Risk estimates for cervical cancer may be similarly susceptible to surveillance bias. Finally, the Working Group noted that PMR studies rely on strong assumptions that may not be valid for firefighter cohorts.]

The mortality study of 10 829 male career firefighters in France (1979–2008) examined cancers of the kidney, bladder, and prostate in firefighters compared with the French general population (Amadeo et al., 2015). The study found no evidence of increased mortality from cancers of the urinary bladder (SMR, 0.73; 95% CI, 0.41–1.21; 15 deaths) or kidney (SMR, 0.63; 95% CI, 0.30–1.16; 10 deaths). Prostate cancer mortality was substantially below the expected rate (SMR, 0.54; 95% CI, 0.31–0.86; 17 deaths). [The Working Group noted that all-cause mortality was also below that expected, which implied a potential for strong bias from healthyworker selection.]

The mortality study of male career firefighters (n = 830) employed by the *Brigade des sapeurs-pompiers de Paris* (Paris Fire Brigade), France (1977–1990) examined all cancers of the urogenital system combined (ICD-9, 180–189) (Deschamps et al., 1995). Urogenital cancer mortality was above the expected rate (SMR, 3.29; 95% CI, 0.40–11.88); however, only two deaths were observed (one from bladder cancer and one from testicular cancer). [Findings based on two deaths from cancers of the urogenital system merit cautious interpretation because of small numbers. The Working Group noted that less than 4% of the cohort was deceased, and that deaths from all causes were about half that expected using reference population rates. Also, all deaths occurred at young ages (range, 31–63 years) indicating a relatively young cohort. Together, these findings implied a strong potential for downward bias in risk estimates from healthy-worker selection.]

The longitudinal studies of cancer mortality (<u>Ma et al., 2005</u>) and incidence (<u>Ma et al., 2006</u>) among career firefighters in Florida, USA, examined several cancers of the urogenital system in analyses stratified by sex. Among male firefighters, there were increased rates of bladder cancer incidence (SIR, 1.29; 95% CI, 1.01-1.62; 73 cases) and mortality (SMR, 1.79; 95% CI, 0.98-3.00; 14 cases) relative to state population rates. There was also an increased incidence of testicular cancer (SIR, 1.60; 95% CI, 1.20-2.09; 54 cases). In contrast, there was no evidence of increased risk for cancers of the kidney or prostate. Among female firefighters, there was evidence of a substantial excess incidence of cervical cancer (SIR, 5.24; 95% CI, 2.93-8.65; 15 cases). There was only one incident event each for bladder and kidney cancer among women; therefore, estimates were unstable. [The large study size and stratification by sex were notable strengths; however, risk estimates among female firefighters were substantively limited by small numbers for most types of cancer. Given improved access to health care among firefighters, differences in cancer screening may have contributed to excess cervical cancer among female firefighters compared with women in the reference group.]

Cancers of the urogenital system (ICD-9, 179–189) were analysed in the PMR study of firefighters in Honolulu, Hawaii, USA (1969–1988) (Grimes et al., 1991). The proportion of urogenital cancers combined was substantially greater than that in the state reference population (PMR, 2.28; 95% CI, 1.28–4.06; [11] deaths). The excess was attributable to prostate cancer (ICD-9, 185) (PMR, 2.61; 95% CI, 1.38–4.97; [9] deaths). The PMR for prostate cancer was elevated in both Caucasian [White] (PMR, 3.70; 95% CI, 1.71–8.02; [6] deaths) and Hawaiian firefighters (PMR, 3.35; 95% CI, 1.07–10.45; [3] deaths); however, few firefighter deaths were observed. The risk among other racial groups was not investigated. [Stratification by race was a notable study strength. The Working Group also noted the lack of standardization of PMRs by age or calendar period as a limitation.]

Cancers of the urogenital system (ICD-7, 177-181) were analysed as a group in a study in Boston, USA, in career firefighters (n = 5655) with \geq 3 years of service between 1915 and 1975 (Musk et al., 1978). The SMR for urogenital cancers was below the expected rate (SMR, 0.92; 95% CI, [0.71–1.17]; 64 deaths) when the state population was used as the referent. [The long follow-up and large study sizes were notable strengths. The Working Group also noted that all-cause mortality was modestly below the expected rate (SMR, 0.91; 95% CI, [0.87-0.94]), implying that there was a small potential for a strong downward bias from healthy-worker selection. Among study limitations, findings were available only for urogenital cancers combined, although numbers appeared to have been sufficient for stable estimates of risk by cancer type.]

The cohort study of cancer incidence in male career firefighters from Melbourne, Australia, (1980–1989) examined cancers of the urinary tract, prostate, and testis (<u>Giles et al., 1993</u>). Prostate cancer incidence was greater than expected, although few cases were observed (SIR, 2.09; 95% CI, 0.67–4.88; 5 cases). There was no evidence of increased risk of urinary tract or testicular cancers, with only four and two cases observed, respectively. [The Working Group noted the study had limited statistical power, given its small size and short observation period.]

The cohort study of male career firefighters (n = 990) employed by the Western Australian Fire Brigade between 1939 and 1978 examined proportionate mortality for cancers of the

urogenital system (Eliopulos et al., 1984). That study calculated an age- and calendar period-standardized PMR for urogenital cancers combined, with deaths among Western Australian men as the reference group. The PMR was not notably elevated (PMR, 1.08; 95% CI, 0.29-2.76); however, only four deaths were observed. [The average follow-up of 17 years was a notable strength of this study. The Working Group also noted that risk estimation was limited to a PMR for all urogenital cancers combined. All-cause mortality was below the expected rate (SMR, 0.80; 95% CI, 0.67–0.96; 116 deaths), implying strong downward bias from healthy-worker selection. The study had limited statistical power given its small size.]

(b) Population-based studies

With one exception (<u>Stang et al., 2003</u>), all studies were previously described in Section 2.1.2(b) and are described in less detail in the present section.

See Table S2.4 (Annex 2, Supplementary material for Section 2, Cancer in Humans, online only, available from: <u>https://publications.iarc.</u> <u>fr/615</u>).

Between 1990 and 2021, four population-based cohort studies were published that reported on the risk of cancers of the urogenital system among firefighters compared with non-firefighters, using employment status as a proxy for exposure (Pukkala et al., 2014; Harris et al., 2018; Zhao et al., 2020; Sritharan et al., 2022), and ten case-control or mortality surveillance studies reported risk estimates for cancers of the urogenital system and employment as a firefighter (Sama et al., 1990; Burnett et al., 1994; Ma et al., 1998; Stang et al., 2003; Bates, 2007; Kang et al., 2008; Tsai et al., 2015; Muegge et al., 2018; Lee et al., 2020; McClure et al., 2021).

Three cohort studies had designs that used national census data to describe the study group (Pukkala et al., 2014; Harris et al., 2018; Zhao et al., 2020). Another study cohort was enumerated using information from an occupational injury and disease claims database and linked to person and cancer registries (<u>Sritharan et al., 2022</u>).

One case-control study on testicular cancer in Germany assessed exposure information, including work history from questionnaires, and used population-based controls obtained from residence registers (Stang et al., 2003). Another eight case-control studies were eventonly designs where cancer cases and controls with other cancers were extracted from the same cancer registry (Sama et al., 1990; Bates, 2007; Kang et al., 2008; Tsai et al., 2015; Lee et al., 2020; McClure et al., 2021) or death certificate database (Ma et al., 1998; Muegge et al., 2018). The remaining study estimated PMRs using information from death certificates obtained from a national occupational mortality surveillance database (Burnett et al., 1994). [The Working Group noted that cancer diagnoses from death certificates may be less accurate than those from cancer registries and cover a smaller fraction of cases than cancer registries if the cancer does not have a high fatality rate.] Job titles in these case-control studies were extracted from the source registries from which study participants had been retrieved. [The Working Group noted that job titles were available for different proportions of cases than controls. Risk estimates may be biased if control cancers are also associated with firefighting or if the rates of the control cancers differ across occupations.] Two partly overlapping case-control studies were based on record linkage from firefighter employment records with incident cancer registry data (Lee et al., 2020; McClure et al., 2021). [The Working Group noted that the study strengths and limitations pertaining to design that were previously described for cancers of the respiratory system in Section 2.1.2(b) also apply to outcomes in the present section. Also, the limitations associated with cancer survival and surveillance bias for studies on cancers of the urogenital system, as

described in Section 2.2.2(a), also apply to these studies.]

Zhao et al. (2020) examined mortality patterns by occupation in a census-based cohort study in the male population of Spain (2001-2011). Age-adjusted MRRs were calculated to compare rates in firefighters with rates in all other occupations. There was elevated but imprecise mortality from cancers of the prostate (MRR, 1.26; 95% CI, 0.67–2.36; 10 deaths) and kidney (MRR, 1.18; 95% CI, 0.57-2.44; 8 deaths), and no evidence of increased mortality from bladder cancer (MRR, 0.62; 95% CI, 0.32-1.17; 10 deaths). The rate ratio for cancer of the renal pelvis was unstable given that there was only one observed death. [The Working Group noted limited statistical power because of few deaths from urogenital cancers among firefighters over the relatively short observation period (10 years).]

Testicular or extra-gonadal germ cell tumour cases (n = 269), histologically confirmed and diagnosed between 1995 and 1997 in participants aged 15-69 years, were examined in a population-based cancer registry study in five regions in Germany (Stang et al., 2003). Control participants from the same regions were randomly selected from residence registries. For ages 15-34 years, each case was matched with two potential controls on 5-year age groups. Similarly, for ages 35-69 years, each case was matched with four potential controls. The overall response proportions were 78% for cases and 57% for controls [The Working Group noted the difference in response proportions for cases and controls, which could have led to selection bias if case firefighters were more willing to participate than control firefighters.] Information on exposures, including detailed work history, was collected primarily by personal interview. Based on four cases, the overall OR (adjusted for history of cryptorchidism) was 4.5 (95% CI, 0.7-31.9). Inclusion of a 5-year lag period or a minimum of 10 years work history as a firefighter decreased the ORs marginally. [The Working Group noted

that this study was based on few cases (1.5%) and controls (0.4%) classified as firefighters. There was potential for selection and recall bias, and exposure assessment quality was rated as minimal.]

The large, census-based cohort study (NOCCA) of cancer incidence in Nordic male career firefighters (1961-2005) reported a modest but relatively precise excess incidence of prostate cancer in the full cohort (SIR, 1.13; 95% CI, 1.05–1.22; 660 cases) (Pukkala et al., 2014). Excess prostate cancer was observed in multiple countries, primarily those with the largest case numbers (SIR for Finland, 1.21, 143 cases; SIR for Norway, 1.16, 137 cases; and SIR for Sweden, 1.11, 347 cases; compared with SIR for Denmark, 1.03, 27 cases; and SIR for Iceland, 0.90, 6 cases). Prostate cancer risk compared with that in the general population was greatest in the youngest age group (SIR for age 30-49 years, 2.59; 95% CI, 1.34-4.52; 12 cases) and within the most recent follow-up period (SIR for 1991–2005, 1.15; 95% CI, 1.05-1.26, 495 cases). The study yielded little evidence of increased risk of cancers of the kidney, bladder, or testis. [The Working Group noted that the pattern of excess prostate cancer risk at younger ages and later periods of observation implied a potential for surveillance bias from improved medical screening. For example, prostate cancer risk was greatest in the period 1991-2005, which coincides with the onset of prostate-specific antigen testing. The Working Group also noted that risk evaluations by country, age, or calendar-period were limited to a select group of cancer sites, precluding detailed evaluation of other urogenital cancers.]

A cohort study of worker compensation claimants in Ontario, Canada, compared site-specific cancer incidence in firefighters (n = 13 642) to that in police and all other occupations, using Cox proportional hazards regression models controlling for age at start of follow-up, birth year, and sex (Sritharan et al., 2022). Elevated risk was observed for cancers of the prostate (HR, 1.43; 95% CI, 1.31–1.57; 492 cases), testis (HR, 2.56;

95% CI, 1.78-3.68; 30 cases), and kidney (HR, 1.52; 95% CI, 1.24-1.87; 94 cases) among firefighters compared with all other workers. Higher risk of cancer of the testis was also observed in firefighters compared with police (HR, 1.96; 95% CI, 1.19–3.23). With police as the referent, firefighters had an elevated incidence of kidney cancer (HR, 1.31; 95% CI, 0.98-1.75). There was no evidence of increased risk of prostate cancer in firefighters compared with police (HR, 0.99; 95% CI, 0.88-1.12). There was no evidence of increased risk of cancer of the bladder in either comparison. [The Working Group noted as study strengths the large study size, access to tumour incidence information, and use of other workers and police as referents. Risk estimates might be biased in either direction given that the type of claims used to identify the cohort may differ by occupation.]

The census-based incidence study of male firefighters (n = 4535) in the CanCHEC (1991– 2010) cohort found a higher prostate cancer risk in firefighters than in other male workers (HR, 1.18; 95% CI, 1.01-1.37; 170 cases) in a model adjusting for age group, region, and education level (<u>Harris et al., 2018</u>). Restricting to prostate cancer diagnosed before age 50 years resulted in a comparable estimate (HR, 1.18; 95% CI, 0.38–3.67; 10 cases). There was also evidence of excess testicular and kidney cancer, although the confidence intervals were wide (HR for testicular cancer, 1.80; 95% CI, 0.85-3.78; 10 cases; HR for kidney cancer, 1.14; 95% CI, 0.74–1.74; 25 cases). No excess incidence was observed for bladder cancer (HR, 0.89; 95% CI, 0.60-1.33; 25 cases). [The Working Group noted in this study the absence of higher risk of early-onset prostate cancer among firefighters, in contrast to findings in other studies (e.g. <u>Pukkala et al., 2014; Barry</u> et al., 2017). This provided some evidence against a strong surveillance bias in prostate cancer risks. Still, given only weak effects, the Working Group could not rule out cancer screening as a plausible

explanation for the observed excess in prostate cancer.]

Site-specific ORs for various incident cancers of both male and female firefighters from Florida, USA, were reported (Lee et al., 2020). Firefighter state certification records were linked with the state cancer registry database. ORs for cancer in female firefighters were reported for cervix uteri (0.41; 95% CI, 0.15-1.12), urinary bladder (1.88; 95% CI, 0.47-7.59) and kidney and renal pelvis (0.59; 95% CI, 0.15-2.36). For the male firefighters, the ORs for cancers of the prostate and testis were increased: OR for prostate, 1.36 (95% CI, 1.27–1.46); and OR for testis, 1.66 (95%) CI, 1.34–2.07). This was not the case for cancer of the penis: 0.79 (95% CI, 0.33–1.90). The ORs for cancers of the urinary bladder (OR, 0.91; 95% CI, 0.75-1.10) and for kidney and renal pelvis (OR, 1.06; 95% CI, 0.90-1.24) were close to the null. Cancers were stratified by stage at diagnosis for men. Risk was somewhat higher for late-stage cancer than for early-stage cancer of the prostate (OR, 1.42; 95% CI, 1.19–1.68; and OR, 1.13; 95% CI, 1.03–1.23; respectively) and for the testis (OR, 1.69; 95% CI, 1.12-2.54; and OR, 1.39; 95% CI, 1.07–1.82; respectively). Finally, ORs for men were stratified by age at diagnosis. The most notable differences were seen for cancers of the prostate – OR for those aged < 50 years, 1.88 (95% CI, 1.49-2.36) versus OR for those aged \geq 50 years, 1.36 (95% CI, 1.26–1.47) – and the urinary bladder – OR for those aged < 50 years, 1.13 (95% CI, 0.72-1.79) versus OR for those aged \geq 50 years, 0.87; 95% CI, 0.71–1.08). [The Working Group noted small numbers for female firefighters and, in particular, the potential for surveillance bias for prostate cancer if firefighters were screened more often for prostate cancer than were the reference occupations.]

McClure et al. (2021) extended the Florida cancer registry-based case-control study of Lee et al. (2020) to assess whether results differed between two different methods of identifying firefighter status. For cancers of the urinary system [not defined], the OR based on state certification records (OR, 1.00; 95% CI, 0.88–1.13; 267 cases) was similar to that based on cancer registry records (OR, 1.01; 95% CI, 0.85–1.20; 138 cases). For cancers of the genital system, the OR was 1.37 (95% CI, 1.28–1.47) based on 1228 state certification cases and 1.10 (95% CI, 0.99–1.22) based on 534 cases from cancer registry job records. [The Working Group noted that the number of available firefighters was different for the two data sources, but results differed only slightly for genital tumours in this example. The cancer groupings were broad and of minimal utility in examining risks for individual genitourinary tumour types.]

Cancer mortality was examined in firefighters compared with non-firefighters in Indiana, USA, for the period 1985–2013 (<u>Muegge et al., 2018</u>). An increased OR for kidney cancer (1.84; 95% CI, 1.17–2.83) was observed. [The Working Group noted as limitations the lack of information on exposure and potential confounders, as well as the event-only death certificate approach, which includes normally less-accurate cancer diagnoses.]

Risk of incident cancer in male firefighters was evaluated by race, using the California Cancer Registry, USA, in 1988-2007 (Tsai et al., 2015). For prostate cancer, the ORs were increased for both White and non-White firefighters: 1.40 (95% CI, 1.19–1.64) and 2.42 (95% CI, 1.53–3.84), respectively. For cancers of testis, urinary bladder, and kidney, the ORs were notably increased only for non-White firefighters: 3.73 (95% CI, 1.26-11.02), 2.37 (95% CI, 1.05-5.33), and 2.59 (95% CI, 1.44–4.80), respectively. <u>Bates (2007)</u> conducted a similar study with the California Cancer Registry, 1988-2003, but these data were included in the study conducted later by Tsai et al. (2015) with data from 1988-2007. [The Working Group noted the high proportion of cancer cases lacking information on occupation in the registry as a limitation.]

Data from the cancer registry-based casecontrol study in Massachusetts, USA, for the period 1982 to 1986 (Sama et al., 1990) were investigated over an extended period between 1987 and 2003 for White men employed as a firefighter, a police officer, or other occupation (Kang et al., 2008). Using police as the reference group, the SMBORs (adjusted for age and smoking) for cancers of the prostate, testis, kidney, and urinary bladder were 0.98 (95% CI, 0.78-1.23), 1.53 (95% CI, 0.75–3.14), 1.34 (95% CI, 0.90–2.01), and 1.22 (95% CI, 0.89-1.69), respectively. Results using all other occupations as the referent were not notably changed, except for kidney cancer (SMBOR, 1.01 (95% CI, 0.74-1.38). [The Working Group noted that a large proportion of the study population lacked occupational information.]

A registry-based case-control study (1982-1986) in Massachusetts, USA, compared risks in men with an occupation as firefighter to other occupations, including police (Sama et al., 1990). Increased SMBOR (adjusted for age alone) for urinary bladder cancer was observed both when police were used as the referent (SMBOR, 2.11; 95% CI, 1.07-1.14; 26 cases) and when the reference group was any non-firefighting job title (SMBOR, 1.59; 95% CI, 1.02-2.50). Stratified by age group [18–54, 55–74, and \geq 75 years] the SMBORs were 1.25 (95% CI, 0.26-5.88), 2.19 (95% CI, 0.99-4.84), and 4.40 (95% CI, 0.42-46.26). [The Working Group noted as a key limitation of this study the absence of occupational information for about the half of the cancer registry population.]

A death certificate-based study of firefighters from 24 US states reported MORs for Black and White men (Ma et al., 1998). For Black firefighters, the MORs for cancers of the prostate and urinary bladder were 1.9 (95% CI, 1.2–3.2; 16 cases) and 1.3 (95% CI, NR; 1 case), respectively. For White firefighters, the MORs for cancers of the prostate and urinary bladder were 1.2 (95% CI, 1.0–1.3; 189 cases) and 1.2 (95% CI, 0.9–1.6; 48 cases), respectively. In addition, White men had MORs for cancers of the testis, kidney, and ureter of 0.6 (95% CI, NR; 1 case), 1.3 (95% CI, 1.0–1.7; 49 cases) and 1.0 (95% CI, NR; 1 case), respectively. [The Working Group noted limited numbers of site-specific cancers, which made results imprecise.]

Burnett et al. (1994) investigated proportionate mortality in White male firefighters compared with the general population in the USA (1984–1990). Mortality for kidney cancer (ICD-9, 189.0-189.2) was above the expected rate for all firefighter deaths (PMR, 1.44; 95%) CI, 1.08–1.89; 53 deaths) and for deaths before age 65 years (PMR, 1.41; 95% CI, 0.90-2.10; 24 deaths). Mortality for bladder cancer (ICD-9, 188) was at the expected rate for all firefighters and deaths before age 65 years. [The Working Group noted that in the absence of rate denominator data, PMRs rely on strong assumptions that may not be valid for firefighter cohorts; therefore, little weight was generally given to these studies for causal inference.]

2.3 Cancers of lymphatic and haematopoietic tissues

2.3.1 Studies reporting occupational characteristics of firefighters

See <u>Table 2.5</u>.

Studies first described in Section 2.1.1 are described in less detail in the present section.

The Working Group identified 24 occupational and population-based cohort studies that had investigated the relationship between occupational exposure as a firefighter and cancers of lymphatic and haematopoietic tissues (Feuer & Rosenman, 1986; Demers et al., 1992a, 1994; Guidotti, 1993; Aronson et al., 1994; Tornling et al., 1994; Zeig-Owens et al., 2011; Ahn et al., 2012; Daniels et al., 2014, 2015; Ahn & Jeong, 2015; Glass et al., 2016a, b, 2017, 2019; Moir et al., 2016; Kullberg et al., 2018; Petersen et al., 2018a, b; Bigert et al., 2020; Pinkerton et al., 2020; Webber et al., 2021; Marjerrison et al., 2022a, b). Of these studies, two were from Asia, seven were from Europe, four were from Oceania, and eleven were from North America. Three other studies are not described in detail as they largely represent earlier follow-up periods of included studies (<u>Heyer et al., 1990; Beaumont et al., 1991;</u> Baris et al., 2001).

The grouping of cancers of the lymphatic and haematopoietic tissues includes the following cancer sites: NHL, Hodgkin lymphoma, leukaemia, multiple myeloma, other lymphatic or haematopoietic cancer, and, less commonly, lymphosarcoma/reticulosarcoma and myelodysplastic syndrome. A challenge of evaluating evidence for this group of cancers is that cancer site classifications, particularly for NHL, have changed over time. For that reason, the relevant ICD revision and codes have been provided, when available. [Myelodysplastic syndrome was reportable only in more recent years.]

In the Republic of Korea, a mortality study in a cohort of 33 442 male professional [career] emergency responders, of whom 29453 (88%) were firefighters, provided information on the risk of cancers of lymphatic and haematopoietic tissues (Ahn & Jeong, 2015). Emergency responders had been employed between 1980 and 2007, and mortality follow-up occurred between 1992 to 2007. During follow-up, there were 15 deaths from all lymphatic and haematopoietic malignancies and 6 deaths from leukaemia among firefighters [ICD codes were not provided in the 2015 publication but, assuming the same coding as the 2012 paper from the same cohort, and on the basis of ICD-10, all lymphatic and haematopoietic malignancies were coded as C81-C96, and leukaemia as C91-C95]. The SMR for all lymphatic and haematopoietic malignancies was 0.91 (95% CI, 0.51–1.50) with the male population of the Republic of Korea as the referent. The SMRs for < 10 years, 10 to < 20 years, and \geq 20 years of employment were 0.80 (95% CI, 0.21-2.04), 0.96 (95% CI, 0.35-2.08) and 0.96 (95% CI, 0.31-2.23),

Table 2.5 Cohort studies reporting occupational characteristics of firefighters and cancers of lymphatic and haematopoietic tissues

Reference, location enrolment/ follow-up period, study design	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments
Ahn & Jeong (2015) Republic of Korea Enrolment, 1980–2007/ follow-up, 1992–2007 Cohort	33 442 men employed as emergency responders for ≥ 1 mo in 1980–2007 with (29 453) and without (3989) firefighting experience and not deceased in 1991 Exposure assessment method: ever employed and categorical duration of employment (years) as first- or second-line firefighters and non-firefighters from employment records	Lymphatic and haematopoietic, mortality Lymphatic and haematopoietic, mortality Leukaemia, mortality Leukaemia, mortality	(SMR): 1 mo to < 10 yr 10 to < 20 yr \geq 20 yr Total Duration of firef (RR): < 10 yr (including non-firefighters) 10 to < 20 yr \geq 20 yr Duration of firef (SMR): 1 mo to < 10 yr 10 to < 20 yr \geq 20 yr Total	4 6 5 15 fighting emj 5 6 5 fighting emj 1 3 2 6	Ployment, 1-yr lag 0.80 (0.21–2.04) 0.96 (0.35–2.08) 0.96 (0.31–2.23) 0.91 (0.51–1.50) Ployment, 1-yr lag 1 1.22 (0.36–4.11) 3.26 (0.67–15.8) Ployment, 1-yr lag 0.33 (0.00–1.86) 0.83 (0.17–2.42) 0.81 (0.09–2.91) 0.66 (0.24–1.44) Ployment, 1-yr lag 1 6.54 (0.50–85.12)	Age, calendar period	Exposure assessment critique: Satisfactory quality. Heterogeneity of direct firefighter exposure within job title. May include both municipal and rural firefighters. Strengths: employment duration and internal comparison limits healthy-worker bias; only professional [career] firefighters were included in the cohort. Limitations: small number of deaths from lymphatic and haematopoietic cancers; no information on personal characteristics or confounders; follow-up time was reasonably short; cohort members were fairly young; no direct measure of exposure.
			10 to < 20 yr $\ge 20 \text{ yr}$	2	6.54 (0.50-85.12) 83.65 (2.21-3166.29)		

Reference, location enrolment/ follow-up period, study design	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments
hn et al. (2012) epublic of 33 416 men employed as emergency responders for	Lymphatic and haematopoietic	Duration of firef (SIR):	ighting emp	ployment, 1-yr lag	Age, calendar	<i>Exposure assessment</i> <i>critique</i> : Satisfactory	
Korea	ea ≥ 1 mo between 1980 and 2007 with (29 438) and	(ICD-10, C81– C96), incidence	1 mo to < 10 yr	13	1.59 (0.84-2.71)	period	quality. Heterogeneity
nrolment,			$\geq 10 \text{ yr}$	19	1.19 (0.72–1.86)		of direct firefighter
980-2007/	without (3978) firefighting		Total	32	1.33 (0.91–1.87)		exposure within job title. May include rural and
ollow-up,	experience and not deceased in 1995	Lymphatic and	SRR:	02	100 (01)1 110/)		
Cohort Exposure assessment method: ever employed and categorical duration of employment (years) as first- or second-line firefighter and non-firefighters from	haematopoietic (ICD-10, C81–	Non- firefighters	4	1		municipal firefighters. <i>Strengths</i> : employment duration and internal comparison limits healthy-worker bias; only professional [career] firefighters were included in the cohort.	
	C96), incidence	Ever employed as a firefighter	32	0.81 (0.28–2.33)			
	NHL (ICD- 10, C82–C85),	Duration of firef (SIR):	ighting emp	ployment, 1-yr lag			
	employment records	incidence	1 mo to < 10 yr	6	1.68 (0.62–3.67)		in the cohort. <i>Limitations</i> : no information on personal characteristics or confounders (except the firefighter cohort had a lower BMI and smoked less than the comparison
			$\geq 10 \text{ yr}$	12	1.69 (0.87–2.96)		
			Total	18	1.69 (1.01–2.67)		
		NHL (ICD-	SRR:				
		10, C82-C85), incidence	Non- firefighters	3	1		
			Ever employed as a firefighter	18	0.52 (0.15–1.78)		population for the SIR analysis); follow-up time
		Leukaemia (ICD- 10, C91–C95),	Duration of firef (SIR):	ighting emp	ployment, 1-yr lag		was reasonably short; cohort members were fair
		incidence	1 mo to < 10 yr	7	1.60 (0.64–3.31)		young; no direct measure of exposure.
			≥ 10 yr	6	0.75 (0.27–1.62)		oi exposure.
		Leukaemia (ICD-	Total SRR:	13	1.05 (0.56–1.79)		
		10, C91-C95), incidence	Non- firefighters	1	1		
			Ever employed as a firefighter	13	1.68 (0.22–13.06)		

Reference, location enrolment/ follow-up period, study design	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments
<u>Marjerrison et al.</u> (<u>2022a)</u> Norway Enrolment,	3881 male professional [career] firefighters (most were full-time) employed in positions entailing active	Hodgkin lymphoma (ICD-10, C81), incidence	SIR: Firefighters	2	0.53 (0.06–1.91)	Age, calendar year	<i>Exposure assessment</i> <i>critique</i> : Satisfactory quality. Included firefighters with current
1950–2019/	firefighting at any of 15 fire	Hodgkin	Year of first em	nlovment (SI	(B)•		or previous positions
follow-up,	departments between 1950	en 1950 lymphoma (ICD-10, C81),	Pre-1950	0	0 (0.00-3.75)		entailing active firefightin
1960-2018	and 2019		1950–1969	2	2.29 (0.28-8.28)		duties but no assessment of length of time in active firefighting positions. Ma
Cohort	Exposure assessment method: employment history	incidence	1970 or after	0	0 (0.00-1.42)		
from personnel records	Hodgkin lymphoma	Time since firs	-			include municipal and	
		< 20 yr	0	0 (0.00–1.70)		rural firefighters.	
		(ICD-10, C81), incidence	20–39 yr	0	0 (0.00-2.19)		Strengths: long length
			\geq 40 yr	2	3.05 (0.37-11.0)		of follow-up (mean, 28 yr); near complete ascertainment of both
		Hodgkin	Duration of em	ployment (S	IR):		
		lymphoma	< 10 yr	0	0 (0.00-2.46)		ascertainment of both cancer incidence and
		(ICD-10, C81),	10–19 yr	0	0 (0.00-3.63)		mortality; analyses by
		incidence	20–29 yr	0	0 (0.00-3.64)		duration and timing of
			≥ 30 yr	2	2.17 (0.26-7.85)		employment.
		NHL (ICD-10,	SIR:				Limitations: probable
		C82–C86, C96), incidence	Firefighters	26	1.17 (0.76–1.71)		healthy-worker effect; low number of cases for some
		NHL (ICD-10,	Year of first em	ployment (SI	(R):		cancer sites; no data on potential confounders ap
		C82–C86, C96),	Pre-1950	6	1.14 (0.42–2.47)		from age, sex, and calend
	incidence	1950-1969	9	1.20 (0.55-2.27)		time.	
			1970 or after	11	1.17 (0.58–2.09)		
		NHL (ICD-10,	Time since firs	t employmen			
		C82–C86, C96),	< 20 yr	4	1.30 (0.35-3.32)		
		incidence	20–39 yr	14	1.50 (0.82–2.52)		
			≥ 40 yr	8	0.81 (0.35-1.61)		

Table 2.5 (co	ntinued)						
Reference, location enrolment/ follow-up period, study design	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments
Marjerrison et al.		NHL (ICD-10,	Duration of emp	ployment (S	IR):	Age,	
<u>(2022a)</u>		C82–C86, C96),	< 10 yr	2	0.72 (0.09-2.61)	calendar	
(cont.)		incidence	10–19 yr	4	1.28 (0.35-3.27)	year	
			20–29 yr	10	1.68 (0.81-3.10)		
			≥ 30 yr	10	0.96 (0.46-1.77)		
		Multiple	SIR:				
		myeloma (ICD-10, C90), incidence	Firefighters	9	0.79 (0.36–1.51)		
		Multiple	Year of first emp	oloyment (SI	(R):		
		myeloma	Pre-1950	5	1.21 (0.39–2.82)		
		(ICD-10, C90),	1950-1969	1	0.25 (0.01-1.40)		
		incidence	1970 or after	3	0.93 (0.19-2.71)		
		Multiple	Time since first	employmen	t (SIR):		
		myeloma	< 20 yr	0	0 (0.00-4.31)		
		(ICD-10, C90),	20-39 yr	4	0.88 (0.24-2.26)		
		incidence	≥ 40 yr	5	0.82 (0.27-1.91)		
		Multiple	Duration of emp	ployment (Sl	IR):		
		myeloma	< 10 yr	1	1.07 (0.03-5.97)		
		(ICD-10, C90), incidence	10–19 yr	0	0 (0.00-2.47)		
		incidence	20–29 yr	4	1.32 (0.36–3.39)		
			≥ 30 yr	4	0.65 (0.18–1.66)		
		Leukaemia (ICD- 10, C91–C95),	SIR: Firefighters	14	0.83 (0.46-1.40)		
		incidence	0				

Table 2.5 (co	ntinued)						
Reference, location enrolment/ follow-up period, study design	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments
<u>Marjerrison et al.</u> (2022a) (cont.)		Leukaemia (ICD- 10, C91–C95), incidence Leukaemia (ICD- 10, C91–C95), incidence Leukaemia (ICD- 10, C91–C95), incidence	Year of first emp Pre-1950 1950-1969 1970 or after Time since first < 20 yr 20-39 yr $\ge 40 \text{ yr}$ Duration of emp < 10 yr	5 4 5 employmen 1 6 7	0.91 (0.29–2.11) 0.72 (0.20–1.84) 0.88 (0.29–2.05) t (SIR): 0.48 (0.01–2.70) 0.92 (0.34–1.99) 0.86 (0.34–1.77) IR): 1.02 (0.12–3.70)	Age, calendar year	
		menerice	10–19 yr 20–29 yr ≥ 30 yr	2 0 10	0.94 (0.11–3.38) 0 (0.00–0.69) 1.20 (0.57–2.20)		
Marjerrison et al. (2022b) Norway Enrolment,	3881 male professional [career] firefighters (most were full-time) employed in positions entailing active	Hodgkin lymphoma (ICD-10, C81), mortality	SMR: Firefighters	0	0 (0.00-2.31)	Age, calendar year	<i>Exposure assessment</i> <i>critique</i> : Satisfactory quality. Included firefighters with current
1950–2019/ follow-up, 1960–2018 Cohort	firefighting at any of 15 fire departments between 1950 and 2019 Exposure assessment method: employment history from personnel records	Hodgkin lymphoma (ICD-10, C81), incidence Hodgkin lymphoma (ICD-10, C81), mortality Hodgkin lymphoma (ICD-10, C81), incidence	Period of follow 1984 or before 1985–1994 1995 or after Period of follow 1984 or before 1985–1994 1995 or after Age at diagnosis ≤ 49 yr 50–69 yr ≥ 70 yr	0 0 < 5 y-up (SMR): 0 0 0	0 (0.00-2.40) 0 (0.00-5.32) 1.01 (0.12-3.67) 0 (0.00-3.80) 0 (0.00-15.7) 0 (0.00-9.40) 0 (0.00-1.51) 1.49 (0.18-5.37) 0 (0.00-7.98)		or previous positions entailing active firefighting duties but no assessment of length of time in active firefighting positions. May include municipal and rural firefighters. <i>Strengths</i> : long length of follow-up (mean, 28 yr); near complete ascertainment of both cancer incidence and mortality; analyses by duration and timing of employment.

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Reference, location enrolment/ follow-up period, study design	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments
Marjerrison et al.		Hodgkin	Age at diagnosis	s (SMR):		Age,	Limitations: probable
(2022b) (cont.)		lymphoma	≤ 49 yr	0	0 (0.00-6.39)	calendar	healthy-worker effect; low
		(ICD-10, C81),	50-69 yr	0	0 (0.00-5.70)	year	number of cases for some
		mortality	≥ 70 yr	0	0 (0.00–9.89)		cancer sites; no data on
		NHL (ICD-10,	SMR:				potential confounders apar
		C82–C86, C96), mortality	Firefighters	9	0.96 (0.44–1.83)		from age, sex, and calendar time.
		NHL (ICD-10,	Period of follow	-up (SIR):			
		C82–C86, C96),	1984 or before	< 5	1.03 (0.21-3.01)		
		incidence	1985-1994	7	2.00 (0.81-4.13)		
			1995 or after	16	1.01 (0.58-1.64)		
		NHL (ICD-10,	Period of follow	-up (SMR):			
		C82–C86, C96),	1984 or before	< 5	0.59 (0.02-3.31)		
		incidence	1985-1994	< 5	1.01 (0.12-3.66)		
			1995 or after	6	1.05 (0.39–2.29)		
		NHL (ICD-10,	Age at diagnosis	s (SIR):			
		C82–C86, C96),	\leq 49 yr	6	1.60 (0.59–3.48)		
		incidence	50-69 yr	13	1.22 (0.65–2.09)		
			≥ 70 yr	7	0.89 (0.36–1.84)		
		NHL (ICD-10,	Age at diagnosis	s (SMR):			
		C82–C86, C96),	\leq 49 yr	0	0 (0.00-2.92)		
		mortality	50-69 yr	5	1.35 (0.44–3.14)		
			≥ 70 yr	< 5	0.87 (0.24-2.22)		

Table 2 5 (a **പ**)

Table 2.5 (co	ntinued)						
Reference, location enrolment/ follow-up period, study design	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments
Marjerrison et al. (2022b) (cont.)		Multiple myeloma (ICD-10, C90), mortality	SMR: Firefighters	7	0.97 (0.39–2.00)	Age, calendar year	
		Multiple myeloma (ICD-10, C90), incidence	Period of follow 1984 or before 1985–1994 1995 or after	-up (SIR): < 5 < 5 < 5	1.39 (0.29–4.07) 1.03 (0.12–3.72) 0.55 (0.15–1.42)		
		Multiple myeloma (ICD-10, C90), mortality	Period of follow 1984 or before 1985–1994 1995 or after		1.36 (0.17–4.93) 2.05 (0.42–5.99)		
		Multiple myeloma (ICD-10, C90), incidence	Age at diagnosis $\leq 49 \text{ yr}$ 50-69 yr $\geq 70 \text{ yr}$		0.47 (0.06–1.69) 0 (0.00–3.81) 0.93 (0.30–2.16) 0.78 (0.21–1.99)		
		Multiple myeloma (ICD-10, C90), mortality	 ∠ 70 yr Age at diagnosis ≤ 49 yr 50-69 yr ≥ 70 yr 		0 (0.00–11.2) 0.70 (0.09–2.55) 1.22 (0.40–2.85)		
		Leukaemia (ICD- 10, C91–C95), mortality	SMR: Firefighters	10	1.00 (0.48–1.84)		
		Leukaemia (ICD- 10, C91–C95), incidence	Period of follow 1984 or before 1985–1994 1995 or after	-up (SIR): < 5 < 5 9	1.18 (0.32–3.03) 0.38 (0.01–2.12) 0.84 (0.38–1.59)		

<u>Marjerrison et al.</u> (2022b) (cont.)		Leukaemia (ICD- 10, C91–C95),	Period of follow					
· · · · · · · · · · · · · · · · · · ·		, ,,		-up (SMR):		Age,		
(cont.)		, ,,	1984 or before	< 5	1.09 (0.22–3.18)	calendar		
		mortality	1985-1994	< 5	0.57 (0.01-3.15)	year		
			1995 or after	6	1.10 (0.40–2.39)			
		Leukaemia (ICD-	Age at diagnosis	s (SIR):				
		10, C91–C95),	\leq 49 yr	< 5	0.42 (0.01–2.37)			
		incidence	50-69 yr	8	1.05 (0.45-2.07)			
			≥ 70 yr	5	0.73 (0.24–1.71)			
		Leukaemia (ICD-	Age at diagnosis	s (SMR):				
		10, C91–C95),	\leq 49 yr	0	0 (0.00-2.62)			
		mortality	50-69 yr	< 5	1.09 (0.30-2.79)			
			≥ 70 yr	6	1.16 (0.43–2.52)			
(2020) f Sweden i	8136 firefighters; male firefighters identified from national censuses in 1960,	NHL (ICD- 10, C83, C85), incidence	SIR: Firefighters	42	1.05 (0.75–1.41)	Age, calendar period	<i>Exposure assessment</i> <i>critique</i> : Satisfactory quality. Unclear if	
	1970, 1980, and 1990	NHL (ICD-	Duration of employment (SIR):				individuals were active	
	Exposure assessment	10, C83, C85),	1–9 yr	1	0.88 (0.02-4.89)		firefighter for whole	
	method: ever employed and categorical duration	incidence	10–19 yr	12	1.10 (0.57–1.93)		employment. May include full-time, part-time,	
	of employment (years) as		20–29 yr	17	1.17 (0.68–1.87)		municipal, and rural	
	firefighter from census		≥ 30 yr	12	0.88 (0.45-1.53)		firefighters.	
5	surveys		Trend-test P val	ue, 0.90			Strengths: near complete	
		NHL (ICD-	Time period (SI	R):			ascertainment of cancer	
		10, C83, C85),	1961–1975	1	0.35 (0.01–1.97)		incidence; long length	
		incidence	1976-1990	10	0.84 (0.40-1.54)		of follow-up (mean, 28 yr); analyses stratified	
			1991-2009	31	1.22 (0.83–1.73)		by calendar period of	
		Multiple	SIR:				employment.	
		myeloma (ICD-10, C90), incidence	Firefighters	26	1.25 (0.82–1.83)			

Table 2.5 (co	ntinued)						
Reference, location enrolment/ follow-up period, study design	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments
<u>Bigert et al.</u>		Multiple	Duration of em	ployment (S	IR):	Age,	Limitations: no data on job
<u>(2020)</u>		myeloma	1–9 yr	0	0 (0.00–7.24)	calendar	duties, employment type,
(cont.)		(ICD-10, C90), incidence	10–19 yr	4	0.77 (0.21–1.96)	period	or potential confounders (aside from age, sex, and
		meldence	20–29 yr	8	1.17 (0.51–2.31)		calendar year); probable
			≥ 30 yr	14	1.70 (0.93–2.85)		healthy-worker hire bias;
			Trend-test P va	lue, 0.11			potential non-differential
		Multiple	Time period (S	IR):			misclassification of
		myeloma	1961–1975	2	1.17 (0.14–4.21)		employment duration.
		(ICD-10, C90), incidence	1976-1990	6	1.07 (0.39–2.32)		
		meldence	1991-2009	18	1.34 (0.79–2.11)		
		Leukaemia (ICD-	SIR:				
		10, C91–C95), incidence	Firefighters	33	0.94 (0.65–1.33)		
		Chronic	SIR:				
		lymphatic leukaemia, incidence	Firefighters	14	0.85 (0.47–1.43)		

Reference, location enrolment/ follow-up period, study design	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments
Kullberg et al.		Lymphatic and	Follow-up perio	d (SIR):		Birth year,	Exposure assessment
(<u>2018)</u> Stockholm,	as a firefighter in Stockholm in 1931–1983	haematopoietic (ICD-7, 200–209),	Full: 1958–2012	18	0.73 (0.43–1.16)	calendar period	<i>critique</i> : Satisfactory quality. Unclear if
Sweden Enrolment, 1931–	rolment, 1931– 83/follow-up, 58–2012 method: ever employed and categorical duration of employment (years) as an	incidence	Former: 1958–1986	3	0.31 (0.06-0.90)		individuals were active firefighters for whole employment. Municipal firefighters. <i>Strengths</i> : long follow-up
1983/follow-up, 1958–2012 Cohort			Extended: 1987–2012	15	1.01 (0.56–1.66)		
Conort		NHL	Follow-up perio	d (SIR):			period; near complete
		(ICD-7, 200), incidence	Full: 1958–2012	6	0.68 (0.25-1.48)		ascertainment of cancer incidence; analyses of
			Former: 1958–1986	1	0.35 (0.01–1.97)		duration and era of employment. <i>Limitations</i> : no data on potential confounders (aside from age, sex, and
			Extended: 1987–2012	5	0.83 (0.27–1.94)		
		Hodgkin	Follow-up perio	d (SIR):			
		lymphoma (ICD-7, 206),	Full: 1958–2012	2	1.39 (0.17–5.00)		calendar year); lack of exposure assessment based on job tasks or fire
		incidence	Former: 1958–1986	1	0.97 (0.02–5.42)		responses.
			Extended: 1987–2012	1	2.41 (0.06–13.4)		
	Multiple	Follow-up perio	d (SIR):				
		myeloma (ICD-7, 203),	Full: 1958–2012	5	1.18 (0.38–2.75)		
		incidence	Former: 1958–1986	0	0 (0.00–2.15)		
				5	1.96 (0.64-4.57)		

Reference, location enrolment/ follow-up period, study design	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments
Kullberg et al.		Leukaemia	Follow-up perio	od (SIR):		Birth year,	
<u>(2018)</u> (cont.)		(ICD-7, 204–207), incidence	Full: 1958–2012	3	0.38 (0.08–1.10)	calendar period	
			Former: 1958–1986	1	0.29 (0.01–1.62)		
			Extended: 1987–2012	2	0.43 (0.05–1.59)		
Tornling et al. (1994) Stockholm, Sweden Enrolment, 1931–1983/ follow-up, 1951– 1986 (mortality), 1958–1986 (incidence) Cohort	1116 for mortality/1091 for incidence; male firefighters employed for ≥ 1 yr by the City of Stockholm between 1931 and 1983 identified from annual enrolment records Exposure assessment method: ever firefighter and duration (years) of firefighting employment from annual enrolment records; number of fires fought ascertained from exposure index developed from fire reports	Lymphatic and haematopoietic (ICD-8, 200– 209), mortality Lymphatic and haematopoietic (ICD-8, 200– 209), incidence	SMR: Firefighters SIR: Firefighters	3	0.44 (0.09–1.27)	Age, calendar period	<i>Exposure assessment</i> <i>critique</i> : Satisfactory/good quality. Enhanced exposur assessment (but based on 10% sample of reports) to differentiate exposure based on number of fires fought accounting for job position, station, and year of exposure. Municipal firefighters. <i>Strengths</i> : long follow-up period; near complete ascertainment of cancer incidence and mortality; assessed exposure to fire responses for some outcomes. <i>Limitations</i> : no data on potential confounders (aside from age, sex, and calendar year); low number

Reference, location enrolment/ follow-up period, study design	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments
Petersen et al.	9061 male firefighters	Hodgkin	Reference group	o (SIR):		Age,	Exposure assessment
<u>(2018a)</u> Denmark Enrolment,	(full-time, part-time, and volunteer) identified from employer, trade union, and	lymphoma (ICD-10, C81), incidence	Firefighters vs general population	13	1.64 (0.95–2.82)	calendar period	<i>critique</i> : Satisfactory quality. Includes part-time and full-time firefighters.
1964–2004/ follow-up, 1968–2014	Danish Civil Registration System records, born on 2 April 1928 or later,		Firefighters vs sample of employees	13	1.35 (0.78–2.32)		Excluded those who did not actually fight fires. Mai include municipal and rural firefighters. <i>Strengths</i> : long period of follow-up; near-complete
Cohort	ohort employed before age 60 yr and 31 December 2004, no cancer diagnosis before employment as a firefighter, and a job title/function indicating actual firefighting exposure Exposure assessment method: ever employed and categorical duration of employment (years), as		Firefighters vs military	13	1.42 (0.82–2.44)		
		1 1	Employment ty	pe (SIR):			ascertainment of cancer
		lymphoma	Full-time	NR	NR		incidence; use of three
		(ICD-10, C81), incidence NHL (ICD-10, C82–C85, C88.3– C88.9), incidence	Part-time or volunteer	NR	2.29 (1.15-4.58)		reference groups to evaluate healthy-worker bias; analyses by proxies of exposure including job task. <i>Limitations</i> : little information on potential confounders.
			SIR: General population referent	37	0.96 (0.69–1.32)		
	well as employment type, job title/function, and work history, ascertained from civil registration, pension,		Sample of working population referent	37	0.97 (0.70-1.33)		
	employer personnel, and trade union membership records		Military employees referent	37	0.97 (0.70–1.34)		
		NHL (ICD-10,	Employment ty	pe (SIR):			
		C82-C85, C88.3-	Full-time	23	1.02 (0.68–1.53)		
		C88.9), incidence	Part-time or volunteer	14	0.87 (0.52–1.47)		
		NHL (ICD-10,	Era of first emp	loyment (SII	R):		
		C82-C85, C88.3-	Pre-1970	13	0.90 (0.52–1.55)		
		C88.9), incidence	1970-1994	18	0.89 (0.56–1.42)		
			1995 or after	6	1.46 (0.65–3.24)		

Reference, location enrolment/ follow-up period, study design	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments		
Petersen et al.		NHL (ICD-10,	Job function (SI			Age,			
<u>(2018a)</u> (cont.)		C82–C85, C88.3– C88.9), incidence	Regular	33	0.91 (0.65–1.29)	calendar period			
(cont.)			Specialized	4	1.53 (0.57–4.08)	period			
		NHL (ICD-10,	Age at first emp						
		C82–C85, C88.3– C88.9), incidence	< 25 yr	15	0.83 (0.50–1.37)				
		(00.7), incluence	25–34 yr	15	1.21 (0.73–2.00)				
			≥ 35 yr	7	0.86 (0.41–1.80)				
		NHL (ICD-10,	Duration of em						
		C82-C85, C88.3-	< 1 yr	8	0.86 (0.43–1.73)				
		C88.9), incidence	$\geq 1 \text{ yr}$	29	0.98 (0.68–1.42)				
			≥ 10 yr	23	0.93 (0.62–1.40)				
			≥ 20 yr	16	0.88 (0.54–1.43)				
		10, C90, C88.0– C88.2), incidence	Reference group (SIR):						
			Firefighters vs general population	8	0.62 (0.31–1.24)				
			Firefighters vs sample of employees	8	0.66 (0.33-1.32)				
			Firefighters vs military	8	0.65 (0.33-1.31)				
		Leukaemia	Reference group						
		(lymphoid) (ICD-10, C91), incidence	Firefighters vs general population	15	0.91 (0.55–1.51)				
			Firefighters vs sample of employees	15	0.97 (0.59–1.61)				
			Firefighters vs military	15	0.88 (0.53–1.47)				

Table 2.5 (co	-						
Reference, location enrolment/ follow-up period, study design	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments
Petersen et al.		Leukaemia (myeloid) (ICD-10, C92), incidence	Reference group	o (SIR):		Age,	
(2018a) (cont.)			Firefighters vs general population	9	0.76 (0.40-1.46)	calendar period	
		Firefighters vs sample of employees	9	0.73 (0.38-1.40)			
		Firefighters vs military	9	0.83 (0.43-1.60)			
Petersen et al. (2018b)	11 775 male firefighters (full-time, part-time, and	Lymphatic and blood forming tissues (ICD- 10, C81–C96), mortality	Employment type (SMR, military reference group):			Age, calendar	<i>Exposure assessment</i> <i>critique</i> : Satisfactory
Denmark	volunteer) identified from		Full-time	17	0.89 (0.56-1.44)	period	quality. Includes part-time and full-time firefighters. Excluded those who did
Enrolment, 1964–2014/	employer, trade union, and Danish Civil Registration		Part-time/ volunteer	5	0.47 (0.20–1.13)		
follow-up, 1970–2014 Cohort	System records, born in 1928 or later, employed before age 60 yr and 31 December	Lymphatic and blood forming	Duration of employment (SMR, military reference group):				not actually fight fires. May include municipal and
Collort	2004, and a job title/function	tissues (ICD-	< 1 yr	4	0.46 (0.17-1.23)		rural firefighters. Strengths: long period of
	indicating actual firefighting	10, C81–C96),	≥1 yr	13	1.25 (0.73-2.16)		follow-up; use of military
	exposure	mortality	≥ 10 yr	12	1.30 (0.74-2.29)		reference group to evaluate
Exposure assessment method: ever employed and categorical duration of employment (years) as a firefighter ascertained from civil registration, pension, employer personnel, and trade union membership records		≥ 20 yr	7	0.88 (0.42–1.85)		healthy-worker bias; analyses by duration of employment. <i>Limitations</i> : little information on potential confounders.	

Reference, location enrolment/ follow-up period, study design	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments
Webber et al.	10 786 FDNY, 8813 CFHS;	NHL, incidence	Group (SIR, US	S reference ra	tes):	Age,	Exposure assessment
<u>(2021)</u> New York	ia, San FDNY cohort included men		CFHS firefighters	43	1.04 (0.77–1.41)	calendar year, race/ ethnicity Age on 11 September 2001, race/	<i>critique</i> : Satisfactory quality. Intensity of exposure at WTC captured but did not consider previous firefighter work. Qualitative assessment based on presence at the WTC site, exposures complex and probably unique to 9/11 disaster. Municipal firefighters. <i>Strengths</i> : ascertainment
City, Chicago, Philadelphia, San			FDNY WTC firefighters	55	1.39 (1.06–1.83)		
Francisco, USA 2001–2016 Cohort		NHL, incidence	SIR (2-year adj surveillance bia		potential		
Conort			FDNY WTC firefighters	NR	1.29 (0.97–1.71)		
	actively employed on	NHL, incidence	Group (RR):				
	11 September 2001 and assumed not to be working		CFHS firefighters	43	1		
at the WTC site Exposure assessment method: presence at WTC site from employment records and duty rosters		FDNY WTC firefighters	55	1.26 (0.80–2.00)	ethnicity	of cancer incidence; comparison of two	
	NHL, incidence	Group (RR, 2-year adjustment for potential surveillance bias):				firefighter cohorts to evaluate bias; adjustment	
		CFHS firefighters	NR	1		for smoking. <i>Limitations</i> : medical surveillance bias; young a of cohort; relatively short length of follow-up.	
		FDNY WTC firefighters	NR	1.21 (0.75–1.94)			

Table 2.5 (continued)

Reference, location enrolment/ follow-up period, study design	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments
Moir et al. (2016) USA Follow-up, 11 September 2001 through 2009 Cohort	11 457 WTC-exposed firefighters; 8220 non-WTC firefighters; White male WTC-exposed firefighters who were employed at FDNY on or after 1 January 1996, actively employed for ≥ 1.5 yr before end of follow-up (31 December 2009), whose identifying information was sent to state cancer registries; contributing person-years at risk at ages 30–70 yr from 11 September 2001 to study end; referent group included firefighters from San Francisco, Chicago, and Philadelphia Exposure assessment method: presence at WTC site from employment records and duty rosters	Haematological, incidence Haematological, incidence Haematological, incidence Haematological, incidence	2001 to 31 Decer Referent group WTC-exposed FDNY firefighters	nber 2004) 12 13 time period 09) diagnos 29 27 ar adjustme	1 1.16 (0.45–3.02) (1 January 2005 to es only) 1 0.97 (0.53–1.76)	Age	<i>Exposure assessment</i> <i>critique</i> : Satisfactory quality. Exposure at WTC captured but did not consider previous firefighter work. Only measure of exposure was being a firefighter at WTC. Exposures complex and probably unique to 9/11 disaster. Urban [municipal] firefighters. <i>Strengths</i> : cancer incidence; comparison with other firefighter cohorts to establish effect of WTC exposures. <i>Limitations</i> : short follow- up period.

Reference, location enrolment/ follow-up period, study design	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments
Zeig-Owens et al.	9853 male FDNY firefighters	Hodgkin	WTC-exposure	status (SIR)	:	Age, race,	Exposure assessment
(2011)employed for ≥ 18 mo,New York City,were active firefighters on 1USAJanuary 1996, with no priorEnrolment,cancer, and, if alive on 121996/follow-up,September 2001, also had	lymphoma, incidence	Non-exposed	≤ 5	0.82 (0.20-3.27)	ethnic	critique: Satisfactory	
		Exposed	0	0 (NR)	origin, calendar	quality. Intensity of exposure at WTC capture	
	NHL, incidence	WTC-exposure status (SIR, 2-year adjustment for potential surveillance bias):			year	but did not consider previous firefighter	
1996–2008	known WTC exposure status		Non-exposed	9	0.83 (0.43-1.60)		work. WTC exposure self-reported using three
Cohort	Exposure assessment		Exposed	20	1.50 (0.97-2.33)		
method: WTC-exposed and non-exposed firefighter from employment records and questionnaires		SIR ratio (exposed vs non-exposed)	NR	1.81 (0.82–3.97)		methods. WTC site exposures complex and probably unique to 9/11	
	Multiple	WTC-exposure	status (SIR)	:		disaster.	
		myeloma,	Non-exposed	0	0 (NR)		Strengths: evaluation of
		incidence	Exposed	≤ 5	1.49 (0.56-3.97)		medical surveillance bias
		Leukaemia,	WTC-exposure	status (SIR)	:		<i>Limitations</i> : healthy-worl hire bias; short length of
		incidence	Non-exposed	7	1.47 (0.63-3.40)		follow-up; young age at
			Exposed	9	1.40 (0.73-2.70)		end of follow-up; little
			SIR ratio (exposed vs non-exposed)	NR	0.98 (0.33–2.77)		information on potentia confounders.

Table 2.5 (continued)

Reference, location enrolment/ follow-up period, study design	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments
Pinkerton et al. (2020) San Francisco, Chicago, and Philadelphia, USA Enrolment, 1950–2009/ follow-up, 1950–2016 Cohort	29 992 municipal career firefighters in the CFHS cohort employed by the fire departments of San Francisco, Chicago, or Philadelphia for ≥ 1 day between 1950 and 2009; exposure–response analyses limited to 19 287 male firefighters of known race hired in 1950 or later and employed for ≥ 1 yr Exposure assessment method: ever-employed as a firefighter, and number of exposed days, fire-runs, fire- hours reconstructed using job-exposure matrix based on job titles and assignments and departmental work history records and historical fire-run and fire- hour data	NHL (ICD-10, C46.3, C82–C85, C88.0, C88.3, C91.4, C96), mortality NHL (ICD-10, C46.3, C82–C85, C88.0, C88.3, C91.4, C96), mortality NHL (ICD-10, C46.3, C82–C85, C88.0, C88.3, C91.4, C96), mortality	Fire department San Francisco Chicago Philadelphia Overall Heterogeneity P Exposed-days m days vs 2500 exp Loglinear without HWSE adjustment RCS without HWSE adjustment Fully adjusted loglinear Fully adjusted RCS Fire-runs (Chica model (HR at 88 10-yr lag): Loglinear without HWSE adjustment RCS without HWSE adjustment RCS without HWSE adjustment Fully adjusted loglinear Fully adjusted loglinear Fully adjusted loglinear Fully adjusted loglinear Fully adjusted loglinear Fully adjusted RCS	30 66 55 151 value, 0.51 odel (HR at ossed-days, 76 76 76 76 76 76 90 and Phil	10-yr lag): 0.94 (0.60–1.50) 0.96 (0.54–1.82) 1.10 (0.60–2.11) 1.08 (0.49–2.64) adelphia only)	Gender, race, age, calendar period Age, race, birthdate (within 5 yr), fire department Age, race, birthdate (within 5 yr), fire department	<i>Exposure assessment</i> <i>critique</i> : Good quality. Minimal bias in exposure assessment in internal analyses. Municipal firefighters. <i>Strengths</i> : long period of follow-up; exposure– response modelling for three metrics of exposure assessed using job-exposure matrices; adjustment for HWSE. <i>Limitations</i> : healthy-worker selection bias in external comparison analyses; little information on potential confounders.

Table 2 5 (a **പ**)

Table 2.5 (co	ntinued)						
Reference, location enrolment/ follow-up period, study design	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments
Pinkerton et al. (2020)		NHL (ICD-10, C46.3, C82–C85,	Fire-hours (Chic 2300 h vs 600 h,		nodel (HR at	Age, race, birthdate	
(cont.)		C88.0, C88.3, C91.4, C96), mortality	Loglinear without HWSE adjustment	40	0.61 (0.35–1.04)	(within 5 yr), fire department	
			RCS without HWSE adjustment	40	0.79 (0.39–1.68)		
			Fully adjusted loglinear	40	0.64 (0.34–1.17)		
			Fully adjusted RCS	40	0.83 (0.38–1.93)		
		Multiple	Fire department	(SMR):		Gender,	
		myeloma (ICD-	San Francisco	12	1.03 (0.53–1.79)	race, age,	
		10, C88.7, C88.9,	Chicago	24	0.86 (0.55-1.27)	calendar	
		C90), mortality	Philadelphia	18	0.97 (0.58–1.54)	period	
			Overall	54	0.93 (0.70-1.21)		
			Heterogeneity P				
		Leukaemia (ICD-	Fire department				
		10, C91.0–C91.3, C91.5–C91.9,	San Francisco	26	0.94 (0.62–1.38)		
		C92–C95),	Chicago	75	1.18 (0.93–1.48)		
		mortality	Philadelphia Overall	49 150	1.12 (0.83–1.48)		
			Heterogeneity P		1.11 (0.94–1.31)		
			received generity F	value, 0.01			

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locationdescription, exposure(histopathology), category or incidence orcases or(95% CI)controlledenrolment/assessment methodincidence orleveldeathsfollow-upmortalityperiod, studydesign
utiti
Pinkerton et al.Leukaemia (ICD-Exposure-days model (HR at 8700 exposed-Age, race,(2020)10, C91.0-C91.3,days vs 2500 exposed-days, 5-yr lag):birthdate
(cont.)C91.5-C91.9, C92-C95),Loglinear721.26 (0.77-2.11)(within 5 yr), fire departmentmortalityadjustment5 yr), fire department
RCS without 72 1.12 (0.61–2.19) HWSE adjustment
Fully adjusted 72 2.32 (1.13–5.19) loglinear
Fully adjusted 72 2.39 (0.91–7.37) RCS
Leukaemia (ICD- 10, C91.0-C91.3,Fire-runs (Chicago and Philadelphia only)model (HR at 8800 runs vs 2100 runs, 5-yr lag):
C92–C95), Loglinear 64 1.07 (0.74–1.52) mortality without HWSE adjustment
RCS without 64 1.46 (0.90–2.43) HWSE adjustment
Fully adjusted 64 1.15 (0.77–1.67) loglinear
Fully adjusted 64 1.89 (1.06–3.48) RCS

Table 2.5 (co	ontinued)						
Reference, location enrolment/ follow-up period, study design	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments
Pinkerton et al.		Leukaemia (ICD-	Fire-hours (Chic		nodel (HR at	Age, race,	
(2020) (cont.)		10, C91.0–C91.3, C91.5–C91.9, C92-C95), mortality	2300 h vs 600 h, Loglinear without HWSE adjustment	5-yr lag): 41	1.07 (0.63–1.77)	birthdate (within 5 yr), fire department	
		·	RCS without HWSE adjustment	41	1.41 (0.71–2.97)	-	
			Fully adjusted loglinear	41	1.17 (0.65–2.05)		
			Fully adjusted RCS	41	1.74 (0.78–4.15)		
		Leukaemia (ICD- 10, C91.0–C91.3, C91.5–C91.9, C92–C95),	Time since first exposure in fire-runs (Chicago and Philadelphia only) fully adjusted loglinear model (HR for 8800 runs vs 2100 runs, 10-yr lag):			Age, race, birthdate (within 5 yr), fire	
		mortality	Lag to < 20 yr	NR	2.56 (1.04-5.75)	department,	
			20 to < 30 yr	NR	0.58 (0.19–1.58)	employment	
			≥ 30 yr	NR	1.12 (0.57-2.08)	duration	
			LRT P value, 0.1	5			
		Leukaemia (ICD- 10, C91.0–C91.3, C91.5–C91.9, C92–C95),	Age at exposure Philadelphia onl model (HR for 8 10-yr lag):	y) fully adj	usted loglinear		
		mortality	< 40 yr	NR	1.42 (0.72–2.63)		
			≥ 40 yr	NR	0.96 (0.51–1.73)		
			LRT <i>P</i> value, 0.4	4			

Table 2.5 (continued)								
Reference, location enrolment/ follow-up period, study design	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments	
<u>Pinkerton et al.</u> (2020) (cont.)		Leukaemia (ICD- 10, C91.0–C91.3, C91.5-C91.9, C92–C95), mortality	Period of expos Philadelphia on model (HR for 8 10-yr lag): Pre-1970 1970 or after LRT <i>P</i> value, 0.0	ly) fully adji 3800 runs vs NR NR		Age, race, birthdate (within 5 yr), fire department, employment duration		
Daniels et al. (2015) San Francisco, Chicago, Philadelphia, USA Enrolment, 1950–2009/ follow-up, 1950– 2009 (mortality), 1985–2009 (incidence) Cohort	19 309; all male career firefighters in the CFHS cohort of known race who were on active duty ≥ 1 day in 1950–2009 in the fire departments of Chicago, Philadelphia, or San Francisco, with ≥ 1 yr of employment Exposure assessment method: number of exposed days, fire-runs, fire-hours reconstructed using job- exposure matrix based on job titles and assignments and departmental work history records and historical fire-run and fire- hour data	 NHL, incidence NHL, incidence NHL, incidence Leukaemia, incidence Leukaemia, incidence Leukaemia, incidence 	Exposed-days n 5-yr lag): 8700 days vs 2500 days Fire-runs (Chic model (HR, line 8800 runs vs 2100 runs Fire-hours (Chi model, 5-yr lag) 2300 h vs 600 h Exposed-days n 5-yr lag): 8700 days vs 2500 days Fire-runs (Chic model (HR, line 8800 runs vs 2100 runs	nodel (HR, p 92 ago and Phi ear model, 5 79 cago only) n : 45 nodel (HR, I 58 ago and Phi ear model, 5 49 cago only) n :	1.07 (0.92–1.28) ladelphia only) -yr lag): 0.79 (0.64–1.10) nodel (HR, power 1.12 (0.89–1.50) RCS model, 0.99 (0.56–1.89) ladelphia only)	Age, race, fire department, birth cohort Age, race, fire department, birth cohort Age, race, birth cohort Age, race, fire department, birth cohort Age, race, fire department, birth cohort Age, race, birth cohort	<i>Exposure assessment</i> <i>critique</i> : Good quality. Minimal bias in exposure assessment in internal analyses. Municipal firefighters. <i>Strengths</i> : long period of follow-up; exposure- response modelling for three metrics of exposure assessed using job- exposure matrices. <i>Limitations</i> : little information on potential confounders.	

Table 2.5 (co	ntinued)						
Reference, location enrolment/ follow-up period, study design	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments
Daniels et al. (2015) (cont.)		Leukaemia, incidence	Time since first loglinear fire-ru only) model (H 5–15 yr 15–25 yr > 25 yr	ıns (Chicago	and Philadelphia	Age, race, fire department, birth cohort	
		Leukaemia, incidence	LRT <i>P</i> value, 0.123 Age at exposure in piecewise loglinear fire- runs (Chicago and Philadelphia only) model (HR at 4600 runs, 5-yr lag):				
			< 40 yr ≥ 40 yr LRT <i>P</i> value, 0.5	NR NR 598	0.95 (0.52–1.62) 1.19 (0.73–1.85)		
		Leukaemia, incidence	runs (Chicago a (HR at 4600 run	nd Philadel ns, 5-yr lag):	se loglinear fire- phia only) model		
			Pre-1970 1970 or after LRT <i>P</i> value, 0.0	NR NR 652	0.95 (0.48–1.72) 1.14 (0.76–1.66)		
Daniels et al. (2014) Chicago, San Francisco, and Philadelphia,	29 993 (24 453 for incidence analyses) male and female career firefighters in the CFHS cohort employed for \geq 1 day in Chicago, San	NHL (ICD-10, C46.3, C82–C85, C88.0, C88.3, C91.4, C96), incidence	SIR: All cancers First primary cancer	170 145	0.99 (0.85–1.15) 0.99 (0.83–1.16)	Gender, race, age, calendar period	<i>Exposure assessment</i> <i>critique</i> : Satisfactory quality. Minimum exposure is 1 day of work as a municipal firefighter.
USA Enrolment, 1950–2009/ follow-up, 1950–	Francisco, or Philadelphia fire departments between 1950 and 2009 Exposure assessment method: ever employed	NHL (ICD-10, C46.3, C82–C85, C88.0, C88.3, C91.4, C96),	Race (SIR, all ca Among men: Caucasian [White]	ancers): 161	1.02 (0.87–1.19)	Age, calendar period	Strengths: long period of follow-up; ascertained incidence outcomes; included female firefighters. Limitations: healthy-
2009 (mortality), 1985–2009 (incidence) Cohort	and categorical duration of employment (years) from employment records	incidence Multiple myeloma (ICD- 10, C88.7, C88.9, C90), incidence	Other SIR: All cancers First primary	7 36 33	0.56 (0.23–1.16) 0.72 (0.50–0.99) 0.75 (0.52–1.06)	Gender, race, age, calendar period	worker hire bias in external comparisons; little information on potential confounders.
			cancer			renou	

Reference, location enrolment/ follow-up period, study design	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments
Daniels et al.		Multiple	Race (SIR, all ca	ncers):		Age,	
(2014) (cont.)	myeloma (ICD- 10, C88.7, C88.9, C90), incidence	Among men: Caucasian [White]	35	0.76 (0.53–1.06)	calendar period		
			Other	NR	0.24 (0.01–1.32)		
		Leukaemia (ICD- 10, C91.0–C91.3,	SIR: All cancers	100	0.94 (0.77-1.15)	Gender, race, age,	
	C91.5–C91.9, C92–C95), incidence	First primary cancer	85	0.93 (0.74–1.15)	calendar period		
		Leukaemia (ICD-				Age,	
	10, C91.0–C91.3, C91.5–C91.9,	Caucasian [White]	88	0.88 (0.71–1.09)	calendar period		
		C92–C95), incidence	Other	11	1.90 (0.95-3.40)		
<u>Demers et al.</u>	2447 male firefighters	Hodgkin	SIR (local county rates):			Age,	<i>Exposure assessment critique</i> : Satisfactory quality. Duration (years)
<u>1994)</u> Seattle and	employed for ≥ 1 yr between 1944 and 1979, alive as of	lymphoma (ICD- 9, 201), incidence	D- Firefighters 1 0.7 (0.0-4.1) cal			calendar period	
Facoma, USA Enrolment,	1 January 1974 and known to be a resident of one of 13	NHL (ICD-	SIR (local count	•			involved in direct firefighting (surrogate
.944–1979/	counties in the catchment	9, 200–202), incidence	Firefighters	7	0.9 (0.4–1.9)		for fire smoke) was not
follow-up,area of the tumour registry $1974-1989$ for ≥ 1 mo; reference group	NHL (ICD- 9, 200–202),	Duration of exp county rates):	osed employ	yment (SIR, local		measured equally in the two study populations.	
Cohort	included 1878 local male police officers	incidence	< 10 yr	1	0.9 (0.0-4.9)		Municipal firefighters. <i>Strengths</i> : use of two
	Exposure assessment		10–19 yr	1	0.6 (0.0-3.5)		comparison groups,
	method: ever employed		20–29 yr	5	1.2 (0.4–2.7)		including comparison
	for \geq 1 yr, and categorical		≥ 30 yr	0	0 (0.0–5.8)		with police officers to limit
duration of employment (years) in direct firefightin		NHL (ICD-		employmen	t (SIR, local county		healthy-worker bias.
		9, 200–202),	rates):				<i>Limitations</i> : little information on potential
	positions from employment	incidanca					
	positions from employment records	incidence	< 20 yr 20–29 yr	2 1	1.9 (0.2–6.7) 0.7 (0.0–3.7)		confounders; small numb

Table 2.5 (c	ontinued)						
Reference, location enrolment/ follow-up period, study design	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments
Demers et al.		NHL (ICD-	IDR:			Age,	
<u>(1994)</u>		9, 200–202),	Local police	2	1	calendar	
(cont.)		incidence	Firefighters	7	1.8 (0.4–13)	period	
		Multiple	SIR (local coun	ty rates):			
		myeloma (ICD-9, 203), incidence	Firefighters	2	0.7 (0.1–2.6)		
		Leukaemia (ICD-	SIR (local coun	ty rates):			
		9, 204–208), incidence	Firefighters	6	1.0 (0.4–2.1)		
		Leukaemia (ICD- 9, 204–208),	Duration of exp county rates):	osed employ	yment (SIR, local		
		incidence	< 10 yr	0	0 (0.0-4.4)		
			10–19 yr	2	1.9 (0.2-6.8)		
			20–29 yr	4	1.1 (0.3–2.8)		
			≥ 30 yr	0	0 (0.0-5.4)		
		Leukaemia (ICD- 9, 204–208),	Years since first rates):	employmen	t (SIR, local county		
		incidence	< 20 yr	1	1.6 (0.0-8.9)		
			20–29 yr	1	1.0 (0.0-5.6)		
			≥ 30 yr	4	0.9 (0.2–2.2)		
		Leukaemia (ICD-	IDR:				
		9, 204–208),	Local police	4	1		
		incidence	Firefighters	6	0.8 (0.2–3.5)		

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Table 2.5 (co	ontinued)									
Reference, location enrolment/ follow-up period, study design	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments			
Demers et al. (1992a) Seattle and Tacoma, Washington; Portland,	4401 male firefighters employed for ≥ 1 yr between 1944 and 1979 in Seattle, Tacoma, or Portland, USA; reference group included	Lymphatic and haematopoietic (ICD-9, 200– 208), mortality Lymphatic and	SMR: Firefighters Duration of ex			Age, calendar period	<i>Exposure assessment</i> <i>critique</i> : Satisfactory/good quality. Duration (years) involved in fire combat (surrogate for fire smoke) was not measured equally			
Oregon, USA	3676 local police officers Exposure assessment	haematopoietic	< 10 yr	4	0.91 (0.2–2.3)		in the three municipal			
Enrolment,	method: ever employed	(ICD-9, 200– 208), mortality	10–19 yr	7	1.46 (0.06–3.0)		firefighter populations.			
1944–1979/	for ≥ 1 yr, and categorical	200), mortanty	20–29 yr	14	1.06 (0.6–1.8)		Strengths: use of two			
follow-up,	duration (years) of exposure		≥ 30 yr	12	2.05 (1.1–3.6)		comparison groups,			
1945–1989 to fire combat from	Lymphatic and	Years since firs	÷ ,			including comparison				
Cohort	employment records	haematopoietic (ICD-9, 200– 208), mortality	< 20 yr	8	1.65 (0.7–3.2)		with police officers to lim healthy-worker bias.			
			20–29 yr	2	0.39 (0.1–1.4)		<i>Limitations</i> : information			
			≥ 30 yr	27	1.48 (1.0–2.2)		on potential confounders			
		Lymphatic and	Age at risk (SM				ascertained mortality outcomes only.			
		haematopoietic (ICD-9, 200–	18–39 yr	5	1.74 (0.6–4.1)					
		208), mortality	40-64 yr	13	0.96 (0.5–1.6)					
			≥ 65 yr	19	1.61 (1.0–2.5)					
		Lymphatic and haematopoietic	IDR:	21	1					
		(ICD-9, 200–	Local police	21	1					
		208), mortality	Firefighters	37	1.03 (0.62–1.73)					
		Lymphosarcoma-	SMR:							
		reticulosarcoma (ICD-9, 200), mortality	Firefighters	7	1.42 (0.57–2.93)					
		Lymphosarcoma-	IDR:							
		reticulosarcoma	Local police	5	1					
		(ICD-9, 200), mortality	Firefighters	7	0.81 (0.30-2.22)					
		Hodgkin lymphoma (ICD- 9, 201), mortality	SMR: Firefighters	3	1.05 (0.22–3.08)					

Table 2.5 (continued)

$ \begin{array}{ c c c c c c c c c c c c c c c c c c c$	Reference, location enrolment/ follow-up period, study design	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments
	<u>Demers et al.</u> (1992a)		 9, 204–208), mortality Leukaemia (ICD- 9, 204–208), mortality Leukaemia (ICD- 9, 204–208), mortality Leukaemia (ICD- 9, 204–208), mortality Leukaemia (ICD- 9, 204–208), mortality Leukaemia (ICD- 9, 204–208), mortality Other lymphatic and haematopoietic (ICD-9, 202, 203), mortality 	Firefighters Duration of exp < 10 yr 10-19 yr 20-29 yr $\geq 30 \text{ yr}$ Years since first < 20 yr 20-29 yr $\geq 30 \text{ yr}$ Age at risk (SMI) 18-39 yr 40-64 yr $\geq 65 \text{ yr}$ IDR: Local police Firefighters SMR: Firefighters IDR: Local police	2 2 4 7 employmen 3 1 11 R): 1 5 9 11 15 12	<pre>/ment (SMR): 1.13 (0.1-4.1) 1.04 (0.1-3.7) 0.73 (0.2-1.9) 2.60 (1.0-5.4) t (SMR): 1.50 (0.3-4.4) 0.50 (0.1-2.8) 1.40 (0.7-2.5) 0.82 (0.1-4.6) 0.95 (0.3-2.2) 1.67 (0.8-3.2) 1 0.80 (0.38-1.70) 1.40 (0.72-2.44)</pre>	calendar	

Reference, location enrolment/ follow-up period, study design	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments
Feuer & Rosenman (1986) New Jersey (NJ), USA 1974–1980 Cohort	263 deceased White male firefighters in the New Jersey Police and Firemen Retirement System (firefighters vested with \geq 10 yr of service, or firefighters who died while on payroll regardless of employment duration); one reference group included 567 White male police deaths Exposure assessment method: ever employed, and categorical duration of employment (years), as a career firefighter from retirement system records	Leukaemia (ICD- 8, 204–207), mortality	Reference popul Firefighters vs US White men Firefighters vs NJ White men Firefighters vs White male NJ police	ation (PMR 4 4 4): [1.86 (0.59–4.49)] [1.77 (0.56–4.27)] [2.76 (0.88–6.65)]	Age, race	<i>Exposure assessment</i> <i>critique</i> : Satisfactory quality. Assessment provides duration of employment categories. May include municipal and rural firefighters. <i>Strengths</i> : comparison with other uniformed service occupation. <i>Limitations</i> : PMR study design lacks event-free follow-up time; short observation period; little information on potential confounders; small number of cases.
Aronson et al. (1994) Toronto, Canada 1950–1989 Cohort	5414 male firefighters employed for ≥ 6 mo at one of six fire departments in Metropolitan Toronto any time between 1950 and 1989 Exposure assessment method: ever employed and categorical duration of employment (years) as municipal firefighter from employment records	Lymphatic and haematopoietic (ICD-9, 200– 208), mortality Lymphosarcoma- reticulosarcoma (ICD-9, 200), mortality Lymphosarcoma- reticulosarcoma (ICD-9, 200), mortality Hodgkin lymphoma (ICD- 9, 201), mortality	SMR: Any employment SMR: Any employment SMR: 10–14 yr of employment SMR: Any employment	18 3 NR 1	0.98 (0.58–1.56) 2.04 (0.42–5.96) 8.33 (1.01–30.1) 0.47 (0.01–2.59)	Age, calendar period	Exposure assessment critique: Satisfactory quality. Unclear if individuals were active firefighters for whole employment. Probably municipal firefighters. Strengths: long period of follow-up; analysis of employment duration. Limitations: healthy-worker hire bias; little information on confounders or exposure; ascertained mortality outcomes only.

Occupational exposure as a firefighter

Table 2.5 (co	ontinued)						
Reference, location enrolment/ follow-up period, study design	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments
<u>Aronson et al.</u> (1994) (cont.)		Multiple myeloma (ICD-9, 203), mortality	SMR: Any employment	1	0.39 (0.01–2.15)	Age, calendar period	
		Leukaemia (lymphoid) (ICD- 9, 204), mortality	SMR: Any employment	4	1.90 (0.52-4.88)		
		Leukaemia (lymphoid) (ICD- 9, 204), mortality	Years since first < 20 yr 20−29 yr ≥ 30 yr	t exposure (S 0 0 4	MR): 0 (0-10.25) 0 (0-9.97) 2.92 (0.80-7.48)		
		Leukaemia (lymphoid) (ICD- 9, 204), mortality Leukaemia	Years of employ < 15 yr 15-29 yr ≥ 30 yr Age (SMR):	yment (SMR) 0 0 4	· · · · · ·		
		(lymphoid) (ICD- 9, 204), mortality Leukaemia (myeloid) (ICD-9, 205), mortality	 < 60 yr ≥ 60 yr SMR: Any employment 	0 4 4	0 (0-4.01) 3.36 (0.92-8.60) 1.20 (0.33-3.09)		

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Reference, location enrolment/ follow-up period, study design	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments
Guidotti (1993) Edmonton and Calgary, Canada 1927–1987 Cohort	3328; all firefighters employed between 1927 and 1987 by either fire departments of Edmonton or Calgary Exposure assessment method: ever employed and categorical duration of employment (years) from employment records; exposure index of years of employment weighted by time spent in proximity to fires based on job classification	Lymphatic and haematopoietic (ICD-9, 200– 208), mortality Lymphatic and haematopoietic (ICD-9, 200– 208), mortality	SMR: Any employment Year of cohort e Pre-1920 1920–1929 1930–1939 1940–1949 1950–1959 1960–1969 1970–1979	10 entry (SMR): 3 0 2 2 1 2 1 2 0	1.26 (0.61–2.32) [2.27 (0.58–6.18)] 0 (NR) [3.23 (0.54–10.66)] [1.33 (0.22–4.40)] [0.43 (0.02–2.12)] [1.85 (0.31–6.12)] 0 (NR)	Age, calendar period	<i>Exposure assessment</i> <i>critique</i> : Good quality. Good approach to differentiate exposure between ranks. Urban [municipal] firefighters. <i>Strengths</i> : long length of follow-up; analyses by duration of employment and exposure index. <i>Limitations</i> : little information on potential confounders; ascertained mortality outcomes only; low number of cases for stratified analyses.
Glass et al. (2019) Australia Enrolment, varied by agency/ follow-up, 1980– 2011 (mortality); 1982–2010 (incidence) Cohort	39 644 female firefighters, both paid [career] (1682) and volunteer (37 962), from nine fire agencies in Australia Exposure assessment method: ever career or volunteer firefighter, ever attended an incident, tertiles of cumulative number of incidents and type of incidents attended from personnel records	Lymphatic and haematopoietic (ICD-10, C81– C96, D45–D46, D47.1, D47.3), incidence NHL (ICD- 10, C82–C85), incidence	SIR: All volunteer firefighters Volunteers who attended incidents SIR: All volunteer firefighters Volunteers who attended incidents	90 37 38 18	0.99 (0.80–1.22) 1.02 (0.72–1.41) 1.00 (0.71–1.38) 1.19 (0.71–1.88)	Age, calendar year	<i>Exposure assessment</i> <i>critique</i> : Good quality. Enhanced exposure assessment to differentiat exposure based on numbo of incidents for volunteer firefighters. Included specific incident types, but early exposure was extrapolated from more recent data. Volunteers mainly rural. <i>Strengths</i> : study of female firefighters; includes predominantly rural firefighters; ascertained exposure to number and type of incidents.

Table 2.5 (co	ntinued)						
Reference, location enrolment/ follow-up period, study design	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments
Glass et al. (2019) (cont.)		Multiple myeloma (ICD-10, C90), incidence	SIR: All volunteer firefighters Volunteers who attended incidents	13 4	1.27 (0.68–2.17) 1.04 (0.28–2.67)	Age, calendar year	<i>Limitations</i> : short length of follow-up; young age at end of follow-up; probable healthy-worker bias; little information on confounders.
		Leukaemia (ICD- 10, C91–C95), incidence	SIR: All volunteer firefighters Volunteers who attended incidents	23 6	1.10 (0.70–1.65) 0.71 (0.26–1.55)		
Glass et al. (2017) Australia Enrolment, date varied by agency (1998–2000)/ follow-up to 30	163 094; all male volunteer firefighters from five fire agencies, enrolled on or after the date on which the agency's roll was complete and who had ever held an	Lymphatic and haematopoietic (ICD-10, C81– C96, D45–D46, D47.1, D47.3), incidence	SIR: All volunteers Volunteers who attended incidents	663 426	0.81 (0.75–0.88) 0.81 (0.74–0.89)	Age, calendar period	<i>Exposure assessment</i> <i>critique</i> : Good quality. Enhanced exposure assessment to differentiate exposure based on number of incidents. Included
November 2011 (mortality) and	active firefighting role Exposure assessment	Lymphatic and haematopoietic	Duration of serv [equivalent to ra		inteers (RIR)		specific incident types, but early exposure was
31 December 2010 (cancer incidence) Cohort	method: ever volunteer firefighter, categorical volunteer duration (years) and era from service records; ever volunteer firefighter	(ICD-10, C81– C96, D45–D46, D47.1, D47.3), incidence	> 3 mo to < 10 yr 10-20 yr \geq 20 yr Trend-test <i>P</i> val	239 126 296	1 0.91 (0.73–1.12) 0.84 (0.70–1.01)		extrapolated from more recent data. Firefighters from rural or peri-urban areas. <i>Strengths</i> : includes
	who attended an incident, tertiles of cumulative emergency incidents from	Lymphatic and haematopoietic (ICD-10, C81–	incidents (RIR):		eers who attended		predominantly rural firefighters; ascertained exposure to number and
	contemporary incident data	C96, D45-D46, D47.1, D47.3), incidence	> 3 mo to < 10 yr 10–20 yr \geq 20 yr Trend-test <i>P</i> val	113 83 237 ue, 0.55	1 1.04 (0.78–1.38) 0.94 (0.74–1.20)		type of incidents. <i>Limitations</i> : short length of follow-up; young age at end of follow-up;

age at end of follow-up; probable healthy-worker bias; little information on confounders.

Table 2.5 (co	ntinued)										
Reference, location enrolment/ follow-up period, study design	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments				
<u>Glass et al. (2017)</u>		Lymphatic and	No. of incidents	attended by	volunteers (RIR):	Age,					
(cont.)		haematopoietic	Baseline	391	1	calendar					
		(ICD-10, C81– C96, D45–D46,	Group 2	24	1.36 (0.90-2.05)	period					
		D47.1, D47.3), incidence	Group 3	11	1.32 (0.72–2.40)						
		Lymphatic and haematopoietic	No. of fire incid (RIR):	ents attende	d by volunteers						
		(ICD-10, C81–	Baseline	392	1						
		C96, D45–D46, D47.1, D47.3),	Group 2	24	1.32 (0.87–1.99)						
		incidence	Group 3	10	1.38 (0.74–2.58)						
		Lymphatic and haematopoietic	No. of structure volunteers (RIR		ts attended by						
		(ICD-10, C81–	Baseline	400	1						
		C96, D45–D46, D47.1, D47.3),	Group 2	18	1.65 (1.03–2.64)						
		incidence	Group 3	8	1.45 (0.72–2.92)						
		Lymphatic and haematopoietic	No. of landscap volunteers (RIR		nts attended by						
		(ICD-10, C81–	Baseline	336	1						
		C96, D45–D46,	Group 2	63	1.08 (0.82–1.41)						
		D47.1, D47.3), incidence	Group 3	27	1.29 (0.87–1.91)						
		Lymphatic and haematopoietic	No. of vehicle fi volunteers (RIR		attended by						
		(ICD-10, C81–	Baseline	393	1						
		C96, D45–D46,	Group 2	22	1.17 (0.76-1.80)						
		D47.1, D47.3), incidence	Group 3	11	1.55 (0.85–2.83)						
		Hodgkin	SIR:								
		lymphoma (ICD-10, C81),	All volunteers	33	0.85 (0.59–1.20)						
		(ICD-10, C81), incidence	Volunteers who attended incidents	23	0.89 (0.56–1.33)						

Reference, location enrolment/ follow-up period, study design	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments		
Glass et al. (2017)		NHL (ICD-	SIR:			Age,			
(cont.)		10, C82–C85),	All volunteers	267	0.83 (0.73-0.94)	calendar			
		incidence	Volunteers who attended incidents	181	0.87 (0.75–1.00)	period			
		NHL (ICD-	Duration of serv	vice, all volu	nteers (RIR):				
		10, C82–C85), incidence	> 3 mo to < 10 yr	100	1				
			10–20 yr	48	0.82 (0.58-1.20)				
			≥ 20 yr	118	0.82 (0.62-1.08)				
			Trend-test P val	ue, 0.16					
		10, C82–C85), incidence	Duration of servincidents (RIR):		ers who attended				
			> 3 mo to < 10 yr	54	1				
			10–20 yr	32	0.81 (0.52-1.25)				
			≥ 20 yr	98	0.79 (0.56–1.13)				
			Trend-test <i>P</i> value, 0.22						
		NHL (ICD-		attended by	volunteers (RIR):				
		10, C82–C85),	Baseline	168	1				
		incidence	Group 2	10	1.30 (0.69–2.47)				
			Group 3	3	0.82 (0.26-2.58)				
		NHL (ICD- 10, C82–C85),	No. of fire incide (RIR):	ents attende	d by volunteers				
		incidence	Baseline	69	1				
			Group 2	11	1.39 (0.75–2.56)				
			Group 3	1	0.32 (0.04-2.25)				
		NHL (ICD- 10, C82–C85),	No. of structure volunteers (RIR		ts attended by				
		incidence	Baseline	172	1				
			Group 2	8	1.67 (0.82–3.40)				
			Group 3	1	0.42 (0.06-2.97)				

Reference, location enrolment/ follow-up period, study design	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments
<u>Glass et al. (2017)</u>		NHL (ICD-	No. of landscap		nts attended by	Age,	
(cont.)		10, C82–C85)	volunteers (RIR			calendar	
		incidence	Baseline	144	1	period	
			Group 2	28	1.09 (0.73–1.64)		
			Group 3	9	1.00 (0.51–1.96)		
		NHL (ICD- 10, C82–C85),	No. of vehicle fi volunteers (RIR):	attended by		
		incidence	Baseline	169	1		
			Group 2	9	1.10 (0.56-2.16)		
			Group 3	3	0.96 (0.31-3.02)		
		NHL (follicular)	SIR:				
		(ICD-10, C82),	All volunteers	74	0.94 (0.73–1.17)		
		incidence	Volunteers who attended incidents	56	1.08 (0.81–1.40)		
		NHL (DLBCL)	SIR:				
		(ICD-10, C83.3),	All volunteers	126	0.82 (0.69-0.98)		
		incidence	Volunteers who attended incidents	82	0.83 (0.66–1.03)		
		Multiple	SIR:				
		myeloma	All volunteers	74	0.75 (0.59-0.94)		
		(ICD-10, C90), incidence	Volunteers who attended incidents	48	0.76 (0.56–1.01)		
		Leukaemia (ICD-	SIR:				
		10, C91–C95),	All volunteers	194	0.90 (0.77-1.03)		
		incidence	Volunteers who attended incidents	1.08	0.78 (0.64–0.94)		

	Population size,	0 1					
	description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments
Glass et al. (2017) (cont.)		Myelodysplastic syndrome (ICD-10, D46), incidence	SIR: All volunteers Volunteers who attended incidents	42 31	0.81 (0.59–1.10) 1.01 (0.69–1.44)	Age, calendar period	
(2016a) Australia Enrolment, 1976–2003/ follow-up, 1976– 2011 (mortality), 1982–2010 (incidence, except two states, 2009) Cohort	30 057; full- (17 394) or part-time (12 663) paid male firefighters employed at one of eight Australian fire agencies for \geq 3 mo from start of personnel records (1976–2003, depending on agency). Exposure assessment method: employed as a part- or full-time firefighter for \geq 3 mo, categorical employment duration (years) and era from employment records; tertiles of cumulative emergency incidents and type of incident attended from contemporary incident data	Lymphatic and haematopoietic (ICD-10, C81– C96, D45–D46, D47.1, D47.3), incidence Lymphatic and haematopoietic (ICD-10, C81– C96, D45–D46, D47.1, D47.3), incidence Lymphatic and haematopoietic (ICD-10, C81– C96, D45–D46, D47.1, D47.3), incidence Lymphatic and haematopoietic (ICD-10, C81– C96, D45–D46, D47.1, D47.3),	(RIR) [equivalent > 3 mo to 10 yr 10-20 yr $\ge 20 \text{ yr}$ Trend-test <i>P</i> value Duration of emp (RIR):	109 43 152 loyment, fu t to rate rat 10 22 75 1e, 0.01 loyment, pa 18 7 18 ne, 0.92 loyment (R	1 2.38 (1.08–5.26) 3.08 (2.32–7.20) art-time firefighters 1 0.83 (0.32–2.11) 1.07 (0.40–2.88)	Age, calendar period	Exposure assessment critique: Good quality. Enhanced exposure assessment to differentiate exposure based on number of incidents, including specific incident types. Included specific incident types, but early exposure was extrapolated from more recent data. Municipal firefighters. Strengths: internal analysis by exposure to number and type of incidents; ascertained cancer incidence. Limitations: healthy-worker hire bias; short length of follow-up; young age at end of follow-up; little information on potential confounders.

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Table 2.5 (co	ontinued)						
Reference, location enrolment/ follow-up period, study design	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments
<u>Glass et al.</u>		Lymphatic and	No. of all incide		l by full-time	Age,	
$\frac{(2016a)}{(aant)}$		haematopoietic (ICD-10, C81–	firefighters (RIF			calendar period	
(cont.)		C96, D45–D46,	Tertile 1	12	1	period	
		D47.1, D47.3),	Tertile 2	11	0.95 (0.42–2.16)		
		incidence	Tertile 3	19	1.06 (0.50–2.24)		
		· · · · · · · · · · · · · · · · · · ·	Trend-test P val		11 6 11		
		Lymphatic and haematopoietic	No. of fire incid firefighters (RIF		d by full-time		
		(ICD-10, C81–	Tertile 1	14	1		
		C96, D45-D46,	Tertile 2	12	0.92 (0.42-2.01)		
		D47.1, D47.3), incidence	Tertile 3	16	0.76 (0.36-1.60)		
		incidence		ue, 0.46			
		Lymphatic and	No. of structure	fire inciden	ts attended by full-		
		haematopoietic	time firefighters	(RIR):			
		(ICD-10, C81–	Tertile 1	15	1		
		C96, D45–D46, D47.1, D47.3),	Tertile 2	17	1.19 (0.59–2.40)		
		incidence	Tertile 3	10	0.46 (0.20-1.05)		
			Trend-test P val				
		Lymphatic and haematopoietic	No. of landscap full-time firefig		nts attended by		
		(ICD-10, C81–	Tertile 1	12	1		
		C96, D45-D46,	Tertile 2	15	1.22 (0.57-2.63)		
		D47.1, D47.3),	Tertile 3	15	0.86 (0.40-1.87)		
		incidence	Trend-test P val	ue, 0.66			
	Lymphatic and haematopoietic		No. of vehicle fi time firefighters		attended by full-		
		(ICD-10, C81–	Tertile 1	13	1		
	C96, D	C96, D45-D46,	Tertile 2	16	1.40 (0.65-2.86)		
		D47.1, D47.3),	Tertile 3	13	0.72 (0.33-1.60)		
		incidence	Trend-test P val	ue, 0.4	. ,		

Reference, location enrolment/ follow-up period, study designPopulation size, description, exposure assessment methodCancer type (histopathology), incidence or mortalityExposure category or levelExposed cases or deathsRisk estimate (95% CI)Covariates controlledCommentsGlass et al. (2016a) (cont.)Hodgkin (ICD-10, C81), incidenceFirefighter statusSIR): Hul-timeAge, calendarAge, calendarMHL (ICD- 10, C82-C85), incidenceMHL (ICD- 10, C82-C85), incidenceFirefighter statusSIR): Hul-timeAge, calendarMHL (ICD- 10, C82-C85), incidenceFirefighter statusSIR): Hul-timeAge, calendarMHL (ICD- 10, C82-C85), incidenceFull-time470.98 (0.72-1.30) 0.95 (0.57-1.49)House
(2016a) lymphoma Full-time 6 0.91 (0.34–1.99) calendar (cont.) (ICD-10, C81), Part-time 4 1.14 (0.31–2.91) period All 10 0.99 (0.48–1.82) NHL (ICD- Firefighter status (SIR): 10, C82–C85), Full-time 47 0.98 (0.72–1.30)
(cont.) (ICD-10, C81), incidence Part-time 4 1.14 (0.31-2.91) period All 10 0.99 (0.48-1.82) NHL (ICD- Firefighter status (SIR): 10, C82-C85), Full-time 47 0.98 (0.72-1.30)
incidence All 10 0.99 (0.48–1.82) NHL (ICD- Firefighter status (SIR): 10, C82–C85), Full-time 47 0.98 (0.72–1.30)
All 10 0.99 (0.48-1.82) NHL (ICD- Firefighter status (SIR): 10, C82-C85), Full-time 47 0.98 (0.72-1.30)
10, C82–C85), Full-time 47 0.98 (0.72–1.30)
incidence Part-time 19 0.95 (0.57–1.49)
All 66 0.97 (0.75–1.24)
NHL (ICD- 10, C82-C85),Duration of employment, full-time firefighters(RIR):
incidence $> 3 \text{ mo to } 10 \text{ yr} 5 \qquad 1$
10–20 yr 9 2.12 (0.71–6.34)
$\geq 20 \text{ yr}$ 31 3.67 (1.28–10.54)
Trend-test P value, 0.01
NHL (ICD- 10, C82-C85),Duration of employment, part-time firefighters(RIR):
incidence $> 3 \text{ mo to } 10 \text{ yr} 6 \qquad 1$
10–20 yr 3 0.95 (0.22–4.18)
$\geq 20 \text{ yr}$ 10 2.27 (0.59–8.71)
Trend-test P value, 0.20
NHL (ICD- Duration of employment (RIR):
10, C82-C85), > 3 mo to 10 yr 11 1
incidence 10–20 yr 12 1.69 (0.74–3.88)
$\geq 20 \text{ yr}$ 41 3.14 (1.42–6.95)
Trend-test <i>P</i> value, < 0.01
NHL (ICD- 10, C82-C85),No. of all incidents attended by full-time firefighters (RIR):
incidence Tertile 1 6 1
Tertile 2 5 0.88 (0.27–2.89)
Tertile 3 7 0.91 (0.30–2.73)
Trend-test P value, 0.86

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Reference, location enrolment/ follow-up period, study design	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments
<u>Glass et al.</u>		NHL (ICD-	No. of fire inci	dents attende	d by full-time	Age,	
<u>(2016a)</u>		10, C82–C85),	firefighters (R	(R):	·	calendar	
(cont.)		incidence	Tertile 1	7	1	period	
			Tertile 2	5	0.78 (0.25-2.45)		
			Tertile 3	6	0.70 (0.23-2.12)		
			Trend-test P v	alue, 0.52			
		NHL (ICD- 10, C82–C85),	No. of structu time firefighte				
		incidence	Tertile 1	8	1		
			Tertile 2	7	0.95 (0.34-2.61)		
			Tertile 3	3	0.32 (0.08-1.23)		
			Trend-test P v	alue, 0.11			
		NHL (ICD- 10, C82–C85),	No. of landscape fire incidents attended by full-time firefighters (RIR):				
		incidence	Tertile 1	6	1		
			Tertile 2	7	1.17 (0.4–3.48)		
			Tertile 3	5	0.65 (0.20-2.16)		
			Trend-test P v	alue, 0.49			
		NHL (ICD- 10, C82–C85),	No. of vehicle fire incidents attended by full- time firefighters (RIR):			5-year- interval age	
		incidence	Tertile 1	5	1	groups	
			Tertile 2	8	1.76 (0.57-5.40)		
			Tertile 3	5	0.85 (0.24-2.98)		
			Trend-test P v	alue, 0.81			

Reference, location enrolment/ follow-up period, study design	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments
Glass et al.		Multiple	Firefighter statu	ıs (SIR):		Age,	
<u>(2016a)</u>		myeloma	Full-time	15	1.14 (0.64–1.89)	calendar	
(cont.)		(ICD-10, C90),	Part-time	3	0.61 (0.13-1.78)	period	
		incidence	All	18	1.00 (0.59-1.58)		
		Leukaemia (ICD-	Firefighter statu	ıs (SIR):			
		10, C91–C95),	Full-time	28	0.92 (0.61-1.33)		
		incidence	Part-time	15	1.21 (0.68-2.00)		
			All	43	1.00 (0.73-1.35)		
		Myelodysplastic	Firefighter statu	ıs (SIR):			
		syndrome	Full-time	4	0.91 (0.25-2.33)		
		(ICD-10, D46),	Part-time	0	0 (NR)		
		incidence	All	4	0.67 (0.18-1.71)		

Reference, location enrolment/ follow-up period, study design	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments
Glass et al. (2016b) Victoria, Australia Enrolment, 1971–1999/ follow-up, 1980– 2011 (mortality), 1982–2012 (incidence) Cohort	614; all male (611) and female (3) employed and volunteer Country Fire Authority trainers and a group of paid [career] Country Fire Authority firefighters who trained at the Fiskville site between 1971 and 1999; all analyses limited to men as no deaths or cancers were observed among women Exposure assessment method: employed or volunteer firefighter trainers and career firefighters who trained at training facility for any period of time, from human resources records, categorized into risk of low, medium, and high chronic exposure to smoke and other agents based on job	Lymphatic and haematopoietic (ICD-10, C81– C96, D45–D46, D47.1, D47.3), incidence	Risk of chronic Low Medium High	c exposure (S 0 4 4	IR): 0 (NR) 1.12 (0.30–2.86) 2.83 (0.77–7.24)	Age, calendar period	Exposure assessment critique: Satisfactory quality. Incorporated categorical level of exposure into assessment for each type of firefighter. Volunteers mainly rural, career firefighters were municipal. Strengths: included firefighter instructors with high potential exposure to smoke and other hazardoux agents; assessed exposure based on job assignment. Limitations: low number of cases; young age at end of follow-up; reported only on the grouping of all lymphatic and haematopoietic cancers.

9/11, World Trade Center disaster, 11 September 2001; BMI, body mass index; CFHS, Career Firefighter Health Study; CI, confidence interval; DLBCL, diffuse large B-cell lymphoma; Fire Department of the City of New York; HR, hazard ratio; HWSE, healthy-worker survivor effect; ICD, International Classification of Diseases; IDR, incidence density ratio; JEM, job-exposure matrix; LRT, likelihood ratio test; mo, month; NHL, non-Hodgkin lymphoma; NJ, New Jersey; NR, not reported; PMR, proportionate mortality ratio; RCS, restricted cubic splines; RIR, relative incidence ratio; RR, rate ratio; SIR, standardized incidence ratio; SMR, standardized mortality ratio; US, United States; vs, versus; WTC, World Trade Center; yr, year.

respectively. The SMR for leukaemia was 0.66 (95% CI, 0.24-1.44) overall, with SMRs of 0.33 (95% CI, 0-1.86), 0.83 (0.17-2.42) and 0.81 (95% CI, 0.09-2.91) for < 10 years, 10 to < 20 years, and \geq 20 years, respectively. ARRs [adjusted rate ratios] were also calculated in internal analyses using a reference group of firefighters with < 10 years of employment and non-firefighters within the cohort. For lymphatic and haematopoietic malignancies, the age and calendar year ARRs were 1.22 (95% CI, 0.36-4.11) for those with 10 to < 20 years of employment and 3.26 (95% CI, 0.67–15.80) for those with \geq 20 years of employment. For leukaemia, the ARRs were 6.54 (95% CI, 0.50-85.12; 3 cases) for those with 10 to < 20 years of employment and 83.65 (95% CI, 2.21–3166.29; 2 cases) for those with \geq 20 years of employment (Ahn & Jeong, 2015). [Although there were no apparent differences in risk with longer employment, the number of cases in each stratum was small, limiting the ability to draw inferences. Although there was increased risk of leukaemia in those with the longest duration in internal analyses, the estimates were not stable because of small numbers of cases. The young age of the cohort (mean age at end of follow-up, 41.3 years) was a limitation, being much younger than the median age at diagnosis for these cancers typically seen in the general population.]

An earlier study in the same cohort (33 416 professional [career] emergency responders; 29 438 firefighters) investigated cancer incidence rather than mortality (Ahn et al., 2012). With cancer incidence follow-up between 1996 and 2007, those ever employed as a firefighter had an age- and calendar year-adjusted SIR of 1.33 (95% CI, 0.91–1.87; 32 cases) for all lymphatic and haematopoietic malignancies [ICD-10, C81–C96] with the national male population of the Republic of Korea as the referent. Stratification by duration of employment (< 10 and \geq 10 years) did not reveal a higher estimate for those employed for a longer duration. For NHL [ICD-10, C82–C85], the overall SIR was 1.69 (95% CI, 1.01–2.67;

18 cases), with similar results for those employed for < 10 years and for \ge 10 years. For leukaemia [ICD-10, C91–C95], the SIR for any employment was 1.05 (95% CI, 0.56–1.79; 13 cases). Although estimates for leukaemia and NHL were elevated for shorter employment duration (< 10 years), they were not stable because of small numbers of cases, and risks did not increase with longer duration (\geq 10 years). An internal analysis comparing firefighters with non-firefighters in the cohort showed that the age- and calendar year-adjusted SRRs were 0.81 (95% CI, 0.28–2.33) for lymphatic and haematopoietic malignancies, 0.52 (95% CI, 0.15-1.78) for NHL, and 1.68 (95% CI, 0.22-13.06) for leukaemia. [The relatively short follow-up (10 years) and young age of the cohort (mean age at the end of follow-up, 41.3 years) were limitations of this study. The elevated risks in the SIR analyses for all cancers of lymphatic and haematopoietic tissues combined and NHL were not observed in the internal analyses, whereas the opposite pattern was seen for leukaemia.]

Two reports from a study in Norway were published in 2022 (Marjerrison et al., 2022a, b); both included 3881 male professional [career] firefighters employed at one of fifteen fire departments around the country. The cohort included mostly full-time firefighters employed between 1950 and 2019, with past or present employment in positions entailing active firefighting duties. Cancer incidence was ascertained through linkage with the national cancer registry, whereas mortality was ascertained from the Cause of Death Registry with follow-up from 1960 through 2018 in both sources. Investigators calculated age- and calendar year-standardized SIRs and SMRs for firefighters compared with the general male population of Norway. For Hodgkin lymphoma (ICD-10, C81), the SIR for ever-employment was 0.53 (95% CI, 0.06-1.91; 2 cases); there were no deaths. The two cases both occurred in the same category of duration, time since first employment, and calendar follow-up period (first employed 1950-1969;

 \geq 40 years since first employment; \geq 30 years for duration of employment; follow-up period, 1995 or after). Both cases were diagnosed at age 50-59 years (SIR, 1.49; 95% CI, 0.18-5.37). For NHL (ICD-10, C82–C86, C96), the SIR was 1.17 (95% CI, 0.76-1.71; 26 cases), whereas the SMR was 0.96 (95% CI, 0.44–1.83; 9 cases). The risks were comparable across categories of year of first employment (before 1950, 1950-1969 and 1970 or after), whereas risks were elevated for time since first employment in the first two categories (< 20 years and 20-39 years), but not for the longest time (≥ 40 years). For time of follow-up, the SIR was elevated in the follow-up period 1985–1994 (SIR, 2.00; 95% CI, 0.81–4.13; 7 cases), but not in any category for mortality. Both the SIR and SMR were elevated in those diagnosed at age 50-69 years (SIR, 1.22; 95% CI, 0.65-2.09; 13 cases; and SMR, 1.35 (95% CI, 0.44–3.14; 5 deaths). For multiple myeloma (ICD-10, C90), neither the SIR nor the SMR showed evidence of association. In stratified analyses, the estimates in most categories were below 1.0 for year of first employment and time since first employment, the exception being an elevated risk (SIR, 1.21; 95% CI, 0.39–2.82) for those first employed before 1950, although the estimate was based on only five cases. The SIR was 1.32 (95% CI, 0.36–3.39; 4 cases) for an employment duration of 20–29 years. For calendar follow-up period, the SIR and SMR for follow-up to the end of 1984 were each elevated but imprecise, and the SMR for follow-up in 1985–1994 was elevated. The SMR, but not the SIR, was elevated for those diagnosed at age \geq 70 years. [The Working Group noted the small number of cases in these categories.] For leukaemia, the SIR was 0.83 (95% CI, 0.46-1.40; 14 cases) and the SMR was 1.00 (95% CI, 0.48–1.84; 10 deaths) for ever-employment, and the SIR was near or above one for an employment duration of < 10 years (SIR, 1.02; 95% CI, 0.12–3.7; 2 cases) and \geq 30 years (SIR, 1.2; 95% CI, 0.57-2.2; 10 cases). There did not appear to be differences by follow-up period or

age at diagnosis for either incidence or mortality. In general, the results were similar for incidence and mortality, with the exceptions noted above. [The analysis of multiple specific subtypes of cancer of lymphatic and haematopoietic tissues was a strength; however, the sample sizes were often small for stratified analyses.]

In a cohort study of 8136 male firefighters in Sweden, firefighters were identified from employment information in the national decennial censuses between 1960 and 1990 (Bigert et al., 2020). Incident cancer diagnoses were ascertained in the Swedish Cancer Registry, with follow-up from 1961 through 2009. Ageand calendar time-standardized SIRs were calculated with the male general population of Sweden as the referent. In addition to analysis of ever-employment, external comparison analyses were also stratified by duration of employment and calendar time period. There were 42 cases of NHL (ICD-10, C83, C85) diagnosed, with an overall SIR for ever-employment of 1.05 (95% CI, 0.75–1.41). By duration of employment, the SIR in firefighters with ≥ 30 years of employment was 0.88 (95% CI, 0.45–1.53; P for trend, 0.90) and the SIR was highest in the most recent time period (1991–2009) at 1.22 (95% CI, 0.83–1.73; 31 cases). There were 26 cases of multiple myeloma (ICD-10, C90), with an overall SIR of 1.25 (95%) CI, 0.82–1.83), and an SIR for \geq 30 years of employment of 1.70 (95% CI, 0.93-2.85; 14 cases; P = 0.11). For leukaemia (ICD-10, C91–C95), the overall SIR was 0.94 (95% CI, 0.65–1.33; 33 cases) and for chronic lymphatic leukaemia (ICD-10 code not provided) it was 0.85 (95% CI, 0.47–1.43; 14 cases). Stratified analyses were not conducted for leukaemia.

A cancer incidence study in a cohort of 1080 male firefighters in Stockholm, Sweden, provided information on the risk of cancer of lymphatic and haematopoietic tissues (Kullberg et al., 2018). Firefighters were identified through annual enrolment records from 15 fire stations and worked for \geq 1 year between 1931 and 1983.

As an update to a previous study (Tornling et al., 1994), this study added 26 years of cancer incidence follow-up from 1958 through 2012 in the Swedish Cancer Registry. The previous study reported three deaths from all haematopoietic cancers. For cancer incidence results, only the more recent study is discussed here. With the male general population of Stockholm County as the referent, the overall SIR for lymphatic and haematopoietic malignancies (ICD-7, 200-209) during the full follow-up period (1958-2012) was 0.73 (95% CI, 0.43-1.16; 18 cases), whereas for the latest follow-up period (1987-2012) the SIR was 1.01 (95% CI, 0.56-1.66; 15 cases). For NHL (ICD-7, 200), the overall SIR was 0.68 (95% CI, 0.25–1.48; 6 cases), whereas for the later time period the SIR was 0.83 (95% CI, 0.27-1.94; 5 cases). For Hodgkin lymphoma (ICD-7, 201), the overall SIR was 1.39 (95% CI, 0.17-5.00; 2 cases) and the SIR for the later follow-up was 2.41 (95% CI, 0.06-13.40; 1 case), whereas for multiple myeloma the SIR for the later follow-up was 1.96 (95% CI, 0.64-4.57; 5 cases). For leukaemia (ICD-7, 204–207), the overall SIR was 0.38 (95%) CI, 0.08–1.10; 3 cases) and the SIR for the recent follow-up period was 0.43 (95% CI, 0.05-1.59; 2 cases). Overall, the results for the later time period were similar to those for the full-time period because most cancers occurred in the later time period. [Analyses of employment duration, latency, and number of fires fought were conducted in the earlier study by Tornling et al. (1994), but results were not reported for cancers of lymphatic and haematopoietic tissues.]

A cohort study of 9061 male firefighters in Denmark compared cancer incidence to that in three different reference groups: (i) the general population of men in Denmark; (ii) a sample of the male working population of Denmark; and (iii) male employees of the Danish military (Petersen et al., 2018a). Cohort members had been employed as firefighters at some time between 1964 and 2004, and cancer incidence follow-up was conducted in the Danish Cancer Registry from 1968 through 2014. With the military employees as the referent, the SIR for Hodgkin lymphoma (ICD-10, C81) was 1.42 (95% CI, 0.82-2.44; 13 cases) and the SIR for NHL (ICD-10, C82-85, C88.3-88.9) was 0.97 (95% CI, 0.70-1.34; 37 cases). With each reference group, the SIR was below one for multiple myeloma (ICD-10, C90, C88.0-C88.2; 8 cases), myeloid leukaemia (ICD-10, C92; 9 cases), and lymphoid leukaemia (ICD-10, C91; 15 cases). With the general population as the referent, the SIR for Hodgkin lymphoma was 2.29 (95% CI, 1.15-4.58) for part-time and volunteer firefighters. The results for Hodgkin lymphoma were not reported for the full-time workers and the number of cases was also not reported. The results for NHL were reported with stratification by employment type, era of first employment, job function (e.g. regular, specialized), age at first employment, and employment duration. The risks were elevated in those employed in or after 1995 (SIR, 1.46; 95% CI, 0.65-3.24; 6 cases), in those with a specialized job function, such as smoke divers, (SIR, 1.53; 95% CI, 0.57-4.08; 4 cases), and in those first employed at age 25-34 years (SIR, 1.21; 95% CI, 0.73-2.00; 15 cases). [The inclusion of three comparison groups allowed for the evaluation of healthy-worker bias. With the exception of Hodgkin lymphoma, for which the estimate was higher when using the general population as the referent, the estimates were very similar regardless of the reference group chosen, indicating that healthy-worker bias did not substantially influence results.]

Cancer mortality was investigated in the same cohort of Danish firefighters described above (Petersen et al., 2018b). An expanded study population of 11 775 male firefighters was followed for mortality in the Danish national death registry from 1970 through 2014. External comparisons were made with the military population as the referent [results with the working population as the referent were not reported for cancers of haematopoietic tissue]. SMRs were calculated for lymphatic and blood forming tissue cancers (ICD-10, C81–C96) for full-time firefighters (17 deaths) and part-time/volunteer firefighters (5 deaths). For both categories, the SMR was below 1.0, although the SMR for part-time/volunteer firefighters was smaller in magnitude. Analyses were also conducted by duration of employment, with modestly elevated risk in the categories of ≥ 1 and ≥ 10 years of employment. [Results were only reported for the larger grouping of all cancers of lymphatic and haematopoietic tissues combined, limiting the ability to make etiological inferences.]

A cancer incidence study in a cohort of 10 786 male firefighters from the FDNY who were exposed to the WTC disaster site and 8813 firefighters in the CFHS, which included firefighters from Philadelphia, Chicago, and San Francisco Fire Departments, provided information on the risk of NHL (Webber et al., 2021). Cancer incidence follow-up was conducted using several state cancer registries selected on the basis of residential history information and began on 11 September 2001 and ended in 2016. There were 55 cases of NHL [ICD-O-3 was used, but codes were not provided to identify NHL] identified in the FDNY cohort and 43 in the CFHS cohort, resulting in SIRs of 1.39 (95% CI, 1.06-1.83) and 1.04 (95% CI, 0.77–1.41), respectively, with the US male general population as the referent. Because WTC-exposed FDNY firefighters undergo free routine health-monitoring examinations, the authors noted concern about medical surveillance bias because of earlier detection of certain cancers. The authors also noted that the median age at diagnosis of NHL in the FDNY cohort was 53.6 years compared with 60.1 years in the CFHS cohort (P < 0.05), indicating the possibility of screening-detected cases of NHL. Therefore, a sensitivity analysis was undertaken, reclassifying the diagnosis dates of any NHL case that was diagnosed \leq 6 months after routine blood tests by delaying the diagnosis dates by 2 years. [The authors stated that 204 cancers were reclassified

overall, but do not mention the number of cases of NHL affected.] In this surveillance bias-adjusted analysis, the SIR for NHL was 1.29 (95% CI, 0.97–1.71). In addition, the authors calculated RRs adjusted for age and race/ethnicity in the FDNY cohort compared with the CFHS cohort. The RR for NHL was 1.26 (95% CI, 0.80–2.00) and the surveillance bias-adjusted RR was 1.21 (95% CI, 0.75-1.94). [The elevated SIR in the WTC-exposed FDNY cohort, but not the CFHS cohort, could indicate either the presence of an exposure unique to the WTC cohort that increased risk or the presence of surveillance bias. Although attenuated, both the SIR and RR remained elevated after the surveillance bias adjustment, suggesting that the WTC exposures may be more likely than bias to be the reason for the elevation.]

An earlier study by Moir et al. (2016) investigated cancer incidence in an overlapping cohort of 11 457 WTC-exposed firefighters in the FDNY compared with a reference pooled cohort of 8220 municipal firefighters from the CFHS cohort. Cancer incidence follow-up was conducted in state cancer registries from 2001 through 2009. Both cohorts were restricted to White men aged 30-70 years who had been employed for \geq 1.5 years before the end of the study, employed on or after 1 January 1996, and employed on 1 September 2001. From 11 September 2001 to 2009, 40 cases of haematological cancers were diagnosed among the WTC-exposed firefighters. The paper noted "hematologic cancers" with no further description, but presumably this included all cancers of lymphatic and haematopoietic tissues.] With the pooled cohort of other firefighters as the referent, the age-adjusted RR for haematological cancers was 1.04 (95% CI, 0.64–1.71). To account for potential medical surveillance bias in the specialized cohort of WTC-exposed firefighters, the researchers also conducted analyses lagging the diagnosis date by 2 years for cases of Hodgkin lymphoma or NHL diagnosed < 6 months after a surveillance chest

CT scan, and all cases of haematological cancers diagnosed < 6 months after a routine blood test. The RR for all haematological malignancies after this correction remained similar at 0.97 (95% CI, 0.58–1.60). Previous follow-up of this cohort to the end of 2008 did not provide evidence of an excess incidence of specific subtypes of haematological cancers, including Hodgkin lymphoma, multiple myeloma, and leukaemia, in WTC-exposed firefighters compared with the general population. However, an elevated rate of NHL was observed with the surveillance bias correction (SIR, 1.50; 95% CI, 0.97-2.33; 20 cases) (Zeig-Owens et al., 2011). [Limitations of this study included the reliance on a one-time assessment of being a firefighter at the WTC disaster site, the grouping of all cancers of lymphatic and haematopoietic tissues together, and the very short follow-up period. Strengths of the study included the ascertainment of cancer incidence and the comparison of two firefighter groups.]

Investigators from NIOSH conducted a mortality study in a cohort of 29 992 male and female municipal career firefighters in the CFHS from San Francisco, Chicago, and Philadelphia (Pinkerton et al., 2020). Mortality follow-up was conducted from 1950 to 2016. With the US general population as the referent, there was an elevated SMR for NHL (ICD-10, C46.3, C82-C85, C88.0, C88.3, C91.4, and C96) (SMR, 1.21; 95% CI, 1.03–1.42; 151 deaths) among firefighters. In internal regression analyses by cumulative exposure to fire responses for NHL, with the referent of 2500 exposed days, the hazard ratio at 8700 exposed days was 1.10 (95% CI, 0.60-2.11; 76 deaths) based on the fully adjusted model (including adjustment for employment duration). There were no associations apparent for number of fire-runs or fire-hours. For leukaemia, the overall SMR among firefighters was modestly elevated (SMR, 1.11; 95% CI, 0.94-1.31; 150 deaths). For the internal exposure-response analyses, the preferred model for this site was based on restricted cubic splines applying a 5-year lag [The authors reported preferring this model for leukaemia based on the nonmonotonic response with increasing risk at low exposures followed by attenuated risk at higher exposure. This pattern required a more flexible exposureresponse function. However, the cause of this attenuation was unclear.] The hazard ratio for the number of exposed days was elevated (HR, 2.39; 95% CI, 0.91–7.37; 72 deaths), as was the analysis based on 8800 fire-runs compared with 2100 fireruns (HR, 1.89; 95% CI, 1.06-3.48; 64 deaths), and 2300 fire-hours compared with 600 fire-hours (HR, 1.74; 95% CI, 0.78-4.15; 41 deaths). [The Working Group noted that this study was among the most informative studies that evaluated cancers of lymphatic and haematopoietic tissues. A limitation of this study was the use of cancer mortality outcomes rather than incidence.]

An earlier study of a subset of firefighters from the same CFHS cohort examined internal exposure-response associations with both cancer mortality and incidence, with follow-up to the end of 2009 (Daniels et al., 2015). The study included 19 309 firefighters of known race hired in 1950 or later and employed for \geq 1 year. Models were adjusted for the same covariates as in Pinkerton et al. (2020), with the exception of employment duration, and only the results for cancer incidence are reviewed here. Overall. there was little evidence of positive associations between exposure to fire responses and incidence of any cancers of lymphatic and haematopoietic tissues in the fully adjusted models. For NHL, there was a modest positive association with 2300 versus 600 fire-hours (HR, 1.12; 95% CI, 0.89-1.50, 45 cases). For leukaemia, the hazard ratio for 8800 versus 2100 fire-runs was 1.08 (95% CI, 0.75-1.84). For leukaemia, hazard ratios based on loglinear models that divided cumulative exposure into time windows were elevated for time since exposure of 5-15 years and 15–25 years, but not for > 25 years and age at exposure < 40 years. [Pinkerton et al. (2020) and Daniels et al. (2015) conducted more formal

adjustments for potential biases than did other studies, including the attempt to adjust for a healthy-worker survivor effect in <u>Pinkerton</u> <u>et al. (2020)</u>. After these adjustments and based on internal analyses, the mortality and incidence results were relatively comparable. Together, these studies were considered informative for the evaluation of cancers of lymphatic and haematopoietic tissues.]

An additional study in the CFHS cohort investigated cancer incidence among 29 993 municipal career firefighters and reported external and internal comparison analyses with follow-up to the end of 2009 (Daniels et al., 2014). The methods were similar to those in the study by <u>Pinkerton et al. (2020)</u>. Cancer incidence follow-up was conducted in state cancer registries relevant to each fire department to the end of 2009, with start years varying from 1985 to 1988. Residential history information was used to select state registries for follow-up. With the US general population as the referent, there were no elevations in the incidence rate of NHL (ICD-10, C46.3, C82-85, C88.0, C88.3, C91.4, and C96), leukaemia (ICD-10, C91.0-C91.3, C91.5-C91.9, and C92–C95), or multiple myeloma (ICD-10, C88.7, C88.9, and C90) among firefighters. In race-stratified analyses, there was an elevated SIR for leukaemia (SIR, 1.90; 95% CI, 0.95–3.40; 11 cases) among non-Caucasian [non-White] firefighters. No other associations by race were apparent.

In a cohort study of 2447 male municipal firefighters from Seattle and Tacoma, USA, cancer incidence was compared with that in the local male general population and in a cohort of male police officers from Washington state (Demers et al., 1994). Participants had been employed for \geq 1 year between 1944 and 1979. Cancer incidence follow-up was conducted from 1974 through 1989 in the regional SEER cancer registry, using residential history information to reduce loss to follow-up. Duration of active-duty employment in direct firefighting positions was ascertained from employment records in the Seattle subcohort. For NHL (ICD-9, 200-202), the overall SIR was 0.9 (95% CI, 0.4–1.9; 7 cases) with the local county population as the referent. The SIR was modestly elevated, although imprecise, for firefighters with 20-29 years of employment (SIR, 1.2; 95% CI, 0.4-2.7), but no elevations were observed for other duration categories. Compared with incidence rates among police, the IDR for NHL was elevated among firefighters but was highly imprecise (IDR, 1.8; 95% CI, 0.4–13). For leukaemia (ICD-9, 204–208), the overall SIR was 1.0 (95% CI, 0.4–2.1; 6 cases) for firefighters compared with the local general population. In analyses of employment duration, the SIR for firefighters with 10-19 years of employment was elevated, but results were highly imprecise (SIR, 1.9; 95% CI, 0.2-6.8; 2 cases). No positive associations were observed for leukaemia in the comparison with police. [This study was limited by a low number of cases of cancer of lymphatic and haematopoietic tissues.]

A previous cohort study of 4401 male municipal firefighters from Seattle, Tacoma, Washington, and Portland, Oregon, USA, investigated the risk of mortality outcomes (Demers et al., 1992a). Firefighters included in this cohort had been employed between 1944 and 1979, and the mortality follow-up period was from 1945 to the end of 1989. In addition to US population rates for the White male general population, a cohort of police from the same cities was also used as a comparison group. With the general population as the referent, SMRs were elevated for lymphatic and haematopoietic malignancies (ICD-9, 200-208), lymphosarcoma-reticulosarcoma (ICD-9, 200), leukaemia (ICD-9, 204–208), and other lymphatic or haematopoietic malignancies (ICD-9, 202, 203), but not for Hodgkin lymphoma. With police as the referent, the mortality IDR was elevated only for other lymphatic or haematopoietic malignancies. SMRs were also calculated evaluating duration of employment (in active firefighting positions for

Seattle and Portland firefighters, or any employment as a firefighter for Tacoma firefighters), time since first employment, and age. For lymphatic and haematopoietic malignancies overall, the SMR was elevated in those with 10-19 years and \geq 30 years duration of employment (SMR, 1.46; 95% CI, 0.06-3.0, 7 cases; and SMR 2.05; 95% CI, 1.1-3.6, 12 cases; respectively). SMRs were also elevated for those with < 20 or ≥ 30 years since first employment. For leukaemia, the SMR was elevated in those with \geq 30 years duration of employment (SMR, 2.6; 95% CI, 1.0-5.4), \geq 30 years since first employment (SMR, 1.4; 95% CI, 0.7–2.5), and age \geq 65 years (SMR, 1.67; 95% CI, 0.8-3.2, 9 deaths). [For several stratified analyses, the number of cases was small.]

A proportionate mortality study of police and firefighters was conducted in New Jersey, USA (Feuer & Rosenman, 1986). Analyses were based on 263 deaths in White male firefighters reported to the state comprehensive retirement system for police and firefighters in 1974–1980. Three reference populations were used to compare mortality proportions among firefighters, including the US general population, the New Jersey general population, and police officers identified in the same data source. [Although duration of employment and latency-based analyses were reported for some outcomes, these were not reported for any cancers of lymphatic and haematopoietic tissues.] For leukaemia (ICD-8, 204-207), the PMR for firefighters was elevated using each of the three reference groups, although estimates were based on only four deaths. The greatest elevation was observed when using the police officers as the referent (PMR, 2.76; 95% CI, [0.88-6.65]).

A mortality study in a cohort of 5414 male career firefighters was conducted in Toronto, Canada (Aronson et al., 1994). Firefighters had been employed between 1950 and 1989 and mortality follow-up was conducted in a national mortality database from 1950 through 1989. Overall, there were 18 deaths from lymphatic and haematopoietic malignancies (ICD-9, 200-208). With the male general population of Ontario as the referent, the overall SMR for lymphatic and haematopoietic malignancies among firefighters was 0.98 (95% CI, 0.58-1.56). For lymphosarcoma/reticulosarcoma (ICD-9, 200), the SMR was elevated, but the estimate was highly imprecise (SMR, 2.40; 95% CI, 0.42-5.96; 3 deaths). There was an increase in the SMR for firefighters employed for 10–14 years, although the estimate was also highly imprecise. [No additional information was provided for this cancer site for duration, time since first employment, or age.] There was one case each of Hodgkin lymphoma and multiple myeloma, with SMR estimates below 1.0 and wide confidence intervals. For lymphoid leukaemia (ICD-9, 204), the SMR was elevated for ever-employment as a firefighter (SMR, 1.90; 95% CI, 0.52-4.88; 4 deaths). All cases of lymphoid leukaemia occurred in firefighters with \geq 30 years since first exposure, \geq 30 years of employment duration, and age \geq 60 years, resulting in elevated, but imprecise, SMRs for these categories. For myeloid leukaemia, the SMR for ever-employment was elevated (SMR, 1.20; 95% CI, 0.33–3.09), although the estimate was based on only four cases. Results stratified by duration, age, and time since employment were not reported for this site. [This study was limited by a low number of deaths from cancers of lymphatic and haematopoietic tissues.]

A mortality study of 3328 municipal firefighters in two cohorts from Calgary and Edmonton, Canada, provided information on the risk of all cancers of lymphatic and haematopoietic tissues combined (Guidotti, 1993). Firefighters had been employed between 1927 and 1987, and mortality follow-up was conducted in both provincial and national sources from 1927 through 1987. Overall, there were 10 deaths from lymphatic and haematopoietic malignancies (ICD-9, 200–208) among the firefighters, resulting in an elevated SMR of 1.26 (95% CI, 0.61–2.32) with the male general population of Alberta as the referent. Year at entry into the cohort was evaluated, and SMRs were elevated for those who entered before 1920 and in 1930–1939, 1940–1949, and 1960–1969. [The reporting of results only for all cancers of lymphatic and haematopoietic tissues combined limited the informativeness of this study.]

A cancer incidence study in an entirely female cohort of 37 962 volunteer firefighters was conducted in Australia (Glass et al., 2019). Cancer incidence follow-up was conducted in a national cancer registry from 1982 through 2010. Work history information describing the number and type of incidents attended was ascertained from fire agency personnel records. With the female general population of Australia as the referent, the SIR for lymphatic and haematopoietic neoplasms (ICD-10, C81-C96, D45-D46, D47.1, and D47.3) among all volunteer firefighters was 0.99 (95% CI, 0.80-1.22; 90 cases), and among those who had attended incidents it was 1.02 (95% CI, 0.72-1.41; 37 cases). For NHL (ICD-10, C82-C85), the SIR for those who had attended incidents was modestly elevated (SIR, 1.19; 95% CI, 0.71-1.88; 18 cases). For multiple myeloma (ICD-10, C90), the SIR was higher for all volunteers (13 cases) than for those who attended incidents (4 cases). A similar pattern was seen for leukaemia (ICD-10, C91–C95) based on 23 and 6 cases, respectively. Results from internal regression analyses by tertile of number of incidents attended were imprecise and did not indicate positive associations for either all lymphatic and haematopoietic malignancies combined or NHL. [In external analyses, the magnitude of reported effect estimates was smaller for volunteers who attended fire incidents than for volunteers overall for multiple myeloma and leukaemia, making it less likely that any increase was attributable to firefighting activities. For NHL, the increase was only seen in those who had attended incidents.]

Two studies of male firefighters in Australia were similar to that focused on female firefighters. The first was a cohort study of cancer incidence among 163 094 male volunteer firefighters from five fire agencies (Glass et al., 2017). A total of 663 cases of lymphohaematopoietic neoplasms (ICD-10, C81-C96, D45-D46, D47.1, and D47.3) were identified among all volunteer firefighters and 426 among the subset of those who had attended fire incidents. With the male general population of Australia as the referent, the SIR for all volunteer firefighters (SIR, 0.81; 95% CI, 0.75-0.88) was the same as that for volunteers who attended incidents (SIR, 0.81; 95% CI, 0.74-0.89). In internal regression analyses, the RIRs [equivalent to rate ratios] for all lymphohaematopoietic neoplasms indicated no elevated risks for any category of duration of service among either the full cohort or those who attended incidents. The rate of all lymphohaematopoietic neoplasms decreased with increasing duration of service among all volunteer firefighters. In contrast, the RIRs were elevated in all categories of exposure based on the number of incidents attended overall, as well as the number of structure fire, landscape fire, and vehicle fire incidents. For NHL (ICD-10, C82-C85), the SIR analyses indicated no evidence of excess risk in all volunteers or in volunteers who attended incidents. The RIRs were elevated for the middle tertile only of the total number of incidents attended (RIR, 1.30; 95% CI, 0.69-2.47; 10 cases), and for the number of fire incidents (RIR, 1.39; 95% CI, 0.75-2.56; 11 cases) and structure fire incidents (RIR, 1.67; 95% CI, 0.82-3.40; 8 cases), although confidence intervals were wide. There was no elevated risk in the higher tertiles of cumulative incidents, or in any category of duration of service. The authors also reported SIRs for volunteers who had attended incidents for some NHL subtypes, including follicular lymphoma (ICD-10, C82) (SIR, 1.08; 95% CI, 0.81-1.40; 56 cases) and diffuse large B-cell lymphoma (ICD-10, C83.3) (SIR, 0.83; 95% CI, 0.66–1.03; 82 cases). Internal analyses were not conducted for the subtypes. SIRs were also reported for Hodgkin lymphoma (ICD-10, C81), multiple myeloma (ICD-10, C90), leukaemia (ICD-10, C91-C95),

and myelodysplastic syndrome (ICD-10, D46), but none were elevated for either the cohort as a whole or for the subset of those who attended incidents. [The analysis of specific NHL subtypes was a strength of this study.]

The second study of male firefighters in Australia was conducted in a cohort of 30 057 paid full-time and part-time firefighters (Glass et al., 2016a). The cohort was enumerated and analysed using similar methods as those used in the studies of volunteer firefighters. Included firefighters had worked between 1976 and 2003 and were primarily municipal or semi-metropolitan firefighters. Cancer incidence follow-up was conducted in a national registry to the end of 2010. With the general male population of Australia as the referent, there was no excess risk of all lymphatic and haematological neoplasms (ICD-10, C81-C96, D45-D46, D47.1, and D47.3) among either full-time or part-time firefighters. In internal regression analyses, the RIRs [equivalent to rate ratios] for duration of employment and all lymphatic and haematological neoplasms combined were elevated for both 10-20 years and \geq 20 years employment for full-time firefighters (RIR, 2.38; 95% CI, 1.08-5.26; 22 cases; and RIR, 3.08; 95% CI, 2.32-7.20; 75 cases; respectively; P for trend, 0.01), but not for part-time firefighters. There were few elevations in the RIRs for all lymphatic and haematological neoplasms across categories of number of any type of fire incident attended, except for tertile 2 for landscape and vehicle fires. For NHL (ICD-10, C82-C85), the SIRs were not elevated for full-time or part-time firefighters in external analyses. In internal analyses, the RIRs were elevated for both 10–20 years and \geq 20 years of employment among full-time firefighters (RIR, 2.12; 95% CI, 0.71-6.34; and RIR, 3.67; 95% CI, 1.28-10.54; respectively; P = 0.01). For part-time firefighters, the RIR was elevated in the \geq 20 years duration category only. For analyses of NHL based on the number and type of incidents attended, there were no apparent positive associations for any

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type of incident. For other cancer types, external comparison analyses indicated no excess risk of Hodgkin lymphoma, multiple myeloma, leukaemia, or myelodysplastic syndrome among firefighters compared with the male population of Australia.

A study of cancer incidence was conducted in a cohort of 614 firefighters and trainers who attended a firefighter-training facility in Australia (Glass et al., 2016b). Three female firefighters were excluded from the analysis. Cancer incidence follow-up was conducted from 1982 through 2012. Participants were grouped into risk categories of low, medium, and high chronic exposure (to smoke and other hazardous agents) on the basis of job assignment. Eight cases of lymphohaematopoietic neoplasms (ICD-10, C81-C96, D45-D46, D47.1, and D47.3) were identified during follow-up. Compared with the general male population of Victoria, participants with an estimated medium risk of chronic exposure had an SIR of 1.12 (95% CI, 0.30-2.86; 4 cases), and those with high risk of chronic exposure had an SIR of 2.83 (95% CI, 0.77-7.24; 4 cases). [This study was limited by the low number of cases in each exposure group and the reporting of risks only by the grouping of all neoplasms of lymphatic and haematopoietic tissues combined.]

2.3.2 Studies only reporting having ever worked as a firefighter

(a) Occupational cohort studies

Studies first described in Section 2.1.2(a) are described in less detail in the present section.

See Table S2.6 (Annex 2, Supplementary material for Section 2, Cancer in Humans, online only, available from: <u>https://publications.iarc.</u> <u>fr/615</u>).

Occupational cohort studies that described incidence or mortality for cancers of lymphatic and haematopoietic tissues in firefighters are included in this section. Cancer sites included in this classification include lymphoma (non-Hodgkin and Hodgkin), lymphosarcoma-reticulosarcoma, multiple myeloma, and leukaemia. Eight studies were included (Musk et al., 1978; Eliopulos et al., 1984; Grimes et al., 1991; Giles et al., 1993; Bates et al., 2001; Ma et al., 2005; 2006; Amadeo et al., 2015). All cohorts assessed in this section were enumerated through record linkage of employment records or certifications. [The grouping of all cancers of lymphatic and haematopoietic tissues together was a limitation of most studies in this section. Furthermore, changes in the classification of these cancers over time made it particularly difficult to compare findings across studies.]

A cohort of all male French firefighters employed on 1 January 1979 was assembled (Amadeo et al., 2015). With follow-up to the end of 2008, there were 42 deaths from lymphohaematopoietic malignancies [ICD codes not given] with an age- and calendar year-adjusted SMR of 0.89 (95% CI, 0.64–1.20) for the 10 829 cohort members compared with the male general population of France.

Two studies were conducted in a cohort of firefighters certified between 1972 and 1999 in Florida, USA; one study assessed cancer incidence (Ma et al., 2006), and the other assessed mortality (Ma et al., 2005). The overall cohort size for both studies was 36 813, including 34 796 men and 2017 women. For cancer incidence, cases were identified through linkage with the Florida Cancer Data System (the Florida cancer registry), and age- and calendar-year adjusted SIRs were calculated separately for men and women with the population of Florida as the referent (Ma et al., 2006). Risks were reported only separately for each sex. [The ICD codes used were not provided; only the ICD-O-3 morphology codes for exclusion were included in the manuscript.] For men, the SIRs were 0.68 (95% CI, 0.54–0.85; 78 cases) for cancers of lymphatic and haematopoietic tissues overall, 1.09 (95% CI, 0.61-1.80; 15 cases) for NHL, 0.77 (95% CI, 0.38-1.38; 11

cases) for Hodgkin lymphoma, and 0.77 (95% CI, 0.47-1.19; 20 cases) for leukaemia. For women, the SIRs were 2.62 (95% CI, 0.96–5.70; 6 cases) for all cancers of lymphatic and haematopoietic tissues, 33.30 (95% CI, 0.44-185.00; 1 case) for NHL, and 6.25 (95% CI, 1.26-18.30; 3 cases) for Hodgkin lymphoma. There were no cases of leukaemia in women. [The Working Group noted that evaluation of specific types of cancer of lymphatic and haematopoietic tissues (NHL, leukaemia) was a strength of this study, but that subtypes within these categories (e.g. NHL subtypes) were not reported.] Mortality was assessed in the same cohort (Ma et al., 2005). With the general population of Florida as the referent, the SMR for men was 0.77 (95% CI, 0.56–1.05; 42 cases) for all lymphatic and haematopoietic malignancies (*n* = 42), 0.65 (95% CI, 0.13–1.90; 3 cases) for lymphosarcoma-reticulosarcoma, 0.23 (95% CI, 0.00-1.30; 1 case) for Hodgkin lymphoma, and 0.84 (95% CI, 0.46-1.42; 14 cases) for leukaemia. For women, the SMR for all lymphatic and haematopoietic malignancies was 1.25 (95% CI, 0.02–6.95; 1 case). There were no deaths among women for lymphosarcoma-reticulosarcoma, Hodgkin lymphoma, or leukaemia. [Codes used for classification were not provided for the mortality analysis but were based on ICD-9.] In men, the risks of lymphatic and haematopoietic malignancies and leukaemia on the basis of incidence and mortality were similar. In women, the risks of lymphatic and haematopoietic malignancies overall and NHL were elevated for cancer incidence, but not for mortality; however, the number of cases was small (6 cases of lymphatic and haematopoietic malignancies and 1 case of NHL), resulting in a wide confidence interval.

A study of 205 deaths among male firefighters in Honolulu, USA, reported a PMR for deaths from cancers of the lymphatic system [ICD-9, 200–209] of 0.95 (95% CI, 0.36–2.50; 4 deaths) (Grimes et al., 1991). [The Working Group noted the lack of standardization of PMRs by age and calendar year as an important limitation.] A study in male firefighters employed for \geq 3 years in Boston, USA, reported SMRs based on deaths from 1915 through 1975 (Musk <u>et al., 1978</u>). With the male general population of Massachusetts as the referent, the SMR for all lymphatic and haematopoietic malignancies [ICD-7, 200–205] among firefighters was 0.63 (95% CI, [0.41–0.94]; 22 deaths). [Confidence intervals were calculated by the Working Group.]

A study of 4221 male paid [career] and volunteer firefighters in New Zealand identified through a database evaluated both cancer incidence (1977-1996) and mortality (1977-1995) (Bates et al., 2001). [Although women were enumerated, only men were included in the analyses.] The SIR for myeloid leukaemia (ICD-9, 205) was 1.81 (95% CI, 0.5-4.6), adjusted for age and calendar year and with the male general population of New Zealand as the referent. There were four deaths from lymphatic or haematopoietic cancers (ICD-9, 200-208) with an SMR of 0.72 (95% CI, 0.2–1.8). [The inclusion of results for myeloid leukaemia was a strength. The reliance on the overall grouping of cancers of lymphatic and haematopoietic tissues for the mortality analysis was a limitation.]

A cohort of 2865 male firefighters in Melbourne, Australia, was followed from 1980 through 1989 for cancer incidence (Giles et al., 1993). Exposure assessment was based on employment records and included firefighters employed between 1917 and 1989. Age- and calendar period-adjusted SIRs were calculated with the general population of the state of Victoria as the referent. For NHL (ICD, 200, 202), the SIR was 1.85 (95% CI, 0.50–4.74; 4 cases). [The Working Group noted that the ICD revision was not specified in the publication.] No cases of leukaemia were diagnosed during this period.

A cohort of 990 male firefighters employed by the Western Australia Fire Brigade was followed from 1939 through 1978 for mortality (<u>Eliopulos</u> <u>et al., 1984</u>). Standardized PMRs were calculated for lymphohaematopoietic malignancies overall [ICD codes not given]. The age- and calendar year-standardized PMR was 1.88 (95% CI, 0.39–5.50; 3 deaths). [Although there were some analyses of duration and time of first employment, this was only applied to death overall and not specifically to cancers of lymphatic and haematopoietic tissues.]

(b) Population-based studies

Studies first described in Section 2.1.2(b) are described in less detail in the present section.

See Table S2.6 (Annex 2, Supplementary material for Section 2, Cancer in Humans, online only, available from: <u>https://publications.iarc.</u> <u>fr/615</u>).

This section includes general population-based studies that evaluated the risks of cancer of lymphatic and haematopoietic tissues among people with the occupation of firefighter and includes four cohort studies derived from census or compensation claims data (Pukkala et al., 2014; Harris et al., 2018; Zhao et al., 2020; Sritharan et al., 2022), two studies based on death certificate data (Burnett et al., 1994; Ma et al., 1998), and six event-only studies using US state cancer registry data (Sama et al., 1990; Bates, 2007; Kang et al., 2008; Tsai et al., 2015; Lee et al., 2020; McClure et al., 2021).

For the cohort studies, occupation as a firefighter was ascertained from census questionnaires, workers' compensation claims data, or death certificates. Comparisons were made with the rest of the enumerated group not employed as a firefighter. All except one study (<u>Sritharan</u> <u>et al., 2022</u>) included only men. The case–control [event-only] studies used patients with other types of cancer (or other causes of death) as controls.

The first census-based study was conducted in Spain (Zhao et al., 2020) and linked data from the 2001 census to the mortality registry to the end of 2011. Among 9 579 759 male cohort members aged 20–64 years and employed on the date of the 2001 census, there were 27 365 firefighters.

Among the firefighters, there were 11 deaths from lymphoma (ICD-10, C81-C83), including two from Hodgkin lymphoma (ICD-10, C81), and seven from leukaemia (ICD-10, C91-C95) for a total of 18 cases of cancers of lymphatic or haematopoietic tissue. Age-standardized MRRs were calculated using the European population as the standard. The MRR was 1.29 (95% CI, 0.69–2.34) for lymphoma, 1.41 (95% CI, 0.34-5.85) for Hodgkin lymphoma, and 0.90 (95% CI, 0.40-2.01) for leukaemia. [Although the overall study size was large, there were few cases of lymphoma and leukaemia among the firefighters because of the short follow-up and young age of the cohort members at the end of follow-up.]

Another census-based study was an analysis of the NOCCA pooled cohort based on census data from five Nordic countries (Denmark, 1970 census; Finland, 1970, 1980, and 1990 censuses; Iceland, 1981 census; Norway, 1970, 1970, and 1980 censuses; and Sweden, 1960, 1970, 1980, and 1990 censuses) that evaluated occupation as a firefighter (Pukkala et al., 2014). Among 15 million respondents to these censuses, 16 422 male firefighters were identified. Overall among those employed as firefighters, there were 82 cases of NHL (ICD-10, C82-C85, C96), 41 cases of multiple myeloma (ICD-10, C90), and 56 cases of leukaemia (ICD-10, C91-C95), including 21 cases of acute myeloid leukaemia. Analyses were conducted by country, with the country-specific rates for the male population used as the referent, by age at follow-up, and by 5-year category of calendar period of follow-up (1961-2005). The overall (all countries combined) SIR for NHL was 1.04 (95% CI, 0.83–1.29), for multiple myeloma it was 1.13 (95% CI, 0.81-1.53), and for leukaemia it was 0.94 (95% CI, 0.71–1.22). Within leukaemia subtypes, the SIR for acute myeloid leukaemia was 1.27 (95% CI, 0.79-1.94). The risk of multiple myeloma was elevated in those diagnosed at age \geq 70 years, with an SIR of 1.69 (95% CI, 1.08–2.51). Other analyses stratified by country,

age, and calendar time of follow-up did not reveal meaningful differences. [The Working Group noted that the large size of the cohort allowed for the evaluation of specific types of cancer of lymphatic and haematopoietic tissues; however, some strata were still limited by small numbers.]

Sritharan et al. (2022) evaluated the cancer experience of firefighters identified from the Occupational Disease Surveillance System (ODSS), a database created from workers' injury and disease claims in Ontario, Canada. The cohort comprising 2 368 226 workers, including 13 642 firefighters and 22 595 police, was linked to the Ontario Cancer Registry to identify cancers diagnosed from 1983 to 2020. Hazard ratios were calculated comparing firefighters to all other workers in the full cohort, as well as to the police identified in the cohort, and were adjusted for age at start of follow-up, birth year, and sex. The hazard ratio for firefighters compared with all other workers was 1.35 (95% CI, 1.11-1.64; 104 cases) for NHL (ICD-10, C82), 1.27 (95%) CI, 0.68–2.37; 10 cases) for Hodgkin lymphoma (ICD-10, C81), 1.18 (95% CI, 0.82–1.70; 29 cases) for myeloma (ICD-10, C90), and 1.35 (95% CI, 1.05–1.73; 64 cases) for leukaemia (ICD-10, C91). The hazard ratio for firefighters compared with police was 1.21 (95% CI, 0.92-1.58) for NHL, 1.33 (95% CI, 0.57–3.12) for Hodgkin lymphoma, 0.94 (95% CI, 0.57–1.53) for multiple myeloma, and 1.15 (95% CI, 0.81-1.62) for leukaemia. [The Working Group noted that results were attenuated when comparing the firefighters with the police rather than with the full worker cohort for NHL, multiple myeloma, and leukaemia, suggesting that selection bias or healthy-worker bias may have influenced the results for the full cohort or, alternatively, that these groups may have shared exposures.]

The CanCHEC study of more than 1.1 million people was created by linking the 1991 census to the Canadian Cancer Registry (<u>Harrisetal., 2018</u>). This study, which identified 4535 male firefighters aged 25–74 who were employed at the time of the census in 1991, included follow-up to the end of 2010. Using all other members of the cohort as the referent, hazard ratios were calculated for Hodgkin lymphoma (5 cases), multiple myeloma (10 cases), NHL (30 cases) and leukaemia (15 cases) for employment as a firefighter adjusted for age group, region, and education level. [Classification was based on ICD-O-3, but codes were not provided for individual cancer sites.] The hazard ratio for Hodgkin lymphoma was 2.89 (95% CI, 1.29–6.46), for multiple myeloma was 1.52 (95% CI, 0.82–2.84), for NHL was 1.00 (95% CI, 0.71–1.41) and for leukaemia was 0.93 (95% CI, 0.55–1.58).

Lee et al. (2020) used linkage between employment records of the Florida State Fire Marshal, USA, and the Florida cancer registry to study associations between firefighter employment and cancers of lymphatic and haematopoietic tissues. Controls were cancer patients diagnosed with any other type of cancer, and ORs were adjusted for age and year of diagnosis. Among 3760 male firefighters, there was no evidence of higher risk of cancers of the lymphatic or haematopoietic tissues. Associations were inverse for all sites (e.g. OR for NHL, 0.88; 95% CI, 0.75-1.03; 168 cases; OR for multiple myeloma, 0.80; 95% CI, 0.59–1.10; 40 cases; and OR for acute myeloid leukaemia, 0.63; 95% CI, 0.41–0.96; 21 cases). There was no clear evidence of heterogeneity of these associations by stage (early versus late stage) or age at cancer diagnosis (age < 50 years, or > 50 years), although sample size limited the ability to assess this for most cancers of lymphatic or haematopoietic tissues other than NHL. Among 168 female firefighters, risk appeared elevated for Hodgkin lymphoma (OR, 1.68; 95% CI, 0.62–4.56; < 10 cases), multiple myeloma (OR, 1.32; 95% CI, 0.33-5.32; < 10 cases), and chronic lymphocytic leukaemia (OR, 2.33; 95% CI, 0.58-9.41; < 10 cases), but inverse for myeloid leukaemia (OR, 0.51; 95% CI, 0.07–3.57; < 10 cases) [The Working Group noted the substantial imprecision of all estimates.] Risk of NHL in female

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firefighters was similar to that in female non-firefighters (OR, 0.98; 95% CI, 0.43–2.21; < 10 cases). [The Working Group noted that case sample size among female firefighters was particularly small (< 10 cases for all cancers of lymphatic and haematopoietic tissues).] A subsequent paper (McClure et al., 2019) compared the firefighter occupation information used in Lee et al. (2020) (from employment records of the Florida State Fire Marshal) with that in occupation records in the Florida cancer registry (an approach used by previous studies). In this analysis, McClure et al. (2019) found that of 3928 firefighters studied by Lee et al., only 679 (17%) had a firefighting-related occupation code in the Florida cancer registry and that this information was differentially distributed by sociodemographic and diagnosis characteristics. McClure et al. (2021) then compared occupation as a firefighter and risk of cancers of lymphatic and haematopoietic tissues using these two different occupation ascertainment approaches. Data were available from the Florida cancer registry for 1981–2014 and from the office of the Florida State Fire Marshal for 1972-2012. Results for leukaemia were similar using the two different occupation information sources but were conflicting for lymphoma (employment as defined by the Florida State Fire Marshal, OR, 0.86; 95% CI, 0.75–0.99; 200 cases; cancer-registry-defined employment, OR, 1.10; 95% CI, 0.90-1.34; 109 cases).

Tsai et al. (2015) conducted a registry-based study using the California Cancer Registry, USA, in 1988–2007. Patients with cancers of the pharynx, stomach, liver, and pancreas were considered as controls. Occupation as a firefighter was associated with increased risk of most cancers of lymphatic and haematopoietic tissue, including multiple myeloma (OR, 1.35; 95% CI, 1.00–1.82; 55 cases), NHL (OR, 1.22; 95% CI, 1.00–1.50; 183 cases) and leukaemia (OR, 1.32; 95% CI, 1.05–1.66; 122 cases), particularly acute myeloid leukaemia (OR, 1.44; 95% CI, 1.02–2.02; 42 cases). Most associations were stronger for non-White individuals. Among non-White cancer patients, firefighters were two to three times as likely as non-firefighters to be diagnosed with NHL (OR, 2.17; 95% CI, 1.20–3.92; 24 cases), multiple myeloma (OR, 3.77; 95% CI, 1.91–7.44; 13 cases), or leukaemia (OR, 3.64; 95% CI, 1.96–6.74; 20 cases). Bates (2007) conducted a similar study with the California Cancer Registry, 1988–2003, but these data were included in the study conducted later by Tsai et al. (2015) with data from 1988–2007.

a cancer registry-based study in In Massachusetts, USA (1987–2003), Kang et al. (2008) calculated SMBORs (adjusted for age and smoking) for cancers of lymphatic and haematopoietic tissues in firefighters compared with two occupation groups: police and all other occupations. Control cancers were those in the Massachusetts registry other than the 25 "cancers of concern" for which at least two previous studies had reported an observed association with firefighting. Compared with male police officers, male firefighters appeared to have lower risk of leukaemia (SMBOR, 0.72; 95% CI, 0.43-1.20; 46 cases), NHL (0.77; 95% CI, 0.31-1.92; 13 cases), and multiple myeloma (SMBOR, 0.76; 95% CI, 0.39–1.48; 29 cases), but the estimates were quite imprecise. Compared with men in other occupations, male firefighters had a similar risk of leukaemia (SMBOR, 0.98; 95% CI, 0.69-1.39), NHL (SMBOR, 1.10, 0.58–2.09), and multiple myeloma (SMBOR, 0.92; 95% CI, 0.58–1.47). Risk of Hodgkin lymphoma appeared to be higher for firefighters than for police (SMBOR, 1.81; 95% CI, 0.72–4.53) or for other occupations (SMBOR, 1.56; 95% CI, 0.71-3.43), although based on only 8 cases. [The Working Group noted that the Kang et al. analyses controlled for smoking status and age. Smoking is a suspected or known risk factor for some but not all types of cancer of lymphatic and haematopoietic tissues, including some types of leukaemia, NHL, and myeloma. Etiological heterogeneity may play a role in null and/or inconsistent results in Kang and other

studies.] Sama et al. (1990) conducted a similar cancer registry-based study in Massachusetts, USA, but covering an earlier time period (1982– 1986) and controlling only for age. In the earlier study, occupation as a firefighter was associated with increased odds of NHL and leukaemia with either group as referent, but associations were stronger with police as the referent - SMBOR for NHL, 3.27 (95% CI, 1.19-8.98; 14 cases); and SMBOR for leukaemia: 2.67 (95% CI, 0.62–11.54; 6 cases). With other occupations as the referent, the SMBORs for occupation as a firefighter were 1.59 (95% CI, 0.89–2.84) for NHL and 1.12 (95% CI, 0.48–2.59) for leukaemia. [The Working Group noted that stronger associations were observed when firefighters were compared with police in <u>Sama et al. (1990)</u> but not in <u>Kang et al. (2008)</u>. Differences included the time period covered and control for smoking in Kang et al. Differences in the distribution of NHL and leukaemia subtypes may also account for differences in findings. Random variation may also have played a role in this inconsistency because of small sample size for most cancers of lymphatic and haematopoietic tissues in both studies.]

Ma et al. (1998) conducted a study of employment as a firefighter and risk of cancers of lymphatic and haematopoietic tissues using occupation codes on male death certificates in 24 US states (1984–1993). Analyses controlled for age and time of death and were stratified by race. Controls were non-cancer causes of death. Among White men, positive associations for occupation as a firefighter were observed both for Hodgkin lymphoma (MOR, 2.4; 95% CI, 1.4–4.1; 13 cases) and for NHL (MOR, 1.4; 95% CI, 1.1–1.7; 76 cases). Smaller associations were observed for multiple myeloma (MOR, 1.1; 95% CI, 0.8-1.6; 28 cases) and leukaemia (MOR, 1.1; 95% CI, 0.8–1.4; 60 cases). Only two cases of cancer of lymphatic and haematopoietic tissues were reported among Black firefighters. [The Working Group noted that etiology as well as survival varies by subtype of cancer of lymphatic and haematopoietic tissues,

and these differences may limit the conclusions that can be drawn from mortality studies.]

Another US mortality surveillance study calculated PMRs for individual causes of death, overall and by age at death, in 27 US states (Burnett et al., 1994). There were 169 deaths from lymphatic and haematopoietic malignancies (PMR, 1.30; 95% CI, 1.11-1.51), of which 85 occurred before age 65 years (PMR, 1.61; 95% CI, 1.29-1.99). For NHL (ICD-9, 200-202), there were 66 deaths overall, resulting in a PMR of 1.32 (95% CI, 1.02-1.67), with 35 deaths under age 65 years (PMR, 1.61; 95% CI, 1.12-2.24). For multiple myeloma (ICD-9, 203), there were 34 deaths overall, of which 11 occurred under age 65 years, resulting in PMRs of 1.48 (95% CI, 1.02-2.07) and 1.36 (95% CI, 0.68-2.43), respectively. Finally, for leukaemia (ICD-9, 204-208), there were 61 deaths overall, of which 33 occurred under age 65 years, resulting in PMRs of 1.19 (95% CI, 0.91-1.53) and 1.71 (95% CI, 1.18-2.40), respectively. [The Working Group noted that point estimates for cancers of lymphatic and haematopoietic tissues were somewhat higher in this study than in others in this section; however, it was hard to evaluate the etiological relevance of these findings given the many limitations of event-only analyses.]

2.4 Cancers of the skin, thyroid, and brain

2.4.1 Studies reporting occupational characteristics of firefighters

Studies first described in Section 2.1.1 are described in less detail in the present section.

See <u>Table 2.7</u>.

The Working Group identified 23 occupational and population-based cohort studies that had investigated the relationship between occupational exposure as a firefighter and risk of skin, thyroid, and/or brain cancer (Feuer & Rosenman, 1986; Vena & Fiedler, 1987; Demers et al., 1992a, 1994; Guidotti, 1993; Aronson et al., 1994; Tornling et al., 1994; Bates et al., 2001; Zeig-Owens et al., 2011; Ahn et al., 2012; Daniels et al., 2014; Glass et al., 2016a, b, 2017, 2019; Petersen et al., 2018b; Kullberg et al., 2018; Bigert et al., 2020; Colbeth et al., 2020a; Pinkerton et al., 2020; Webber et al., 2021; Marjerrison et al., 2022a, b). One of these studies was from Asia, six were from Europe, fifteen were from North America, and five were from Oceania. Four of these studies were excluded because they represented earlier follow-up of included studies (Heyer et al., 1990; Beaumont et al., 1991; Baris et al., 2001) or covered similar data to that in an included study (Demers et al., 1992b).

A cohort study of cancer incidence among 33 416 male professional [career] emergency responders (of whom 29 438, or 88%, were fire-fighters) in the Republic of Korea provided information on the risk of cancers of the brain and thyroid (<u>Ahn et al., 2012</u>). Emergency responders had been employed between 1980 and 2007, and cancer incidence follow-up took place from 1996 through 2007. With the national male population as the referent, there was no evidence of an increased risk of brain cancer among fire-fighters, based on only four cases (SIR, 0.53; 95% CI, 0.14–1.36). The SIR for thyroid cancer among firefighters was null (SIR, 1.00; 95% CI, 0.60–1.56; 19 cases).

An incidence and mortality study in a cohort of 3881 male professional [career] firefighters from several departments in Norway provided information on the risk of cutaneous melanoma, non-melanoma skin cancer, brain and other central nervous system cancers, and thyroid cancer (Marjerrison et al., 2022a, b). The cohort included mostly full-time firefighters employed between 1950 and 2019, with past or present employment in positions entailing active firefighting duties. The follow-up period for both cancer incidence and mortality analyses was from 1960 through 2018. For those ever employed as a firefighter, the incidence (SIR,

Reference, location, enrolment/follow- up period, study design	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments
Ahn et al. (2012) Republic of Korea Enrolment, 1980–2007/follow- up, 1996–2007 Cohort	33 416 men employed as emergency responders for ≥ 1 mo in 1980–2007 with (29 438) and without (3978) firefighting experience and not deceased in 1995 Exposure assessment method: ever employed and categorical duration of employment (years) as first- or second- line firefighter and non-firefighters from employment records	Brain and other CNS (ICD-10, C70–C72), incidence Brain and other CNS (ICD-10, C70–C72), incidence Thyroid, incidence	(SIR): 1 mo to < 10 yr ≥ 10 yr Total SRR: Non- firefighters Ever employed as a firefighter	2 2 4 0 4	 bloyment, 1-yr lag 0.74 (0.08–2.66) 0.42 (0.05–1.51) 0.53 (0.14–1.36) 0 (NR) NR bloyment, 1-yr lag 1.21 (0.55–2.29) 0.86 (0.41–1.59) 1.00 (0.60–1.56) 1 2.17 (0.29–16.51) 	Age, calendar period	Exposure assessment critique: Satisfactory quality. Heterogeneity of direct firefighter exposure within job title. May include rural and municipal firefighters. Strengths: employment duration and internal comparison limits healthy- worker bias; only professional [career] firefighters were included in the cohort. Limitations: no information on personal characteristics or confounders (except the firefighter cohort had a lower BMI and smoked less than the comparison population for the SIR analysis); follow-up time was reasonably short; cohort members were fairly young; no direct measure of

Table 2.7 Cohort studies reporting occupational characteristics of firefighters and cancers of the skin, thyroid, and brain

Reference, location, enrolment/follow- up period, study design	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments
Marjerrison et al.	3881 male	Melanoma,	SIR:			Age,	Exposure assessment
<u>(2022a)</u>	professional [career]	incidence	Firefighters	47	1.30 (0.95-1.73)	critique: Satisfactory quality.	
Norway	firefighters (most were	Melanoma,	Year of first em	ployment (SI	R):		Included firefighters with
Enrolment, 1950–2019/follow-	full-time) employed in positions entailing	incidence	Pre-1950	8	1.38 (0.59-2.71)		current or previous positions entailing active firefighting
up, 1960–2018 active firefighting Cohort at any of 15 fire departments between 1950 and 2019 Exposure assessment			1950-1969	19	1.53 (0.92-2.38)		duties but no assessment
			1970 or after	20	1.11 (0.68–1.72)		of length of time in active
		Melanoma,	Time since firs	t employmen	t (SIR):		firefighting positions. May
	incidence	< 20 yr	9	1.33 (0.61–2.53)		include municipal and rural	
	1		20-39 yr	21	1.36 (0.84-2.08)		firefighters.
	method: employment history from		≥ 40 yr	17	1.21 (0.70-1.94)		<i>Strengths</i> : long length of follow-up (mean, 28 yr);
	personnel records	Melanoma,	Duration of em	ployment (Sl	IR):		near complete ascertainment
	personner records	incidence	< 10 yr	10	1.84 (0.88-3.38)		of both cancer incidence
			10–19 yr	5	0.85 (0.27-1.98)		and mortality; analyses
			20–29 yr	13	1.38 (0.73-2.35)		by duration and timing of
			≥ 30 yr	19	1.23 (0.74-1.92)		employment.
		Non-melanoma	SIR:				<i>Limitations</i> : probable healthy- worker effect; no data on
		skin cancer (ICD-10, C44) excluding BCC, incidence	Firefighters	35	0.99 (0.69–1.37)		potential confounders apart from age, sex, and calendar time.
		Non-melanoma	Year of first em	ployment (SI	R):		
		skin cancer	Pre-1950	9	0.72 (0.33-1.37)		
		(ICD-10, C44)	1950-1969	17	1.10 (0.64–1.76)		
		excluding BCC, incidence	1970 or after	9	1.20 (0.55–2.28)		

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Reference, location, enrolment/follow- up period, study design	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments
<u>Marjerrison et al.</u>		Non-melanoma	Time since first	employmen	t (SIR):	Age,	
<u>(2022a)</u>		skin cancer	< 20 yr	3	2.14 (0.44-6.26)	calendar year	
(cont.)		(ICD-10, C44)	20-39 yr	8	0.97 (0.42-1.96)		
		excluding BCC, incidence	≥ 40 yr	24	0.93 (0.59–1.38)		
		Non-melanoma	Duration of emp				
		skin cancer	< 10 yr	3	1.02 (0.21-2.98)		
		(ICD-10, C44)	10–19 yr	5	1.56 (0.51-3.63)		
		excluding BCC, incidence	20–29 yr	7	0.83 (0.34–1.72)		
		mendence	≥ 30 yr	20	0.96 (0.58–1.48)		
Marjerrison et al. 3881 male (2022b) professional [career]		Melanoma,	SMR:			Age,	Exposure assessment
	mortality	Firefighters	13	1.55 (0.83–2.65)	calendar year	<i>critique</i> : Satisfactory quality. Included firefighters with	
Norway Enrolment,	firefighters (most were full-time) employed	d incidence	Period of follow	-			current or previous positions entailing active firefighting duties but no assessment
1950–2019/follow-	in positions entailing		1984 or before	5	1.25 (0.40-2.91)		
up, 1960–2018	active firefighting		1985–1994	11	2.09 (1.04-3.74)		
Cohort	at any of 15 fire		1995 or after	31	1.15 (0.78–1.63)		of length of time in active
	departments between	Melanoma,	Period of follow-up (SMR):				firefighting positions. May
	1950 and 2019 Exposure assessment	mortality	1984 or before	< 5	1.41 (0.17–5.08)		include municipal and rural firefighters.
	method: employment		1985–1994	< 5	2.83 (0.77–7.25)		<i>Strengths</i> : long length of
	history from		1995 or after	7	1.26 (0.51–2.60)		follow-up (mean, 28 yr);
	personnel records	Melanoma, incidence	Age at diagnosis				near complete ascertainmen
		Incluence	\leq 49 yr	10	1.21 (0.58–2.22)		of both cancer incidence
			50–69 yr	24	1.42 (0.91–2.12)		and mortality; analyses
		261	≥ 70 yr	13	1.18 (0.63–2.01)		by duration and timing of employment.
		Melanoma, mortality	Age at diagnosis		0 (0 00 1 0 1)		<i>Limitations</i> : probable health
		mortanty	$\leq 49 \text{ yr}$	0	0 (0.00–1.94)		worker effect; no data on
			50–69 yr	10	2.63 (1.26-4.84)		potential confounders apart
			≥ 70 yr	< 5	0.99 (0.20–2.88)		from age, sex, and calendar time.

. . . . 7 (continued)

Reference, location, enrolment/follow- up period, study design	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments
<u>Marjerrison et al.</u> (2022b) (cont.)		Non-melanoma skin cancer (ICD-10, C44) excluding BCC, mortality	SMR: Firefighters	< 5	0.95 (0.02–5.31)	Age, calendar year	
		Non-melanoma	Period of follow	-up (SIR):			
		skin cancer	1984 or before	< 5	0.77 (0.09-2.77)		
		(ICD-10, C44)	1985-1994	< 5	0.60 (0.12-1.77)		
		excluding BCC, incidence	1995 or after	30	1.07 (0.73–1.53)		
		Non-melanoma	Period of follow	up (SMR):			
		skin cancer	1984 or before	0	0 (0.00-16.2)		
		(ICD-10, C44)	1985-1994	0	0 (0.00–18.1)		
		excluding BCC, mortality	1995 or after	< 5	1.43 (0.04–7.97)		
		Non-melanoma	Age at diagnosis	(SIR):			
		skin cancer	≤ 49 yr	< 5	1.32 (0.16-4.78)		
		(ICD-10, C44)	50-69 yr	10	1.02 (0.49–1.88)		
		excluding BCC, incidence	≥ 70 yr	23	0.95 (0.60–1.43)		
		Non-melanoma	Age at diagnosis	(SMR):			
		skin cancer	≤ 49 yr	0	0 (0.00-103)		
		(ICD-10, C44)	50-69 yr	0	0 (0.00-10.5)		
		excluding BCC, mortality	≥ 70 yr	< 5	1.36 (0.03–7.58)		
		Brain and other	SIR:				
		CNS (ICD-10, C70–C72), incidence	Firefighters	28	1.31 (0.87–1.09)		
		Brain and other CNS (ICD-10, C70–C72), mortality	SMR: Firefighters	14	1.41 (0.77–2.37)		

Reference, location, enrolment/follow- up period, study design	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments
Marjerrison et al.		Thyroid,	SIR:			Age,	
<u>(2022b)</u>	incidence	Firefighters	6	1.45 (0.53-3.15)	calendar year		
(cont.)		Thyroid,	SMR:				
		mortality	Firefighters	< 5	2.41 (0.29-8.70)		
		Thyroid,	Period of follow	-up (SIR):			
		incidence	1984 or before	< 5	1.22 (0.03-6.78)		
			1985-1994	0	0 (0.00-5.05)		
		1995 or after	5	1.83 (0.59-4.27)			
	Thyroid,	Thyroid,	Period of follow	-up (SMR):			
		mortality	1984 or before	< 5	4.60 (0.12-25.6)		
			1985-1994	0	0 (0.00-18.32)		
			1995 or after	< 5	2.22 (0.06-12.38)		
		Thyroid,	Age at diagnosis	s (SIR):			
		incidence	≤ 49 yr	< 5	0.75 (0.02-4.19)		
			50-69 yr	< 5	2.06 (0.56-5.27)		
			≥ 70 yr	< 5	1.14 (0.03-6.35)		
		Thyroid,	Age at diagnosis	s (SMR):			
		mortality	≤ 49 yr	0	0 (0.00-48.5)		
			50-69 yr	< 5	2.83 (0.07-15.8)		
			≥ 70 yr	< 5	2.4 (0.06–13.4)		

Reference, location, enrolment/follow- up period, study design	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments
Bigert et al. (2020)8136 male firefighters	Melanoma,	SIR:			Age,	Exposure assessment	
Sweden	identified from	incidence	Firefighters	69	1.22 (0.95–1.54)	calendar	<i>critique</i> : Satisfactory quality Unclear if individuals
Enrolment	national censuses in	Melanoma,	Duration of en	nployment (Sl	IR):	period	
1960–1990/follow- up, 1961–2009	1960, 1970, 1980, and 1990	incidence	1–9 yr	0	0 (0.00-2.30)		were active firefighters for whole employment. May
Cohort	Exposure		10–19 yr	17	1.24 (0.72–1.98)		include full-time, part- time, municipal, and rural
	assessment method:		20–29 yr	27	1.42 (0.94-2.07)		
questionnaire; ever employed and categorical duration		≥ 30 yr	25	1.11 (0.72–1.65)		firefighters.	
		Trend-test P va	alue, 0.11			Strengths: near complete	
	Melanoma,	Time period (S	SIR):			ascertainment of cancer	
	of employment (years) as firefighter from census surveys	incidence	1961-1975	5	1.56 (0.51-3.65)		incidence; long length of
			1976-1990	14	1.10 (0.60-1.85)		follow-up (mean, 28 yr); analyses stratified by calend
			1991-2009	50	1.23 (0.91-1.62)		period of employment.
		Non-melanoma	SIR:				<i>Limitations</i> : no data on job
		skin cancer, incidence	Firefighters	101	1.48 (1.20–1.80)		duties, employment type, or potential confounders (aside
		Non-melanoma	Duration of en	nployment (SI	from age, sex, and calendar		
		skin cancer,	1–9 yr	0	0 (0.00-3.70)		year); probable healthy-work
		incidence	10–19 yr	28	1.82 (1.21-2.62)		hire bias; potential non-
			20–29 yr	35	1.56 (1.09-2.17)		differential misclassificatio of employment duration.
			\geq 30 yr	38	1.28 (0.91–1.76)		or employment duration.
			Trend-test P va	alue, < 0.01			
		Non-melanoma	Time period (S	SIR):			
	skin cancer,	1961–1975	2	0.87 (0.11-3.16)			
		incidence	1976-1990	15	1.28 (0.71-2.11)		
			1991-2009	84	1.55 (1.23-1.92)		
	Brain and other	SIR:		. ,			
		CNS (ICD-10, C70–C72), incidence	Firefighters	38	0.89 (0.63–1.23)		
		Brain, incidence	SIR:				
		(glioma)	Firefighters	18	0.94 (0.56-1.48)		

Reference, location, enrolment/follow- up period, study design	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments
Kullberg et al.	1080 men who worked	Melanoma,	Follow-up period	d (SIR):		Birth year,	Exposure assessment
(2018)	\geq 1 yr as a firefighter	incidence	Full: 1958-2012	3	0.30 (0.06-0.88)	calendar	critique: Satisfactory quality.
Stockholm, Sweden Enrolment,	in Stockholm between 1931 and 1983		Former: 1958–1986	1	0.39 (0.01–2.18)	period	Unclear if individuals were active firefighters for whole
1931–1983/follow- 1p, 1958–2012	Exposure assessment method: ever		Extended: 1987–2012	2	0.27 (0.03-0.97)		employment. Municipal firefighters.
Cohort	employed and categorical duration	Non-melanoma	Follow-up period	d (SIR):			<i>Strengths</i> : long follow- up period; near complete
	of employment	skin cancer,	Full: 1958–2012	17	0.85 (0.49-1.35)		ascertainment of cancer
	(years) as an urban incidence [municipal] firefighter	incidence	Former: 1958–1986	5	1.49 (0.48-3.48)	incidence; analyses o duration and era of employment.	incidence; analyses of
	from annual enrolment records		Extended: 1987–2012	12	0.72 (0.37–1.25)		Limitations: no data on
		Brain and other	Follow-up period	d (SIR):			potential confounders (aside
		nervous system	Full: 1958–2012	8	1.16 (0.50-2.28)		from age, sex, and calendar
		(ICD-7 193), incidence	Former: 1958–1986	6	1.68 (0.62–3.66)		year); lack of exposure assessment based on job task or fire responses.
			Extended: 1987–2012	2	0.60 (0.07–2.15)		of me responses.
<u>Fornling et al.</u>	1116 for	Brain, mortality	SMR:			Age,	Exposure assessment
<u>(1994)</u>	mortality/1091 for		Firefighters	5	2.79 (0.91-6.51)	calendar	critique: Satisfactory/good
Stockholm, Sweden	incidence; male	Brain, incidence	SIR:			period	quality. Enhanced exposure
Enrolment, 931–1983/follow-	firefighters employed for ≥ 1 yr by the		Firefighters	5	1.37 (0.44-3.20)		assessment (but based on 10% sample of reports) to
1951–1985/10110w-	City of Stockholm	Brain, mortality	Age (SMR):				differentiate exposure based
mortality), 1958–	between 1931 and		< 50 yr	0	0 (0-9.88)		on number of fires fought
986 (incidence)	1983 identified from		50-64 yr	2	2.62 (0.32-9.45)		accounting for job position,
Cohort	annual enrolment		≥ 65 yr	3	4.59 (0.95–13.41)		station, and year of exposure
	records	Brain, mortality	Duration of emp	loyment (SI			Municipal firefighters.
			< 20 yr	0	0 (0-8.25)		
			20-30 yr	2	3.04 (0.37-10.97)		
			> 30 yr	3	[4.37 (0.90-12.78)]		

Reference, location, enrolment/follow- up period, study design	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments
<u>Tornling et al.</u> (<u>1994)</u> (cont.)	Exposure assessment method: ever firefighter and duration (years) of firefighting employment from annual enrolment records; number of fires fought ascertained from exposure index developed from fire reports	Brain, mortality Brain, mortality	Latency (SMR): < 30 yr 30-40 yr > 40 yr No. of fires (SMF < 800 800-1000 > 1000	0 3 2 8): 0 1 4	0 (0-6.43) 5.07 (1.05-14.81) 3.20 (0.39-11.15) 0 (0-6.11) 2.62 (0.07-14.62) 4.96 (1.35-12.70)	Age, calendar period	<i>Strengths</i> : long follow- up period; near complete ascertainment of cancer incidence and mortality; assessed exposure to fire responses for some outcomes. <i>Limitations</i> : no data on potential confounders (aside from age, sex, and calendar year); low number of cases.
Petersen et al. (2018a) Denmark Enrolment, 1964–2004/follow- up, 1968–2014 Cohort	9061 male firefighters (full-time, part- time, and volunteer) identified from employer, trade union, and Danish Civil Registration System records, born 2 April 1928 or later, employed before age 60 yr and 31 December 2004, no cancer diagnosis before employment as a firefighter, and a job title/function indicating actual firefighting exposure	Melanoma, incidence Melanoma, incidence	Reference group Firefighters vs general population Firefighters vs sample of employees Firefighters vs military Employment typ Full-time Part-time or volunteer	70 70 70	1.24 (0.98–1.57) 1.28 (1.01–1.61) 1.05 (0.83–1.33) 1.28 (0.94–1.74) 1.19 (0.83–1.70)	Age, calendar period	Exposure assessment critique: Satisfactory quality. Includes part-time and full-time firefighters. Excluded those who did not actually fight fires. May include municipal and rural firefighters. Strengths: long period of follow-up; near-complete ascertainment of cancer incidence; use of three reference groups to evaluate healthy-worker bias; analyses by proxies of exposure including job task. Limitations: little information on potential confounders.

Petersen et al. (2018a) (cont.)Exposure assessment method: ever employed and categorical duration of employment (years), as well as employment type, job title/function, and work history, accrtained from civil registration, pension membership recordsMelanoma, incidenceEra of first employment (SIR): $1970-1994$ Age, calendar periodWelanoma, incidence1970-1994321.07 (0.76-1.51)periodMelanoma, and work history, ascertained from civil registration, pension membership recordsMelanoma, incidenceL43 (0.83-2.47)calendar periodMelanoma, incidenceMelanoma, incidenceSpecialized92.44 (1.27-4.70)Melanoma, employment type, incidenceMelanoma, incidence25-34 yr150.77 (0.47-1.28)25-34 yr150.77 (0.47-1.28)25 yr1.19 (0.88-1.60)2 1 yr571.28 (0.99-1.66)1.90 (0.84-1.43)2 1 yr571.29 (0.99-1.61)20 yr242 0 yr240.96 (0.64-1.43)Method: we general population20 yr240.09 (0.64-1.43)Chter skin (ICD- incidenceRefrence group (SIR): we general population1.01 (0.90-1.12)Vis general population311.01 (0.90-1.12)Vis general population3180.86 (0.77-0.96)Miltary population3180.96 (0.83-1.11)No Chter skin (ICD- incidenceEmployment type (SIR): employeesMinicidence Priefighters3180.07 (0.90-1.26)<	Reference, location, enrolment/follow- up period, study design	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments
$ \begin{array}{ ccnl.} \\ \mbox{employment} \\ \mbox{ferm} \\ fer$			Melanoma,	Era of first empl	oyment (SIF	R):	Age,	
$\begin{array}{cccccccccccccccccccccccccccccccccccc$			incidence	Pre-1970	25	1.42 (0.96–2.11)		
$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	(cont.)			1970-1994	32	1.07 (0.76–1.51)	period	
$ \begin{array}{cccccccccccccccccccccccccccccccccccc$				1995 or after	13	1.43 (0.83-2.47)		
$ \begin{array}{cccccccccccccccccccccccccccccccccccc$			Melanoma,	Job function (SI	R):			
job title/function, and work history, accertained from civil registration, pension, employer personnel, and trade union membership records Network incidence Network incidenc			incidence	Regular	61	1.15 (0.90-1.48)		
ascertained from civil registration, pension, employer personnel, and trade union membership records		job title/function,		Specialized	9	2.44 (1.27-4.70)		
$ \begin{array}{llllllllllllllllllllllllllllllllllll$			and work history, Melanoma, A	Age at first emp	loyment (SII	R):		
$ \begin{array}{cccccccccccccccccccccccccccccccccccc$		registration, pension,	inclucie	< 25 yr	38	1.47 (1.07–2.02)		
and trade union membership records Melanoma, incidence $4 extrm{ yr}$ $4 extrm{ yr}$ $2 extrm{ yr}$ $4 extrm{ yr}$ $2 extrm{ yr}$ $3 extrm{ 107}$ 1.52 (0.95-2.45) 1.07 (0.62-1.85) $2 extrm{ 177}$ 1.28 (0.99-1.66) $2 extrm{ 197}$ $2 extrm{ 137}$ 1.19 (0.88-1.60) $2 extrm{ 20}$ $2 extrm{ 20}$				25–34 yr	15	0.77 (0.47-1.28)		
membership recordsMelanoma, incidenceDuration of employment (SIR):< 1 yr				≥ 35 yr	17	1.52 (0.95-2.45)		
$\begin{array}{cccccccccccccccccccccccccccccccccccc$			membership records Melanoma,	Duration of emp	ployment (SI	R):		
$ \begin{array}{llllllllllllllllllllllllllllllllllll$		*		< 1 yr	13	1.07 (0.62–1.85)		
$ \begin{array}{llllllllllllllllllllllllllllllllllll$				≥1 yr	57	1.28 (0.99–1.66)		
Other skin (ICD- 10, C44, C46.0), incidence Reference group (SIR): Firefighters 318 1.00 (0.90–1.12) vs general population - Firefighters 318 1.01 (0.90–1.12) vs sample of employees - Firefighters vs 318 0.86 (0.77–0.96) military - Other skin (ICD- 10, C44, C46.0), incidence Employment type (SIR): Full-time 180 0.96 (0.83–1.11) Part-time or 138 1.07 (0.90–1.26)				≥ 10 yr	43	1.19 (0.88–1.60)		
10, C44, C46.0), incidence Firefighters 318 1.00 (0.90-1.12) vs general population Firefighters 318 1.01 (0.90-1.12) Vs sample of employees Firefighters vs 318 0.86 (0.77-0.96) Military Other skin (ICD- 10, C44, C46.0), incidence Employment type (SIR): 0.96 (0.83-1.11) Part-time or 138 1.07 (0.90-1.26)				≥ 20 yr	24	0.96 (0.64–1.43)		
incidence vs general population Firefighters 318 1.01 (0.90–1.12) vs sample of employees Firefighters vs 318 0.86 (0.77–0.96) military Other skin (ICD- 10, C44, C46.0), incidence Full-time 180 0.96 (0.83–1.11) Part-time or 138 1.07 (0.90–1.26)			Other skin (ICD-	Reference group	(SIR):			
vs sample of employees Firefighters vs 318 0.86 (0.77–0.96) military Other skin (ICD- Employment type (SIR): 10, C44, C46.0), Full-time 180 0.96 (0.83–1.11) incidence Part-time or 138 1.07 (0.90–1.26)				vs general	318	1.00 (0.90–1.12)		
military Other skin (ICD- Employment type (SIR): 10, C44, C46.0), Full-time 180 0.96 (0.83–1.11) incidence Part-time or 138 1.07 (0.90–1.26)				vs sample of	318	1.01 (0.90–1.12)		
10, C44, C46.0), incidenceFull-time1800.96 (0.83-1.11)Part-time or1381.07 (0.90-1.26)				military		0.86 (0.77–0.96)		
incidence Part-time or 138 1.07 (0.90–1.26)			·		-			
Fait-time of 138 1.07 (0.90-1.20)								
			incidence		138	1.07 (0.90–1.26)		

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Reference, location, enrolment/follow- up period, study design	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments
Petersen et al. (2018a) (cont.)		Other skin (ICD- 10, C44, C46.0), incidence Other skin (ICD- 10, C44, C46.0), incidence Other skin (ICD- 10, C44, C46.0), incidence Other skin (ICD- 10, C44, C46.0), incidence Brain (ICD- 10, C71, C75.1–C75.3,	Era of first empl Pre-1970 1970–1994 1995 or after Job function (SI Regular Specialized Age at first empl < 25 yr 25-34 yr $\ge 35 \text{ yr}$ Duration of empl < 1 yr $\ge 10 \text{ yr}$ $\ge 20 \text{ yr}$ Reference group Firefighters vs general	126 159 33 R): 287 31 loyment (SII 132 117 69 bloyment (SI 66 252 219 159	0.97 (0.81-1.15) 1.04 (0.89-1.21) 0.98 (0.70-1.38) 0.97 (0.86-1.09) 1.49 (1.04-2.11) 2): 0.89 (0.75-1.05) 1.18 (0.98-1.41) 0.99 (0.78-1.26)	Age, calendar period	
		D33.0-D33.2, D43.0-D43.2, D35.2-D35.4, D44.3-D44.5), incidence	population Firefighters vs sample of employees Firefighters vs	33 33	0.87 (0.62–1.23)		

Table 2.7 (cont	inued)								
Reference, location, enrolment/follow- up period, study design	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments		
Petersen et al.		Other parts of	Reference group	(SIR):		Age,			
(2018a) (cont.)		CNS (ICD-10, C72, D33.3– D33.9, D43.3–	Firefighters vs general population	12	1.39 (0.79–2.45)	calendar period			
		D43.9), incidence	D43.9), incidence	D43.9), incidence	Firefighters vs sample of employees	12	1.47 (0.83–2.58)		
			Firefighters vs military	12	1.31 (0.74–2.30)				
		Thyroid,	Reference group	(SIR):					
		incidence	Firefighters vs general population	6	1.21 (0.54–2.69)				
			Firefighters vs sample of employees	6	1.18 (0.53–2.63)				
			Firefighters vs military,	6	1.05 (0.47–2.35)				

Table 3.7 /a **א**

Reference, location, enrolment/follow- up period, study design	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments
<u>Webber et al. (2021)</u>	10 786 FDNY, 8813	Melanoma,	Group (SIR, US	reference ra	tes):	Age,	Exposure assessment critique
USA 2001–2016	CFHS; FDNY and CFHS cohorts;	incidence	CFHS	70	1.39 (1.07–1.79)	calendar year, race/	Satisfactory quality. Intensit
Cohort	male firefighters who were active		firefighters FDNY WTC firefighters	96	1.59 (1.30–1.96)	ethnicity	of exposure at WTC captured but did not consider previous firefighter work. Qualitative
	on 11 September 2001; FDNY cohort included men who	Melanoma, incidence	e	ment for pot	ential surveillance		assessment based on presence at the WTC site, exposures
	worked at the WTC site any time between		FDNY WTC firefighters	NR	1.59 (1.30–1.96)		complex and probably unique to 9/11 disaster. Municipal firefighters. <i>Strengths</i> : ascertainment of cancer incidence; comparison of two firefighter cohorts to
	11 September 2001 and 25 July 2002; CFHS cohort included	Melanoma, incidence	Group (RR): Non-Hispanic White:			Age on 11 September 2001	
	men who were actively employed on		CFHS firefighters	NR	1		evaluate bias. <i>Limitations</i> : medical
	11 September 2001 and assumed not to be		FDNY WTC firefighters	NR	1.12 (0.80–1.57)		surveillance bias; young age cohort; relatively short lengt
	working at the WTC site	Thyroid,	Group (SIR, US	reference ra	tes):	Age,	of follow-up.
	Exposure assessment method: presence	incidence	CFHS firefighters	15	1.01 (0.61–1.67)	calendar year, race/	
	at WTC site from employment records		FDNY WTC firefighters	46	2.37 (1.78–3.17)	ethnicity	
	and duty rosters	Thyroid, incidence	SIR (2-yr adjustr bias):	ment for pot	ential surveillance		
			FDNY WTC firefighters	46	2.01 (1.47–2.75)		
		Thyroid, incidence	Group (RR): CFHS firefighters	15	1	Age on 11 September 2001, race/	
			FDNY WTC firefighters	46	2.53 (1.37-4.70)	ethnicity	

Reference, location, enrolment/follow- up period, study design	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments
Webber et al. (2021) (cont.)		Thyroid, incidence	Group RR (2-yr surveillance bias		for potential	Age on 11 September	
			CFHS firefighters	NR	1	2001, race/ ethnicity	
			FDNY WTC firefighters	NR	2.11 (1.14-3.90)		
<u>Colbeth et al.</u> (<u>2020a)</u> New York, USA 12 September 2001	14 987 male firefighters and emergency medical service personnel	Thyroid, incidence	Group (RR): Rochester Epidemiology Project	99	1	Age	<i>Exposure assessment critique</i> Good quality. Intensity of exposure at WTC captured but did not consider
through 2018 Cohort	monitored through the Fire Department– WTC Health Program		FDNY WTC firefighters	72	2.3 (1.7–3.2)		previous firefighter work. Five ordinal categories of exposure intensity based
	(arrived at the WTC disaster site between the morning of 11 September 2001	Thyroid, incidence	Period (RR vs Rochester Epidemiology Project): Early (to 31 NR 1.8 (1.1–3.0) December 2009)				on time of arrival at WTC site. Exposures complex and probably unique to 9/11 disaster. Urban [municipal]
	and 25 July 2002); reference group	d 25 July 2002);	Late (1 January 2010 or later)	NR	2.5 (1.6-3.8)		firefighters. Strengths: cohort was defined
	included members of the Rochester	Thyroid, incidence	Symptom type (Project):	RR vs Roch	ester Epidemiology		before exposure; apparently appropriate matching
	Epidemiology Project		Asymptomatic	53	3.1 (2.1-4.7)		comparison population.
	cohort Exposure assessment method: questionnaire; presence at WTC site from employment records and duty		Symptomatic	12	0.8 (0.4–1.5)		<i>Limitations</i> : comparison group not from a fire department; misclassification of diagnosis; no information on size or stage of cancer.

confounders.

Table 2.7 (cont	inued)						
Reference, location, enrolment/follow- up period, study design	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments
Zeig-Owens et al. (2011) New York City, USA Enrolment, 1996/ follow-up, 1996– 2008 Cohort	9853 male FDNY firefighters employed for ≥ 18 mo, were active firefighters on 1 January 1996, with no prior cancer, and, if alive on 12 September 2001, also had known WTC exposure status Exposure assessment method: questionnaire; WTC-exposed and unexposed firefighters from employment records and questionnaires	Melanoma, incidence Thyroid, incidence	WTC-exposure Non-exposed Exposed SIR ratio (exposed vs non-exposed) WTC-exposure potential surve Non-exposed Exposed SIR ratio (exposed vs non-exposed	15 33 NR e status (SIR,	0.95 (0.57–1.58) 1.54 (1.08–2.18) 1.61 (0.87–2.99) 2-yr adjustment for	Age, race, ethnic origin, calendar year	<i>Exposure assessment critique</i> : Satisfactory quality. Intensity of exposure at WTC captured but did not consider previous firefighter work. WTC exposure self-reported using three methods. WTC site exposures complex and probably unique to 9/11 disaster. <i>Strengths</i> : evaluation of medical surveillance bias. <i>Limitations</i> : healthy-worker hire bias; short length of follow-up; young age at end of follow-up; little information on potential confounders.
Pinkerton et al. (2020) San Francisco, Chicago, and Philadelphia, USA Enrolment, 1950–2009/follow- up, 1950–2016 Cohort	29 992 municipal career firefighters in the CFHS cohort employed by the fire departments of San Francisco, Chicago, or Philadelphia for ≥ 1 day between 1950 and 2009; exposure- response analyses limited to 19 287 male firefighters of known race hired in 1950 or later and employed for ≥ 1 yr	Skin (ICD-10, C43-C44, C46.0, C46.9), mortality Skin (ICD-10, C43-C44, C46.0, C46.9), mortality	Fire department San Francisco Chicago Philadelphia Overall Heterogeneity J Exposed-days r vs 2500 exposed Fully adjusted RCS	18 35 25 78 P value, 0.79 nodel (HR at	1.21 (0.72–1.92) 1.00 (0.70–1.39) 1.02 (0.66–1.51) 1.05 (0.83–1.31) t 8700 exposed-days r lag): 0.83 (0.32–2.46)	Gender, race, age, calendar period Age, race, birthdate (within 5 yr), fire department, employment duration	<i>Exposure assessment critique</i> : Good quality. Minimal bias in exposure assessment in internal analyses. Municipal firefighters. <i>Strengths</i> : long period of follow-up; exposure-response modelling for three metrics of exposure assessed using job- exposure matrices; adjustment for HWSE. <i>Limitations</i> : healthy-worker selection bias in external comparison analyses; little information on potential

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Reference, location, enrolment/follow- up period, study design	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments	
<u>Pinkerton et al.</u> (2020) (cont.)	Exposure assessment method: ever employed as a firefighter, and number of exposed days, fire-runs, fire-	Skin (ICD-10, C43–C44, C46.0, C46.9), mortality	Fire-runs (Chica model (HR at 88 lag): Fully adjusted RCS			Age, race, birthdate (within 5 yr), fire department, employment duration		
	using job-exposure matrix based on job titles and assignments and departmental work history records and historical fire-run	matrix based on job titles and assignments and departmental work history records	Brain and other nervous system (ICD-10, C47, C70–C72), mortality	Fire department San Francisco Chicago Philadelphia Overall Heterogeneity P	20 37 29 86	1.21 (0.74–1.87) 0.89 (0.63–1.23) 1.01 (0.68–1.45) 0.99 (0.79–1.23)	Gender, race, age, calendar period	
		Brain and other nervous system (ICD-10, C47, C70–C72), mortality Brain and other nervous system (ICD-10, C47, C70–C72), mortality	e ,	odel (HR at -days, 10-yr 45 ago and Phil	0.46 (0.18–1.38) adelphia only)	Age, race, birthdate (within 5 yr), fire department, employment duration		

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Table 2.7 (continued) Reference, Population size, Cance

Reference, location, enrolment/follow- up period, study design	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments
Daniels et al. (2014)		Melanoma,	SIR:			Gender, race,	Exposure assessment
Chicago, San Francisco and	incidence analyses) male and female	incidence	All cancers	141	0.87 (0.73–1.03)	age, calendar period	<i>critique</i> : Satisfactory quality. Minimum exposure is 1 day
Philadelphia, USA	career firefighters		Fire departmen			period	of work as a municipal
Enrolment,	in the CFHS cohort	incidence	San Francisco	56	1.89 (1.43–2.46)		firefighter. <i>Strengths</i> : long period of follow-up; ascertained
1950-2009/follow-	employed for		Chicago	44	0.56 (0.41-0.76)		
up, 1950–2009	\geq 1 day in Chicago,		Philadelphia	41	0.75 (0.54–1.02)		
(mortality), 1985–	2009 (incidence) Philadelphia fire Cohort departments between 1950 and 2009 Exposure assessment method: ever employed and categorical duration	Brain and other	SIR:				incidence outcomes; included
		nervous system	All cancers	51	1.02 (0.76–1.34)		female firefighters.
Conort		(ICD-10, C47, C70–C72), incidence	First primary cancer	48	1.06 (0.78–1.41)		<i>Limitations</i> : healthy- worker hire bias in external comparisons; little
		Brain and other	Fire departmen	t (SIR, all ca	ncers):		information on potential
		nervous system (ICD-10, C47, C70–C72),	San Francisco	17	1.95 (1.14–3.12)		confounders.
			Chicago	13	0.53 (0.28-0.91)		
	of employment (years)		Philadelphia	21	1.25 (0.77–1.91)		
	from employment records	incidence	Heterogeneity <i>F</i>				
	100103	Brain and other nervous system (ICD-10, C47,	Race, men (SIR, all cancers):			Age,	
			Caucasian [White]	49	1.05 (0.78–1.39)	calendar period	
		C70–C72), incidence	Other	< 5	0.67 (0.08–2.42)		
		Brain and other	Age (SIR, all can	ncers):		Gender, race,	
		nervous system	17–64 yr	26	1.00 (0.65–1.46)	age, calendar	
		(ICD-10, C47,	65 to ≥ 85 yr	25	1.04 (0.67–1.54)	period	
		C70–C72), incidence	Heterogeneity <i>P</i>	value, 1.00			
		Thyroid and	SIR:				
		other endocrine glands, incidence	All cancers	28	0.91 (0.60–1.31)		
		Thyroid and	Fire departmen	t (SIR, all ca	ncers):		
		other endocrine	San Francisco	< 5	0.72 (0.20-1.84)		
		glands, incidence	Chicago	15	0.98 (0.55-1.61)		
			Philadelphia	9	0.91 (0.42-1.72)		

Reference, location, enrolment/follow- up period, study design	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments
<u>Daniels et al. (2014)</u> (cont.)		Thyroid, incidence Thyroid, incidence	SIR: All cancers Fire departmer San Francisco Chicago Philadelphia	25 nt (SIR, all ca < 5 13 9	0.87 (0.56–1.28) ncers): 0.57 (0.12–1.68) 0.90 (0.48–1.55) 0.97 (0.44–1.85)	Gender, race, age, calendar period	
Demers et al. (1994) Seattle and Tacoma, USA Enrolment, 1944–1979/follow- up, 1974–1989 Cohort	2447 male firefighters employed for ≥ 1 yr between 1944 and 1979, alive as of 1 January 1974 and known to be a resident of one of 13 counties in the catchment area of the tumour registry for ≥ 1 mo; reference group included 1878 local male police officers Exposure assessment method: ever employed for ≥ 1 yr, and categorical duration of employment (years) in direct firefighting positions from employment records	Melanoma, incidence Melanoma, incidence Melanoma, incidence Brain, incidence Brain, incidence	SIR (local count Firefighters Duration of exp county rates): < 10 yr 10–19 yr 20–29 yr ≥ 30 yr Years since first rates): < 20 yr 20–29 yr ≥ 30 yr 20–29 yr ≥ 30 yr IDR: Local police Firefighters SIR (local count Firefighters	9 posed employ 0 4 4 1 t employmen 2 2 5 6 9 sty rates): 4	1.2 (0.6–2.3) /ment (SIR, local 0 (0.0–2.6) 2.3 (0.6–5.8) 1.1 (0.3–2.7) 2.4 (0.1–13) t (SIR, local county 1.3 (0.2–4.4) 1.2 (0.1–4.3) 1.2 (0.1–4.3) 1.2 (0.4–2.8) 1 1.0 (0.4–1.8) 1.1 (0.3–2.9) /ment (SIR, local 1.6 (0.0–8.8) 0 (0.0–4.6) 1.6 (0.3–4.6)	Age, calendar period	<i>Exposure assessment critique:</i> Satisfactory quality. Duration (years) involved in direct firefighting (surrogate for fire smoke) was not measured equally in the two study populations. Municipal firefighters. <i>Strengths</i> : use of two comparison groups, including comparison with police officers to limit healthy- worker bias. <i>Limitations</i> : little information on potential confounders.

Reference, location, enrolment/follow- up period, study design	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments
Demers et al. (1994) (cont.)		Brain, incidence	Years since first rates): < 20 yr	employment 0	6 (SIR, local county 0 (0.0–7.1)	Age, calendar period	
			20–29 yr	0	0 (0.0-4.5)		
		Brain, incidence	\geq 30 yr IDR:	4	1.9 (0.5–4.9)		
		,	Local police	2	1		
			Firefighters	4	1.4 (0.2–11)		
		Thyroid,	SIR (local count	y rates):			
		incidence	Firefighters	1	0.8 (0.2-4.2)		
Demers et al.4401 male firefighters $(1992a)$ employed for ≥ 1 yrSeattle and Tacoma,between 1944 and	employed for ≥ 1 yr between 1944 and	Skin (ICD-9, 172, 173), mortality Skin (ICD-9, 172,	SMR: Firefighters IDR:	6	0.98 (0.36–2.13)	Age, calendar period	Exposure assessment critique Satisfactory/good quality. Duration (years) involved in
Washington; Portland, Oregon,	1979 in Seattle, Tacoma, or Portland,	173), mortality	Local police	4	1		fire combat (surrogate for fire smoke) was not measured
USA Enrolment,	USA; reference group included 3676 local	Brain and other	Firefighters SMR:	6	1.12 (0.27–4.76)		equally in the three municip firefighter populations.
Initiated 50/0 focal $1944-1979/follow-$ up, $1945-1989$ Cohortmethod: everemployed for ≥ 1 yr,and categorical	nervous system (ICD-9, 191, 192, 237.5–237.7, 239.6–239.7), mortality	Firefighters	22	2.09 (1.31-3.17)		Strengths: use of two comparison groups, includir comparison with police officers to limit healthy- worker bias.	
	duration (years)	Brain and other	IDR:				Limitations: little information
	of exposure to fire combat from	nervous system	Local police	8	1		on potential confounders;
	employment records	(ICD-9, 191, 192, 237.5–237.7, 239.6–239.7), mortality	Firefighters	22	1.88 (0.82–4.31)		ascertained mortality outcomes only.

Table 2.7 (cont	inued)						
Reference, location, enrolment/follow- up period, study design	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments
Demers et al.		Brain and other	Duration of exp	osed employ	ment (SMR):	Age,	
<u>(1992a)</u>	<u>.992a)</u>	nervous system (ICD-9, 191,	< 10 yr	5	2.57 (0.8-6.0)	calendar	
(cont.)			10–19 yr	8	3.53 (1.5-7.0)	period	
		192, 237.5–237.7,	20–29 yr	6	1.24 (0.5-2.7)		
	mortality Brain and other nervous system (ICD-9, 191, 192, 237.5–237.7, 239.6–239.7),	239.6–239.7), mortality	≥ 30 yr	3	2.04 (0.4–5.9)		
		Brain and other	Years since first	t employmen	t (SMR):		
		< 20 yr	6	2.45 (0.9-5.3)			
			20–29 yr	2	0.73 (0.1-2.6)		
			≥ 30 yr	14	2.63 (1.4-4.4)		
		Brain and other	Age at risk (SM	R):			
		nervous system	18–39 yr	5	3.75 (1.2-8.7)		
		(ICD-9, 191,	40-64 yr	11	1.66 (0.8–3.0)		
		192, 237.5–237.7, 239.6–239.7),	≥ 65 yr	6	2.34 (0.9–5.1)		
		mortality	a. (P				
		Brain and other	SMR:				
		nervous system (ICD-9, 191, 192), mortality	Firefighters	18	2.07 (1.23-3.28)		
		Brain and other	IDR:				
		nervous system	Local police	8	1		
		(ICD-9, 191, 192), mortality	Firefighters	18	1.63 (0.70–3.79)		

(1987) career firefighters CNS (ICI	dathar					
	Brain and other CNS (ICD-8, 191,	Years worked a	s a firefighter		Age,	<i>Exposure assessment critique:</i> Minimal quality. Only assessed ever-employment and duration of employment as a municipal firefighter. <i>Strengths</i> : long length of
Buffalo, New York, employed by the City 192), mor		1–9 yr	1	[3.33 (0.2–16.4)]	calendar period	
USA of Buffalo for ≥ 5 yr,	rtanty	10–19 yr	2	[3.33 (0.6–11.0)]	period	
1950–1979 with $\ge 1 \text{ yr}$		20–29 yr	3	[3.75 (1.0–10.2)]		
Cohort as a firefighter		30–39 yr	0	0 (NR)		
Exposure assessment		\geq 40 yr	0	0 (NR)		follow-up.
method: ever-	1 .1	Total	6	2.36 (0.86–5.13)		<i>Limitations</i> : healthy-worker hire bias; little information
	Brain and other CNS (ICD-8, 191, 192), mortality	Calendar year o				on potential confounders
		1950-1959	3	[5.0 (1.3–13.6)]		or exposure to firefighting activities.
employment records		1960-1969	0	0 (NR)		
р. ·	1 (1	1970–1979	3	[2.73 (0.7–7.4)]		
Brain and CNS (ICI		Year of hire (SN				
192), mor		Pre-1930	1	[1.54 (0.1–7.6)]		
,		1930-1939	0	0 (NR)		
		1940–1949	4	[4.94 (1.6-11.9)]		
Brain and	d othou	1950 or after	1 (SMD):	[1.61 (0.1-8.0)]		
CNS (ICI		Years of latency		[4.02(1.1, 11.7)]		
192), mor		< 20 yr	3	[4.02 (1.1-11.7)]		
	/	20–29 yr 30–39 yr	3 0	[4.58 (1.3–13.6)] 0 (NR)		
		30–39 yr 40–49 yr	0	0 (NR) 0 (NR)		
		20-49 yr $\geq 50 \text{ yr}$	0	0 (NR) 0 (NR)		

Reference, location, enrolment/follow- up period, study design	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments
Feuer & Rosenman	euer & Rosenman 263 deceased White	Skin, mortality	Reference popul	ation (PMR):	Age and	Exposure assessment critique: Satisfactory quality. Assessment provides duration of employment categories. May include municipal and rural firefighters. Strengths: comparison with other uniformed service occupation. Limitations: PMR study design lacks event-free follow- up time; short observation period; little information on
<u>(1986)</u> New Jersey, USA	male firefighters in the New Jersey		Firefighters vs US	4	[2.70 (0.86-6.52)]	calendar period	
1974–1980 Cohort	rt Retirement System		Firefighters vs NJ	4	[1.90 (0.61-4.6)]		
with ≥ 10 yr of service, or firef	(firefighters vested with ≥ 10 yr of service, or firefighters		Firefighters vs White male NJ police	4	[1.35 (0.43-3.26)]		
	who died while on	Skin, mortality	Duration of emp	oloyment (P	MR):		
	payroll regardless of employment		< 20 yr	0	0 (NR)		
	duration); one		20–25 yr	1	[1.82 (0.09-8.98)]		
	reference group		> 25 yr	3	[3.88 (0.99–10.56)]		
	included 567 White	Skin, mortality	Latency (PMR):				potential confounders; small
	male police deaths		< 22 yr	1	[1.15 (0.06-5.67)]		number of cases.
	Exposure assessment method: ever		22–27 yr	1	[1.68 (0.08-8.29)]		
	employed, and categorical duration of employment (years), as a career firefighter from retirement system		> 27 yr	2	[3.14 (0.53–10.37)]		

records

Reference, location, enrolment/follow- up period, study design	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments
Aronson et al.5414 male firefighters (1994) employed for ≥ 6 moToronto, Canadaat one of six fire	Melanoma, mortality	SMR: Any employment	2	0.73 (0.09–2.63)	Age, calendar period	<i>Exposure assessment</i> <i>critique</i> : Satisfactory quality. Unclear if individuals were	
1950–1989	departments in	Melanoma,	Years since first	exposure (S	MR).	F	active firefighters for whole
Cohort	Metropolitan Toronto between 1950 and 1989 Exposure assessment method: ever employed and categorical duration of employment (years) as municipal firefighter from	mortality	< 20 yr	1	0.95 (0.02–5.31)		employment. Likely municipa
		,	20–29 yr	1	1.30 (0.03-7.24)		firefighters. <i>Strengths</i> : long period of follow-up, analysis of employment duration.
			$\geq 30 \text{ yr}$	0	0 (0-3.97)		
		Melanoma,	Years of employ				
		mortality	< 15 yr	1	1.10 (0.03-6.12)		<i>Limitations</i> : healthy-worker
			15–29 yr	1	0.90 (0.02-5.02)		hire bias; little information
			\geq 30 yr	0	0 (0-5.27)		on confounders or exposure;
		Melanoma,	Age (SMR):				ascertained mortality outcomes only.
	employment records	mortality	< 60 yr	2	0.94 (0.11-3.41)		outcomes only.
			$\geq 60 \text{ yr}$	0	0 (0-5.86)		
		Brain and other	SMR:				
		nervous system (ICD-9, 191, 192), mortality	Any employment	14	2.01 (1.10-3.37)		
		Brain and other	Years since first	t exposure (S	MR):		
		nervous system	< 20 yr	6	2.83 (1.04-6.16)		
		(ICD-9, 191, 192),	20–29 yr	2	0.99 (0.12-3.56)		
		mortality	≥ 30 yr	6	2.12 (0.78-4.62)		
		Brain and other	Years of employ	ment (SMR)):		
		nervous system	< 15 yr	5	2.62 (0.85-6.11)		
		(ICD-9, 191, 192),	15–29 yr	3	1.06 (0.22-3.10)		
		mortality	≥ 30 yr	5	2.29 (0.75-5.35)		
		Brain and other	Age (SMR):				
		nervous system	< 60 yr	10	1.99 (0.95–3.66)		
		(ICD-9, 191, 192), mortality	≥ 60 yr	4	2.04 (0.56-5.22)		

Reference, location, enrolment/follow- up period, study design	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments
Guidotti (1993) Edmonton and Calgary, Canada 1927–1987 Cohort	3328; all firefighters employed between 1927 and 1987 by either of the fire departments of Edmonton or Calgary Exposure assessment method: ever employed and categorical duration of employment (years) from employment records exposure index of years of employment weighted by time spent in proximity to fires based on job classification	Brain, mortality	SMR: Any employment	3	1.47 (0.30–4.29)	Age, calendar period	<i>Exposure assessment critique</i> : Good quality. Good approach to differentiate exposure between ranks. Municipal firefighters. <i>Strengths</i> : long length of follow-up; analyses by duration of employment and exposure index. <i>Limitations</i> : little information on potential confounders; ascertained mortality outcomes only; low number of cases for stratified analyses.
Glass et al. (2019) Australia Enrolment, varied by agency/follow- up, 1980–2011 (mortality); 1982– 2010 (incidence) Cohort	39 644 female firefighters, both paid [career] (1682) and volunteer (37 962), from nine fire agencies in Australia Exposure assessment method: ever career or volunteer firefighter, ever attended an incident, tertiles of cumulative number of incidents and type of incidents attended from personnel records	Melanoma, incidence Melanoma, incidence	SIR: All volunteer firefighters Volunteers who attended incidents No. of incidents [equivalent to ra Zero incidents Tertile 1 Tertile 2 Tertile 3 Trend-test <i>P</i> val	ate ratios]: 61 20 18 17	1.25 (1.05–1.46) 1.11 (0.84–1.44) ers (RIR) 1 1.04 (0.63–1.73) 0.82 (0.48–1.38) 0.84 (0.49–1.44)	Age, calendar year	<i>Exposure assessment critique</i> : Good quality. Enhanced exposure assessment to differentiate exposure based on number of incidents for volunteer firefighters. Included specific incident types, but early exposure was extrapolated from more recent data. Volunteers mainly rural. <i>Strengths</i> : study of female firefighters; includes predominantly rural firefighters; ascertained exposure to number and type of incidents.

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Reference, location, enrolment/follow- up period, study design	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments
<u>Glass et al. (2019)</u>		Melanoma,	No. of fire incide	ents, all volu	inteers (RIR):	Age,	Limitations: short length of
(cont.)	incidence	Zero incidents	66	1	calendar year		
			Tertile 1	21	1.10 (0.67–1.80)		follow-up; probable healthy- worker bias; little information on confounders.
			Tertile 2	13	0.68 (0.37-1.23)		
			Tertile 3	16	0.84 (0.48-1.45)		on contounders.
			Trend-test P value	ue, 0.42			
		Melanoma, incidence	No. of structure (RIR):	fire inciden	ts, all volunteers		
			Zero incidents	99	1		
			Tertile 1	5	0.53 (0.21-1.30)		
			Tertile 2	7	0.66 (0.31-1.43)		
			Tertile 3	5	0.47 (0.19-1.17)		
			Trend-test P value	ue, 0.89			
		Melanoma, incidence	No. of landscape fire incidents, all volunteers (RIR):				
			Zero incidents	71	1		
			Tertile 1	18	1.11 (0.66–1.87)		
			Tertile 2	12	0.67 (0.36-1.23)		
			Tertile 3	15	0.83 (0.48-1.46)		
			Trend-test P value	ue, 0.41			
		Melanoma, incidence	No. of vehicle fir (RIR):	e incidents,	all volunteers		
			Zero incidents	97	1		
			Tertile 1	9	1.38 (0.69–2.75)		
			Tertile 2	5	0.72 (0.29–1.76)		
			Tertile 3	5	0.71 (0.29–1.75)		
			Trend-test P valu	ue, 0.24			

inued)						
Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments
<u>Glass et al. (2019)</u>	Brain and other	SIR:			Age,	
	C70–C72),	All volunteer firefighters	15	1.00 (0.56–1.65)	calendar year	
		Volunteers who attended incidents	6	0.95 (0.35–2.07)		
	Brain, incidence	SIR:				
		All volunteer firefighters	13	0.92 (0.49–1.57)		
		Volunteers who attended incidents	5	0.84 (0.27–1.97)		
	Thyroid and	SIR:				
	other endocrine (ICD-10, C73–	All volunteer firefighters	41	1.00 (0.72–1.36)		
C	C75), incidence	Volunteers who attended incidents	15	0.81 (0.45-1.33)		
	Thyroid,	SIR:				
incidence	incidence	All volunteer firefighters	39	0.97 (0.69–1.33)		
		Volunteers who attended incidents	14	0.77 (0.42–1.29)		
	description, exposure	Population size, description, exposure assessment methodCancer type (histopathology), incidence or mortalityBrain and other CNS (ICD-10, C70-C72), incidenceBrain and other CNS (ICD-10, C70-C72), incidenceBrain, incidenceBrain, incidenceThyroid and other endocrine (ICD-10, C73- C75), incidenceThyroid,Thyroid,	Population size, description, exposure assessment methodCancer type (histopathology), incidence or mortalityExposure category or levelBrain and other CNS (ICD-10, C70-C72), incidenceSIR: All volunteer firefighters Volunteers who attended incidentsBrain, incidenceSIR: All volunteer firefighters Volunteers who attended incidentsBrain, incidenceSIR: All volunteer firefighters Volunteers who attended incidentsBrain, incidenceSIR: All volunteer firefighters Volunteers who attended incidentsThyroid and other endocrine (ICD-10, C73- C75), incidenceSIR: All volunteer firefighters Volunteers who attended incidentsThyroid, incidenceSIR: All volunteer firefighters Volunteers who attended incidentsThyroid, incidenceSIR: All volunteer firefighters Volunteers who attended incidentsThyroid, incidenceSIR: All volunteer firefighters Volunteers who attended incidents	Population size, description, exposure assessment methodCancer type (histopathology), incidence or mortalityExposure category or levelExposed cases or deathsBrain and other CNS (ICD-10, C70-C72), incidenceSIR: All volunteer firefighters Volunteers who attended incidents15Brain, incidenceSIR: All volunteer firefighters Volunteers who attended incidents13Brain, incidenceSIR: All volunteer firefighters Volunteers who attended incidents13Brain, incidenceSIR: All volunteer firefighters Volunteers who attended incidents13Thyroid and other endocrine (ICD-10, C73- C75), incidenceSIR: All volunteer firefighters41Thyroid and other endocrine (ICD-10, C73- C75), incidenceSIR: All volunteer firefighters41Thyroid, incidenceSIR: All volunteer firefighters15Volunteers who attended incidents539Thyroid, incidenceSIR: All volunteer firefighters39Thyroid, incidenceSIR: All volunteer firefighters39Volunteers who attended incidence14	Population size, description, exposure assessment methodCancer type (histopathology), incidence or mortalityExposure category or levelExposed cases or deathsRisk estimate (95% CI)Brain and other CNS (ICD-10, C70-C72), incidenceSIR: All volunteer frefighters151.00 (0.56-1.65) (0.056-1.65)Brain and other CNS (ICD-10, C70-C72), incidenceSIR: All volunteer frefighters0.95 (0.35-2.07) who attended incidentsBrain, incidenceSIR: All volunteers volunteers frefighters0.92 (0.49-1.57) frefightersBrain, incidenceSIR: All volunteer frefighters0.92 (0.49-1.57) frefightersThyroid and other endocrine (ICD-10, C73- C75), incidenceSIR: All volunteer frefighters1.00 (0.72-1.36) frefightersThyroid, incidenceSIR: All volunteer frefighters1.00 (0.72-1.33) (0.45-1.33) who attended incidents0.97 (0.69-1.33) frefighters	Population size, description, exposur assessment methodCancer type (histopathology) incidence or mortalityExposur category or levelExpose, cases or deathsRisk estimate (95% CI)Covariates controlledBrain and other C70 - C72), incidenceSIR: All volunteer frefighters151.00 (0.56 - 1.65) 0.95 (0.35 - 2.07)Age, calendar yearVolunteers who attended incidenceSIR: All volunteers frefighters0.95 (0.35 - 2.07)Age, calendar yearBrain, incidenceSIR: All volunteers frefighters0.92 (0.49 - 1.57)All volunteer frefightersBrain, incidenceSIR: All volunteers frefighters0.92 (0.49 - 1.57)All volunteer frefightersBrain, incidenceSIR: All volunteers frefighters0.92 (0.49 - 1.57)All volunteer frefightersThyroid and other endocrine (ICD-10, C73- C75), incidenceSIR: All volunteer frefighters1.00 (0.72 - 1.36)Thyroid, incidenceSIR: All volunteers who attended incidents1.00 (0.72 - 1.33)All volunteer frefightersThyroid, incidenceSIR: All volunteers volunteers volunteers0.97 (0.69 - 1.33)All volunteer volunteerThyroid, incidenceSIR: Volunteers volunteers volunteersAll volunteer volunteers390.97 (0.42 - 1.29)

Reference, location, enrolment/follow- up period, study design	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments
Glass et al. (2017)163 094 all maleAustraliavolunteer firefightersEnrolment, datefrom five fire agenciesvaried by agencyenrolled on or after(1998–2000)/follow-the date on which	volunteer firefighters from five fire agencies enrolled on or after the date on which	Melanoma, incidence	SIR: All volunteers Volunteers who attended incidents	912 590	1.00 (0.93–1.06) 0.98 (0.91–1.07)	Age, calendar period	<i>Exposure assessment critique</i> : Good quality. Enhanced exposure assessment to differentiate exposure based on number of incidents.
up to 30 November	the agency's roll was	Melanoma,	Era of first servi	ce (SIR):		Included specific incident	
2011 (mortality) and 31 December	complete and who had ever held an active	incidence	Pre-1970	168	0.80 (0.69-0.93)		types, but early exposure was extrapolated from more recen
2010 (cancer	firefighting role		1970-1994	381	1.00 (0.90-1.10)		data. Firefighters from rural
incidence)	cidence) Exposure assessment ohort method: ever volunteer firefighter, categorical volunteer duration (years)		1995 or after	363	1.12 (1.01–1.24)		or peri-urban areas.
Cohort		Melanoma, incidence	Duration of serv [equivalent to ra		nteers (RIR)		Strengths: includes predominantly rural firefighters; ascertained exposure to number and type of incidents. Limitations: short length of follow-up; young age at end of
			> 3 mo to 10 yr	336	1		
			10–20 yr	194	1.04 (0.87-1.24)		
	and era from service records; ever		≥ 20 yr	370	0.92 (0.78-1.08)		
	volunteer firefighter		Trend-test P valu	1e, 0.29			
	who attended an incident, tertiles	Melanoma, incidence	Duration of service, volunteers who attended incidents (RIR):				follow-up; probable healthy worker bias; little informati
	of cumulative		> 3 mo to 10 yr	176	1		on confounders.
	emergency incidents		10–20 yr	134	1.12 (0.89–1.41)		
	from contemporary incident data		≥ 20 yr	292	0.95 (0.77-1.16)		
	incluent data		Trend-test P valu	1e, 0.52			
		Melanoma,	No. of incidents	attended by	volunteers (RIR):		
		incidence	Baseline	558	1		
			Group 1	18	0.71 (0.45-1.14)		
			Group 2	14	1.20 (0.71-2.04)		
		Melanoma, incidence	No. of fire incidents attended by volunteers (RIR):				
			Baseline	559	1		
			Group 1	17	0.67 (0.41-1.08)		
			Group 2	14	1.42 (0.83-2.41)		

Reference, location, enrolment/follow- up period, study design	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments		
<u>Glass et al. (2017)</u> cont.)		Melanoma, incidence	No. of structure volunteers (RIR		ts attended by	Age, calendar			
			Baseline	570	1	period			
			Group 1	13	0.82 (0.47-1.42)				
			Group 2	7	0.92 (0.44-1.93)				
		Melanoma, incidence	No. of landscape volunteers (RIR		ats attended by				
			Baseline	486	1				
			Group 1	80	0.95 (0.75-1.20)				
			Group 2	24	0.86 (0.57-1.29)				
		Melanoma, incidence	No. of vehicle fin volunteers (RIR		attended by				
			Baseline	558	1				
			Group 1	23	0.85 (0.56-1.30)				
			Group 2	9	0.89 (0.46–1.72)				
		Brain and other	SIR:						
		CNS (ICD-10,	All volunteers	116	0.86 (0.71-1.04)				
		C70–C72), incidence	Volunteers who attended incidents	81	0.91 (0.73–1.14)				
		Brain and other	Era of first servi	ce (SIR):					
		CNS (ICD-10,	Pre-1970	25	0.86 (0.56-1.27)				
		С70–С72),	1970-1994	34	0.61 (0.42-0.85)				
		incidence	1995 or after	57	1.16 (0.88–1.50)				
		Brain, incidence	SIR:						
			All volunteers	114	0.88 (0.73-1.06)				
		Volunteers who attended incidents	80	0.94 (0.74–1.17)					

Reference, location, enrolment/follow- up period, study design	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments
<u>Glass et al. (2017)</u> (cont.)		Thyroid and other endocrine (ICD-10, C73– C75), incidence Thyroid and other endocrine (ICD-10, C73– C75), incidence Thyroid, incidence	SIR: All volunteers Volunteers who attended incidents Era of first servio Pre-1970 1970–1994 1995 or after SIR: All volunteers Volunteers	62 33 ce (SIR): 10 21 31 58 30	0.81 (0.62–1.04) 0.65 (0.45–0.92) 0.85 (0.41–1.57) 0.64 (0.40–0.98) 0.98 (0.66–1.39) 0.83 (0.63–1.07) 0.64 (0.43–0.92)	Age, calendar period	
Glass et al. (2016a) Australia Enrolment, 1976–2003/follow- up, 1976–2011 (mortality), 1982– 2010 (incidence, except two states, 2009) Cohort	ia (17 394) or part- time (12 663) paid male firefighters 5-2011 employed at one of ity), 1982- eight Australian cidence, fire agencies for start of personnel records (1976–2003, depending on agency)	Melanoma, incidence Melanoma, incidence Melanoma,	(RIR) [equivaler > 3 mo to 10 yr 10-20 yr ≥ 20 yr Trend-test <i>P</i> value	209 89 298 bloyment, funt to rate rat 35 50 122 ue, 0.79	1.45 (1.26–1.66) 1.43 (1.15–1.76) 1.44 (1.28–1.62) Ill-time firefighters ios]: 1 1.26 (0.80–2.00) 1.11 (0.68–1.81) art-time firefighters	Age, calendar period	<i>Exposure assessment critique</i> Good quality. Enhanced exposure assessment to differentiate exposure based on number of incidents, including specific incident types. Included specific incident types, but early exposure was extrapolated from more recent data. Municipal firefighters. <i>Strengths</i> : internal analysis
		Melanoma, incidence		(RIR): > 3 mo to 10 yr 10−20 yr ≥ 20 yr Trend-test <i>P</i> valu	36 15 36	1 0.88 (0.46–1.69) 1.64 (0.83–3.23)	

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Reference, location, enrolment/follow- up period, study design	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments
<u>Glass et al. (2016a)</u>	Exposure assessment	Melanoma,	Duration of emp	oloyment (R	IR):	Age,	
(cont.)	method: employed	incidence	> 3 mo to 10 yr	71	1	calendar	
	as a part- or full-		10–20 yr	65	1.14 (0.80–1.64)	period	
≥ 3 mc emplo (years)	time firefighter for ≥ 3 mo, categorical		≥ 20 yr	158	1.23 (0.84-1.80)		
	employment duration		Trend-test P valu	1e, 0.29			
	(years) and era from employment records;	Melanoma, incidence	No. of incidents firefighters (RIR		full-time		
	tertiles of cumulative		Tertile 1	26	1		
	emergency incidents		Tertile 2	36	1.37 (0.82-2.27)		
and type of inci- attended from contemporary incident data	and type of incident		Tertile 3	31	0.82 (0.48-1.40)		
			Trend-test P valu	1e, 0.40			
		Melanoma, incidence	No. of fire incide firefighters (RIR		d by full-time		
			Tertile 1	24	1		
			Tertile 2	36	1.55 (0.92–2.60)		
			Tertile 3	33	0.92 (0.54-1.59)		
			Trend-test P valu	1e, 0.68			
		Melanoma, incidence	No. of structure time firefighters		ts attended by full-		
			Tertile 1	30	1		
			Tertile 2	29	0.98 (0.59–1.64)		
			Tertile 3	34	0.80 (0.48-1.33)		
			Trend-test P valu	1e, 0.38			
		Melanoma, incidence	No. of landscape time firefighters		nts attended by full-		
			Tertile 1	24	1		
			Tertile 2	40	1.62 (0.97–2.70)		
			Tertile 3	29	0.86 (0.50-1.50)		
			Trend-test P valu	1e 0.50			

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Table 2.7 (continued)

Reference, location, enrolment/follow- up period, study design	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments
<u>Glass et al. (2016a)</u>		Melanoma,	No. of vehicle fin	e incidents	attended by full-	Age,	
(cont.)		incidence	time firefighters			calendar	
			Tertile 1	26	1	period	
			Tertile 2	38	1.56 (0.94–2.58)		
			Tertile 3	29	0.81 (0.47-1.39)		
			Trend-test P val	ue, 0.39			
		Melanoma, incidence	Duration of emp (SIR):	oloyment, fu	ll-time firefighters		
			> 3 mo to 10 yr	35	1.33 (0.93-1.85)		
			10–20 yr	50	1.50 (1.12-1.98)		
			$\geq 20 \text{ yr}$	122	1.46 (1.22–1.75)		
		Melanoma, incidence		oloyment, pa	art-time firefighters		
			> 3 mo to 10 yr	36	1.34 (0.94–1.86)		
			10–20 yr	15	1.01 (0.56-1.66)		
			$\geq 20 \text{ yr}$	36	1.78 (1.25-2.46)		
		Melanoma, incidence	Era of first empl (SIR):	oyment, full	-time firefighters		
			Pre-1970	75	1.58 (1.24-1.98)		
			1970-1994	108	1.35 (1.10-1.63)		
			1995 or after	26	1.58 (1.03-2.31)		
		Melanoma, incidence	Era of first empl (SIR):	oyment, par	t-time firefighters		
			Pre-1970	18	2.32 (1.38-3.67)		
			1970-1994	45	1.23 (0.90-1.65)		
			1995 or after	26	1.43 (0.94-2.10)		
		Melanoma, incidence	No. of incidents firefighters (RIR		part-time		
			Tertile 1	9	1		
			Tertile 2	7	0.64 (0.23-1.73)		
			Tertile 3	14	0.90 (0.35-2.26)		
			Trend-test P val	ue, 0.89	. ,		

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Reference, location, enrolment/follow- up period, study design	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments
<u>Glass et al. (2016a)</u>		Melanoma,	No. of fire incid		d by part-time	Age,	
(cont.)		incidence	firefighters (RI			calendar period	
			Tertile 1	9	1	period	
			Tertile 2 Tertile 3	9 12	0.80 (0.31–2.03) 0.75 (0.29–1.92)		
			Trend-test P va		0.75 (0.29–1.92)		
		Melanoma, incidence		e fire inciden	ts attended by part-		
			Tertile 1	10	1		
			Tertile 2	7	0.58 (0.22–1.53)		
			Tertile 3	13	0.71 (0.28–1.77)		
			Trend-test P va	lue, 0.49			
		Melanoma, incidence	No. of landscap part-time firefi		its attended by		
			Tertile 1	10	1		
			Tertile 2	7	0.58 (0.22–1.53)		
			Tertile 3	13	0.76 (0.31–1.85)		
			Trend-test P va				
		Melanoma, incidence	No. of vehicle f time firefighter		attended by part-		
			Tertile 1	9	1		
			Tertile 2	9	0.93 (0.37–2.34)		
			Tertile 3	12	0.85 (0.34–2.11)		
			Trend-test P va				
		Brain and other	Firefighter stat				
		CNS (ICD-10,	Full-time	17	0.78 (0.45–1.24)		
		C70–C72), incidence	Part-time	13	1.37 (0.73–2.35)		
			All	30	0.96 (0.65–1.37)		

Reference, location, enrolment/follow- up period, study design	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments
<u>Glass et al. (2016a)</u> (cont.)		Brain and other CNS (ICD-10, C70–C72), incidence	Duration of emp (SIR): > 3 mo to 10 yr		ll-time firefighters 0.71 (0.15–2.08)	Age, calendar period	
			> 5 mo to 10 yr 10–20 yr	3 4	0.71 (0.13–2.08) 0.81 (0.22–2.07)	periou	
			$\geq 20 \text{ yr}$	4 10	0.81(0.22-2.07) 0.80(0.38-1.47)		
		Brain and other CNS (ICD-10, C70–C72),	•		art-time firefighters		
			> 3 mo to 10 yr	4	0.94 (0.26-2.41)		
	incidence	10–20 yr	3	1.37 (0.28-4.00)			
			≥ 20 yr	6	2.02 (0.74-4.40)		
		Brain and other CNS (ICD-10, C70–C72), incidence	Era of first emple (SIR):	oyment, full	-time firefighters		
			Pre-1970	6	0.82 (0.30-1.79)		
			1970-1994	8	0.67 (0.29–1.32)		
			1995 or after	3	1.12 (0.23-3.27)		
		Brain and other CNS (ICD-10,	Era of first emple (SIR):	oyment, par	t-time firefighters		
		С70–С72),	Pre-1970	5	4.40 (1.43-10.26)		
		incidence	1970-1994	6	1.11 (0.41–2.42)		
			1995 or after	2	0.68 (0.08-2.46)		
		Brain, incidence	Firefighter status	s (SIR):			
			Full-time	16	0.76 (0.44–1.24)		
			Part-time	12	1.32 (0.68–2.31)		
			All	28	0.93 (0.62–1.35)		
		Brain, incidence	Duration of emp (SIR):	oloyment, fu	ll-time firefighters		
			> 3 mo to 10 yr	3	0.75 (0.15–2.19)		
			10–20 yr	4	0.85 (0.23-2.18)		
			$\geq 20 \text{ yr}$	9	0.75 (0.34-1.42)		

Reference, location, enrolment/follow- up period, study design	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments
<u>Glass et al. (2016a)</u> (cont.)		Brain, incidence	Duration of emp (SIR):	loyment, pa	rt-time firefighters	Age, calendar	
`			> 3 mo to 10 yr	3	0.75 (0.15-2.18)	period	
			10–20 yr	3	1.43 (0.29-4.18)		
			$\geq 20 \text{ yr}$	6	2.09 (0.77-4.55)		
		Brain, incidence	•	oyment, full	-time firefighters		
			Pre-1970	5	0.71 (0.23-1.65)		
			1970-1994	8	0.70 (0.30-1.39)		
			1995 or after	3	1.18 (0.24-3.44)		
		Brain, incidence	Era of first emple (SIR):	oyment, par	t-time firefighters		
			Pre-1970	5	4.54 (1.47-10.59)		
			1970-1994	6	1.16 (0.43-2.53)		
			1995 or after	1	0.36 (0.01-2.00)		
		Thyroid and	Firefighter status	s (SIR):			
		other endocrine	Full-time	13	1.08 (0.58-1.85)		
		(ICD-10, C73-	Part-time	7	1.16 (0.47–2.39)		
		C75), incidence	All	20	1.11 (0.68–1.71)		
		Thyroid and other endocrine	Duration of emp (SIR):	oloyment, fu	ll-time firefighters		
		(ICD-10, C73–	> 3 mo to 10 yr	3	1.02 (0.21-2.98)		
		C75), incidence	10–20 yr	6	1.87 (0.69-4.06)		
			≥ 20 yr	4	0.70 (0.19–1.78)		
		Thyroid and other endocrine	Duration of emp (SIR):	oloyment, pa	rt-time firefighters		
		(ICD-10, C73–	> 3 mo to 10 yr	2	0.62 (0.07-2.22)		
			10–20 yr	2	1.44 (0.17–5.20)		
			≥ 20 yr	3	2.24 (0.46-6.54)		

Reference, location, enrolment/follow- up period, study design	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments
<u>Glass et al. (2016a)</u>		Thyroid and		oyment, full	-time firefighters	Age,	
(cont.)		other endocrine	(SIR):			calendar	
		(ICD-10, C73– C75), incidence	Pre-1970	2	0.78 (0.09–2.83)	period	
		07 <i>5</i>), incluence	1970–1994	7	0.96 (0.38–1.97)		
			1995 or after	4	1.85 (0.50-4.72)		
		Thyroid and other endocrine	Era of first empl (SIR):	oyment, par	t-time firefighters		
		(ICD-10, C73–	Pre-1970	3	7.02 (1.45–20.51)		
		C75), incidence	1970-1994	4	1.24 (0.34-3.18)		
			1995 or after	0	0 (NR)		
		Thyroid,	Firefighter statu	s (SIR):			
		incidence	Full-time	13	1.18 (0.63-2.01)		
			Part-time	7	1.26 (0.51-2.59)		
			All	20	1.20 (0.74-1.86)		
		Thyroid, incidence	Duration of emp (SIR):	oloyment, fu	ll-time firefighters		
			> 3 mo to 10 yr	3	1.11 (0.23-3.25)		
			10–20 yr	6	2.03 (0.75-4.43)		
			≥ 20 yr	4	0.76 (0.21–1.94)		
		Thyroid, incidence	Duration of emp (SIR):	oloyment, pa	rt-time firefighters		
			> 3 mo to 10 yr	2	0.67 (0.08-2.41)		
			10–20 yr	2	1.56 (0.19-5.62)		
			$\geq 20 \text{ yr}$	3	2.44 (0.50-7.14)		
		Thyroid, incidence	Era of first empl (SIR):	oyment, full	-time firefighters		
			Pre-1970	2	0.87 (0.11-3.15)		
			1970-1994	7	1.04 (0.42-2.14)		
			1995 or after	4	1.99 (0.54-5.08)		

Reference, location, enrolment/follow- up period, study design	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments
<u>Glass et al. (2016a)</u> (cont.)		Thyroid, incidence	Era of first emple (SIR):	oyment, par	t-time firefighters	Age, calendar	
		Pre-1970	3	7.78 (1.60-22.74)	period		
		1970-1994	4	1.35 (0.37-3.45)			
			1995 or after	0	0 (NR)		
Glass et al. (2016b)614; all male (611) andVictoria, Australiafemale (3) employedEnrolment,and volunteer1971–1999/follow-Country Fireup, 1980–2011Authority trainers(mortality), 1982–and a group of paid2012 (incidence)Country FireCohortAuthority firefighterswho trained at the Fiskville site from	Melanoma, incidence	Risk of chronic e (SIR):	exposure an	d firefighter group	Age, calendar	<i>Exposure assessment</i> <i>critique</i> : Satisfactory quality.	
		Low	3	1.43 (0.29-4.18)	period	Incorporated categorical lev of exposure into assessment for each type of firefighter.	
		Medium	5	1.51 (0.49-3.52)			
		– Paid [career]	3	2.45 (0.50-7.15)		Volunteers mainly rural,	
		-Volunteer	2	0.96 (0.12-3.47)		paid [career] firefighters wer	
	Authority firefighters		–Volunteer with Fiskville start date	2	1.01 (0.12–3.66)		municipal. Strengths: included firefighte instructors with high potential exposure to smoke and other hazardous agents; assessed exposure based on job assignment. Limitations: low number of
	1971 to 1999; all analyses limited to		–With Fiskville HR start date	5	3.06 (1.00-7.15)		
	men as no deaths or		High	6	4.59 (1.68-9.99)		
	cancers were observed among women		–With Fiskville HR start date	6	5.25 (1.93–11.4)		
	Exposure assessment method: employed or volunteer firefighter	Brain and other CNS (ICD-10,	Risk of chronic exposure and firefighter group (SIR):				cases; young age at end of follow-up.
	trainers and career	С70-С72),	Low	0	0 (NR)		
	firefighters who	incidence	Medium	4	5.74 (1.56–14.7)		
	trained at training		-Paid [career]	2	7.59 (0.92–27.4)		
	facility for any period		-Volunteer	2	4.62 (0.56–16.67)		
of low, medium, and high chronic exposu	resource records, categorized into risk		–Volunteer with Fiskville start date	0	0 (NR)		
	high chronic exposure to smoke and other		-With Fiskville HR start date		5.76 (0.70-20.8)		
	agents based on job		High	1	3.63 (0.09–20.3)		
	assignment		–With Fiskville HR start date	1	4.15 (0.11–23.1)		

Table 2.7 (cont	tinued)								
Reference, location, enrolment/follow- up period, study design	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments		
<u>Bates et al. (2001)</u> New Zealand	4305; the cohort comprised all male	Melanoma, incidence	Follow-up perio		1.2((0.0.1.0))	<i>Exposure assessment</i> <i>critique</i> : Satisfactory quality			
Enrolment, 1977 (4221) and female	mendence	1977-1996	23	1.26 (0.8–1.9)	calendar period	Heterogeneity of direct			
through June 1995/	(84) firefighters		1990–1996	15	1.49 (0.8–2.5)	period	firefighter exposure within		
follow-up, 1977-	(paid [career] and	Melanoma, incidence	Duration of pai				job classification. May incluc urban [municipal] and rural firefighters.		
1995 (mortality),	volunteer) employed		0–10 yr	7	1.72 (0.7–3.5)				
1977–1996	as a career firefighter		11–20 yr	6	1.75 (0.6–3.8)				
Cohort also worke	for ≥ 1 yr and who		> 20 yr	6	1.67 (0.6–3.6)		Strengths: ascertained both		
	career firefighter for	Melanoma, incidence	Trend-test P va	,			incidence and mortality outcomes.		
	\geq 1 day between 1977		-		teer service (SIR):		<i>Limitations</i> : little information		
	and 1995; all analyses	incidence	0–10 yr	4	1.58 (0.4–4.0)		on confounders; significant		
	limited to men due		11–20 yr	6	1.83 (0.7–4.0)		loss to follow-up; low numbe of cases in stratified analyses		
	to small numbers of		> 20 yr	9	1.70 (0.8–3.2)				
	women		Trend-test P va	lue, 0.93					
	Exposure assessment method: ever employed and categorical duration of employment (years)	nethod: ever incidence	SMR: Firefighters vs male New Zealand population	2	0.65 (0.1–2.4)				
	from employment	Brain, incidence	Follow-up perio	od (SIR):					
	records		1977–1996	5	1.27 (0.4-3.0)				
			1990-1996	3	1.59 (0.3-4.6)				
		Brain, mortality	SMR:						
			Firefighters vs male New Zealand population	2	0.68 (0.1–2.4)				

9/11, World Trade Center disaster, 11 September 2001; BCC, basal cell carcinoma; BMI, body mass index; CFHS, Career Firefighter Health Study; CI, confidence interval; CNS, central nervous system; FDNY, Fire Department of the City of New York; HR, hazard ratio; HWSE, healthy-worker survivor effect; ICD, International Classification of Diseases; IDR, incidence density ratio; JEM, job-exposure matrix; LRT, likelihood ratio test; NJ, New Jersey; NR, not reported; PMR, proportionate mortality ratio; RCS, restricted cubic splines; RIR, relative incidence ratio; RR, rate ratio; SIR, standardized incidence ratio; SMR, standardized mortality ratio; SRR, standardized rate ratio; US, United States; vs, versus; WTC, World Trade Center; yr, year.

1.30; 95% CI, 0.95-1.73; 47 cases) and mortality (SMR, 1.55; 95% CI, 0.83-2.65; 13 deaths) of cutaneous melanoma appeared higher than in the general male population of Norway. There was little evidence to suggest that the risk of non-melanoma skin cancer was higher than in the general population, whether based on incidence (SIR, 0.99; 95% CI, 0.69-1.37; 35 cases) or mortality (SMR, 0.95; 95% CI, 0.02–5.31; < 5 deaths). There was some evidence to suggest that the risk of cancer of the thyroid was raised when the general population was the referent, whether based on incidence (SIR, 1.45; 95% CI, 0.53-3.15; 6 cases) or mortality (SMR, 2.41; 95% CI, 0.29-8.70; < 5 deaths). Similarly, there was some evidence to suggest that the risk of brain and other central nervous system cancers was higher than in the general population, whether based on incidence (SIR, 1.31; 95% CI, 0.87–1.90; 28 cases) or mortality (SMR, 1.41; 95% CI, 0.77–2.37; 14 deaths). Separate stratified analyses were also conducted examining calendar period of first employment, duration of employment, time since first employment, period of follow-up, and age at diagnosis, although results for most of these were very imprecise. For melanoma, the SIR was raised for follow-up from 1985 through 1994, the SMR was raised for firefighters aged 50-69 years at diagnosis, and there was some evidence of an increased SIR regardless of year of first employment, years since first employment, and duration of employment. The estimate for non-melanoma skin cancer incidence increased from below unity to 1.20 with more recent year of first employment. There were no other findings of note in the stratified analyses.

A census-based cancer incidence study in a cohort of 8136 male firefighters in Sweden provided information on the risk of melanoma, non-melanoma skin cancer, and brain cancer (<u>Bigert et al., 2020</u>). Employment information was ascertained from national decennial censuses between 1960 and 1990. Cancer incidence data were ascertained from the Swedish Cancer Registry with follow-up from 1961 through 2009. The SIR for ever-employment as a firefighter was raised for non-melanoma skin cancer (SIR, 1.48; 95% CI, 1.20–1.80; 101 cases), with SIRs decreasing with increasing duration of employment (P < 0.01) and increasing for cancers diagnosed in more recent calendar periods (no results from test for trend were provided). The SIR for the most recent cancers (diagnosed 1991-2009) was 1.55 (95% CI, 1.23–1.92; 84 cases). The SIR for cutaneous melanoma appeared to be raised (SIR, 1.22; 95% CI, 0.95-1.54; 69 cases), and there was no apparent relation with duration of employment or calendar year of diagnosis. The SIR was not raised for cancer of the brain (SIR, 0.89; 95% CI, 0.63–1.23; 38 cases). Stratified results were not presented for brain cancer.

A cancer incidence study in a cohort of 1080 male firefighters in Stockholm, Sweden provided information on the risk of melanoma, non-melanoma skin cancer, and brain cancer (Kullberg et al., 2018). Firefighters were identified through annual enrolment records from 15 fire stations and had worked for ≥ 1 year between 1931 and 1983. This was an update to a previous study (Tornling et al., 1994) and added 26 years of cancer incidence follow-up from 1958 through 2012 in the Swedish Cancer Registry. The overall SIR for melanoma diagnosed any time during the follow-up period (1958–2012) was below one (SIR, 0.30; 95% CI, 0.06–0.88; 3 cases), and the overall SIR was not raised for non-melanoma skin cancer (SIR, 0.85; 95% CI, 0.49-1.35; 17 cases). The SIR for brain cancer was modestly elevated (SIR, 1.16; 95% CI, 0.50-2.28; 8 cases), although the confidence interval was wide.

The earlier study of the same cohort also investigated both cancer incidence and mortality in a slightly larger population of 1116 male firefighters with mortality follow-up from 1951 through 1986 (<u>Tornling et al., 1994</u>) and provided information on the risk of brain cancer. Exposure to fire events was assessed using reports of fires fought by the Stockholm fire brigade between

1933 and 1983. With male regional mortality rates as the referent, the overall SMR for brain cancer mortality appeared raised (SMR, 2.79; 95% CI, 0.91-6.51; 5 cases). In stratified analyses, the SMRs for brain cancer were statistically imprecise but appeared raised in firefighters aged \geq 65 years (SMR, 4.59; 95% CI, 0.95–13.41; 3 cases), 30-40 years after first exposure (SMR, 5.07; 95% CI, 1.05-14.81; 3 cases), and in firefighters who had attended more than 1000 fires (SMR, 4.96; 95% CI, 1.35-12.70; 4 cases). SMRs were not raised for different latencies or fewer fires attended, or within other strata of age or years of employment. SMRs appeared to increase with increasing age, years of employment, and number of fires attended. Stratified results for brain cancer incidence outcomes were similar to those for mortality. [The Working Group noted that the exposure assessment method was a strength and that the number of deaths from brain cancer was small.]

A cancer incidence study in a cohort of 9061 male full-time, part-time, and volunteer firefighters provided information on the risk of melanoma, brain cancer, and thyroid cancer (Petersen et al., 2018a). Cohort members had been employed as firefighters at some time between 1964 and 2004, and cancer incidence follow-up was conducted in the Danish Cancer Registry from 1968 through 2014. External comparisons were made with the general male population, a random sample of the employed Danish population, and the Danish military. The SIR for melanoma was raised in firefighters compared with a sample of Danish employees (SIR, 1.28; 95% CI, 1.01-1.61; 70 cases), and with the general population (SIR, 1.24; 95% CI, 0.98-1.57), but not when compared with the military (SIR, 1.05; 95% CI, 0.83–1.33). An excess of melanoma was also observed among those with a "specialized" job function who were presumed to have a heavier exposure to smoke (SIR, 2.44; 95% CI, 1.27-4.70; 9 cases) and in those who were aged < 25 years at first employment (SIR, 1.47; 95% CI, 1.07-2.02;

38 cases) compared with the general population. The SIR was also raised for non-melanoma skin cancer in those with a specialized job function (SIR, 1.49; 95% CI, 1.04-2.11; 31 cases) compared with the general population. Otherwise, there was no apparent relation between employment type, era of first employment, age at first employment, or employment duration and the incidence of melanoma or non-melanoma skin cancer. The SIR estimates for thyroid cancer were modestly raised when using all three comparison populations (SIRs ranged from 1.05 to 1.21) but were imprecise. The overall SIR estimates for brain cancer were below one for all three comparison populations. Stratified analyses were not available for thyroid cancer or brain cancer.

[The investigation of cancer mortality in the same cohort by <u>Petersen et al. (2018b)</u> did not report results for brain or thyroid cancer. Skin cancer outcomes were combined with those for bone cancer in analyses, making these results uninformative for the risk of skin cancer alone.]

A cancer incidence study in a cohort of 10 786 male firefighters from the FDNY exposed to the WTC disaster site and 8813 firefighters in the CFHS, which included firefighters from Philadelphia, Chicago, and San Francisco fire departments, provided information on the risk of melanoma and cancer of the thyroid (Webber et al., 2021). Cancer incidence follow-up was conducted using several state cancer registries selected on the basis of residential history information and began on 11 September 2001 and ended in 2016. With the US male general population as the referent, overall SIRs for melanoma were increased in both the FDNY (SIR, 1.59; 95% CI, 1.30-1.96; 96 cases) and CFHS (SIR, 1.39; 95% CI, 1.07-1.79; 70 cases) cohorts. After adjustment for medical surveillance bias with the addition of a 2-year lag to the diagnosis date of certain cases, the SIR for melanoma for the FDNY cohort was unchanged. Among non-Hispanic White men, the risk of melanoma appeared modestly increased in FDNY firefighters compared with

CFHS firefighters in internal comparisons, but the estimate was relatively imprecise (RR, 1.12; 95% CI, 0.80–1.57). With the US male general population as the referent, SIRs for thyroid cancer were increased for the FDNY cohort (SIR, 2.37; 95% CI, 1.78-3.17; 46 cases) but appeared to be the same for the CFHS cohort (SIR, 1.01; 95% CI, 0.61–1.67; 15 cases). After applying the adjustment for medical surveillance bias, the SIR for thyroid cancer for the FDNY cohort remained high (SIR, 2.01; 95% CI, 1.47–2.75). In internal comparison analyses, the risk of thyroid cancer was increased in FDNY firefighters compared with CFHS firefighters (RR, 2.53; 95% CI, 1.37-4.70). This was also the case after adjustment for surveillance bias (RR, 2.11; 95% CI, 1.14–3.90). [The Working Group noted that this study was limited by a possible incompletely controlled effect of greater medical surveillance bias in FDNY firefighters than in CFHS firefighters or the US general population. This bias may be particularly influential on results for thyroid cancer.]

A study of 14 987 male firefighters employed by FDNY and who had worked on the WTC disaster site between September 2001 and July 2002 provided information on the risk of thyroid cancer (Colbeth et al., 2020a). Age-adjusted relative rates [rate ratios or RRs] were calculated using a reference group that the authors described as "demographically similar" (all male residents of Olmsted County, Minnesota, from 1 January 2000 to 31 December 2018). The age-adjusted RRs were higher among firefighters overall (RR, 2.3; 95% CI, 1.7-3.2; 72 cases) and in subgroups for cancers detected in early (RR for 2001–2009, 1.8; 95% CI, 1.1-3.0) or late (RR for 2010-2018, 2.5; 95% CI, 1.6-3.8) calendar periods, and for cases that were asymptomatic (RR, 3.1; 95% CI, 2.1-4.7; 53 cases). However, the rate did not appear to be raised for symptomatic cancers (RR, 0.8; 95% CI, 0.4-1.5; 12 cases). [The Working Group concurred with the authors' conclusion that the thyroid cancer excess was attributable to asymptomatic cancers and that this was probably because of increased medical surveillance in the firefighter group compared with the reference group.]

An earlier cancer incidence study of an overlapping cohort of 9853 male FDNY firefighters reported risks among WTC-exposed and unexposed firefighters for additional cancer sites, including melanoma and thyroid cancer (Zeig-Owens et al., 2011). Cancer incidence follow-up was conducted in state cancer registries from 1996 through 2008. With the US male general population as the referent, the SIR for melanoma was raised when restricted to exposed persontime in firefighters (SIR, 1.54; 95% CI, 1.08–2.18; 33 cases) but not when restricted to unexposed person-time in firefighters (SIR, 0.95; 95% CI, 0.57-1.58; 15 cases). For thyroid cancer, the SIR (corrected for medical surveillance bias) was raised when restricted to exposed person-time in firefighters (SIR, 2.17; 95% CI, 1.23–3.82; 12 cases) but not when restricted to unexposed persontime in firefighters (SIR, 0.59; 95% CI, 0.15-2.36; \leq 5 cases). [The Working Group noted that the increased risk of thyroid cancer and melanoma may be influenced by medical surveillance bias in this cohort.]

A mortality study was carried out in a cohort of 29 992 male and female municipal career firefighters in the USA. The CFHS from San Francisco, Chicago, and Philadelphia provided information on the risk of cancers of the prostate, kidney, and urinary bladder (Pinkerton et al., 2020). Mortality follow-up was conducted from 1950 through 2016. With the US general population as the referent, the SMRs among firefighters for melanoma and other skin cancers (SMR, 1.05; 95% CI, 0.83-1.31; 78 cases) and for brain cancer (SMR, 0.99; 95% CI, 0.79-1.23; 86 cases) were not elevated overall. Results stratified by municipal fire department were similar and likewise not elevated. In internal regression analyses, there was also no suggestion of an association between the number of exposed days or fire-runs and either cancer site (fire-hours were not evaluated

because of small numbers). [The Working Group noted that the use of mortality outcomes was a limitation for the assessment of melanoma risk because of potential outcome misclassification.]

An additional study of the CFHS cohort investigated cancer incidence among 29 993 municipal career firefighters and reported external and internal comparison analyses with follow-up to the end of 2009 (Daniels et al., 2014). The methods were similar to those used in the study by Pinkerton et al. (2020). Cancer incidence follow-up was conducted in state cancer registries relevant to each fire department to the end of 2009, with start years varying between 1985 and 1988. Residential history information was used to select state registries for follow-up. With the US general population as the referent, the overall SIR among firefighters for cancers of the brain and other nervous system tissues (including all primary cancers) was not elevated (SIR, 1.02; 95% CI, 0.76-1.34; 51 cases). There was strong evidence of heterogeneity in the results for different fire departments for brain cancer incidence (P = 0.007), with the San Francisco Fire Department subcohort having an elevated rate (SIR, 1.95; 95% CI, 1.14-3.12; 17 cases) and the Chicago Fire Department subcohort having a reduced rate (SIR, 0.53; 95% CI, 0.28-0.91; 13 cases). There was no suggestion of heterogeneity by age (P = 1.0). For thyroid cancer, the overall SIR among firefighters was not elevated (SIR, 0.87; 95% CI, 0.56-1.28; 25 cases). Similar results were seen for the individual fire department subcohorts and for the expanded case definition of "thyroid and other endocrine glands". For melanoma, the overall SIR among firefighters was not elevated (SIR, 0.87; 95% CI, 0.73-1.03; 141 cases). There appeared to be marked heterogeneity between the results for melanoma for different fire departments (no formal test results were available), with the San Francisco Fire Department having an elevated rate (SIR, 1.89; 95% CI, 1.43-2.46; 56 cases) and the Chicago Fire Department having a reduced rate (SIR,

0.56; 95% CI, 0.41–0.76; 44 cases). [The Working Group noted that a strength of this study was that results for melanoma were standardized by race to reduce confounding by skin tone.]

A cancer incidence study in a cohort of 2447 male municipal firefighters from Seattle and Tacoma, USA, provided information on the risk of melanoma, and cancers of the brain and thyroid, in comparison to that in the local male general population and in a cohort of male police officers from Washington state (Demers et al., 1994). Firefighters had been employed for \geq 1 year between 1944 and 1979, and cancer incidence follow-up was conducted from 1974 through 1989 in the regional SEER cancer registry using residential history information to reduce loss to follow-up. With the local general population as the referent, the overall SIR for melanoma appeared modestly raised (SIR, 1.2; 95% CI, 0.6-2.3; 9 cases), and the SIR for brain cancer was close to unity and imprecise (SIR, 1.1; 95% CI, 0.3-2.9; 4 cases). All four cases of brain cancer occurred in firefighters with \geq 30 years since first employment, giving a raised, but still imprecise, SIR for this group (SIR, 1.9; 95% CI, 0.5-4.9; 4 cases). Apart from this, duration of employment, time since first employment, and comparisons with police officers as the reference group yielded little evidence of positive associations for melanoma or cancer of the brain. However, analyses were statistically imprecise because of small case numbers. There was only one case of thyroid cancer.

An earlier study of 4401 male municipal firefighters, who included firefighters from Portland (Oregon), Seattle, and Tacoma, reported findings for mortality from cancer of the skin (melanoma and non-melanoma skin cancer combined) and cancer of the brain and nervous system (Demers et al., 1992a). The mortality follow-up period was from 1945 to the end of 1989. Comparison of mortality rates was made with US White males in the general population and with a cohort of local male police officers. With the general

population as the referent, the overall SMR for skin cancer among firefighters was close to one (SMR, 0.98; 95% CI, 0.36-2.13; 6 deaths), and with the police officers as the referent, there was little evidence of an increase in skin cancer mortality (IDR, 1.12; 95% CI, 0.27-4.76). There were too few deaths from skin cancer to allow stratification by age or employment characteristics. Mortality from brain and nervous system cancers (ICD-9, 191 and 192) was higher (SMR, 2.07; 95% CI, 1.23-3.28; 18 deaths) than that in the general population, although the association was attenuated when police officers were used as the reference group (IDR, 1.63; 95% CI, 0.7–3.79). The SMR for brain and nervous system tumours (ICD-9, 191, 192, 237.5–237.7, 239.6–239.7) was raised for 10-19 years of exposed employment $(SMR, 3.53; 95\% CI, 1.5-7.0; 8 deaths), \ge 30 years$ after first employment (SMR, 2.63; 95% CI, 1.4-4.4; 14 deaths), and people aged 18-39 years (SMR, 3.75; 95% CI, 1.2-8.7; 5 deaths), but there was no clear relation with duration of exposed employment, years since first employment, or age. Stratified analyses for brain cancer mortality were limited by the small number of cases.

A mortality study in a cohort of 1867 White male municipal firefighters who worked for the City of Buffalo, USA, provided information on the risk of brain cancer (Vena & Fiedler, 1987). Firefighters had been employed in the occupation for \geq 1 year between 1950 and 1979 and mortality follow-up was from 1950 through 1979. With the US White male general population as the referent, the overall SMR for brain cancer appeared raised but was imprecise (SMR, 2.36; 95% CI, 0.86–5.13; 6 deaths). In stratified analyses, SMRs were raised for those working as a firefighter for 20-29 years (SMR, 3.75; 95% CI, [1.0–10.2]; 3 deaths), and for latencies of < 20 years (SMR, 4.02; 95% CI, [1.1–11.7]; 3 deaths) and 20-29 years (SMR, 4.58; 95% CI, [1.3–13.6]; 3 deaths). There was no clear positive relation between brain cancer mortality and the categories of duration of employment or other

time-related characteristics. [This study was limited by the small number of cases.]

A proportionate mortality study of deceased police and firefighters was conducted in New Jersey, USA (Feuer & Rosenman, 1986). Analyses were based on 263 deaths in White male firefighters that were reported to the state comprehensive retirement system for police and firefighters in 1974–1980. There were four deaths from skin cancer (all types combined) among firefighters. Overall PMR estimates were elevated for skin cancer mortality when using either the general population (national and state) or police officers as the referent, although estimates were imprecise. Analyses stratified by duration of employment and latency were too imprecise to make inferences.

A mortality study in a cohort of 5414 male career firefighters in Toronto, Canada, who had worked for \geq 6 months between 1950 and 1989 provided information on the risk of melanoma and cancer of the brain and other nervous system tissues (Aronson et al., 1994). Mortality follow-up was conducted in a national mortality database from 1950 through 1989. There were only two deaths from melanoma. With the male general population of Ontario as the referent, the SMR for brain cancer among firefighters was raised overall (SMR, 2.01; 95% CI, 1.10–3.37; 14 deaths) and in those with < 20 years since first exposure (SMR, 2.83; 95% CI, 1.04-6.16; 6 deaths). There was little evidence of a relation between SMR and duration of employment, time since first exposure, or age.

A study of 3328 municipal firefighters in two cohorts from Calgary and Edmonton, Canada, investigated mortality from melanoma and brain cancer (<u>Guidotti, 1993</u>). Firefighters had been employed between 1927 and 1987 and mortality follow-up was conducted in both provincial and national sources from 1927 through 1987. Results showed no deaths from melanoma. With the general population of Alberta as the referent, the SMR for brain cancer appeared to be raised but was very imprecise (SMR, 1.47; 95% CI, 0.30-4.29; 3 deaths).

A cancer incidence study in an entirely female cohort of 37 962 volunteer firefighters in Australia provided information on the risk of melanoma, cancer of the thyroid, and brain and other central nervous system cancers (Glass et al., 2019). Cancer incidence follow-up was conducted in a national cancer registry from 1982 through 2010. Work history information describing the number and type of incidents attended was ascertained from fire agency personnel records. With the female general population of Australia as the referent, SIRs were above one for melanoma among all volunteer firefighters (SIR, 1.25; 95% CI, 1.05-1.46; 147 cases) and also among those who had attended incidents (SIR, 1.11; 95% CI, 0.84-1.44; 57 cases). External comparison results showed no excess of brain or thyroid cancer incidence among either group of volunteers. In internal regression analyses, there was no association between any tertile of the number of incidents attended and the rate of melanoma relative to firefighters who never attended incidents. Trend tests across tertile categories did not suggest a relation between risk of melanoma and the total number of incidents overall (P = 0.53) or all fire incidents (P = 0.42), structure fire incidents (P = 0.89), landscape fire incidents (P = 0.41), or vehicle fire incidents (P = 0.24). [The Working Group noted that the volunteer firefighters were more likely to live in rural areas and may have had more sun exposure through outdoor jobs (e.g. farming) than people who live in cities. In Australia, more than 85% of people live in cities and using the general population as the reference group in external comparisons may have introduced positive confounding. Non-melanoma skin cancer results were not available.]

Using the same methods as those in the study of female firefighters, cancer incidence was also investigated in a parallel cohort of 163 094 male volunteer firefighters in Australia (Glass et al., 2017). With the male general population

(SIR, 1.00; 95% CI, 0.93-1.06; 912 cases), brain cancer (SIR, 0.88; 95% CI, 0.73-1.06; 114 cases) (a similar result was found for brain and other central nervous system cancers), or thyroid cancer (SIR, 0.83; 95% CI, 0.63-1.07; 58 cases). In internal regression analyses, there was little suggestion that risk of melanoma was related to duration of service (P = 0.29). All results were similar when analyses were restricted to volunteer firefighters who attended incidents. Analysis by incident type (using tertiles of number of incidents attended) suggested risk of melanoma increased with increasing number of total and fire incidents, but confidence intervals were wide and there was no formal trend test. There was no association suggested with structure fire incidents, landscape fire incidents, or vehicle fire incidents. The SIR for melanoma appeared to increase with more recent calendar time periods and was raised for the most recent time period of 1995 or later (SIR, 1.12; 95% CI, 1.01-1.24; 363 cases). There was little evidence suggesting increased risk of brain and other central nervous system cancers or thyroid cancer in external or internal comparison analyses. Using methods similar to those in the two

of Australia as the referent, SIRs for all volun-

teer firefighters were not increased for melanoma

studies of volunteer firefighters, a cancer incidence study in a cohort of 30 057 paid full-time and part-time male firefighters in Australia provided information on the risk of melanoma and cancers of the brain and thyroid (Glass et al., 2016a). Included firefighters had worked between 1976 and 2003 and were primarily municipal or semi-metropolitan firefighters. Cancer incidence follow-up was conducted in a national registry to the end of 2010. With the male general population of Australia as the referent, the SIR for melanoma overall was elevated for all firefighters (SIR, 1.44; 95% CI, 1.28-1.62; 298 cases) and was also elevated within each stratum of full-time and part-time firefighters. The SIR for melanoma among full-time firefighters was raised regardless of duration of employment and year of diagnosis and was elevated in both categories of duration of employment in internal regression analyses. However, internal analyses by number of incidents attended did not indicate a positive monotonic relation between risk of melanoma for all incident types, fire incidents (P = 0.68), structure fire incidents (P = 0.38), landscape fire incidents (P = 0.50), or vehicle fire incidents (P = 0.39). The SIR for brain cancer among all firefighters was not raised (SIR, 0.93; 95% CI, 0.62–1.35; 28 cases), although it was raised for thyroid cancer (SIR, 1.20; 95% CI, 0.74–1.86; 20 cases).

A study of cancer incidence was conducted in a cohort of 614 firefighters and trainers who attended a firefighter-training facility in Australia (Glass et al., 2016b). Three female firefighters were excluded from the analysis. Cancer incidence follow-up was conducted from 1982 through 2012. Participants were grouped into risk categories of low, medium, and high chronic exposure (to smoke and other hazardous agents) on the basis of job assignment. With the male general population of Victoria as the referent, a raised SIR for melanoma was observed among firefighters with a high risk of chronic exposure (SIR, 4.59; 95% CI, 1.68-9.99; 6 cases) but not among those with a low (SIR, 1.43; 95% CI, 0.29–4.18; 3 cases) or medium (SIR, 1.51; 95% CI, 0.49–3.52; 5 cases) risk of chronic exposure. A raised SIR for brain and other central nervous system cancers was observed among firefighters with a medium risk of chronic exposure (SIR, 5.74; 95% CI, 1.56–14.7; 4 cases).

A mortality and cancer incidence study in a cohort of 4305 paid [career] and volunteer firefighters in New Zealand provided information on the risk of melanoma and cancer of the brain (Bates et al., 2001). The cohort included 84 female firefighters who were excluded from the analysis. Included firefighters had worked for \geq 1 year as a career firefighter and were employed for \geq 1 day between 1977 and 1995. Follow-up for cancer mortality and incidence was conducted in a national data source to the end of 1995 (for mortality) or 1996 (for incidence). With the male general population of New Zealand as the referent, the overall SIR among firefighters appeared slightly raised for melanoma (SIR, 1.26; 95% CI, 0.8–1.9; 23 cases) and for brain cancer incidence (SIR, 1.27; 95% CI, 0.4–3.0; 5 cases), although the estimate for brain cancer was imprecise. Results were similar when restricted to recent calendar years (1990-1996) of diagnosis. There was no evidence of a positive relation between melanoma incidence and either duration of career service (P = 0.97) or duration of total (career and volunteer) service (P = 0.93). Similar analyses for brain cancer were not reported. Results for melanoma and brain cancer mortality were based on only two cases.

2.4.2 Studies only reporting having ever worked as a firefighter

(a) Occupational cohort studies

Studies first described in Section 2.1.2(a) are described in less detail in the present section.

See Table S2.8 (Annex 2, Supplementary material for Section 2, Cancer in Humans, online only, available from: <u>https://publications.iarc.</u> <u>fr/615</u>).

Six studies that assessed cancer among firefighters from five retrospective occupational cohorts were reviewed (Musk et al., 1978; Grimes et al., 1991; Giles et al., 1993; Ma et al., 2005, 2006; Amadeo et al., 2015). A descriptive study of skin cancer incidence and mortality among firefighters in Scotland was not reviewed because it lacked measures of association (Ide, 2014). A cohort study by <u>Deschamps et al. (1995)</u> that followed firefighters in Paris, France, for 14 years and compared mortality with that of the male general population of France was also not reviewed because it did not report tabulated results for skin, thyroid, or brain cancer. However, in the discussion the authors noted that they did not observe any cases of brain cancer in this

cohort. Five of the reviewed studies compared cancer incidence or mortality rates in a firefighter cohort to those in one or more general population reference groups, controlling for age and calendar year; the other study (Grimes et al., 1991) examined proportionate mortality. [A potential limitation for estimating associations for cancers of the skin, thyroid, and brain was that most of the studies lacked information on tumour histology, which may bias findings towards the null for certain tumour types if occupation as a firefighter is causally associated with some, but not all, tumour types. An additional limitation was that none of the studies included information on potential confounding factors specific to these cancer sites including, for cancers of the skin, early-age sunburn and non-firefighting-related sun exposure and, for cancers of the thyroid, body mass index (BMI) or history of ionizing radiation exposure. The studies of thyroid cancer incidence may be susceptible to surveillance bias for firefighters who underwent routine occupational health screening. Many of the estimates for the reviewed cancer sites were based on a small sample size, resulting in imprecise risk estimates that hindered interpretation.]

Amadeo et al. (2015) compared the mortality experience of male career firefighters (n = 10829) in France to that of the male general population. This cohort followed career firefighters (who were actively employed in 1979) for up to 29 years. No excess skin cancer was observed. The SMR, based on five deaths, was 0.65 (95% CI, 0.21–1.51). [A limitation of this study was that skin cancer was defined as any malignant neoplasm of skin, including melanoma and non-melanoma skin cancers, which may have different etiologies.]

Ma and colleagues followed a cohort of career firefighters in Florida, USA, from 1981 through 1999 and reported incidence (<u>Ma et al., 2006</u>) and mortality (<u>Ma et al., 2005</u>) for cancers of the skin, brain, and thyroid compared with that in the ageand calendar year-standardized general population of Florida. Excess incident non-melanoma skin cancer (ICD-O-3, C44) was observed among both male and female firefighters (Ma et al., 2006), with SIRs of 1.17 (95% CI, 0.95–1.42; 99 cases) and 3.01 (95% CI, 0.97-7.03; 5 cases), respectively. A lower incidence of cancers of the brain (ICD-10, C71) was seen among male firefighters than in the general population (SIR, 0.58; 95% CI, 0.31-0.97; 14 cases). A higher incidence of thyroid cancer (C73) was seen among both male firefighters and female firefighters, although the latter was based on six cases, with SIRs of 1.77 (95% CI, 1.08-2.73) and 3.97 (95% CI, 1.45-8.65), respectively. Ma et al. (2005) observed no excess of skin cancer mortality among male firefighters (SMR, 0.89; 95% CI, 0.52-1.42; 17 deaths). In a sensitivity analysis restricted to the 15 deaths occurring in firefighters certified between 1972 and 1976, the subgroup with the longest estimated occupational exposure had an SMR of 1.21 (95% CI, 0.68-2.00). No excess mortality was observed for cancers of the brain and central nervous system among male firefighters (SMR, 0.66; 95% CI, 0.35-1.13; 13 deaths), with a similar finding among the subset who entered the cohort between 1972 and 1976. A higher rate of mortality from thyroid cancer was seen in the firefighters than in the general population (SMR, 4.82; 95% CI, 1.30-12.3; 4 deaths). None of the 38 deaths among women firefighters was attributed to cancers of the skin, brain, or thyroid. [The Working Group noted that a strength of these two studies was the availability of results for male and female firefighters; however, findings for incident cancers were imprecise because of the relatively young age at end of follow-up of the firefighters. Although 7% of the cohort members were lost to follow-up, this was unlikely to introduce substantial bias unless the loss was strongly influenced by cancer diagnosis, which may be more likely for cancers with poorer prognosis (e.g. glioma).]

<u>Grimes et al. (1991)</u> examined proportionate mortality for 205 deaths among male firefighters with \geq 1 year of service in the City of Honolulu fire department, Hawaii, USA (1969–1988). The PMR for deaths from brain and other cancers of the central nervous system was 3.78 (95% CI, 1.22–11.71; [3] deaths) with the state population as the referent, with no indication of effect modification by race (Caucasian [White] versus Pacific Islander). [The Working Group noted the lack of standardization of PMRs by age and calendar year as an important limitation.]

<u>Musk et al. (1978)</u> examined the mortality experience of 5655 male firefighters employed for \geq 3 years between 1915 and 1975 in Boston, Massachusetts, USA. On the basis of eight cases, mortality from cancers of the brain and central nervous system (ICD-7, 193) was similar to that in both the state and US populations (SMR, 1.03; 95% CI, [0.48–1.95]; and SMR, 1.13; 95% CI, [0.52–2.14]; respectively).

<u>Giles et al. (1993)</u> studied cancer incidence among 2865 male career firefighters from Melbourne, Victoria, Australia, compared with the adult male state population. The rate of mortality from melanoma was similar to that in the general population (SMR, 1.08; 95% CI, 0.35–2.53; 5 deaths). [Strengths of this study were the inclusion of operational firefighter personnel only (who were likely to have responded to fires), and the reporting of melanoma of the skin (ICD-9, 172) rather than all skin cancers. Limitations included the lack of description of linkage methods with the national cancer registry and resulting inability to assess related potential bias because of matching errors.]

(b) Population-based studies

Studies first described in Section 2.1.2(b) are described in less detail in the present section.

See Table S2.8 (Annex 2, Supplementary material for Section 2, Cancer in Humans, online only, available from: <u>https://publications.iarc.</u> <u>fr/615</u>).

During the period 1990–2021, four studies in population-based cohorts investigated firefighters' risk of cancers of the skin (melanoma and non-melanoma), thyroid, and brain (<u>Pukkala</u> et al., 2014; <u>Harris et al., 2018</u>; <u>Zhao et al., 2020</u>; <u>Sritharan et al., 2022</u>), and eight case-control studies reported results for cancers of the skin, thyroid, and brain among firefighters in the USA (<u>Sama et al., 1990</u>; <u>Ma et al., 1998</u>; <u>Bates, 2007</u>; <u>Kang et al., 2008</u>; <u>Tsai et al., 2015</u>; <u>Muegge et al., 2018</u>; <u>Lee et al., 2020</u>; <u>McClure et al., 2021</u>). One mortality surveillance study evaluated PMRs for skin cancer and for brain and other nervous system cancers among firefighters compared with the national general population in the USA (<u>Burnett et al., 1994</u>).

Three of the cohort studies were based on census data, and compared sex-, age-, and calendaryear-adjusted cancerincidence (Pukkala et al., 2014; Harris et al., 2018) or mortality (Zhao et al., 2020) among firefighters to that for reference groups. The fourth study examined a relatively large cohort via linkage of a Canadian occupational injury and disease claim database to person and cancer registries (Sritharan et al., 2022).

Four of the case-control studies were based on incident cancer registry information only, including self-reported job information, and both site-specific cancer cases and controls diagnosed with other cancers were extracted from the same registries (Sama et al., 1990; Bates, 2007; Kang et al., 2008; Tsai et al., 2015). Two overlapping case-control studies were based on record linkage of firefighter employment records with incident cancer registry data (Lee et al., 2020; McClure et al., 2021). The two remaining studies examined records limited to information obtained from death certificates, including cancer diagnosis and job title (Ma et al., 1998; Muegge et al., 2018). [The Working Group noted that the study strengths and limitations pertaining to design that were previously described for cancers of the respiratory system in Section 2.1.2(b) also apply to cancer types in the present section. Also, the limitations associated with cancer survival, surveillance bias, and lack of information on

potential confounders for studies of the same cancers, as described in Section 2.4.2(a), also apply to studies in this section.]

Cancer mortality was examined prospectively (2001–2011) in a census-based cohort of men aged 20–64 years employed in Spain in 2001 (Zhao et al., 2020). Age-standardized MRRs were calculated for firefighters compared with all other occupations. MRRs were 1.07 (95% CI, 0.63–1.81) for brain cancer, 2.34 (95% CI, 0.53–10.29) for thyroid cancer, and 0.63 (95% CI, 0.19–2.10) for melanoma. [The Working Group noted the small number of cases, which made estimates imprecise. A strength was the use of the working population as the referent.]

The large Nordic linkage study (NOCCA), including 16 422 male firefighters and based on linkage of census data (1960-1990) and nationwide cancer registry data (1961-2005), found an overall increased risk of non-melanoma skin cancer (SIR, 1.33; 95% CI, 1.10-1.59) and (similarly) of melanoma (SIR, 1.25; 95% CI, 1.03–1.51) (Pukkala et al., 2014). The SIR for thyroid cancer was 1.28 (95% CI, 0.75–2.05). The overall SIR for brain cancer was 0.86 (95% CI, 0.66-1.10) and was 0.92 (95% CI, 0.64-1.30) in the subgroup of glioma. [The Working Group noted the evaluation of brain cancer subtype and the long follow-up period as strengths. The main limitation was the lack of information on duration and intensity of firefighting.]

Cancer incidence was explored in a cohort of 13 642 firefighters from Ontario, Canada (Sritharan et al., 2022). The study used information from an occupational injury and disease claims database (ODSS) and linked claimants between 1983 and 2019 to a person register and to the Ontario Cancer Registry. Workers were followed from the first claim date to first cancer diagnosis date, emigration out of Ontario, attained age of 85 years, death, or study end in 2020, whichever was earliest. Site-specific cancer risk, comparing cancer incidence in firefighters with that in all other occupations and in police, was assessed using Cox proportional hazards regression, controlling for age at start of follow-up, birth year, and sex. When comparing firefighters with all other workers, the hazard ratio was 2.38 (95% CI, 1.99–2.84) for melanoma, 1.26 (95% CI, 0.91–1.74) for brain cancer, and 1.11 (95% CI, 0.76–1.62) for thyroid cancer. The excesses were greatly attenuated when the police group was used as the referent. [The Working Group noted that the relatively large size, inclusion of women, and access to tumour information were study strengths. Among limitations, exposure information was limited to the job title available at the time of the worker compensation claim, which may introduce bias in either direction.]

CanCHEC, a census and cancer registrybased study from Canada (1991–2010), estimated risks of incident cancers in firefighters (Harris et al., 2018). The census used data collected in 1991 for about 20% of the households in Canada. Firefighter status was assessed on the basis of the longest-held job in the previous year, and the cohort was restricted to men aged 25-74 years at census. Average follow-up time was almost 18 years. Adjusted hazard ratios (for age group, region, and education level) for brain and thyroid cancers were 1.11 (95% CI, 0.61-2.01) and 1.35 (95% CI, 0.61-3.02), respectively. The adjusted hazard ratio for melanoma was elevated (1.67; 95% CI, 1.17-2.37) [The Working Group noted the relatively large population of firefighters and the long follow-up period, and adjustment for educational level as strengths. The main limitation was the lack of information on duration and intensity of firefighting.]

A case-control study reported age- and calendar year-adjusted ORs for various incident primary cancers of male and female firefighters from Florida, USA (Lee et al., 2020). Career firefighter certification records (1972 or after) were linked with state cancer registry data (1981–2014) to identify cases in firefighters. Controls were individuals with all other cancer types, excluding the cancer of interest. ORs for

melanoma of the skin were increased in both female and male firefighters, with estimates of 1.68 (95% CI, 0.97-2.90) and 1.56 (95% CI, 1.39–1.76), respectively. Elevated ORs were also observed for thyroid cancer in male and female firefighters, with estimates of 2.17 (95% CI, 1.78–2.66) and 2.42 (95% CI, 1.56–3.74), respectively. In contrast, brain cancer was elevated only among female firefighters (OR, 2.54; 95% CI, 1.19–5.42). For men, ORs were further stratified by tumour stage. Only the ORs for thyroid cancer differed between early-stage cancer (OR, 1.78; 95% CI, 1.38–2.31) and late-stage cancer (OR, 2.70; 95% CI, 1.94–3.76). Finally, the ORs for men were stratified by age < 50 years and ≥ 50 years at diagnosis. The ORs for both melanoma (1.87; 95% CI, 1.55–2.26) and thyroid cancer (2.55; 95% CI, 1.96–3.31) tended to be higher in the younger firefighters. A study by McClure et al. (2021) evaluated the impact of misclassification of firefighter status within this cohort by comparing two occupation ascertainment methods. The ORs calculated when firefighter status was obtained from the cancer registry were compared with those when the designation of firefighter was obtained from state firefighter certification. ORs for all skin cancers were 1.06 (95% CI, 0.87-1.29) based on 109 cases in firefighters identified from the cancer registry, and 1.54 (95% CI, 1.37–1.73) based on 316 cases in firefighters identified from certification records. [The Working Group noted small numbers for female firefighters and consequently imprecise results in the study by Lee et al. (2020). Further, McClure et al. (2021) found that a high proportion of firefighters was not identified by job title from the cancer registry. Therefore, ascertainment of firefighting exposure classification from cancer registries alone resulted in the potential for exposure misclassification.]

ORs for cancer mortality were examined among firefighters compared with non-firefighters in Indiana, USA, using death certificate records for the period 1985–2013 (Muegge et al., 2018). People aged \geq 18 years at death, with known race and ethnicity, were identified as either firefighters or non-firefighters (reference group) using job information recorded at the time of death. Each firefighter was matched on attained age, sex, race, ethnicity, and year of death to four randomly selected non-firefighter deaths. An increased OR for cancer of the brain and nervous system (1.98; 95% CI, 1.23-3.12) was observed. [The Working Group noted that the use of death certificates may result in misclassification of both job and cancer diagnosis. Furthermore, this source of information is less accurate for cancers with higher survival rates. Finally, the study did not provide a specific definition of brain cancer, which comprises a diverse group of cancers with different survival rates.]

Cancer risk by race was examined in a registry-based case-control study of 678 132 cases of cancer diagnosed among adult men in California, USA, during the period 1988–2007, and which included 3996 diagnoses of cancer among firefighters (Tsai et al., 2015). This study included only men from the California Cancer Registry for whom information on longest-held job was available. Cases of cancers not thought to be associated with firefighting, i.e. cancers of the pharynx, stomach, liver, and pancreas, were used as controls. Increased ORs were observed for melanoma (OR, 1.75; 95% CI, 1.44-2.13) and brain cancer (OR, 1.54; 95% CI, 1.19–2.00). Rates of these cancers were notably increased in the subgroup of non-White firefighters, although this was based on small numbers (OR for melanoma, 4.51; 95% CI, 1.85-10.97; and OR for brain cancer, 3.58; 95% CI, 1.65-7.74). The OR for thyroid cancer was also elevated (OR, 1.27; 95%) CI, 0.88–1.84). <u>Bates (2007)</u> conducted a similar study using the California Cancer Registry, 1988-2003, but these data were also included in the study by Tsai et al. (2015). [The Working Group noted a high proportion of cancer registrants missing occupational information overall in the registry, which may bias results unpredictably, if missingness is related to occupational or demographic factors.]

An incidence-based cancer registry study in Massachusetts, USA, reported site-specific cancer risks in White male firefighters identified in the state cancer registry (1987-2003) (Kang et al., 2008). Longest-held job, identified from the same registry, was classified as firefighter, police, or other occupations, and the methodology was similar to that in an earlier study (Sama et al., 1990) that considered cancer diagnoses in 1982-1986. Age- and smoking-adjusted SMBORs were calculated for firefighters on the basis of two reference groups: occupations other than firefighters, and police employees. In Kang et al. (2008), the SMBORs for cancer of the brain were increased when using police officers (SMBOR, 1.90; 95% CI, 1.10-3.26) and all other occupations (SMBOR, 1.36; 95% CI, 0.87-2.12) as referents. SMBORs for melanoma and thyroid cancer were not elevated for either reference group. In the earlier study (Sama et al., 1990), the age-adjusted SMBOR for melanoma (18 cases) was elevated when police were used as the referent (SMBOR, 2.92; 95% CI, 1.70-5.03), and to a lesser extent when other employed men were used as the referent (SMBOR, 1.38; 95% CI, 0.60–3.19). The ORs for brain and other nervous system cancers were based on only five cases. [The Working Group noted that the number of cases was small in both studies, and that about the half of the population had no occupational information, which may bias results unpredictably.]

A death certificate-based case-control study in 24 US states (1984–1993) reported MORs for Black and White male firefighters. All non-cancer deaths were used as controls (<u>Ma</u> <u>et al., 1998</u>). The MORs for melanoma, non-melanoma skin cancer, and thyroid cancer for White firefighters were 1.4 (95% CI, 1.0–1.9), 1.0 (95% CI, 0.5–1.9), and 1.3 (95% CI, NR), respectively. The MOR for brain and central nervous system cancer was highly elevated for Black firefighters (MOR, 6.9; 95% CI, 3.0–16.0), but not for White firefighters (MOR, 1.0; 95% CI, 0.8–1.4). [The Working Group noted limited numbers for most cancers, and typically inaccurate occupational information from death certificates, which can bias results to the null. Further, death certificate data is a poor means of identifying non-melanoma skin cancer, which has a low fatality rate.]

Proportionate mortality was investigated in White male US firefighters from 27 states compared with the age-adjusted deceased White male general population, in 1984-1990 (Burnett et al., 1994). Deceased firefighters (n = 5744)were identified by the coded occupation listed on the death certificate. The PMR for melanoma was elevated both overall (PMR, 1.63; 95% CI, 1.15-2.23) and for firefighters aged < 65 years (PMR, 1.67; 95% CI, 1.07-2.48). No increased PMRs were reported for cancers of the brain (PMR, 1.03; 95% CI, 0.73-1.41) and nervous system (PMR, 0.85; 95% CI, 0.52-1.34). [The Working Group noted that PMR analyses might overestimate the cancer risks in firefighters if their overall risk of death were below the risk in the comparison group.]

2.5 Cancers of the colon and rectum, oesophagus, stomach, and other sites

2.5.1 Studies reporting occupational characteristics of firefighters

Studies first described in Section 2.1.1 are described in the present section in less detail.

See <u>Table 2.9</u>.

The Working Group identified 24 occupational and population-based cohort studies that investigated the relation between occupational exposure as a firefighter and risk of cancer of the oralcavity,pharynx,breast,oesophagus,stomach, pancreas, liver, and colon and rectum (Feuer & Rosenman, 1986; Vena & Fiedler, 1987; Demers

Table 2.9 Cohort studies reporting occupational characteristics of firefighters and cancers of the colon and rectum, oesophagus, stomach, and other sites

location des	scription, exposure sessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments
(2015)emeRepublic of Koreafor 3Enrolment,with1980–2007/follow-(398up, 1992–2007expCohortdecoExpmetandof eas filinenomnom	hergency responders $\geq 1 \text{ mo in 1980-2007}$ th (29 453) and without 289) firefighting perience and not ceased in 1991 posure assessment ethod: ever employed d categorical duration employment (years) first- or second- e firefighter and n-firefighters from aployment records	Stomach, mortality Stomach, mortality Colon and rectum, mortality Colon and rectum, mortality	Duration of firef 1-yr lag (SMR): 1 mo to < 10 yr 10 to < 20 yr ≥ 20 yr Overall Duration of firef 1-yr lag (RR): < 10 yr (including non- firefighters) 10 to < 20 yr ≥ 20 yr Duration of firef 1-yr lag (SMR): 1 mo to < 10 yr 10 to < 20 yr ≥ 20 yr Overall Duration of firef 1-yr lag (RR): < 10 yr (including non- firefighters) 10 to < 20 yr ≥ 20 yr Overall Duration of firef 1-yr lag (RR): < 10 yr (including non- firefighters) 10 to < 20 yr	11 9 14 34 fighting emp 12 9 14 fighting emp 2 5 5 12	0.89 (0.44–1.59) 0.50 (0.23–0.95) 0.60 (0.33–1.00) 0.63 (0.43–0.88) bloyment, 1 0.63 (0.27–1.50) 1.03 (0.44–2.44) bloyment, 0.46 (0.05–1.67) 0.81 (0.26–1.90) 0.63 (0.20–1.48) 0.65 (0.34–1.14)	Age, calendar period	<i>Exposure assessment</i> <i>critique</i> : Satisfactory quality. Heterogeneity of direct firefighter exposure within job title. May include both municipal and rural firefighters. <i>Strengths</i> : employment duration and internal comparison limits healthy-worker bias; only professional [career] firefighters were included in the cohort. <i>Limitations</i> : no information on personal characteristics or confounders; follow-up time was reasonably short; cohort members were fairly young; no direct measure of exposure.
			≥ 20 yr	5	1.29 (0.27-6.08)		

Reference, location enrolment/follow- up period, study design	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments
<u>Ahn & Jeong</u> (2015)		Liver and bile ducts, mortality	Duration of fire 1-yr lag (SMR):	fighting emp	bloyment,	Age, calendar period	
(cont.)			1 mo to < 10 yr	14	0.69 (0.38-1.16)		
			10 to < 20 yr	13	0.43 (0.23-0.73)		
			≥ 20 yr	23	0.58 (0.37-0.87)		
			Overall	50	0.55 (0.41-0.73)		
		Liver and bile ducts, mortality	Duration of fire 1-yr lag (RR):	fighting emp	ployment,		
			< 10 yr (including non- firefighters)	14	1		
			10 to < 20 yr	13	0.78 (0.37-1.66)		
			≥ 20 yr	23	1.82 (0.85-3.90)		

Reference, location enrolment/follow- up period, study design	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments
Ahn et al. (2012) Republic of Korea Enrolment, 1980–2007/follow- up, 1996–2007 Cohort	33 416 men employed as emergency responders for ≥ 1 mo in 1980–2007 with (29 438) and without (3978) firefighting experience and not deceased in 1995 Exposure assessment method: ever employed and categorical duration of employment (years) as first- or second- line firefighter and non-firefighters from employment records	Oesophagus, incidence	Duration of firefighting employment, 1-yr lag (SIR):			Age, calendar period	<i>Exposure assessment</i> <i>critique</i> : Satisfactory
			1 mo to < 10 yr	0	0 (NR)		quality. Heterogeneity of direct firefighter exposure within job title May include rural and municipal firefighters. <i>Strengths</i> : employment duration and internal comparison limits healthy-worker bias; onl
			≥ 10 yr	6	0.94 (0.34-2.05)		
		Oesophagus, incidence	Overall SRR:	6	0.75 (0.28–1.64)		
			Non- firefighters	0	0 (NR)		
			Ever employed as a firefighter	6	NR		
		Stomach, incidence	Duration of firefighting employment, 1-yr lag (SIR):				professional [career] firefighters were included
			1 mo to < 10 yr	29	0.98 (0.66–1.41)		in the cohort. <i>Limitations</i> : no information on personal characteristics or confounders (except the firefighter cohort had a lower BMI and smoked less than the comparison population for the SIR
			$\geq 10 \text{ yr}$	77	0.92 (0.72–1.14)		
		Stomach, incidence	Overall SRR:	106	0.93 (0.76–1.13)		
			Non- firefighters	8	1		
			Ever employed as a firefighter	106	1.09 (0.53–2.25)		
		Colon and rectum, incidence	Duration of firefighting employment, 1-yr lag (SIR):				analysis); follow-up time was reasonably short;
			1 mo to < 10 yr	20	1.35 (0.82-2.08)		cohort members were fairly young; no direct measure of exposure.
			≥ 10 yr	52	1.25 (0.95-1.63)		
			Overall	72	1.27 (1.01–1.59)		
		Colon and rectum, incidence	SRR:				
			Non- firefighters	10	1		
			Ever employed as a firefighter	72	0.55 (0.26-1.19)		

Reference, location enrolment/follow- up period, study design	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments
<u>Ahn et al. (2012)</u> (cont.)		Liver and bile ducts, incidence	Duration of fires (SIR):	fighting emp	ployment, 1-yr lag	Age, calendar period	
			1 mo to < 10 yr	21	0.97 (0.60-1.49)	•	
			≥ 10 yr	53	0.80 (0.60-1.05)		
			Overall	74	0.84 (0.66-1.06)		
		Liver and bile	SRR:				
		ducts, incidence	Non- firefighters	1	1		
			Ever employed as a firefighter	74	5.10 (0.71-36.85)		
		Gallbladder and extrahepatic bile	Duration of fire: (SIR):	fighting emj	ployment, 1-yr lag		
		ducts (ICD-	1 mo to < 10 yr	2	1.04 (0.12-3.74)		
		10, C23–C24),	≥ 10 yr	5	0.76 (0.25-1.78)		
		incidence	Overall	7	0.82 (0.33-1.70)		
		Gallbladder and extrahepatic bile ducts (ICD-	SRR:				
			Non- firefighters	1	1		
		10, C23–C24), incidence	Ever employed as a firefighter	7	0.48 (0.06-3.94)		
		Pancreas, incidence	Duration of fire: (SIR):	fighting emj	ployment, 1-yr lag		
			1 mo to < 10 yr	4	1.80 (0.49-4.62)		
			≥ 10 yr	5	0.93 (0.25-2.37)		
			Overall	9	0.95 (0.44-1.81)		
		Pancreas,	SRR:				
		incidence	Non- firefighters	1	1		
			Ever employed as a firefighter	9	0.58 (0.07-4.58)		

Reference, location enrolment/follow- up period, study design	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments
<u>Ahn et al. (2012)</u> (cont.)		Bone and articular cartilage	Duration of fire (SIR):	fighting emp	ployment, 1-yr lag	Age, calendar period	
		(ICD-10, C40–	1 mo to < 10 yr	1	1.33 (0.02–7.40)		
		C41), incidence	≥ 10 yr	3	2.37 (0.48-6.92)		
			Overall	4	1.98 (0.53-5.07)		
		Bone and	SRR:		. ,		
		articular cartilage (ICD-10, C40–	Non- firefighters	2	1		
		C41), incidence	Ever employed as a firefighter	4	0.24 (0.04–1.37)		
<u>Marjerrison et al.</u>	3881 male professional	Oral cavity,	SIR:			Age,	Exposure assessment
<u>(2022b)</u>	[career] firefighters (most	incidence	Firefighters	< 5	0.73 (0.20-1.86)	calendar year	critique: Satisfactory
Norway	were full-time) employed	Oral cavity,	SMR:				quality. Included
Enrolment,in positions entailing1950-2019/follow-active firefighting at anyup, 1960-2018of 15 fire departmentsCohortbetween 1950 and 2019	mortality	Firefighters	0	0 (0.00-3.04)		firefighters with current or previous positions	
	Pharynx,	SIR:				entailing active firefighting duties but no	
	incidence	Firefighters	11	1.61 (0.80-2.88)			
	Exposure assessment	Pharynx,	SMR:				assessment of length of
	method: employment	mortality	Firefighters	< 5	1.05 (0.29-2.69)		time in active firefighting
	history from personnel records	Oesophagus,	SIR:				positions. May include
	records	incidence	Firefighters	13	1.55 (0.83-2.66)		municipal and rural firefighters.
		Oesophagus,	SMR:				Strengths: long length
		mortality	Firefighters	13	1.82 (0.97-3.11)		of follow-up (mean,
		Oesophagus,	Period of follow-up (SIR):			28 yr); near complete	
		incidence	1984 or before	< 5	2.15 (0.44-6.29)		ascertainment of both
			1985-1994	< 5	1.60 (0.19-5.78)		cancer incidence and mortality; analyses by
			1995 or after	8	1.40 (0.60-2.76)		duration and timing of
		Oesophagus,	Period of follow	-up (SMR):			employment.
		mortality	1984 or before	< 5	2.35 (0.48-6.86)		Limitations: probable
			1985–1994	< 5	1.74 (0.21–6.29)		healthy-worker effect;
			1995 or after	8	1.69 (0.73–3.33)		no data on potential confounders apart from age, sex, and calendar time.

Reference, location enrolment/follow- up period, study design	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments
Marjerrison et al.		Oesophagus,	Age at diagnosi	s (SIR):		Age,	
<u>(2022b)</u>		incidence	≤ 49 yr	0	0 (0.00-6.22)	calendar year	
(cont.)			50-69 yr	7	1.54 (0.62–3.17)		
			≥ 70 yr	6	1.80 (0.66-3.91)		
		Oesophagus,	Age at diagnosi	s (SMR):			
		mortality	≤ 49 yr	0	0 (0.00–9.96)		
			50-69 yr	7	1.88 (0.76-3.88)		
			≥ 70 yr	6	1.91 (0.70-4.16)		
		Stomach,	SIR:				
		incidence	Firefighters	38	1.35 (0.95–1.85)		
		Stomach,	SMR:				
		mortality	Firefighters	28	1.28 (0.85-1.84)		
		Stomach,	Period of follow				
		incidence	1984 or before	15	1.39 (0.78-2.29)		
			1985-1994	10	1.64 (0.79-3.02)		
			1995 or after	13	1.15 (0.61–1.96)		
		Stomach,	Period of follow	-up (SMR):			
		mortality	1984 or before	12	1.35 (0.70-2.36)		
			1985-1994	9	1.88 (0.86-3.56)		
			1995 or after	7	0.85 (0.34–1.75)		
		Stomach,	Age at diagnosi	s (SIR):			
		incidence	$\leq 49 \text{ yr}$	< 5	1.34 (0.28-3.91)		
			50-69 yr	21	1.56 (0.97-2.39)		
			≥ 70 yr	14	1.11 (0.61–1.87)		
		Stomach,	Age at diagnosi		. , ,		
		mortality	≤ 49 yr	< 5	1.93 (0.40-5.63)		
			50-69 yr	12	1.20 (0.62–2.10)		
			≥ 70 yr	13	1.25 (0.67–2.14)		
		Colon, incidence	SIR:		. (
		,	Firefighters	74	1.24 (0.98-1.56)		

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Reference, location enrolment/follow- up period, study design	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments
Marjerrison et al.		Colon, mortality	SMR:			Age,	
<u>(2022b)</u>			Firefighters	34	1.26 (0.87-1.76)	calendar year	
(cont.)		Colon, incidence	Period of follow	v-up (SIR):			
			1984 or before	16	2.02 (1.15-3.28)		
			1985-1994	14	1.41 (0.77-2.37)		
			1995 or after	44	1.05 (0.77-1.42)		
		Colon, mortality	Period of follow	v-up (SMR):			
			1984 or before	10	2.33 (1.12-4.29)		
			1985-1994	9	1.79 (0.82-3.39)		
			1995 or after	15	0.85 (0.48-1.40)		
		Colon, incidence	Age at diagnosi	s (SIR):			
			≤ 49 yr	< 5	0.80 (0.16-2.33)		
			50-69 yr	29	1.16 (0.78-1.67)		
			≥ 70 yr	42	1.36 (0.98-1.84)		
		Colon, mortality A	Age at diagnosi	s (SMR):			
			≤ 49 yr	< 5	0.75 (0.02-4.19)		
			50–69 yr	16	1.63 (0.93-2.65)		
			≥ 70 yr	17	1.07 (0.62-1.72)		
		Rectum,	SIR:				
		incidence	Firefighters	37	0.96 (0.68-1.33)		
		Rectum,	SMR:				
		mortality	Firefighters	18	1.16 (0.69–1.84)		
		Rectum,	Period of follow	-up (SIR):			
		incidence	1984 or before	< 5	0.63 (0.17-1.62)		
			1985-1994	6	0.86 (0.31-1.87)		
			1995 or after	27	1.07 (0.71–1.56)		
		Rectum,	Period of follow	-up (SMR):			
		mortality	1984 or before	*	0.89 (0.18-2.60)		
			1985-1994	< 5	0.57 (0.07-2.05)		
			1995 or after	13	1.51 (0.80-2.58)		

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inued) Population size, description, exposure assessment method Cancer type (histopathology), incidence or mortality Exposure category or level Rectum, incidence Age at diagn ≤ 49 yr 50-69 yr

(histopathology), incidence or mortality	category or level	cases or deaths	(95% CI)	controlled
Rectum,	Age at diagnosis	(SIR):		Age,
incidence	\leq 49 yr	< 5	1.22 (0.25-3.56)	calendar year
	50-69 yr	16	0.83 (0.47-1.35)	
	≥ 70 yr	18	1.07 (0.64–1.70)	
Rectum,	Age at diagnosis	(SMR):		
mortality	≤ 49 yr	0	0 (0.00-3.97)	
	50-69 yr	< 5	0.62 (0.17-1.58)	
	≥ 70 yr	14	1.70 (0.93–2.85)	
Liver (HCC),	SIR:			
incidence	Firefighters	8	1.43 (0.62–2.81)	
Liver (HCC),	SMR:			
mortality	Firefighters	7	1.38 (0.56-2.85)	
Bile duct and	SIR:		. ,	
gallbladder, incidence	Firefighters	< 5	1.13 (0.31–2.89)	
Bile duct and	SMR:			
gallbladder, mortality	Firefighters	< 5	2.01 (0.55-5.15)	
Liver, gall	SIR:			
bladder, biliary ducts, incidence	Firefighters	12	1.31 (0.68–2.29)	
Liver, gall	SMR:			
bladder, biliary ducts, mortality	Firefighters	11	1.56 (0.78–2.79)	
Liver, gall	Period of follow-	up (SIR):		
bladder, biliary	1984 or before	5	3.62 (1.17-8.44)	
ducts, incidence	1985–1994	< 5	1.46 (0.18–5.29)	
	1995 or after	5	0.78 (0.25-1.82)	
Liver, gall	Period of follow-	up (SMR):		
bladder, biliary	1984 or before	< 5	3.03 (0.83-7.75)	
ducts, mortality	1985–1994	< 5	1.91 (0.23-6.89)	
	1995 or after	5	1.07 (0.35-2.50)	

Exposed

Risk estimate

Covariates

Comments

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Table 2.9 (continued)

Reference,

enrolment/follow-

up period, study

Marjerrison et al.

location

design

<u>(2022b)</u>

(cont.)

Reference, location enrolment/follow- up period, study design	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments
Marjerrison et al.		Liver, gall	Age at diagnos	is (SIR):		Age,	
<u>(2022b)</u>		bladder, biliary	\leq 49 yr	< 5	1.45 (0.04-8.07)	calendar year	
(cont.)		ducts, incidence	50-69 yr	< 5	0.91 (0.25-2.33)		
			≥ 70 yr	7	1.72 (0.69-3.55)		
		Liver, gall	Age at diagnos	is (SMR):			
		bladder, biliary	≤ 49 yr	< 5	1.95 (0.05–10.9)		
		ducts, mortality	50-69 yr	< 5	1.26 (0.34-3.24)		
			≥ 70 yr	6	1.78 (0.65-3.87)		
		Pancreas,	SIR:				
		incidence	Firefighters	24	1.22 (0.78–1.81)		
		Pancreas,	SMR:				
		mortality	Firefighters	20	1.09 (0.67–1.68)		
<u>Bigert et al. (2020)</u> Sweden	8136 male firefighters identified from national	Pharynx, incidence	SIR:	10	1 0 4 (0 55 1 50)	Age, calendar period	<i>Exposure assessment</i> <i>critique</i> : Satisfactory
Enrolment	censuses in 1960, 1970,	Oesophagus, incidence	Firefighters	13	1.04 (0.55–1.78)	period	quality. Unclear if individuals were active firefighters for whole
1960–1990/follow-	1980, and 1990		SIR:	12			
up, 1961–2009	Exposure assessment		Firefighters	13	0.71 (0.38–1.21)		
Cohort	method: questionnaire;	Stomach, incidence	SIR:	(0	1.00 (0.02, 1.20)		employment. May include
	ever employed and	Stomach,	Firefighters Duration of em	60	1.08 (0.83–1.39)		full-time, part-time,
	categorical duration of employment (years) as	incidence	1–9 yr	4	1.43 (0.39–3.66)		municipal, and rural firefighters.
	firefighter from census	mendence	1–9 yr 10–19 yr	4 22	1.23 (0.77–1.86)		<i>Strengths</i> : near complete
	surveys		20–29 yr	18	1.00 (0.59–1.57)		ascertainment of cancer
			$\geq 30 \text{ yr}$	16	0.97 (0.55 - 1.58)		incidence; long length
			Trend-test <i>P</i> va		0.97 (0.35-1.30)		of follow-up (mean, 28 yr); analyses stratified
		Stomach,	Time period (S				by calendar period of
		incidence	1961–1975	16	1.85 (1.06-3.00)		employment.
			1976–1990	22	1.16 (0.73–1.76)		. /
			1991-2009	22	0.79 (0.49–1.19)		
		Colon, incidence	SIR:		(
		,	Firefighters	101	1.01 (0.82-1.23)		

Table 2.9 (cont	inued)						
Reference, location enrolment/follow- up period, study design	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments
		Rectum, incidence	SIR: Firefighters	63	0.89 (0.69–1.14)	Age, calendar period	<i>Limitations</i> : no data on job duties; employment type,
		Liver and bile ducts, incidence	SIR: Firefighters	15	0.89 (0.50–1.47)	I	or potential confounders (aside from age, sex, and calendar year); probable
		Pancreas, incidence Soft tissue	SIR: Firefighters SIR:	43	1.17 (0.85–1.58)		healthy-worker hire bias; potential non-differential misclassification of
		sarcoma, incidence	Firefighters	15	1.46 (0.82–2.41)		employment duration.
Kullberg et al. (2018) Stockholm, Sweden Enrolment, 1931–1983/follow- up, 1958–2012	1080 men who worked ≥ 1 yr as a firefighter in Stockholm between 1931 and 1983 Exposure assessment method: ever employed	Lip, incidence	Follow-up perio Full: 1958–2012 Former: 1958–1986	2	1.45 (0.18–5.26) 1.42 (0.04–7.91)	Birth year, calendar period	<i>Exposure assessment</i> <i>critique</i> : Satisfactory quality. Unclear if individuals were active firefighters for whole employment.
Cohort	and categorical duration of employment (years)		Extended: 1987–2012	1	1.49 (0.38–8.32)		<i>Strengths</i> : long follow-up period; near complete
	as an urban [municipal] firefighter from annual enrolment records	Oesophagus, incidence	Follow-up perio Full: 1958–2012	5 5	0.99 (0.32–2.30)		ascertainment of cancer incidence; analyses of duration and era of
			Former: 1958–1986	1	0.43 (0.01–2.38)		employment. Municipal firefighters.
			Extended: 1987–2012	4	1.46 (0.40-3.75)		<i>Limitations</i> : no data on potential confounders
		Stomach, incidence	Follow-up perio Full: 1958–2012	od (SIR): 27	1.89 (1.25–2.75)		(aside from age, sex, and calendar year); lack of exposure assessment
			Former: 1958–1986	20	2.21 (1.35-3.41)		based on job tasks or fire responses.
			Extended: 1987–2012	7	1.35 (0.54–2.78)		

Reference, location enrolment/follow- up period, study design	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments
Kullberg et al.		Stomach,	Age at risk (SI	R):		Birth year,	
(2018)		incidence	< 50 yr	2	3.18 (0.39-11.49)	calendar	
(cont.)			50-64 yr	8	2.38 (1.03-4.70)	period	
			≥ 65 yr	17	1.65 (0.96-2.65)		
			Trend-test P va	alue, 0.07			
		Stomach,	Duration of er	nployment (S	IR):		
		incidence	1–9 yr	0	0 (NR)		
			10–19 yr	2	2.02 (0.50-8.06)		
			20–29 yr	7	2.03 (0.97-4.26)		
			≥ 30 yr	18	2.05 (1.29-3.26)		
			Trend-test P va	alue, 0.19			
		Stomach,	Period of first	employment	(SIR):		
		incidence	1902-1939	15	1.81 (1.09-3.01)		
			1940-1959	8	1.77 (0.88-3.55)		
			1960-1983	4	2.72 (1.02-7.26)		
			Trend-test P va	alue, 0.69			
		Colon, incidence	Follow-up per	iod (SIR):			
			Full: 1958–2012	20	0.86 (0.53–1.34)		
			Former: 1958–1986	8	0.92 (0.40–1.81)		
			Extended: 1987–2012	12	0.83 (0.43-1.46)		
		Rectum,	Follow-up per	iod (SIR):			
		incidence	Full: 1958–2012	18	1.25 (0.74–1.98)		
			Former: 1958–1986	10	1.74 (0.83–3.19)		
			Extended: 1987–2012	8	0.93 (0.40–1.82)		

Table 2.0 /a **.**:..

Reference, location enrolment/follow- up period, study design	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments
Kullberg et al.		Liver and bile	Follow-up peri	od (SIR):		Birth year,	
(2018) (cont.)		ducts, incidence	Full: 1958–2012	7	0.79 (0.32–1.63)	calendar period	
			Former: 1958–1986	4	0.90 (0.25-2.31)		
			Extended: 1987–2012	3	0.68 (0.14-2.00)		
		Pancreas,	Follow-up peri	od (SIR):			
		incidence	Full: 1958–2012	10	1.06 (0.51–1.94)		
			Former: 1958–1986	6	1.23 (0.45–2.68)		
			Extended: 1987–2012	4	0.87 (0.24-2.23)		

Reference, location enrolment/follow- up period, study design	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments
Tornling et al.	1116 for mortality/1091	Stomach,	SMR:			Age, calendar	Exposure assessment
<u>(1994)</u>	for incidence; male	mortality	Firefighters	12	1.21 (0.62–2.11)	period	critique: Satisfactory/
Stockholm, Sweden Enrolment,	firefighters employed for ≥ 1 yr in the City of	Stomach,	Age (SMR):				good quality. Enhanced exposure assessment (but based on 10% sample of reports) to differentiate exposure based on numbe of fires fought accounting
1931–1983/follow-	Stockholm in 1931–1983,	mortality	< 50 yr	1	1.90 (0.05–10.57)		
up, 1951–1986	identified from annual		50-64 yr	4	1.61 (0.44–4.12)		
(mortality), 1958–	enrolment records		≥ 65 yr	7	1.01 (0.41–2.08)		
1986 (incidence)	Exposure assessment	Stomach,	Duration of er	nployment (S			
Cohort	method: ever firefighter	mortality	< 20 yr	1	1.08 (0.03-6.04)		for job position, station,
	and duration (years) of firefighting employment		20-30 yr	5	1.05 (0.34–2.45)		and year of exposure. Municipal firefighters.
	from annual enrolment		> 30 yr	6	1.41 (0.52–3.07)		Strengths: long follow-up
	records; number of fires	Stomach,	Latency (SMR				period; near complete
	fought ascertained from	mortality	< 30 yr	2	1.92 (0.23-6.92)		ascertainment of cancer incidence and mortality; assessed exposure to fire responses for some outcomes.
	exposure index developed		30-40 yr	3	1.40 (0.29-4.09)		
	from fire reports		> 40 yr	7	1.04 (0.42–2.13)		
		Stomach,	No. of fires (SI				
		mortality	< 800	1	0.51 (0.01–2.87)		<i>Limitations</i> : no data on
			800-1000	2	0.59 (0.07–2.12)		potential confounders
		0. 1	> 1000	9	1.96 (0.90-3.72)		(aside from age, sex, and
		Stomach, incidence	SIR:	10			calendar year).
			Firefighters	18	1.92 (1.14–3.04)		
		Stomach, incidence	Age (SIR):	1	2 0 4 (0 02 11 25)		
		mendence	< 50 yr	1	2.04 (0.03–11.35)		
			50–64 yr	6	2.58 (0.94–5.61)		
		Stores ab	$\geq 65 \text{ yr}$	11 malazza ant (S	1.68 (0.84–3.00)		
		Stomach, incidence	Duration of er				
		menuence	< 20 yr	1	1.02 (0.01–5.68)		
			20-30 yr > 30 yr	5 12	1.18 (0.38–2.75) 2.89 (1.49–5.05)		

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$\begin{array}{cccc} \begin{tabular}{ c c c c } \hline Tornling et al. \\ (1994) & incidence & & < 30 \ yr & 5 \\ & & 30-40 \ yr & 12 \\ & & > 40 \ yr & 1 \\ \hline & & > 40 \ yr & 1 \\ \hline & & \\ $	4.81 (1.55–11.22) 6.06 (3.13–10.59) 0.16 (0–0.88) 1.04 (0.12–3.76) 1.37 (0.37–3.52)	Age, calendar period	
(cont.) $30-40 \text{ yr} \qquad 12$ $> 40 \text{ yr} \qquad 1$ $Stomach, \qquad No. of fires (SIR):$ incidence $< 800 \qquad 2$ $800-1000 \qquad 4$ $> 1000 \qquad 14$ $Colon, mortality \qquad SMR:$ $Firefighters \qquad 6$ $Colon, incidence \qquad SIR:$ $Firefighters \qquad 8$ $Rectum, \qquad SMR:$ $mortality \qquad Firefighters \qquad 8$ $Rectum, \qquad SMR:$ $mortality \qquad Firefighters \qquad 8$ $Rectum, \qquad SIR:$ $mortality \qquad Firefighters \qquad 8$ $Rectum, \qquad SIR:$ $mortality \qquad Firefighters \qquad 8$ $Rectum, \qquad SIR:$ $Incidence \qquad Firefighters \qquad 8$ $Rectum, \qquad SIR:$ $Incidence \qquad Firefighters \qquad 10$ $Liver (HCC), \qquad SMR:$ $mortality \qquad Firefighters \qquad 4$	6.06 (3.13–10.59) 0.16 (0–0.88) 1.04 (0.12–3.76)	period	
$\begin{array}{cccc} & & & & & & & & & & & & & & & & & $	0.16 (0-0.88)		
Stomach, incidenceNo. of fires (SIR): < 800 2 $800-1000$ 4 > 1000 14Colon, mortalitySMR: Firefighters6Colon, incidenceSIR: Firefighters6Colon, incidenceSIR: Firefighters8Rectum, mortalitySMR: Firefighters8Rectum, incidenceSIR: Firefighters10Liver (HCC), mortalitySMR: Firefighters10Liver (HCC), mortalitySMR: Firefighters4	1.04 (0.12–3.76)		
$\begin{array}{llllllllllllllllllllllllllllllllllll$			
$\begin{array}{cccc} & & & & & & & & & & & & & & & & & $			
 > 1000 14 Colon, mortality SMR: Firefighters Colon, incidence SIR: Firefighters 8 Rectum, SMR: mortality Firefighters 8 Rectum, SIR: incidence Firefighters 10 Liver (HCC), SMR: mortality Firefighters 4 	$1\ 37\ (0\ 37-3\ 52)$		
Colon, mortalitySMR: Firefighters6Colon, incidenceSIR: Firefighters6Colon, incidenceSIR: Firefighters8Rectum,SMR: mortality5Rectum,SIR: Firefighters8Rectum,SIR: Incidence10Liver (HCC),SMR: Firefighters4	1.57(0.57-5.52)		
Firefighters 6 Colon, incidence SIR: Firefighters 8 Rectum, SMR: mortality Firefighters 8 Rectum, SIR: incidence Firefighters 10 Liver (HCC), SMR: mortality Firefighters 4	2.64 (1.36-4.61)		
Colon, incidenceSIR:Firefighters8Rectum,SMR:mortalityFirefighters8Rectum,SIR:incidenceFirefighters10Liver (HCC),SMR:mortalityFirefighters4			
Firefighters8Rectum,SMR:mortalityFirefighters8Rectum,SIR:incidenceFirefighters10Liver (HCC),SMR:mortalityFirefighters4	0.85 (0.31-1.85)		
Rectum,SMR:mortalityFirefighters8Rectum,SIR:10Liver (HCC),SMR:10Liver (HCC),Firefighters4			
mortalityFirefighters8Rectum,SIR:incidenceFirefighters10Liver (HCC),SMR:mortalityFirefighters4	0.90 (0.39-1.77)		
Rectum, SIR: incidence Firefighters 10 Liver (HCC), SMR: mortality Firefighters 4			
Rectum,SIR:incidenceFirefighters10Liver (HCC),SMR:mortalityFirefighters4	2.07 (0.89-4.08)		
Liver (HCC), SMR: mortality Firefighters 4			
Liver (HCC), SMR: mortality Firefighters 4	1.70 (0.81-3.12)		
mortality Firefighters 4			
	1.49 (0.41-3.81)		
	(0.11 0.01)		
incidence Firefighters 4	0.85 (0.23-2.18)		
Pancreas, SMR:	0.00 (0.20 2.10)		
mortality Firefighters 5	0.84 (0.27-1.96)		
Pancreas, SIR:	0.01(0.2/ 1.90)		
incidence Firefighters 6			

Reference, location enrolment/follow- up period, study design	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments
<u>Petersen et al.</u> (2018a)	9061 male firefighters (full-time, part-time,	Lip, incidence	Reference group Firefighters	(SIR): 4	1.04 (0.39-2.78)	Age, calendar period	<i>Exposure assessment critique</i> : Satisfactory
Denmark Enrolment,	and volunteer) identified from employer, trade		vs general population	-	101 (0.05 200)	*	quality. Includes part-time and full-time firefighters.
1964–2004/follow- up, 1968–2014 Cohort	union, and Danish Civil Registration System records, born 2 April 1928		Firefighters vs sample of	4	1.13 (0.42–3.01)		Excluded those who did not actually fight fires. May include municipal
Conort	or later, employed before age 60 yr and 31 December		employees Firefighters vs military	4	1.60 (0.60-4.28)		and rural firefighters. Strengths: long period of follow-up; near-complete ascertainment of cancer incidence; use of three reference groups to evaluate healthy-worker bias; analyses by proxies of exposure including job task. Limitations: little information on potential confounders.
	2004, no cancer diagnosis before employment as a	Mouth (ICD-10,	Reference group	(SIR):			
	firefighter, and a job title/ function indicating actual firefighting exposure	C03-C06, C46.2), incidence	Firefighters vs general population	7	0.60 (0.28–1.25)		
	Exposure assessment method: ever employed and categorical duration		Firefighters vs sample of employees	7	0.57 (0.27-1.19)		
	of employment (years), as well as employment		Firefighters vs military	7	0.61 (0.29–1.27)		
	type, job title/function, and work history,	Pharynx,	Reference group	(SIR):			
	ascertained from civil registration, pension,	incidence	Firefighters vs general population	20	0.91 (0.59–1.41)		
	employer personnel, and trade union membership records		Firefighters vs sample of employees	20	0.94 (0.60–1.45)		
			Firefighters vs military	20	0.87 (0.56–1.35)		

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Reference, ocation enrolment/follow- 1p period, study lesign	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments
Petersen et al.		Oesophagus,	Reference group	o (SIR):		Age, calendar	
2018a) (cont.)		incidence	Firefighters vs general population	21	0.99 (0.65–1.53)	period	
			Firefighters vs sample of employees	21	1.05 (0.68–1.61)		
			Firefighters vs military	21	1.18 (0.77–1.81)		
		Stomach,	Reference group	o (SIR):			
		incidence	Firefighters vs general population	27	1.09 (0.75–1.59)		
			Firefighters vs sample of employees	27	1.12 (0.77–1.63)		
			Firefighters vs military	27	1.26 (0.87–1.84)		
		Colon, incidence	Reference group	o (SIR):			
			Firefighters vs general population	57	0.73 (0.57–0.95)		
			Firefighters vs sample of employees	57	0.77 (0.59–0.99)		
			Firefighters vs military	57	0.70 (0.54-0.90)		
		Colon, incidence	Employment ty				
			Full-time	39	0.79 (0.58-1.08)		

Reference, ocation enrolment/follow- 1p period, study lesign	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments
etersen et al.		Colon, incidence	Era of first emp	loyment (SII	R):	Age, calendar	
<u>2018a)</u>			Pre-1970	31	0.78 (0.55-1.11)	period	
cont.)			1970-1994	24	0.73 (0.49-1.09)		
			1995 or after	2	0.40 (0.10-1.59)		
	Colon, incidence	Job function (SI	IR):				
			Regular	53	0.73 (0.56-0.96)		
			Specialized	4	0.78 (0.29-2.08)		
		Colon, incidence	Age at first emp	oloyment (SI	R):		
			< 25 yr	33	0.85 (0.60-1.19)		
			25–34 yr	13	0.59 (0.34-1.02)		
			≥ 35 yr	11	0.65 (0.36-1.18)		
	Colon, incidence	Duration of em	ployment (S				
			< 1 yr	16	0.70 (0.43-1.14)		
			$\geq 1 \text{ yr}$	41	0.75 (0.55-1.02)		
			≥ 10 yr	39	0.82 (0.60-1.12)		
			≥ 20 yr	31	0.84 (0.59–1.20)		
		Rectum,	Reference group	p (SIR):			
		incidence	Firefighters vs general population	64	1.22 (0.95–1.55)		
			Firefighters vs sample of employees	64	1.24 (0.97–1.58)		
			Firefighters vs military	64	1.20 (0.94–1.53)		
		Rectum, incidence	Employment ty	-	11((0.04, 1.60)		
		incluence	Full-time	38	1.16 (0.84–1.60)		
			Part-time or volunteer	26	1.31 (0.89–1.92)		

Table 2.9 (cont	Table 2.9 (continued)							
Reference,	Population size,	Cancer type						
location	description, exposure	(histopathology),						
enrolment/follow-	assessment method	incidence or						

up period, study design	mort			deaths		
Petersen et al.	Rectu	um, l	Era of first emplo	oyment (SIR):	Age, calendar
<u>(2018a)</u>	incide	ence]	Pre-1970	37	1.47 (1.06-2.02)	period
(cont.)			1970–1994	24	1.01 (0.68-1.51)	
			1995 or after	3	0.80 (0.26-2.49)	
	Rectu	um, J	ob function (SII	R):		
	incide	ence]	Regular	58	1.18 (0.91–1.53)	
		5	Specialized	6	1.72 (0.77-3.84)	
	Rectu	um, "	Age at first empl	oyment (SIR	.):	
	incide	ence .	< 25 yr	29	1.13 (0.79–1.63)	
		2	25–34 yr	19	1.25 (0.80-1.96)	
		2	≥ 35 yr	16	1.36 (0.83-2.22)	
	Rectu	um, l	Duration of emp	loyment (SI	R):	
	incide	ence .	< 1 yr	16	1.08 (0.66-1.77)	
		2	≥ 1 yr	48	1.27 (0.96-1.68)	
			≥ 10 yr	38	1.16 (0.85–1.60)	
			≥ 20 yr	33	1.32 (0.94–1.85)	
	Liver	· (HCC),	Reference group	(SIR):		
	incid	1	Firefighters vs general population	14	0.97 (0.58–1.64)	
]	Firefighters vs sample of employees	14	0.98 (0.58–1.65)	
			Firefighters vs military	14	1.17 (0.69–1.98)	

Exposure

category or level Exposed

cases or

deaths

Risk estimate

(95% CI)

Covariates

controlled

Comments

Reference, location enrolment/follow- up period, study design	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments
Petersen et al.		Bile duct/	Reference group	o (SIR):		Age, calendar	
(<u>2018a)</u> (cont.)		gallbladder, incidence	Firefighters vs general population	5	0.99 (0.41–2.37)	period	
			Firefighters vs sample of employees	5	1.04 (0.43–2.50)		
			Firefighters vs military	5	1.02 (0.42–2.44)		
		Pancreas,	Reference group	o (SIR):			
		incidence	Firefighters vs general population	34	1.20 (0.86–1.68)		
			Firefighters vs sample of employees	34	1.27 (0.91–1.78)		
			Firefighters vs military	34	1.28 (0.92–1.80)		
		Pancreas,	Employment ty	pe (SIR):			
		incidence	Full-time	27	1.54 (1.05-2.25)		
			Part-time or volunteer	7	0.65 (0.31–1.37)		
		Pancreas,	Era of first emp	loyment (SII	R):		
		incidence	Pre-1970	22	1.63 (1.08-2.48)		
			1970-1994	10	0.78 (0.42-1.45)		
			1995 or after	2	1.02 (0.26-4.08)		
		Pancreas,	Job function (SI	(R):			
		incidence	Regular	31	1.17 (0.83–1.67)		
			Specialized	3	1.60 (0.52-4.97)		
		Pancreas,	Age at first emp	loyment (SI	R):		
		incidence	< 25 yr	23	1.68 (1.12-2.53)		
			25-34 yr	3	0.36 (0.12-1.13)		
			\geq 35 yr	8	1.27 (0.63-2.53)		

Table	2.9 (c	ontinu	ied)

Reference, location enrolment/follow- up period, study design	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments	
Petersen et al.		Pancreas,	Duration of en	nployment (S	IR):	Age, calendar		
<u>(2018a)</u>		incidence	< 1 yr	14	1.79 (1.05-3.01)	period		
(cont.)			$\geq 1 \text{ yr}$	20	0.98 (0.63-1.52)			
			≥ 10 yr	13	0.74 (0.43-1.27)			
			≥ 20 yr	10	0.74 (0.40-1.37)			
<u>Petersen et al.</u> (<u>2018b)</u> Denmark	018b)(full-time, part-time, and volunteer) identifiedoesophagusenmarkand volunteer) identified(ICD-10, C00- C15), mortalitynrolment,from employer, tradeC15), mortality064-2014/follow- p, 1970-2014Registration SystemOral cavity and	oesophagus	Employment t group): Full-time	ype (SMR, m 24	ilitary reference 1.27 (0.85–1.89)	Age, calendar period	<i>Exposure assessment</i> <i>critique</i> : Satisfactory quality. Includes part-tim	
Enrolment, 1964–2014/follow-		from employer, trade union, and Danish Civil		Part-time/ volunteer	8	0.63 (0.32–1.27)		and full-time firefighters. Excluded those who did not actually fight fires.
Cohort		oesophagus (ICD-10, C00–	Duration of en reference grou Full-time firefighters:		MR, military		May include municipal and rural firefighters. <i>Strengths</i> : long period of follow-up; use of military	
		< 1 yr	11	1.39 (0.77–2.51)		reference group to		
	firefighting exposure		$\geq 1 \text{ yr}$	13	1.18 (0.68–2.03)		evaluate healthy-worker bias; analyses by duration of employment.	
	Exposure assessment		≥ 10 yr	11	1.13 (0.63–2.05)			
	method: ever employed		≥ 20 yr	10	1.21 (0.65-2.25)			
	and categorical duration of employment (years) as a firefighter ascertained	s stomacn,	Employment type (SMR, military reference group):				<i>Limitations</i> : few data on potential confounders.	
	from civil registration,		Full-time	17	1.96 (1.22–3.16)			
pension, employer personnel, and trade union membership records	pension, employer		Part-time/ volunteer	1	0.18 (0.03–1.31)			
		Stomach, mortality	Duration of en reference grou		MR, military			
		Full-time firefighters:						
			< 1 yr	8	2.13 (1.07-4.26)			
			$\geq 1 \text{ yr}$	9	1.84 (0.95-3.53)			
			≥ 10 yr	8	1.85 (0.93-3.70)			
			$\geq 20 \text{ yr}$	7	1.90 (0.91-3.99)			

Reference, location enrolment/follow- up period, study design	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments
Petersen et al.		Colon,		ype (SMR, m	ilitary reference	Age, calendar	
(2018b) (cont.)	nt.) junction, sma intestines, mortality Colon,	junction, small	group): Full-time	25	1.11 (0.75–1.64)	period	
		,	Part-time/ volunteer	8	0.66 (0.33–1.32)		
		Colon, rectosigmoid	Duration of er (SMR, militar				
		junction, small	< 1 yr	14	1.31 (0.78-2.22)		
		intestines,	$\geq 1 \text{ yr}$	11	0.92 (0.51-1.66)		
		mortality	≥ 10 yr	11	1.03 (0.57-1.86)		
			$\geq 20 \text{ yr}$	8	0.87 (0.43-1.73)		
		Rectum, mortality	Employment t group):	type (SMR, m	ilitary reference		
		·	Full-time	12	1.04 (0.59-1.83)		
			Part-time/ volunteer	8	1.34 (0.67–2.69)		
		Rectum, mortality	Duration of er (SMR, militar		ull-time firefighters oup):		
		·	< 1 yr	5	0.91 (0.38–2.18)		
			≥ 1 yr	7	1.16 (0.56-2.44)		
			$\geq 10 \text{ yr}$	5	0.93 (0.39-2.23)		
			$\geq 20 \text{ yr}$	4	0.86 (0.32-2.29)		

Table 2.9 (cont	inued)						
Reference, location enrolment/follow- up period, study design	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments
Moir et al. (2016) USA Follow-up, 11 September 2001 through 2009 Cohort	11 457 White male WTC-exposed firefighters (and 8220 non-WTC firefighters) who were employed at FDNY on or after 1 January 1996, actively employed for ≥ 1.5 yr before end of follow-up (31 December 2009), whose identifying information was sent to state cancer registries; contributing person-years at risk at ages 30–70 yr from 11 September 2001 to study end; referent group included firefighters from San Francisco, Chicago, and Philadelphia Exposure assessment method: presence at WTC site from employment records and duty rosters	Colon, incidence Colon, incidence	2001 to 31 Dece. Referent group WTC-exposed FDNY firefighters	y time perio mber 2004) 6 6 time perioc 109, diagnos 15	1 0.73 (0.33–1.59) od (11 September diagnoses only): 1 1.69 (0.42–6.80) 1 (1 January 2005 to es only): 1 0.49 (0.17–1.30)	Age	<i>Exposure assessment</i> <i>critique</i> : Satisfactory quality. Exposure at WTC captured but did not consider previous firefighter work. Only measure of exposure was being a firefighter at WTC. Exposures complex and probably unique to 9/11 disaster. Urban [municipal] firefighters. <i>Other comments</i> : only first primaries were included. <i>Strengths</i> : relatively large cohort. <i>Limitations</i> : short period of follow-up; aimed to investigate effect of WTC exposure, not to firefighting per se.

Reference, location enrolment/follow- up period, study design	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments
Zeig-Owens et al.	9853 male FDNY	Oesophagus,	WTC-exposure	status (SIR):		Age, race,	
(<u>2011)</u>	firefighters employed	incidence	Non-exposed	≤ 5	0.44 (0.06–3.13)	ethnic origin,	
New York City, USA	for ≥ 18 mo, were active		Exposed	≤ 5	0.58 (0.15-2.32)	calendar year	
Enrolment, 1996/follow-up, 1996–2008	firefighters on 1 January 1996, with no prior cancer, and, if alive on 12	Stewark	SIR ratio (exposed vs non-exposed)	NR	1.32 (0.12–14.53)		
Cohort known WTC-exposus status	September 2001, also had known WTC-exposure	Stomach,	WTC-exposure	status (SIR):	:		
	1	incidence	Non-exposed	≤ 5	1.23 (0.40-3.83)		
	Exposure assessment		Exposed	8	2.24 (0.98-5.25)		
	method: WTC-exposed and unexposed firefighter from employment records		SIR ratio (exposed vs non-exposed)	NR	1.82 (0.44–7.49)		
	and questionnaires	Colon, incidence	WTC-exposure status (SIR):				evaluation of medical
			Non-exposed	9	1.01 (0.53-1.94)		surveillance bias.
			Exposed	21	1.52 (0.99-2.33)		Strengths: evaluation of medical surveillance bias
			SIR ratio (exposed vs non-exposed)	NR	1.50 (0.69–3.27)		<i>Limitations</i> : healthy- worker hire bias; short length of follow-up; your
		Pancreas,	WTC-exposure status (SIR):				age at end of follow-up;
		incidence	Non-exposed Exposed SIR ratio (exposed vs	≤ 5 ≤ 5 NR	0.31 (0.04-2.20) 0.78 (0.29-2.09) 2.52 (0.28-22.59)		little information on potential confounders.

San Francisco, Chicago, Philadelphia, USA Enrolment, 1950–2009/follow- up, 1950–2016cohort employed by the fire departments of San Francisco, Chicago, or Philadelphia for ≥ 1 day between 1950 and 2009; up, 1950–2016Chicago Francisco, Chicago, or Philadelphia for ≥ 1 day between 1950 and 2009; up, 1950–2016Minimal bias in expansion assessment mortalityMinimal bias in expansion assessment mortalityCohortanalyses limited to 19 287 male firefighters of known race hired in 1950 or later and employed for ≥ 1 yr Exposure assessment method: ever employed as a firefighter, and number of exposed days, fire-runs, fire-hours reconstructed using job-exposure matrix based on job titlesOesophagus, mortalityRace (SMR): Mon-White ≥ 65 yr1.36 (1.07–1.68)Minimal bias in expansion assessment mortalityCesophagus, matrix based on job titlesOesophagus, mortalityMinimal bias in expansion Overall1.33 (1.10–1.55)Minimal bias in expansion analyses. Municipal firefighters.Strengths: Limitations: healthy- worker seposure matrix based on job titlesOesophagus, mortalityMinimal bias in expansion (Withiut HWSE1.36 (1.07–1.68)Minimal bias in expansion analyses.Strengths: Limitations: healthy- worker seposure matrix based on job titlesOesophagus, mortalityRace (SMR): Strengths: (65 yr1.26 (0.94–1.64)Strengths: long personse of exposed-days, fire-runs, fire-hours reconstructed using job-exposure matrix based on job titlesOesophagus, mortalityMinimal bias in expansion (9000000000000000000000000000000000000	Reference, location enrolment/follow- up period, study design	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments
and assignments and adjustment adjustment department department department department department department department RCS without 82 0.60 (0.36–1.02) records and historical fire- run and fire-hour data adjustment Fully adjusted 82 0.73 (0.40–1.36) loglinear Fully adjusted 82 0.65 (0.33–1.36)	(2020) San Francisco, Chicago, Philadelphia, USA Enrolment, 1950–2009/follow- up, 1950–2016	firefighters in the CFHS cohort employed by the fire departments of San Francisco, Chicago, or Philadelphia for \geq 1 day between 1950 and 2009; exposure-response analyses limited to 19 287 male firefighters of known race hired in 1950 or later and employed for \geq 1 yr Exposure assessment method: ever employed as a firefighter, and number of exposed days, fire-runs, fire-hours reconstructed using job-exposure matrix based on job titles and assignments and departmental work history records and historical fire-	mortality Oesophagus, mortality Oesophagus, mortality Oesophagus,	San Francisco Chicago Philadelphia Overall Heterogeneity P Race (SMR): White Non-White Age (SMR): < 65 yr ≥ 65 yr Heterogeneity P Exposed-days m vs 2500 exposed Loglinear without HWSE adjustment RCS without HWSE adjustment Fully adjusted loglinear	26 68 39 133 2 value, 0.71 > 128 < 5 54 79 2 value, 0.70 nodel (HR at 1-days, 10-yr 82 82 82	1.39 (1.08–1.77) 1.18 (0.84–1.62) 1.31 (1.10–1.55) 1.38 (1.15–1.64) 0.50 (0.14–1.28) 1.26 (0.94–1.64) 1.35 (1.07–1.68) 38700 exposed-days 1ag): 0.63 (0.40–1.00) 0.60 (0.36–1.02) 0.73 (0.40–1.36)	age, calendar period Age, race, birthdate (within	<i>critique</i> : Good quality. Minimal bias in exposure assessment in internal analyses. Municipal firefighters. <i>Strengths</i> : long period of follow-up; exposure- response modelling for three metrics of exposure assessed using job-exposure matrices; adjustment for HWSE.

Reference, location enrolment/follow- up period, study design	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments
<u>Pinkerton et al.</u> (2020) (cont.)		Oesophagus, mortality	Fire-runs (Chica model (HR at 88 10-yr lag):			Age, race, birthdate (within	
			Loglinear without HWSE adjustment	72	0.97 (0.68–1.36)	5 yr), fire department	
			RCS without HWSE adjustment	72	1.15 (0.74–1.81)		
			Fully adjusted loglinear	72	1.10 (0.75–1.58)		
			Fully adjusted RCS	72	1.45 (0.88–2.44)		
		Oesophagus, mortality	Fire-hours (Chic vs 600 h, 10-yr la		nodel (HR at 2300 h		
			Loglinear without HWSE adjustment	45	0.91 (0.53–1.51)		
			RCS without HWSE adjustment	45	0.95 (0.50–1.83)		
			Fully adjusted loglinear	45	1.17 (0.65–2.05)		
			Fully adjusted RCS	45	1.31 (0.64–2.75)		
		Oesophagus, mortality		a only) fully	fire-runs (Chicago adjusted loglinear 2100 runs,	Age, race, birthdate (within 5 yr), fire	
			Lag to < 20 yr 20 to < 30 yr	NR NR	1.10 (0.36–3.05) 0.92 (0.37–2.12)	department, employment duration	
			\geq 30 yr LRT <i>P</i> value, 0.8	NR 4	1.26 (0.69–2.15)		

Table 2.0 (contin

Table 2.9 (cont	(inued)						
Reference, location enrolment/follow- up period, study design	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments
<u>Pinkerton et al.</u> (2020) (cont.)		Oesophagus, mortality	Age at exposure Philadelphia or model (HR for 10-yr lag):	nly) fully adj	usted loglinear	Age, race, birthdate (within 5 yr), fire	
			< 40 yr	NR	1.25 (0.69-2.15)	department,	
			$\geq 40 \text{ yr}$	NR	0.96 (0.50-1.76)	employment	
			LRT <i>P</i> value, 0.		. ,	duration	
			Period of expos Philadelphia or model (HR for 10-yr lag):	nly) fully adj			
			Pre-1970	NR	2.00 (1.01-3.69)		
			1970 or after	NR	0.81 (0.49-1.30)		
			LRT <i>P</i> value, 0.	04			
		Stomach,	Fire departmen	nt (SMR):		Gender, race,	
		mortality	San Francisco	27	1.13 (0.75–1.65)	age, calendar	
			Chicago	62	1.15 (0.88–1.48)	period	
			Philadelphia	35	0.90 (0.62–1.25)		
			Overall	124	1.06 (0.88–1.27)		
			Heterogeneity	P value, 0.46			
		Stomach,	Race (SMR):			Gender, age,	
		mortality	White	118	1.09 (0.91–1.31)	calendar	
			Non-White	6	0.68 (0.25–1.48)	period	
		Stomach,	Age (SMR):				
		mortality	< 65 yr	40	0.74 (0.53–1.01)		
			≥ 65 yr	84	1.34 (1.07–1.65)		
			Heterogeneity	P value, < 0.0)]		

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Reference, location enrolment/follow- up period, study design	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments
Pinkerton et al. (2020)		Stomach, mortality	Exposed-days m vs 2500 exposed		t 8700 exposed-days	Age, race, birthdate	
(cont.)		mortanty	Loglinear without HWSE adjustment	52	1.13 (0.62–2.16)	(within 5 yr), fire department	
			RCS without HWSE adjustment	52	1.00 (0.50–2.19)		
			Fully adjusted loglinear	52	1.75 (0.74-4.53)		
			Fully adjusted RCS	52	1.40 (0.51-4.44)		
		Stomach, mortality	Fire-runs (Chicago and Philadelphia only) model (HR at 8800 runs vs 2100 runs, 10-yr lag):				
			Loglinear without HWSE adjustment	45	1.07 (0.68–1.62)		
			RCS without HWSE adjustment	45	1.28 (0.73–2.28)		
			Fully adjusted loglinear	45	1.25 (0.76–1.95)		
			Fully adjusted RCS	45	1.67 (0.87–3.31)		

Table 2.9 (cont	inued)						
Reference, location enrolment/follow- up period, study design	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments
Pinkerton et al.		Stomach,			nodel (HR at 2300 h	Age, race,	
(2020) (cont.)		mortality	vs 600 h, 10-yr l Loglinear	ag): 30	1.34 (0.7–2.45)	birthdate (within 5 yr), fire	
			without HWSE adjustment			department	
			RCS without HWSE adjustment	30	1.37 (0.62–3.20)		
			Fully adjusted loglinear	30	1.45 (0.71–2.87)		
			Fully adjusted RCS	30	1.54 (0.63-3.94)		
		Stomach, mortality	and Philadelphi	a only) fully	fire-runs (Chicago adjusted loglinear 2100 runs, 10-yr	Attained age, race, birthdate (within	
			Lag to < 20 yr	NR	1.45 (0.42–4.31)	5 yr) and	
			20 to < 30 yr	NR	1.69 (0.55–4.67)	department, employment	
			\geq 30 yr LRT <i>P</i> value, 0.6	NR	0.92 (0.38–1.93)	duration	
		Small intestine,	Fire department			Gender, race,	
		colon (ICD-	San Francisco	59	0.99 (0.75-1.27)	age, calendar	
		10, C17–C18),	Chicago	189	1.37 (1.19–1.58)	period	
		mortality	Philadelphia	122	1.28 (1.07–1.53)		
			Overall	370	1.27 (1.14–1.40)		
			Heterogeneity P	value, 0.08			
		Small intestine,	Race (SMR):			Gender, age,	
		colon (ICD-	White	359	1.30 (1.17–1.44)	calendar	
		10, C17–C18), mortality	Non-White	11	0.67 (0.34–1.21)	period	

Reference, location enrolment/follow- up period, study design	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments
Pinkerton et al.		Small intestine,	Age (SMR):			Gender, race,	
(2020)		colon (ICD-	< 65 yr	104	1.01 (0.82–1.22)	age, calendar	
(cont.)		10, C17–C18), mortality	≥ 65 yr	266	1.40 (1.24–1.58)	period	
		mortanty	Heterogeneity P				
		Colon, mortality	Exposed-days m vs 2500 exposed		t 8700 exposed-days t lag):	Age, race, birthdate	
			Loglinear without HWSE adjustment	145	0.83 (0.58–1.18)	(within 5 yr), fire department	
			RCS without HWSE adjustment	145	0.77 (0.51–1.17)		
			Fully adjusted loglinear	145	0.87 (0.56–1.38)		
			Fully adjusted RCS	145	0.75 (0.45-1.31)		
	Colon, mortality	Fire-runs (Chica model (HR at 88 lag):		ladelphia only) 2100 runs, 10-yr			
			Loglinear without adjustment	132	0.83 (0.63–1.08)		
			RCS without HWSE adjustment	132	0.80 (0.58–1.09)		
			Fully adjusted loglinear	132	0.89 (0.66–1.18)		
			Full adjusted RCS	132	0.87 (0.61–1.23)		

Reference, location enrolment/follow- up period, study	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments
design		,					
Pinkerton et al. (2020)		Colon, mortality	Fire-hours (Chi vs 600 h, 10-yr l		nodel (HR at 2300 h	Age, race, birthdate	
(cont.)			Loglinear without HWSE adjustment	100	0.79 (0.54–1.12)	(within 5 yr), fire department	
			RCS without HWSE adjustment	100	0.79 (0.51–1.21)		
			Fully adjusted loglinear	100	0.84 (0.56-1.26)		
			Fully adjusted RCS	100	0.84 (0.52–1.36)		
		Colon, mortality	and Philadelphi	ia only) fully	fire-runs (Chicago adjusted loglinear 2100 runs, 10-yr	Age, race, birthdate (within 5 yr), fire	
			Lag to < 20 yr	NR	0.64 (0.26-1.48)	department,	
			20 to < 30 yr	NR	0.76 (0.36-1.49)	employment	
			\geq 30 yr	NR	1.13 (0.71–1.73)	duration	
			LRT P value, 0.3				
		Rectum,	Fire departmen			Gender, race,	
		mortality	San Francisco	20	1.33 (0.81-2.06)	age, calendar	
		,	Chicago	52	1.53 (1.14–2.01)	period	
			Philadelphia	25	1.02 (0.66–1.51)		
			Overall	97	1.32 (1.07–1.16)		
			Heterogeneity <i>I</i>		1.02 (1.07 1.10)		
		Rectum,	Race (SMR):	varae, 0.25		Gender, age,	
		mortality	White	> 92	1.36 (1.10-1.66)	calendar	
			Non-White	< 5	0.72 (0.15–2.11)	period	
		Rectum,	Age (SMR):		0.72 (0.13-2.11)	Gender, race,	
		mortality	< 65 yr	40	1.21 (0.87–1.65)	age, calendar	
			$\geq 65 \text{ yr}$	57	1.41 (1.07–1.83)	period	
			2 05 yi				

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Reference, location enrolment/follow- up period, study design	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments
Pinkerton et al. (2020)		Rectum, mortality	Exposed-days m vs 2500 exposed		t 8700 exposed-days	Age, race, birthdate	
(cont.)		mortanty	Loglinear without HWSE adjustment	42	0.45 (0.24–0.88)	(within 5 yr), fire department	
			RCS without HWSE adjustment	42	0.41 (0.21–0.83)	-	
			Fully adjusted loglinear	42	0.49 (0.21–1.19)		
			Fully adjusted RCS	42	0.43 (0.17–1.20)		
		Rectum, mortality	Fire-runs (Chicago and Philadelphia only) model (HR at 8800 runs vs 2100 runs, 10-yr lag):				
			Loglinear without HWSE adjustment	34	0.32 (0.16-0.61)		
			RCS without HWSE adjustment	34	0.39 (0.17–0.87)		
			Fully adjusted loglinear	34	0.36 (0.16-0.75)		
			Fully adjusted RCS	34	0.47 (0.18–1.22)		

run and fire-hour data

Reference, location enrolment/follow- up period, study design	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments
<u>Pinkerton et al.</u> (2020) (cont.)		Rectum, mortality	and Philadelph model (HR for lag): Lag to < 20 yr 20 to < 30 yr \ge 30 yr LRT <i>P</i> value, 0.	ia only) fully 8800 runs vs NR NR NR 54	fire-runs (Chicago v adjusted loglinear s 2100 runs, 10-yr 0.18 (0.02–1.51) 0.80 (0.15–3.30) 0.24 (0.06–0.80)	Age, race, birthdate (within 5 yr), fire department, employment duration	
		Breast, mortality	Fire departmen San Francisco Chicago Philadelphia Overall Heterogeneity J	NR NR NR 10	2.11 (0.58-5.41) 1.16 (0.38-2.71) 0.53 (0.01-2.94) 1.24 (0.59-2.27)	Gender, race, age, calendar period	
Daniels et al. (2015) San Francisco, Chicago, Philadelphia, USA Enrolment,	19 309; all male career firefighters in the CFHS cohort of known race who were on active duty for \geq 1 day from 1950 through 2009 in the fire	Oesophagus, incidence Oesophagus, incidence	e ,	nodel (HR, l 54 cago and Phi	1 / ·	Age, race, fire department, birth cohort Age, race, fire department,	<i>Exposure assessment</i> <i>critique</i> : Good quality. Minimal bias in exposur assessment in internal analyses. Municipal firefighters.
1950–2009/follow- up, 1950–2009 (mortality), 1985– 2009 (incidence) Cohort	departments of Chicago, Philadelphia, or San Francisco with ≥ 1 yr of employment Exposure assessment method: number of exposed days, fire-runs,	Oesophagus, incidence	8800 runs vs 2100 runs Fire-hours (Chi model, 10-yr la 2300 h vs 600 h		1.22 (0.89–1.88) nodel (HR, linear 0.57 (NR–1.10)	birth cohort Age, race, birth cohort	Strengths: long period of follow-up; exposure- response modelling for three metrics of exposur assessed using job- exposure matrices. <i>Limitations</i> : little
	fire-hours reconstructed using job-exposure matrix based on job titles and assignments and departmental work history records and historical fire-	Colon and rectum, incidence	Exposed-days r lag): 8700 days vs 2500 days	nodel (HR, _F 289	oower model, 10-yr 0.92 (0.84–1.01)	Age, race, fire department, birth cohort	<i>Limitations</i> : little information on potentia confounders.

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Table 2.9 (cont	-						
Reference, location enrolment/follow- up period, study design	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments
Daniels et al. (2015) (cont.)		Colon and rectum, incidence	Fire-runs (Chio model (HR, log 8800 runs vs 2100 runs			Age, race, fire department, birth cohort	
			Fire-hours (Ch model, 10-yr la	g):	nodel (HR, linear	Age, race, birth cohort	
			2300 h vs 600 h	158	0.78 (0.63–1.04)		
Daniels et al. (2014) San Francisco, Chicago, Philadelphia, USA Enrolment, 1950–2009/follow- up 1950–2009 (mortality), 1985– 2009 (incidence)	29 993 (24 453 for incidence analyses); male and female career firefighters in the CFHS cohort employed for ≥ 1 day in Chicago, San Francisco, or Philadelphia fire departments between 1950 and 2009	Oral cavity and pharynx combined, incidence Oesophagus, incidence	SIR: All cancers First primary cancer SIR: All cancers First primary cancer	174 148 90 80	1.39 (1.19–1.62) 1.41 (1.20–1.66) 1.62 (1.31–2.00) 1.71 (1.36–2.13)	Gender, race, age, calendar period	<i>Exposure assessment</i> <i>critique</i> : Satisfactory quality. Minimum exposure is 1 day of work as a municipal firefighter. <i>Strengths</i> : long period of follow-up; ascertained incidence outcomes; included female
Cohort	Exposure assessment method: ever employed and categorical duration of employment (years) from employment records	Oesophagus, incidence Stomach, incidence	Race (SIR, all c Among men: Caucasian [White] Other SIR: All cancers	87 < 5 93	1.70 (1.36–2.09) 0.73 (0.15–2.15) 1.15 (0.93–1.40)	Age, calendar period Gender, race, age, calendar	firefighters. <i>Limitations</i> : healthy- worker hire bias in external comparisons; little information on potential confounders.
		Stomach, incidence	First primary cancer Race (SIR, all c Among men: Caucasian [White] Other	72 ancers): 87 6	1.02 (0.80–1.28) 1.19 (0.96–1.47) 0.76 (0.28–1.66)	period Age, calendar period	
			Other	0	0.70 (0.20-1.00)		

Reference, location enrolment/follow- up period, study design	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments
Daniels et al. (2014) (cont.)		Small intestine, colon (ICD- 10, C17–C18), incidence	SIR: All cancers First primary cancer	398 351	1.21 (1.09–1.33) 1.29 (1.16–1.43)	Gender, race, age, calendar period	
		Small intestine, colon (ICD-	Race (SIR, all ca Among men:	ancers):		Age, calendar period	
		10, C17–C18), incidence	Caucasian [White]	379	1.23 (1.11–1.36)		
		Colon, incidence	Other SIR:	18	0.90 (0.53-1.42)	Gender, race, age, calendar	
			All cancers First primary cancer	381 335	1.21 (1.09–1.34) 1.28 (1.15–1.43)	period	
		Rectum, incidence	SIR: All cancers	166	1.11 (0.95–1.30)	Gender, race, age, calendar	
			First primary cancer	140	1.09 (0.91–1.28)	period	
		Rectum, incidence	Race (SIR, all ca Among men:	ancers):		Age, calendar period	
			Caucasian [White]	159	1.16 (0.99–1.36)		
		Breast, incidence	Other SIR:	7	0.62 (0.25–1.28)	Gender, race,	
			All cancers First primary cancer	26 24	1.26 (0.82–1.85) 1.32 (0.84–1.96)	age, calendar period	

Reference, location enrolment/follow- up period, study design	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments
Demers et al.	2447 male firefighters	Oral cavity	SIR (local cour	nty rates):		Age, calendar	Exposure assessment
$\begin{array}{ll} \underline{994} \\ employed for \geq 1 \ yr \\ between 1944 \ and 1979, \\ common \\ end \\ common \\ end $	and pharynx, incidence	Firefighters	11	1.1 (0.6–2.0)	period	<i>critique</i> : Satisfactory quality. Duration (years)	
Tacoma,	alive as of 1 January 1974	Oral cavity	IDR:				involved in direct
Washington, USA	and known to be a resident of one of 13 counties in	and pharynx,	Local police	8	1		firefighting (surrogate for fire smoke) was not
Enrolment, 1944–1979/follow-	the catchment area of	incidence	Firefighters	11	0.8 (0.3–1.9)		measured equally in the
up, 1974–1989 Cohort	b, 1974–1989 bhort ≥ 1 mo; reference group included 1878 local male police officers Exposure assessment method: ever employed	Oral cavity and pharynx,	Duration of ex county rates):	posed employ	yment (SIR, local		two study populations. Municipal firefighters.
Contra			< 10 yr	2	1.4 (0.2–5.1)		Strengths: use of two
			10–19 yr	4	2.5 (0.7-6.4)		comparison groups,
			20–29 yr	2	0.3 (0.0-1.2)		including comparison
			≥ 30 yr	3	3.9 (0.8–11)		with police officers to lim
for ≥ 1 yr, and categorical duration of employment (years) in direct	Oral cavity and pharynx,	Years since firs rates):	st employmen	t (SIR, local county		healthy-worker bias. <i>Limitations</i> : little information on potential	
	(years) in direct firefighting positions from employment records	incidence	< 20 yr	1	1.5 (0.0-8.2)		confounders; small number of cases for som outcomes.
			20–29 yr	1	0.5 (0.0-2.7)		
	1 7		≥ 30 yr	9	1.3 (0.6-2.4)		
		Oesophagus,	SIR (local cour	nty rates):			
		incidence	Firefighters	4	1.3 (0.4–3.3)		
		Oesophagus, incidence	Duration of ex county rates):	posed employ	yment (SIR, local		
			< 10 yr	0	0 (0.0–9.3)		
			10–19 yr	2	4.8 (0.6-17.2)		
			20-29	2	1.0 (0.1-36.1)		
			≥ 30 yr	0	0 (0.0-12)		
	Oesophagus, incidence	Years since firs rates):	st employmen	nt (SIR, local county			
			< 20 yr	0	0 (0.0-36.5)		
			20–29 yr	2	4.3 (0.5-15.4)		
			≥ 30 yr	2	0.8 (0.1-2.8)		
		Stomach,	SIR (local cour	nty rates):			
		incidence	Firefighters	8	1.4 (0.6-2.7)		

Reference, location enrolment/follow- up period, study design	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments
Demers et al.		Stomach,	IDR:			Age, calendar	
<u>(1994)</u>		incidence	Local police	7	1	period	
(cont.)			Firefighters	8	0.4 (0.1–1.2)		
		Stomach, incidence	Duration of ex county rates):	posed employ			
			< 10 yr	2	3 (0.4–11)		
			10–19 yr	1	1.2 (0.0-6.9)		
			20–29 yr	4	1.1 (0.3–2.9)		
			≥ 30 yr	1	1.4 (0.0-8.1)		
		Stomach, incidence	Years since firs rates):	t employmen			
			< 20 yr	0	0 (0.0–15.7)		
			20–29 yr	2	2.3 (0.3-8.3)		
			≥ 30 yr	6	1.3 (0.5-2.8)		
		Colon, incidence	SIR (local cour	nty rates):			
		Colon, incidence	Firefighters	23	1.1 (0.7–1.6)		
			IDR:				
			Local police	8	1		
			Firefighters	23	1.3 (0.6-3.0)		
		Colon, incidence	Duration of exposed employment (SIR, local county rates):				
			< 10 yr	2	0.8 (0.1-2.9)		
			10–19 yr	2	0.7 (0.1–2.6)		
			20–29 yr	15	1.1 (0.6–1.9)		
			≥ 30 yr	4	1.5 (0.4–3.9)		
		Colon, incidence	Years since first employment (SIR, local county rates):				
			< 20 yr	0	0 (0.0-5.7)		
			20–29 yr	3	1.2 (0.3-3.5)		
			≥ 30 yr	20	1.1 (0.7–1.7)		

Reference, location enrolment/follow- up period, study design	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments
Demers et al.		Colon, incidence	Duration of exposed employment (IDR):			Age, calendar	
<u>(1994)</u>			< 10 yr	2	1	period	
(cont.)			10–19 yr	2	1.0 (0.1–7.2)		
			20–29 yr	15	1.3 (0.3–5.9)		
		≥ 30 yr	4	1.8 (0.3–11.6)			
		Colon, incidence	Duration of exp	osed employ	yment (IDR):		
			< 10 yr vs local police	2	1.0 (0.2–4.8)		
			10–19 yr vs local police	2	0.9 (0.2–4.4)		
			20–29 yr vs local police	15	1.4 (0.6–3.2)		
			\geq 30 yr vs local police	4	2.0 (0.5-8.0)		
		Rectum,	SIR (local county rates):				
		incidence	Firefighters	12	1.0 (0.5-1.8)		
		Rectum,	IDR:				
		incidence	Local police	5	1		
			Firefighters	12	1.3 (0.5-3.9)		
		Rectum, incidence	Duration of exposed employment (SIR, local county rates):				
			< 10 yr	2	1.4 (0.2-4.9)		
			10–19 yr	3	1.9 (0.4–5.4)		
			20–29 yr	5	0.7 (0.2–1.6)		
		Rectum, incidence	\geq 30 yr	2	1.6 (0.2–5.6)		
			Years since first employment (SIR, local county rates):				
		< 20 yr	0	0 (0.0-8.8)			
			20–29 yr	4	2.2 (0.6-5.7)		
			\geq 30 yr	8	0.8 (0.4–1.7)		
		Pancreas,	SIR (local count	ty rates):	· · · ·		
		incidence	Firefighters	6	1.1 (0.4–2.3)		

Reference, location enrolment/follow- up period, study design	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments
<u>Demers et al.</u> (1994) (cont.)		Pancreas, incidence Breast, incidence	IDR: Local police Firefighters SIR (local cour Firefighters	3 6 nty rates): 1	1 1.1 (0.3–5.5) 2.4 (0.1–13.3)	Age, calendar period	
Demers et al. (1992a) Seattle and Tacoma, Washington, and Portland, Oregon, USA Enrolment, 1944–1979/follow- up, 1944–1989	4401 male firefighters employed for ≥ 1 yr between 1944 and 1979 in Seattle, Tacoma, or Portland, USA; reference group included 3676 local police officers Exposure assessment method: ever employed for ≥ 1 yr, and categorical duration (years) of exposure to fire combat from employment records	Oral cavity and pharynx combined, mortality Oesophagus, mortality Stomach, mortality Colon, mortality	SMR: Firefighters SMR: Firefighters SMR: Firefighters SMR:	7 6 16	0.81 (0.33–1.66) 0.83 (0.30–1.80) 1.07 (0.61–1.73)	Age, calendar period	<i>Exposure assessment</i> <i>critique</i> : Satisfactory/good quality. Duration (years) involved in fire combat (surrogate for fire smoke) was not measured equally in the three municipal firefighter populations. <i>Strengths</i> : use of two comparison groups, including comparison with police officers to lim healthy-worker bias. <i>Limitations</i> : little information on potential
Cohort		Colon, mortality	Firefighters IDR: Local police Firefighters	24 8 24	0.85 (0.54–1.26) 1 1.58 (0.73–3.43)		
		Colon, mortality	Duration of ex < 10 yr 10−19 yr 20−29 yr ≥ 30 yr	posed emplo 4 2 9 9	yment (SMR): 1.40 (0.4–3.6) 0.54 (0.1–2.0) 0.62 (0.3–1.2) 1.21 (0.6–2.3)		confounders; ascertained mortality outcomes only.
		Colon, mortality Colon, mortality	Years since firs < 20 yr 20-29 yr $\ge 30 \text{ yr}$	1 3 20			
			Age at risk (SM 18–39 yr 40–64 yr ≥ 65 yr	IR): 1 10 13	1.38 (0.1–8.2) 0.78 (0.4–1.4) 0.86 (0.5–1.5)		

Table 2.9 (cont	tinued)						
Reference, location enrolment/follow- up period, study design	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments
<u>Demers et al.</u> (<u>1992a)</u> (cont.)		Rectum, mortality Rectum,	SMR: Firefighters IDR:	8	0.95 (0.41–1.87)	Age, calendar period	
		mortality	Local police	5	1		
		Liver and bile	0	0.89 (0.30–2.66)			
		ducts, mortality Liver and bile ducts, mortality	Firefighters IDR:	6	1.19 (0.44–2.59)		
			Local police	4	1		
		Pancreas,	Firefighters SMR:	6	0.71 (0.19–2.71)		
		mortality	Firefighters	14	0.89 (0.49-1.49)		
Vena & Fiedler1867 White male career(1987)firefighters employed byBuffalo, New York,the City of Buffalo forUSA ≥ 5 yr, with ≥ 1 yr as a1950–1979firefighterCohortExposure assessmentmethod: ever-	firefighters employed by the City of Buffalo for	Oesophagus, mortality Stomach,	SMR: Firefighters SMR:	3	1.34 (0.27–3.91)	Only assessed ever- employment and dura of employment as a	<i>critique</i> : Minimal quality. Only assessed ever-
	firefighter Exposure assessment	mortality Colon, mortality	Firefighters SMR:	7	1.19 (0.48–2.46)		
			Firefighters	16	1.83 (1.05-2.97)		municipal firefighter. Strengths: long length of
		Colon, mortality	Years worked as a firefighter (SMR):				follow-up.
			1–9 yr	0	0 (NR)		<i>Limitations</i> : healthy- worker hire bias; little information on potential confounders or exposure to firefighting activities.
			10–19 yr	1	[1.25 (0.1-6.2)]		
			20–29 yr	2	[0.87 (0.1-2.9)]		
			30–39 yr	5	[1.43 (0.5–3.2)]		
			≥ 40 yr	8	[4.71 (2.2-8.9)]		
		Colon, mortality	Calendar year of death (SMR):				
			1950–1959	3	[1.76 (0.4–4.8)]		
			1960-1969	4	[1.38 (0.4 - 3.3)]		
			1970–1979	9	[2.20 (1.1-4.0)]		

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Reference, location enrolment/follow- up period, study design	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments
Vena & Fiedler		Colon, mortality	Year of hire (SI	MR):		Age, calendar	
<u>(1987)</u>			Pre-1930	10	[2.27 (1.2-4.1)]	period	
(cont.)			1930-1939	4	[2.35 (0.7-5.7)]		
			1940-1949	4	[1.11 (0.2-3.7)]		
			1950 or after	0	0 (NR)		
		Colon, mortality	Years of latency	y (SMR):			
			< 20 yr	0	0 (NR)		
			20–29 yr	2	[1.30 (0.2-4.4)]		
			30–39 yr	4	[1.51 (0.5-3.6)]		
			40-49 yr	7	[2.65 (1.2–5.3)]		
			≥ 50 yr	3	[2.85 (0.7–7.4)]		
		Rectum,	SMR:				
		mortality	Firefighters	7	2.08 (0.83-4.28)		
		Liver and bile	SMR:				
		ducts, mortality	Firefighters	2	0.98 (0.11-3.52)		
		Pancreas,	SMR:				
		mortality	Firefighters	2	0.38 (0.04-1.36)		

Reference, ocation enrolment/follow- 1p period, study lesign	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments
<u>Feuer & Rosenman</u> (1986) New Jersey (NJ),	263 deceased White male firefighters in the New Jersey Police and	Digestive (ICD- 8, 150–159), mortality	Reference popul Firefighters vs US White men): [1.45 (0.91–2.20)]	Age, race	<i>Exposure assessment</i> <i>critique</i> : Satisfactory quality. Assessment provides duration of employment categories.
JSA 974–1980	Firemen Retirement System (firefighters vested with > 10 yr of service, or		Firefighters vs NJ White men	20	[1.11 (0.70–1.69)]		
Cohort with \geq 10 yr of service, or firefighters who died while on payroll regardless of employment duration); one reference group included 567 White male police deaths Exposure assessment method: ever employed,		Firefighters vs White male NJ police	20	[0.91 (0.57–1.38)]		May include municipal and rural firefighters. <i>Strengths</i> : comparison with other uniformed service occupation. <i>Limitations</i> : PMR study	
	Digestive (ICD- 8, 150–159),	Duration of emp	oloyment (Pl	MR):			
		$\leq 20 \text{ yr}$	5	[1.24 (0.45-2.75)]			
	mortality	20–25 yr	5	[0.96 (0.35-2.13)]		design lacks event-free	
		> 25 yr	10	[1.15 (0.58–2.05)]		follow-up time; short	
		Digestive (ICD-	Latency (PMR):				observation period; littl information on potentia confounders.
	and categorical duration	8, 150–159),	$\leq 22 \text{ yr}$	4	[0.92 (0.29-2.22)]		
	of employment (years), as a career firefighter from	mortality	22–27 yr	7	[1.28 (0.56-2.53)]		
	retirement system records		> 27 yr	9	[1.10 (0.54-2.02)]		
Aronson et al.	5414 male firefighters	Pharynx,	SMR:			Age, calendar	Exposure assessment
<u>1994)</u> Coronto, Canada	employed for ≥ 6 mo at one of six fire departments	mortality	Any employment	4	1.39 (0.38–3.57)	period	<i>critique</i> : Satisfactory quality. Unclear if
950-1989	in Metropolitan Toronto	Pharynx,	Years since first	exposure (SI	MR):		individuals were active
Cohort	any time between 1950 and 1989	mortality	< 20 yr	0	0 (0-9.46)		firefighters for whole
	Exposure assessment		20–29 yr	1	1.22 (0.03-6.80)		employment. Probably municipal firefighters.
	method: ever employed		≥ 30 yr	3	1.81 (0.37-5.28)		Strengths: long period
	and categorical duration	Pharynx,	Years of employ	ment (SMR)	:		of follow-up; analysis of
of employment (years) as	mortality	< 15 yr	1	2.33 (0.06-12.96)		employment duration.	
	municipal firefighter from		15–29 yr	0	0 (0-3.26)		Limitations: healthy-
employment records	employment records		≥ 30 yr	3	2.33 (0.48-6.80)		worker hire bias; little information on confounders or exposu ascertained mortality outcomes only.

Reference, location enrolment/follow- up period, study design	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments
Aronson et al.		Pharynx,	Age (SMR):			Age, calendar	
<u>(1994)</u>		mortality	< 60 yr	1	0.62 (0.02-3.44)	period	
(cont.)			≥ 60 yr	3	2.40 (0.49-7.01)		
		Oesophagus,	SMR:				
		mortality	Any employment	2	0.40 (0.05-1.43)		
		Stomach,	SMR:				
		mortality	Any employment	7	0.51 (0.20–1.05)		
		Colon, mortality	SMR:				
			Any employment	11	0.60 (0.30-1.08)		
		Rectum,	SMR:				
		mortality	Any employment	13	1.71 (0.91–2.93)		
		Rectum,	Years since firs	t exposure (S			
		mortality	< 20 yr	1	1.35 (0.03–7.53)		
			20–29 yr	2	1.46 (0.18–5.27)		
			≥ 30 yr	10	1.82 (0.87–3.36)		
		Rectum,	Years of employ	yment (SMR):		
		mortality	< 15 yr	0	0 (0-4.67)		
			15–29 yr	5	2.35 (0.76-5.48)		
			≥ 30 yr	8	1.74 (0.75–3.43)		
		Rectum,	Age (SMR):				
		mortality	< 60 yr	4	1.39 (0.38–3.56)		
			≥ 60 yr	9	1.91 (0.87–3.63)		
		Liver and bile	SMR:				
		ducts, mortality	Any employment	2	0.84 (0.10-3.05)		
		Pancreas,	SMR:				
		mortality	Any employment	14	1.40 (0.77–2.35)		

Reference, location enrolment/follow- up period, study design	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments
Aronson et al.		Pancreas,	Years since firs	t exposure (S	MR):	Age, calendar	
<u>(1994)</u>		mortality	< 20 yr	1	1.03 (0.03-5.74)	period	
(cont.)			20–29 yr	2	0.95 (0.12-3.44)		
			\geq 30 yr	11	1.59 (0.80-2.85)		
		Pancreas,	Years of emplo	yment (SMR)			
		mortality	< 15 yr	2	1.75 (0.21-6.34)		
			15–29 yr	3	0.96 (0.20-2.79)		
			\geq 30 yr	9	1.61 (0.74-3.05)		
		Pancreas,	Age (SMR):				
		mortality	< 60 yr	4	0.97 (0.27-2.49)		
			$\geq 60 \text{ yr}$	10	1.70 (0.81-3.13)		
Guidotti (1993) Edmonton and Calgary, province of Alberta, Canada	3328; all firefighters employed between 1927 and 1987 by either of the fire departments of	Oral cavity and pharynx combined, mortality	SMR: Any employment	2	1.14 (0.14–4.10)	Age, calendar period	<i>Exposure assessment</i> <i>critique</i> : Good quality. Good approach to differentiate exposure between ranks. Municipal firefighters. <i>Strengths</i> : long length of follow-up; analyses by duration of employment and exposure index. <i>Limitations</i> : little
1927–1987 Cohort	Edmonton or Calgary Exposure assessment method: ever employed and categorical duration	Stomach, mortality Colon and	SMR: Any employment SMR:	6	0.81 (0.30–1.76)		
fro	of employment (years) from employment records; exposure index of years of	rectum, mortality	Any employment	14	1.61 (0.88–2.71)		
	employment weighted by	Colon and	Year of cohort	entry (SMR):			information on potential
	time spent in proximity	rectum, mortality	Pre-1920	4	[1.49 (0.47–3.60)]		confounders; ascertained
	to fires based on job		1920–29	0	0 (NR)		mortality outcomes only
	classification		1930–39	2	[2.65 (0.44-8.76)]		low number of cases for stratified analyses.
			1940-49	2	[1.23 (0.21-4.05)]		otratilited allary ses.
			1950–59	3	[1.49 (0.38-4.07)]		
			1960-69	2	[3.40 (0.57–11.2)]		
			1970–79	0	0 (NR)		

Reference, location enrolment/follow- up period, study design	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments
<u>Guidotti (1993)</u>		Colon and	Latency (SMR):			Age, calendar	
(cont.)		rectum, mortality	< 20 yr	2	[1.48 (0.25-4.90)]	period	
			20–29 yr	5	[2.68 (0.98-5.93)]		
			30–39 yr	3	[1.24 (0.32–3.39)]		
			40–49 yr	2	[1.20 (0.20-3.96)]		
			≥ 50 yr	2	[1.46 (0.24-4.82)]		
		Colon and rectum, mortality	Exposure index	(SMR):			
			0	0	0 (NR)		
			> 0 to < 1	2	[2.83 (0.47-9.31)]		
		1–9	6	[4.58 (1.86-9.53)]			
		≥ 10	6	[0.90 (0.37-1.88)]			
		rectum, mortality	Latency, exposi	re index > 0	, < 1 (SMR):		
			< 20 yr	0	0 (NR)		
			20–29 yr	1	[5.48 (0.28-27.4)]		
			30–39 yr	1	[5.95 (0.29-29.0)]		
			40–49 yr	0	0 (NR)		
			≥ 50 yr	0	0 (NR)		
		Colon and	Latency, exposi	ıre index 1–9	9 (SMR):		
		rectum, mortality	< 20 yr	1	[2.31 (0.12–11.5)]		
			20–29 yr	3	[11.46 (2.94–31.4)]		
			30–39 yr	1	[3.50 (0.17–17.0)]		
			40-49 yr	0	0 (NR)		
			≥ 50 yr	1	[5.80 (0.29-29.0)]		
		Colon and	Latency, exposi	are index ≥ 1	0 (SMR):		
		rectum, mortality	< 20 yr	1	[1.59 (0.08–7.83)]		
			20–29 yr	1	[0.70 (0.04-3.47)]		
			30–39 yr	1	[0.51 (0.03-2.52)]		
			40–49 yr	2	[1.36 (0.23-4.50)]		
			≥ 50 yr	1	[0.85 (0.04-4.22)]		

Reference, location enrolment/follow- up period, study design	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments
Guidotti (1993)	Pancreas,	SMR:			Age, calendar		
cont.)	.) mortality Pancreas,	mortality	Any employment	5	1.55 (0.50-3.62)	period	
		Latency (SMR):					
		mortality	< 20 yr	0	0 (NR)		
			20–29 yr	1	[1.13 (0.06-5.54)]		
			30–39 yr	1	[0.97 (0.05-4.79)]		
			40-49 yr	0	0 (NR)		
			≥ 50 yr	3	[7.16 (1.82–19.4)]		
		Pancreas,	Exposure index	(SMR):			
		mortality	0	0	0 (NR)		
			> 0 to < 1	0	0 (NR)		
			1–9	1	[2.12 (0.11-10.5)]		
			≥ 10	4	[1.65 (0.52-3.97)]		
					/]		

Reference, location enrolment/follow- up period, study design	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments
Glass et al. (2019) Australia Enrolment, varied by agency/follow- up, 1980–2011 (mortality); 1982– 2010 (incidence) Cohort	both paid [career] (1682) varied and volunteer (37 962), llow- from nine fire agencies in Australia 1982– Exposure assessment	Lip, oral cavity, and pharynx, incidence Colon, incidence Rectum, incidence	SIR: Volunteer firefighters Volunteer firefighters who attended incidents SIR: Volunteer firefighters Volunteer firefighters who attended incidents SIR: Volunteer firefighters Volunteer firefighters Volunteer firefighters Volunteer firefighters	16 7 81 31 38 14	0.81 (0.46–1.32) 0.87 (0.35–1.79) 1.09 (0.87–1.36) 1.12 (0.76–1.59) 1.35 (0.95–1.85) 1.26 (0.69–2.12)	Age, calendar period	<i>Exposure assessment</i> <i>critique</i> : Good quality. Enhanced exposure assessment to differentiate exposure based on number of incidents for volunteer firefighters. Included specific incident types, but early exposure was extrapolated from more recent data. Volunteers mainly rural. <i>Strengths</i> : study of female firefighters; includes predominantly rural firefighters; ascertained exposure to number and type of incidents. <i>Limitations</i> : short length of follow-up; young
		Colon and rectum, incidence	who attended incidents No. of incidents [equivalent to ra Zero incidents Tertile 1 Tertile 2 Tertile 3 Trend-test <i>P</i> val	ate ratios]: 57 11 20 18	ers (RIR) 1 0.74 (0.39–1.41) 1.15 (0.69–1.92) 1.34 (0.78–2.29)		age at end of follow-up; probable healthy-worker bias; little information on confounders.

Reference, location enrolment/follow- up period, study design	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments
<u>Glass et al. (2019)</u>		Colon and	No. of fire incid	ents, all volu	inteers (RIR):	Age, calendar	
(cont.)		rectum, incidence	Zero incidents	58	1	period	
			Tertile 1	11	0.81 (0.43-1.55)		
			Tertile 2	19	1.33 (0.79–2.24)		
			Tertile 3	18	1.45 (0.85-2.47)		
			Trend-test P val	ue, 0.13			
		Colon and rectum, incidence	No. of structure (RIR):	e fire inciden	ts, all volunteers		
			Zero incidents	78	1		
			Tertile 1	6	1.20 (0.52–2.76)		
			Tertile 2	10	1.55 (0.80-3.00)		
		Colon and rectum, incidence	Tertile 3	12	2.08 (1.13-3.84)		
			Trend-test P val	ue, 0.26			
			No. of landscap (RIR):	e fire incider	nts, all volunteers		
			Zero incidents	65	1		
			Tertile 1	7	0.62 (0.28–1.36)		
			Tertile 2	17	1.18 (0.69–2.02)		
			Tertile 3	17	1.31 (0.77–2.24)		
			Trend-test P val	ue, 0.11			
		Colon and rectum, incidence	No. of vehicle fi (RIR):	re incidents,	all volunteers		
			Zero incidents	86	1		
			Tertile 1	7	1.98 (0.91-4.33)		
			Tertile 2	6	1.30 (0.57–2.97)		
			Tertile 3	7	1.59 (0.73-3.46)		
			Trend-test P val	ue, 0.73			

Reference, location enrolment/follow- up period, study design	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments
<u>Glass et al. (2019)</u> (cont.)		Breast, incidence	SIR: Volunteer firefighters Volunteer firefighters who attended incidents	349 142	0.96 (0.86–1.06) 0.93 (0.78–1.09)	Age, calendar period	
Glass et al. (2017) Australia Enrolment, date varied by agency (1998–2000)/ follow-up to 30 November 2011 (mortality) and 31 December 2010 (cancer incidence) Cohort	163 094; all male volunteer firefighters from five fire agencies enrolled on or after the date on which the agency's roll was complete and who had ever held an active firefighting role Exposure assessment method: ever volunteer firefighter, categorical volunteer duration (years) and era from service records; ever volunteer firefighter who attended an incident; tertiles of cumulative emergency incidents from contemporary incident data	Lip, oral cavity, and pharynx, incidence Lip, oral cavity, and pharynx, incidence Lip, oral cavity, and pharynx, incidence	SIR: All volunteers Volunteers who attended incidents Duration of serv [equivalent to ra > 3 mo to 10 yr 10–20 yr ≥ 20 yr Trend-test <i>P</i> val Duration of serv incidents: < 3 mo to 10 yr 10–20 yr ≥ 20 yr Trend-test <i>P</i> val	ate ratios]: 82 48 111 ue, 0.64 vice, volunte 41 33 86	0.71 (0.63–0.81) 0.70 (0.60–0.82) Inteers (RIR) 1 1.05 (0.73–1.50) 1.08 (0.79–1.46) Pers who attended 1 1.18 (0.74–1.87) 1.15 (0.76–1.72)	Age, calendar period	Exposure assessment critique: Good quality. Enhanced exposure assessment to differentiate exposure based on number of incidents. Included specific incident types, but early exposure was extrapolated from more recent data. Firefighters from rural or peri-urban areas. Strengths: includes predominantly rural firefighters; ascertained exposure to number and type of incidents. Limitations: short length of follow-up; young
		Oesophagus, incidence	SIR: All volunteers Volunteers who attended incidents	77 57	0.65 (0.52–0.82) 0.76 (0.57–0.98)		age at end of follow-up; probable healthy-worker bias; little information on confounders.

Reference, location enrolment/follow- up period, study design	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments
<u>Glass et al. (2017)</u>		Stomach,	SIR:			Age, calendar	
(cont.)		incidence	All volunteers	116	0.69 (0.57–0.83)	period	
			Volunteers who attended incidents	74	0.69 (0.55–0.87)		
	Colon and	SIR:					
		rectum, incidence	All volunteers	897	0.85 (0.80-0.91)		
			Volunteers who attended incidents	553	0.82 (0.76–0.89)		
		Colon and	Era of first servi	ce (SIR):			
		rectum, incidence	Pre-1970	283	0.87 (0.77-0.97)		
			1970-1994	336	0.83 (0.74-0.92)		
			1995 or after	278	0.86 (0.76-0.97)		
		Colon and	Duration of serv	vice, all volu	inteers (RIR):		
		rectum, incidence	> 3 mo to 10 yr		1		
			10–20 yr	147	0.87 (0.71–1.07)		
			≥ 20 yr	469	1.01 (0.86–1.18)		
			Trend-test P val				
		Colon and rectum, incidence	incidents (RIR):		eers who attended		
			< 3 mo to 10 yr		1		
			10–20 yr	91	0.98 (0.75–1.29)		
			$\geq 20 \text{ yr}$	354	1.09 (0.87–1.35)		
			Trend-test P val				
		Colon and rectum, incidence			v volunteers (RIR):		
		rectum, mendence	Baseline	517	1		
			Group 2 Group 3	32 4	1.35 (0.94–1.93) 0.35 (0.13–0.94)		
			Group 5	ч	0.55 (0.15-0.94)		

. . . . 20 (continued)

Reference, location enrolment/follow- up period, study design	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments
<u>Glass et al. (2017)</u>			No. of fire incid	ents, attende	ed by volunteers	Age, calendar	
(cont.)		rectum, incidence	(RIR):			period	
			Baseline	518	1		
		Group 2	33	1.33 (0.94–1.89)			
			Group 3	2	0.20 (0.05-0.80)		
	Colon and rectum, incidence	No. of structure volunteers (RIR		ts, attended by			
		Baseline	530	1			
		Group 2	21	1.43 (0.92–2.21)			
		Group 3	2	0.26 (0.07-1.05)			
	Colon and rectum, incidence	No. of landscap volunteers (RIR					
			Baseline	429	1		
			Group 2	96	1.25 (1.00-1.56)		
			Group 3	28	0.98 (0.67-1.44)		
		Colon and rectum, incidence	No. of vehicle fi volunteers (RIR				
			Baseline	519	1		
			Group 2	31	1.24 (0.87-1.79)		
		Colon, incidence	Group 3 SIR:	3	0.31 (0.10-0.98)		
		Colon, mendence	All volunteers	526	0.87 (0.80-0.95)		
			Volunteers	333	0.87 (0.78–0.97)		
			who attended				
			incidents				
		Rectum,	SIR:				
		incidence	All volunteers	301	0.90 (0.80-1.01)		
			Volunteers who attended incidents	181	0.84 (0.72–0.97)		

Table 2.9 (cont	tinued)						
Reference, location enrolment/follow- up period, study design	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments
Glass et al. (2017) (cont.)		Liver and bile ducts, incidence	SIR: All volunteers Volunteers who attended incidents	39 18	0.33 (0.23–0.45) 0.24 (0.14–0.37)	Age, calendar period	
		Pancreas, incidence	SIR: All volunteers	116	0.74 (0.61–0.89)		
			Volunteers who attended incidents	77	0.77 (0.61–0.97)		
		Breast, incidence	SIR: All volunteers Volunteers who attended incidents	12 12	0.83 (0.43–1.45) 1.29 (0.67–2.26)		

Reference, location enrolment/follow- up period, study design	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments		
Glass et al. (2016a)	30 057 full-time (17 394)	30 057 full-time (17 394) Lip	Lip, oral cavity,	Firefighter statu	s (SIR):		Age, calendar	Exposure assessment	
Australia	or part-time (12 663) paid	and pharynx,	Full-time	55	0.95 (0.71-1.23)	period	critique: Good quality.		
Enrolment,	male firefighters employed	incidence	Part-time	21	0.89 (0.55-1.36)		Enhanced exposure		
1976–2003/follow- up, 1976–2011	at one of eight Australian fire agencies for $\geq 3 \mod 3$		All	76	0.93 (0.73-1.16)		assessment to differentiate exposure based on		
(mortality), 1982– 2010 (incidence,	from start of personnel records (1976–2003,	Lip, oral cavity, and pharynx,	Duration of emp (RIR) [equivaler		ull-time firefighters tios]:		number of incidents, including specific incident		
except two states,	depending on agency)	incidence	> 3 mo to 10 yr	9	1		types. Included specific incident types, but early exposure was extrapolated from more recent data.		
2009)	Exposure assessment		10–20 yr	12	1.37 (0.58-3.29)				
Cohort	method: employed as		≥ 20 yr	34	1.42 (0.60-3.38)				
	a part- or full-time		Trend-test P val	ue, 0.46					
	firefighter for \geq 3 mo, categorical employment duration (years) and era	Lip, oral cavity, and pharynx,	l pharynx, (RIR):				Municipal firefighters. Strengths: internal analysi		
	from employment records;	incidence	> 3 mo to 10 yr	11	1		by exposure to number and type of incidents;		
	tertiles of cumulative		10–20 yr	6	1.50 (0.52-4.37)		ascertained cancer		
	emergency incidents and		≥ 20 yr	4	1.24 (0.35-4.42)		incidence.		
	type of incident attended		Trend-test P val	ue, 0.65			Limitations: healthy-		
	from contemporary	Lip, oral cavity,	Duration of emp	ployment (R	RIR):		worker hire bias; short		
	incident data	and pharynx,	> 3 mo to 10 yr	20	1		length of follow-up; young		
		incidence	10–20 yr	18	1.23 (0.64-2.36)		age at end of follow-up; little information on		
			$\geq 20 \text{ yr}$	38	1.11 (0.57-2.16)		potential confounders.		
			Trend-test P val	ue, 0.78			Potonia como anacio		
		Digestive (ICD-	Firefighter statu	s (SIR):					
		10, C15–C25),	Full-time	230	1.00 (0.87-1.14)				
		incidence	Part-time	85	0.99 (0.79–1.23)				
			All	315	1.00 (0.89-1.11)				
					- (

Reference, location enrolment/follow- up period, study design	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments
<u>Glass et al. (2016a)</u> (cont.)		Digestive (ICD- 10, C15–C25),	Duration of emp (RIR):	ployment, fu	ıll-time firefighters	Age, calendar period	
		incidence	> 3 mo to 10 yr	20	1		
			10–20 yr	27	0.78 (0.43-1.41)		
			≥ 20 yr	183	0.92 (0.56-1.53)		
			Trend-test P val	ue, 0.97			
		Digestive (ICD- 10, C15–C25), incidence	Duration of emp (RIR):	ployment, p	art-time firefighters		
			< 3 mo to 10 yr	25	1		
			10–20 yr	17	0.93 (0.48-1.80)		
			≥ 20 yr	43	1.12 (0.58–2.13)		
			Trend-test P val	ue, 0.70			
		Digestive (ICD-	Duration of emp	ployment (R			
		10, C15–C25),	< 3 mo to 10 yr	45	1		
		incidence	10–20 yr	44	0.75 (0.49–1.15)		
			≥ 20 yr	226	0.88 (0.61-1.26)		
			Trend-test P val	ue, 0.73			
		Digestive (ICD- 10, C15–C25), incidence	No. of incidents firefighters (RIR		v full-time		
			Tertile 1	20	1		
			Tertile 2	18	0.95 (0.50-1.81)		
			Tertile 3	28	0.87 (0.49–1.55)		
			Trend-test P val	ue, 0.63			

Reference, location enrolment/follow- up period, study design	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments
<u>Glass et al. (2016a)</u> (cont.)		Digestive (ICD- 10, C15-C25),	No. of fire incid firefighters (RI		d by full-time	Age, calendar period	
		incidence	Tertile 1	15	1	-	
			Tertile 2	18	1.44 (0.72-2.87)		
			Tertile 3	33	1.28 (0.69-2.38)		
			Trend-test P va	lue, 0.50			
		Digestive (ICD- 10, C15–C25),	No. of structur time firefighter		ts attended by full-		
		incidence	Tertile 1	17	1		
			Tertile 2	18	1.23 (0.63-2.40)		
			Tertile 3	31	1.07 (0.59–1.95)		
			Trend-test P va	lue, 0.88	. ,		
		Digestive (ICD- 10, C15–C25), incidence	No. of landscap time firefighter		nts attended by full-		
			Tertile 1	14	1		
			Tertile 2	24	1.87 (0.96-3.62)		
			Tertile 3	28	1.32 (0.69-2.52)		
			Trend-test P va				
		Digestive (ICD- 10, C15–C25),	No. of vehicle f time firefighter				
		incidence	Tertile 1	15	1		
			Tertile 2	18	1.54 (0.77-3.09)		
			Tertile 3	33	1.48 (0.80-2.73)		
			Trend-test P va	lue, 0.25			
		Oesophagus,	Firefighter stat	us (SIR):			
		incidence	Full-time	12	0.76 (0.39-1.33)		
			Part-time	5	0.85 (0.28-1.98)		
			All	17	0.78 (0.46-1.26)		
		Stomach,	Firefighter stat	us (SIR):	. ,		
		incidence	Full-time	24	0.98 (0.63-1.46)		
			Part-time	9	1.03 (0.47–1.96)		
			All	33	0.99 (0.68–1.39)		

Reference, location enrolment/follow- up period, study design	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments
<u>Glass et al. (2016a)</u>		Colon and	Firefighter statu	s (SIR):		Age, calendar	
(cont.)		rectum, incidence	Full-time	157	1.09 (0.92-1.27)	period	
			Part-time	57	1.06 (0.80-1.37)		
			All	214	1.08 (0.94-1.23)		
		Colon and rectum, incidence	Duration of emp (RIR):	ployment, fu	ıll-time firefighters		
			> 3 mo to 10 yr	14	1		
			10–20 yr	20	0.79 (0.39-1.57)		
			≥ 20 yr	123	0.91 (0.50-1.66)		
		Colon and rectum, incidence	Duration of emp (RIR):	ployment, p			
			< 3 mo to 10 yr	16	1		
			10–20 yr	11	0.96 (0.42-2.19)		
			≥ 20 yr	30	1.32 (0.59-2.92)		
			Trend-test P val	ue, 0.45			
		Colon and	Duration of emp	oloyment (R			
		rectum, incidence	< 3 mo to 10 yr	30	1		
			10–20 yr	31	0.80 (0.48-1.34)		
			≥ 20 yr	153	0.97 (0.62-1.51)		
			Trend-test P val	ue, 0.89			
		Colon and rectum, incidence	No. of incidents attended by full-time firefighters (RIR):				
			Tertile 1	16	1		
			Tertile 2	15	0.98 (0.48-1.99)		
			Tertile 3	23	0.84 (0.44-1.59)		
			Trend-test P val	ue, 0.56			

Reference, location enrolment/follow- up period, study design	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments
<u>Glass et al. (2016a)</u> (cont.)		Colon and rectum, incidence	No. of fire inci- firefighters (RI		d by full-time	Age, calendar period	
			Tertile 1	12	1	1	
			Tertile 2	13	1.28 (0.58-2.83)		
			Tertile 3	29	1.30 (0.66-2.56)		
			Trend-test P va	alue, 0.47			
		Colon and rectum, incidence		re fire inciden	ts attended by full-		
			Tertile 1	15	1		
			Tertile 2	13	0.97 (0.46-2.05)		
			Tertile 3	26	0.95 (0.50-1.80)		
			Trend-test P va	alue, 0.88			
		Colon and rectum, incidence	No. of landsca time firefighter		nts attended by full-		
			Tertile 1	10	1		
			Tertile 2	21	2.26 (1.06-4.82)		
			Tertile 3	23	1.42 (0.67-2.99)		
			Trend-test P va	alue, 0.56			
		Colon and rectum, incidence	No. of vehicle t time firefighter		attended by full-		
			Tertile 1	13	1		
			Tertile 2	13	1.28 (0.59-2.77)		
			Tertile 3	28	1.34 (0.69-2.60)		
			Trend-test P va	alue, 0.40			
		Liver and bile	Firefighter stat	us (SIR):			
		ducts, incidence	Full-time	8	0.52 (0.23-1.03)		
			Part-time	4	0.64 (0.17–1.64)		
			All	12	0.56 (0.29-0.97)		
		Pancreas,	Firefighter stat	us (SIR):			
		incidence	Full-time	22	1.07 (0.67–1.62)		
			Part-time	7	0.93 (0.37–1.91)		
			All	29	1.03 (0.69–1.48)		

Reference, location enrolment/follow- up period, study design	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments
<u>Glass et al. (2016a)</u>		Breast, incidence	Firefighter stat	tus (SIR):		Age, calendar	
(cont.)			Full-time	5	2.49 (0.81-5.82)	period	
			Part-time	1	1.31 (0.03–7.32)		
			All	6	2.17 (0.80-4.72)		
<u>Glass et al. (2016b)</u>	614; all male (611) and	Digestive (ICD-	Risk of chroni	c exposure (S	IR):	Age, calendar	Exposure assessment
Victoria, Australia Enrolment, 1971–1999/follow- up, 1980–2011 (mortality), 1982– 2012 (incidence) Cohort	female (3) employed and volunteer Country Fire Authority trainers and a group of paid [career] Country Fire Authority firefighters who trained at the Fiskville site from 1971 to 1999; all analyses limited to men as no deaths or cancers were observed among women Exposure assessment method: employed or volunteer firefighter trainers and career firefighters who trained at training facility for any period of time from human resource records, categorized into risk of low, medium, and high chronic exposure to smoke and other agents based on job assignment	10, C15–C25), incidence	Low Medium High	0 9 3	0 (NR): 1.25 (0.57–2.38) 1.02 (0.21–2.99)	period	<i>critique</i> : Satisfactory quality. Incorporated categorical level of exposure into assessment for each type of firefighter Volunteers mainly rural, paid [career] firefighters were municipal. <i>Strengths</i> : included firefighter instructors with high potential exposure to smoke and other hazardous agents; assesse exposure based on job assignment. <i>Limitations</i> : low number of cases; young age at end of follow-up.

Reference, location enrolment/follow- up period, study design	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments
Bates et al. (2001)	4305, comprising all male Oesophagus,	Follow-up peri	od (SIR):		Age, calendar	Exposure assessment	
New Zealand	(4221) and female (84)	incidence	1977-1996	3	1.67 (0.3-4.9)	period	critique: Satisfactory
Enrolment, 1977	firefighters (paid [career]		1990-1996	2	1.80 (0.2-6.5)		quality. Heterogeneity of
through June 1995/ follow-up, 1977–	and volunteer) employed as a career firefighter	Stomach,	Follow-up peri	od (SIR):			direct firefighter exposure within job classification.
1995 (mortality),	for ≥ 1 yr and who	incidence	1977-1996	3	0.76 (0.2–2.2)		May include urban
1977–1996	for ≥ 1 yr and who also worked as a career		1990-1996	2	0.89 (0.1-3.2)		[municipal] and rural
(incidence)	firefighter for ≥ 1 day	Stomach,	SMR:				firefighters.
Cohort		95; mortality o men	Firefighters vs male New Zealand population	3	1.16 (0.2–3.4)		Strengths: ascertained both incidence and mortality outcomes <i>Limitations</i> : little information on confounders; significant loss to follow-up; low number of cases in stratified analyses.
	Exposure assessment	Colon, incidence	Follow-up peri	od (SIR):			
	method: ever employed		1977–1996	7	0.60 (0.2–1.2)		
	and categorical duration		1990–1996	4	0.58 (0.2–1.5)		
	of employment (years)	Colon, incidence	Duration of pa				
	from employment records	Colon, mendence	0–10 yr	1	0.41 (0.0–2.3)		
			11–20 yr	1	0.46 (0.0–2.6)		
			> 20 yr	5	1.37 (0.4-3.2)		
			Trend-test <i>P</i> va		1.57 (0.4-5.2)		
		Colon, incidence			teer service (SIR):		
		Colon, mendence	0–10 yr	1	0.82 (0.0-4.6)		
			11–20 yr	1	0.58 (0.0-3.3)		
			> 20 yr	5	0.92 (0.3–2.1)		
			Trend-test <i>P</i> va		0.92 (0.9-2.1)		
		Colon, mortality	SMR:	iuc, 0.01			
			Firefighters vs male New Zealand population	6	1.19 (0.4–2.6)		

Reference, location enrolment/follow- up period, study design	Population size, description, exposure assessment method	Cancer type (histopathology), incidence or mortality	Exposure category or level	Exposed cases or deaths	Risk estimate (95% CI)	Covariates controlled	Comments
Bates et al. (2001)		Rectum,	Follow-up peri	od (SIR):		Age, calendar	
(cont.)		incidence	1977-1996	9	1.15 (0.5–2.2)	period	
			1990-1996	5	1.08 (0.3-2.5)		
		Rectum,	Duration of pa	id service (SI	IR):		
		incidence	0–10 yr	2	1.22 (0.1-4.4)		
			11–20 yr	2	1.38 (0.2–5.0)		
			> 20 yr	4	1.61 (0.4–4.1)		
			Trend-test P va	lue, 0.74			
		Rectum,	Duration of pa	id and volun	teer service (SIR):		
		incidence	0–10 yr	1	1.23 (0.0-6.8)		
			11–20 yr	2	1.75 (0.2–6.3)		
			> 20 yr	5	1.35 (0.4-3.1)		
			Trend-test P va	lue, 0.97			
		Rectum,	SMR:				
	mortality	mortality	Firefighters vs male New Zealand population	4	1.21 (0.3–3.1)		
		Pancreas,	Follow-up perie	od (SIR):			
		incidence	1977–1996	3	1.28 (0.3-3.7)		
			1990-1996	3	2.17 (0.4-6.4)		

9/11, World Trade Center disaster, 11 September 2001; CI, confidence interval; FDNY, Fire Department of the City of New York; HCC, hepatocellular carcinoma; HR, hazard ratio; HWSE, healthy-worker survivor effect; ICD, International Classification of Diseases; IDR, incidence density ratio; LRT, likelihood ratio test; mo, month; NJ, New Jersey; NR, not reported; PMR, proportionate mortality ratio; RCS, restricted cubic splines; RIR, relative incidence ratio; RR, rate ratio; SIR, standardized incidence ratio; SMR, standardized mortality ratio; SRR, standardized rate ratio; US, United States; vs, versus; WTC, World Trade Center; yr, year.

et al., 1992a, 1994; Guidotti, 1993; Aronson et al., 1994; Tornling et al., 1994; Bates et al., 2001; Zeig-Owens et al., 2011; Ahn et al., 2012; Daniels et al., 2014, 2015; Ahn & Jeong, 2015; Glass et al., 2016a, b, 2017, 2019; Moir et al., 2016; Petersen et al., 2018a, b; Kullberg et al., 2018; Bigert et al., 2020; Pinkerton et al., 2020; Marjerrison et al., 2022b). Two of these studies were from Asia, six from Europe, eleven from North America, and five from Oceania. Results for other cancer sites not described here or elsewhere in Section 2 were considered uninformative to the evaluation (e.g. cancer of the bone, eye).

(a) Cancers of the digestive tract

Ahn & Jeong (2015) conducted a cohort mortality study among 33442 professional [career] emergency responders in the Republic of Korea. Emergency responders had been employed between 1980 and 2007, and mortality follow-up took place from 1992 through 2007. Below, cancer mortality results among the subcohort of firefighters (n = 29 453, 88% of total cohort) are reported. With the male population of the Republic of Korea as the referent, the overall SMRs were 0.63 (95% CI, 0.43-0.88) for stomach cancer, 0.65 (95% CI, 0.34-1.14) for colorectal cancer, and 0.55 (95% CI, 0.41-0.73) for cancer of the liver and intrahepatic bile duct. The external comparisons showed no associations with longer duration of employment for any of these sites. In internal analyses of employment duration, for which firefighters employed for < 10 years and other emergency responders served as reference groups, age- and calendar year-adjusted estimates above unity for longer employment durations were seen for colorectal cancer (ARR [adjusted rate ratio] for \geq 10 years to < 20 years, 1.40; 95% CI, 0.33-5.87; and ARR for ≥ 20 years, 1.29; 95% CI, 0.27–6.08) and for cancer of the liver and intrahepatic bile ducts $(ARR \text{ for } \ge 20 \text{ years}, 1.82; 95\% \text{ CI}, 0.85-3.90).$

In the same cohort as described above, <u>Ahn et al. (2012)</u> conducted a cancer incidence

study among professional [career] emergency responders in the Republic of Korea with cancer incidence follow-up from 1996 through 2007. National male cancer incidence rates served as the referent, and analyses were conducted overall and by duration of employment (< 10 versus \geq 10 years). SIRs below unity were seen for cancers of the oesophagus, stomach, liver and intrahepatic bile ducts, and pancreas, but estimates were imprecise. In internal comparisons with non-firefighter emergency responders as the referent, SRRs were elevated but imprecise for cancers of the stomach and liver and intrahepatic bile ducts (SRR, 1.09; 95% CI, 0.53-2.25; and SRR, 5.10; 95% CI, 0.71-36.85; respectively). The overall SIR for colorectal cancer was elevated (SIR, 1.27; 95% CI, 1.01-1.59) but did not increase with longer duration of employment.

Marjerrison et al. (2022b) compared cancer incidence and mortality in a cohort of 3881 male professional [career] firefighters with cancer rates in the general population in Norway. The cohort included mostly full-time firefighters employed between 1950 and 2019, with past or present employment in positions entailing active firefighting duties. The follow-up period for both cancer incidence and mortality analyses was from 1960 through 2018. For oesophageal cancer among those ever employed as a firefighter, both incidence and mortality rates were greater than expected (SIR, 1.55; 95% CI, 0.83-2.66; and SMR, 1.82; 95% CI, 0.97-3.11). The highest risks were seen in the earliest follow-up period (up to and including 1984) and oldest age at diagnosis (\geq 70 years), but estimates were imprecise. Stomach cancer risk was moderately elevated, with an imprecise risk estimate (SIR, 1.35; 95% CI, 0.95–1.85). Risk of colon cancer was elevated, with an SIR of 1.24 (95% CI, 0.98-1.56); the SMR of 1.26 (95% CI, 0.87-1.76) was of similar magnitude, but less precise. Incidence and mortality of colon cancer was elevated in the earliest follow-up period: SIR, 2.02 (95% CI, 1.15–3.28); and SMR, 2.33 (95% CI, 1.12-4.29). Smaller and less precise

excess risks were seen for follow-up in 1985–1994. Overall risk of rectal cancer was at the expected level (SIR, 0.96; 95% 0.68–1.33). SIR for overall risk of cancer of the liver, gallbladder, and biliary ducts was 1.31 (95% CI, 0.68–2.29), and SMR was 1.56 (95% CI, 0.78–2.79). For analyses by calendar period of follow-up, risk was elevated in the earliest period (SIR, 3.62; 95% CI, 1.17–8.44), based on five cases only. Pancreatic cancer incidence and mortality were slightly above unity, but estimates were imprecise (SIR, 1.22; 95% CI, 0.78–1.81; and SMR, 1.09; 95% CI, 0.67–1.68).

Bigert et al. (2020) investigated cancer incidence in a cohort of 8136 male firefighters in Sweden. Employment information was ascertained from national decennial censuses between 1960 and 1990. Cancer incidence data were ascertained from the Swedish Cancer Registry with follow-up from 1961 through 2009. With the national male general population as the referent, the overall SIR for stomach cancer was 1.08 (95% CI, 0.83–1.39). Analysis of duration of employment was performed for stomach cancer, but no increasing risk with longer employment duration was seen (P for trend, 0.75). The SIR for stomach cancer was highest in the earliest calendar follow-up period from 1961 through 1975 (SIR, 1.85; 95% CI, 1.06-3.00). The overall SIR for pancreatic cancer was 1.17 (95% CI, 0.85-1.58). No excess risk of cancers of the oesophagus (SIR, 0.71; 95% CI, 0.38–1.21), colon (SIR, 1.01; 95% CI, 0.82–1.23), rectum (SIR, 0.89; 95% CI, 0.69–1.14), or liver and bile ducts (SIR, 0.89; 95%) CI, 0.50–1.47) was observed.

A cancer incidence study in a cohort of 1080 male firefighters in Stockholm, Sweden, provided information on the risk of cancers of the digestive system (Kullberg et al., 2018). Firefighters were identified through annual enrolment records from 15 fire stations and had worked for \geq 1 year between 1931 and 1983. As an update to a previous study (Tornling et al., 1994), this study added 26 years of cancer incidence follow-up from 1958 through 2012 in the Swedish Cancer Registry.

With the male general population of Stockholm County as the referent, the overall SIR for stomach cancer for the full follow-up period (1958–2012) was 1.89 (95% CI, 1.25–2.75), with the extended follow-up period (1987–2012) contributing 7 of the 27 total cases, yielding an SIR of 1.35 (95% CI, 0.54–2.78). Stomach cancer risk decreased with increasing age (*P* for trend, 0.07) but did not vary with duration of employment (*P* for trend, 0.19) or period of first employment (*P* for trend, 0.69). The overall SIR for rectum cancer was 1.25 (95% CI, 0.74–1.98), but was somewhat higher for the follow-up period 1958–1986 (SIR, 1.74; 95% CI, 0.83–3.19). Rates for cancers of the oesophagus (SIR, 0.99; 95% CI, 0.32-2.30), pancreas (SIR, 1.06; 95% CI, 0.51–1.94), liver and bile ducts (SIR, 0.79; 95% CI, 0.32-1.63), and colon (SIR, 0.86; 95% CI, 0.53–1.34) did not deviate from expected values.

In the original analysis of this cohort, <u>Torn-</u> ling et al. (1994) investigated both cancer mortality and incidence in a slightly larger population (n = 1116). Follow-up was from 1951 through 1986 for mortality and from 1958 through 1986 for cancer incidence. Comparisons were made with the regional male general population. For each firefighter, exposure to fire events was assessed using reports of fires fought by the Stockholm fire brigade between 1933 and 1983. Overall, the risk of stomach cancer mortality was only slightly increased, and the estimate was imprecise (SMR, 1.21; 95% CI, 0.62–2.11). Both stomach cancer mortality and incidence increased with greater number of fire responses (SMR, 1.96; 95% CI, 0.90-3.72; and SIR, 2.64; 95% CI, 1.36-4.61, respectively, for > 1000 fires). The numbers of colon cancer deaths and cases were essentially as expected, whereas rectum cancer mortality was elevated (SMR, 2.07; 95% CI, 0.89–4.08). For liver cancer, an elevated mortality rate was observed, although the estimate was imprecise (SMR, 1.49; 95% CI, 0.41–3.81). Imprecise estimates for pancreatic cancer mortality were seen (SMR, 0.84; 95% CI, 0.27-1.96) based on five deaths.

[The Working Group noted that the exposure assessment method was a strength.]

Petersen et al. (2018a) studied cancer incidence in a cohort of 9061 male full-time, parttime, and volunteer firefighters employed between 1964 and 2004 in Denmark. Follow-up was from 1968 through 2014, and three alternative comparison groups were used in the overall analyses: the general Danish population; a sample of the working population; and a cohort of military employees. For cancers of the colon, rectum, and pancreas, additional analyses by employment type (e.g. full-time, other), era of first employment, job function (e.g. regular, specialized), age at first employment, and duration of employment were performed with the general population as referent. For cancers of the oesophagus and the stomach, comparisons with the cohort of military employees showed the most elevated rates among firefighters, with SIRs of 1.18 (95% CI, 0.77-1.81) and 1.26 (95% CI, 0.87-1.84), respectively. Risk of cancer of the colon, rectum, and pancreas did not vary with choice of reference group. The overall risk of colon cancer was consistently below the expected value in all comparisons (SIR, 0.73; 95% CI, 0.57-0.95; relative to the general population), and in all strata of age at first employment and duration of employment. The overall risks of cancers of the rectum and pancreas were above the expected values, with SIRs of 1.22 (95% CI, 0.95-1.55) and 1.20 (95% CI, 0.86–1.68), respectively, with the general population as the referent. Rectal cancer risk was elevated among those first employed before 1970 (SIR, 1.47; 95% CI, 1.06-2.02), and numbers were higher than expected for the group of specialized firefighters (SIR, 1.72; 95% CI, 0.77-3.84) and for those employed for \geq 20 years (SIR, 1.32; 95% CI, 0.94-1.85). For pancreatic cancer, elevated risk was seen for full-time employees (SIR, 1.54; 95% CI, 1.05–2.25), for first employment at < 25 years (SIR, 1.68; 95% CI, 1.12-2.53), and for an employment duration of < 1 year (SIR, 1.79; 95% CI, 1.05-3.01). The SIR for liver cancer was elevated

in firefighters compared with military personnel (SIR, 1.17; 95% CI, 0.69–1.98), but was at unity compared with other reference populations.

Cancer mortality was investigated in the same cohort of Danish firefighters described above (Petersen et al., 2018b). An expanded study population of 11 775 male firefighters were followed for mortality in the Danish national death registry from 1970 through 2014. With the military as the referent, the stomach cancer mortality rate was elevated among full-time firefighters (SMR, 1.96; 95% CI, 1.22-3.16) and in all strata of employment duration, specifically for < 1 year of employment (SMR, 2.13; 95% CI, 1.07-4.26). Mortality from rectal cancer and "other intestinal cancers" (colon, rectosigmoid, and small intestine) was not different from unity. There was also no evidence of a trend between employment duration and mortality from "other intestinal cancer" or cancer of the rectum.

Moir et al. (2016) and Zeig-Owens et al. (2011) reported results on the incidence of specific cancers of the digestive tract among a cohort of firefighters employed at the FDNY who were present at the WTC disaster site. The studies used different criteria for inclusion and exclusion, and cohorts comprised 11 457 (Moir et al., 2016) and 9853 (Zeig-Owens et al., 2011) FDNY firefighters, respectively. Moir et al. (2016) compared cancer incidence among WTC-exposed firefighters with that in 8220 non-WTC exposed firefighters employed at the same time in cohorts from San Francisco, Chicago, and Philadelphia (combined into the CFHS, and described in Pinkerton et al., 2020). Cancer incidence follow-up was conducted in state registries from 11 September 2001 through 2009. The RR for colon cancer among the WTC-exposed firefighters when considering the whole follow-up period was 0.73 (95% CI, 0.33–1.59). In their first follow-up of this cohort, Zeig-Owens et al. (2011) compared cancer incidence for WTC-exposed and unexposed personyears in the FDNY cohort with that in the US male general population from 1996 through 2008. The ratios of SIRs for exposure versus non-exposure were elevated for cancers of the oesophagus (SIR ratio, 1.32; 95% CI, 0.12–14.53), stomach (SIR ratio, 1.82; 95% CI, 0.44–7.49), colon (SIR ratio, 1.50; 95% CI, 0.69–3.27), and pancreas (SIR ratio, 2.52; 95% CI, 0.28–22.59), but estimates were imprecise with wide confidence intervals. [The Working Group noted that the SIR ratio is not a standard epidemiological effect measure.]

Three studies of both cancer mortality and incidence have been conducted among municipal career firefighters in the CFHS employed at fire departments in San Francisco, Chicago, and Philadelphia, USA. Most recently, <u>Pinkerton et al.</u> (2020) updated previous analyses by Daniels et al. (2014) with cancer mortality follow-up from 1950 extended through 2016. Compared with that in the US general population, risk of oesophageal cancer was elevated in all municipal fire departments, with an overall SMR of 1.31 (95% CI, 1.10-1.55), but no consistent associations with fire-response exposure metrics in internal regression analyses were observed. For stomach cancer, SMRs above unity were seen in the San Francisco and Chicago subcohorts (SMR for San Francisco subcohort, 1.13; 95% CI, 0.75-1.65; and SMR for Chicago subcohort, 1.15; 95% CI, 0.88-1.48), but estimates were somewhat imprecise. In the fully adjusted regression models, the HRs for stomach cancer according to the number of exposed days (8700 versus 2500 exposed-days), fire-runs (8800 versus 2100 runs), and fire-hours (2300 versus 600 hours), all incorporating a 10-year lag period, were 1.75 (95% CI, 0.74-4.53), 1.25 (95% CI, 0.76–1.95), and 1.45 (95% CI, 0.71–2.87), respectively. Risk of cancer of the small intestine and colon combined was elevated overall (SMR, 1.27; 95% CI, 1.14-1.40) in external comparisons, driven by elevated risks in the Chicago and Philadelphia subcohorts, but the exposureresponse analyses for colon cancer (separately) showed lower HRs with higher exposure. SMRs for cancer of the small intestine and colon were specifically elevated among firefighters of White

race and age \geq 65 years. Mortality from cancer of the rectum was elevated in the San Francisco and Chicago subcohorts, with an overall SMR of 1.32 (95% CI, 1.07–1.61), and among White firefighters only, but differences were not observed between those aged < 65 years or > 65 years. In internal regression analyses, a higher number of exposed days and fire-runs was associated with a lower risk of rectal cancer (HR for exposed days, 0.49; 95% CI, 0.21–1.19; and HR for fire-runs, 0.36; 95% CI, 0.16–0.75), in the fully adjusted model).

An earlier study of a subset of 19 309 firefighters from the same CFHS cohort examined internal exposure-response associations with both cancer mortality and incidence with follow-up to the end of 2009 (Daniels et al., 2015). Methods were similar to those used in Pinkerton et al. (2020); however, results in the present study were not adjusted for employment duration. No consistent pattern of risk associated with higher exposure was observed for cancer of the oesophagus. For cancers of the colon and rectum combined, HRs associated with cancer incidence were below unity for all exposure metrics: the HRs were 0.92 (95% CI, 0.84-1.01), 0.89 (95% CI, 0.72–1.09) and 0.78 (95% CI, 0.63-1.04) for exposed-days, fire-hours, and fireruns, respectively.

An additional study in the CFHS cohort investigated cancer incidence among 29 993 municipal career firefighters and reported external and internal comparison analyses with follow-up to the end of 2009 (Daniels et al., 2014). The methods were similar to those used in the study by Pinkerton et al. (2020). Cancer incidence follow-up was conducted in state cancer registries relevant to each fire department to the end of 2009, with start years varying between 1985 and 1988. With the US general population as the referent, excess risks were observed overall for cancers of the oesophagus (1.62; 95% CI, 1.31–2.00), stomach (SIR, 1.15; 95% CI, 0.93-1.40), colon (SIR, 1.21; 95% CI, 1.09-1.34), and rectum (SIR, 1.11; 95% CI, 0.95-1.30).

Demers et al. (1994) studied cancer incidence in a cohort of 2447 male municipal firefighters who had been employed for ≥ 1 year between 1944 and 1979 in Seattle and Tacoma, Washington, USA. Firefighters were followed for cancer from 1974 through 1989 in the regional SEER cancer registry, using residential history information to reduce loss to follow-up. Duration of active-duty employment in direct firefighting positions was ascertained from employment records in the Seattle subcohort. With the local general male population as the referent, there was no evidence of an overall excess of cancers of the oesophagus, stomach, colon, rectum, or pancreas among firefighters. For colon cancer, risk increased monotonically with longer duration of exposed employment, with an IDR for firefighters with ≥ 30 years of employment of 1.8 (95% CI, 0.3-11.6) compared with firefighters employed < 10 years. Also, compared with incidence rates among police officers, colon cancer risk in the group of firefighters with the longest duration of employment (\geq 30 years) was elevated but imprecise (RR, 2.0; 95% CI, 0.5-8.0). [The Working Group noted that trend tests were not conducted, and that for many analyses the number of cancer cases was small.]

In a cohort study of cancer mortality, Demers et al. (1992a) included firefighters employed in Portland, Oregon, in addition to the Seattle and Tacoma cohorts mentioned above. The mortality follow-up period was from 1945 through 1989. Mortality rates for the US general population and for police officers from the same cities served as referents. Mortality was examined overall and in stratified analyses by years of fire combat exposure (in Seattle and Portland firefighters only), years since first employment as a firefighter, and age at risk. For colon cancer, the overall SMR was 0.85 (95% CI, 0.54-1.26) for firefighters compared with US men, but above unity when comparing with local police (IDR, 1.58; 95% CI, 0.73–3.43), although this estimate was imprecise. No association with duration of exposed employment,

time since first employment, or age at risk was observed. [Trend tests were not reported.] SMRs for rectal, oesophageal, and pancreatic cancers were below unity, but estimates were imprecise with wide confidence intervals.

Vena & Fiedler (1987) investigated cancer mortality in a cohort of 1867 White male municipal firefighters who had been employed between 1950 and 1979 in Buffalo, USA. Mortality follow-up was from 1950 through 1979, and comparisons were made with mortality rates among US White men in the general population. Overall, more deaths than expected were seen among firefighters for cancers of the oesophagus (SMR, 1.34; 95% CI, 0.27-3.91; 3 deaths), stomach (SMR, 1.19; 95% CI, 0.48-2.46; 7 deaths), and rectum (SMR, 2.08; 95% CI, 0.83–4.28; 7 deaths). For colon cancer, the SMR was elevated overall (1.83; 95% CI, 1.05-2.97) and in the categories with the longest duration of employment (SMR for employment \geq 40 years, 4.71; 95% CI, [2.2–8.9]), longest latency (SMR for \geq 50 years since first employment, 2.85; 95% CI, [0.7-7.4]), and most recent period of death (SMR for death during 1970-1979, 2.20; 95% CI, [1.1-4.0]). For pancreatic cancer, mortality was close to unity (SMR, 0.89; 95% CI, 0.49-1.49). [This study was limited by the small numbers of cases.]

Feuer & Rosenman (1986) conducted a PMR study that included 263 deceased firefighters from New Jersey, USA, who died in 1974-1980. Comparisons were made with the White male general populations of the USA and of New Jersey, as well as New Jersey White police officers. Mortality from digestive tract cancers (ICD-8, 150–159, i.e. cancers of the oesophagus, stomach, small intestine, large intestine, rectum and rectosigmoid junction, liver and intrahepatic bile ducts, gallbladder and bile ducts, pancreas, peritoneum and retroperitoneal tissue, and unspecified digestive organs) was higher than expected (PMR, 1.45; 95% CI, [0.91–2.20]) compared with that in US White men, although the estimate was attenuated when compared with New Jersey men, and below unity with New Jersey police officers as the referent. Analyses by duration of employment or time since first employment did not indicate any mortality trends.

Aronson et al. (1994) investigated cancer mortality in a cohort of 5414 male career firefighters employed for ≥ 6 months in Toronto, Canada (n = 5414). Firefighters had been employed between 1950 and 1989, and mortality follow-up was conducted in a national mortality database from 1950 through 1989. With the male general population of Ontario as the referent, there was no evidence of an increased risk of cancers of the oesophagus, stomach, or colon. The overall SMR for rectal cancer mortality was 1.71 (95% CI, 0.91–2.93), and risk increased with time since first employment. The overall SMR for cancer of the pancreas was 1.40 (95% CI, 0.77-2.35), but no consistent pattern was seen with time since first employment or duration of employment.

Guidotti (1993) examined cancer mortality in a cohort of 3328 firefighters who had been employed between 1927 and 1987 in Edmonton and Calgary, Canada. Mortality follow-up was conducted in both provincial and national sources from 1927 through 1987. External comparisons were made with the male general population of Alberta. SMRs were stratified according to employment characteristics, and an exposure index (with values of 0, > 0 to < 1, 1–9, and \geq 10) was created on the basis of years of firefighter service weighted by an estimate of the relative time spent in proximity to fires according to job classification. With the general population as the referent, mortality was not elevated overall for stomach cancer (SMR, 0.81; 95% CI, 0.30-1.76). For cancer of the colon and rectum combined, the overall SMR was 1.61 (95% CI, 0.88–2.71) based on 14 deaths. Analyses stratified by year of cohort entry (first employment), latency, the exposure index value, and latency by exposure index generally yielded unstable estimates with wide confidence intervals. Colorectal cancer mortality was highest in

the latency period 20–29 years after first employment, with an SMR of 2.68 (95% CI, [0.98–5.93]); 5 deaths), and in the exposure index group "1–9" (SMR, 4.58; 95% CI, [1.86–9.53]; 6 deaths). The SMR for pancreatic cancer was elevated at 1.55 (95% CI, 0.50–3.62), although the estimate was based on only five deaths. Three deaths from pancreatic cancer occurred \geq 50 years after first employment (SMR, 7.16; 95% CI, [1.82–19.4]). [The Working Group noted that the number of cases was low for many of the comparisons, and estimates were imprecise.]

<u>Glass et al. (2019)</u> investigated cancer incidence in a cohort of female volunteer firefighters (n = 37 962). Cancer incidence follow-up was conducted in a national cancer registry from 1982 through 2010. Work history information describing the number and type of incidents attended was ascertained from fire agency personnel records. The female general population of Australia served as the referent in external comparison analyses. For all volunteers, the overall SIRs for cancers of the colon and rectum were 1.09 (95% CI, 0.87-1.36) and 1.35 (95% CI, 0.95-1.85), respectively. Results were similar in separate analyses restricted to volunteers who had attended incidents. In internal regression analyses, the RIR [equivalent to rate ratio] for colorectal cancer in the highest tertile of total number of incidents attended was 1.34 (95% CI, 0.78-2.29). For structure fire incidents specifically, the corresponding RIR was 2.08 (95% CI, 1.13-3.84).

Using the same methods as in the study of female firefighters, cancer incidence was also investigated in a parallel cohort of 163 094 male volunteer firefighters in Australia (Glass et al., 2017). With the male general population of Australia as the referent, the overall SIRs among firefighters who had attended incidents were lower than expected for cancers of the oesophagus, stomach, pancreas, and liver. SIRs for cancers of the colon and rectum overall and by period of first employment were below unity, and no trends were seen with period of employment or duration of service. Internal regression analyses by number and type of incident attended generally showed the highest estimates among firefighters in the intermediate tertile of exposure group, whereas risk estimates were below those of the referent in the highest tertile group. For all fire incidents, the RIR [equivalent to rate ratio] was 1.33 (95% CI, 0.94–1.89) in the intermediate group and 0.20 (95% CI, 0.05–0.80) in the highest group. In the analysis of vehicle fire incidents, the highest RIR was found in the intermediate group (RIR, 1.24; 95% CI, 0.87–1.79). Estimates in the highest tertile of exposure were imprecise because of small numbers of cases in that group.

Using similar methods as in the two studies of volunteer firefighters, mortality and cancer incidence were studied in a cohort of 30 057 paid full-time and part-time firefighters in Australia (Glass et al., 2016a). Included firefighters had workedbetween 1976 and 2003 and were primarily municipal or semi-metropolitan firefighters. Cancer incidence follow-up was conducted in a national registry to the end of 2010. With the male general population of Australia as the referent, SIRs among all firefighters were at unity or below for cancers of the oesophagus, stomach, and pancreas. Overall, risk of cancers of the digestive tract combined (ICD-10, C15-C25, i.e. cancers of the oesophagus, stomach, small intestine, colon, rectum and rectosigmoid junction, anus and anal canal, liver and intrahepatic bile ducts, gallbladder, biliary tract, and pancreas) was at the expected level, and estimates were similar among full-time and part-time firefighters. In internal regression analyses, risk of cancers of the digestive tract did not increase by duration of employment, and no positive trends were seen with increasing number or type of incident attended. Risk of colorectal cancer was similar among fulltime and part-time firefighters (overall SIR, 1.08; 95% CI, 0.94-1.23). No association with duration of employment was seen for either group in internal analyses. Among full-time firefighters,

attendance at landscape fires was positively associated with elevated risk in the second tertile of the exposure distribution compared with the lowest tertile (RIR [equivalent to rate ratio], 2.26; 95% CI, 1.06–4.82).

<u>Glass et al. (2016b)</u> studied cancer incidence in a small cohort of 614 firefighter trainers and firefighters who attended a firefighter-training facility in Australia. Cancer incidence follow-up was conducted from 1982 through 2012. Participants were grouped into risk categories of low, medium, and high for chronic exposure (to smoke and other hazardous agents) on the basis of job assignment. With the male general population of Victoria as the referent, the SIR for digestive tract cancers combined was highest in the group with medium risk of chronic exposure (SIR, 1.25; 95% CI, 0.57–2.38).

Bates et al. (2001) investigated cancer incidence and mortality in a cohort of 4305 paid [career] and volunteer New Zealand firefighters who had been employed as a career firefighter for \geq 1 year and worked between 1977 and 1995. The cohort included 84 female firefighters who were excluded from the analysis. External comparisons were made with the male general population of New Zealand. Follow-up for cancer mortality and incidence was conducted in a national data source to the end of 1995 (for mortality) or 1996 (for incidence). For cancer of the oesophagus, a modestly elevated SIR was observed (SIR, 1.67; 95% CI, 0.3-4.9), although the estimate was imprecise and based on only three cases. Limiting the follow-up period to 1990–1996 gave an SIR of 1.80 (95% CI, 0.2-6.5). For stomach cancer, mortality was slightly higher and incidence slightly lower than unity, but estimates were imprecise (SMR, 1.16; 95% CI, 0.2-3.4; and SIR, 0.76; 95% CI, 0.2–2.2). A modestly elevated, but imprecise, incidence rate of pancreatic cancer was seen (SIR, 1.28; 95% CI, 0.3-3.7). Overall mortality from colon cancer was modestly elevated (SMR, 1.19; 95% CI, 0.4-2.6), whereas incidence was reduced (SIR, 0.60; 95% CI,

0.2-1.2), but both estimates were imprecise. The SIR for colon cancer was 1.37 (95% CI, 0.4–3.2) for firefighters with > 20 years of career service, with a P for trend of 0.18. When volunteer service was included, the SIR for > 20 years of paid and volunteer service was 0.92 (95% CI, 0.3–2.1; P for trend, 0.81). Mortality and incidence of rectal cancer was modestly increased, although the estimates were imprecise (SMR, 1.21; 95% CI, 0.3–3.1; and SIR, 1.15; 95% CI, 0.5–2.2). Analysis by duration of exposure in career service showed monotonically increasing estimates above unity, but *P* for trend was 0.74. [The Working Group noted that, for rectal cancer, all of the SIRs stratified by duration of employment were greater than the overall SIR.]

(b) Cancers of other sites

In the studies included in the present section, results for other cancer sites not reviewed elsewhere in Section 2 were reported sporadically. [The Working Group noted that most analyses for these other cancer sites were based on small numbers because of the rarity of the cancer types or because the cancers were sex-specific and that estimates generally were statistically imprecise.]

Marjerrison et al. (2022b) reported an SIR for cancer of the pharynx of 1.61 (95% CI, 0.80-2.88), based on 11 cases. In the study by **Bigert et al.** (2020), the SIR for pharyngeal cancer was 1.04 (95% CI, 0.55-1.78), based on 13 cases. Petersen et al. (2018b) combined oral and oesophageal cancer in their analysis and observed a moderately elevated SMR among full-time employed firefighters (SMR, 1.27; 95% CI, 0.85-1.89), whereas the SMR was below unity for part-time firefighters or volunteers. The highest elevation of risk was seen among firefighters with < 1 year of employment (SMR, 1.39; 95% CI, 0.77-2.51). For oral and pharyngeal cancer, Demers et al. (1994) reported an SIR of 1.1 (95% CI, 0.6-2.0) when using local general population reference rates, but risk was below unity when using local police officers as the reference group (IDR, 0.8; 95% CI, 0.3–1.9). No consistent trends were seen with duration of employment or time since first employment. Altogether, seven deaths from oral or pharyngeal cancer were observed by **Demers** et al. (1992a), giving an SMR of 0.81 (95% CI, 0.33-1.66). In <u>Aronson et al. (1994)</u>, four deaths by pharyngeal cancer were reported, resulting in an SMR of 1.39 (95% CI, 0.38-3.57). Three of the deaths occurred ≥ 30 years since first employment (SMR, 1.81; 95% CI, 0.37-5.28). Guidotti (1993) reported an SMR for oral and pharyngeal cancer of 1.14 (95% CI, 0.14-4.10). The SIR for cancers of the lip, oral cavity, and pharynx was below unity for female volunteer firefighters in Glass et al. (2019). Among all male volunteer firefighters, the SIR for cancers of the lip, oral cavity and pharynx was 0.71 (95% CI, 0.63–0.81) and was similar in the subgroup who had attended incidents Glass et al. (2017). Among male paid firefighters, SIRs for cancers of the lip, oral cavity, and pharynx were at or below the expected values among full-time and part-time firefighters in Glass et al. (2016a). For full-time firefighters, risk was elevated with longer duration of employment (P = 0.46).

Overall SIRs for cancer of the gall bladder ranged from 0.99 to 1.04 in <u>Petersen et al. (2018a)</u> in firefighters compared with the three reference populations analysed, based on five observed cases. <u>Ahn et al. (2012)</u> found a slightly reduced SIR for cancer of the gall bladder and extrahepatic bile ducts (SIR, 0.82; 95% CI, 0.33–1.70), based on seven cases.

Risk of soft tissue cancer was moderately elevated in <u>Bigert et al. (2020)</u> (SIR, 1.46; 95% CI, 0.82–2.41, 15 cases). In <u>Ahn et al. (2012)</u>, the SIR for cancers of bone and articular cartilage was elevated but imprecise (SIR, 1.98; 95% CI, 0.53–5.07; 4 cases).

2.5.2 Studies only reporting having ever worked as a firefighter

(a) Occupational cohort studies

Studies first described in Section 2.1.2(a) are described in less detail in the present section.

See Table S2.10 (Annex 2, Supplementary material for Section 2, Cancer in Humans, online only, available from: <u>https://publications.iarc.</u> <u>fr/615</u>).

Altogether, eight occupational cohort studies reporting on the risk of cancers of the colon and rectum, oesophagus, stomach, pancreas, and other sites among firefighters were available (Musk et al., 1978; Eliopulos et al., 1984; Grimes et al., 1991; Giles et al., 1993; Deschamps et al., 1995; Ma et al., 2005, 2006; Amadeo et al., 2015). Incidence of cancer was studied in Ma et al. (2006) and Giles et al. (1993), whereas the remaining studies provided estimates for mortality as SMRs (Musk et al., 1978; Deschamps et al., 1995; Ma et al., 2005; Amadeo et al., 2015) or PMRs (Eliopulos et al., 1984; Grimes et al., 1991).

(i) Cancers of the digestive tract

Cancer mortality was investigated in a cohort comprising 10 829 firefighters employed in 1979 and covering 93% of the population of France (Amadeo et al., 2015). Follow-up was to the end of 2008, and comparisons were made with the male general population of France. For cancers of the oesophagus, stomach, and liver, mortality was close to the expected values, with SMRs of 0.93 (95% CI, 0.67-1.27; 40 deaths), 1.15 (95% CI, 0.77–1.65; 29 deaths), and 1.10 (95% CI, 0.80–1.46; 46 deaths), respectively. Colon cancer mortality was lower than expected (SMR, 0.73; 95% CI, 0.44–1.04). Moderately elevated mortality ratios were seen for cancers of the rectum (SMR, 1.36; 95% CI, 0.86-2.04; 23 deaths) and pancreas (SMR, 1.27; 95% CI, 0.92-1.72; 42 deaths), but precision was low.

Deschamps et al. (1995) reported on mortality in a cohort comprising 830 male firefighters in Paris, France. Firefighters had a minimum of 5 years of service on 1 January 1977, and follow-up was until 1 January 1991 (14 years). With the male general population of France as the referent, mortality from digestive tract cancers (i.e. ICD-9, 150-159; including oesophagus, stomach, small intestine including duodenum, colon, rectum, rectosigmoid junction and anus, liver and intrahepatic bile ducts, gallbladder and extrahepatic bile ducts, pancreas, retroperitoneum and peritoneum, and other and ill-defined sites within the digestive organs and peritoneum) was modestly elevated, but the estimate was imprecise (SMR, 1.14; 95% CI, 0.37–2.66; 5 deaths).

Ma et al. (2006) examined cancer incidence in a cohort of 34 796 male and 2017 female career firefighters certified since 1972 in Florida, USA, with follow-up from 1981 through 1999. Comparisons were made with cancer rates in Florida. Among men, the SIR for colon cancer was 1.16 (95% CI, 0.92-1.45; 78 cases). For cancers of the oesophagus, stomach, rectum, and pancreas, risk estimates were below unity, but with wide confidence intervals. Among women, no cases of cancer of the oesophagus, stomach, or pancreas occurred. In a mortality study in the same cohorts as described above (Ma et al., 2005), follow-up was from 1972 through 1999. In male firefighters, stratified analyses were also made for those certified between 1972 and 1976, among whom the most cases occurred. For cancers of the oesophagus, stomach, and pancreas, SMRs among men were below unity and did not differ essentially between the full cohort and the cohort restricted to firefighters certified in 1972-1976, whereas no cases occurred among the female firefighters. Mortality rates for colon cancer were modestly increased among male firefighters compared with the general population, but the precision was low (SMR, 1.14; 95% CI, 0.81-1.56; 38 deaths). Among women, only one death from

colon cancer was observed (SMR, 2.27; 95% CI, 0.03-12.7).

Grimes et al. (1991) conducted a proportionate mortality analysis of causes of death in 1969–1988 among 205 deceased male firefighters employed by the City and County of Honolulu, Hawaii. The firefighters had been employed for \geq 1 year and comparison was made with male mortality rates for the general population of Hawaii. Stratified analyses were also made for Caucasian [White] and Hawaiian firefighters. The PMR for cancer of the stomach was 0.79 (95% CI, 0.30–2.09; [4] deaths) overall. Colon cancer deaths were fewer among firefighters than in the general population, with none occurring among the Hawaiian firefighters.

Musk et al. (1978) conducted a cohort mortality study among 5655 firefighters with \geq 3 years of service between 1915 and 1975 in Boston, USA. Firefighters were identified from employment records. Information on cause of death came from death certificates, which were lacking for 194 confirmed deaths (7.9%). Mortality for cancers of the digestive tract (i.e. oesophagus, stomach, small intestine including duodenum, colon, rectum, liver, and intrahepatic bile ducts, gallbladder and extrahepatic bile ducts, pancreas, peritoneum, and unspecified sites within digestive organs) was below unity when compared with that for Massachusetts men, but at unity when compared with that for US White men.

Giles et al. (1993) conducted a cancer incidence study of 2865 male operational firefighters employed between 1917 and 1989 by the fire brigade in Melbourne, Australia. Follow-up was from 1980 through 1989, and comparisons were made with the State of Victoria as the reference group. For colorectal cancer overall, the SIR was elevated but imprecise (SIR, 1.36; 95% CI, 0.62–2.59; 9 cases), driven by the risk in the age group \geq 65 years (SIR, 3.65; 95% CI, 1.13–7.94; 6 cases). Risk of pancreatic cancer was at the expected level.

Eliopulos et al. (1984) conducted a PMR study among 990 firefighters employed between 1939 and 1978 in Western Australia. For stomach cancer and intestinal cancer, mortality ratios were elevated but imprecise (PMR, 2.02; 95% CI, 0.65–4.70; 5 deaths; and PMR, 1.59; 95% CI, 0.43–4.07; 4 deaths, respectively). [The Working Group noted that cancer codes were not stated, but as the ICD-8 classification system was used, the group "intestinal cancer" was presumed to comprise the small intestines (including duodenum), large intestine, and rectum.]

(ii) Cancers of other sites

In the studies included in the present section, results for cancer sites not included elsewhere were reported sporadically. Results on these sites are presented below. [The Working Group noted that most analyses in this group were based on small numbers because of the rarity of the cancer sites and that therefore estimates generally were imprecise.]

In <u>Deschamps et al. (1995)</u>, the SMR for pharyngeal cancer was 0.81 (95% CI, 0.10–2.93), based on two deaths. For lip, oral cavity, and pharynx cancers, <u>Ma et al. (2006)</u> found a lower incidence rate among male firefighters than in the general population (SIR, 0.67; 95% CI, 0.47–0.91; 39 cases), whereas no cases occurred among women. Mortality from buccal/pharyngeal cancer was lower among male firefighters in <u>Ma et al. (2005)</u> (SMR, 0.42; 95% CI, 0.17–0.87; 7 deaths). For cancer of the upper aerodigestive tract (i.e. lip, tongue, oral cavity, pharynx, oesophagus, nose and sinuses, and larynx), <u>Giles</u> et al. (1993) reported an SIR of 1.46 (95% CI, 0.53–3.18; 6 cases).

The incidence rate of breast cancer among men was lower than expected in <u>Ma et al. (2006)</u> (SIR, 0.51; 95% CI, 0.06–1.84; 2 cases), whereas in <u>Ma et al. (2005)</u>, the mortality rate for male breast cancer was substantially elevated (SMR, 7.41; 95% CI, 1.99–19.0; 4 deaths). Among women (<u>Ma</u> <u>et al., 2006</u>), breast cancer risk was as expected (SIR, 0.96; 95% CI, 0.46–1.76; 10 cases). <u>Amadeo et al. (2015)</u> identified one death from breast cancer in men (SMR, 0.76; 95% CI, 0.02–4.23).

<u>Ma et al. (2006)</u> found risk of bone and soft tissue sarcoma to be as expected among men. Based on one case among women, the SIR for soft tissue sarcoma was 5.56 (95% CI, 0.07–30.91). Mortality from bone cancer among male firefighters in <u>Ma et al. (2005)</u> did not differ from that expected, based on one death; and no deaths from bone cancer occurred among female firefighters.

(b) Population-based studies

Studies first described in Section 2.1.2(b) are described in less detail in the present section.

See Table S2.10 (Annex 2, Supplementary material for Section 2, Cancer in Humans, online only, available from: <u>https://publications.iarc.</u> <u>fr/615</u>).

Three cohort studies (two in Europe and one in Canada) examined the risk of cancers of the digestive tract and other cancers among firefighters by linking national census records to national tumour registry or death records (Pukkala et al., 2014; Harris et al., 2018; Zhao et al., 2020). An additional cohort study in Canada examined the risk of cancer among firefighters who were former claimants of workers compensation linked to cancer registry records (Sritharan et al., 2022). Case-control (and similar) studies included seven "event-only" studies conducted in the USA that used cancer registry records to identify cancer cases (Sama et al., 1990; Bates, 2007; Kang et al., 2008; Tsai et al., 2015; Langevin et al., 2020; Lee et al., 2020; McClure et al., 2021) and three other US studies that relied solely on death certificates as the source of both occupation and underlying cause of death (Ma et al., 1998; Muegge et al., 2018).

(i) Cancers of the digestive tract

The most recent European study was by Zhao et al. (2020), who linked Spanish census data to a national mortality registry. The study population consisted of 9.5 million employed men, aged 20–64 years in 2001, who were followed for 10 years. Among 27 365 firefighters, excesses of cancers of the stomach (MRR, 1.32; 95% CI, 0.88–1.98) and oesophagus (MRR, 1.11; 95% CI, 0.64–1.92) were observed, although all estimates were imprecise. Mortality for rectal cancer was close to that expected (MRR, 1.08; 95% CI, 0.57–2.04), and no excess was observed for cancers of the colon, liver, or pancreas.

Pukkala et al. (2014) presented a more comprehensive set of results from a census linkage of 15 million people (the NOCCA cohort) from all five Nordic countries (1961–2005). A total of 16 422 men reported their occupation as firefighter. With the Nordic general population as the referent, there were modest excesses of pancreatic cancer (SIR, 1.17; 95% CI, 0.94–1.45) and colon cancer (SIR, 1.14; 95% CI, 0.99–1.31), and a larger excess of gallbladder cancer (SIR, 1.45; 95% CI, 0.86–2.29). The risks of cancers of the oesophagus, stomach, rectum, and liver were similar to those expected.

Sritharan et al. (2022) investigated cancer incidence in a cohort of 13 642 firefighters compared with other members of a large cohort of 2 368 226 workers and with a subset of police officers in the cohort in Ontario, Canada. The study group was enumerated using information from an occupational injury and disease claims database and linkage to the provincial tumour registry and other electronic health records. There was no evidence of increased incidence of cancers of the oesophagus, stomach, or liver among firefighters compared with either the cohort overall or police officers. There were relatively precise excesses of both colon (HR, 1.39; 95% CI, 1.19–1.63; 152 cases) and pancreatic (HR, 1.34; 95% CI, 1.02-1.76; 53 cases) cancer in firefighters compared with all other workers, but not compared with police. There were also excesses of rectal cancer (HR compared with other workers, 1.18; 95% CI, 0.93–1.51; and HR compared with police, 1.19; 95% CI, 0.85–1.68; 66 cases) and lip cancer (HR compared with other workers, 1.61; 95% CI, 0.89–2.92; and HR compared with police, 1.35; 95% CI, 0.57–3.22; 11 cases).

Harris et al. (2018) conducted the CanCHEC study using the 1991 Canadian census. The cohort included 1.1 million employed men, of whom 4535 reported their occupation as firefighter, who were followed up for cancer incidence through 2010. Elevated but imprecise risks were observed for cancers of the oesophagus (HR, 1.31; 95% CI, 0.68–2.51) and pancreas (HR, 1.38; 95% CI, 0.83–2.29) in firefighters compared with other employed people who participated in the census, whereas no evidence of an excess was seen for cancers of the stomach, colon, rectum, or liver. [The Working Group noted that parallel analyses were also conducted of police and members of the armed forces, who were chosen because they share some characteristics with firefighters. Colon cancer was elevated in police, but no other excess of cancers of the digestive tract were observed in either group.]

Lee et al. (2020) used records for 1972-2012 from the office of the Florida State Fire Marshal, USA, to identify cancer cases in male and female firefighters linked to the state cancer registry. No excess was observed for cancers of the oesophagus, stomach, colon, rectum, pancreas, or liver among men, although excesses of cancers of the stomach (OR, 1.85; 95% CI, 0.46–7.49) and rectum (OR, 2.02; 95% CI, 0.90-4.58) were observed for women, both based on fewer than 10 cases. A subanalysis identified a somewhat increased risk of late-stage diagnosis for cancers of the oesophagus, colon, and liver among male firefighters. A subsequent paper by the same group (McClure et al., 2021) demonstrated that relying on cancer registry data for occupational information was prone to errors that can cause bias in either direction. For cancers of the digestive system, similar ORs were obtained when firefighters were ascertained using only the registry data (OR, 0.96; 95% CI, 0.84–1.10) and when using the data from the office of the Fire Marshall (OR, 0.93; 95% CI, 0.85–1.03), even though the latter data identified twice as many cancers in firefighters.

Muegge et al. (2018) used death certificates from the state of Indiana, USA, for a mortality study of firefighters. Four non-firefighters per firefighter, matched on year of death, age at death, sex, and race/ethnicity, were randomly chosen as the comparison population. An increased risk of mortality from pancreatic cancer was observed (OR, 1.45; 95% CI, 1.01–2.06; 46 deaths) among firefighters, although no results for other specific cancer sites in the digestive tract were presented. [The Working Group noted that the major limitation of such studies is the reliance on death certificates to identify both occupation and cancer, which is likely to result in misclassification of both firefighting and cancer and has the potential for selection bias.]

Tsai et al. (2015) used data from the California Cancer Registry, USA, 1988–2007, to identify 3996 male firefighters, including wildland firefighters. An excess of oesophageal cancer was observed (OR, 1.59; 95% CI, 1.20-2.09), attributable to adenocarcinoma (OR, 1.85; 95% CI, 1.34–2.55), and was observed in White firefighters and in firefighters with other races/ethnicities (among non-White firefighters, the OR was 2.14; 95% CI, 0.81–5.65). Modestly elevated risks were also observed for cancers of the colorectum (OR, 1.10; 95% CI, 0.93-1.31), liver (OR, 1.07; 95% CI, 0.75–1.53), and pancreas (OR, 1.10; 95% CI, 0.83-1.46), whereas no excess was observed for stomach cancer. Bates (2007) conducted a similar study with the California Cancer Registry, USA, in 1988–2003, but these data were included in the study conducted later by Tsai et al. (2015) with data from 1988–2007.

Kang et al. (2008) conducted a study that relied on records from the state cancer registry in Massachusetts, USA, from 1987 through 2003 to identify usual occupation as well as cancer. A total of 2125 cancers were identified among White male firefighters. Twenty-five cancer types of concern for firefighters were evaluated, and the remaining cancers were the controls. SMBORs were adjusted for age and smoking status. Firefighters had an increased risk of colon cancer when compared with police (SMBOR, 1.36; 95% CI, 1.04-1.79) and, although reduced, when compared with other occupations (SMBOR, 1.15; 95% CI, 0.93-1.43), and colon cancer risk increased with age. Firefighters also had a somewhat increased risk of liver cancer when compared with police (SMBOR, 1.15; 95% CI, 0.55-2.41) or with all other occupations (SMBOR, 1.19; 95% CI, 0.69-2.06), but these estimates were less precise. No excesses of cancers of the oesophagus, stomach, rectum, or pancreas were observed when firefighters were compared with police or with all other occupations. Sama et al. (1990) conducted an earlier study that also relied on records from the state cancer registry in Massachusetts, USA, and used the same design as Kang et al. (2008) but had a substantially shorter (but non-overlapping) follow-up period (1982-1986) and did not adjust for smoking. Only men were included, and the risks for nine cancer sites were assessed, with the remaining sites acting as controls. This study observed excesses of cancers of the colon (SMBOR, 1.20; 95% CI, 0.80-1.82) and rectum (SMBOR, 1.35; 95% CI, 0.84-2.19) among firefighters compared with the general population, but not with the police. In contrast, an excess of pancreatic cancer (SMBOR, 3.19; 95% CI, 0.72-14.15) was observed compared with the police, but not with the general population; however, all estimates were imprecise.

<u>Ma et al. (1998)</u> used death certificates from 24 states of the USA as the sole source of both occupation and underlying cause of death in 1984– 1993. Among White male firefighters, modestly elevated risks were observed for cancers of the pancreas (MOR, 1.2; 95% CI, 1.0-1.5), stomach (MOR, 1.2; 95% CI, 0.9–1.6), liver (MOR, 1.2; 95% CI, 0.9–1.7), and rectum (MOR, 1.1; 95% CI, 0.8-1.6), whereas no evidence of an excess was observed for cancers of the oesophagus or colon. Among Black male firefighters, excesses were observed for cancers of the colon (MOR, 2.1; 95% CI, 1.1-4.0), pancreas (MOR, 2.0; 95% CI, 0.9-4.6), and stomach (MOR, 1.4; 95% CI, NR; 4 deaths), based on much smaller numbers (no deaths from cancers of the rectum or liver were observed). In an earlier report, Burnett et al. (1994) used data from 27 states for a proportionate mortality analysis of White male firefighters in 1984–1990. An excess of rectal cancer was identified (PMR, 1.48; 95% CI, 1.05-2.05), which was substantially higher among firefighters who died before age 65 years (PMR, 1.86; 95% CI, 1.10-2.94). No other results for cancers of the digestive tract were reported. Of the 27 states reported, 24 were the same as those reported by <u>Ma et al. (1998)</u> for a somewhat longer time period.

(ii) Cancers of other sites

Other cancer sites, not considered in previous sections, were also examined in some studies, and results for cancers of the lip, oral cavity, pharynx, soft tissue sarcoma/connective tissue, bone, and breast are discussed here. Zhao et al. (2020) reported an increased risk of oropharyngeal (MRR, 1.34; 95% CI, 0.81-2.21; 18 deaths), breast (MRR, 3.04; 95% CI, 0.42-21.78; 1 death), and bone cancer (MRR, 1.11; 95% CI, 0.16-7.92; 1 death) among Spanish firefighters. Sritharan et al. (2022) reported a similar risk of breast cancer among female firefighters compared with all other workers (HR, 0.97; 95% CI, 0.46-2.03) and with police (HR, 0.78; 95% CI, 0.36-1.71). In the NOCCA study, Pukkala et al. (2014) reported a greater than expected number of soft tissue cancers (SIR, 1.16; 95% CI, 0.69-1.84) among Nordic firefighters, but the incidence rates of cancers of the lip, oral cavity, and pharynx

were at or below expected rates. Harris et al. (2018) found a higher rate of lip cancer among firefighters (HR, 2.09; 95% CI, 0.87-5.06) than among others, but the incidence of oral cavity cancer was as expected. Lee et al. (2020) reported results separately for men and women for cancers of the oral cavity and pharynx combined (OR for men, 0.85; 95% CI, 0.72–0.99; and OR for women, 1.26; 95% CI, 0.47-3.40), soft tissue (OR for men, 0.93; 95% CI, 0.65–1.34; and OR for women, 0.69; 95% CI, 0.10-4.95), bone (OR for men, 0.72; 95% CI, 0.36-1.44; and OR for women, 3.90; 95% CI, 0.97–15.71). They reported a deficit of breast cancers among female firefighters. Langevin et al. (2020) reported no association between ever-employment or duration of employment as a firefighter and cancers of head and neck (all combined), oral cavity, oropharynx (SCC), or hypopharynx (SCC), although there were very few firefighters as cases or controls in the study.

Muegge et al. (2018) reported an increased risk of cancers of the oral cavity and pharynx combined (OR, 2.15; 95% CI, 1.19-3.79) and of connective tissue (OR, 2.50; 95% CI, 1.01-5.86) for the death certificate study in Indiana, USA. <u>Tsai et al. (2015)</u> reported unremarkable results, mainly based on very small numbers, for cancers of lip, pharynx, and soft tissues for the California registry-based study. Kang et al. (2008) reported below-null, close-to-null, or highly imprecise results for cancers of the lip, oral cavity, and pharynx, soft tissue sarcoma, and male breast for firefighters compared with either police or with other occupations in the Massachusetts registry-based study. Ma et al. (1998) reported mortality findings for cancer of the pharynx among Black firefighters (OR, 7.6; 95% CI, 1.3-46.4) and, among White firefighters, for cancers of the lip (MOR, 5.9; 95% CI, 1.9-18.3), soft tissue sarcoma (MOR, 1.6; 95% CI, 1.0-2.7), and bone (MOR, 1.0; 95% CI, NR). [The Working Group noted that findings were not consistently provided for these cancers and estimates were often based on small numbers.]

2.6 Cancer of all sites combined

2.6.1 Studies reporting occupational characteristics of firefighters

See Table S2.11 (Annex 2, Supplementary material for Section 2, Cancer in Humans, online only, available from: <u>https://publications.iarc.</u> <u>fr/615</u>).

Studies first described in Section 2.1.1 are described in less detail in the present section.

The Working Group identified 26 occupational and population-based cohort studies that had investigated the relationship between occupational exposure as a firefighter and risk of cancer of all sites combined (Feuer & Rosenman, 1986; Vena & Fiedler, 1987; Demers et al., 1992a, 1994; Giles et al., 1993; Guidotti, 1993; Aronson et al., 1994; Tornling et al., 1994; Bates et al., 2001; Zeig-Owens et al., 2011; Ahn et al., 2012; Daniels et al., 2014, 2015; Ahn & Jeong, 2015; Glass et al., 2016a, b, 2017, 2019; Kullberg et al., 2018; Petersen et al., 2018a, b; Bigert et al., 2020; Pinkerton et al., 2020; Webber et al., 2021; Marjerrison et al., 2022a, b). Two of these studies were from Asia, seven were from Europe, twelve were from North America, and six were from Oceania. [The Working Group noted that, although analysis of all cancers combined enhances the statistical power to observe an effect because of increased case numbers, interpretation of the results is seriously limited by the very heterogenous etiology and pathology of cancers at the different sites.]

Ahn & Jeong (2015) conducted a cohort mortality study among 33 442 professional [career] emergency responders in the Republic of Korea. Emergency responders had been employed between 1980 and 2007, and mortality follow-up took place from 1992 through 2007. In the subcohort of firefighters (n = 29 453, 88% of the total cohort) compared with the male population of the Republic of Korea, the SMR for cancer of all sites combined was lower than expected overall (SMR, 0.58; 95% CI, 0.50–0.68) and in all categories of duration of employment (< 10 years, 10-20 years, and ≥ 20 years). Internal analyses of employment duration, for which firefighters employed for < 10 years and other emergency responders served as reference groups, showed age- and calendar-year ARR [adjusted rate ratio] estimates of 1.54 (95% CI, 1.02–2.31) for firefighters employed for ≥ 20 years. [The Working Group noted the young average age at end of follow-up (41.3 years), which strongly indicated a downward selection bias from a healthy-worker hire effect.]

In the same cohort as above, <u>Ahn et al. (2012)</u> conducted a cancer incidence study among professional [career] emergency responders with cancer incidence follow-up from 1996 through 2007 in the Republic of Korea. National cancer incidence rates for men served as the referent, and analyses were conducted overall and by duration of employment (< 10 years versus \geq 10 years). Risk of cancer of all sites combined was not different from that for the general population (SIR, 0.97; 95% CI, 0.88–1.06) or, in the internal analyses, for the non-firefighter emergency responders (SRR, 0.83; 95% CI, 0.59–1.16). No increased risk with duration of employment (< 10 years versus \geq 10 years) was seen.

Marjerrison et al. (2022a, b) investigated cancer incidence and mortality in a cohort of 3881 male professional [career] firefighters in Norway compared with the male general population. The cohort included mostly full-time firefighters employed between 1950 and 2019 with past or present employment in positions entailing active firefighting duties. The follow-up period for both cancer incidence and mortality analyses was from 1960 through 2018. Among those ever employed as a firefighter, the SIR for all cancer sites combined was 1.15 (95% CI, 1.07-1.23). Increased risks were seen for firefighters with longer duration of employment (SIR for \ge 30 years, 1.19; 95% CI, 1.09–1.30), for those first employed before 1950 (SIR, 1.29; 95% CI, 1.15–1.44), and for those with \geq 40 years since

first employment (SIR, 1.18; 95% CI, 1.08–1.29). For mortality, the overall SMR for all cancers combined was 1.08 (95% CI, 0.97–1.20). In the earliest follow-up period (to the end of 1984), an SIR of 1.21 (95% CI, 1.02–1.43) and SMR of 1.25 (95% CI, 1.00–1.55) was observed. Elevated incidence and mortality were also seen in the age group \geq 70 years (SIR, 1.23; 95% CI, 1.11–1.36; and SMR, 1.20; 95% CI, 1.05–1.38).

<u>Bigert et al. (2020)</u> investigated cancer incidence in a cohort of 8136 male firefighters in Sweden. Employment information was ascertained from national decennial censuses between 1960 and 1990. Cancer incidence data were ascertained from the Swedish Cancer Registry with follow-up from 1961 through 2009. With the national male general population as the referent, risk of all cancers combined did not deviate from the expected value overall (SIR, 1.03; 95% CI, 0.97–1.09) or by duration of employment (P = 0.19).

A cancer incidence study in a cohort of 1080 male firefighters in Stockholm, Sweden, provided information on the risk of all cancers combined (Kullberg et al., 2018). Firefighters were identified through annual enrolment records from 15 fire stations and had worked for ≥ 1 year between 1931 and 1983. As an update to a previous study (Tornling et al., 1994), this study added 26 years of cancer incidence follow-up from 1958 through 2012 in the Swedish Cancer Registry. With the male general population of Stockholm County as the referent, the overall SIR for all cancers combined was lower than expected (0.81; 95% CI, 0.71–0.91). In stratified analyses, there were statistically significant trends of increasing overall SIR for cancer with increasing age (P for trend, < 0.01), longer employment duration (P for trend, 0.03), and earlier period of hire (P for trend, < 0.01), although there was no excess of cancer overall in any stratum.

In the original analysis of this cohort, <u>Tornling et al. (1994)</u> investigated both cancer mortality and incidence. Follow-up for mortality

was from 1951 through 1986 and for cancer incidence from 1958 through 1986. Comparisons were made with the male regional general population. For each firefighter, exposure to fire events was assessed using reports of fires fought by the Stockholm fire brigade between 1933 and 1983. Mortality from cancer of all sites was equal to that expected. In stratified analyses, SMRs above 1.00 were seen for the highest age category (SMR, 1.09; 95% CI, 0.85–1.39), the longest employment duration (SMR, 1.09; 95% CI, 0.79-1.46), and the highest number of fire responses (SMR, 1.20; 95% CI, 0.90–1.57). SIRs did not vary with the number of fire responses. [The Working Group noted that the exposure assessment method was a strength and that trend tests were not performed.]

Petersen et al. (2018a) studied cancer incidence in a cohort of 9061 male full-time, parttime, and volunteer firefighters in Denmark. Follow-up was from 1968 through 2014, and three external comparison groups were used: the general population of Denmark, a sample of the working population, and a cohort of military employees. Additional analyses by employment type (e.g. full-time, other), era of first employment, job function (e.g. regular, specialized), age at first employment, and duration of employment were performed with the general population as referent. For cancer of all sites combined, overall estimates varied very little with choice of referent, with the SIR using the general population as the reference group being 1.02 (95%) CI, 0.96–1.09). Risks were modestly elevated for employment before 1970 (SIR, 1.12; 95% CI, 1.02-1.22), specialized firefighters (SIR, 1.12; 95% CI, 0.88–1.39), age < 25 years at first employment (SIR, 1.12; 95% CI, 1.03-1.22), and for duration of employment of < 1 year (SIR, 1.14; 95% CI, 1.02 - 1.27).

Cancer mortality was investigated in the same cohort of firefighters in Denmark described above (<u>Petersen et al., 2018b</u>). An expanded study population of 11 775 male firefighters was followed for mortality in the Danish national

death registry from 1970 through 2014. External comparisons were made with a sample of the working population and with a cohort of military employees. The overall SMR for all cancers combined was not elevated compared with that for either of the reference groups; however, with restriction to full-time firefighters the SMR was 1.12 (95% CI, 1.00–1.26) compared with the military referent. Overall cancer mortality decreased monotonically with longer duration of employment, with an SMR of 1.18 (95% CI, 0.99–1.40) for a duration of < 1 year. [The Working Group noted that a trend test was not performed.]

Webber et al. (2021) investigated cancer incidence in a cohort of 10 786 male firefighters from the FDNY and exposed to the WTC disaster site. Comparisons were made with the US male general population and with 8813 presumed non-WTC exposed firefighters employed during the same period from the CFHS (which included firefighters from San Francisco, Chicago, and Philadelphia). Cancer follow-up was from 11 September 2001 through 2016. With the US general population as the referent, the overall SIR for all cancers combined was elevated among the FDNY WTC-exposed firefighters (SIR, 1.15; 95% CI, 1.08–1.23) but not among the CFHS firefighters (SIR, 1.05; 95% CI, 0.98-1.12). To adjust for potential medical surveillance bias because of free and routine health examinations in the WTC-exposed FDNY cohort, additional analyses with the diagnosis date of select cases delayed by 2 years were performed. With this adjustment, the SIR for the FDNY firefighters was attenuated (SIR, 1.09; 95% CI, 1.02-1.16). Internal comparison regression analyses with the CFHS cohort as the referent, with and without adjustment for potential surveillance bias, yielded RRs of 1.07 (95% CI, 0.96–1.18 and 1.13 (95% CI,1.02–1.25), respectively. [The Working Group noted the importance of investigating potential surveillance bias attributable to enhanced screening in this firefighter cohort. Although increased medical attention would tend to elevate risk

estimates, results indicated that the effect on cancer of all sites combined was present, but modest. The opposite contributions of healthyworker bias and surveillance bias complicated interpretation of results from this cohort.]

In a previous follow-up of cancer incidence among WTC exposed firefighters, Zeig-Owens et al. (2011) compared exposed and unexposed person-time in the FDNY cohort, which included 9853 male FDNY firefighters. Cancer incidence follow-up was conducted in state cancer registries from 1996 through 2008. With the US male general population as the referent, exposure at the WTC site was associated with higher incidence of all cancers combined (SIR, 1.10; 95% CI, 0.98-1.25) than was no exposure (SIR, 0.84; 95% CI, 0.71-0.99), with a ratio of SIRs of 1.32 (95% CI, 1.07-1.62). Sensitivity analyses with different cohort restrictions and inclusion of multiple primary cancer diagnoses did not meaningfully change the ratio of SIRs. No difference was seen by calendar period of follow-up (before or after 31 December 2004). [The Working Group noted that the SIR ratio is not a standard epidemiological effect measure.]

Three studies of both cancer mortality and incidence have been conducted among municipal career firefighters in the CFHS who were employed at fire departments in San Francisco, Chicago, and Philadelphia, USA. Most recently, Pinkerton et al. (2020) updated previous analyses by Daniels et al. (2014) with cancer mortality follow-up from 1950 extended through 2016. With the US general population as the referent, the overall SMR for all cancers combined was elevated in the full cohort (SMR, 1.12; 95% 1.08–1.16) and specifically among firefighters in the Chicago subcohort (SMR, 1.20; 95% 1.15–1.26). Significant heterogeneity between the fire department subcohorts was noted (heterogeneity P value, < 0.01). Stratified analyses showed that SMRs were lower than expected (SMR, 0.79; 95% CI, 0.68-0.93) among non-White firefighters and higher than expected among White firefighters (SMR, 1.14; 95% CI, 1.10–1.18) and firefighters aged \geq 65 years (SMR, 1.22; 95% CI, 1.17–1.27). In internal regression analyses, the choice of regression model had little impact on estimates for all cancers combined, but covariate adjustment for duration of employment generally produced estimates that were higher than those without adjustment. Comparing hazard rates at the 75th and the 25th percentile of the exposure distributions, the fully adjusted model gave adjusted hazard ratios of 1.14 (95% CI, 1.00–1.31) for number of exposed days, 1.02 (95% CI, 0.94–1.11) for fire-runs, and 1.08 (95% CI, 0.96–1.21) for fire-hours.

An earlier study of a subset of 19 309 firefighters from the same CFHS cohort examined both cancer mortality and incidence and reported internal exposure–response associations with follow-up to the end of 2009 (Daniels et al., 2015). Methods were similar to those used in <u>Pinkerton et al. (2020)</u>; however, results in the present study were not adjusted for employment duration. Results showed no evidence of an association for cancer of all sites combined with any of the exposure metrics of number of exposed days, fire-runs, or fire-hours.

An additional study of the CFHS cohort investigated cancer incidence among 29 993 municipal career firefighters and reported external and internal comparison analyses with follow-up to the end of 2009 (Daniels et al., 2014). The methods were similar to those in the study by Pinkerton et al. (2020). Cancer incidence follow-up was conducted in state cancer registries relevant to each department to the end of 2009, with start years varying between 1985 and 1988. For the incidence of all cancers combined (including all primary cancers), slightly increased risk was observed in firefighters (SIR, 1.09; 95% CI, 1.06-1.12) compared with the US general population. In Caucasian [White] men, an excess risk was observed (SIR, 1.10; 95% CI, 1.07-1.13), whereas non-White men had an SIR slightly below unity (SIR, 0.92; 95% CI, 0.81-1.05).

Among women, overall cancer incidence was modestly elevated, but imprecise (SIR, 1.24; 95% CI, 0.89–1.69).

Cancer incidence was studied in a cohort of 2447 male firefighters who had been employed for ≥ 1 year between 1945 and 1979 in the cities of Seattle and Tacoma, Washington, USA (Demers et al., 1994). Follow-up was conducted in a regional cancer registry for the period 1974–1989. There was no evidence of an overall excess risk of cancer of all sites combined, with comparisons with local county rates and local police rates yielding similar results. Risk also did not increase with duration of exposed employment or time since first employment.

In an earlier cohort study, <u>Demers et al.</u> (1992a) investigated cancer mortality in 4401 male municipal firefighters from the cities of Seattle and Tacoma, Washington, and Portland, Oregon, USA. Mortality follow-up was from 1944 through 1989. SMRs for all cancers combined were at unity when compared with US national mortality rates and with mortality rates for police officers from the same cities.

Vena & Fiedler (1987) studied mortality in a cohort of 1867 White male firefighters employed in Buffalo, USA, during 1950–1979. Mortality follow-up was from 1950 through 1979, and comparisons were made with mortality rates among US White men in the general population. Overall cancer mortality was similar to that expected (SMR, 1.09; 95% CI, 0.89–1.32) but was increased in firefighters with an employment duration of \geq 40 years (SMR, 2.20; 95% CI, [1.5–3.1]). Mortality from all malignant neoplasms also tended to increase with increasing latency of time since first employment.

<u>Feuer & Rosenman (1986)</u> conducted a PMR study that included 263 deceased firefighters from New Jersey, USA, who died during 1974– 1980. Comparisons were made with the US White male and New Jersey White male general populations, as well as New Jersey White police officers. With US White males as the referent, the PMR for all cancer sites combined was 1.15 (95% CI, [0.90–1.45]). Estimates were closer to unity when using the two alternative reference groups. Stratified analyses by duration of employment showed a higher estimate for those employed for > 25 years (PMR, 1.09; 95% CI, [0.77–1.51]) than for those employed \leq 20 years (PMR, 0.91; 95% CI, [0.53–1.47]).

Aronson et al. (1994) investigated cancer mortality among a cohort of 5414 male career firefighters employed for ≥ 6 months in Toronto, Canada. Firefighters had been employed between 1950 and 1989, and mortality follow-up was conducted in a national mortality database from 1950 through 1989. With the male general population of Ontario as the referent, the SMR for all malignant neoplasms combined was 1.05 (95% CI, 0.91–1.20), and the highest mortality was seen among those with the shortest time since first employment (< 20 years) and shortest duration of employment (< 15 years).

Guidotti (1993) examined cancer mortality in a cohort of 3328 firefighters employed and followed-up from 1927 through 1987 in Edmonton and Calgary, Canada. External comparisons were made with the general male population of Alberta. SMRs were stratified according to employment characteristics, and an exposure index (with values of 0, > 0 to < 1, 1–9, and \geq 10) was created on the basis of years of firefighter service weighted by an estimate of the relative time spent in proximity to fires according to job classification. With the general population as the referent, the overall SMR for all cancers combined was 1.27 (95% CI, 1.02-1.55). No clear pattern with latency period of first employment was observed, but SMRs were higher with 40-49 years (SMR, 1.76; 95% CI, [1.15-2.61]) or \geq 50 years since first employment (SMR, 1.44; 95% CI, [0.82-2.36]) than with first employment in more recent times. The SMR was 1.67 (95%: [0.73–3.31]) for those in the lowest exposure index category and 1.96 (95% CI, [1.09-3.27]) in the second lowest exposure category. Stratified

analyses of exposure index by time since first employment showed no clear association with mortality from all cancers combined. [The Working Group noted the low number of cases in stratified analyses.]

In a large cohort of Australian female paid [career] (n = 1682) and volunteer (n = 37962)firefighters, Glass et al. (2019) investigated both mortality and cancer incidence. Cancer incidence follow-up was conducted in a national cancer registry from 1982 through 2010. The general female population of Australia served as the reference group in external comparison analyses. Information on the number of incidents attended was ascertained from personnel records and categorized in tertiles by type of incident. Among the subset of career firefighters, the SIR for all cancers combined was 1.15 (95% CI, 0.80-1.67). Among volunteer firefighters, there was no excess of all cancers combined using either incidence or mortality outcomes. In internal regression analyses of cancer incidence, there was a modest elevation in the rate of cancer among volunteer firefighters in the highest tertile of the number of total incidents attended compared with firefighters who had never attended incidents (RIR [equivalent to rate ratio], 1.14; 95% CI, 0.93-1.38). Trend tests did not suggest positive trends in the rate of cancer with increasing tertile for any incident type.

Using the same methods as those in the study of female firefighters, cancer incidence was also investigated in a parallel cohort of 163 094 male volunteer firefighters in Australia (Glass et al., 2017). With the male general population of Australia as the referent, overall cancer mortality and incidence were similar and lower than expected in all volunteers and the subset who had attended incidents, respectively (SMR, 0.59; 95% CI, 0.57–0.62; and SIR, 0.86; 95% CI, 0.84–0.88). Internal regression analysis showed decreasing mortality with longer duration of service (P < 0.01). With more incidents attended, relative mortality ratios (RMR) [rate ratios] for

all cancers combined were consistently above unity, specifically for attendance at structure fires (RMR, 1.38; 95% CI, 1.00-1.91) and vehicle fires (RMR, 1.29; 95% 1.00-1.66) among firefighters in the intermediate tertile of exposure. For overall cancer incidence, associations with the number of incidents attended were more attenuated than for mortality, with the highest risk estimate being an RIR [equivalent to rate ratio] of 1.20 (95% CI, 1.01-1.42) for attendance at structure fires among those in the intermediate tertile group. In the subset of volunteer firefighters who attended incidents, the RIR for duration of service of 10-20 years was 1.09 (95% CI, 1.00–1.20; *P* = 0.25) compared with < 10 years of service.

Using similar methods as those in the two studies of volunteer firefighters, mortality and cancer incidence were studied in a cohort of 30 057 paid full-time and part-time male firefighters in Australia (Glass et al., 2016a). Included firefighters had worked between 1976 and 2003 and were primarily municipal or semi-metropolitan firefighters. Cancer incidence and mortality follow-up were conducted in national registries to the end of 2010 and 2011, respectively. For all cancer sites combined, mortality was lower than expected (SMR, 0.81; 95% CI, 0.74-0.89), but incidence was higher than expected (SIR, 1.09; 95% CI, 1.03-1.14) among firefighters overall compared with the male general population of Australia. Stratified results were similar for fulltime and part-time firefighters. In internal regression analyses, no trend was seen with increasing duration of employment. Among full-time firefighters, increasing attendance at all incidents and all fire incidents was positively associated with the incidence of all cancers combined, specifically for landscape fires in the second tertile of the number of incidents attended (SIR, 1.54; 95% CI, 1.18-1.99) and for vehicle fires (SIR for second tertile, 1.48; 95% CI, 1.13-1.93; and SIR for third tertile, 1.34; 95% 1.04–1.71; *P* = 0.04).

Glass et al. (2016b) studied cancer incidence and mortality in a small cohort of 614 firefighter trainers and firefighters who attended a firetraining facility in Australia. Cancer incidence follow-up was conducted from 1982 through 2012 and mortality follow-up from 1980 through 2011. Participants were grouped into risk categories of low, medium, and high chronic exposure (to smoke and other hazardous agents) on the basis of job assignment. For all cancers combined, the SMR was 1.47 (95% CI, 0.54–3.19; 6 deaths) among firefighters in the "high risk of chronic exposure" group compared with the male general population of Victoria. The SIR for cancers of all sites combined was low in the "low risk of chronic exposure" group (SIR, 0.40; 95% CI, 0.15-0.87) and elevated in the "high risk of chronic exposure" group (SIR, 1.85; 95% CI, 1.2–2.73). Sensitivity analyses differentiating between paid [career] and volunteer firefighters in the medium-risk group or using different sources for start date, did not change estimates for mortality, but had a larger impact on the incidence estimates. In the high-risk group, selection of an alternative source for start date elevated the SIR to 2.06 (95% CI, 1.32–3.06).

Bates et al. (2001) investigated cancer incidence and mortality in a cohort of 4305 paid [career] and volunteer New Zealand firefighters who had been employed as a career firefighter for \geq 1 year and between 1977 and 1995. The cohort included 84 female firefighters who were excluded from analysis. Follow-up for cancer mortality and incidence was conducted in a national data source to the end of 1995 (for mortality) or 1996 (for incidence). External comparisons were made with the male general population of New Zealand. No excess incidence or mortality among firefighters was seen for all cancer combined in the overall analysis or, for incidence, after stratification by calendar period of follow-up. For career and volunteer service combined, 11-20 years of service gave an SIR of 1.75 (95% CI, 1.2-2.5), which was reduced to

near-unity with > 20 years of service (SIR, 1.04; 95%: CI, 0.8–1.4). For duration of career service only, all estimates were closer to unity.

Giles et al. (1993) conducted a cancer incidence study of 2865 male operational firefighters employed by the fire brigade in Melbourne, Australia, between 1917 and 1989. Cancer incidence follow-up was from 1980 through 1989, and comparisons were made with the general population of the state of Victoria as the reference group. The overall SIR for all cancers combined was 1.13 (95% CI, 0.84-1.48). The SIR was specifically elevated among those aged \geq 65 years (SIR, 2.14; 95% CI, 1.32-2.37). Decreasing SIRs were seen with increasing time since first employment, and no trend test was reported. With duration of employment, the highest SIR was seen among firefighters with employment of 15–29 years (SIR, 1.39; 95% CI, 0.85–2.15).

2.6.2 Studies only reporting having ever worked as a firefighter

(a) Occupational cohort studies

Studies first described in Section 2.1.2(a) are described in less detail in the present section.

See Table S2.12 (Annex 2, Supplementary material for Section 2, Cancer in Humans, online only, available from: <u>https://publications.iarc.</u> <u>fr/615</u>).

Altogether, nine occupational cohort studies in firefighters reported on risk of cancer of all sites combined (Mastromatteo, 1959; Musk et al., 1978; Eliopulos et al., 1984; Grimes et al., 1991; Deschamps et al., 1995; Ide, 1998; Ma et al., 2005, 2006; Amadeo et al., 2015). [One of these studies, Ide (1998), investigated a highly selected group of 505 firefighters aged 20–54 years who died (n = 17) or retired from service because of ill health (n = 488). This study was not considered informative and is therefore not further considered here.] Cancer incidence was evaluated only in Ma et al. (2006), whereas the remaining studies provided estimates for mortality as SMRs (Mastromatteo, 1959; Musk et al., 1978; Deschamps et al., 1995; Ma et al., 2005; Amadeo et al., 2015), PMRs (Grimes et al., 1991), or both (Eliopulos et al., 1984). None of the studies had, or used, information on duration of employment, and analyses were based on registration as a firefighter at a single time-point, in some studies with a qualifier of duration of employment for $\geq 1, 3$, or 5 years (Musk et al., 1978; Grimes et al., 1991; Deschamps et al., 1995, respectively). Periods of follow-up were generally long, ranging from 13 (Grimes et al., 1991) to 39 years (Eliopulos et al., 1984).

<u>Amadeo et al. (2015)</u> investigated all-cancer mortality in a cohort comprising 10 829 firefighters employed in 1979 and covering 93% of the population of France. Follow-up was through 2008 and comparisons were made with the male general population of France. The SMR for all cancer sites combined was near the expected value (SIR, 0.95; 95% CI, 0.88–1.02).

Deschamps et al. (1995) reported on mortality in a cohort comprising 830 male firefighters in Paris, France, with a minimum of 5 years of service on 1 January 1977. Follow-up was until 1 January 1991 (14 years). With the male general population of France as the referent, the SMR for all cancer sites combined was 0.89 (95% CI, 0.53–1.40).

Ma et al. (2006) examined cancer incidence in a cohort of 34 796 male and 2017 female career firefighters certified since 1972 in Florida. Linkage was performed with the state-wide Florida cancer registry, and comparisons were made with Florida state cancer rates. Risk of cancer of all sites was lower among male firefighters (SIR, 0.84; 95% CI, 0.79–0.90) and was elevated among female firefighters (SIR, 1.63; 95% CI, 1.22–2.14), with 970 and 52 cancer cases, respectively, compared with the general population.

In a mortality study of the same cohort as described above (<u>Ma et al., 2005</u>), follow-up was from 1972 through 1999. In male firefighters,

stratified analyses were also made for those certified between 1972 and 1976, among whom most cases occurred. The mortality rate from cancer of all sites combined was below that expected among males and was similar in the restricted cohort and the full cohort (SMR in the full cohort, 0.85; 95% CI, 0.77–0.94). Among women, the all-cancer mortality rate was as expected.

<u>Grimes et al. (1991)</u> conducted a proportionate mortality analysis of causes of death during 1969–1988 among 205 deceased firefighters employed by the city and county of Honolulu, Hawaii, USA. The firefighters had been employed for \geq 1 year, and comparisons were made with mortality rates for the male general population in Hawaii. PMRs were modestly elevated for cancers of all sites combined (overall PMR, 1.19; 95% CI, 0.96–1.49), and were somewhat higher for Hawaiian than for Caucasian [White] firefighters.

Musk et al. (1978) conducted a cohort mortality study among 5655 firefighters with \geq 3 years of service in Boston, USA, during 1915– 1975. Firefighters were identified from employment records. Information on cause of death came from death certificates, which were lacking for 194 confirmed deaths (7.9%). Mortality for cancer of all sites combined was below unity in the total cohort (SMR, 0.86; 95% CI, [0.77–0.95]) and among active firefighters (SMR, 0.73; 95% CI, [0.60–0.89]) when compared with that in Massachusetts men.

Mastromatteo (1959) conducted a cohort mortality study of all 1832 active and retired firefighters employed by the city fire department of Toronto, Ontario, Canada, from 1918 to 1954. A total of 325 firefighters (31%) were lost to follow-up after termination of work and were censored at that time. Comparison was made with mortality rates among male residents in Ontario (1921–1953) and with specifically calculated mortality rates among men in urban areas of Ontario (1937–1959). Mortality from cancer of all sites combined was moderately elevated, but imprecise, in firefighters compared with Ontario men, and similar to that in men in urban areas of Ontario. [The Working Group noted the large loss to follow-up in this study, which rendered the result less informative.]

Eliopulos et al. (1984) studied cancer mortality from 1939 through 1978 among 990 firefighters in Western Australia compared with the male general population of Western Australia. The SMR for all cancer sites was close to that expected (SMR, 1.09; 95% CI, 0.74–1.56).

(b) Population-based studies

Studies first described in Section 2.1.2(b) are described in less detail in the present section.

See Table S2.12 (Annex 2, Supplementary material for Section 2, Cancer in Humans, online only, available from: <u>https://publications.iarc.</u> <u>fr/615</u>).

Altogether, eight population-based studies reported on risk of cancer of all sites combined among firefighters, including five cohort studies (<u>Hansen, 1990; Pukkala et al., 2014; Harris et al.,</u> 2018; <u>Zhao et al., 2020; Sritharan et al., 2022</u>) and three studies based on death records (<u>Burnett</u> et al., 1994; <u>Ma et al., 1998; Muegge et al., 2018</u>).

Zhao et al. (2020) followed 9.5 million employed men aged 20-64 years, identified from the 2001 Spanish census, for a period of 10 years via data linkage to a national mortality registry. There was no evidence of increased risk of all cancers combined (MRR, 1.00; 95% CI, 0.89-1.12) among 27 365 firefighters compared with all other occupations. [The Working Group noted that the major limitations of this study were the lack of information on duration or other exposure-related information and the minimal information on potential confounding factors. In addition, the short follow-up time limited the power of this study. The main strength of the study was the use of national census data, which allowed the identification of all firefighters in 2001.]

Pukkala et al. (2014) in the NOCCA study conducted a census linkage of 15 million people from all five Nordic countries (1961-2005). A total of 16 422 males reported their occupation as firefighter. With the Nordic general population as the referent, a small excess of all cancers combined (excluding non-melanomaskin cancer) was observed (SIR, 1.06; 95% CI, 1.02-1.11). [The Working Group noted that the major limitations of this study were the lack of information on duration or other exposure related information and minimal information on potential confounding factors. The major strengths of this study were its use of high-quality tumour registry data and the use of national census data, which allowed the identification of all firefighters at the census time-points.]

Sritharan et al. (2022) investigated cancer incidence in a cohort of 13642 firefighters employed in Ontario, Canada, compared with other members of a large cohort of 2 368 226 workers and separately with 22 595 police from the same cohort. The study group was enumerated and followed-up using information from an occupational injury and disease claims database and linkage to the provincial tumour registry and other electronic health records. An increased risk of overall cancer incidence was observed in firefighters compared with all other workers in the cohort (HR, 1.23; 95% CI, 1.17–1.29) but not with police (HR, 1.03; 95% CI, 0.96–1.09).

Harris et al. (2018) conducted the CanCHEC study, which was similar to the study carried out by <u>Pukkala et al. (2014)</u> using the 1991 Canadian census, although Harris and colleagues adjusted for education level in addition to age and geographical region. The cohort included 1.1 million employed men, of whom 4535 reported their occupation as firefighter, with follow-up to the end of 2010. The overall cancer incidence was similar to that for other employed men (HR, 1.04; 95% CI, 0.96–1.14). [The Working Group noted that the major limitations of this study were the lack of information on duration or other exposure-related information and the minimal information on potential confounding factors. Its major strengths were the use of tumour registry data and the use of national census data, which allowed the identification of all firefighters in 1991.]

Muegge et al. (2018) used death certificates from Indiana, USA, for a mortality study using a case-control analysis among firefighters. Four non-firefighters per firefighter, matched on year of death, age at death, sex, and race/ethnicity, were randomly chosen as the comparison population. An increased risk of overall cancer mortality was observed (OR, 1.19; 95% CI, 1.08-1.30) based on 857 cancer deaths among firefighters. [The Working Group noted that the authors used non-standard analytical methods similar to the MOR analysis proposed as an alternative to the PMR. Another major limitation of this study was the reliance on death certificates to identify both occupation and cancer (which is likely to result in misclassification of both), and the lack of information on duration or other exposure-related information, which limits the ability to draw conclusions regarding causality. This study also had minimal information on potential confounding factors, other than sex and race.]

Ma et al. (1998) used death certificates from 24 states in the USA as the sole source of both occupation and underlying cause of death in 1984-1993. There were 1817 cancer deaths observed among White male firefighters (MOR, 1.1; 95% CI, 1.1-1.2) and 66 among Black firefighters (MOR, 1.2; 95% CI, 0.9-1.5). In an earlier report, Burnett et al. (1994) used data from 27 states for a proportionate mortality analysis of White male firefighters in 1984-1990. An excess of all cancers combined was identified (PMR, 1.10; 95% CI, 1.06-1.14). Twenty-four of the 27 states were the same as those reported by Ma et al. (1998) for a somewhat longer time period. [The Working Group noted that the major limitations of these studies were the reliance on death certificates to identify both occupation

and cancer, which is likely to result in misclassification of both. Results may also be biased if the cancer sites chosen as controls are associated with firefighting. In addition, death certificates lack information on duration or other exposure-related information, which limits the ability to draw conclusions regarding causality. These studies also had no information on potential confounding factors, other than sex and race.]

2.7 Case reports

Twelve case reports or series describing the occurrence of cancers of any site in individuals occupationally exposed as a firefighter were reviewed (Bates & Lane, 1995; Cucchi, 2003; Bianchi et al., 2007; Wolfe et al., 2012; Cormack, 2013; Schrey et al., 2013; Sugi et al., 2013; Antoniv et al., 2017; Landgren et al., 2018; Geiger et al., 2020; Brinchmann et al., 2022; Park et al., 2022). The Working Group determined that seven of these reports were not informative to this review as they did not provide information on occupational exposures other than the patient's occupation as a firefighter. These publications included four reports that each presented a brief clinical description of a rare tumour in a firefighter: a benign clavicular neoplasm (Sugi et al., 2013); a diffuse mesothelioma of the pericardium (Cucchi, 2003); a peritoneal mesothelioma (Cormack, 2013); and an extramedullary head and neck tumour (Schrey et al., 2013). Also included in this group of publications was a report describing 99 cases of pleural mesothelioma diagnosed in residents of Trieste province, Italy, one of whom was a firefighter (Bianchi et al., 2007); a description of the clinical course of Chernobyl-exposed patients with laryngeal cancer (Antoniv et al., 2017); and a clinical description of mycosis fungoides among eight people exposed to flame-retardant clothing (with no description of the patient's occupation) (Park et al., 2022). The five case reports and case series reviewed provided detailed descriptions of risk factor information relevant to the occurrence of cancer at sites reported in epidemiological studies reviewed in the present monograph: metastatic melanoma (Brinchmann et al., 2022); renal cell carcinoma (Geiger et al., 2020); multiple myeloma (Landgren et al., 2018); testicular cancer (Bates & Lane, 1995); and SCC of the skin (Wolfe et al., 2012). One of these case reports further provided support for non-burning heat exposure as a mechanism for SCC in wildland firefighters (Wolfe et al., 2012).

Brinchmann et al. (2022) described a case of metastatic melanoma (primary site unknown) in a male firefighter with 33 years (1973–2006) of occupational exposure as a firefighter. The patient had worked as a structural [municipal] firefighter in an industrial urban environment and had responded to diverse types of fires, including industrial, residential, vehicular, and brush. He also oversaw departmental trainings. The discussion noted probable occupational exposure to solar radiation and polychlorinated biphenyls (PCBs), both of which are considered by IARC to be carcinogenic agents with suffi*cient* evidence in humans for melanoma (Lauby-Secretan et al., 2013). [The Working Group did not find the report informative for the review because no exposures unique to firefighting were discussed and no direct evidence of exposure to PCBs or solar radiation was provided.]

Geiger et al. (2020) reported on a case series of four firefighters in Washington state, USA, who were diagnosed with kidney cancer found incidentally on imaging. Cases were identified by a retrospective review of electronic healthcare records from a single clinic in a search for patients with a history of a firefighting career who had been diagnosed with renal cell carcinoma between 2014 and 2019. Abstracted information included duration of firefighting employment, as well as known risk factors for renal cancer, including age and BMI at diagnosis, smoking history, and family history of renal cancer. Career firefighting tenure among cases ranged from 8 to 40 years. Among the firefighters, age at diagnosis ranged from 31 to 59 years and three patients were aged < 40 years, whereas the authors noted that in the general population less than 5% of renal cancers are diagnosed in patients aged 20-40 years. None of the cases had a reported history of smoking [causally associated with renal cancer] and BMI ranged from 28 to 31 kg/m². [The Working Group noted that few agents associated with occupational exposure have been identified by the IARC Monographs programme with sufficient evidence of carcinogenicity for renal cancer: these include trichloroethylene and X- and gamma-radiation. The strengths of this case series included information on duration of career firefighting experience and a set of behavioural and medical risk factors. The limitations included that smoking history and lifetime occupation may be underreported or misclassified in medical records. Interpretation was clouded by the lack of description of the clinic source population. The reporting of BMI at the time of diagnosis (as opposed to a considerable time before diagnosis) was also a limitation since body-weight loss may result from renal cancer.]

Landgren et al. (2018) described the clinical characteristics of 16 patients with multiple myeloma among FDNY WTC-exposed firefighters. The cases were diagnosed between 11 September 2001 and 1 July 2017 and identified from the 11 959 non-Hispanic White male firefighters in the FDNY cohort who consented to participate in the research. The diagnosis of multiple myeloma was confirmed by linkage with population-based cancer registries and a review of FDNY WTC Health Program records. Cohort members of ethnicity other than non-Hispanic White (n = 959) were not included in this case series. The median age at diagnosis was 57 years (range, 38–76 years), and the median time between 11 September 2001 and diagnosis was 12 years (range, 1-16 years). Of the cases of multiple myeloma, fourteen had peripheral blood samples evaluated and lightchain proteins were detected in seven (50%; 95%

CI, 27–73%). [The Working Group noted that a strength of this case series was its robust casefinding approach. Limitations included that WTC disaster exposure was not described for the cases, and no additional information was given on other firefighting or occupational exposures. The authors also conducted serological screening for monoclonal gammopathy of undetermined significance (MGUS, the precursor state for most multiple myeloma diagnoses) and lightchain MGUS (LC-MGUS) among 781 FDNY firefighters. However, this serological analysis was not reviewed in the present section as it was beyond the scope of a case series. The Working Group noted that investigation of MGUS and LC-MGUS, as precursors of multiple myeloma, may reveal common causal pathways; however, this cross-sectional survey was not reviewed elsewhere in the present monograph because of the descriptive nature of the analysis.]

In a case report, Wolfe et al. (2012) described SCCs of the skin on the lower extremities diagnosed in 2005 in a 65-year-old Caucasian [White] man with 28 years occupational experience as a wildland firefighter in Florida, USA. The patient had incurred chronic heat exposure to the lower extremities and reported 15-hour workdays with daily exposure of an hour (4 feet [1.2 m] or less from the fire line). PPE included wildfire protective trousers and boots. The patient had a history of 13 SCCs below the knee in the 4 years preceding the current diagnosis; in the next 3 years he developed 28 SCCs between the ankle and midthigh. All SCCs developed on the heat-exposed front and side of the legs and none on the back of the legs. The authors noted that in the 1970s wildland firefighting teams began prioritizing controlled burns, which can result in longer and more proximate heat exposure than the previously prioritized wildfire suppression activities. They hypothesized that changes in the epithelium attributable to lifetime chronic non-burning heat exposure, as well as to solar radiation, may have predisposed this wildland firefighter to SCC formation. [The Working Group noted that this single case report was of interest since it points to chronic non-burning heat exposure as a potential mechanism for SCC of the skin among wildland firefighters. Limitations included that, although cumulative heat exposure to the lower extremities was quantified, the methods used to do so were not described. Similarly, although type of PPE used was described, frequency of use was not.]

Bates & Lane (1995) reported on an investigation of four cases of testicular cancer diagnosed among firefighters employed in Wellington, New Zealand. The cases were found incidentally when the Wellington fire department was used as a comparison group for another study of occupational exposure in firefighters after an industrial fire in December 1984. Three cases of testicular cancer were identified among Wellington firefighters during that study period, December 1984 to December 1988. The fourth case was diagnosed in January 1989. Information about the cancer diagnosis (e.g. date, laterality) and risk factors for testicular cancer (e.g. age, ancestry, family history of cancer, occupational history, injuries, and cryptorchidism) was gathered by medical record review and through interviews with the patients. All cases were histologically confirmed as germ cell testicular cancer. Age of diagnosis ranged from 24 to 59 years. The cases were fulltime firefighters employed for 6-19 years (mean, 13 years) and all had been exposed to smoke. No common risk factors for testicular cancer were reported. [The Working Group concluded that this systematically conducted case investigation was minimally informative for the present monograph since it lacked details of firefighting exposures. However, a retrospective cohort study that compared testicular cancer incidence and mortality among all paid [career] firefighters in New Zealand in 1977-1996 with that in the general population is reviewed in Section 2.2.2 (Bates et al., 2001).]

2.8 Meta-analyses

2.8.1 Meta-analyses of cancer risk among firefighters

Seven meta-analyses investigating the association between occupational exposure as a firefighter and risk of cancer were available to the Working Group (Howe & Burch, 1990; LeMasters et al., 2006; Youakim, 2006; Sritharan et al., 2017; Jalilian et al., 2019; Soteriades et al., 2019; Casjens et al., 2020). Three of the available meta-analyses were published before the previous evaluation of firefighting by the IARC Monographs programme (Volume 98) in October 2007 (IARC, 2010). The Working Group for Volume 98 conducted a separate meta-analysis that showed increased meta-relative risks for cancer of the testis (1.47; 95% CI, 1.20–1.80; fixed effects, 6 studies), prostate (1.30; 95% CI, 1.12–1.51; random effects, 16 studies), and NHL (1.21; 95% CI, 1.08-1.36; fixed effects, 7 studies). One of the more recent meta-analyses focused on only prostate cancer (Sritharan et al., 2017). Further, an overview of systematic reviews of cancer incidence and mortality was available; this overview included 104 original studies, of which some overlapped, that were published between 1959 and 2018 (Laroche & L'Espérance, 2021). All meta-analyses overlapped concerning included studies, outcome (incidence and mortality), and the cancer sites evaluated. For the present review, the Working Group considered in detail two meta-analyses (Jalilian et al., 2019; Casjens et al., 2020) that included as many of the most relevant and recent studies as possible, in addition to the meta-analysis of only prostate cancer (Sritharan et al., 2017). A fourth recently published metaanalysis was considered less informative because it only included studies published until 2007 (Soteriades et al., 2019).

The meta-analysis of only prostate cancer incidence and mortality included 26 studies of firefighters published from 1980 to 2017 (<u>Sritharan</u> et al., 2017). Meta-risk estimates were calculated based on random effects models and were similar for incidence (1.17; 95% CI, 1.08–1.28, $I^2 = 72\%$) and mortality (1.12; 95% CI, 0.92–1.36, $I^2 = 50\%$). [The Working Group noted that the similarity between incidence and mortality estimates provided evidence against a strong medical surveillance bias. The heterogeneity variance estimator was not reported.]

A meta-analysis of cancer incidence and mortality studies published before 1 January 2018 combined information from 48 casecontrol and cohort studies using random effects meta-analysis models (Jalilian et al., 2019). Only results for male firefighters or male and female firefighters combined were included. Studies were largely conducted in the USA (41% of incidence studies and 54% of mortality studies). Case ascertainment periods were from 1950 to 2014 for incidence studies and from 1921 to 2011 for mortality studies. Studies of volunteer and trainee firefighters were excluded. Included studies used predominantly national, regional, or local external comparison populations. [Studies from the Nordic countries may have had overlapping study populations with cases included more than once in meta-estimates.] For all cancers combined, both the overall summary of incidence risk estimate (SIRE) (12 studies) and summary of mortality risk estimate (SMRE) (22 studies) among firefighters were at unity: 0.99 (95% CI, 0.93–1.05) and 0.99 (95% CI, 0.92–1.06), respectively. Small increased risks were seen for incidence of cancer of the colon (SIRE, 1.14; 95% CI, 1.06–1.23; 10 studies), rectum (SIRE, 1.09; 95% CI, 1.00-1.20; 10 studies), prostate (SIRE, 1.15; 1.05-1.27; 17 studies), bladder (SIRE, 1.12; 95% CI, 1.04-1.21; 14 studies), and thyroid (SIRE, 1.22; 95% CI, 1.01-1.48; 10 studies), and for melanoma (SIRE, 1.21; 95% CI, 1.02-1.45; 11 studies). The SIREs were over 1.3 for only two cancer sites: cancer of the testis (SIRE, 1.34; 95%) CI, 1.08–1.68; 9 studies) and cancer of the pleura (mesothelioma) (SIRE, 1.60; 95% CI, 1.09-2.34;

5 studies). For cancer mortality, only the estimates for rectal cancer (SMRE, 1.36; 95% CI, 1.18–1.57; 12 studies) and NHL (SMRE, 1.42; 95% CI, 1.05–1.90; 8 studies) were elevated. [The Working Group noted that results from cohort and case–control studies were pooled into one meta-effect estimate, which may have biased results. The heterogeneity variance estimator was not reported.]

The most recent meta-analysis included 25 cohort studies of both incidence and mortality outcomes (Casjens et al., 2020) published during 1959-2018. Only cohort studies of cancer in male career full-time firefighters that included the general population as the referent in external comparisons were included. Studies of exposure to catastrophic events (e.g. the WTC responders) were excluded. Meta-risk estimates for incidence and mortality outcomes were calculated separately and based on inverse-variance random effect models. Models were fitted using the Paule-Mandel heterogeneity variance estimator. [Some of the studies in the Nordic countries may have had overlapping study populations with cases included more than once in meta-estimates.] The meta-estimates for the incidence (meta-standardized incidence ratio, meta-SIR, 1.00; 95% CI, 0.93-1.07; 9 studies) and mortality (metastandardized mortality ratio, meta-SMR, 0.97; 95% CI, 0.89-1.05; 17 studies) of all cancers combined were similar to the general population. [The Working Group noted that a high proportion of the estimates for specific cancers, 18 of 37 cancer sites for incidence and 13 of 30 mortality sites, were based on a small number of studies and estimates were statistically imprecise.] Elevated risks were found for incidence of colon cancer (meta-SIR, 1.11; 95% CI, 1.00-1.21; 6 studies), bladder cancer (meta-SIR, 1.18; 95% CI, 1.01-1.34; 6 studies), and mesothelioma (meta-SIR, 1.46; 95% CI, 1.01-1.90; 2 studies). For mortality, increases were seen for cancers of the rectum (meta-SMR, 1.35; 95% CI, 1.12-1.59; 9 studies) and bladder (1.72; 95% CI, 1.05-2.38;

7 studies). Finally, stratification of risks by three calendar periods (related to potential differences in exposure and the use of personal protective equipment) and three geographical regions was provided. [The Working Group noted that information on the proportion of full-time career firefighters within the included cohorts was not available for all studies. This meta-analysis only included results using a general population referent, which were more prone to bias because of the healthy-worker hire effect and surveillance bias than were results using other uniformed service workers as the referent. Stratified estimates were based on small numbers of studies.]

2.8.2 Working Group meta-analysis

The Working Group conducted a metaanalysis of the most recently available epidemiological studies on the association between occupational exposure as a firefighter and cancer. The methods, analysis, and results of this work are described in detail in a stand-alone publication (DeBono et al., 2023). Briefly, the objective was to conduct a meta-analysis of the association between ever-employment and duration of employment as a firefighter and cancer incidence and mortality. Information was abstracted from studies published until 13 June 2022. Studies were evaluated for the influence of key biases on results. Random-effects meta-analysis models were used to estimate associations with 12 selected cancer sites. The impact of bias was explored in sensitivity analyses.

The overall results are presented in <u>Table</u> 2.13, and results for selected cancer sites are also illustrated using forest plots in <u>Fig. 2.1</u>, <u>Fig. 2.2</u>, <u>Fig. 2.3</u>, <u>Fig. 2.4</u>, <u>Fig. 2.5</u>, <u>Fig. 2.6</u>, <u>Fig. 2.7</u>, <u>Fig. 2.8</u>, and <u>Fig. 2.9</u>. There was evidence of positive associations between occupational exposure as a fire-fighter and cancer incidence for several cancer types, including cancers of the urinary bladder, testis, prostate, thyroid, and colon, and mesothelioma, NHL, and melanoma. Associations for

Outcome	No. of studies ^a	Meta-rate ratio ^b (95% CI)	I ^{2 c} (%)	Q P value	τ^2
Incidence (SIR, RR, HR)					
All cancers (C00-C95)	14	1.05 (0.99-1.11)	87	< 0.01	0.008
Stomach (C16)	12	1.00 (0.87-1.15)	33	0.12	0.002
Colon (C18)	10	1.19 (1.07-1.32)	37	0.11	0.007
Lung (C33–C34)	14	0.85 (0.75-0.96)	78	< 0.01	0.032
Melanoma (C43)	12	1.36 (1.15-1.62)	83	< 0.01	0.062
Mesothelioma (C45)	7	1.58 (1.14-2.20)	8	0.36	0.009
Prostate (C61)	14	1.21 (1.12-1.32)	81	< 0.01	0.015
Testis (C62)	11	1.37 (1.03-1.82)	56	0.01	0.084
Kidney (C64–C66)	12	1.09 (0.92-1.29)	55	0.01	0.035
Bladder (C67–C68)	10	1.16 (1.08-1.26)	0	0.71	0
Brain and nervous (C47, C70-C72)	11	1.01 (0.86-1.18)	5	0.40	0.003
Thyroid (C73)	10	1.28 (1.02-1.61)	40	0.09	0.055
Non-Hodgkin lymphoma (C82–C85)	13	1.12 (1.01-1.25)	0	0.51	0.007
<i>Mortality (SMR, RR)</i> ^d					
All cancers (C00-C95)	18	0.96 (0.88-1.06)	87	< 0.01	0.026
Stomach (C16)	13	1.05 (0.87-1.28)	41	0.06	0.045
Colon (C18)	9	1.03 (0.78-1.37)	63	< 0.01	0.079
Lung (C33–C34)	12	0.96 (0.86-1.06)	55	0.01	0.008
Melanoma (C43)	4	1.05 (0.48-2.30)	0	0.43	0.093
Mesothelioma (C45)	3	1.75 (0.83-3.69)	0	0.56	0
Prostate (C61)	11	1.07 (0.95-1.20)	30	0.16	0
Kidney (C64–C66)	9	1.10 (0.66-1.83)	53	0.03	0.199
Bladder (C67–C68)	9	1.22 (0.70-2.11)	67	< 0.01	0.267
Brain and nervous (C47, C70-C72)	11	1.33 (0.98-1.79)	53	0.02	0.098
Thyroid (C73)	4	1.90 (0.36-10.00)	58	0.07	0.671
Non-Hodgkin lymphoma (C82–C85)	5	1.20 (1.03-1.40)	0	0.74	0

Table 2.13 Meta-rate ratios for selected cancers in male career firefighters compared with a general, uniformed service, or working population referent

CI, confidence interval; HR, hazard ratio; RR, rate ratio; SIR, standardized incidence ratio; SMR, standardized mortality ratio. ^a Results from the studies by <u>Daniels et al. (2014)</u> and <u>Pinkerton et al. (2020)</u> included a small number of women. <u>Petersen et al. (2018a)</u> included part-time/volunteer firefighters for cancers of the kidney, stomach, thyroid, and brain, and for mesothelioma. Some results from overlapping study populations were excluded.

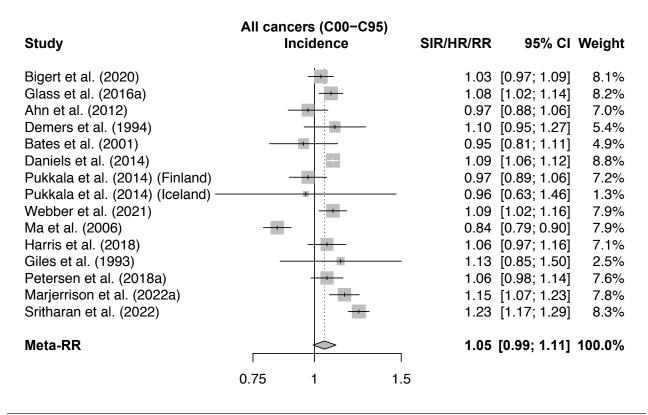
^b Random-effects models were used with between-study variance estimated using the restricted maximum-likelihood estimator. Hartung– Knapp–Sidik–Jonkman (HKSJ) adjustments and an ad hoc variance correction (using wider confidence intervals) were used to calculate confidence intervals.

^c See Figure 1 in <u>DeBono et al. (2023)</u> for individual study results and generic inverse-variance meta-analysis statistics. The variance of individual study estimates was based on the reported confidence interval bounds and may differ from estimates obtained using exact methods when there are few cases.

^d Outcomes with fewer than three available studies were not meta-analysed.

From DeBono et al. (2023), CC-BY-3.0.

Fig. 2.1 Forest plot of individual study results and meta-rate ratios for incidence of all cancers in firefighters compared with a general, uniformed service, or working population referent



CI, confidence interval; HR, hazard ratio; meta-RR, meta-rate ratio; RR, rate ratio; SIR, standardized incidence ratio.

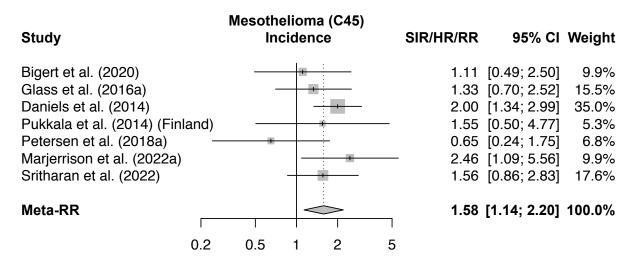
Heterogeneity: $I^2 = 87\%$, $\tau^2 = 0.0079$, P < 0.01

Random-effects models were used with the restricted maximum-likelihood estimator. Hartung–Knapp–Sidik–Jonkman (HKSJ) adjustments and an ad hoc variance correction were used to calculate confidence intervals for summary estimates. Calculated study intervals may differ from reported values because of differences in variance estimation methods.

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bladder cancer and NHL were modest in magnitude. For mortality outcomes, associations were attenuated compared with incidence outcomes for cancers of the prostate and colon and melanoma, whereas they were similar or greater in magnitude for cancers of the bladder and lung, NHL, and mesothelioma. Since the most recent meta-analysis on cancer in firefighters (Casjens et al., 2020), three new cohort studies (Marjerrison et al., 2022a, b; Sritharan et al., 2022; Zhao et al., 2020) and two cohorts with extended follow-up (Bigert et al., 2020; Pinkerton et al., 2020) have been published that were included in the Working Group's meta-analysis. Our results from comparable analyses were consistent with those previously reported and suggested more strongly positive associations for the incidence of testicular, colon, and prostate cancer, and for mesothelioma and melanoma. Applying a causal interpretation to our findings requires additional considerations regarding the influence of bias and the plausibility of exposures in the occupation to cause specific cancer types over time. Results of the meta-analysis are described in detail in the evidence synthesis (Section 2.9) within the context of causal inference for cancer hazard identification in humans.

Fig. 2.2 Forest plot of individual study results and meta-rate ratios for incidence of mesothelioma in firefighters compared with a general, uniformed service, or working population referent



CI, confidence interval; HR, hazard ratio; meta-RR, meta-rate ratio; RR, rate ratio; SIR, standardized incidence ratio.

Heterogeneity: $I^2 = 8\%$, $\tau^2 = 0.0093$, P = 0.36

Random-effects models were used with the restricted maximum-likelihood estimator. Hartung–Knapp–Sidik–Jonkman (HKSJ) adjustments and an ad hoc variance correction were used to calculate confidence intervals for summary estimates. Calculated study intervals may differ from reported values because of differences in variance estimation methods. From DeBono et al. (2023), CC-BY-3.0.

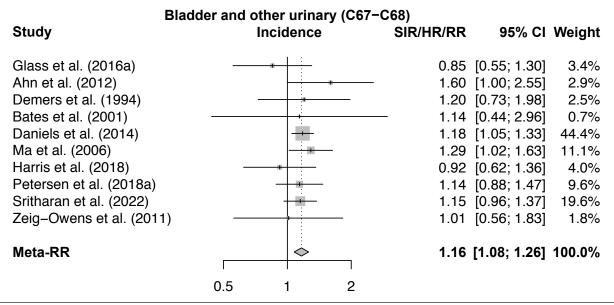
2.9 Evidence synthesis for cancer in humans

In total, 52 cohort and case–control studies (including PMR and other "event-only" studies), 12 case reports, and 7 meta-analyses were available for the evaluation of the association between occupational exposure as a firefighter and cancer incidence or mortality. Many of these studies were published since the first evaluation of firefighting by the *IARC Monographs* programme in 2007 (IARC, 2010), which included 42 studies.

2.9.1 Original studies evaluated

Many of the available studies were in occupational cohorts, which typically reported results for several different cancer types and for all cancers combined. Some of these studies provided results on cancer incidence, some on cancer mortality, and a few on both. In assessing the carcinogenicity of occupational exposure as a firefighter, the greatest weight was accorded to findings from cohort studies because of their lower potential for bias compared with other designs. In general, the cohort studies of incidence were given higher weight than studies of mortality because of the relatively poorer quality of cancer information obtained from death certificates, and lower sensitivity for identifying cases of certain cancer types with higher survivability, e.g. testicular cancer. However, the Working Group considered that mortality results may occasionally complement and inform the interpretation of incidence results for certain cancer types that may be prone to surveillance bias, such as cancers of the prostate, colon, and thyroid. The cohort studies all had retrospective designs and typically lacked information on important potential confounders apart from age, sex, and calendar period, such as tobacco smoking, alcohol drinking, sun exposure habits, and leisure time physical activity.

Fig. 2.3 Forest plot of individual study results and meta-rate ratios for incidence of cancers of the urinary bladder and other and unspecified urinary organs excluding kidney, renal pelvis, and ureter in firefighters compared with a general, uniformed service, or working population referent



CI, confidence interval; HR, hazard ratio; meta-RR, meta-rate ratio; RR, rate ratio; SIR, standardized incidence ratio.

Heterogeneity: $I^2 = 0\%$, $\tau^2 = 0$, P = 0.71

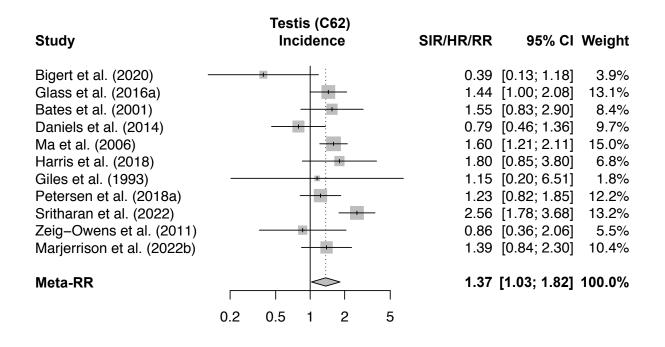
Random-effects models were used with the restricted maximum-likelihood estimator. Hartung-Knapp-Sidik-Jonkman (HKSJ) adjustments and an ad hoc variance correction were used to calculate confidence intervals for summary estimates. Calculated study intervals may differ from reported values because of differences in variance estimation methods. From DeBono et al. (2023), CC-BY-3.0.

Very few case-control or "event-only" studies provided such information.

Studies based only on information from either mortality or cancer registries (e.g. proportionate mortality or other "event-only" studies) were reviewed but given little weight because of the high potential for exposure misclassification and/or selection bias. Occupational surveillance studies (n = 36) that did not investigate cancer in firefighters a priori were excluded from further consideration because of the potential for publication bias (e.g. selective reporting of only positive findings in the searchable abstract). [Some of these studies were included in the previous monograph on occupational exposure as a firefighter (IARC, 2010), reducing the overlap in studies evaluated in the two monographs.] Finally, 12 case-report or case-series studies describing the occurrence of cancers of any site in individuals occupationally exposed as a firefighter were available to the Working Group. Seven were considered uninformative and were not reviewed further because they lacked information on occupational exposures outside the patient's occupation as a firefighter, and five of those reviewed by the Working Group were not considered further because they lacked details about firefighting exposures.

Some of the studies reviewed by the Working Group provided details about aspects of exposure, such as duration of work as a firefighter, full-time or part-time employment status, volunteer versus career work status, number of fire responses, and types of fires attended (e.g. structure, wildland), whereas others included only

Fig. 2.4 Forest plot of individual study results and meta-rate ratios for incidence of cancer of the testis in firefighters compared with a general, uniformed service, or working population referent



CI, confidence interval; HR, hazard ratio; meta-RR, meta-rate ratio; RR, rate ratio; SIR, standardized incidence ratio.

Heterogeneity: $I^2 = 56\%$, $\tau^2 = 0.0843$, P = 0.01

Random-effects models were used with the restricted maximum-likelihood estimator. Hartung–Knapp–Sidik–Jonkman (HKSJ) adjustments and an ad hoc variance correction were used to calculate confidence intervals for summary estimates. Calculated study intervals may differ from reported values because of differences in variance estimation methods.

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information on ever versus never having worked as a firefighter. The Working Group's critique of the quality of exposure assessment in the reviewed studies is summarized in Section 1.8.1.

A detailed definition of the agent, including various types of firefighter (e.g. career, volunteer, structure, wildland) has been described in Section 1.2. Although the work of these groups of firefighters may entail different underlying exposures, the available epidemiological data did not in general allow for making inferences by type of firefighting. Studies of firefighters included in the FDNY WTC-disaster responders cohort (Zeig-Owens et al., 2011; Webber et al., 2021) were included in the evaluation but were considered somewhat less informative, given the probable increased cancer surveillance in these firefighters compared with the reference populations used. Although some information was available on volunteer firefighters in a few studies, participants in most studies were (or were presumed to be) career firefighters. The Working Group was unable to make separate conclusions about whether the association between occupational exposure as a firefighter and cancer differed between female and male firefighters, given the paucity of data for women. Therefore, although the evaluation of the Working Group was primarily based on evidence derived from male municipal career firefighters, there was no evidence to suggest that results would not also apply to women or to other types of firefighter.

Fig. 2.5 Forest plot of individual study results and meta-rate ratios for incidence of melanoma in firefighters compared with a general, uniformed service, or working population referent

	Melanoma (C43)			
Study	Incidence	SIR/RR	95% CI	Weight
Bigert et al. (2020)	<u>—</u>	1.22	[0.96; 1.55]	9.9%
Glass et al. (2016a)		1.45	[1.26; 1.66]	11.4%
Demers et al. (1994)	<u> </u>	1.20	[0.61; 2.35]	4.3%
Bates et al. (2001)	- <u>-</u> -	1.26	[0.82; 1.94]	6.9%
Daniels et al. (2014)		0.87	[0.73; 1.03]	11.0%
Pukkala et al. (2014) (Finland)		1.16	[0.73; 1.84]	6.5%
Pukkala et al. (2014) (Iceland)		— 1.83	[0.13; 26.15]	0.4%
Webber et al. (2021)		1.59	[1.29; 1.95]	10.5%
Harris et al. (2018)		1.58	[1.11; 2.25]	8.1%
Giles et al. (1993)		1.08	[0.40; 2.90]	2.4%
Petersen et al. (2018a)		1.28	[0.94; 1.74]	8.8%
Marjerrison et al. (2022a)	<u> </u>	1.30	[0.96; 1.75]	9.0%
Sritharan et al. (2022)		2.38	[1.99; 2.84]	10.9%
Meta-RR		1.36	[1.15; 1.62]	100.0%
C	0.1 0.5 1 2 10			

CI, confidence interval; HR, hazard ratio; meta-RR, meta-rate ratio; RR, rate ratio; SIR, standardized incidence ratio.

Heterogeneity: $I^2 = 83\%$, $\tau^2 = 0.0619$, P < 0.01

Random-effects models were used with the restricted maximum-likelihood estimator. Hartung–Knapp–Sidik–Jonkman (HKSJ) adjustments and an ad hoc variance correction were used to calculate confidence intervals for summary estimates. Calculated study intervals may differ from reported values because of differences in variance estimation methods. From <u>DeBono et al. (2023), CC-BY-3.0</u>.

2.9.2 Meta-analysis

Eight meta-analyses were available, including one performed by the Working Group in 2007 (IARC, 2010). Two were published relatively recently and captured selected studies published until 2018 (see Section 2.8.1). To improve upon some methodological approaches in these analyses, and to include the most recent studies, the Working Group performed an updated metaanalysis of studies of incidence and mortality, including cohort studies published until 13 June 2022 (DeBono et al., 2023; see Section 2.8.2). Estimates of meta-rate ratios (meta-RR) were computed for each cancer site, including I^2 and *P* values as estimates of residual between-study variance (heterogeneity). The following cancer types were examined: mesothelioma, urinary bladder, testis, NHL, prostate, melanoma, colon, brain, thyroid, lung, stomach, kidney, and all cancers combined. These were chosen on the basis of suggested positive findings in previous meta-analyses, findings from studies in the literature review, and the conclusions of the previous evaluation by the *IARC Monographs* programme. Other cancer sites were not considered further in the meta-analysis. Fig. 2.6 Forest plot of individual study results and meta-rate ratios for incidence of cancer of the prostate in firefighters compared with a general, uniformed service, or working population referent

	Prostate (C61)			
Study	Incidence	SIR/HR/RR	95% CI	Weight
Bigert et al. (2020)		1.06	[0.96; 1.17]	10.1%
Glass et al. (2016a)		1.23	[1.10; 1.37]	9.6%
Ahn et al. (2012)		1.32	[0.65; 2.70]	1.2%
Demers et al. (1994)		1.40	[1.13; 1.74]	6.3%
Bates et al. (2001)		1.08	[0.55; 2.11]	1.3%
Daniels et al. (2014)	+	1.03	[0.97; 1.09]	11.0%
Pukkala et al. (2014) (Finland)		1.21	[1.02; 1.43]	7.7%
Pukkala et al. (2014) (Iceland)		0.90	[0.37; 2.19]	0.8%
Webber et al. (2021)		1.55	[1.39; 1.73]	9.6%
Ma et al. (2006)		1.10	[0.90; 1.34]	6.8%
Harris et al. (2018)		1.15	[0.99; 1.34]	8.3%
Giles et al. (1993)	*	- 2.09	[0.77; 5.64]	0.6%
Petersen et al. (2018a)		1.12	[0.95; 1.33]	7.8%
Sritharan et al. (2022)		1.43	[1.31; 1.57]	10.2%
Marjerrison et al. (2022b)	-	1.18	[1.03; 1.35]	8.8%
Meta-RR	÷ ◆		[1.12; 1.32]	100.0%
0.2	0.5 1 2	5		

CI, confidence interval; HR, hazard ratio; meta-RR, meta-rate ratio; RR, rate ratio; SIR, standardized incidence ratio. Heterogeneity: $I^2 = 81\%$, $\tau^2 = 0.0146$, P < 0.01

Random-effects models were used with the restricted maximum-likelihood estimator. Hartung–Knapp–Sidik–Jonkman (HKSJ) adjustments and an ad hoc variance correction were used to calculate confidence intervals for summary estimates. Calculated study intervals may differ from reported values because of differences in variance estimation methods.

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2.9.3 Exposure assessment and misclassification of exposure

As described in Section 1.8.1, many studies considered by the Working Group classified exposure on the basis of ever having worked as a firefighter, without further information on specific firefighting activities. A minority of studies captured specific job duties within fire departments, such as fire combat, fire inspection, training, or administrative positions. The number of fires and types, such as structure versus wildland, were documented only in a small number of studies. Duration of employment was the surrogate used most often for level of exposure, although a few studies used more sophisticated measures of exposure, such as number and/or types of fire responses, or duration of employment in active firefighting roles.

A challenge to assessing cancer risk among firefighters is potential exposure to a wide range of established and suspected human carcinogens

Fig. 2.7 Forest plot of individual study results and meta-rate ratios for incidence of non-Hodgkin lymphoma in firefighters compared with a general, uniformed service, or working population referent

non–Hodgkin lymphoma (C82–C85)						
Study	Incidence	SIR/HR/RR	95% CI	Weight		
Bigert et al. (2020)	<u>+</u>	1.05	[0.77; 1.44]	8.7%		
Glass et al. (2016a)			[0.73; 1.32]	9.7%		
Ahn et al. (2012)	<u> </u>		[1.04; 2.75]			
Demers et al. (1994)			[0.41; 1.96]			
Daniels et al. (2014)				20.3%		
Pukkala et al. (2014) (Finland)	;		[0.62; 1.58]	4.5%		
Pukkala et al. (2014) (I mand) Pukkala et al. (2014) (Iceland) —	Ē.		[0.02, 1.36]			
. , . ,			•			
Webber et al. (2021)	:		[0.97; 1.71]	10.3%		
Ma et al. (2006)			[0.63; 1.87]	3.4%		
Harris et al. (2018)	 _:		[0.71; 1.41]			
Giles et al. (1993)			[0.60; 5.70]			
Petersen et al. (2018a)			[0.68; 1.53]			
Marjerrison et al. (2022a)			[0.78; 1.75]	5.8%		
Sritharan et al. (2022)		1.35	[1.11; 1.64]	17.1%		
Meta-RR	∳	1.12	[1.01; 1.25]	100.0%		
		' •				
0.1	0.5 1 2 1	0				

CI, confidence interval; HR, hazard ratio; meta-RR, meta-rate ratio; RR, rate ratio; SIR, standardized incidence ratio.

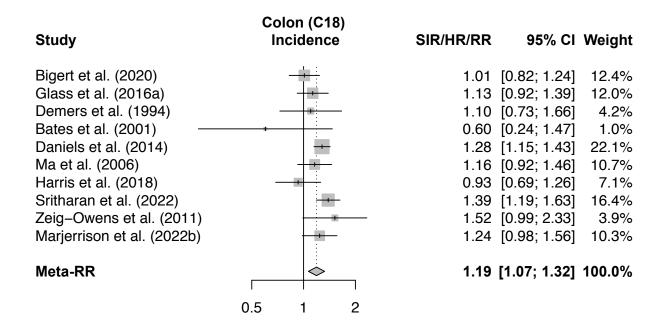
Heterogeneity: $I^2 = 0\%$, $\tau^2 = 0.068$, P = 0.51

Random-effects models were used with the restricted maximum-likelihood estimator. Hartung–Knapp–Sidik–Jonkman (HKSJ) adjustments and an ad hoc variance correction were used to calculate confidence intervals for summary estimates. Calculated study intervals may differ from reported values because of differences in variance estimation methods. From <u>DeBono et al. (2023), CC-BY-3.0</u>.

(see Section 1, Table 1.1), which may vary based on duties, types of fire being fought, calendar era, or the individual characteristics of a particular fire. Although duration of employment may be positively correlated with some firefighting exposures, it may not be closely correlated with an exposure such as fire smoke, which can vary greatly even within departments and can decline with longer employment because of diminishing front-line fire combat duties as seniority accrues. In addition, associations between cancer and duration of employment can be affected by the healthy-worker survivor bias. Information on

the number and/or types of fires represents a further improvement, which may provide better surrogates of exposure to fire smoke but will still not capture specific exposures that vary by individual fire events.

In the present evaluation, the Working Group attempted to classify studies on the basis of the quality of their exposure assessment. However, there was a wide range of potential exposures to consider, and very few were well captured, even by the best surrogates. Misclassification of exposure to specific hazards was considered common in studies assessing only employment Fig. 2.8 Forest plot of individual study results and meta-rate ratios for incidence of cancer of the colon in firefighters compared with a general, uniformed service, or working population referent



CI, confidence interval; HR, hazard ratio; meta-RR, meta-rate ratio; RR, rate ratio; SIR, standardized incidence ratio.

Heterogeneity: $I^2 = 37\%$, $\tau^2 = 0.0066$, P = 0.11

Random-effects models were used with the restricted maximum-likelihood estimator. Hartung–Knapp–Sidik–Jonkman (HKSJ) adjustments and an ad hoc variance correction were used to calculate confidence intervals for summary estimates. Calculated study intervals may differ from reported values because of differences in variance estimation methods.

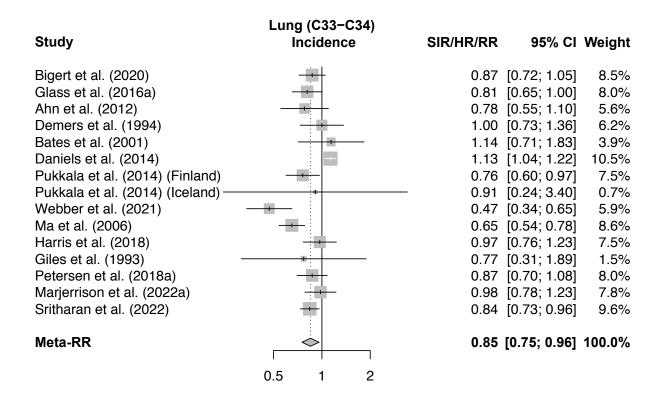
From DeBono et al. (2023), CC-BY-3.0.

in the occupation. Assessment of exposure in almost all cohort studies would have been done independently of the eventual diagnosis of disease and should therefore be non-differential in nature, and as such may be expected to bias associations towards the null.

2.9.4 Confounding, surveillance bias, and selection bias

As "occupational exposure as a firefighter" reflects a range of different potentially carcinogenic exposures (as noted in Section 1), the Working Group defined confounders for this agent as carcinogenic exposures that occur outside of the firefighting occupation, such as chemical or other exposures from previous or concurrent occupations (e.g. asbestos exposure from construction work not related to the firefighter job). The role of confounding from such exposures is difficult to ascertain because of the potential contribution of the same exposures (e.g. physical activity, UV radiation, and asbestos) both within and outside of firefighter occupational activities.

The impact of confounding on the observed associations was somewhat unclear, since most studies did not control for confounders other than age, sex, and calendar time in analyses. The included cohort studies primarily compared cancer rates in general population groups with those among firefighters, and distributions of several potentially important risk factors may be Fig. 2.9 Forest plot of individual study results and meta-rate ratios for incidence of cancer of the lung in firefighters compared with a general, uniformed service, or working population referent



CI, confidence interval; HR, hazard ratio; meta-RR, meta-rate ratio; RR, rate ratio; SIR, standardized incidence ratio.

Heterogeneity: $I^2 = 78\%$, $\tau^2 = 0.0319$, P < 0.01

Random-effects models were used with the restricted maximum-likelihood estimator. Hartung–Knapp–Sidik–Jonkman (HKSJ) adjustments and an ad hoc variance correction were used to calculate confidence intervals for summary estimates. Calculated study intervals may differ from reported values because of differences in variance estimation methods. From <u>DeBono et al. (2023), CC-BY-3.0</u>.

quite different in these two groups. This could be an important source of bias in some of the studies considered by the Working Group. For example, available information on smoking prevalence in firefighters compared with the general community was sparse, and was mostly for the USA, but the available published information suggested that the prevalence of smoking has been lower in firefighters than in the general population since at least the early 1990s (Haddock et al., 2011; Phan et al., 2022). This would mean that differences in smoking between firefighters and a comparison group from the general population could be a source of negative confounding for smoking-related cancers. Of note, the differences in risk factor distributions between firefighters and the comparison populations may also have changed over time, making it additionally difficult to assess the impact of this lack of information.

Notably, some confounders may be operating in opposite directions. For example, physical activity lowers the risk of several cancers, whereas chemical exposures outside of the firefighter occupation may increase risks. However, the relative importance of specific confounders varies by cancer type. Smoking is a risk factor for many cancers, but concern about this factor as a confounder of the reported positive associations was mitigated by the observed lower risk of lung cancer among firefighters. Potential confounding from sources of chemical exposures such as benzene and diesel engine exhaust outside of the occupation as a firefighter may be most relevant for cancers such as NHL, lung, and bladder. Again, associations in opposite directions (e.g. NHL and bladder compared with lung cancer) in the same study mitigate concern about the potential impact of these confounders. Finally, as noted in Section 1.2, there was some evidence that alcohol intake is heavier in firefighters. For cancers associated with alcohol use (e.g. positively for colon cancer and inversely for NHL), alcohol use cannot be ruled out as a potential confounder (although it may create bias towards the null for NHL).

Most cohort studies relied on employment or other record linkages to enumerate their study populations. These studies are therefore less susceptible to issues related to selection into a study, and selection bias from this source should generally not be a major factor in interpretation of results from these studies.

However, other biases are of potential concern, including those related to healthyworker biases, such as healthy-hire and healthyworker survivor biases. Healthy-worker hire bias would tend to diminish effect estimates since at the start of employment the exposed population is generally healthier than the general population used for comparison. This might be of particular concern for occupations such as firefighting for which there are often physical requirements for employment eligibility. The majority of studies used a general population as the referent. As the healthy-worker hire bias tends to diminish with time, studies with short follow-up are most vulnerable (e.g. Giles et al., 1993; Demers et al., 1994; Bates et al., 2001; Ma et al., 2006; Ahn et al., 2012; Glass et al., 2016a; Harris et al.,

2018; Webber et al., 2021). Studies that used other working populations as the referent and those that conducted internal analyses would also be less susceptible to this bias. Finally, as described in the Working Group's meta-analysis (<u>DeBono et al., 2023</u>), a sensitivity analysis excluding studies identified as being particularly susceptible to healthy-worker hire bias (Vena & Fiedler, 1987; Zeig-Owens et al., 2011; Ahn & Jeong, 2015; Glass et al., 2016a; Bigert et al., 2020; Webber et al., 2021) was conducted. The estimates for mesothelioma and cancers of the testis and kidney were slightly increased when these studies were excluded, suggesting that the healthy-worker hire bias may have led to underestimation of the associations for these cancers.

The healthy-worker survivor bias occurs when less-healthy workers reduce their workplace exposures through a change in employment or job tasks and would tend to diminish the magnitude of effect estimates in internal comparison analyses of cumulative exposure or employment duration (Arrighi & Hertz-Picciotto, 1994). In one mortality study that reported internal exposure–response analyses, the authors evaluated this effect by adjusting for employment duration and demonstrated some evidence of this bias for cancers of the lung and bladder, for example (Pinkerton et al., 2020).

The potential for surveillance bias in cancer incidence studies is of concern for this occupational group. Firefighters may often participate in occupational screening or cancer awareness programmes or have more access to medical care because of their employment. In this case, cancers that are detected more frequently because of heightened awareness in firefighters could lead to positive associations when compared with the general population. It is of particular concern for cancer sites at which tumours are more likely to be indolent and slow-growing (e.g. prostate, thyroid, and melanoma) and that would not be diagnosed or would be diagnosed later in the general population, in which medical surveillance is less frequent. It is of less concern for cancer sites for which no or limited screening programmes exist, such as brain. In addition, mortality studies overall and studies on cancers with a very low rate of survival, such as lung cancer or mesothelioma, are less susceptible to this bias. In its meta-analysis (DeBono et al., 2023), the Working Group examined the potential for such bias by estimating the meta-RR for cancer sites that may be susceptible to surveillance bias and reported risk estimated using follow-up before 1990, when a strong screening bias was thought to be less influential. There was little evidence of a bias in melanoma incidence risk estimates from increasing cancer surveillance over time (see Section 2.8.2). In contrast, excess prostate cancer incidence decreased slightly after restricting follow-up to before 1990, which suggested that surveillance bias might at least partially explain the excess risk observed in the main analysis.

2.9.5 Mesothelioma

Mesothelioma is a rare cancer. It is well established that there is a dose-dependent causal association between asbestos exposure and mesothelioma, and there are positive trends in population-level risk associated with increasing exposure via asbestos production and use. The average latency period between asbestos exposure and disease occurrence is long $(\geq 30 \text{ years})$. Other than asbestos, three agents (erionite, fluoro-edenite fibrous amphibole, and occupation as a painter) are listed by the IARC Monographs programme as having sufficient evidence for mesothelioma in humans (IARC, 2023). The examination of mesothelioma in the available occupational mortality studies of firefighters was further hampered by the lack of a cause-of-death ICD code before the late 1990s (i.e. before ICD-10).

Municipal firefighters may be exposed to asbestos during multiple activities that can disturb building materials containing asbestos, such as fire suppression, overhaul, rescue, and recovery. Exposure could also occur from resuspension of asbestos fibres from contaminated apparatus and firefighting gear (see Section 1.5.1).

There were 13 studies providing information on mesothelioma or pleural cancers among firefighters. The most informative studies were several recent (2014-2022) observational studies of municipal career firefighters compared with non-firefighter populations (Daniels et al., 2014; Pukkala et al., 2014; Glass et al., 2016a; Bigert et al., 2020; Pinkerton et al., 2020; Marjerrison et al., 2022b; Sritharan et al., 2022). Significant excess incidence of mesothelioma was observed in the meta-analysis carried out by the Working Group (meta-RR, 1.58; 95% CI, 1.14–2.20; $I^2 = 8\%$), which combined information from seven cohort studies, including 70 mesothelioma cases from more than 1.5 million person-years of observation (DeBono et al., 2023). Among these studies, the mesothelioma SIRs ranged from 0.65 in a study of Danish firefighters (Petersen et al., 2018a) to 2.46 in a study of Norwegian firefighters (Marjerrison et al., 2022b). Only the Danish study reported less-than-expected mesothelioma risk, based on four cases. More than half of the Danish cohort comprised part-time and volunteer firefighters for whom information was not separable from that of career firefighters. Excluding that study from the meta-analysis increased the effect estimate (meta-RR, 1.70; 95% CI, 1.30-2.22) and reduced the residual heterogeneity ($I^2 = 0\%$).

Meta-regression revealed an inverse association between mesothelioma risk and employment duration on the basis of three studies (Glass et al., 2016a; Bigert et al., 2020; Marjerrison et al., 2022a). The estimate was imprecise and strongly influenced by markedly greater risk in the lowest duration category (0–10 years). This category comprised the fewest observed cases (one to three) per study and less than one expected case each, possibly resulting in unstable estimates. Disease latency could not be addressed in the model, although <u>Marjerrison et al. (2022a)</u> found that six of seven observed cases occurred 40 years after first employment (SIR, 3.47; 95% CI, 1.27–7.55).

Overall, there was consistent evidence of excess mesothelioma among municipal career firefighters compared with non-firefighter groups. The relatively new reporting of excess mesothelioma may reflect overall improvements in ascertainment, larger study sizes, longer follow-up, and increasing use of cancer registries versus death certificates. The effect size appeared strong relative to associations seen for other cancer sites. Asbestos exposure, which has been linked to municipal firefighting activities (see Section 1.1), is the primary cause of mesothelioma. Although there was an inverse association with employment duration in the meta-analysis (based on few studies), the long latent period of mesothelioma was not accounted for and may have affected regression estimates. An important limitation was the absence of information on asbestos exposures occurring outside of firefighting. For example, firefighters may have worked in previous and concurrent jobs associated with occupational asbestos exposure in the military, in construction, or elsewhere (Elbaek Pedersen et al., 2020). There were no studies available that directly examined confounding by asbestos exposures outside of firefighting. However, full occupational histories covering the period 1964–2015 were examined in the cohort of Danish firefighters, and only slightly greater prevalence of work in shipyards, construction, and as insulators was reported among part-time and volunteers than among career firefighters (Elbaek Pedersen et al., 2020). This was evidence against differential distribution of asbestos-related employment as a reasonable explanation of the risk difference observed between career fighters and part-time/volunteers or general population referents. Further, mesothelioma incidence was increased in Australian male career firefighters (Glass et al., 2016a), but

not among volunteers (Glass et al., 2017), who were most likely to hold additional employment elsewhere. These findings did not support a strong bias from other sources of asbestos, but they are tempered somewhat by other potential differences, such as that volunteers may work in a predominantly rural area compared with the urban settings of most career firefighters. The Working Group concluded that there was no compelling evidence that firefighters have a greater potential for asbestos exposure outside of firefighting activities than do reference populations and concluded that, despite the lack of prior exposure information, exposures not connected to firefighting work were unlikely to fully explain the observed results. Given consistency across studies, strength of association, and an absence of other potential risk factors or sources of strong bias that could fully explain the association, chance, bias, and confounding were reasonably ruled out as explanations for the positive association seen between occupational exposure as a firefighter and mesothelioma.

2.9.6 Cancer of the urinary bladder

There were 27 studies providing information on cancers of the urinary bladder. Of these, the Working Group meta-analysis (DeBono et al., 2023) combined information from 10 goodquality (i.e. lacking potential for a strong bias) cohort studies examining cancer incidence in career firefighters (Demers et al., 1994; Bates et al., 2001; Ma et al., 2006; Zeig-Owens et al., 2011; Ahn et al., 2012; Daniels et al., 2014; Glass et al., 2016a; Harris et al., 2018; Petersen et al., 2018a; Sritharan et al., 2022). Modest but precise excess incidence of bladder cancer was observed (meta-RR, 1.16; 95% CI, 1.08-1.26), with no indication of between-study heterogeneity ($I^2 = 0\%$; P = 0.71). Most weight (44%) was given to the large study of municipal career firefighters in the USA (SIR, 1.18; 95% CI, 1.05-1.33) (Daniels et al., 2014). The meta-analysis did not include the cohort study of Norwegian firefighters by Marjerrison et al. (2022a) (SIR, 1.25; 95% CI, 0.97-1.25; 69 cases), which examined incidence of all cancers of the urinary tract combined (bladder, ureter, and renal pelvis) (ICD-10, C65-C68) or the cohort study of Swedish firefighters by Bigert et al. (2020) (SIR, 1.08; 95% CI, 0.89-1.31; 109 cases) using a broader case definition of ICD-10 C66-C68. Both reported similar excess risk to that reported in the meta-analysis. The meta-analysis estimate for mortality was similar in magnitude to incidence; however, the estimate was less precise because of residual between-study variance ($I^2 = 67\%$) and fewer studies aggregated (n = 9) (<u>Vena & Fiedler, 1987</u>; Demers et al., 1992a; Guidotti, 1993; Aronson et al., 1994; Bates et al., 2001; Ma et al., 2005; Amadeo et al., 2015; Pinkerton et al., 2020; Zhao et al., 2020). Marjerrison et al. (2022b) reported 14% excess mortality from cancer of the urinary tract in Norwegian firefighters, based on 15 cases. Among the few studies examining cancer risk among women, excess mortality or incidence for bladder cancer was found in studies of career firefighters in the USA (Ma et al., 2006; Daniels et al., 2014). Excess incidence of urinary tract cancers was not found among Australian female volunteer firefighters (Glass et al., 2017).

Meta-regression revealed an inverse association between employment duration and bladder cancer incidence (slope = -0.017; *P* = 0.06), with no evidence of residual between-study variance (P = 0.75) (DeBono et al., 2023). There was no evidence of a positive exposure-response association between bladder cancer incidence and number of exposed-days, fire-runs, or firehours in career firefighters in the USA (Daniels et al., 2015). Similarly, there was no evidence of a positive trend in bladder cancer incidence with number or type of fire incident in internal analyses of cancer in firefighters in Australia (Glass et al., 2016a). However, Pinkerton et al. (2020) found a strong indication of confounding by employment duration in the regression model of bladder cancer and exposed-days, where the exposure–response estimate shifted from a negative to a positive association after controlling for employment duration. Thus, the Working Group concluded that time-varying confounding from a healthy-worker survivor bias may be masking a true exposure–response association.

An important consideration for bladder cancer is that firefighter exposures include both known and suspected human bladder carcinogens, e.g. PAH, soot, diesel engine exhaust (see Table 1.1 and <u>IARC</u>, 2023), thereby strengthening the evidence for a plausible causal association.

In summary, there was consistent evidence in good-quality longitudinal studies of a modest association between firefighter exposure and bladder cancer risk. Evidence of an exposureresponse association between bladder cancer risk and exposure surrogates was lacking in most studies. However, this finding may stem from residual confounding attributable to a healthyworker survivor bias, among other causes, therefore diminishing its weight against causality (Arrighi & Hertz-Picciotto, 1994; Stayner et al., 2003; Buckley et al., 2015). Tobacco smoking is a risk factor for bladder cancer and could therefore theoretically confound results. However, tobacco smoking is a much stronger risk factor for lung cancer than for bladder cancer, and in studies that reported on both cancer sites there was no increased risk of lung cancer, which argues against strong positive confounding, but rather suggests negative confounding attenuating the estimated bladder cancer risk. Thus, the Working Group concluded that chance, bias, and confounding could be reasonably ruled out as alternative explanations of the observed excess bladder cancer risk among firefighters.

2.9.7 Cancer of the testis

Cancer of the testis is rare, and incidence peaks at ages that are young compared with those for other cancer sites. Mortality rates have declined sharply since the mid-1970s in highincome countries because of advancements in treatment (<u>Purdue et al., 2005; Thun et al., 2017</u>), which makes mortality studies less informative than incidence studies for this evaluation. Potential firefighter exposures include some compounds with *limited* evidence of human testicular carcinogenicity, e.g. perfluorooctanoic acid (PFOA) (see Table 1.1).

The evaluation included 20 studies providing information on cancer of the testis among firefighters. Of these, the most informative were 11 good- to moderate-quality cohort studies of cancer incidence published between 1993 and 2022 (Giles et al., 1993; Bates et al., 2001; Ma et al., 2006; Zeig-Owens et al., 2011; Daniels et al., 2014; Glass et al., 2016a; Harris et al., 2018; Petersen et al., 2018a; Bigert et al., 2020; Marjerrison et al., 2022b; Sritharan et al., 2022). The Working Group meta-analysis resulted in an elevated summary estimate (meta-RR, 1.37; 95% CI, 1.03–1.82) with significant heterogeneity $(I^2 = 56\%; P = 0.01)$ (<u>DeBono et al., 2023</u>). The model combined effect estimates ranging from 0.39 in the Swedish firefighters (Bigert et al., <u>2020</u>) to 2.56 in the Canadian study of firefighters identified through workers compensation claims (Sritharan et al., 2022). All except three studies (Zeig-Owens et al., 2011; Daniels et al., 2014; Bigert et al., 2020) reported greater than expected risk. Removing the Canadian study with the highest effect estimate from the meta-analysis only slightly reduced its magnitude (meta-RR, 1.31; 95% CI, 1.04-1.64) but increased precision and reduced heterogeneity ($I^2 = 26\%$, P = 0.20). There was no evidence of a positive association between testicular cancer incidence and employment duration (P = 0.46) from only three available studies (Bates et al., 2001; Glass et al., 2016a; Petersen et al., 2018a). There was no evidence of a positive exposure-response association between testicular cancer and any exposure proxy examined in the Australian study, although cases were few (Glass et al., 2016a). Estimates of

testicular cancer incidence in studies excluded from meta-analyses, including those from exposure contrasts, were inconsistent and imprecise. Among relevant firefighting exposures, as noted above, there is *limited* evidence of an association between PFOA, which is a component in aqueous film-forming foam (AFFF) used in firefighting, and testicular cancer (IARC, 2016). However, the extent of AFFF exposure among firefighters examined in the relevant studies was unclear. Studies have examined the potential association between extreme temperature and testicular cancer; however, findings were inconsistent (McGlynn & Trabert, 2012). Standardized screening methods are not available, and most testicular cancers are found by self- or medical examination. On the basis of tumour behaviour and progression, early detection is not likely to explain the excess risk (IQWiG, 2021). Given scarce information on plausible exposures for testicular cancer, the effect size observed, heterogeneity in results among relevant studies and inconsistent findings across available exposure contrasts, chance and bias could not be reasonably ruled out as alternative explanations for the observed excess risk.

2.9.8 Melanoma

The Working Group reviewed 26 studies that reported results for incidence or mortality of cutaneous melanoma (hereafter referred to as "melanoma"). The synthesis was primarily informed by studies that were assessed as having an exposure assessment of good or satisfactory quality (see Table 1.8.1).

The Working Group's meta-analysis (DeBono et al., 2023) revealed an excess of melanoma incidence among firefighters compared with the general population (meta-RR, 1.36; 95% CI, 1.15–1.62), based on 12 studies (Giles et al., 1993; Demers et al., 1994; Bates et al., 2001; Daniels et al., 2014; Pukkala et al., 2014; Glass et al., 2016a; Harris et al., 2018; Petersen et al., 2018a; Bigert et al., 2020; Webber et al., 2021; Marjerrison et al., 2022a; Sritharan et al., 2022). The meta-RR was elevated similarly across categories of duration of employment as a firefighter. There was considerable heterogeneity in the meta-analysis ($I^2 = 83\%$; P < 0.01), reducing confidence in the meta-estimate. The meta-RR for melanoma incidence was similar in a sensitivity analysis restricted to studies that were less likely to be subject to surveillance bias but was attenuated in an analysis restricted to comparisons with people in the uniformed services. Little evidence of excess melanoma mortality was seen (1.05; 95% CI, 0.48-2.30), based on four studies. This latter finding may support a role of surveillance bias, shared exposures, or non-differential misclassification by occupation.

Five cohort studies that included an exposure assessment categorized as "good" quality reported estimates for melanoma incidence. Four of these studies showed an excess risk (<u>Glass et al., 2016a</u>, <u>b</u>, 2019; <u>Webber et al., 2021</u>). One conducted among male volunteer firefighters in Australia (<u>Glass et al., 2017</u>) did not. Volunteer firefighters are more likely than career firefighters to live in rural areas and may have more sun exposure through outside jobs (e.g. farming) than people who live in cities.

Although firefighters are occupationally exposed to agents known to cause melanoma, including solar radiation (IARC, 2012) and PCBs (IARC, 2015) (see Section 1, Table 1.1), causal factors that could confound this relation were generally not controlled for in the reviewed studies, for example, early-age sunburn, non-firefighting-related sun exposure, and skin tone. For example, if the firefighter cohorts included a higher proportion of participants with light skin than did the reference population, this could be a source of positive confounding for melanoma. The race-standardized SIR from a study of municipal career firefighters in the USA showed no excess incidence of melanoma overall (Daniels et al., 2014). Further, four of the cohort studies reported incidence results for both melanoma and non-melanoma skin cancer (Kullberg et al., 2018; Petersen et al., 2018a; Bigert et al., 2020; Marjerrison et al., 2022a). Incidence at the latter site, which in contrast to melanoma has exposure to soot as an established cause, was increased in only one of the studies (Bigert et al., 2020). Given the modest effect size, the lack of information about whether exposures to some of the known causes of skin cancer (e.g. solar radiation, PCBs) were more common in firefighters than in the comparison populations hindered the interpretation of the positive findings.

Overall, the Working Group considered healthy-worker biases to be unlikely for melanoma and noted the potential for inflated risk effects because of uncontrolled confounding from UV exposure, surveillance bias, heterogeneity in results, and small numbers in some studies (resulting in unstable estimates). In summary, the Working Group concluded that, although a positive association between occupational exposure as a firefighter and incidence of melanoma is plausible, surveillance bias, confounding, and chance could not be ruled out.

2.9.9 Non-Hodgkin lymphoma

The Working Group included 26 published studies in its review of occupational exposure as a firefighter and risk of NHL. Firefighters are potentially exposed to agents that have either sufficient or limited evidence for causal associations with NHL, including exposure to PAHs in combustion products, benzene, and infections (see Section 1). The Working Group noted that the definition of NHL was not reported consistently across the studies, partly because the definition of NHL has changed over time. Therefore, the ICD codes were listed for each study to aid in interpretation. Importantly, multiple myeloma and lymphocytic leukaemia are now included in the most recent definition of NHL published by the World Health Organization (Swerdlow et al.,

2008), but none of the studies reviewed in the present monograph included multiple myeloma or lymphocytic leukaemia in their definitions of NHL. The results for multiple myeloma are described briefly below, and the results for lymphocytic leukaemia are embedded within the discussion of leukaemia as defined in previous classifications.

The cohort studies were generally considered to be the most informative, as described in Section 2.9.1. Among these, seven reported on duration of employment as a firefighter and cancer incidence. One study that was considered to have a good-quality exposure assessment (Glass et al., 2016a) reported a higher risk of NHL (ICD-10, C82–C85) with longer (10–19 years and \geq 20 years) compared with shorter (< 10 years) duration of full-time work as a firefighter, albeit based on five cases in the reference group. Another study with an exposure assessment of satisfactory quality (Marjerrison et al., 2022a) found some evidence of a stronger SIR for NHL (ICD-10, C82-C86 and C96) with more years of employment as a firefighter, but this was not observed for the firefighters who worked the longest (\geq 30 years). The other five studies, all with exposure assessments of good or satisfactory quality, showed no evidence of duration effects: <u>Demers et al., 1994</u> (ICD-9, 200–202); Ahn et al., 2012 (ICD-10, C82–C85); Glass et al., 2017 (ICD-10, C82-C85); Petersen et al., 2018a (ICD-10, C82–85 and C88.3–C88.9); and <u>Bigert</u> et al., 2020 (ICD-10, C83 and C85). Among studies that constructed more extensive exposure metrics (such as number of events attended, fire-hours), there was no notable evidence of exposure-response associations between proxies of firefighting exposures and NHL.

In the meta-analysis (<u>DeBono et al., 2023</u>), 13 cohort studies provided effect estimates for NHL incidence (<u>Giles et al., 1993</u>; <u>Demers et al., 1994</u>; <u>Ma et al., 2006</u>; <u>Ahn et al., 2012</u>; <u>Daniels et al., 2014</u>; <u>2014</u>; <u>Pukkala et al., 2014</u>; <u>Glass et al., 2016a</u>; <u>Harris et al., 2018</u>; <u>Petersen et al., 2018a</u>; <u>Bigert</u> et al., 2020; Webber et al., 2021; Marjerrison et al., 2022a; Sritharan et al., 2022) and five for NHL mortality (Demers et al., 1992a; Aronson et al., 1994; Ma et al., 2005; Pinkerton et al., 2020; Marjerrison et al., 2022b). The meta-analysis showed a similar modest excess in both incidence (meta-RR, 1.12; 95% CI, 1.01-1.25), and mortality (meta-RR, 1.20; 95% CI, 1.03-1.40). The heterogeneity for both estimates was low $(I^2 = 0\%)$; P = 0.51 for incidence, and P = 0.74 for mortality). These results were also robust in analyses considering different reference groups, follow-up length, and age at follow-up, or excluding those studies with concerns about potential biases. This meta-estimate for NHL incidence was slightly weaker than, but similar to, that in the previous evaluation by the IARC Monographs programme in which occupation as a firefighter was reviewed (meta-RR, 1.21, 1.08–1.36; 6 studies; IARC, 2010). Notably, only three studies overlapped in the two meta-analyses because of the addition of more recent publications and the restriction to cohort studies in the current meta-analysis. Although female firefighters were largely not included in the present meta-analysis, a study of female volunteer firefighters who attended fire incidents (Glass et al., 2019) also reported a similar point estimate (SIR, 1.19; 95% CI, 0.71-1.88; 18 cases).

Although none of the studies in this review included multiple myeloma in their definition of NHL, there were 13 studies with exposure assessments of good or satisfactory quality that reported on multiple myeloma separately. Most studies reported no evidence for an association with multiple myeloma, often based on a very small number of cases (Aronson et al., 1994; Glass et al., 2016a, 2017; Petersen et al., 2018a; Marjerrison et al., 2022a). Glass et al. (2019) reported an SIR of 1.27 for all female volunteers, however, the SIR was attenuated (1.04) when restricted to volunteers who attended fire incidents, but was based on a very small number of cases. There was some evidence of an association in **Bigert et al.** (2020), where the overall SIR

was 1.25 and increased to 1.70 among firefighters who had worked for \geq 30 years. One other study provided nominal support for an association (<u>Kullberg et al., 2018</u>), with an SIR of 1.96 based on five cases in the extended follow-up period from 1987 through 2012. Overall, the Working Group concluded that a positive association was not seen in the body of evidence for multiple myeloma.

The Working Group noted modestly positive associations between occupation as a firefighter and risk of NHL, including across several well-designed studies. The Working Group considered that the likelihood of strong surveillance bias or healthy-worker biases was low. However, inconsistency in results and the modest effect size, hovering close to the null value, clouded interpretation of the evidence for NHL. Although confounding could not be ruled out, the Working Group considered that if uncontrolled confounding were an issue, the lack of control would most probably have attenuated observed associations rather than increase them. Importantly, NHL comprises more than 40 subtypes (Swerdlow et al., 2008) with documented etiological heterogeneity for many exposures (Morton et al., 2014). This may have an impact on both the overall association with occupation as a firefighter and the importance of potential confounders. Changing definitions of NHL over time may also have led to some heterogeneity in results, particularly if there were heterogeneity in the association with occupation as a firefighter according to NHL subtype. Overall, there was a lack of consistent positive associations in the body of evidence, and chance or alternative explanations of the observed excess risk could not be ruled out.

2.9.10 Cancer of the prostate

Cancer of the prostate is a common cancer. There are no conclusive risk factors for prostate cancer apart from age. However, there is *limited* evidence for a causal association with cancer of the prostate in humans for arsenic, cadmium and night shift work (<u>IARC, 2023</u>), and firefighters are potentially exposed to all three hazards (see Section 1.1).

There were 34 studies that provided useable information on cancer of the prostate: 23 occupational cohort studies; six cohort studies in the general population; and five "event-only" studies of cancer end-points.

The Working Group considered that 12 cohort studies (providing 13 sets of results) with exposure assessments of good or satisfactory quality were particularly informative (<u>Demers et al.</u>, <u>1992a</u>, <u>1994</u>; <u>Tornling et al.</u>, <u>1994</u>; <u>Daniels et al.</u>, <u>2014</u>; <u>Glass et al.</u>, <u>2016a</u>, <u>2017</u>; <u>Kullberg et al.</u>, <u>2018</u>; <u>Petersen et al.</u>, <u>2018a</u>, <u>b</u>; <u>Bigert et al.</u>, <u>2020</u>; <u>Pinkerton et al.</u>, <u>2020</u>; <u>Marjerrison et al.</u>, <u>2022a</u>, <u>b</u>). However, the overall findings and conclusions were similar when all available studies were included.

The meta-analysis performed by the Working Group (<u>DeBono et al., 2023</u>) incorporating most of the cohort studies found an increased incidence of cancer of the prostate (meta-RR, 1.21; 95% CI, 1.12–1.32), but with high heterogeneity ($I^2 = 81\%$; *P* < 0.01) (Giles et al., 1993; Demers et al., 1994; Bates et al., 2001; Ma et al., 2006; Ahn et al., 2012; Daniels et al., 2014; Pukkala et al., 2014; Glass et al., 2016a; Harris et al., 2018; Petersen et al., 2018a; Bigert et al., 2020; Webber et al., 2021; Marjerrison et al., 2022b; Sritharan et al., 2022), and no clear increase for mortality (meta-RR, 1.07; 95% CI, 0.95–1.20; $I^2 = 30\%$; P = 0.16) (Vena & Fiedler, 1987; Demers et al., 1992a; Guidotti, 1993; Aronson et al., 1994; Tornling et al., 1994; Ma et al., 2005; Amadeo et al., 2015; Petersen et al., 2018b; Pinkerton et al., 2020; Zhao et al., 2020; Marjerrison et al., 2022b). For incidence, the effect estimates from the individual studies ranged from 0.90 to 2.09, with all except one of the studies having an estimate of above one. For mortality, the relative risk estimates ranged from

0.54 to 1.46, with eight of the eleven estimates being above one.

There was no consistent relationship across the studies between increased risk and any of age at diagnosis, time since employment, duration of employment, or other proxy measures of exposure. There was a consistent observation of excess prostate cancer risk at younger ages among studies with follow-up after prostate-specific antigen testing (e.g. <u>Daniels et al., 2014; Pukkala et al., 2014; Kullberg et al., 2018; Marjerrison et al., 2022b</u>).

All studies used the general population as the comparison population, which raised the possibility of a healthy-worker hire effect biasing the measure of effect downwards, but several studies also conducted internal analyses (Glass et al., 2016a, 2017; Pinkerton et al., 2020).

The Working Group noted evidence indicating increased medical surveillance for prostate cancer in the firefighter populations studied (Jakobsen et al., 2022). There was no clear evidence from the meta-analysis performed by the Working Group that this resulted in important bias, but such increased surveillance might be difficult to identify. For this reason, the two WTC studies (Zeig-Owens et al., 2011; Webber et al., 2021), which comprised cohorts that the Working Group considered likely to have undergone increased surveillance when compared with the reference populations used, were not considered to be among the key studies used for the evidence synthesis. These two studies were excluded from the meta-analysis in a sensitivity analysis.

Overall, the Working Group found there was evidence suggesting that the risk of cancer of the prostate is positively associated with occupational exposure as a firefighter. However, given the possibility of detection bias arising from increased medical surveillance, the lack of a consistent relation with any of the included exposure metrics, and the statistical imprecision of the estimates in many of the studies, accompanied by high heterogeneity in the meta-analysis, the Working Group concluded that chance, bias, and confounding could not be ruled out with reasonable confidence.

2.9.11 Cancer of the colon

Cancer of the colon is one of the most common incident cancers in the world (Rawla et al., 2019). Incidence rates vary by sex and are associated with several genetic, hereditary, or familial factors. A number of individual risk factors have been well established, particularly concerning physical activity, tobacco smoking, and alcohol consumption. Further, there is *limited* evidence for a causal association between night shift work and colon cancer in humans (IARC, 2023), and firefighters are exposed to this hazard (see Section 1.5.2).

In the meta-analysis performed by the Working Group (DeBono et al., 2023), a modest excess was observed for incidence of cancer of the colon (meta-RR, 1.19; 95% CI, 1.07–1.32; $I^2 = 37\%$; P = 0.11). For mortality, the meta-RR was 1.03 (95% CI, 0.78–1.37). There was a positive association between colon cancer incidence and employment duration in meta-regression; however, the estimate was largely imprecise given that only three studies were available for aggregation. Information was insufficient to examine mortality.

Eight cohort studies of good or satisfactory exposure assessment quality including primarily career firefighters (Aronson et al., 1994; Demers et al., 1994; Bates et al., 2001; Daniels et al., 2014; Glass et al., 2016a; Petersen et al., 2018b; Bigert et al., 2020; Pinkerton et al., 2020; Marjerrison et al., 2022b) reported on overall incidence or mortality of colon cancer.

Compared with incidence rates in the general population, elevated overall SIRs for colon cancer (1.21 and 1.24) were reported by <u>Daniels et al. (2014)</u> and <u>Marjerrison et al. (2022b)</u>. For mortality, SMRs in the same cohorts were

elevated by 26% and 27% (<u>Pinkerton et al., 2020</u>; <u>Marjerrison et al., 2022b</u>). Point estimates below unity were found in two studies comparing firefighters with general population reference groups (<u>Aronson et al., 1994</u>; <u>Petersen et al., 2018a</u>).

Few studies attempted to assess internal exposure-response associations. Among the most informative, consistent inverse associations between intestinal/rectal cancer and exposeddays, fire-runs, and fire-hours were observed for all models of cancer incidence and mortality in pooled studies of male career firefighters in the USA (Daniels et al., 2015; Pinkerton et al., 2020), and there was no evidence of a strong healthy-worker survivor bias that could explain these findings (Pinkerton et al., 2020). In other large studies, there was little evidence of a positive association between colorectal cancer incidence and the number and type of fire incidents attended among male career firefighters (Glass et al., 2016a) or volunteers (Glass et al., 2017) in Australia. Two earlier smaller studies found some indications of increasing incidence or mortality rates with longer employment duration, but case numbers were low, and substantial deviations from expected numbers of colon cancer cases or deaths were not seen (Demers et al., 1994; Bates et al., 2001).

Among volunteer firefighters, significant deficits in risk of incident colon cancer were observed among men (<u>Glass et al., 2017</u>), whereas a modest but imprecise elevation was seen among women (<u>Glass et al., 2019</u>).

Firefighters are required to have a high level of physical fitness to enter their profession and might, therefore, be expected to have a higher level of physical activity, which has been associated with a decreased risk of colon cancer (see Section 1.2.5) and could attenuate any association between colon cancer and occupation. However, recent survey studies from the USA and United Kingdom have indicated a higher prevalence of overweight among firefighters than in the general population (<u>Poston et al., 2011; Munir</u> et al., 2012) and a higher frequency of drinking five or more alcoholic beverages on an occasion (Kanny et al., 2013), but little historical information is available. In addition, there is the potential for medical surveillance bias attributable to screening, which may contribute to elevations in point estimates among firefighters compared with the general population.

Overall, the Working Group found some evidence suggesting that risk of cancer of the colon is associated with work as a firefighter. However, there was a lack of consistency among the positive results, and a potential for healthy survivor and surveillance bias. As a result, the potential for chance, bias, or confounding could not be ruled out with reasonable confidence.

2.9.12 Cancer of the brain and other cancers of the central nervous system

The Working Group synthesis for brain and other cancers of the central nervous system in humans was primarily informed by the metaanalysis of DeBono et al. (2023), as well as by studies assessed as having an exposure assessment of good or adequate quality. The meta-analysis found an excess in mortality (meta-RR, 1.33; 95% CI, 0.98–1.79; $I^2 = 53\%$; P = 0.02), but not incidence (meta-RR, 1.01; 95% CI, 0.86–1.18; *I*² = 5%; P = 0.40). This was an unexpected finding given the high fatality rates of these tumours in adults. Among three cohort studies that had good exposure assessments and included mortality, one reported excess mortality (Tornling et al., 1994), and two did not (Guidotti, 1993; Pinkerton et al., 2020). Three studies with satisfactory exposure assessments reported an excess of mortality from brain and other cancers of the central nervous system (Demers et al., 1992a; Aronson et al., 1994; Marjerrison et al., 2022b); another reported a null association (Bates et al., 2001). All the individual studies reporting incidence had null findings, many of which were imprecise. Overall, the Working Group concluded that a positive association was not seen in the body of evidence for cancers of the brain and central nervous system.

2.9.13 Cancer of the thyroid

The Working Group reviewed 21 studies that reported results for thyroid cancer incidence or mortality. The synthesis was primarily informed by studies assessed as having an exposure assessment of good or satisfactory quality (as defined in Section 1.8), as well as by the meta-analysis performed by the Working Group (DeBono et al., 2023). Of five studies with an exposure assessment considered "good" and that included incidence estimates for thyroid cancer, two studies in FDNY WTC-exposed firefighters reported an excess incidence of thyroid cancer (<u>Colbeth</u> et al., 2020a; Webber et al., 2021) but, as noted in Section 2.4, this finding was probably subject to a strong surveillance bias. Of three other studies with exposure assessments classified as "good," one reported slightly elevated estimates for thyroid cancer, but based on few cases (Glass et al., 2016a), and two reported null findings (Glass et al., 2017, 2019), including among female volunteer firefighters in Australia (Glass et al., 2019). In the meta-analysis performed by the Working Group, the meta-RR for thyroid cancer mortality was elevated, but based on only four studies; the meta-RR for incidence was also elevated (meta-RR, 1.28; 95% CI, 1.02-1.61; $I^2 = 40\%$; P = 0.09). However, the meta-estimate for cancer incidence was attenuated in most sensitivity analyses, including when studies most likely to have been influenced by surveillance bias and healthy-worker effects were excluded.

The Working Group noted a lack of precision for most point estimates for thyroid cancer, and the strong possibility of overestimated associations attributable to the effect of medical surveillance bias on thyroid cancer incidence. Overall, the Working Group found little evidence that the risk of cancer of the thyroid is credibly associated with occupational exposure as a firefighter.

2.9.14 Cancer of the lung

Cancer of the lung is a common cancer, and tobacco smoking is the strongest and most important risk factor. Firefighters are potentially exposed to several known human lung carcinogens (see Table 1.1).

There were 34 studies that provided information on cancer of the lung: 28 cohort studies, five "event-only" studies, and 1 case–control study. The overall findings and conclusions were similar regardless of the exposure quality of the studies included.

The meta-analysis performed by the Working Group (DeBono et al., 2023), which incorporated estimates from most of the cohort studies, found an inverse association for lung cancer incidence (meta-RR, 0.85; 95% CI, 0.75–0.96; 14 cohort studies; $I^2 = 78\%$; P < 0.01), and no association for mortality (meta-RR, 0.96; 95% CI, 0.86–1.06; 12 cohort studies; $I^2 = 55\%$; P = 0.01). The relative risk estimates from the individual studies for incidence ranged from 0.47 to 1.14, with all except three of the studies having estimates below one. For mortality, the relative risk estimates ranged from 0.58 to 1.63, with all except three of the studies having estimates below one.

There was no consistent relationship across the studies between increased risk of lung cancer and age at diagnosis, time since employment, duration of employment, or other measures of exposure.

Although no increase in risk was identified, the Working Group noted several factors that clouded the interpretation of the study findings, most of which would be expected to bias the estimate of effect downwards in relevant studies: the healthy-worker hire effect, young age of included participants, short follow-up period, and potential negative confounding from smoking in studies with more recent follow-up. For many of the studies, the participants were relatively young during much of the follow-up period, ages at which the healthy-worker effect was likely to be more evident than might be expected at older ages. Many studies also had a relatively short follow-up, providing less opportunity for cancers related to exposure to have occurred. However, restriction to studies with longer and older periods of follow-up in the meta-analysis did not indicate positive associations. Most studies did not have information about smoking for the included firefighters or the comparison population. One large pooled international case-control study with this information showed no increased lung cancer risk, either with or without smoking adjustment (Bigert et al., 2016).

Overall, the Working Group found little evidence that the risk of cancer of the lung is positively associated with occupational exposure as a firefighter.

2.9.15 Cancer of the kidney

For cancer of the kidney, the meta-analysis conducted by the Working Group (DeBono et al., 2023) found a slightly elevated risk for incidence (meta-RR, 1.09; 95% CI, 0.92–1.29; $I^2 = 55\%$; P = 0.01) based on 12 cohort studies and for mortality (meta-RR, 1.10; 95% CI, 0.66-1.83; $I^2 = 53\%$; P = 0.03) based on nine studies. There were four studies that evaluated duration of employment (Ahn et al., 2012; Glass et al., 2016a, 2017; Marjerrison et al., 2022a), with no patterns of increasing risk with increasing duration found in any except Glass et al. (2016a). Although there were elevations observed in some strata for other measures of exposure, inferences were limited by very small numbers and showed no consistent patterns. Overall, the Working Group found little evidence that the risk of cancer of the kidney is positively associated with occupational exposure as a firefighter.

2.9.16 Leukaemia

There were 24 cohort studies that evaluated leukaemia risk among firefighters. Nine studies reported null findings (Demers et al., 1994; Ahn et al., 2012; Ahn & Jeong, 2015; Glass et al., 2016a, 2017, 2019; Kullberg et al., 2018; Bigert et al., 2020; Marjerrison et al., 2022a), including some studies that were informative for other cancer sites. In two studies, each with six exposed cases, there was some evidence of increased risk of leukaemia with longer duration of employment (Demers et al., 1992a; Aronson et al., 1994), although there was a noted lack of precision because of small numbers. In a well-conducted study of municipal career firefighters in the USA, there was an elevated risk among 11 non-Caucasian [non-White] male firefighters (SIR, 1.90; 95% CI, 0.95-3.40) but not in 88 Caucasian [White] males (Daniels et al., 2014). In the same cohort, mortality analyses revealed no overall excess of leukaemia, although there was some evidence of an exposure-response relation for the number of fire-runs and fire-hours (Pinkerton et al., 2020). Most studies did not evaluate myeloid and lymphoid malignancies separately, and no differences were apparent. Overall, the Working Group concluded that a positive association was not seen in the body of evidence for leukaemia.

2.9.17 Other cancer sites

The Working Group also considered the evidence for a causal association between occupational exposure as a firefighter and other cancer types. For example, some studies observed an increased risk of cancers of the stomach and larynx. However, in examining the full body of evidence, few studies observed an excess risk of greater than 20%, and meta-analyses found the risk of stomach cancer among firefighters to be similar to that in the general population (DeBono et al., 2023). The six studies that examined stomach cancer risk in relation to duration

of employment found no evidence of an association. The only study to examine the relation between exposure to fire responses and stomach cancer did find a positive association (<u>Pinkerton</u> <u>et al., 2020</u>). The few studies to examine laryngeal cancer by indicators of firefighting activities, including duration of employment, showed inconsistent results based on small numbers of cases. Overall, the Working Group found little evidence that the risk of cancers of the stomach and larynx is positively associated with occupational exposure as a firefighter.

2.9.18 All cancers combined

The meta-analysis performed by the Working Group for male firefighters and all cancers combined (DeBono et al., 2023) showed little evidence of an increase in the meta-rate ratio for either incidence (meta-RR, 1.05; 95% CI, 0.99-1.11) or mortality (meta-RR, 0.99; 95% CI, 0.96–1.06). The heterogeneities of both estimates were high ($I^2 = 87\%$). As seen above, the incidence of some of the most frequent cancers, i.e. prostate, colon, and bladder cancer, which together account for about one third of all cancers in men, was raised and may have contributed to an overall increase, which was not observed. Therefore, the Working Group found little evidence that the risk of all cancers combined is associated with occupational exposure as a firefighter.

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