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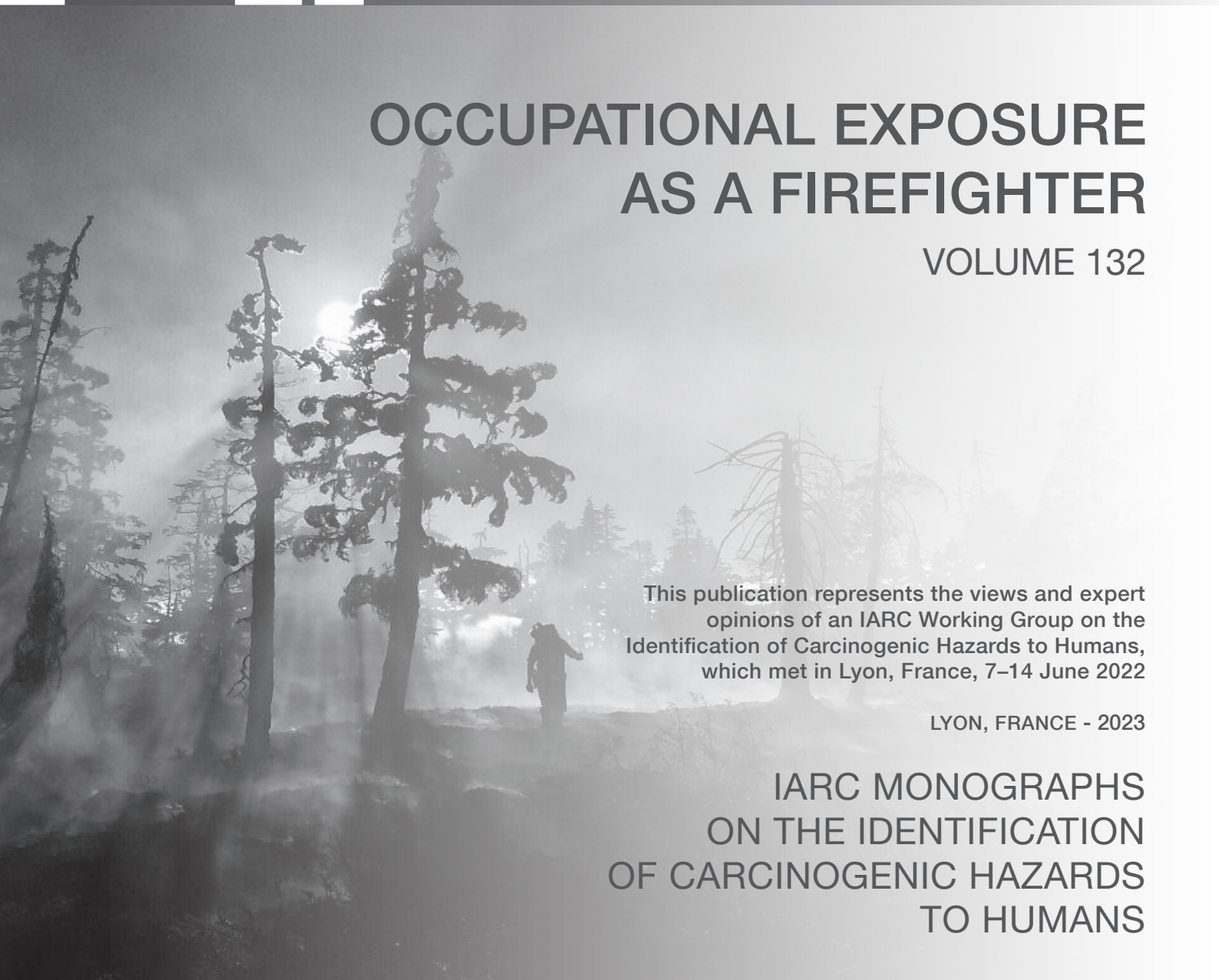

OCCUPATIONAL EXPOSURE AS A FIREFIGHTER

VOLUME 132

This publication represents the views and expert opinions of an IARC Working Group on the Identification of Carcinogenic Hazards to Humans, which met in Lyon, France, 7–14 June 2022

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IARC MONOGRAPHS ON THE IDENTIFICATION OF CARCINOGENIC HAZARDS TO HUMANS

International Agency for Research on Cancer

World Health Organization

Table S1.30 Exposure assessment review and critique for mechanistic studies on cancer and occupational exposure as a firefighter

Reference and mechanistic end-point (key characteristic, KC)	What was the study design? (if not a standard design, a brief description)	Study location and exposure period.	What methods were used for the exposure assessment? (incl. data source, environmental and biological measurements etc.)	What was the exposure definition?	Was exposure assessment qualitative, semiquantitative or quantitative?	Concerns noted on exposure classification/ measurements	What firefighting activities (or type of firefighters) were assessed?	Information collected on PPE use, and its effect on exposure if applicable	What exposure metrics were derived for use in analyses (e.g. average exposure, exposure duration, cumulative exposure etc.)?	What was the timing of exposure relative to the outcome?	Was there potential for co-exposures to other carcinogens outside of firefighting exposures?	Was there potential for differential exposure misclassifications ?
Abreu et al. (2017) Genotoxic; oxidative stress	Cross-sectional	Portugal, 2014	Self-report	Volunteer firefighter	Semiquantitative	No data on individual exposures or tasks	Wildland firefighting	PPE use largely unknown	Duration (< 7, 7–15, > 15 yr)	Predates	27% smokers	No
Adetona et al. (2013b) Oxidative stress	Pre/post	Savannah River, USA, 2004	Personal air sampling	$PM_{2.5}$, CO	Quantitative	–	Wildland prescribed burn	None used	8-hour TWA of $PM_{2.5}$ and CO	Outcome samples at end of shift	Smoking data collected, but not reported	No
Adetona et al. (2017) Chronic inflammation	Pre/post	USA, 2015	Personal air sampling	$PM_{2.5}$, black carbon, CO	Quantitative	–	Holding, lighting in wildland prescribed burns	None used	8-hour TWA of $PM_{2.5}$	Same day	No	No
Adetona et al. (2019) Genotoxic; oxidative stress	Pre/post	USA, 2015	Personal air sampling, biomonitoring	$PM_{2.5}$, black carbon, CO, 1-HP	Quantitative	–	Holding, lighting in wildland prescribed burns	None used	8-hour TWA of $PM_{2.5}$, black carbon and CO. Urinary 1-HP	Same day	Data collected on smoking, diet, medication	No
Aldrich et al. (2016) Chronic inflammation	Repeated measurements	WTC USA, 9/2001	Self-report	Presence as firefighter at WTC	Semiquantitative	No data on individual exposures or tasks	WTC firefighting	No information	None used in the analysis	Outcome 10+ yr after exposure	Yes	No

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Al-Malki et al. (2008) Oxidative stress	Cross-sectional	Saudi Arabia, year not specified	Self-report	Working as a firefighter	Qualitative	No data on individual exposures or tasks	Fighting fires (general)	No information	None	Within an hour	Yes – no information given	No
Almeida et al. (2007) Chronic inflammation	Cross-sectional	Portugal, 2005–2006	Self-report	Active firefighter for at least 5 yr	Semiquantitative	No data on individual exposures or tasks	Wildland (forest) firefighting	Respiratory protection used	Duration of occupation. Prior history of smoke intoxication (yes/no)	After years of exposure	Smoking	Healthy worker effect
Andersen et al. (2018b) Genotoxic, chronic inflammation, immunosuppression	Pre/post	Denmark, 2015–2016	Skin wipes, biomonitoring	PAH, 1-HP	Quantitative	–	Smoke diving training	Full PPE including SCBA, used	Total PAHs skin wipes, urinary 1-HP	Same/next day and 14 days before/after	Yes	No
Andersen et al. (2018a) Genotoxic; oxidative stress, chronic inflammation	Pre/post	Denmark, year not specified	Particulates, skin wipes, biomonitoring self-report	PM, PAHs, 1-HP, fire smoke	Quantitative	Difficulties in estimating particulate exposure	Municipal firefighter	PPE was used and effects estimated	Total PAH from skin wipes, urinary 1-HP	Same day	Included current smokers	No

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Beitel et al. (2020) Receptor-mediated effects	Pre/post	Tucson (AZ), USA, year not specified	Personal wipe samples, biological (urinary) monitoring	Polycyclic aromatic hydrocarbons (PAHs) and hydroxylated PAHs	Quantitative	–	Training structure fire	PPEs worn; effect of particulate blocking hood tested	Cross-shift change in urinary hydroxylated PAH concentration	Changes from before to immediately after exposure at controlled fire	No	No
Bergström et al. (1997) Chronic inflammation	Cross-sectional	[Sweden], year not specified	[self-report]	Active (voluntary) firefighter for at least 3 yr	Qualitative	Narrative on type of fires fought or type of exposure in last 3 mo, but not systematic and not directly linked with outcome No data on individual exposures or tasks	Fighting fires (general)	PPE, yes/no	Ever exposure	Unclear: active firefighters, but variable when last exposure occurred	Smoking	Healthy worker effect

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Bodienkova & Ivanskaia (2003) Immunosuppression	Cross-sectional	Shelekhov, Russian Federation [1992]	Firefighting at an incident	Firefighting exposure at a cable product and PVC fire at a factory	Qualitative	Not apparent how firefighting was determined	Structural [municipal] firefighting at a factory	None used	Involvement in a specific firefight	Not clear but likely between > 7 and 11 yr before	Possible and was not apparent that such e.g. smoking and environmental exposures were controlled in analysis	Not enough information to determine
Bodienkova & Ivanskaia (2003) Immunosuppression	Case series	Not stated	Not enough information to determine	Employed as a firefighter	Qualitative	Not enough information to determine	Not enough information to determine	None used	None	Not stated	Not enough information to determine	Not enough information to determine
Borges et al. (2021) Immunosuppression	Cross-sectional	Aracaju, Brazil, 2021	Employment at a fire brigade/department	Working as a firefighter	Qualitative	No exposure relevant to variation of outcome among subjects was measured	Military firefighters	None used	None	Unclear	Yes (smoke exposure probably but no information about this was collected); control for co-exposures that were collected not controlled in analysis	No

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Burgess et al. (2002) Chronic inflammation	Pre/post	USA	Personal air sampling, biomonitoring	Smoke: Carbon monoxide, Carboxyhemoglobin, Nitrogen dioxide, Sulfur dioxide, Hydrogen cyanide, Formaldehyde, Acetaldehyde, Hydrochloric acid, Sulfuric acid, Benzene, Respirable dust	Quantitative	None	Overhaul, structure fires	Yes, described	Average exposure	Baseline and directly after firefighting	Smoking	No
Chernyak & Grassman (2020) Receptor-mediated effects	Cross-sectional	Shelekhovo, Russian Federation 1992	Biomonitoring	Polychlorinated dioxins, furans, and biphenyls (PCDDs, PCDFs, and PCBs)	Quantitative	None	Firefighting at cable factory fire	None used	Lipid concentration of PCDDs, PCDFs, and PCBs as chronic marker of exposure	17–18 yr after exposure to cable factory fire	Yes, smoking was accounted for in analyses	No
Cherry et al. (2021b) Chronic inflammation	Repeated measurements	Canada, 2016–2020	Self-report, air sampling	$PM_{2.5}$, heat, noise	Quantitative	None	Wildland firefighting	Yes, adjusted for	Cumulative exposure, average exposure, peak (highest day), days since last deployment,	Outcome measured within 19 days of the start of the fire and 14–18 weeks later.	Smoking	No

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									days since last fire			
Chia et al. (1990) Other relevant information	Pre/post trial	Malaysia 1990	Controlled combustion of diesel oil, petrol, and wood dust, plastic. No quantitative measurements	Being exposed to smoke in test chamber for approx. 11 min	Qualitative		New recruits were compared to ffs with mean 4.6 yr of service	None used	None	Before versus 1, 6 and 24 h after	No	No
Cho et al. (2014) Chronic inflammation	Nested case-cohort	USA, 2001–2008 [typo 2011–2008]	Self-report	Presence as firefighter at WTC	Qualitative	No data on individual exposures or tasks	WTC firefighting	No information	"WTC exposure intensity," based on arrival time: (i) Presented on the morning of 9/11/2001 and (ii) Arrived between afternoon on 9/11/2001 and 9/12/2001	Up to 7 yr after exposure	Smoking, other fires	No
Christison et al. (2021) Receptor-mediated effects	Pre/post	USA, year not specified	Self-report	Physical strain – self report muscle soreness	Qualitative	None	Wildland firefighting critical training	None used	NA	Physiological changes from immediately before, through training, to	No	No

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										immediately after exposure		
Clarity et al. (2021) Immortalization	Cross-sectional	San Francisco (CA), USA, < 2015	Biomonitoring	PFAS, OPFRs, PBDEs	Quantitative	None	[Municipal firefighters]	None used	Average exposure	Exposure still ongoing as a firefighter but outcome measured at least 5 yr since employment	Yes. Other potential exposures were controlled for in analyses	Estimation of OPFR exposure by urine concentration of metabolites could have been affected by recent exposures from other sources since the biomarkers have short half-lives
Cleven et al. (2019) Chronic inflammation	Nested case–control	WTC, USA 11–24 September, 2001	Self-report	Presence as firefighter at WTC	Semiquantitative	No data on individual exposures or tasks	WTC firefighting	No information	Date of arrival	Exposure before diagnosis	Yes	No
Cordeiro et al. (2021) Chronic inflammation	Pre/post	Brazil, 2018–2019	Experimental setting	Heat, by-products of combustion	Qualitative		Structural [municipal] firefighting	All used RPE	Recent exposure	Outcome measured pre-exposure, after 1 week, and after 4 weeks	Smoking	No

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Darcey et al. (1992) Genotoxic	Pre/post	Kuwait, 1991	Self-report	Smoke exposure	Qualitative	No objective or quantitative measurements of exposure available, potential recall bias or non-differential misclassification	Fighting oil fires	None used	NA	Before vs after exposure	Unclear	Unlikely
Diaz-Castro et al. (2020a) Receptor-mediated effects	RCT	Spain, year not specified	Experimental setting	Physical exertion (strenuous exercise) and supplement	Qualitative	None	[Municipal firefighters]	NA	NA	Physiological changes from immediately before to immediately after strenuous exercise exposure	No	No
Diaz-Castro et al. (2020b) Cell proliferation	RCT	Spain, year not specified	Experimental setting	Physical exertion (strenuous exercise) and supplement	Qualitative	None	[Municipal firefighters]	NA	NA	Physiological changes from immediately before to immediately after strenuous	No	No

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										exercise exposure		
Ferguson et al. (2016) Oxidative stress, chronic inflammation	Pre/post	USA, year not specified	Experimental setting	Woodsmoke ($PM_{2.5}$)	Quantitative	None	Wildland firefighting (simulated)	NA	$PM_{2.5}$ concentrations	Immediately pre-post	No	No
Fireman et al. (2004) Chronic inflammation, immortalization	Cross-sectional	New York City, USA, 2001	Self-report, biomonitoring	At WTC on first morning	Qualitative/ semiquantitative	Particulate exposure only from settled dust	WTC firefighting	No information	Number of work days continuous and dichotomised (< 10 or ≥ 10 workdays)	Exposure 10 mo prior	Yes	No
Ford et al. (1992) Multiple characteristics	Cross-sectional	New York City, USA, 1992	Employment records	Employed as ff	Qualitative	No data on individual exposures or tasks	[Municipal firefighters]	None used	None	Predates	Unclear	Unlikely
Gaughan et al. (2014a) Oxidative stress	Cross-sectional	USA, 2011	Self-report, biomonitoring	Fire smoke	Quantitative	None	Wildland firefighting	None used	Levoglucosan concentration	Predates	Smoking	Other sources than woodsmoke may affect urinary levels of levoglucosan (Naeher et al., 2013)

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Gaughan et al. (2014b) Chronic inflammation	Cross-sectional	USA, 2007–2009	Employment records	Employed as ff	Qualitative	No data on individual exposures or tasks	Structural [municipal] firefighters	Not reported	None	Predates	Smoking	No
Gianniou et al. (2016) Chronic inflammation	Cross-sectional	Greece, year not specified	Self-report	Firefighter or comparison group	Quantitative	Little information on exposures	[Municipal firefighters]	Some used (unspecified)	Years employed	Not specified	Yes	No
Gianniou et al. (2018) Chronic inflammation	Repeated measurements	Greece, 2008	Self-report	Operation as wildland firefighter; time away from firefighting	Qualitative	Poorly described	Wildland (forest) firefighting	No information	Hours dichotomized at 10	Reassessed 3 mo after end of firefighting	Yes	No
Goldfarb et al. (2021) Chronic inflammation	Cross-sectional	New York City, USA, 2001	Self-report	WTC firefighting	Qualitative	No data on individual exposures or tasks	WTC firefighting	No information	“WTC exposure intensity,” based on arrival time	Predates	Smoking	No
Goodrich et al. (2021) Epigenetic	Cross-sectional	4 US cities, 2016–2018	Employment records	Working as an active firefighter	Qualitative		Fire fighting	None used	None	Predates	Yes	No

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Goodrich et al. (2022) Epigenetic	Pre/post	Tucson (AZ), USA, 2015–2018	Employment and fire response records	Responding to fires, total or structure, measured by number of fire runs or hours spent at fires	Semiquantitative	No direct measurements of exposure intensity or composition	Responding to fires, either any fire or structure fire	None used	Cumulative fire hours and fire runs for all fires and structure fires-only	Before versus after 20 to 37 mo	Yes	Unlikely
Greven et al. (2011) Chronic inflammation	Cross-sectional	Netherlands, 2008–2009	Self-report	Fire smoke	Quantitative	Based on self-report, which may be complicated by recall, particularly with regards to the frequency. No measurements of exposure available	Fighting fires (general)	No information	Frequency, time since exposure, ever exposure, duration	Outcome after exposure	Smoking	Self-reported exposure may be biased by health condition
Greven et al. (2012) Chronic inflammation	Repeated measurements	Netherlands, 2009	Self-report, biomonitoring	Fire smoke; particle count	Qualitative and quantitative	Self-reported. No measurements of exposure available.	Municipal fire brigades	SCBA yes/no	Recent exposure	Blood within 24 h post-exposure, after a week and 3 mo. Sputum within 5 days. Spirometry and methacholine	Smoking	Possibly more reported by those having symptoms

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										provocation 1-week post-exposure		
Gündüzöz et al. (2018) Oxidative stress	Cross-sectional	Türkiye, year not specified	Self-report; biomonitoring	Employment status; concentration arsenic in spot urine sample	Qualitative and quantitative	Rationale for arsenic unclear	[Municipal firefighters]	None used	Employment as a firefighter; average exposure	Sample on the day of respiratory assessment	Unknown	No
Gurney et al. (2021) Oxidative stress	Pre/post	[Montana], USA, year not specified	Participation in firefighter training	Pre-wildland firefighting season training including control burns on 7 days and physical exercise on 2 days	Qualitative	None	Wildland firefighters	None used	Participation in firefighter training	Exposure ongoing through the period (1–11 days) of outcome measurements	No (everyone was own control)	Oxidative exposures outside work in periods between sample collection
Hejl et al. (2013) Chronic inflammation	Pre-post	USA, 2011	Personal air sampling	$PM_{2.5}$, CO	Quantitative	None	Lighting, holding, wildland prescribed burn	None used	Average exposure	Same day	One smoker	No
Hena et al. (2018) Chronic inflammation	Repeated measurements	New York City, New York, USA 2001	Self-report	9/11 WTC smoke exposure	Qualitative	None	WTC firefighting	None used	None	Follow-up clinical examination – 14 yr following	Information collected on insecticide exposure; not	No

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										WTC smoke exposure; average of 6 yr following diagnosis	assessed in the analyses	
Hengstler et al. (1995) Genotoxic	Cross-sectional	Germany, year not specified	Area sampling, self-report	Working in contaminated area after fire	Qualitative	No individual measurements of exposure available	Cleaning after fire	None used	None	Predates	Unclear	Unlikely
Hong et al. (2000) Oxidative stress	Mendelian randomization	Republic of Korea, year not specified	Employment records	Firefighting hours in previous 5 days	Semiquantitative	Qualitative measure of recent exposure using only length of activity	Structural [municipal] firefighters	None used	No exposure; low exposure; high exposure	Hours worked in previous 5 days	Smoking considered	No
Huang et al. (2010b) Chronic inflammation, immunosuppression, receptor-mediated effects	Pre/post trial	Mississippi, USA, year not specified	Experimental setting	Physical and psychological (mental challenge) stress	Qualitative	None	[General firefighters]	NA	NA	Change immediately after from immediately before and through experimental exposures	No	No
Huang et al. (2010a) Immunosuppression	Pre/post trial	Mississippi, USA, year not specified	Experimental setting	Physical and psychological stress	Qualitative	None	[General firefighters]	NA	NA	Change immediately after from	No	No

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										immediately before and through experimental exposures		
Jasra et al. (2022) Genotoxic, epigenetic	Cross-sectional	WTC, USA 11–24 September, 2001	Employment records	Presence as firefighter at WTC	Qualitative	No data on individual exposures or tasks	WTC firefighting	No information		Exposure 12 to 14 yr before biomonitoring	Yes	No
Jeong et al. (2018) Multiple characteristics	Cross-sectional	Tucson (AZ) USA, 2018	Employment records	Years of service as ff	Semiquantitative	No data on individual exposures or tasks	[General fire department]	None used	Years of service as ff	Predates	Unclear	Unlikely
Josyula et al. (2007) Chronic inflammation	Cross-sectional	USA, 2004	[Employment records]	Firefighter	Qualitative	No data on individual exposures or tasks	[General fire department]	No information	–	After	Smoking	–
Jung et al. (2021) Multiple characteristics	Pre/post	Tucson (AZ), USA, 2 yr starting in 2015	Employment records, official fire response records	Employment duration, cumulative fire hours, cumulative fire runs, days since last fire call; stratified by type of fire	Semiquantitative	None	[General fire department]	None used	Employment duration, cumulative fire hours, cumulative fire runs, days since last fire call;	Before vs after approx. 2 yr exposure	Smokers were excluded	Unlikely

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									stratified by type of fire			
Kazemi et al. (2018) Receptor-mediated effects	Repeated measurements	Islamic Republic of Iran, year not specified	[Employment records]	Work-shift rotation	Qualitative	None	Firefighting in petrochemical company	NA	Two shift work rotations: 7 night, 7 day and 7 off; 4 night, 4 day and 4 off	Outcome measured immediately after exposure	No	No
Keir et al. (2017) Genotoxic, oxidative stress	Pre/post	Canada, 2015–2016	Dermal and personal PAH; biomonitoring (urinary hydroxylated PAH)	Structural [municipal] firefighters on shifts of interest	Quantitative	None	Structural [municipal] firefighting	PPE used, effects not discussed	Concentration of PAH metabolites	Pre, post shift and for following 18 h	No	No
Kern et al. (1993) Chronic inflammation	Cross-sectional	Rhode Island, USA, 1979–1990	Employment records	Employed as a firefighter	Qualitative	No data on individual exposures or tasks	[General fire department]	None used	None	10–16 yr since employment as a firefighter	Smoking reported by 24% of participants; not accounted for in analyses	No
Kim et al. (2018) Chronic inflammation; receptor-mediated effects	Pre/post trial	[Republic of Korea]	Experimental setting	Heat (200–300 °C), smoke	Qualitative	None	Live-fire simulation	PPE used	High vs room temperature, smoke vs non-smoke	Outcome measurements directly before and after	–	No

Table S1.30 Exposure assessment review and critique for mechanistic studies on cancer and occupational exposure as a firefighter

Reference and mechanistic end-point (key characteristic, KC)	What was the study design? (if not a standard design, a brief description)	Study location and exposure period.	What methods were used for the exposure assessment? (incl. data source, environmental and biological measurements etc.)	What was the exposure definition?	Was exposure assessment qualitative, semiquantitative or quantitative?	Concerns noted on exposure classification/ measurements	What firefighting activities (or type of firefighters) were assessed?	Information collected on PPE use, and its effect on exposure if applicable	What exposure metrics were derived for use in analyses (e.g. average exposure, exposure duration, cumulative exposure etc.)?	What was the timing of exposure relative to the outcome?	Was there potential for co-exposures to other carcinogens outside of firefighting exposures?	Was there potential for differential exposure misclassifications ?
										exposure, after 4 h and 24 h		
Kuan et al. (2019) Epigenetic	Cross-sectional	WTC, USA 11–24 September, 2001	Self-reported detailed exposure information from WTC responders	Exposure index based on time, location and tasks of WTC response	Semiquantitative	No direct measurements of exposure intensity or composition	Time, location and tasks of WTC response	Yes, included explicitly in exposure index	Exposure-ranking index	More than 10 yr before	Yes	No
Kudaeva & Budarina (2005) Immunosuppression	Cross-sectional	Russian Federation, period not specified	Occupation; career length	Employment as a firefighter and length of career	Qualitative and semiquantitative	Not apparent how employment status and history were obtained	Unclear	None used	Occupation and employment history	Ongoing employment as firefighter but time since last exposure at a fire not given	Possible and was not apparent that such e.g. smoking and environmental exposures were controlled in analysis	Not enough information to determine
Kudaeva & Budarina (2007) Immunosuppression	Cross-sectional	[Russian Federation], period not specified	Occupation; career length; firefighting at an incident with complex exposures; exposure to psychological stress	Employment as a firefighter and length of career	Qualitative and semiquantitative	Not apparent how the exposure metrics were collected	Structural [municipal] firefighting at an incident; unclear for the other groups of firefighters	None used	Occupation and employment history including involvement in a specific firefight; unclear what metric was used	Ongoing employment as firefighter but time since last fire exposure or the fire with complex	Possible and was not apparent that such e.g. smoking and environmental exposures were	Not enough information to determine

Table S1.30 Exposure assessment review and critique for mechanistic studies on cancer and occupational exposure as a firefighter

Reference and mechanistic end-point (key characteristic, KC)	What was the study design? (if not a standard design, a brief description)	Study location and exposure period.	What methods were used for the exposure assessment? (incl. data source, environmental and biological measurements etc.)	What was the exposure definition?	Was exposure assessment qualitative, semiquantitative or quantitative?	Concerns noted on exposure classification/ measurements	What firefighting activities (or type of firefighters) were assessed?	Information collected on PPE use, and its effect on exposure if applicable	What exposure metrics were derived for use in analyses (e.g. average exposure, exposure duration, cumulative exposure etc.)?	What was the timing of exposure relative to the outcome?	Was there potential for co-exposures to other carcinogens outside of firefighting exposures?	Was there potential for differential exposure misclassifications ?
									for psychological stress	exposure not given	controlled in analysis	
Lam et al. (2020) Chronic inflammation	Cross-sectional	USA, 2001	Self-report	Presence as firefighter at WTC	Qualitative	No data on individual exposures or tasks	WTC firefighting	No information	None	Predates	No	No
Li et al. (2004) Genotoxic	Cross-sectional	Tokyo, [1998]	Biomonitoring	Sarin exposure	Quantitative		Disaster	None used	Level of sarin exposure	Predates by about 3 yr	Unclear	Unlikely
Lim et al. (2020) Receptor-mediated effects	Pre/post	Republic of Korea, year not specified	Employment records	Work-shift rotation	Qualitative	None	[General fire department]	NA	Shift work in 3-, 6-, 9-, and 21-day cycles.	Outcome measured during and immediately after exposure	No	No
Liou et al. (1989) Genotoxic	Cross-sectional	Washington (DC), USA, [1988]	Self-report	Employment as firefighter and self-reported number of fires fought in the previous day, week, month, and average of fires/year	Qualitative & semiquantitative	Estimates of fire exposure by recall, subject to bias, potential non-differential misclassification	General fire department	Self-report of frequency of mask wearing	Employment as ff, number of fires fought in the preceding 24 h, and month and average fires/1 year	Predates	Tobacco, charcoal broiled meat, alcohol	Unlikely
Lofrano-Porto et al. (2020) Receptor-mediated effects	Cross-sectional	Florida, USA, year not specified	Biomonitoring	Employment as firefighter	Quantitative	None	General fire department	None used	Serum testosterone concentration in firefighters – its	Timing of measurement of testosterone	Potential non-firefighting co-exposures	No – associations with firefighting exposures not investigated

Table S1.30 Exposure assessment review and critique for mechanistic studies on cancer and occupational exposure as a firefighter

Reference and mechanistic end-point (key characteristic, KC)	What was the study design? (if not a standard design, a brief description)	Study location and exposure period.	What methods were used for the exposure assessment? (incl. data source, environmental and biological measurements etc.)	What was the exposure definition?	Was exposure assessment qualitative, semiquantitative or quantitative?	Concerns noted on exposure classification/ measurements	What firefighting activities (or type of firefighters) were assessed?	Information collected on PPE use, and its effect on exposure if applicable	What exposure metrics were derived for use in analyses (e.g. average exposure, exposure duration, cumulative exposure etc.)?	What was the timing of exposure relative to the outcome?	Was there potential for co-exposures to other carcinogens outside of firefighting exposures?	Was there potential for differential exposure misclassifications ?
									relationship with firefighting exposure was not analysed	relative to firefighting exposures not reported	not accounted for in analysis	
Loupasakis et al. (2015) Chronic inflammation	Repeated measurements	USA, 2001	Self-report	Presence as firefighter at WTC	Qualitative	No data on individual exposures or tasks	WTC firefighting	No information	Time since exposure	After	Smoking	-
Luria et al. (1982) Receptor-mediated effects	Cross-sectional	Cleveland (OH), USA, year not specified	Biomonitoring	Employment as firefighter	Quantitative	None	[General firefighters]	None used	Serum testosterone concentration in firefighters – its relationship with firefighting exposure was not analysed	Timing of measurement of testosterone relative to firefighting exposures not reported	Potential non-firefighting co-exposures not accounted for in analysis	No – associations with firefighting exposures not investigated
Ma et al. (2020) Oxidative stress, immortalization	Pre/post	Denmark year not specified	Exposure at firefighter training	Smoke exposure at firefighter training	Qualitative	None	None	Full PPE including SCBA (not assessed since all wore this)	Engagement in training exercise	From immediately before to after	No	No
Macedo et al. (2015)	RCT	Brazil 2012	Physical fitness test and intervention	Physical fitness test and use of RES or placebo for 90 days	Binary	None	Military firefighters	No information	None	Immediately before and	Diet was recorded but not reported	No

Table S1.30 Exposure assessment review and critique for mechanistic studies on cancer and occupational exposure as a firefighter

Reference and mechanistic end-point (key characteristic, KC)	What was the study design? (if not a standard design, a brief description)	Study location and exposure period.	What methods were used for the exposure assessment? (incl. data source, environmental and biological measurements etc.)	What was the exposure definition?	Was exposure assessment qualitative, semiquantitative or quantitative?	Concerns noted on exposure classification/ measurements	What firefighting activities (or type of firefighters) were assessed?	Information collected on PPE use, and its effect on exposure if applicable	What exposure metrics were derived for use in analyses (e.g. average exposure, exposure duration, cumulative exposure etc.)?	What was the timing of exposure relative to the outcome?	Was there potential for co-exposures to other carcinogens outside of firefighting exposures?	Was there potential for differential exposure misclassifications ?
Oxidative stress, chronic inflammation										after fitness test		
Main et al. (2013) Chronic inflammation	Pre/post	Australia, year not specified	[Employment records]	Wildfire suppression shifts	Qualitative	No data on individual exposures or tasks	Wildfire suppression	No information	None	Pre- and post-shift	–	No
Main et al. (2020) Chronic inflammation	Pre/post	Australia, 2009	[Employment records]	Wildfire suppression shift	Qualitative	No data on individual exposures or tasks	Wildfire suppression	No information	–	Pre- and post-shift	–	No
McAllister et al. (2018) Oxidative stress	Pre/post trial	USA, year not specified	Heat and supplement intervention	Heat	Binary	None	Simulated location and removal of victim	Used throughout	Heat/no heat	Outcome biomarkers before and after exercise	No	No
McAllister et al. (2020) Oxidative stress, chronic inflammation	Pre/post trial	USA, year not specified	Feeding intervention	Time-restricted feeding	Qualitative	None	Physical exercise – not specific to firefighting	NA	Time-restricted feeding	Pre-post measurements	No	Healthy selection
McAllister et al. (2021)	Pre/post trial	USA, year not specified	Physical exercise and intervention	Physical exercise in a time-restricted feeding intervention	Qualitative	None	Fire simulation	NA	Engagement in physical exercise	Pre-post measurements by	No	Healthy selection

Table S1.30 Exposure assessment review and critique for mechanistic studies on cancer and occupational exposure as a firefighter

Reference and mechanistic end-point (key characteristic, KC)	What was the study design? (if not a standard design, a brief description)	Study location and exposure period.	What methods were used for the exposure assessment? (incl. data source, environmental and biological measurements etc.)	What was the exposure definition?	Was exposure assessment qualitative, semiquantitative or quantitative?	Concerns noted on exposure classification/ measurements	What firefighting activities (or type of firefighters) were assessed?	Information collected on PPE use, and its effect on exposure if applicable	What exposure metrics were derived for use in analyses (e.g. average exposure, exposure duration, cumulative exposure etc.)?	What was the timing of exposure relative to the outcome?	Was there potential for co-exposures to other carcinogens outside of firefighting exposures?	Was there potential for differential exposure misclassifications ?
Chronic inflammation; receptor-mediated effects										intervention status		
Min et al. (2020) Multiple characteristics	Cross-sectional	Republic of Korea, 2019	Employment records	Shift work vs day work	Qualitative	Only shift differences were considered, no other ff exposures	[General fire department]	None used	None	Predates	Only shift work was evaluated	Unlikely
Montague et al. (2022) Immunosuppression	Repeated measurements	Colorado, USA, 2020–2021	Self-report	Occupation	Qualitative	Misreporting possible for self-reported occupation	Unspecified; not enough information to determine and may include multiple types	Access to COVID-19 related respiratory protection (dust mask and eye protection) at the workplace	Employment as a firefighter	Outcome measured 2 times across 2–3 mo without information about firefighting exposures during the period	Yes, possible effects of non-occupational related exposures to smoke or the causative agent of outcome of interest, SARS-CoV-2, not considered	Yes, due to possible misreporting but possible minimal

Table S1.30 Exposure assessment review and critique for mechanistic studies on cancer and occupational exposure as a firefighter

Reference and mechanistic end-point (key characteristic, KC)	What was the study design? (if not a standard design, a brief description)	Study location and exposure period.	What methods were used for the exposure assessment? (incl. data source, environmental and biological measurements etc.)	What was the exposure definition?	Was exposure assessment qualitative, semiquantitative or quantitative?	Concerns noted on exposure classification/ measurements	What firefighting activities (or type of firefighters) were assessed?	Information collected on PPE use, and its effect on exposure if applicable	What exposure metrics were derived for use in analyses (e.g. average exposure, exposure duration, cumulative exposure etc.)?	What was the timing of exposure relative to the outcome?	Was there potential for co-exposures to other carcinogens outside of firefighting exposures?	Was there potential for differential exposure misclassifications ?
Oliveira et al. (2020) Genotoxic, oxidative stress	Cross-sectional	Portugal, year not specified	Biomonitoring	Urinary biomarkers of PAH exposure	Quantitative	No pre-exposure measures	Active wildland firefighting	No information	PAH metabolite corrected for creatinine	Sample collected within 48 h	Smoking collected and used to stratify	No
Orris et al. (1986) Chronic inflammation	Case series	Chicago, USA, 1986	Self-report	Burning plastic, tar, wood, silicon tetrachloride and wood furniture.	Qualitative	Self-reported exposures may be incomplete	Structural [municipal] firefighters	No information	None	Predates	No	No
Ouyang et al. (2012) Epigenetic	Cross-sectional	Cincinnati, USA, 2012	Employment records	Employed as ff, duration of service	Semiquantitative	No data on individual exposures or tasks	None	None used	Duration of ff service	Predates	Unclear	Unlikely
Park et al. (2016) Oxidative stress	Pre/post trial	Republic of Korea, year not specified	Wearing of PPE	Use of PPE weighting 22 kg	Qualitative	None	[General fire department]	Designed to estimate effect of wearing PPE	None	Samples before and after activity	No	No
Patel & Nixon (2022) Other relevant information	Case series	Australia, 2021	Employment records, self-report of wearing black rubber mask	Wearing black rubber mask while working as an active firefighter	Qualitative	None	None	Wearing black rubber mask was the exposure	None	Predates	Yes	No

Table S1.30 Exposure assessment review and critique for mechanistic studies on cancer and occupational exposure as a firefighter

Reference and mechanistic end-point (key characteristic, KC)	What was the study design? (if not a standard design, a brief description)	Study location and exposure period.	What methods were used for the exposure assessment? (incl. data source, environmental and biological measurements etc.)	What was the exposure definition?	Was exposure assessment qualitative, semiquantitative or quantitative?	Concerns noted on exposure classification/ measurements	What firefighting activities (or type of firefighters) were assessed?	Information collected on PPE use, and its effect on exposure if applicable	What exposure metrics were derived for use in analyses (e.g. average exposure, exposure duration, cumulative exposure etc.)?	What was the timing of exposure relative to the outcome?	Was there potential for co-exposures to other carcinogens outside of firefighting exposures?	Was there potential for differential exposure misclassifications ?
Peters et al. (2018) Oxidative stress	Experimental randomized control trial	Montana, Missouri, USA, year not specified	Experimental exposure to controlled combustion of wood	Exposure to smoke with quantification of $PM_{2.5}$	Quantitative	None	None. Subjects were residents in the community	NA	Exposure to woodsmoke	Immediately pre-exposure versus immediately post, and 1 h after	No (everyone was own control)	No
Ranadive et al. (2021) Receptor-mediated effects	Cross-sectional	Florida, USA, year not specified	Firefighter employment (testosterone was the actual exposure)	Mediating exposure (serum testosterone) for other outcomes	Quantitative	None	None	None used	Serum testosterone concentration in firefighters – its relationship (or of the outcomes) with firefighting exposure was not analysed	Timing of measurement of testosterone relative to firefighting exposures or study outcomes not reported	Potential non-firefighting co-exposures not accounted for in analysis	No – associations with firefighting exposures not investigated
Ray et al. (2005) Genotoxic	Cross-sectional	Kolkata & Howrah, India, approximately 2005	Apparently self-report	Employed as ff ≥ 10 yr	Semiquantitative	No data on individual exposures or tasks	[General fire department]	None used	Duration of ff service: 10–19 vs ≥ 20 yrs	Predates	Unclear	Unlikely
Ricaud et al. (2021) Immunosuppression	Cross-sectional	Montreal, Canada, year not specified	Self-reported employment status	Employment as a firefighter; dichotomized firefighter career length	Qualitative and semiquantitative	Apparent reliance on recall for career length but this	Structural [municipal] firefighting	None used	Cumulative – career length	Ongoing exposures; not clear when last	Yes, other sources of exposure to AhR ligands e.g.	Yes, because information was apparently collected based on self-report and

Table S1.30 Exposure assessment review and critique for mechanistic studies on cancer and occupational exposure as a firefighter

Reference and mechanistic end-point (key characteristic, KC)	What was the study design? (if not a standard design, a brief description)	Study location and exposure period.	What methods were used for the exposure assessment? (incl. data source, environmental and biological measurements etc.)	What was the exposure definition?	Was exposure assessment qualitative, semiquantitative or quantitative?	Concerns noted on exposure classification/ measurements	What firefighting activities (or type of firefighters) were assessed?	Information collected on PPE use, and its effect on exposure if applicable	What exposure metrics were derived for use in analyses (e.g. average exposure, exposure duration, cumulative exposure etc.)?	What was the timing of exposure relative to the outcome?	Was there potential for co-exposures to other carcinogens outside of firefighting exposures?	Was there potential for differential exposure misclassifications ?
						should be minimal				exposure occurred	secondhand smoking	seemingly depended on self-recall
Rothman et al. (1993) Genotoxic	Repeated measurements	California, USA, 1988	Self-report	Firefighting activities	Semiquantitative	Activities documented by recall, potential for bias or non-differential misclassification; limited breathing zone measurements of PAH suggested low exposures during typical ff activities	Wildland firefighting	Proportion of time wearing cloth mask	Cumulative hours of ff activities in prior time period, number of seasons of ff activity, min of diesel exhaust exposure/day	Predates	Charcoal broiled meat by dietary recall questionnaire	Unlikely
Roy et al. (2003) Receptor-mediated effects	Repeated measurements	United Kingdom, year not specified	Self-report	Psychological stress	Semiquantitative	Effect of intraindividual variation in exposure measures on outcomes were analysed since	[General fire department]	NA	Average DSI score across each 16-day monitoring period, and STAI, BDI, and job strain scores	Immediately following 16-day work-shifts	34 of 72 self-reported smoking and not accounted for in analyses	Subjective self-reported measures with the potential of ratings being affected by mood

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Reference and mechanistic end-point (key characteristic, KC)	What was the study design? (if not a standard design, a brief description)	Study location and exposure period.	What methods were used for the exposure assessment? (incl. data source, environmental and biological measurements etc.)	What was the exposure definition?	Was exposure assessment qualitative, semiquantitative or quantitative?	Concerns noted on exposure classification/ measurements	What firefighting activities (or type of firefighters) were assessed?	Information collected on PPE use, and its effect on exposure if applicable	What exposure metrics were derived for use in analyses (e.g. average exposure, exposure duration, cumulative exposure etc.)?	What was the timing of exposure relative to the outcome?	Was there potential for co-exposures to other carcinogens outside of firefighting exposures?	Was there potential for differential exposure misclassifications ?
						mood can affect ratings provided for stress questionnaires			at the end of each 16-day monitoring period; also highest and lowest scores across the four 16-day monitoring period over a 1-year follow-up			
Santos et al. (2020) Immunosuppression	RCT	Location and year of exposure not stated	Experimental setting	4-month physical training with or without nutritional supplement at the ending 5-week period	Qualitative	None	NA	NA	Supplemented vs placebo	Change immediately after from immediately before supplement intervention	Smoking reported by some participants; not accounted for in analyses	No
Singh et al. (2018) Chronic inflammation	Repeated measurements	USA, 2001–2017	Self-report	Presence as firefighter at WTC	Semiquantitative	No data on individual exposures or tasks	WTC firefighting	No information	Intensity (high = morning of 9/11; moderate = after noon 9/11 to 9/12; low = 9/13 to 9/24)	Up to 7 yr after exposure	Smoking	No

Table S1.30 Exposure assessment review and critique for mechanistic studies on cancer and occupational exposure as a firefighter

Reference and mechanistic end-point (key characteristic, KC)	What was the study design? (if not a standard design, a brief description)	Study location and exposure period.	What methods were used for the exposure assessment? (incl. data source, environmental and biological measurements etc.)	What was the exposure definition?	Was exposure assessment qualitative, semiquantitative or quantitative?	Concerns noted on exposure classification/ measurements	What firefighting activities (or type of firefighters) were assessed?	Information collected on PPE use, and its effect on exposure if applicable	What exposure metrics were derived for use in analyses (e.g. average exposure, exposure duration, cumulative exposure etc.)?	What was the timing of exposure relative to the outcome?	Was there potential for co-exposures to other carcinogens outside of firefighting exposures?	Was there potential for differential exposure misclassifications ?
Smith et al. (2004) Immunosuppression	Pre/post	[Illinois], USA, year not specified	Participation in firefighter training	Firefighter training exposure	Qualitative	None	Firefighter training	None used	Participation in firefighter training	Immediately before 4th day of training and after 7th day	No	No
Smith et al. (2005) Immunosuppression ; receptor-mediated effects	Pre/post trial	Illinois, USA, year not specified	Experimental design	Firefighting	Qualitative	None	Live-fire firefighting drills	NA	NA	Change from immediately before experimental exposures to immediately and 90 min after	No	No
Smith et al. (2019) Chronic inflammation; immortalization	RCT	USA, year not specified	Experimental design	Simulated firefighting in an aspirin intervention study	Quantitative	None	Simulated structural [municipal] firefighter activity	Full PPE including SCBA	NA	Immediate post activity	No	No
Swiston et al. (2008) Chronic inflammation	Cross-sectional	Canada, 2004–2005	Self-report, personal air sampling	Wood smoke (CO)	Semiquantitative	Self-report dependent on individual judgement	Forest firefighting	No information	Average	Baseline and after exposure	Smoking	No

Table S1.30 Exposure assessment review and critique for mechanistic studies on cancer and occupational exposure as a firefighter

Reference and mechanistic end-point (key characteristic, KC)	What was the study design? (if not a standard design, a brief description)	Study location and exposure period.	What methods were used for the exposure assessment? (incl. data source, environmental and biological measurements etc.)	What was the exposure definition?	Was exposure assessment qualitative, semiquantitative or quantitative?	Concerns noted on exposure classification/ measurements	What firefighting activities (or type of firefighters) were assessed?	Information collected on PPE use, and its effect on exposure if applicable	What exposure metrics were derived for use in analyses (e.g. average exposure, exposure duration, cumulative exposure etc.)?	What was the timing of exposure relative to the outcome?	Was there potential for co-exposures to other carcinogens outside of firefighting exposures?	Was there potential for differential exposure misclassifications ?
Trowbridge et al. (2022) Receptor-mediated effects	Cross-sectional	San Francisco, USA, 2014–2015	Occupation and biomarker measurement	Employment as firefighter and urine levels of organophosphate flame retardants	Qualitative and quantitative	Self-reported occupation but unlikely misclassification because through fire departments and organizations; spot urine samples	Structural [municipal] firefighters	Information on SCBA use but effect on outcome not assessed	Biomarkers seem more reflective of acute exposure	Ranging from within one day to one month since exposure	Yes, exposure to products containing flame retardants and other carcinogens outside work not incorporated in design/measurement	Yes, spot urine samples were collected; biomarker levels could be impacted by exposures outside work
Tsukiji et al. (2014) Chronic inflammation	Nested case–control study	USA, 2001–2008	Self-report	Presence as firefighter at WTC	Qualitative	No data on individual exposures or tasks	WTC firefighting	No information	"WTC exposure intensity," based on arrival time	Up to 7 yr after exposure	Smoking, other fires	No
Vinnikov et al. (2021) Receptor-mediated effects	Cross-sectional	Kazakhstan, year not specified	Self-report	Occupation -job role as a firefighter	Qualitative	Limitation of resolution of job role classification that is collected	[General fire department]	None used	Job role and fire department	Cross-sectional study – ongoing exposure with	Yes (smoking was mentioned) but not analysed with respect to	Yes, current or past overlap of job roles with other categories

Table S1.30 Exposure assessment review and critique for mechanistic studies on cancer and occupational exposure as a firefighter

Reference and mechanistic end-point (key characteristic, KC)	What was the study design? (if not a standard design, a brief description)	Study location and exposure period.	What methods were used for the exposure assessment? (incl. data source, environmental and biological measurements etc.)	What was the exposure definition?	Was exposure assessment qualitative, semiquantitative or quantitative?	Concerns noted on exposure classification/ measurements	What firefighting activities (or type of firefighters) were assessed?	Information collected on PPE use, and its effect on exposure if applicable	What exposure metrics were derived for use in analyses (e.g. average exposure, exposure duration, cumulative exposure etc.)?	What was the timing of exposure relative to the outcome?	Was there potential for co-exposures to other carcinogens outside of firefighting exposures?	Was there potential for differential exposure misclassifications ?
						at the time of recruitment				respect to occupation	outcome of interest (serum testosterone) and exposure metric	
Walker et al. (2015) Chronic inflammation; immunosuppression	Pre/post trial	Australia, year not specified	Experimental setting	Heat	Qualitative	None	Simulated firefighting search and rescue	NA	NA	Change from immediately before experimental exposures to immediately after through 24 h after	No	No
Walker et al. (2017) Chronic inflammation; immunosupression	Pre/post trial	Australia, year not specified	Experimental setting	Heat	Qualitative	None	Simulated firefighting search and rescue	NA	NA	Change from immediately before experimental exposures to immediately after through 24 h after	No	No

Table S1.30 Exposure assessment review and critique for mechanistic studies on cancer and occupational exposure as a firefighter

Reference and mechanistic end-point (key characteristic, KC)	What was the study design? (if not a standard design, a brief description)	Study location and exposure period.	What methods were used for the exposure assessment? (incl. data source, environmental and biological measurements etc.)	What was the exposure definition?	Was exposure assessment qualitative, semiquantitative or quantitative?	Concerns noted on exposure classification/ measurements	What firefighting activities (or type of firefighters) were assessed?	Information collected on PPE use, and its effect on exposure if applicable	What exposure metrics were derived for use in analyses (e.g. average exposure, exposure duration, cumulative exposure etc.)?	What was the timing of exposure relative to the outcome?	Was there potential for co-exposures to other carcinogens outside of firefighting exposures?	Was there potential for differential exposure misclassifications ?
Watkins et al. (2019a) Chronic inflammation	Pre/post trial	United Kingdom, year not specified	Experimental setting	Fire exercises	Qualitative	None	Fire exercises	NA	Type of exercise (demo, attack, compartment)	Before, during and after exercise	No	No
Watkins et al. (2019b) Chronic inflammation	Pre/post trial	United Kingdom, year not specified	Experimental setting	Heat	Qualitative	None	Fire service instruction	Fire protective clothing (all)	Number of [heat] exposures	Before, during and after exposure	No	No
Watkins et al. (2021) Chronic inflammation	Cross-sectional	United Kingdom, year not specified	Self-report	Heat	Quantitative	Self-reported frequency, hard to recall	Training and operational capacity	No information	Number of fire exposures	Before and > 12 h after heat exposure	No	No
Watt et al. (2016) Immunosuppression	Pre/post trial	United Kingdom, year not specified	Experimental setting	Heat	Quantitative	The drills apparently included fire and the potential confounding effect of smoke was not considered	Structure fire instruction drills	PPE including self-contained breathing apparatus used during exposure; the effect on outcome not tested	NA	Changes from before to immediately after exposure	No	No

Table S1.30 Exposure assessment review and critique for mechanistic studies on cancer and occupational exposure as a firefighter

Reference and mechanistic end-point (key characteristic, KC)	What was the study design? (if not a standard design, a brief description)	Study location and exposure period.	What methods were used for the exposure assessment? (incl. data source, environmental and biological measurements etc.)	What was the exposure definition?	Was exposure assessment qualitative, semiquantitative or quantitative?	Concerns noted on exposure classification/ measurements	What firefighting activities (or type of firefighters) were assessed?	Information collected on PPE use, and its effect on exposure if applicable	What exposure metrics were derived for use in analyses (e.g. average exposure, exposure duration, cumulative exposure etc.)?	What was the timing of exposure relative to the outcome?	Was there potential for co-exposures to other carcinogens outside of firefighting exposures?	Was there potential for differential exposure misclassifications ?
Webb et al. (2011) Chronic inflammation; receptor-mediated effects	Pre/post trial	Mississippi, USA, year not specified	Experimental setting	Physical and psychological stress	Qualitative	None	[General fire department]	NA	NA	Change immediately after from immediately before and through experimental exposures	No	No
Weiden et al. (2021) Chronic inflammation	Cross-sectional	USA, 2001–2020	Self-report	Presence as firefighter at WTC	Qualitative	No data on individual exposures or tasks	WTC firefighting	No information	Time since event	Predates	Smoking	No
Witteveen et al. (2010) Receptor-mediated effects	Cross-sectional	Netherlands, year not specified	Employment records, self-report questionnaire, biomarker (saliva, blood) collection	Exposure to major air disaster (negative life event – NLE)	Semiquantitative	No data on individual exposures or tasks	Air disaster	NA	Aggregate traumatic stress exposure	Exposure occurred 8 yr or more before outcome was measured	Yes. Other potential exposures were controlled for in analyses	Yes, because exposure assessment was through self-report; potential for NLE to have been assigned to incorrect period
Wolkow et al. (2015a) Chronic inflammation	Pre/post trial	Australia, year not specified	Experimental setting	Sleep restriction (max 4 h) vs control (8 h)	Qualitative	None	Simulated physical wildland firefighting work circuit	NA	Sleep restricted vs control	Pre and post exposure	No	No

Table S1.30 Exposure assessment review and critique for mechanistic studies on cancer and occupational exposure as a firefighter

Reference and mechanistic end-point (key characteristic, KC)	What was the study design? (if not a standard design, a brief description)	Study location and exposure period.	What methods were used for the exposure assessment? (incl. data source, environmental and biological measurements etc.)	What was the exposure definition?	Was exposure assessment qualitative, semiquantitative or quantitative?	Concerns noted on exposure classification/ measurements	What firefighting activities (or type of firefighters) were assessed?	Information collected on PPE use, and its effect on exposure if applicable	What exposure metrics were derived for use in analyses (e.g. average exposure, exposure duration, cumulative exposure etc.)?	What was the timing of exposure relative to the outcome?	Was there potential for co-exposures to other carcinogens outside of firefighting exposures?	Was there potential for differential exposure misclassifications ?
Wolkow et al. (2015b) Chronic inflammation; receptor-mediated effects	Pre/post trial	Australia, year not specified	Experimental setting	Sleep restriction	Qualitative	None	Simulated wildfire suppression work	No information	Sleep restricted vs control	Pre and post exposure	No	No
Wolkow et al. (2016a) Chronic inflammation; receptor-mediated effects	Pre/post trial	Australia, year not specified	Experimental setting	Sleep restriction (max 4 h) vs control (8 h)	Qualitative	None	Simulated physical wildland firefighting work circuit	NA	Sleep restricted vs control	Pre and post exposure	No	No
Wolkow et al. (2016b) Chronic inflammation; receptor-mediated effects	Pre/post trial	Australia, year not specified	Experimental setting	Sleep restriction (max 4 h) vs control (8 h)	Qualitative	None	Simulated firefighting deployment	NA	Sleep restricted vs control	Pre and post exposure	No	No

Table S1.30 Exposure assessment review and critique for mechanistic studies on cancer and occupational exposure as a firefighter

Reference and mechanistic end-point (key characteristic, KC)	What was the study design? (if not a standard design, a brief description)	Study location and exposure period.	What methods were used for the exposure assessment? (incl. data source, environmental and biological measurements etc.)	What was the exposure definition?	Was exposure assessment qualitative, semiquantitative or quantitative?	Concerns noted on exposure classification/ measurements	What firefighting activities (or type of firefighters) were assessed?	Information collected on PPE use, and its effect on exposure if applicable	What exposure metrics were derived for use in analyses (e.g. average exposure, exposure duration, cumulative exposure etc.)?	What was the timing of exposure relative to the outcome?	Was there potential for co-exposures to other carcinogens outside of firefighting exposures?	Was there potential for differential exposure misclassifications ?
Wolkow et al. (2017) Chronic inflammation; receptor-mediated effects	Pre/post trial	Australia, year not specified	Experimental setting	Temperature: hot condition (day, 33 °C, night, 23 °C) vs control (day, 19 °C, 18 °C at night)	Qualitative	None	Simulated physical wildland firefighting work circuit	NA	Hot vs control condition	Outcome measurement during exposure	No	no
Wright-Beatty et al. (2014) Chronic inflammation	Pre/post trial	Canada, year not specified	Experimental setting	Ambient humidity in high heat	Qualitative	None	Physical activity	NA	Dry heat vs humid heat	Outcome measurements before, during and after exposure	No	No
Wu et al. (2020a) Oxidative stress; chronic inflammation	Pre/post	USA, 2015–2019	Personal monitoring of $PM_{2.5}$	Firefighter during the shift of interest	Quantitative	None	Lighting, holding, prescribed wildland burns	No information	TWA of $PM_{2.5}$. estimation of carbon black	Same day (pre-post)	Information collected, not reported	No
Wu et al. (2020b) Genotoxic; oxidative stress	Pre/post	USA, 2015	Burn compared with non-burn days	Participation in a wildland prescribed burn	Qualitative, quantitative	None	Wildland firefighting, prescribed burns. Tasks not specified	No RPE used	NA	Same/next day	No information	No

Table S1.30 Exposure assessment review and critique for mechanistic studies on cancer and occupational exposure as a firefighter

Reference and mechanistic end-point (key characteristic, KC)	What was the study design? (if not a standard design, a brief description)	Study location and exposure period.	What methods were used for the exposure assessment? (incl. data source, environmental and biological measurements etc.)	What was the exposure definition?	Was exposure assessment qualitative, semiquantitative or quantitative?	Concerns noted on exposure classification/ measurements	What firefighting activities (or type of firefighters) were assessed?	Information collected on PPE use, and its effect on exposure if applicable	What exposure metrics were derived for use in analyses (e.g. average exposure, exposure duration, cumulative exposure etc.)?	What was the timing of exposure relative to the outcome?	Was there potential for co-exposures to other carcinogens outside of firefighting exposures?	Was there potential for differential exposure misclassifications ?
Yucesoy et al. (2008) Chronic inflammation	Cross-sectional	USA, 1988–2003	Employment records	Active firefighter	Qualitative	No data on individual exposures or tasks	[General fire department]	No information	–	After	Smoking	Healthy worker effect
Zhou et al. (2019) Epigenetic	Cross-sectional	Tucson, Arizona, USA, 2018	Employment records	Years of service as ff	Semiquantitative	No data on individual exposures or tasks	[General fire department]	None used	Years of service as ff	Predates	–	No

KC2, key characteristic of carcinogens – "is genotoxic"; KC4, key characteristic of carcinogens – "induces epigenetic alterations"; KC5, key characteristic of carcinogens – "induces oxidative stress"; KC6, key characteristic of carcinogens – "induces chronic inflammation"; KC7, key characteristic of carcinogens – "is immunosuppressive"; KC8, key characteristic of carcinogens – "modulates receptor-mediated effects"; KC9, key characteristic of carcinogens – "causes immortalization"; KC10, key characteristic of carcinogens – "alters cell proliferation, cell death, or nutrient supply".

CO, carbon monoxide; FDNY, Fire Department of the City of New York; ff, firefighter; 1-HP, 1-hydroxypyrene; NA, not applicable; NLE, negative life event; OPFRs, organophosphate flame retardants; PAH, polycyclic aromatic hydrocarbons; PBDEs, polybrominated diphenyl ethers; PCBs, polychlorinated biphenyls; PCDDs, polychlorinated dibenzodioxins; PCDFs, polychlorinated dibenzofurans; PFAS, per- and polyfluoroalkyl substances; PM, particulate matter; $PM_{2.5}$, fine particulate matter 2.5 µm or less in diameter; PPE, personal protective equipment; RCT, randomized control trial; RES, resveratrol; TWA, time-weighted average exposure concentration for a conventional 8-hour workday and a 40-hour workweek; RPE, respiratory protection equipment; SCBA, self-contained breathing apparatus; vs, versus; WTC, World Trade Center.

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