2.5 Cancer of the prostate

2.5.1 Cohort studies

See Table 2.5.1 (red meat) and Table 2.5.2 (processed meat, web only; available at: http://monographs.iarc.fr/ENG/Monographs/vol114/index.php)

The quality of the studies was evaluated based on sample size, quality of reporting of the type of meat, consideration of relevant confounders, study design issues (e.g. population- vs hospital-based design, response rates), and exposure assessment, including validation of dietary questionnaires. The Working Group considered total energy intake, BMI, and race as important potential confounders. Cancer of the prostate poses a special problem compared with other sites because there is a broad range of clinical behaviours, and the classification is not uniform across studies (e.g. grade, stage, Gleason score, or other definitions of clinical aggressiveness). In addition, the widespread use of prostate-specific antigen (PSA) testing, which may be associated with dietary habits, further complicates the interpretation of epidemiological findings.

More than 20 cohort studies have reported on the intake of red meat or processed meat and the incidence or mortality (when incident cases were also considered) from prostate cancer, spanning from 1984 to 2011. The Americas, Asia, and Europe were represented, with studies from Japan, Norway, the Netherlands, the United Kingdom, and the USA.

The most informative cohorts were published by Schuurman et al. (1999), Michaud et al. (2001), Cross et al. (2005) (PLCO randomized trial), Rodriguez et al. (2006), Park et al. (2007), Allen et al. (2008), Koutros et al. (2008), Agalliu et al. (2011), and Major et al. (2011), and several of these studies were included in a pooled analysis of 15 prospective cohort studies (Wu et al., 2016).

Studies with fewer than 100 exposed cases are not described further in the text or tables (e.g. Gann et al., 1994; Giovannucci et al., 1993; Loh et al., 2010; Phillips & Snowdon, 1983; Richman et al., 2011; Rohrmann et al., 2007; Sander et al., 2011; Snowdon et al., 1984; Veierød et al., 1997; Wu et al., 2006).

(a) Pooling Project of Prospective Studies of Diet and Cancer

The Pooling Project of Prospective Studies of Diet and Cancer (DCPP) (Wu et al., 2016) pooled data from 15 of the prospective cohorts conducted globally (Ahn et al., 2008; Neuhouser et al., 2007; Rohrmann et al., 2007; Rodriguez et al., 2006; Larsson et al., 2009; Allen et al., 2008; Michaud et al., 2001; Kurahashi et al., 2008; Muller et al., 2009; Park et al., 2007; Schuurman et al., 1999; Sinha et al., 2009; Kristal et al., 2010; Cross et al., 2005). The individual studies included in the DCPP are not described in detail in the text and tables because the analysis was superseded by Wu et al. (2016).

Among over 700 000 men, 52 683 incident cases of prostate cancer, including 4924 advanced cases, were identified. Methods of ascertainment of meat intake and outcome measures were harmonized across cohorts (all dietary instruments were validated). Median intakes of red meat ranged from 10.3 g/day in a Japanese cohort to 109 g/day in a Melbourne cohort.

A modest positive association was found between the highest category of red meat consumption and prostate tumours identified as advanced stage at diagnosis (RR, 1.19; 95% CI, 1.01–1.40; P_{trend} = 0.07; $P_{heterogeneity}$ = 0.47). For processed meat, the corresponding relative risk was 1.17 (95% CI, 0.99–1.39; P_{trend} = 0.10; $P_{heterogeneity}$ = 0.94). Positive associations between red meat, and inverse associations between poultry intake, and advanced cancers were limited to North American studies.

(b) Studies not included in the pooling project

Among a cohort of farmers in the Agricultural Health Study in the USA involved in pesticide application, Koutros et al. (2008) reported on the 668 prostate cancer cases that were identified, including 140 with advanced-stage prostate cancer. The response rate was low (about 50%). Slight increases in incident prostate cancer risk were noticed with quintiles of red meat intake, with no dose–response relationship (P_{trend} = 0.76). Doneness was associated with risk. For the second tertile of intake of well-done meat (median, 40.6 g/day), the relative risk was 1.12 (95% CI, 0.92–1.37), and for the third tertile of intake of well-done meat (median, 80.3 g/day), it was 1.26 (95% CI, 1.02–1.54; P_{trend} = 0.03). When this was limited to advanced cases, the relative risk for the second versus the first tertile (40.6 vs 18.0 g/day) was 1.63 (95% CI, 1.06–2.52), and for the third tertile versus the first tertile (median, 80.3 g/day), it was 1.97 (95% CI, 1.26–3.08; P_{trend} = 0.004). [Red meat was not clearly defined; doneness was for total meat.]

Major et al. (2011) conducted a study on African Americans within the NIH-AARP study. Levels of HAAs and polycyclic aromatic hydrocarbons (PAHs) from meats were ascertained by linking data to the NCI Computerized Heterocyclic Amines Resource for Research in Epidemiology of Disease (CHARRED) database. Haem iron intake was estimated. No association between incident prostate cancer and red meat intake was found, except for red meat cooked at high temperatures: the relative risk for the second (median, 11.40 g per 1000 kcal) versus the first tertile (3.49 g per 1000 kcal) was 1.18 (95% CI, 1.0–1.38), and for the third tertile (median, 24.74 g per 1000 kcal), it was 1.22 (95% CI, 1.03–1.44). The relative risk of the estimated exposure to the mutagen DiMeIQx for the second tertile (median, 0.93 ng per 1000 kcal) was 1.15 (95% CI, 0.93–1.42), and for the third tertile, it was 1.3 (95% CI, 1.05–1.61; P_{trend} = 0.02). No associations were observed with intake of other HAAs. The results for processed meat were inconclusive. [The Working Group noted that red meat included all types of beef and pork.]

Agalliu et al. (2011) described a nested case–cohort study in a Canadian cohort, with 702 cases and 1979 controls (subcohort), who were alumni of the University of Alberta. Elevated relative risks were reported for red meat, but none reached statistical significance, except Q5 (median, 3.1 oz [~87.8 g/day]) vs Q1 (median, 0.7 oz [~19.8 g/day]); the relative risk was 1.44 (95% CI, 1.06–1.95). There was no dose–response relationship. [The Working Group noted that red meat was not defined.]

2.5.2 Case–control studies

See Table 2.5.3 (red meat) and Table 2.5.4 (processed meat, web only; available at: http://monographs.iarc.fr/ENG/Monographs/vol114/index.php)

More than 20 case–control studies were considered, six with a population-based design. The Working Group considered first the population-based studies that tended to be more informative, given the uncertainty in the choice of hospital controls, who were affected by diseases that could have possibly had an impact on dietary habits. Studies with fewer than 100 cases were excluded (see details below).

(a) Population-based studies

Slattery et al. (1990) was not considered here because meat intake was considered together with estimated intake of saturated fats. Studies by Nowell et al. (2004) and Ukoli et al. (2009) were excluded because numbers were small, or dietary assessment was limited.

Norrish et al. (1999) conducted a population-based study in New Zealand that included 317 cases and 480 controls randomly selected from electoral rolls. They used a 107-item FFQ. An association was found with intake of browned

beef steaks. The odds ratios were 1.36 (95% CI, 0.84–2.18) for medium/lightly browned and 1.68 (95% CI, 1.02–2.77) for well browned. Similar, but not statistically significant, associations were found in advanced cases. The researchers also looked separately at other types of red meats, including pork, lamb, and minced beefand, processed meats including sausage, and bacon, with null results.

Wright et al. (2011) conducted a population-based study that included 1754 cases and 1645 controls identified by random digit dialling. Response rates were high (78%) in cases and lower (67%) in controls. Detailed clinical data were obtained for the cases. Disease aggressiveness was based on a composite variable incorporating Gleason score stage and PSA, where more aggressive cases were defined by a Gleason score of ≥ 7, non-localized stage, or PSA > 20 ng/mL at the time of diagnosis. A positive association was found with increasing servings per day (1 serving/day) of red meat. The odds ratios were 1.21 (95% CI, 0.97–1.51) for 0.59–1.09 servings/day and 1.43 (95% CI, 1.11–1.84) for > 1.09 servings/day. [The definition of red meat was unclear.] Similar associations were found among less and more aggressive cancer cases.

Joshi et al. (2012) conducted a study in the USA, with 717 localized and 1140 advanced incident cases, in a multiethnic population. Controls were selected with a "neighbourhood walking algorithm" or randomly from a health care financing organization. [The degree of selection bias with this type of procedure was uncertain, as selection was conditioned by local characteristics, such as the social structure of the neighbourhood and the nature of the financing organization.] The response rate was not given. Accurate dietary histories were collected with a modified version of the Block FFQ. No association with red meat intake was found, except when hamburgers cooked at high temperatures were considered, and only among advanced cases. The odds ratios were 1.3 (95% CI, 1.0–1.6) for low frequency (< 4.4 g/1000 kcal) versus never, 1.4 (95% CI, 1.0–1.8) for medium frequency (≥ 4.4 to < 7.9 g/1000 kcal), and 1.7 (95% CI, 1.3–2.2) for high frequency (≥ 7.9 g/1000 kcal). Associations were particularly strong for pan-fried red meat; subgroup analyses and multiple comparisons were considered. Previously, John et al. (2011) had reported on the San Francisco Bay Area portion of this study (John et al., 2011). In that study, advanced prostate cancer cases showed an association with increasing tertiles of total red meat intake versus no intake. The odds ratios were 1.1 (95% CI, 0.68–1.79), 1.65 (95% CI, 1.02–2.65), and 1.53 (95% CI, 0.93–2.49; P_{trend} = 0.02). Similar associations with advanced cases were found for hamburgers, steaks, and processed meat. The odds ratios for processed meat (increasing tertiles versus no intake) were 1.25 (95% CI, 0.85–1.83), 1.15 (95% CI, 0.77–1.71), and 1.57 (95% CI, 1.04–2.36), again with no clear dose–response. This study also examined cooking methods and meat mutagens.

(b) Hospital-based studies

The following hospital-based studies were given less weight for different reasons: Bashir et al. (2014), as no details given on the choice of controls; Li et al. (2014), as no response rates and limited exposure assessment; Mahmood et al. (2012), as no details on exposure assessment and no response rates; Punnen et al. (2011), as no response rates, no adjustment for total energy intake, and only cases with Gleason ≥ 7 included; Rodrigues et al. (2011), as no response rates and no adjustment for energy intake; Román et al. (2014), as no response rates and source of controls not identified; Rosato et al. (2014), as no response rates and results not given for meat as such; Salem et al. (2011), as diagnoses in controls not specified and poor dietary history; Sonoda et al. (2004), as no response rates and limited adjustment for confounders; Subahir et al. (2009), as diseases of controls not specified and no response rates; Sung et al. (1999), as no response rates, unclear

adjustment for confounders, and limited dietary history; Walker et al. (2005), as no response rates for controls and only dietary patterns examined; and De Stefani et al. (1995), as the distinction between red and white meat was unclear. These studies are not further described in the text and tables.

Deneo-Pellegrini et al. (1999) described a study in Uruguay with cancer-free controls, with small numbers. For red meat and for processed meat, the slightly elevated odds ratios were not statistically significant. An update of the same study was published by the same authors with similar results (Deneo-Pellegrini et al. (2012).

Aune et al. (2009) conducted a hospital-based study on multiple cancers in Uruguay, with 345 histologically confirmed cases. A 64-item FFQ validated was used. An association was found with red meat. The odds ratio for the second (150 to < 250 g/day) versus the first (0 to < 150 g/day) tertile was 1.56 (95% CI, 1.15–2.13), and the odds ratio for the third (250–600 g/day) versus the first tertile was 1.87 (95% CI, 1.08–3.21; P_{trend} = 0.001). No association was found with processed meat. [The Working Group noted that the results were adjusted for energy intake, BMI, and numerous other risk factors.]

Among those given less priority, Punnen et al. (2011) is worth mentioning because of the relatively large size of the study (466 cases). They found an association with an increasing intake of grilled beef. The odds ratios were 1.5 (95% CI, 1.03–2.19) for low intake versus none, 1.69 (95% CI, 1.19–2.38) for medium intake versus none, and 1.61 (95% CI, 1.13–2.28) (P_{trend} = 0.004) for high intake versus none. The odds ratios with increasing intake of grilled hamburgers versus no intake were 1.41 (95% CI, 0.99–2.01), 1.58 (95% CI, 1.11–2.24), and 1.86, (95% CI, 1.28–2.71; P_{trend} = 0.001).

Di Maso et al. (2013) published results based on data from a large hospital-based study in Italy (1294 cases, non-neoplastic controls). They reported slightly elevated odds ratios for red meat, which were not statistically significant.

(c) Other studies

Amin et al. (2008), in Canada, recruited 1356 subjects with increased PSA undergoing a prostate biopsy, comparing those with a cancer diagnosis with the others. All men were asked to respond to a self-administered, validated FFQ (included only 12 food groups) before the procedure; the procedure was a biopsy administered after a rising serum PSA level or a suspicious digital rectal examination. Increased odds ratios with intake of red meat (including ham and sausages) were found, with an apparent dose–response relationship across quintiles. The odds ratio for Q4 (5 servings/week) versus Q1 (1 serving/week) was 2.31 (95% CI, 1.32–2.46), and for Q5 (data missing or unavailable) versus Q1, it was 2.91 (95% CI, 1.56–4.87; P_{trend} = 0.027). [The Working Group noted that there was apparently a low response rate among controls. This study was of interest because both cases and controls had high PSA. That is, screening was not a source of confounding, the FFQ was administered when PSA was measured, and the identification of cases occurred after, so recall bias could be reasonably ruled out. Red meat included ham and sausages and so corresponded to red meat and processed meat combined.]

Table 2.5.1 Cohort studies on consumption of red meat and cancer of the prostate

Reference, location, enrolment/follow-up period, study design	Population size, description, exposure assessment method	Organ site	Exposure category or level	Exposed cases/ deaths	Risk estimate (95% CI)	Covariates controlled
Koutros et al. (2008) USA Recruitment, 1993–1997 Cohort study	23 080 men, 197 017 person-years, 668 prostate cancer cases (140 advanced); Agricultural Health Study included 57 311 licenced pesticide applicators from Iowa and North Carolina; 23 080 available for analysis Exposure assessment method: questionnaire; frequency of intake of hamburgers, beef steaks, chicken, pork chops/ham steaks, and bacon/sausage in the last 12 mo; doneness of total meat and cooking methods [red meat was not clearly defined]	Prostate: incident cases	Red meat (median, g/day)			Age, state of residence, race, smoking, family history of prostate cancer
			Q1 (23.2)	145	1.00	
			Q2 (42.5)	143	1.28 (1.15–1.62)	
			Q3 (60.9)	121	1.15 (0.90–1.48)	
			Q4 (81.6)	109	1.16 (0.90–1.50)	
			Q5 (122.3)	95	1.11 (0.84–1.46)	
			Trend-test *P* value: 0.76			
		Prostate: incident cases	Doneness level, well- and very well-done total meat (median, g/day)			
			T1 (18.0)	187	1.00	
			T2 (40.6)	212	1.12 (0.92–1.37)	
			T3 (80.3)	214	1.26 (1.02–1.54)	
			Trend-test *P* value: 0.03			
		Prostate: (aggressive/ advanced)	Doneness level, very well-done total meat (median, g/day)			
			T1 (18.0)	35	1.00	
			T2 (40.6)	51	1.63 (1.06–2.52)	
			T3 (80.3)	54	1.97 (1.26–3.08)	
			Trend-test *P* value: 0.004			
		Prostate: incident cases	Doneness level, rare or medium total meat (median, g/day)			
			T1 (0)	239	1.00	
			T2 (18.0)	205	1.06 (0.87–1.29)	
			T3 (63.0)	169	1.04 (0.84–1.29)	
			Trend-test *P* value: 0.8			

Table 2.5.1 (continued)

Reference, location, enrolment/follow-up period, study design	Population size, description, exposure assessment method	Organ site	Exposure category or level	Exposed cases/ deaths	Risk estimate (95% CI)	Covariates controlled
Agalliu et al. (2011) Canada 1995–1998 Cohort study	702 cases and 1979 controls (subcohort); prospective cohort of 73 909 men and women, mainly alumni of the University of Alberta, (34 291 men) Exposure assessment method: questionnaire; 166 food items and validated; red meat was not defined	Prostate	Quintiles of red meat intake [median, g/day]			Age, race, BMI, physical activity, education
			Q1 [19.8]	108	1.00	
			Q2 [36. 8]	124	1.10 (0.80–1.50)	
			Q3 [48.2]	151	1.33 (0.98–1.80)	
			Q4 [62.3]	128	1.18 (0.87–1.61)	
			Q5 [87.8]	150	1.44 (1.06–1.95)	
			Trend-test *P* value: 0.04			
		Prostate (aggressive/ advanced)	Quintiles of red meat intake [median, g/day]			
			Q1 [19.8]	28	1.00	
			Q2 [36.8]	40	1.44 (0.85–2.43)	
			Q3 [48.2]	37	1.30 (0.76–2.23)	
			Q4 [62.3]	32	1.17 (0.67–2.03)	
			Q5 [87.8]	36	1.38 (0.80–2.39)	
			Trend-test *P* value: 0.10			
Major et al. (2011) USA Enrolment, 1995–1996 Cohort study	Prospective cohort of 7949 men; from National Institutes of Health – American Association of Retired Persons (NIH-AARP) Diet and Health Study; men and women aged 50–57 yr; 556 401 people, including 9304 African American men (after exclusions, 7949) Exposure assessment method: questionnaire; 124-item FFQ on previous 12 mo; "red meat" included all types of beef and pork	Prostate	Quintiles of red meat (median intake, g/1000 kcal)			Age, BMI, smoking, education, marital status, alcohol consumption, health status, family history of prostate cancer, family history of diabetes, fruit intake
			Q1 (8.42)	244	1.00	
			Q2 (19.35)	225	0.99 (0.82–1.19)	
			Q3 (29.17)	226	1.05 (0.87–1.26)	
			Q4 (40.32)	213	1.01 (0.83–1.24)	
			Q5 (60.92)	181	0.92 (0.75–1.14)	
			Trend-test *P* value: 0.48			
		Prostate	Tertiles of red meat cooked at high temperatures (median intake, g/1000 kcal)			
			T1 (3.49)	365	1.00	
			T2 (11.40)	373	1.18 (1.00–1.38)	
			T3 (24.74)	351	1.22 (1.03–1.44)	
			Trend-test *P* value: 0.04			

Table 2.5.1 (continued)

Reference, location, enrolment/follow-up period, study design	Population size, description, exposure assessment method	Organ site	Exposure category or level	Exposed cases/ deaths	Risk estimate (95% CI)	Covariates controlled
Major et al. (2011) USA Enrolment, 1995–1996 Cohort study (cont.)		Prostate	Tertiles of red meat cooked at low temperatures (median intake, g/1000 kcal)			
			T1 (6.63)	405	1.00	
			T2 (15.36)	368	0.91 (0.78–1.06)	
			T3 (29.06)	316	0.84 (0.71–0.99)	
			Trend-test *P* value: 0.05			
		Prostate: advanced cases	Tertiles of red meat cooked at high temperatures (median intake, g/1000 kcal)			
			T1 (3.49)	34	1.00	
			T2 (11.40)	35	1.23 (0.74–2.06)	
			T3 (24.74)	39	1.44 (0.83–2.47)	
			Trend-test *P* value: 0.20			
Wu et al. (2016) International pooled cohort consortium 1985–2009 Cohort study	842 149 men; consortium of 15 cohort studies (52 683 incident prostate cancer cases, including 4924 advanced cases) Exposure assessment method: questionnaire	Prostate (aggressive/ advanced)	Quintiles of red meat intake (g/day)			Marital status, race, education, BMI, height, alcohol intake, total energy intake, smoking status, family history of prostate cancer, physical activity, history of diabetes, multivitamin use
			Q1 (< 20)	NR	1.00	
			Q2 (20 to < 40)	NR	1.02 (0.89–1.16)	
			Q3 (40 to < 60)	NR	1.11 (0.96–1.27)	
			Q4 (60 to < 100)	NR	1.05 (0.91–1.21)	
			Q5 (≥ 100)	NR	1.19 (1.01–1.40)	
			Trend-test *P* value: 0.07			

BMI, body mass index; FFQ, food frequency questionnaire; mo, month; NR, not reported; yr, year

Table 2.5.3 Case–control studies on consumption of red meat and cancer of the prostate

Reference, location, enrolment	Population size, description, exposure assessment method	Organ site	Exposure category or level	Exposed cases/deaths	Risk estimate (95% CI)	Covariates controlled
Deneo-Pellegrini et al. (1999) Uruguay 1994–1997	Cases: 175; localized cancers, 25%; regional cancers, 72%; disseminated cancers, 3% Controls: 233; hospital patients with conditions unrelated to diet, mainly mild surgical conditions, and no cancers Exposure assessment method: questionnaire; 64 food items; red meat was beef and lamb	Prostate	Red meat, quartiles Q1 Q2 Q3 Q4 Trend-test *P* value: 0.17	 32 61 36 46	 1.0 1.5 (0.9–2.7) 1.7 (0.9–3.3) 1.7 (0.8–3.4)	Age, residence, urban/rural, education, family history, BMI, energy intake
Norrish et al. (1999) New Zealand 1996–1997	Cases: 317; population-based, histologically confirmed cases Controls: 480; controls were randomly selected from electoral rolls and matched by age Exposure assessment method: questionnaire; self-administered, 107-item FFQ	Prostate Prostate: advanced cases	Beef steak doneness Medium or lightly browned vs never eaten Well done or well browned vs never eaten Trend-test *P* value: 0.03 Beef steak doneness Medium or lightly browned vs never eaten Well done or well browned vs never eaten Trend-test *P* value: 0.16	 163 123 NR NR	 1.36 (0.84–2.18) 1.68 (1.02–2.77) 1.38 (0.78–2.42) 1.56 (0.86–2.81)	Age, socioeconomic status, total NSAIDs, total energy intake
Amin et al. (2008) Canada 2003–2006	Cases: 386 men; cohort of 1356 subjects with increased PSA who underwent prostate biopsy; cases were those with cancer at biopsy Controls: 268 men; controls had high PSA, but non-malignant lesions at biopsy Exposure assessment method: questionnaire; self-administered FFQ with 12 food groups; repeated questionnaires among 50 subjects to validate the FFQ and exclude recall bias	Prostate	Red meat, ham, and sausages; quintiles Q1 Q2 Q3 Q4 Q5 Trend-test *P* value: 0.027	 NR NR NR NR NR	 1.00 1.55 (0.85–1.69) 1.97 (0.74–2.73) 2.31 (1.32–2.46) 2.91 (1.56–4.87)	Age, ethnicity, education, family history, smoking, alcohol, sexually transmitted infection, cystitis

Table 2.5.3 (continued)

Reference, location, enrolment	Population size, description, exposure assessment method	Organ site	Exposure category or level	Exposed cases/deaths	Risk estimate (95% CI)	Covariates controlled
Aune et al. (2009) Uruguay 1996–2004	Cases: 345; recruited in four major hospitals in Montevideo Controls: 2032; controls had non-neoplastic diseases not related to smoking or drinking, and no recent changes in dietary habits Exposure assessment method: questionnaire; 64 food items; FFQ tested for reproducibility (correlation coefficient between two assessments was 0.77 for red meat); red meat was defined as fresh meat, including lamb and beef	Prostate	Red meat (g/day), tertiles T1 (0 to < 150) T2 (150 to < 250) T3 (250–600) Trend-test *P* value: 0.001	 125 179 41	 1.00 1.56 (1.15–2.13) 1.87 (1.08–3.21)	Residence; age; education; income; interviewer; smoking; alcohol; intake of grains and fatty foods, fruits and vegetables; energy intake; BMI; other dietary habits
John et al. (2011) USA 1997–2000	Cases: 726; population-based, aged 40–70 yr; non-Hispanic, whites and African Americans; SEER codes 41–85 Controls: 527; controls identified with random digit dialling and randomly selected from the rosters of beneficiaries of the Health Care Financing Administration; frequency-matched by age and ethnicity Exposure assessment method: questionnaire; 74-item food questionnaire; red meat was all types of beef and pork	Prostate: advanced cases	Hamburgers (g/1000 kcal per day), tertiles No red meat consumed T1 T2 T3 Trend-test *P* value: 0.005	 42 144 150 195	 1.00 1.21 (0.75–1.95) 1.33 (0.82–2.14) 1.79 (1.10–2.92)	Age, race, socioeconomic status, family history, BMI, calorie intake, fat, fruits, vegetables
		Prostate: advanced cases	Red meat (g/1000kcal per day), tertiles No red meat consumed T1 T2 T3 Trend-test *P* value: 0.02	 42 128 190 171	 1.00 1.10 (0.68–1.79) 1.65 (1.02–2.65) 1.53 (0.93–2.49)	
		Prostate: localized cases	Red meat (g/1000kcal per day), tertiles No red meat consumed T1 T2 T3 Trend-test *P* value: 0.62	 58 156 157 156	 1.00 0.71 (0.39–1.27) 1.12 (0.63–2.01) 0.91 (0.49–1.69)	

Table 2.5.3 (continued)

Reference, location, enrolment	Population size, description, exposure assessment method	Organ site	Exposure category or level	Exposed cases/deaths	Risk estimate (95% CI)	Covariates controlled
Punnen et al. (2011) USA 2001–2004	Cases: 466; hospital-based. incident histologically confirmed cases; only aggressive cases (Gleason score ≥ 7) Controls: 511; controls were men older than 50 yr undergoing medical examination, with PSA < 4; frequency-matched by age, ethnicity, and medical centre Exposure assessment method: questionnaire; SQFFQ; estimation of exposure to mutagens	Prostate	Grilled beef intake Low intake vs none Medium vs none High vs none Trend-test *P* value: 0.004 Grilled hamburger intake Low vs none Medium vs none High vs none Trend-test *P* value: 0.001	 85 124 129 106 126 120	 1.50 (1.03–2.19) 1.69 (1.19–2.38) 1.61 (1.13–2.28) 1.41 (0.99–2.01) 1.58 (1.11–2.24) 1.86 (1.28–2.71)	Age, ethnicity, medical centre, family history, smoking, BMI, prior history of PSA testing, education level, n-3 fatty acid intake
Wright et al. (2011) USA 1993–1996	Cases: 1754; population-based study; cases identified from the SEER Registries Controls: 1645; population controls identified by random digit telephone dialling and matched by age Exposure assessment method: questionnaire; self-administered FFQ on usual dietary intake during 3–5 yr before the reference date; [red meat not clearly defined]	Prostate Prostate: less aggressive cancer Prostate: more aggressive cancer	Red meat (servings/day) ≤ 0.58 0.59–1.09 > 1.09 Trend-test *P* value: <0.01 Red meat (servings/day) ≤ 0.58 0.59–1.09 > 1.09 Trend-test *P* value: 0.02 Red meat (servings/day) ≤ 0.58 0.59–1.09 > 1.09 Trend-test *P* value: 0.01	 NR NR NR NR NR NR NR NR NR	 1.00 1.21 (0.97–1.51) 1.43 (1.11–1.84) 1.00 1.11 (0.87–1.42) 1.38 (1.05–1.82) 1.00 1.43 (1.06–1.96) 1.55 (1.10–2.20)	Age, PSA screening history, BMI, total caloric intake

Table 2.5.3 (continued)

Reference, location, enrolment	Population size, description, exposure assessment method	Organ site	Exposure category or level	Exposed cases/deaths	Risk estimate (95% CI)	Covariates controlled
Deneo-Pellegrini et al. (2012) Uruguay 1996–2004	Cases: 326; hospital-based study; localized cancers, 25%; regional cancers, 72%; and disseminated cancers, 3% Controls: 652; hospital controls; conditions not related to smoking, drinking and no recent dietary changes (minor surgical conditions); matched 2:1 on age and residence Exposure assessment method: questionnaire; 64 food items; red meat was beef and lamb	Prostate	T1 T2 T3 Trend-test *P* value: 0.17	95 119 112	1.00 1.28 (0.90–1.81) 1.28 (0.90–1.82)	Age, residence, urban/rural, BMI, education, family history, energy intake, other types of meats
Joshi et al. (2012) USA 1997–1998	Cases: 717 localized, 1140 advanced; multiethnic, population-based; incident cases identified through cancer registries Controls: 1096; controls selected with neighbourhood walk algorithm or randomly selected from the Health Care Financing Administration Exposure assessment method: questionnaire; red meat was all types of beef and pork, hamburgers, and steak	Prostate: advanced cases	High-temperature cooked hamburger (g/1000 kcal/day) Never/rarely (0) Low (> 0 to < 4.4) Medium (≥ 4.4 to < 7.9) High (> 7.9) Trend-test *P* value: < 0.001	 501 310 145 183	 1.0 1.3 (1.0–1.6) 1.4 (1.0–1.8) 1.7 (1.3–2.2)	Age, BMI, caloric intakes, family history, fat intake, alcohol, smoking, fruit intake, vegetable intake
		Prostate: advanced cases	Red meat (g/1000 kcal per day), quintiles Q1 (≥ 0 to < 4.6) Q2 (≥ 4.6 to < 8.9) Q3 (≥ 8.9 to < 14.4) Q4 (≥ 14.4 to < 23.3) Q5 (≥ 23.3) Trend-test *P* value: 0.667	 209 200 250 257 223	 1.0 0.9 (0.7–1.2) 1.2 (0.9–1.5) 1.1 (0.8–1.5) 1.0 (0.8–1.4)	

Table 2.5.3 (continued)

Reference, location, enrolment	Population size, description, exposure assessment method	Organ site	Exposure category or level	Exposed cases/deaths	Risk estimate (95% CI)	Covariates controlled
Joshi et al. (2012) USA 1997–1998 (cont.)		Prostate: localized cases	Red meat (g/1000 kcal per day), quintiles			
			Q1 (≥ 0 to < 4.6)	124	1.0	
			Q2 (≥ 4.6 to < 8.9)	142	1.2 (0.8–1.6)	
			Q3 (≥ 8.9 to < 14.4)	140	1.1 (0.8–1.5)	
			Q4 (≥ 14.4 to < 23.3)	141	1.0 (0.7–1.4)	
			Q5 (≥ 23.3)	168	1.1 (0.8–1.6)	
			Trend-test *P* value: 0.822			
		Prostate: advanced cases	High-temperature cooked red meat (g/1000 kcal per day)			
			Never/rarely (0)	133	1.0	
			Low (> 0 to < 9.4)	457	1.1 (0.9–1.5)	
			Medium (≥ 9.4 to < 16.9)	274	1.4 (1.0–1.9)	
			High (≥ 16.9)	275	1.4 (1.0–1.9)	
			Trend-test *P* value: 0.026			
		Prostate: advanced cases	Well-done red meat (g/1000 kcal per day)			
			Never/rarely (0)	392	1.0	
			Low (> 0 to < 6.1)	355	1.2 (0.9–1.4)	
			Medium (≥ 6.1 to < 11.0)	161	1.1 (0.8–1.4)	
			High (≥ 11.0)	231	1.4 (1.1–1.8)	
			Trend-test *P* value: 0.013			
		Prostate: advanced cases	Pan-fried red meat (g/1000 kcal per day)			
			Never/rarely (0)	538	1.0	
			Low (> 0.0 to < 5.0)	297	1.2 (1.0–1.5)	
			Medium (≥ 5.0 to < 9.8)	137	1.2 (0.9–1.6)	
			High (≥ 9.8)	167	1.3 (1.0–1.8)	
			Trend-test *P* value: 0.035			

Table 2.5.3 (continued)

Reference, location, enrolment	Population size, description, exposure assessment method	Organ site	Exposure category or level	Exposed cases/deaths	Risk estimate (95% CI)	Covariates controlled
Di Maso et al. (2013) Italy and Switzerland 1991–2002	Cases: 1294; hospitalized incident cases Controls: 11 656; hospital controls; non-neoplastic conditions unrelated to alcohol, diet, and tobacco; frequency-matched to cases Exposure assessment method: questionnaire; red meat was beef, veal, pork, horse meat, and half of the first course, including meat sauce (e.g. lasagne, pasta/rice with bologna sauce)	Prostate	Red meat (g/day) 60–89 vs < 60 ≥ 90 vs < 60 Trend-test *P* value: 0.14	 385 453	 1.17 (0.96–1.42) 1.15 (0.96–1.39)	Centre, age, education, BMI, smoking, alcohol, vegetable intake, fruit intake
		Prostate	Increase of 50 g/day	NR	1.07 (0.97–1.18)	

BMI, body mass index; FFQ, food frequency questionnaire; NR, not reported; NSAID, nonsteroidal anti-inflammatory drug; PSA, prostate-specific antigen; SEER, Surveillance, Epidemiology, and End Results; SQFFQ, semi-quantitative food frequency questionnaire; yr, year

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