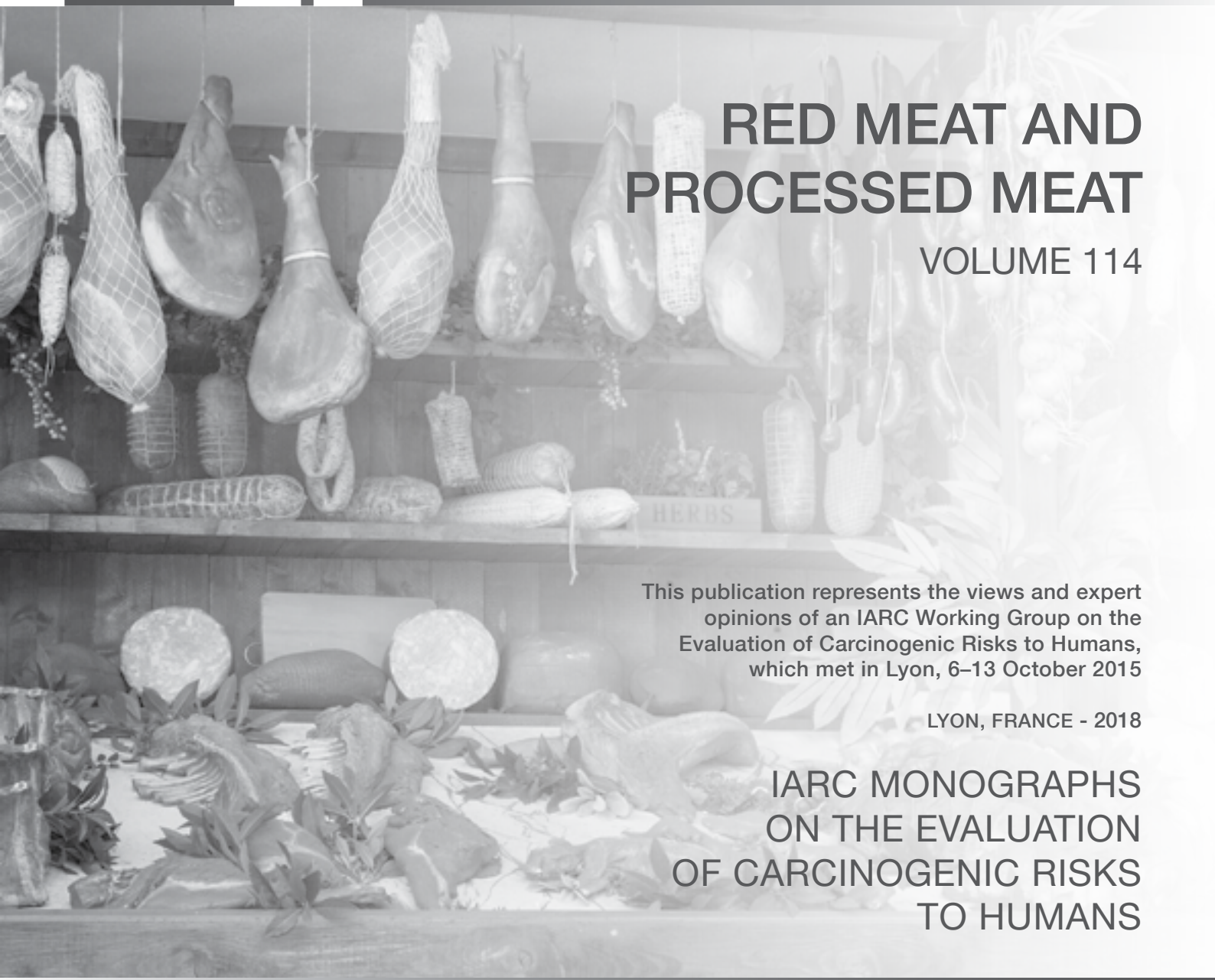
IARC MONOGRAPHS



RED MEAT AND PROCESSED MEAT

VOLUME 114

This publication represents the views and expert opinions of an IARC Working Group on the Evaluation of Carcinogenic Risks to Humans, which met in Lyon, 6–13 October 2015

LYON, FRANCE - 2018

IARC MONOGRAPHS ON THE EVALUATION OF CARCINOGENIC RISKS TO HUMANS

International Agency for Research on Cancer

World Health Organization

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://publications.iarc.fr/564)

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://publications.iarc.fr/564)

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 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
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 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
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 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
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 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
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			Age, ethnicity, medical centre, family history, smoking, BMI, prior history of PSA testing, education level, n-3 fatty acid intake
			Low intake vs none	85	1.50 (1.03–2.19)	
			Medium vs none	124	1.69 (1.19–2.38)	
			High vs none	129	1.61 (1.13–2.28)	
			Trend-test *P* value: 0.004			
			Grilled hamburger intake			
			Low vs none	106	1.41 (0.99–2.01)	
			Medium vs none	126	1.58 (1.11–2.24)	
			High vs none	120	1.86 (1.28–2.71)	
			Trend-test *P* value: 0.001			
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	Red meat (servings/day)			Age, PSA screening history, BMI, total caloric intake
			≤ 0.58	NR	1.00	
			0.59–1.09	NR	1.21 (0.97–1.51)	
			> 1.09	NR	1.43 (1.11–1.84)	
			Trend-test *P* value: <0.01			
		Prostate: less aggressive cancer	Red meat (servings/day)			
			≤ 0.58	NR	1.00	
			0.59–1.09	NR	1.11 (0.87–1.42)	
			> 1.09	NR	1.38 (1.05–1.82)	
			Trend-test *P* value: 0.02			
		Prostate: more aggressive cancer	Red meat (servings/day)			
			≤ 0.58	NR	1.00	
			0.59–1.09	NR	1.43 (1.06–1.96)	
			> 1.09	NR	1.55 (1.10–2.20)	
			Trend-test *P* value: 0.01			

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. (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 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
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 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
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

References

Agalliu I, Kirsh VA, Kreiger N, Soskolne CL, Rohan TE (2011). Oxidative balance score and risk of prostate cancer: results from a case-cohort study. *Cancer Epidemiol*, 35(4):353–61. doi:10.1016/j.canep.2010.11.002 PMID:21145797

Ahn J, Moslehi R, Weinstein SJ, Snyder K, Virtamo J, Albanes D (2008). Family history of prostate cancer and prostate cancer risk in the Alpha-Tocopherol, Beta-Carotene Cancer Prevention (ATBC) Study. *Int J Cancer*, 123(5):1154–9. doi:10.1002/ijc.23591 PMID:18546266

Allen NE, Key TJ, Appleby PN, Travis RC, Roddam AW, Tjønneland A et al. (2008). Animal foods, protein, calcium and prostate cancer risk: the European Prospective Investigation into Cancer and Nutrition. *Br J Cancer*, 98(9):1574–81. doi:10.1038/sj.bjc.6604331 PMID:18382426

Amin M, Jeyaganth S, Fahmy N, Bégin LR, Aronson S, Jacobson S et al. (2008). Dietary habits and prostate cancer detection: a case-control study. *Can Urol Assoc J*, 2(5):510–5. doi:10.5489/cuaj.918 PMID:18953447

Aune D, De Stefani E, Ronco A, Boffetta P, Deneo-Pellegrini H, Acosta G et al. (2009). Meat consumption and cancer risk: a case-control study in Uruguay. *Asian Pac J Cancer Prev*, 10(3):429–36. PMID:19640186

Bashir MN, Ahmad MR, Malik A (2014). Risk factors of prostate cancer: a case-control study in Faisalabad, Pakistan. *Asian Pac J Cancer Prev*, 15(23):10237–40. doi:10.7314/APJCP.2014.15.23.10237 PMID:25556453

Cross AJ, Peters U, Kirsh VA, Andriole GL, Reding D, Hayes RB et al. (2005). A prospective study of meat and meat mutagens and prostate cancer risk. *Cancer Res*, 65(24):11779–84. doi:10.1158/0008-5472.CAN-05-2191 PMID:16357191

De Stefani E, Fierro L, Barrios E, Ronco A (1995). Tobacco, alcohol, diet and risk of prostate cancer. *Tumori*, 81(5):315–20. PMID:8804446

Deneo-Pellegrini H, De Stefani E, Ronco A, Mendilaharsu M (1999). Foods, nutrients and prostate cancer: a case-control study in Uruguay. *Br J Cancer*, 80(3-4):591–7. doi:10.1038/sj.bjc.6690396 PMID:10408871

Deneo-Pellegrini H, Ronco AL, De Stefani E, Boffetta P, Correa P, Mendilaharsu M et al. (2012). Food groups and risk of prostate cancer: a case-control study in Uruguay. *Cancer Causes Control*, 23(7):1031–8. doi:10.1007/s10552-012-9968-z PMID:22544454

Di Maso M, Talamini R, Bosetti C, Montella M, Zucchetto A, Libra M et al. (2013). Red meat and cancer risk in a network of case-control studies focusing on cooking practices. *Ann Oncol*, 24(12):3107–12. doi:10.1093/annonc/mdt392 PMID:24121119

Gann PH, Hennekens CH, Sacks FM, Grodstein F, Giovannucci EL, Stampfer MJ (1994). Prospective study of plasma fatty acids and risk of prostate cancer. *J Natl Cancer Inst*, 86(4):281–6. doi:10.1093/jnci/86.4.281 PMID:8158682

Giovannucci E, Rimm EB, Colditz GA, Stampfer MJ, Ascherio A, Chute CG et al. (1993). A prospective study of dietary fat and risk of prostate cancer. *J Natl Cancer Inst*, 85(19):1571–9. doi:10.1093/jnci/85.19.1571 PMID:8105097

John EM, Stern MC, Sinha R, Koo J (2011). Meat consumption, cooking practices, meat mutagens, and risk of prostate cancer. *Nutr Cancer*, 63(4):525–37. doi:10.1080/01635581.2011.539311 PMID:21526454

Joshi AD, Corral R, Catsburg C, Lewinger JP, Koo J, John EM et al. (2012). Red meat and poultry, cooking practices, genetic susceptibility and risk of prostate cancer: results from a multiethnic case-control study. *Carcinogenesis*, 33(11):2108–18. doi:10.1093/carcin/bgs242 PMID:22822096

Koutros S, Cross AJ, Sandler DP, Hoppin JA, Ma X, Zheng T et al. (2008). Meat and meat mutagens and risk of prostate cancer in the Agricultural Health Study. *Cancer Epidemiol Biomarkers Prev*, 17(1):80–7. doi:10.1158/1055-9965.EPI-07-0392 PMID:18199713

Kristal AR, Arnold KB, Neuhouser ML, Goodman P, Platz EA, Albanes D et al. (2010). Diet, supplement use, and prostate cancer risk: results from the prostate cancer prevention trial. *Am J Epidemiol*, 172(5):566–77. doi:10.1093/aje/kwq148 PMID:20693267

Kurahashi N, Inoue M, Iwasaki M, Sasazuki S, Tsugane AS; Japan Public Health Center-Based Prospective Study Group (2008). Dairy product, saturated fatty acid, and calcium intake and prostate cancer in a prospective cohort of Japanese men. *Cancer Epidemiol Biomarkers Prev*, 17(4):930–7. doi:10.1158/1055-9965.EPI-07-2681 PMID:18398033

Larsson SC, Akesson A, Wolk A (2009). Dietary acrylamide intake and prostate cancer risk in a prospective cohort of Swedish men. *Cancer Epidemiol Biomarkers Prev*, 18(6):1939–41. doi:10.1158/1055-9965.EPI-09-0280 PMID:19505926

Li ML, Lin J, Hou JG, Xu L, Cui XG, Xu XX et al. (2014). Environmental and psycho-social factors related to prostate cancer risk in the Chinese population: a case-control study. *Biomed Environ Sci*, 27(9):707–17. PMID:25256860

Loh YH, Mitrou PN, Bowman R, Wood A, Jeffery H, Luben RN et al. (2010). MGMT Ile143Val polymorphism, dietary factors and the risk of breast, colorectal and prostate cancer in the European Prospective Investigation into Cancer and Nutrition (EPIC)-Norfolk study. *DNA Repair (Amst)*, 9(4):421–8. doi:10.1016/j.dnarep.2010.01.002 PMID:20096652

Mahmood S, Qasmi G, Ahmed A, Kokab F, Zahid MF, Afridi MI et al. (2012). Lifestyle factors associated with the risk of prostate cancer among Pakistani men. *J Ayub Med Coll Abbottabad*, 24(2):111–5. PMID:24397069

Major JM, Cross AJ, Watters JL, Hollenbeck AR, Graubard BI, Sinha R (2011). Patterns of meat intake and risk of prostate cancer among African-Americans in a large prospective study. *Cancer Causes Control*, 22(12):1691–8. doi:10.1007/s10552-011-9845-1 PMID:21971816

Michaud DS, Augustsson K, Rimm EB, Stampfer MJ, Willet WC, Giovannucci E (2001). A prospective study on intake of animal products and risk of prostate cancer. *Cancer Causes Control*, 12(6):557–67. doi:10.1023/A:1011256201044 PMID:11519764

Muller DC, Severi G, Baglietto L, Krishnan K, English DR, Hopper JL et al. (2009). Dietary patterns and prostate cancer risk. *Cancer Epidemiol Biomarkers Prev*, 18(11):3126–9. doi:10.1158/1055-9965.EPI-09-0780 PMID:19861522

Neuhouser ML, Barnett MJ, Kristal AR, Ambrosone CB, King I, Thornquist M et al. (2007). (n-6) PUFA increase and dairy foods decrease prostate cancer risk in heavy smokers. *J Nutr*, 137(7):1821–7. doi:10.1093/jn/137.7.1821 PMID:17585037

Norrish AE, Ferguson LR, Knize MG, Felton JS, Sharpe SJ, Jackson RT (1999). Heterocyclic amine content of cooked meat and risk of prostate cancer. *J Natl Cancer Inst*, 91(23):2038–44. doi:10.1093/jnci/91.23.2038 PMID:10580030

Nowell S, Ratnasinghe DL, Ambrosone CB, Williams S, Teague-Ross T, Trimble L et al. (2004). Association of SULT1A1 phenotype and genotype with prostate cancer risk in African-Americans and Caucasians. *Cancer Epidemiol Biomarkers Prev*, 13(2):270–6. doi:10.1158/1055-9965.EPI-03-0047 PMID:14973106

Park SY, Murphy SP, Wilkens LR, Henderson BE, Kolonel LN (2007). Fat and meat intake and prostate cancer risk: the multiethnic cohort study. *Int J Cancer*, 121(6):1339–45. doi:10.1002/ijc.22805 PMID:17487838

Phillips RL, Snowdon DA (1983). Association of meat and coffee use with cancers of the large bowel, breast, and prostate among Seventh-Day Adventists: preliminary results. *Cancer Res*, 43(5):Suppl: 2403s–8s. PMID:6831464

Punnen S, Hardin J, Cheng I, Klein EA, Witte JS (2011). Impact of meat consumption, preparation, and mutagens on aggressive prostate cancer. *PLoS One*, 6(11):e27711. doi:10.1371/journal.pone.0027711 PMID:22132129

Richman EL, Kenfield SA, Stampfer MJ, Giovannucci EL, Chan JM (2011). Egg, red meat, and poultry intake and risk of lethal prostate cancer in the prostate-specific antigen-era: incidence and survival. *Cancer Prev Res (Phila)*, 4(12):2110–21. doi:10.1158/1940-6207.CAPR-11-0354 PMID:21930800

Rodrigues IS, Kuasne H, Losi-Guembarovski R, Fuganti PE, Gregório EP, Kishima MO et al. (2011). Evaluation of the influence of polymorphic variants CYP1A1 2B, CYP1B1 2, CYP3A4 1B, GSTM1 0, and GSTT1 0 in prostate cancer. *Urol Oncol*, 29(6):654–63. doi:10.1016/j.urolonc.2010.01.009 PMID:20884258

Rodriguez C, McCullough ML, Mondul AM, Jacobs EJ, Chao A, Patel AV et al. (2006). Meat consumption among Black and White men and risk of prostate cancer in the Cancer Prevention Study II Nutrition Cohort. *Cancer Epidemiol Biomarkers Prev*, 15(2):211–6. doi:10.1158/1055-9965.EPI-05-0614 PMID:16492907

Rohrmann S, Platz EA, Kavanaugh CJ, Thuita L, Hoffman SC, Helzlsouer KJ (2007). Meat and dairy consumption and subsequent risk of prostate cancer in a US cohort study. *Cancer Causes Control*, 18(1):41–50. doi:10.1007/s10552-006-0082-y PMID:17315319

Román MD, Niclis C, Tumas N, Díaz MP, Osella AR, Muñoz SE (2014). Tobacco smoking patterns and differential food effects on prostate and breast cancers among smokers and nonsmokers in Córdoba, Argentina. *Eur J Cancer Prev*, 23(4):310–8. doi:10.1097/CEJ.0000000000000044 PMID:24871563

Rosato V, Edefonti V, Bravi F, Bosetti C, Bertuccio P, Talamini R et al. (2014). Nutrient-based dietary patterns and prostate cancer risk: a case-control study from Italy. *Cancer Causes Control*, 25(4):525–32. doi:10.1007/s10552-014-0356-8 PMID:24515125

Salem S, Salahi M, Mohseni M, Ahmadi H, Mehrsai A, Jahani Y et al. (2011). Major dietary factors and prostate cancer risk: a prospective multicenter case-control study. *Nutr Cancer*, 63(1):21–7. PMID:21161822

Sander A, Linseisen J, Rohrmann S (2011). Intake of heterocyclic aromatic amines and the risk of prostate cancer in the EPIC-Heidelberg cohort. *Cancer Causes Control*, 22(1):109–14. doi:10.1007/s10552-010-9680-9 PMID:21103922

Schuurman AG, van den Brandt PA, Dorant E, Goldbohm RA (1999). Animal products, calcium and protein and prostate cancer risk in The Netherlands Cohort Study. *Br J Cancer*, 80(7):1107–13. doi:10.1038/sj.bjc.6690472 PMID:10362125

Sinha R, Park Y, Graubard BI, Leitzmann MF, Hollenbeck A, Schatzkin A et al. (2009). Meat and meat-related compounds and risk of prostate cancer in a large prospective cohort study in the United States. *Am J Epidemiol*, 170(9):1165–77. doi:10.1093/aje/kwp280 PMID:19808637

Slattery ML, Schumacher MC, West DW, Robison LM, French TK (1990). Food-consumption trends between adolescent and adult years and subsequent risk of prostate cancer. *Am J Clin Nutr*, 52(4):752–7. doi:10.1093/ajcn/52.4.752 PMID:2403069

Snowdon DA, Phillips RL, Choi W (1984). Diet, obesity, and risk of fatal prostate cancer. *Am J Epidemiol*, 120(2):244–50. doi:10.1093/oxfordjournals.aje.a113886 PMID:6465122

Sonoda T, Nagata Y, Mori M, Miyanaga N, Takashima N, Okumura K et al. (2004). A case-control study of diet and prostate cancer in Japan: possible

protective effect of traditional Japanese diet. *Cancer Sci*, 95(3):238–42. doi:10.1111/j.1349-7006.2004.tb02209.x PMID:15016323

Subahir MN, Shah SA, Zainuddin ZM (2009). Risk factors for prostate cancer in Universiti Kebangsaan Malaysia Medical Centre: a case-control study. *Asian Pac J Cancer Prev*, 10(6):1015–20. PMID:20192575

Sung JF, Lin RS, Pu YS, Chen YC, Chang HC, Lai MK (1999). Risk factors for prostate carcinoma in Taiwan: a case-control study in a Chinese population. *Cancer*, 86(3):484–91. doi:10.1002/(SICI)1097-0142(19990801)86:3<484::AID-CNCR17>3.0.CO;2-P PMID:10430257

Ukoli FA, Taher K, Egbagbe E, Lomotey M, Oguike T, Akumabor P et al. (2009). Association of self-reported consumption of cooked meat, fish, seafood and eggs with prostate cancer risk among Nigerians. *Infect Agent Cancer*, 4:Suppl 1: S6. doi:10.1186/1750-9378-4-S1-S6 PMID:19208211

Veierød MB, Laake P, Thelle DS (1997). Dietary fat intake and risk of prostate cancer: a prospective study of 25,708 Norwegian men. *Int J Cancer*, 73(5):634–8. doi:10.1002/(SICI)1097-0215(19971127)73:5<634::AID-IJC4>3.0.CO;2-Y PMID:9398038

Walker M, Aronson KJ, King W, Wilson JW, Fan W, Heaton JP et al. (2005). Dietary patterns and risk of prostate cancer in Ontario, Canada. *Int J Cancer*, 116(4):592–8. doi:10.1002/ijc.21112 PMID:15825170

Wright JL, Neuhouser ML, Lin DW, Kwon EM, Feng Z, Ostrander EA et al. (2011). AMACR polymorphisms, dietary intake of red meat and dairy and prostate cancer risk. *Prostate*, 71(5):498–506. doi:10.1002/pros.21267 PMID:20945498

Wu K, Hu FB, Willett WC, Giovannucci E (2006). Dietary patterns and risk of prostate cancer in U.S. men. *Cancer Epidemiol Biomarkers Prev*, 15(1):167–71. doi:10.1158/1055-9965.EPI-05-0100 PMID:16434606

Wu K, Spiegelman D, Hou T, Albanes D, Allen NE, Berndt SI et al. (2016). Associations between unprocessed red and processed meat, poultry, seafood and egg intake and the risk of prostate cancer: A pooled analysis of 15 prospective cohort studies. *Int J Cancer*, 138(10):2368–82. doi:10.1002/ijc.29973 PMID:26685908