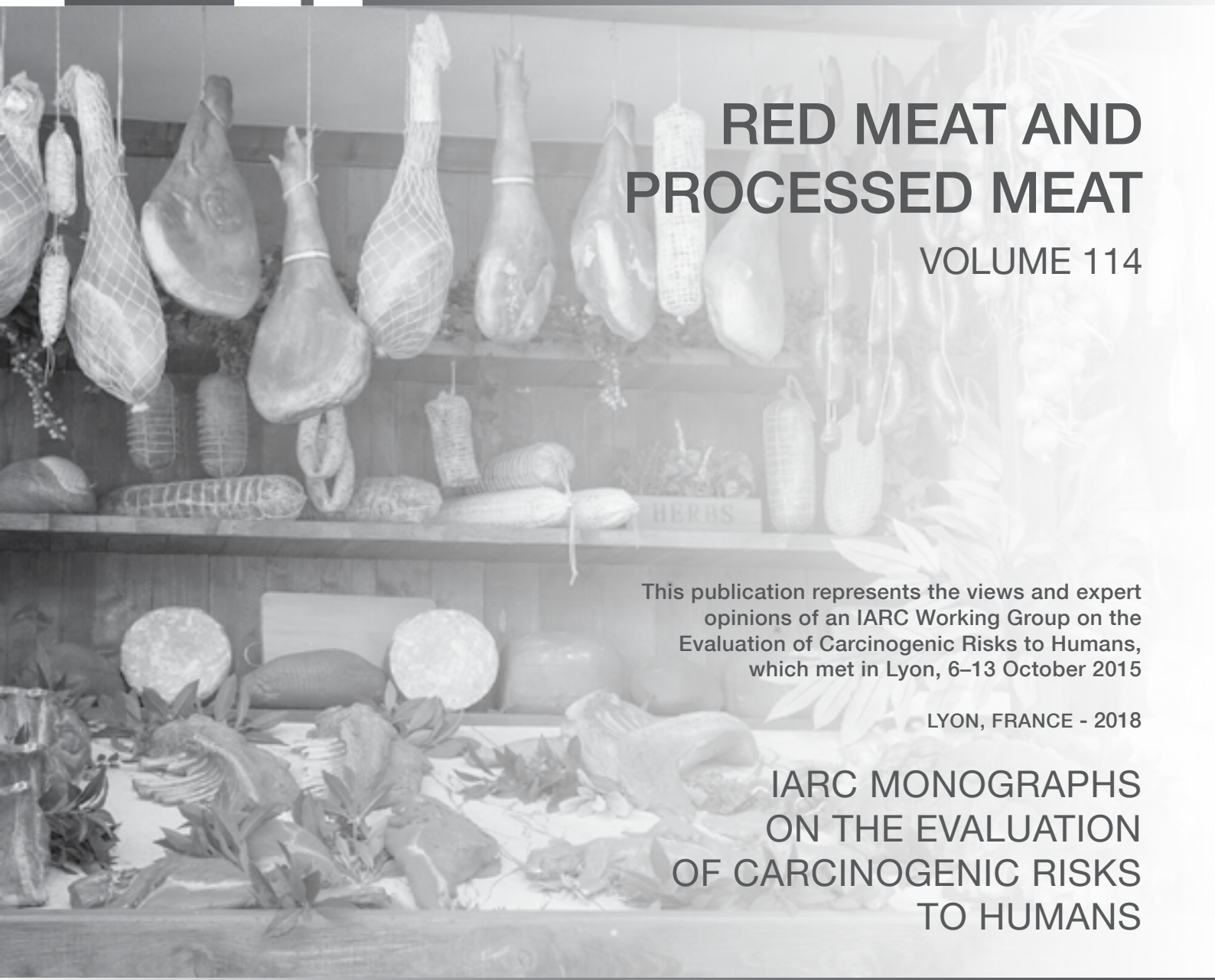
IARC MONOGRAPHS



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

2.4 Cancer of the pancreas

2.4.1 Cohort studies

Cohort studies on cancer of the pancreas have been conducted in North America, Europe, and Asia. Considering the high mortality rate for cancer of the pancreas, both studies of incidence and mortality were included in the review. Studies investigating the association between consumption of red meat or specific red meats, such as beef, pork, or other meats, are reviewed first, followed by studies on consumption of processed meat or specific processed meat items, such as ham or bacon. Findings for red meat and processed meat combined are presented only when a study did not present data for either type of meat separately.

For studies reporting on more than one type of meat, the descriptive details are given in the section the first time the study is cited, while only the key results are provided for subsequent citations. The Working Group's comments, if any, on the study's strengths and limitations are also presented only the first time a study is cited, unless different issues were noted in each analysis. Studies that did not adjust for important potential confounders for pancreatic cancer, including age, smoking, BMI, and energy intake, are noted.

After reviewing all of the available studies, the Working Group excluded the following groups of publications from further consideration: studies reporting fewer than 100 cases (e.g. Zheng et al., 1993), due to their limited statistical power; studies reporting risk estimates that were not specific for red meat intake (e.g. Yun et al., 2008; Berjia et al., 2014; Hirayama, 1990); and reports on study populations that were included in or updated by subsequent reports (e.g. Khan et al., 2004; Cross et al., 2007; Iso et al., 2007).

(a) Red meat

See Table 2.4.1

In the Alpha-Tocopherol, Beta-Carotene Cancer Prevention (ATBC) Study cohort in Finland (Stolzenberg-Solomon et al., 2002), 27 111 male smokers aged 50–69 years were followed from 1985 to 1997, and 163 developed pancreatic cancer. The median value of red meat intake was 128.7 g/day for non-cases. The adjusted hazard ratio for the highest quintile versus the lowest quintile of consumption was 0.95 (95% CI, 0.58–1.56; P_{trend} = 0.71). Beef and pork also did not show any association. [The Working Group noted that the definition of red meat was not reported. Subjects were male smokers with largely atypical diets, so generalizability of the results was limited.]

In the Nurses' Health Study (NHS), 178 pancreatic cancer cases were observed over 18 years of follow-up in 88 802 women (Michaud et al., 2003). Diet was assessed by questionnaire four times during follow-up. The definition of red meat included processed meat, so those results are not reported here. For the highest versus the lowest quintile of consumption of beef, pork, or lamb as a main dish, the multivariate hazard ratio was 0.75 (95% CI, 0.41–1.40). Updating the dietary exposures reportedly produced similar results, but data were not shown. [The Working Group noted that the sample size was small.]

Nöthlings et al. (2005) observed positive associations between red meat, beef, and pork consumption and pancreatic cancer incidence in 190 545 men from the Multiethnic Cohort Study in Hawaii and California, USA. During 7 years of follow-up, 482 incident pancreatic cancers occurred. For the highest compared with the lowest quintiles, after adjusting for important confounders, the multivariate relative risks for intakes of red meat, beef, and pork were 1.45 (95% CI, 1.19–1.76; $P_{trend} < 0.01$), 1.21 (95% CI, 0.99–1.47; P_{trend} = 0.03), and 1.53 (95% CI, 1.25–1.87; $P_{trend} < 0.01$), respectively. [The Working Group noted that the sample size was large, and the cohort included considerable dietary heterogeneity due to the multi-ethnic background. There was no adjustment for BMI.]

In a population-based cohort of 61 433 Swedish women recruited for mammography screening, Larsson et al. (2006) reported a positive association between long-term red meat consumption, measured by two surveys 10 years apart, and pancreatic cancer risk. During follow-up from 1987 to 2004, 172 incident cases of pancreatic cancer were observed. After adjusting for important confounders, the multivariate hazard ratio for the highest versus the lowest number of servings per week of red meat was 1.73 (95% CI, 0.99–2.98). A dose–response relationship was observed (P_{trend} = 0.01). [The Working Group noted that using surveys from two time points enabled the effect of long-term exposure to be seen. The cohort was restricted to women. The sample size was small.]

In the Japan Collaborative Cohort (JACC) Study, Lin et al. (2006) evaluated the relationship between dietary factors, including meat, and risk of pancreatic cancer death; 46 465 men and 64 327 women aged 40–79 years were followed up, and 300 deaths from pancreatic cancer were recognized. After adjustment, the multivariate relative risks for the highest compared with the lowest category of intake of beef were 2.3 (95% CI, 0.83–6.39; P_{trend} = 0.33; 4 observed deaths) for men and 0.98 (95% CI, 0.14–7.11; P_{trend} = 0.74; 1 observed death) for women. The corresponding results for pork were 1.63 (95% CI, 0.62–4.26; P_{trend} = 0.34; 5 observed deaths) for men and 1.71 (95% CI, 0.71–4.09; P_{trend} = 0.35; 6 observed deaths) for women. [The Working Group noted that, while the total number of deaths was not small, the number of observed deaths among the highest category of intake was small. BMI and total energy were not adjusted.]

In a case–cohort analysis of the Netherlands Cohort Study (NLCS), Heinen et al. (2009) observed no association between intake of red meat or individual red meat items and pancreatic cancer risk. The study consisted of 120 852 men and women, and 350 pancreatic cancer cases, identified during 13 years of follow-up. Meat consumption was assessed using a validated FFQ with 150 items. For the highest compared with the lowest quintile, after adjusting for important confounders, the multivariate relative risks for intakes of red meat, beef, pork, and minced meat were 0.75 (95% CI, 0.52–1.09; P_{trend} = 0.23), 1.20 (95% CI, 0.84–1.72; P_{trend} = 0.61), 0.75 (95% CI, 0.52–1.08; P_{trend} = 0.27), and 0.78 (95% CI, 0.54–1.10; P_{trend} = 0.16), respectively. The corresponding value for intake of liver, categorized into two groups, was 1.05 (95% CI, 0.83–1.33). [The Working Group noted that red meat was clearly defined as not including processed meat. BMI was not adjusted.]

In the Iowa Women's Health Study (IWHS), Inoue-Choi et al. (2011) assessed multiple aspects of dietary intake among 34 642 postmenopausal women. A total of 256 pancreatic cancer cases during the period from 1986 to 2007 were included in the analysis. No statistically significant associations were observed between intake of red meat and pancreatic cancer (HR, 0.97; 95% CI, 0.65–1.44; for the highest vs lowest consumption category; P_{trend} = 0.79). [The Working Group noted that the definition of red meat was not reported. The follow-up was nearly complete. BMI and energy were not adjusted.]

Among the 62 581 subjects randomized to screening in the Prostate, Lung, Colorectal and Ovarian (PLCO) Cancer Screening Trial in the USA (Anderson et al., 2012), 248 cases of exocrine pancreatic cancer were identified during follow-up from 1993 to 2007. The multivariate hazard ratios for the highest versus the lowest quintile of intake of red meat by doneness preference were 0.84 (95% CI, 0.55–1.29; P_{trend} = 0.36) for rare to medium well done and 1.60 (95% CI, 1.01–2.54; P_{trend} = 0.04) for well to very well done. When quintiles 1–4 were combined, the corresponding values for the highest quintile of "red barbecued meat" [definition not reported] were 0.79 (95% CI, 0.55–1.13; 39 exposed cases) for rare to medium well done and 1.35 (95% CI, 1.00–1.83; 56 exposed cases) for well to very well

done. Pancreatic cancer was significantly associated with consumption of fried (HR, 1.74; 95% CI, 1.05–2.90) and grilled or barbecued pork chops (HR, 1.80; 95% CI, 1.04–3.13), but not with any other cooking method or preference of doneness for pork chops, hamburger, or steak. [The Working Group noted that BMI was not adjusted. The definitions of red meat and barbecued meat were not reported.]

Rohrmann et al. (2013) examined the association between meat consumption and risk of pancreatic cancer in the European Prospective Investigation into Cancer and Nutrition (EPIC) study. A total of 477 202 EPIC participants from 10 European countries recruited between 1992 and 2000 were included in the analysis. Eight hundred and sixty-five non-endocrine pancreatic cancer cases were observed during follow-up to 2008. After adjusting for important confounders, no significant association between consumption of red meat and pancreatic cancer was observed; the multivariate relative risk for the fourth compared with the first quantile of intake was 1.07 (95% CI, 0.83–1.38). [The Working Group took note of the large international study encompassing diverse diets.]

(b) Processed meat

See Table 2.4.2 (web only; available at: http://publications.iarc.fr/564)

In the ATBC Study cohort (Stolzenberg-Solomon et al., 2002), the median value of processed meat intake was 61.2 g/day. After adjusting for important confounders, no association was observed for processed meat (highest vs lowest quintile multivariate HR,1.04; 95% CI, 0.66–1.65).

In the NHS, the adjusted hazard ratio for the highest versus the lowest quintile of processed meat consumption was 1.28 (95% CI, 0.86–1.92; $P_{trend} = 0.10$) (Michaud et al., 2003) Analyses using dietary exposures updated during follow-up produced similar results. [The Working Group noted that repeated surveys enabled changes in diet to be considered, and exposure updates did not alter the results. BMI was not adjusted.]

Nöthlings et al. (2005) observed a positive association between processed meat consumption and pancreatic cancer incidence in the Multiethnic Cohort Study. For the highest compared with the lowest quintile, after adjusting for important confounders, the multivariate relative risk for intake of processed meat was 1.68 (95% CI, 1.35–2.07; $P_{trend} < 0.01$).

In a population-based cohort of 61 433 Swedish women, Larsson et al. (2006) found no association between pancreatic cancer risk and processed meat consumption at baseline or in the long term, measured using two surveys 10 years apart. For long-term processed meat consumption, the multivariate hazard ratio for the highest versus the lowest number of servings per week was 0.94 (95% CI, 0.61–1.44; $P_{trend} = 0.70$). Results for baseline consumption were similar. [The Working Group noted that using surveys from two time points enabled the effect of long-term exposure to be seen. The cohort was restricted to women.]

In the JACC Study (Lin et al., 2006), for the highest compared with the lowest category, the multivariate relative risks for intakes of ham and sausage were 1.82 (95% CI, 0.62–4.26; $P_{trend} = 0.34$; 7 observed deaths) for men and 0.93 (95% CI, 0.29–2.99; $P_{trend} = 0.63$; 3 observed deaths) for women.

In the NLCS (Heinen et al., 2009), for the highest compared with the lowest category of processed meat intake, the multivariate relative risk was 0.93 (95% CI, 0.65–1.35; $P_{trend} = 0.97$; 70 exposed cases). [A detailed validated FFQ with 150 items was used.] Among subjects randomized to screening in the PLCO trial in the USA (Anderson et al., 2012), the multivariate hazard ratio for the highest versus the lowest tertile of bacon/sausage consumption by doneness preference was 0.99 (95% CI, 0.73–1.35) for crisp or charred compared with cooked to a lesser degree of doneness. [The Working Group noted that

BMI was not adjusted. Information on cooking method preferences was available.]

In the EPIC study, Rohrmann et al. (2013) did not find a significant relation between consumption of processed meat and pancreatic cancer (multivariate RR per 50 g/day increase, 0.93; 95% CI, 0.71–1.23).

During follow-up of the NIH-AARP cohort, until 2006, where 2193 pancreatic cancer cases were identified, Jiao et al. (2015) investigated the joint associations between pancreatic cancer and processed meat consumption and intake of advanced glycation end products (AGEPs). The multivariate hazard ratio for the highest compared with the lowest quintile of processed meat consumption was 1.03 (95% CI, 0.92–1.37; P_{trend} = 0.28). Further adjustment for AGEPs did not alter the results.

(c) Red meat and processed meat combined

Coughlin et al. (2000), in a cohort of 483 109 men and 619 199 women from the Cancer Prevention Study (CPS) II (CPS-II), confirmed 3751 pancreatic cancer deaths during follow-up from 1982 to 1996. The red meat variable used in the analysis included processed meat items. The multivariate-adjusted hazard ratios for the highest versus the lowest quintile for this variable were 1.1 (95% CI, 0.9–1.2) in men and 0.9 (95% CI, 0.8–1.0) in women. [The Working Group noted that this was a large study with a low percentage of men and women lost to follow-up. Red meat and processed meat were combined.]

Based on a follow-up of the NIH-AARP study cohort from 1995 to 2000 with 836 cases, Stolzenberg-Solomon et al. (2007) reported a statistically significant association between pancreatic cancer risk and red meat consumption for men (adjusted HR, 1.42; 95% CI, 1.05–1.91; highest vs lowest category of consumption), but not for women (HR, 0.69 ; 95% CI, 0.83–1.35) or for both sexes combined (HR, 1.06; 95% CI, 0.83–1.35). [The Working Group noted that the red meat variable included processed items.]

Jiao et al. (2015) investigated the risk of pancreatic cancer associated with red meat consumption and intake of AGEPs in the same cohort. For the highest compared with the lowest quintile of intake among men, the multivariate hazard ratios for red meat and red meat cooked at a high temperature were 1.35 (95% CI, 1.07–1.70; P_{trend} = 0.05) and 1.18 (95% CI, 0.89–1.56; P_{trend} = 0.01), respectively. The hazard ratios were attenuated and no longer significant after further adjustment for AGEPs. Data on the association between meat consumption and pancreatic cancer risk were not reported for women. [The Working Group noted that this was a large study, but the definition of red meat may have included processed meat items, as per the report based on follow-up through 2000.]

2.4.2 Case–control studies

Case–control studies on cancer of the pancreas have been conducted in North America, Europe, and Asia. Considering the high mortality rate for cancer of the pancreas, both studies of incidence and mortality data were included in the review. The studies were considered based on the quality of reporting of the type of meat, study design issues (e.g. population- vs hospital-based design), sample size, and exposure assessment, including validation of dietary questionnaires and inclusion of relevant confounders. Studies that did not adjust for important potential confounders (see Section 2.4.1) are noted.

As for cohort studies, case–control studies that investigated the association with consumption of total red meat or specific red meats are presented first, followed by studies that investigated the association with consumption of processed meat. Study details and Working Group comments are provided only the first time a study is cited, unless important differences were noted.

After reviewing all of the available studies, studies with fewer than 100 cases (e.g. Kadlubar

et al., 2009; Luckett et al., 2012), papers reporting only dietary patterns (e.g. Bosetti et al., 2013; Chan et al., 2013) or preserved processed items including eggs (e.g. Ji et al., 1995), and overlapping studies of the same population (e.g. Hu et al., 2011) were excluded from further consideration. Studies that did not report pertinent odds ratios (e.g. Li et al., 2007) were excluded when only crude odds ratios could be calculated from the data presented.

(a) Red meat

See Table 2.4.3

Lyon et al. (1993) reported the results of a population-based case–control study of cancer of the exocrine pancreas conducted from 1984 to 1987 in Utah, USA; 149 cases of pancreatic cancer were identified from the Utah Cancer Registry, and 363 controls were identified by random digit dialling or health insurance records of those older than 65 years. Dietary intake data were collected from a 32-item FFQ administered to proxy respondents for cases and controls. Red meat was defined as beef and pork. The multivariate odds ratios for the highest versus the lowest level of red meat consumption were 1.41 (95% CI, 0.72–2.75; P_{trend} = 0.30) in men and 1.44 (95% CI, 0.65–3.20; P_{trend} = 0.45) in women. [The Working Group noted that the study was small, and BMI and energy were not adjusted.]

Ji et al. (1995) reported findings for red meat consumption in a population-based case–control study conducted from 1990 to 1993 in Shanghai, China. Pancreatic cancer cases (n = 451) were identified by a rapid reporting system. Controls (n = 1552) were selected Shanghai residents, frequency-matched to cases by sex and age. Interviews with next of kin were conducted for 38% of cases and 10% of controls. Usual meat intake over the previous 5 years was ascertained from an 86-item questionnaire. The multivariate odds ratios for the highest versus the lowest quartile of red meat consumption were 0.73 (95% CI, 0.47–1.12; P_{trend} = 0.24) in men and 1.24 (95% CI, 0.73–2.13; P_{trend} = 0.86) in women. [The Working Group noted that processed meat was not included. This study was large, but a substantial number of case and control interviews were performed with next of kin. BMI and energy were not adjusted. No validation data for FFQ were reported.]

In a population-based case–control study, conducted from 1995 to 1999 in California, USA, Chan et al. (2007), reported the results of red meat consumption. Dietary intake of red meat was collected from a validated, 131-item SQFFQ. Cases were 532 pancreatic cancer patients from the Northern California Cancer Center. Controls were 1701 area residents identified by random digit dialling, and frequency-matched to cases by sex and age. Compared with a frequency of < 1 time/month, the multivariate odds ratios for ≥ 2 times/week frequency of beef or lamb intake as a main dish and pork intake as a main dish were 2.2 (95% CI, 1.0–4.5; 14 exposed cases) and 0.6 (95% CI, 0.3–1.1; P_{trend} = 0.2; 11 exposed cases), respectively. Results for total red meats, including processed red meats, were also reported. [The Working Group noted that the study design was sound.]

Hu et al. (2008) reported the results of a population-based case–control study of pancreatic cancer conducted from 1994 to 1997 in eight Canadian provinces. Dietary intake of red meat was collected from a mailed, validated questionnaire with 69 items. Cases were 628 individuals identified from provincial cancer registries. Controls were 5039 individuals selected from a random sample within the provinces. The multivariate odds ratio for the highest versus the lowest quartile of frequency of red meat consumption was 1.1 (95% CI, 0.9–1.5; P_{trend} = 0.31). [The Working Group noted that the sample size was large, and a validated FFQ was used.]

In a population-based case–control study, Anderson et al. (2009) reported the results of red meat consumption from 2003 to 2007 in Canada. Dietary intake of red meat was collected

from a mailed FFQ. Cases were 422 pancreatic cancer patients identified by the Ontario Cancer Registry. Controls were 312 subjects recruited through random digit dialling. The age-adjusted odds ratio for > 3 servings/week versus ≤ 1 serving/week of red meat consumption was 1.49 (95% CI, 0.98–2.28). Adjusting for other factors, such as smoking and education, did not alter the results. [The Working Group noted that the exact definition of red meat was not reported. This study was large, but the questionnaire was not validated. BMI and energy were not adjusted.]

Tavani et al. (2000), using data from a hospital-based case–control study of several cancers in northern Italy in 1983–1996, reported results for red meat consumption and pancreatic cancer. Cases were 362 hospital patients younger than 75 years with confirmed pancreatic cancer. Controls were 7990 patients younger than 75 years admitted to the same network of hospitals as the cancer cases for acute non-cancer conditions. Dietary intake of red meat over the previous 2 years was collected by FFQ, which defined red meat as beef, veal, or pork, excluding processed items. The multivariate odds ratio for the highest (≥ 7 times/week) versus the lowest (≤ 3 times/week) level of red meat consumption was 1.6 (95% CI, 1.2–2.1). [The participation of cases and controls was similar and almost complete. The questionnaire was not tested for validity, but reproducibility was reported to be satisfactory. BMI and energy were not adjusted.] Similar findings were reported in an earlier paper based on the same study (Soler et al., 1998), which also provided data for liver consumption (OR, 1.43; 95% CI, 1.01–1.99). [The Working Group noted that the study population appeared to overlap with those studied by Soler et al. (1998), Tavani et al. (2000), Polesel et al. (2010), and Di Maso et al. (2013).]

Polesel et al. (2010) reported the results of a hospital-based case–control study of pancreatic cancer conducted from 1991 to 2008 in northern Italy. [The study population appeared to overlap with that studied by Tavani et al. (2000).] Cases were 326 men and women with incident pancreatic cancer. Controls were 652 hospital patients admitted for acute conditions. Dietary intake of red meat was collected from a validated questionnaire with 78 items. Cooking methods were assessed for all meats combined. After adjusting for important potential confounders, the multivariate odds ratio for the highest versus the lowest quintile of red meat consumption was 1.99 (95% CI, 1.18–3.36). Data were also reported for pork and processed meat combined (multivariate OR, 1.25; 95% CI, 0.85–1.84; $P_{trend} = 0.27$). [The definition of red meat was not reported. and data were not reported for pork and processed meat separately. The Working Group judged the data on cooking methods to be uninformative, as they were reported only for all meats combined. The response rate was high for both cases and controls.]

Di Maso et al. (2013) also reported results of a hospital-based case–control study that partially overlapped with that of Tavani et al. (2000). Red meat was defined as including beef, veal, pork, horse meat, and meat sauces. The multivariate odds ratio for pancreatic cancer was 1.51 (95% CI, 1.25–1.82) per 50 g/day increment. Associations with red meat cooked in different ways were also examined, with no significant heterogeneity identified between meats cooked by roasting/grilling, boiling/stewing, and frying/pan-frying. [The Working Group noted that the results of later, overlapping studies were similar to those reported by Tavani et al. (2000), and the Tavani et al. study had a large number of cases and controls, and the definition of red meat was clearly described and did not include processed meat.]

(b) Processed meat

See Table 2.4.4 (web only; available at: http://publications.iarc.fr/564)

Lyon et al. (1993), in a population-based case–control study of cancer of the exocrine pancreas

in Utah, USA (previously described in Section 2.4.2(a)), assessed dietary intake of nitrated meats (bacon, sausages, and hot dogs) with a standardized questionnaire. The multivariate odds ratios for the highest versus the lowest level of nitrated meat consumption were 2.77 (95% CI, 1.34–5.72; $P_{trend} < 0.001$) in men and 1.08 (95% CI, 0.48–2.42; $P_{trend} = 0.15$) in women.

In a population-based case–control study in Japan from 1987 to 1992, Ohba et al. (1996) reported on the association with ham and sausage consumption. Cases were 141 pancreatic cancer patients identified from hospitals. Controls were 282 subjects randomly selected from telephone books. Dietary data were collected from an FFQ, which was administered in person to cases and by mail to controls. Only the univariate odds ratio was reported for consumption of ham/sausage > 3 times/week (OR, 0.89; 95% CI, 0.44–1.77). [The Working Group noted that this study had several limitations: sample size was small, data collection methods were different for cases and controls; questionnaire was not validated, and only univariate analysis was conducted for processed meats.]

In a population-based case–control study in California, USA (Chan et al., 2007) (as previously described in Section 2.4.2(a)), the multivariate odds ratios for intake ≥ 2 times/week versus < 1 time/month of sausage, kielbasa, salami, bologna, other processed meat sandwiches, beef or pork hot dogs were 1.8 (95% CI, 1.3–2.6) and 1.9 (95% CI, 1.3–3.0), respectively. For intake of bacon ≥ 4 times/week, the odds ratio was 1.9 (95% CI, 1.0–3.5), and for intake of beef or pork hot dogs ≥ 1 time/week, the odds ratio was 1.1 (95% CI, 0.8–1.4; $P_{trend} = 0.9$).

In a population-based case–control study of pancreatic cancer in eight Canadian provinces [previously described in Section 2.4.2(a)], Hu et al. (2008) reported that the multivariate odds ratio for the highest versus the lowest level of processed meat consumption was 1.4 (95% CI, 1.0–1.9; $P_{trend} = 0.01$).

In a hospital-based case–control study, Mizuno et al. (1992) reported the results of ham/sausage consumption and pancreatic cancer incidence from 1989 to 1990 in seven cooperating hospitals in Japan. Cases were 124 pancreatic cancer patients identified in seven cooperating hospitals in Japan. Controls were 124 sex- and age-matched patients with non-cancer conditions. Information was collected by questionnaire, but details were not reported. The sex- and age-adjusted odds ratio for consuming ham/sausage ≥ 3 times/week was 1.05 (95% CI, 0.54–2.04). [The Working Group noted that this study was small. Details of dietary assessment were not reported, and only age and sex were adjusted.]

A hospital-based case–control study in northern Italy by Soler et al. (1998), partially overlapping with studies by Tavani et al. (2000), Polesel et al. (2010), and Di Maso et al. (2013), reported a multivariate odds ratio for the highest versus the lowest frequency of ham and sausage consumption of 1.64 (95% CI, 1.24–2.18). [The Working Group took note of the high participation of cases and controls. BMI and energy were not adjusted.]

(c) Red meat and processed meat combined

Anderson et al. (2002) reported the results of a population-based case–control study of pancreatic cancer conducted from 1994 to 1998 in the upper Midwestern USA. Cases were 193 (approximately 30% participation rate) patients recruited from hospitals. Controls were 674 (59% response rate) subjects selected from drivers' licence lists or USA Health Care Financing Administration records. Dietary intake of red meat was collected from in-person interviews using an FFQ. After adjusting for potential confounders, the multivariate odds ratios for the highest versus the lowest quintile of consumption for red and processed meat combined were 2.2 (95% CI, 1.4–3.4) for grilled or barbecued meats, 1.4 (95% CI, 0.7–2.6) for fried meats, and 0.7 (95% CI, 0.4–1.2) for

broiled meats. [The Working Group noted that red meat and processed meat were combined. Detailed information on the cooking methods was available. This study had limited power, and BMI and energy were not adjusted.]

2.4.3 Meta-analyses

Associations between pancreatic cancer and consumption of red meat and processed meat were estimated in two meta-analyses published in 2012: Larsson & Wolk (2012), focused on prospective studies, and Paluszkiewicz et al. (2012), considered both cohort and case–control studies.

Larsson & Wolk (2012), in a meta-analysis based on 11 prospective studies with 6643 cases identified through PubMed and Embase searches through November 2011, reported on red and processed meat consumption. An increase in red meat consumption of 120 g/day was associated with a meta-relative risk of 1.13 (95% CI, 0.93–1.39; $P_{\text{heterogeneity}} < 0.001$; 11 studies). For processed meat, the relative risk for a 50 g/day increase in consumption was 1.19 (95% CI, 1.04–1.36; $P_{\text{heterogeneity}} = 0.46$; 7 studies). [The Working Group noted that there were no studies missing. Studies considering specific items of red or processed meat were also included. No evidence of publication bias was found.]

Paluszkiewicz et al. (2012) included cohort studies and case–control studies identified through MEDLINE, PubMed, Cochrane Library, Embase, CANCERLIT, Scopus, and Google Scholar through 2010. Six cohort studies and four case–control studies provided data for red meat. For the highest versus the lowest category of red meat intake, a statistically significant increased risk was observed for case–control studies (OR, 1.48; 95% CI, 1.25–1.76; $P_{\text{heterogeneity}} = 0.7716$), but not for cohort studies (RR, 1.14; 95% CI, 0.94–1.38; $P_{\text{heterogeneity}} = 0.004$). Analyses for processed meat were not reported. [The Working Group noted that several electronic databases were searched for relevant studies. Study quality was assessed, but how quality scores were used in the analysis was not reported. No analyses of sensitivity or publication bias were reported.]

Two large prospective studies were published since these meta-analyses, both showing no association overall between red or processed meat consumption and pancreatic cancer risk (Rohrmann et al., 2013; Jiao et al., 2015). However, results in Jiao et al. (2015) were positive for red meat before adjusting for AGEP consumption.

Table 2.4.1 Cohort studies on consumption of red meat and cancer of the pancreas

Reference, location, enrolment/follow-up period,	Population size, description, exposure assessment method	Organ site	Exposure category or level	Exposed cases/ deaths	Risk estimate (95% CI)	Covariates controlled
Coughlin et al. (2000) USA 1982–1996	483 109 men and 619 199 women; American Cancer Society volunteers Exposure assessment method: questionnaire; four-page, self-administered questionnaire; total red meat included beef, pork, ham, hamburgers, liver, sausages, bacon, and smoked meats	Pancreas	Red meat, quartiles Men: Q1 Q2 Q3 Q4 Red meat, quartiles Women: Q1 Q2 Q3 Q4	 454 425 461 447 421 458 314 345	 1.0 1.1 (0.9–1.2) 1.1 (0.9–1.2) 1.1 (0.9–1.2) 1.0 1.0 (0.9–1.1) 0.9 (0.7–1.0) 0.9 (0.8–1.0)	Age, race, education, family history of pancreatic cancer, history of gallstones, BMI, smoking, alcohol, citrus fruits and juices, vegetables, history of diabetes mellitus
Stolzenberg-Solomon et al. (2002) Finland 1985–1997	27 111; male smokers aged 50–69 yr Exposure assessment method: questionnaire; 200-item dietary history questionnaire	Pancreas	Red meat (g/day) ≤ 93.0 > 93.0 to ≤ 117.3 > 117.3 to ≤ 141.6 > 141.6 to ≤ 175.6 ≥ 175.6 Trend-test *P* value: 0.71 Beef (g/day) ≤ 10.8 > 10.8 to ≤ 17.5 > 17.5 to ≤ 25.1 > 25.1 to ≤ 36.8 ≥ 36.8 Trend-test *P* value: 0.28 Pork (g/day) ≤ 25.2 > 25.2 to ≤ 33.1 > 33.1 to ≤ 41.2 > 41.2 to ≤ 52.5 ≥ 52.5 Trend-test *P* value: 0.96	 NR NR NR NR NR NR NR NR NR NR NR NR NR NR NR	 1.00 0.88 (0.54–1.44) 0.84 (0.51–1.39) 1.28 (0.81–2.01) 0.95 (0.58–1.56) 1.00 1.09 (0.66–1.81) 1.11 (0.67–1.83) 1.19 (0.73–1.96) 1.30 (0.79–2.12) 1.00 1.00 (0.61–1.61) 0.99 (0.61–1.60) 0.94 (0.57–1.53) 1.01 (0.62–1.64)	Age, smoking, total energy

Table 2.4.1 Cohort studies on consumption of red meat and cancer of the pancreas

Reference, location, enrolment/follow-up period,	Population size, description, exposure assessment method	Organ site	Exposure category or level	Exposed cases/ deaths	Risk estimate (95% CI)	Covariates controlled
Michaud et al. (2003) USA 1980–1998	88 802; female registered nurses aged 30–55 yr from the USA Exposure assessment method: questionnaire; validated FFQ, assessed dietary intake in 1980, 1984, 1986, and 1990 using an SQFFQ (61 items in 1980, 131 items other years)	Pancreas	Beef, pork, or lamb as main dish (frequency)			Smoking, BMI, diabetes, total energy intake, physical activity, height, menopausal status
			Baseline consumption: < 3 times/mo	29	1.00	
			1 time/wk	60	0.97 (0.62–1.51)	
			2–4 times/wk	67	0.89 (0.56–1.42)	
			≥ 5 times/wk	22	0.75 (0.41–1.40)	
			Trend-test *P* value: 0.33			
			Beef, pork, or lamb as sandwich or mixed dish (frequency)			
			Baseline consumption: < 3 times/mo	21	1.00	
			1 time/wk	57	1.13 (0.68–1.86)	
			2–4 times/wk	55	0.91 (0.55–1.52)	
			≥ 5 times/week	45	0.95 (0.55–1.62)	
			Trend-test *P* value: 0.60			
Nöthlings et al. (2005) USA 1993–2001	190 545; African American, Latino, Japanese American, native Hawaiian, and Caucasian residents of Hawaii and California, aged 45–75 yr Exposure assessment method: questionnaire; quantitative FFQ	Pancreas	Red meat (quintile median, g/1000 kcal per day)			Sex, time in study, age at cohort entry, ethnicity, history of diabetes mellitus, familial history of pancreatic cancer, smoking status, energy intake
			4.5	86	1.00	
			11.0	95	1.06 (0.87–1.29)	
			16.8	113	1.27 (1.05–1.54)	
			23.4	83	1.03 (0.84–1.26)	
			35.0	105	1.45 (1.19–1.76)	
			Trend-test *P* value: 0.01			
			Beef (quintile median, g/1000 kcal per day)			
			3.1	93	1.00	
			7.7	103	1.01 (0.84–1.22)	
			11.8	103	1.08 (0.89–1.30)	
			16.7	89	1.02 (0.84–1.24)	
			25.9	94	1.21 (0.99–1.47)	
			Trend-test *P* value: 0.03			

Table 2.4.1 Cohort studies on consumption of red meat and cancer of the pancreas

Reference, location, enrolment/follow-up period,	Population size, description, exposure assessment method	Organ site	Exposure category or level	Exposed cases/ deaths	Risk estimate (95% CI)	Covariates controlled
Nöthlings et al. (2005) USA 1993–2001 (cont.)			Pork (quintile median, g/1000 kcal per day)			
			0.4	75	1.00	
			1.8	87	1.14 (0.93–1.40)	
			3.5	95	1.12 (0.91–1.39)	
			5.7	112	1.44 (1.18–1.76)	
			9.7	113	1.53 (1.25–1.87)	
			Trend-test *P* value: 0.01			
Larsson et al. (2006) Sweden 1987–2004	61 433; women born between 1914 and 1948 and residing in Uppsala and Västmanland counties, central Sweden Exposure assessment method: questionnaire; 67- and 96-item FFQ; "red meat" was minced meat (hamburgers, meatballs, meatloaf, etc.); casserole with beef, pork, or veal; and whole beef (steaks, roasts, etc.)	Pancreas	Red meat (servings/wk)			Age, BMI, smoking, alcohol intake, education, total energy intake, folate, processed meat, poultry, eggs
			Baseline consumption: < 1.5	38	1.00	
			1.5 to < 2.5	32	1.15 (0.70–1.89)	
			2.5 to < 4.0	76	1.30 (0.85–2.00)	
			≥ 4.0	26	1.33 (0.77–2.31)	
			Trend-test *P* value: 0.07			
			Red meat (servings/wk)			
			Updated average consumption: < 1.5	31	1.00	
			1.5 to < 2.5	42	1.62 (1.00–2.64)	
			2.5 to < 4.0	70	1.34 (0.85–2.13)	
			≥ 4.0	29	1.73 (0.99–2.98)	
			Trend-test *P* value: 0.01			
Lin et al. (2006) Japan 1988–1999	110 792 (46 465 men, 64 327 women); Japanese residing in 45 areas throughout Japan Exposure assessment method: questionnaire; 33-item FFQ	Pancreas	Beef (frequency)			Age, area, pack-years of smoking
			Men: 0–2 times/mo	65	1.00	
			1–4 times/wk	25	0.60 (0.37–0.99)	
			Almost every day	4	2.30 (0.83–6.39)	
			Trend-test *P* value: 0.33			

Table 2.4.1 Cohort studies on consumption of red meat and cancer of the pancreas

Reference, location, enrolment/follow-up period,	Population size, description, exposure assessment method	Organ site	Exposure category or level	Exposed cases/ deaths	Risk estimate (95% CI)	Covariates controlled
Lin et al. (2006) Japan 1988–1999 (cont.)			Beef (frequency)			
			Women: 0–2 times/mo	61	1.00	
			1–4 times/wk	35	1.10 (0.69–1.74)	
			Almost every day	1	0.98 (0.14–7.11)	
			Trend-test *P* value: 0.74			
			Pork (frequency)			
			Men: 0–2 times/mo	34	1.00	
			1–4 times/wk	67	1.15 (0.74–1.80)	
			Almost every day	5	1.63 (0.62–4.26)	
			Trend-test *P* value: 0.34			
			Pork (frequency)			
			Women: 0–2 times/mo	39	1.00	
			1–4 times/wk	71	1.11 (0.69–1.67)	
			Almost every day	6	1.71 (0.71–4.09)	
			Trend-test *P* value: 0.35			
Stolzenberg-Solomon et al. (2007) USA 1995–2000	537 302; National Institutes of Health – American Association of Retired Persons (NIH-AARP) Diet and Health Study Exposure assessment method: questionnaire	Pancreas	Red meat consumption (highest vs lowest category)			Smoking, energy-adjusted saturated fat
			Men	147	1.42 (1.05–1.91)	
			Women	47	0.69 (0.45–1.05)	

Table 2.4.1 Cohort studies on consumption of red meat and cancer of the pancreas

Reference, location, enrolment/follow-up period,	Population size, description, exposure assessment method	Organ site	Exposure category or level	Exposed cases/ deaths	Risk estimate (95% CI)	Covariates controlled
Heinen et al. (2009) The Netherlands 1986–1999	120 852; men and women aged 55–69 yr at enrolment Exposure assessment method: questionnaire; 150-item FFQ	Pancreas	Red meat, quintiles			Sex, age, energy intake, smoking, alcohol, diabetes, hypertension, vegetable and fruit intake
			Q1	70	1.00	
			Q2	69	0.98 (0.69–1.39)	
			Q3	67	0.93 (0.65–1.34)	
			Q4	84	1.14 (0.80–1.61)	
			Q5	60	0.75 (0.52–1.09)	
			Trend-test *P* value: 0.23			
			Beef, quintiles			
			Q1	65	1.00	
			Q2	75	1.16 (0.81–1.66)	
			Q3	70	0.99 (0.69–1.42)	
			Q4	56	0.81 (0.56–1.18)	
			Q5	84	1.20 (0.84–1.72)	
			Trend-test *P* value: 0.61			
			Pork, quintiles			
			Q1	76	1.00	
			Q2	64	0.85 (0.60–1.22)	
			Q3	70	0.89 (0.63–1.26)	
			Q4	80	1.01 (0.72–1.43)	
			Q5	60	0.75 (0.52–1.08)	
			Trend-test *P* value: 0.27			
			Minced meat, quintiles			
			Q1	75	1.00	
			Q2	65	0.79 (0.56–1.13)	
			Q3	84	1.02 (0.73–1.43)	
			Q4	61	0.75 (0.52–1.07)	
			Q5	65	0.78 (0.54–1.10)	
			Trend-test *P* value: 0.16			
			Liver (g/day)			
			> 0	130	1.05 (0.83–1.33)	

Table 2.4.1 Cohort studies on consumption of red meat and cancer of the pancreas

Reference, location, enrolment/follow-up period,	Population size, description, exposure assessment method	Organ site	Exposure category or level	Exposed cases/ deaths	Risk estimate (95% CI)	Covariates controlled
Inoue-Choi et al. (2011) Iowa, USA 1986–2007	34 642; postmenopausal women aged 55 to 69 yr Exposure assessment method: questionnaire; FFQ	Pancreas	Red meat (mean, servings/wk)			Age, race, education, alcohol intake, smoking, physical activity
			2.0	54	1.00	
			3.5	43	0.85 (0.57–1.28)	
			5.0	52	0.99 (0.67–1.47)	
			7.0	55	1.06 (0.72–1.55)	
			9.0	52	0.97 (0.65–1.44)	
			Trend-test *P* value: 0.79			
Anderson et al. (2012) USA 1993–2007	62,581; women and men aged 55–74 yr Exposure assessment method: FFQ (170 questions)	Pancreas	Red meat, rare to medium well done			Age, sex, education, diabetes, dietary fat intake, cigarette smoking history, race
			Q1	53	1.00	
			Q2	57	1.11 (0.76–1.63)	
			Q3	43	0.81 (0.54–1.21)	
			Q4	50	0.91 (0.61–1.34)	
			Q5	45	0.84 (0.55–1.29)	
			Trend-test *P* value: 0.364			
			Red meat, well to very well done			
			Q1	39	1.00	
			Q2	58	1.52 (1.01–2.29)	
			Q3	47	1.25 (0.81–1.92)	
			Q4	49	1.37 (0.88–2.12)	
			Q5	55	1.60 (1.01–2.54)	
			Trend-test *P* value: 0.039			
			Red barbecued meat, rare to medium well done			
			Q1–Q4	209	1.00	
			Q5	39	0.79 (0.55–1.13)	
			Red barbecued meat, well to very well done			
			Q1–Q4	192	1.00	
			Q5	56	1.35 (1.00–1.83)	
			Pork chops, cooking method			
			Do not eat	19	1.00	
			Baked	67	1.44 (0.86–2.40)	
			Oven-broiled	31	1.78 (1.00–3.17)	
			Pan-fried	86	1.74 (1.05–2.90)	
			Grilled or barbecued	42	1.80 (1.04–3.13)	

Table 2.4.1 Cohort studies on consumption of red meat and cancer of the pancreas

Reference, location, enrolment/follow-up period,	Population size, description, exposure assessment method	Organ site	Exposure category or level	Exposed cases/ deaths	Risk estimate (95% CI)	Covariates controlled
Anderson et al. (2012) USA 1993–2007 (cont.)			Hamburger, cooking method			
			Do not eat	11	1.00	
			Oven-broiled	23	1.11 (0.54–2.30)	
			Pan-fried	75	1.32 (0.69–2.51)	
			Grilled or barbecued	133	1.43 (0.77–2.67)	
			Steak, cooking method			
			Do not eat	20	1.00	
			Oven-broiled	76	1.15 (0.70–1.89)	
			Pan-fried	32	1.10 (0.62–1.94)	
			Grilled or barbecued	119	0.93 (0.57–1.50)	
			Hamburger, doneness preference			
			Do not eat	10	1.00	
			Rare or medium rare	26	1.40 (0.67–2.93)	
			Medium	38	0.88 (0.43–1.78)	
			Medium well done	60	1.04 (0.53–2.06)	
			Well done	99	1.32 (0.68–2.55)	
			Very well done	15	1.39 (0.62–3.11)	
			Steak, doneness preference			
			Do not eat	13	1.00	
			Rare or medium rare	72	1.43 (0.79–2.61)	
			Medium	55	0.99 (0.54–1.83)	
			Medium well done	61	1.16 (0.64–2.13)	
			Well done	35	1.19 (0.62–2.26)	
			Very well done	12	1.68 (0.76–3.70)	
Rohrmann et al. (2013) Europe 1992–2008	477 202; European Prospective Investigation into Cancer and Nutrition (EPIC) participants from 10 European countries Exposure assessment method: questionnaire	Pancreas	Red meat intake (g/day)			Area, sex, age, height, weight, physical activity index, smoking, education, history of diabetes mellitus, total energy
			0 to < 20	176	1.00	
			20 to < 40	215	1.01 (0.82–1.24)	
			40 to < 80	291	0.99 (0.80–1.22)	
			≥ 80	183	1.07 (0.83–1.38)	
			Per 50 g observed	865	1.05 (0.94–1.17)	
			Per 50 g calibrated	865	1.03 (0.93–1.14)	

Table 2.4.1 Cohort studies on consumption of red meat and cancer of the pancreas

Reference, location, enrolment/follow-up period,	Population size, description, exposure assessment method	Organ site	Exposure category or level	Exposed cases/ deaths	Risk estimate (95% CI)	Covariates controlled
Rohrmann et al. (2013) Europe 1992–2008 (cont.)			Red meat intake (g/day)			
			Men: 0 to < 20	58	1.00	
			20 to < 40	84	1.01 (0.71–1.43)	
			40 to < 80	134	0.95 (0.67–1.35)	
			≥ 80	120	0.94 (0.63–1.40)	
			Trend-test *P* value: 0.53			
			Red meat intake (g/day)			
			Women: 0 to < 20	118	1.00	
			20 to < 40	131	1.01 (0.78–1.31)	
			40 to < 80	157	1.00 (0.76–1.32)	
			≥ 80	63	1.23 (0.87–1.75)	
Jiao et al. (2015) USA 1995–2006	567 169; members of the National Institutes of Health – American Association of Retired Persons (NIH-AARP) aged 50–71 yr, in six states Exposure assessment method: questionnaire; 124-item, 12-mo FFQ	Pancreas	Red meat intake (g/1000 kcal)			Age, race, education, diabetes, smoking status, first-degree family history of cancer, BMI, alcohol consumption, carbohydrate intake, saturated fat
			Men: 0–30.2	242	1.00	
			30.3–51.8	268	1.19 (0.99–1.42)	
			51.9–76.6	282	1.09 (0.90–1.32)	
			76.7–115.5	302	1.17 (0.95–1.43)	
			115.6–972.8	313	1.35 (1.07–0.70)	
			Trend-test *P* value: 0.05			
			Red meat cooked at high temperatures (g/1000 kcal)			
			Men: 0–9.2	245	1.00	
			9.3–18.0	255	0.87 (0.69–1.10)	
			18.1–29.7	294	1.23 (0.98–1.54)	
			29.8–49.2	300	1.01 (0.78–1.30)	
			49.3–693.7	313	1.18 (0.89–1.56)	
			Trend-test *P* value: 0.01			

BMI, body mass index; CVI, confidence interval; FFQ, food frequency questionnaire; mo, month; NR, not reported; SQFFQ, semi-quantitative food frequency questionnaire; wk, week; yr, year

Table 2.4.3 Case–control studies on consumption of red meat and cancer of the pancreas

Reference, location, enrolment	Population size, description, exposure assessment method	Organ site	Exposure category or level	Exposed cases/deaths	Risk estimate (95% CI)	Covariates controlled
Lyon et al. (1993) Utah, USA 1984–1987	Cases: 149; Utah Cancer Registry Controls: 363; random digit dialling and health care financing records Exposure assessment method: questionnaire; 32-item FFQ; red meat included beef and pork	Pancreas	Red meat Men: Low	30	1.00	Age, smoking, consumption of coffee and alcohol
			Medium	16	0.64 (0.30–1.37)	
			High	41	1.41 (0.72–2.75)	
			Trend-test *P* value: 0.3			
			Red meat Women: Low	16	1.00	
			Medium	23	1.05 (0.47–2.34)	
			High	21	1.44 (0.65–3.20)	
			Trend-test *P* value: 0.45			
Ji et al. (1995) Shanghai, China 1990–1993	Cases: 451; rapid reporting system; residents in Shanghai aged 30–74 yr Controls: 1552; Shanghai general population, frequency-matched by age and sex Exposure assessment method: questionnaire; 86-item FFQ; no validation data were reported	Pancreas	Red meat (servings/mo) Men: ≤ 13.7	NR	1.00	Age. income, smoking, green tea drinking (females only), response status
			13.8–22.5	NR	0.64 (0.42–0.99)	
			22.6–37.7	NR	0.76 (0.50–1.15)	
			≥ 37.8	NR	0.73 (0.47–1.12)	
			Trend-test *P* value: 0.24			
			Red meat (servings/mo) Women: ≤ 10.7	NR	1.00	
			10.7–19.8	NR	1.34 (0.81–2.21)	
			19.9–33.1	NR	0.83 (0.47–1.43)	
			≥ 33.0	NR	1.24 (0.73–2.13)	
			Trend-test *P* value: 0.86			

Table 2.4.3 Case–control studies on consumption of red meat and cancer of the pancreas

Reference, location, enrolment	Population size, description, exposure assessment method	Organ site	Exposure category or level	Exposed cases/deaths	Risk estimate (95% CI)	Covariates controlled
Tavani et al. (2000) Italy 1983–1996	Cases: 362; patients at several hospitals aged < 75 yr Controls: 7990; patients aged < 75 yr in the same network of hospitals for acute non-cancer conditions Exposure assessment method: questionnaire; FFQ with approximately 40 foods; red meat defined as beef, veal, and pork, excluding canned and preserved	Pancreas	Red meat consumption (median, times/wk) 3 5 7 Trend-test *P* value: ≤ 0.01	 115 120 127	 1.0 1.2 (0.9–1.6) 1.6 (1.2–2.1)	Age; year of recruitment; sex; education; smoking habits; alcohol, fat, fruit, and vegetable intakes
Anderson et al. (2002) USA 1994–1998	Cases: 193; incident cases aged ≥ 20 yr from area hospitals and clinics Controls: 674; aged ≥ 20 yr from drivers' licence and health care financing records; matched by age, sex, and race Exposure assessment method: questionnaire; in-person FFQ; "red meat" included bacon, sausage, and ham	Pancreas	Grilled/barbecued red meat (g/day) 0 0.9–3.5 3.7–10.7 10.8–88.0 Trend-test *P* value: < .001 Fried red meat (g/day) 0–1.1 1.2–4.6 4.7–11.5 11.7–24.1 24.2–192.6 Trend-test *P* value: 0.90 Broiled red meat (g/day) 0–0.49 0.50–4.90 5.00–11.70 12.00–171.10 Trend-test *P* value: 0,08	 77 14 36 66 25 26 55 44 43 102 31 28 32	 1.0 1.4 (0.7–2.7) 1.2 (0.7–1.9) 2.2 (1.4–3.4) 1.0 1.1 (0.6–2.0) 1.9 (1.1–3.3) 1.6 (0.9–2.8) 1.4 (0.7–2.6) 1.0 0.9 (0.5–1.4) 0.7 (0.4–1.1) 0.7 (0.4–1.2)	Age, sex, smoking, education, race, diabetes, red meat cooked by other methods

Table 2.4.3 Case–control studies on consumption of red meat and cancer of the pancreas

Reference, location, enrolment	Population size, description, exposure assessment method	Organ site	Exposure category or level	Exposed cases/deaths	Risk estimate (95% CI)	Covariates controlled
Chan et al. (2007) USA 1995–1999	Cases: 532; from Northern California Cancer Center and aged 21–85 yr Controls: 1701; general population, identified by random digit dialling; matched by age and sex Exposure assessment method: questionnaire; validated, 131-item FFQ; red meat included bacon and other processed meats	Pancreas	Beef or lamb as main dish (frequency)			Age, sex, energy intake, BMI, race, education, smoking, diabetes
			< 1 time/mo	107	1.0	
			1–3 times/mo	175	1.2 (0.9–1.6)	
			1 time/wk	127	1.1 (0.8–1.5)	
			2–4 times/wk	102	1.4 (1.0–2.0)	
			≥ 5 times/wk	14	2.2 (1.0–4.5)	
			Trend-test *P* value: 0.03			
			Pork as main dish (frequency)			
			< 1 time/mo	132	1.0	
			1–3 times/mo	113	0.9 (0.7–1.2)	
			1 time/wk	57	0.9 (0.6–1.4)	
			≥ 2 times/wk	11	0.6 (0.3–1.1)	
			Trend-test *P* value: 0.2			
			Hamburger (frequency)			
			< 1 time/mo	230	1.0	
			1–3 times/mo	134	1.1 (0.8–1.4)	
			1 time/wk	92	1.3 (1.0–1.7)	
			≥ 2 times/wk	70	1.7 (1.2–2.4)	
			Trend-test *P* value: 0.005			
Hu et al. (2008) Canada 1994–1997	Cases: 628; aged 20–76 yr from provincial cancer registries Controls: 5039; random sample within provinces, frequency-matched by age and sex Exposure assessment method: questionnaire; Block FFQ, short version (69 items)	Pancreas	Red meat (servings/wk)			Age, province, education, BMI, sex, alcohol use, smoking, total vegetable and fruit intake, total energy intake
			Q1	NR	1.0	
			Q2	NR	1.2 (0.9–1.5)	
			Q3	NR	1.3 (1.0–1.7)	
			Q4	NR	1.1 (0.9–1.5)	
			Trend-test *P* value: 0.31			

Table 2.4.3 Case–control studies on consumption of red meat and cancer of the pancreas

Reference, location, enrolment	Population size, description, exposure assessment method	Organ site	Exposure category or level	Exposed cases/deaths	Risk estimate (95% CI)	Covariates controlled
Anderson et al. (2009) Canada 2003–2007	Cases: 422; Ontario Cancer Registry Controls: 312; random digit dialling Exposure assessment method: questionnaire; mailed questionnaire, but a full FFQ was not administered; validity was not reported	Pancreas	Red meat (servings/wk) ≤ 1 2–3 > 3	 99 151 131	 1.00 1.16 (0.78–1.72) 1.49 (0.98–2.28)	Age
Polesel et al. (2010) Italy 1991–2008	Cases: 326; incident cases admitted to major general hospitals Controls: 652; hospital patients with various acute conditions, matched by study centre, sex, and age Exposure assessment method: questionnaire; 78-item FFQ on average weekly consumption in the past 2 yr; meat-cooking methods assessed, but definition of red meat was not specified	Pancreas	Red meat (median, servings/wk) 1.00 2.25 3.25 4.25 6.25 Trend-test *P* value: 0.01 Pork and processed meat (median, servings/wk) 1.50 3.00 5.00 Trend-test *P* value: 0.27	 43 51 51 84 97 89 115 122	 1.00 1.26 (0.75–2.12) 1.69 (0.98–2.91) 1.79 (1.09–2.96) 1.99 (1.18–3.36) 1.00 1.18 (0.81–1.73) 1.25 (0.85–1.84)	Year of interview, education, tobacco smoking, alcohol drinking, self-reported history of diabetes, BMI, total energy, study centre, age, sex
Di Maso et al. (2013) Italy, Switzerland 1991–2009	Cases: 326; incident cases from major hospitals Controls: 652; patients in the same hospitals with acute conditions Exposure assessment method: questionnaire; validated FFQ; red meat included beef, veal, pork, horse meat, and meat sauces	Pancreas	Red meat intake (g/day) < 60 60–89 ≥ 90 Increase of 50 g/day Trend-test *P* value: < 0.01	 96 96 134 326	 1.00 1.42 (0.98–2.07) 2.18 (1.51–3.16) 1.51 (1.25–1.82)	Study centre, age, sex, education, year, BMI, tobacco, alcohol, fruit and vegetable consumption

BMI, body mass index; CI, confidence interval; FFQ, food frequency questionnaire; mo, month; NR, not reported; wk, week; yr, year

References

Anderson KE, Sinha R, Kulldorff M, Gross M, Lang NP, Barber C et al. (2002). Meat intake and cooking techniques: associations with pancreatic cancer. *Mutat Res*, 506-507:225–31. doi:10.1016/S0027-5107(02)00169-0 PMID:12351162

Anderson KE, Mongin SJ, Sinha R, Stolzenberg-Solomon R, Gross MD, Ziegler RG et al. (2012). Pancreatic cancer risk: associations with meat-derived carcinogen intake in the Prostate, Lung, Colorectal, and Ovarian Cancer Screening Trial (PLCO) cohort. *Mol Carcinog*, 51(1):128–37. doi:10.1002/mc.20794 PMID:22162237

Anderson LN, Cotterchio M, Gallinger S (2009). Lifestyle, dietary, and medical history factors associated with pancreatic cancer risk in Ontario, Canada. *Cancer Causes Control*, 20(6):825–34. doi:10.1007/s10552-009-9303-5 PMID:19194662

Berjia FL, Poulsen M, Nauta M (2014). Burden of diseases estimates associated to different red meat cooking practices. *Food Chem Toxicol*, 66:237–44. doi:10.1016/j.fct.2014.01.045 PMID:24491261

Bosetti C, Bravi F, Turati F, Edefonti V, Polesel J, Decarli A et al. (2013). Nutrient-based dietary patterns and pancreatic cancer risk. *Ann Epidemiol*, 23(3):124–8. doi:10.1016/j.annepidem.2012.12.005 PMID:23332711

Chan JM, Wang F, Holly EA (2007). Pancreatic cancer, animal protein and dietary fat in a population-based study, San Francisco Bay Area, California. *Cancer Causes Control*, 18(10):1153–67. doi:10.1007/s10552-007-9054-0 PMID:17805983

Chan JM, Gong Z, Holly EA, Bracci PM (2013). Dietary patterns and risk of pancreatic cancer in a large population-based case-control study in the San Francisco Bay Area. *Nutr Cancer*, 65(1):157–64. doi:10.1080/01635581.2012.725502 PMID:23368926

Coughlin SS, Calle EE, Patel AV, Thun MJ (2000). Predictors of pancreatic cancer mortality among a large cohort of United States adults. *Cancer Causes Control*, 11(10):915–23. doi:10.1023/A:1026580131793 PMID:11142526

Cross AJ, Leitzmann MF, Gail MH, Hollenbeck AR, Schatzkin A, Sinha R (2007). A prospective study of red and processed meat intake in relation to cancer risk. *PLoS Med*, 4(12):12 (e 325): e325 doi:10.1371/journal.pmed.0040325 PMID:18076279

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

Heinen MM, Verhage BA, Goldbohm RA, van den Brandt PA (2009). Meat and fat intake and pancreatic cancer risk in the Netherlands Cohort Study. *Int J Cancer*, 125(5):1118–26. doi:10.1002/ijc.24387 PMID:19452526

Hirayama T (1990). [A large scale cohort study on the effect of life styles on the risk of cancer by each site] *Gan No Rinsho*, (Spec No):233–42. PMID:2313877

Hu J, La Vecchia C, DesMeules M, Negri E, Mery L, Group CCRE; Canadian Cancer Registries Epidemiology Research Group (2008). Meat and fish consumption and cancer in Canada. *Nutr Cancer*, 60(3):313–24. doi:10.1080/01635580701759724 PMID:18444165

Hu J, La Vecchia C, Morrison H, Negri E, Mery L; Canadian Cancer Registries Epidemiology Research Group (2011). Salt, processed meat and the risk of cancer. *Eur J Cancer Prev*, 20(2):132–9. doi:10.1097/CEJ.0b013e3283429e32 PMID:21160428

Inoue-Choi M, Flood A, Robien K, Anderson K (2011). Nutrients, food groups, dietary patterns, and risk of pancreatic cancer in postmenopausal women. *Cancer Epidemiol Biomarkers Prev*, 20(4):711–4. doi:10.1158/1055-9965.EPI-11-0026 PMID:21278328

Iso H, Kubota Y; Japan Collaborative Cohort Study for Evaluation of Cancer (2007). Nutrition and disease in the Japan Collaborative Cohort Study for Evaluation of Cancer (JACC). *Asian Pac J Cancer Prev*, 8:Suppl: 35–80. PMID:18260705

Ji BT, Chow WH, Gridley G, Mclaughlin JK, Dai Q, Wacholder S et al. (1995). Dietary factors and the risk of pancreatic cancer: a case-control study in Shanghai China. *Cancer Epidemiol Biomarkers Prev*, 4(8):885–93. PMID:8634662

Jiao L, Stolzenberg-Solomon R, Zimmerman TP, Duan Z, Chen L, Kahle L et al. (2015). Dietary consumption of advanced glycation end products and pancreatic cancer in the prospective NIH-AARP Diet and Health Study. *Am J Clin Nutr*, 101(1):126–34. doi:10.3945/ajcn.114.098061 PMID:25527756

Kadlubar S, Anderson JP, Sweeney C, Gross MD, Lang NP, Kadlubar FF et al. (2009). Phenotypic CYP2A6 variation and the risk of pancreatic cancer. *JOP*, 10(3):263–70. PMID:19454817

Khan MM, Goto R, Kobayashi K, Suzumura S, Nagata Y, Sonoda T et al. (2004). Dietary habits and cancer mortality among middle aged and older Japanese living in Hokkaido, Japan by cancer site and sex. *Asian Pac J Cancer Prev*, 5(1):58–65. PMID:15075007

Larsson SC, Håkanson N, Permert J, Wolk A (2006). Meat, fish, poultry and egg consumption in relation to risk of pancreatic cancer: a prospective study. *Int J Cancer*, 118(11):2866–70. doi:10.1002/ijc.21732 PMID:16385571

Larsson SC, Wolk A (2012). Red and processed meat consumption and risk of pancreatic cancer: meta-analysis of prospective studies. *Br J Cancer*, 106(3):603–7. doi:10.1038/bjc.2011.585 PMID:22240790

Li D, Day RS, Bondy ML, Sinha R, Nguyen NT, Evans DB et al. (2007). Dietary mutagen exposure and risk of pancreatic cancer. *Cancer Epidemiol Biomarkers Prev*, 16(4):655–61. doi:10.1158/1055-9965.EPI-06-0993 PMID:17416754

Lin Y, Kikuchi S, Tamakoshi A, Yagyu K, Obata Y, Inaba Y et al. (2006). Dietary habits and pancreatic cancer risk in a cohort of middle-aged and elderly Japanese. *Nutr Cancer*, 56(1):40–9. doi:10.1207/s15327914nc5601_6 PMID:17176216

Luckett BG, Su LJ, Rood JC, Fontham ET (2012). Cadmium exposure and pancreatic cancer in south Louisiana. *J Environ Public Health*, 2012:180186. doi:10.1155/2012/180186 PMID:23319964

Lyon JL, Slattery ML, Mahoney AW, Robison LM (1993). Dietary intake as a risk factor for cancer of the exocrine pancreas. *Cancer Epidemiol Biomarkers Prev*, 2(6):513–8. PMID:8268766

Michaud DS, Giovannucci E, Willett WC, Colditz GA, Fuchs CS (2003). Dietary meat, dairy products, fat, and cholesterol and pancreatic cancer risk in a prospective study. *Am J Epidemiol*, 157(12):1115–25. doi:10.1093/aje/kwg098 PMID:12796048

Mizuno S, Watanabe S, Nakamura K, Omata M, Oguchi H, Ohashi K et al. (1992). A multi-institute case-control study on the risk factors of developing pancreatic cancer. *Jpn J Clin Oncol*, 22(4):286–91. PMID:1434027

Nöthlings U, Wilkens LR, Murphy SP, Hankin JH, Henderson BE, Kolonel LN (2005). Meat and fat intake as risk factors for pancreatic cancer: the multiethnic cohort study. *J Natl Cancer Inst*, 97(19):1458–65. doi:10.1093/jnci/dji292 PMID:16204695

Ohba S, Nishi M, Miyake H (1996). Eating habits and pancreas cancer. *Int J Pancreatol*, 20(1):37–42. PMID:8872522

Paluszkiewicz P, Smolińska K, Dębińska I, Turski WA (2012). Main dietary compounds and pancreatic cancer risk. The quantitative analysis of case-control and cohort studies. *Cancer Epidemiol*, 36(1):60–7. doi:10.1016/j.canep.2011.05.004 PMID:22018953

Polesel J, Talamini R, Negri E, Bosetti C, Boz G, Lucenteforte E et al. (2010). Dietary habits and risk of pancreatic cancer: an Italian case-control study. *Cancer Causes Control*, 21(4):493–500. doi:10.1007/s10552-009-9480-2 PMID:20091114

Rohrmann S, Linseisen J, Nöthlings U, Overvad K, Egeberg R, Tjønneland A et al. (2013). Meat and fish consumption and risk of pancreatic cancer: results from the European Prospective Investigation into Cancer and Nutrition. *Int J Cancer*, 132(3):617–24. doi:10.1002/ijc.27637 PMID:22610753

Soler M, Chatenoud L, La Vecchia C, Franceschi S, Negri E (1998). Diet, alcohol, coffee and pancreatic cancer: final results from an Italian study. *Eur J Cancer Prev*, 7(6):455–60. doi:10.1097/00008469-199812000-00005 PMID:9926293

Stolzenberg-Solomon RZ, Pietinen P, Taylor PR, Virtamo J, Albanes D (2002). Prospective study of diet and pancreatic cancer in male smokers. *Am J Epidemiol*, 155(9):783–92. doi:10.1093/aje/155.9.783 PMID:11978580

Stolzenberg-Solomon RZ, Cross AJ, Silverman DT, Schairer C, Thompson FE, Kipnis V et al. (2007). Meat and meat-mutagen intake and pancreatic cancer risk in the NIH-AARP cohort. *Cancer Epidemiol Biomarkers Prev*, 16(12):2664–75. doi:10.1158/1055-9965.EPI-07-0378 PMID:18086772

Tavani A, La Vecchia C, Gallus S, Lagiou P, Trichopoulos D, Levi F et al. (2000). Red meat intake and cancer risk: a study in Italy. *Int J Cancer*, 86(3):425–8. doi:10.1002/(SICI)1097-0215(20000501)86:3<425::AID-IJC19>3.0.CO;2-S PMID:10760833

Yun YH, Lim MK, Won YJ, Park SM, Chang YJ, Oh SW et al. (2008). Dietary preference, physical activity, and cancer risk in men: national health insurance corporation study. *BMC Cancer*, 8(1):366 doi:10.1186/1471-2407-8-366 PMID:19077256

Zheng T, Boyle P, Willett WC, Hu H, Dan J, Evstifeeva TV et al. (1993). A case-control study of oral cancer in Beijing, People's Republic of China. Associations with nutrient intakes, foods and food groups. *Eur J Cancer B Oral Oncol*, 29B(1):45–55. doi:10.1016/0964-1955(93)90010-C PMID:8180577