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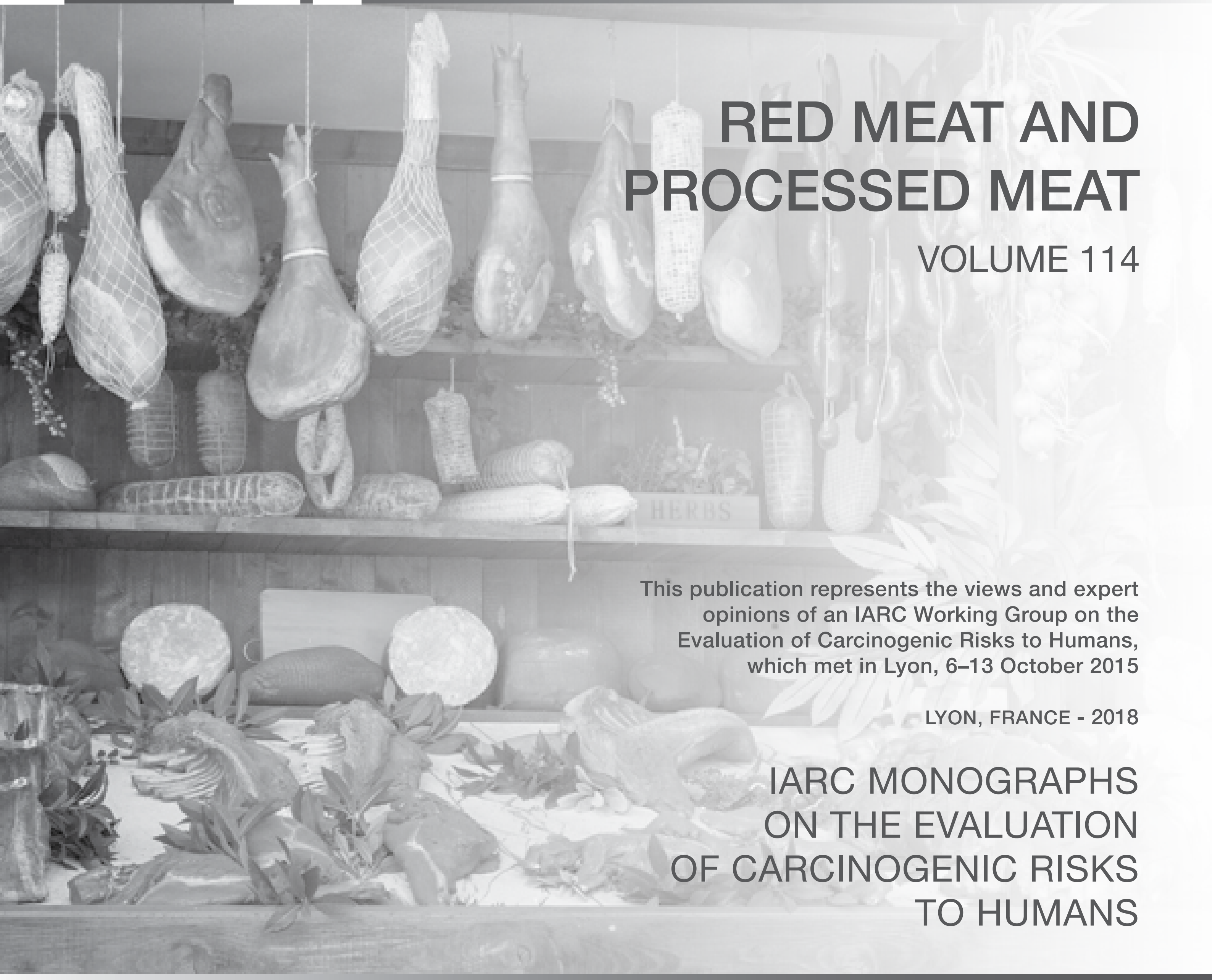

RED MEAT AND PROCESSED MEAT

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2.2 Cancer of the colorectum

2.2.1 Cohort studies

This section includes prospective cohort studies and case–control studies nested within prospective studies on the association between red or processed meat intake and risk of cancer of the colorectum. The most recent publication of a cohort study, or the publication with the highest number of cases in the analysis, was included in the review. The results of superseded studies were not detailed.

This evaluation excluded prospective studies with colorectal cancer mortality, rather than incidence, as the end-point, and study results on the association between meat intake and colorectal cancer risk when the definition of meat intake included poultry and/or fish. Studies on dietary patterns and studies with fewer than 100 cases in the analyses were also not included.

The results of the included studies are presented according to the type of meat investigated: red meat (i.e. unprocessed red meat), processed meat, and red meat and processed meat combined. When studies reported on two or more of these types of meat, only the data for red meat and processed meat considered separately were treated in detail. A few studies that reported results only for particular aspects of meat consumption, such as doneness or type of meat, are described in this section, but these studies are not included in the tables. Studies on gene–exposure interactions are described in the section of the corresponding meat type, as are studies on the association between cooking methods or meat doneness levels and colorectal cancer.

As studies with greater precision can be considered more informative, particularly when the strength of the association appears to be weak to moderate, the descriptions of the studies are ordered for each section by the number of cases in the analysis, and tables are ordered chronologically. Other study quality criteria are indicated in the text when relevant. The study results most pertinent to the evaluation are included in the tables. Other findings of interest are briefly described in the text.

(a) Red meat

Fourteen cohort studies and two cohort consortia provided informative data on the association between red meat and risk of colorectal cancer (see Table 2.2.1). A few studies investigated specific types of red meat only. The results of these studies are described at the end of this section.

The New York University Women's Health Study (NYUWHS) enrolled women aged 34–65 years at mammographic screening clinics from 1985 to 1991, and followed them up until 1994 through a combination of direct contact and record linkage to cancer registries. A 70–food item, modified Block questionnaire was used to assess diet. Colorectal cancer risk was not significantly associated with red meat intake. The relative risk (RR) for the highest compared with the lowest quartile was 1.23 (95% confidence interval, CI, 0.68–2.22) (Kato et al., 1997). [The Working Group noted that the amount of red meat intake was not reported in the publication, and the study was small (100 cases in the analysis).]

In a nested case–control study using data from the Monitoring Project on Cardiovascular Disease Risk Factors study in the Netherlands (Tiemersma et al., 2002), 102 incident colorectal cancer cases were identified during 8.5 years of follow-up, and a random sample of 537 controls were matched for sex and age. The odds ratio (OR) for consumption of red meat ≥ 5 times/week compared with ≤ 3 times/week was 1.6 (95% CI, 0.9–2.9). In an analysis stratified by sex, a positive association was observed in men (OR, 2.7; 95% CI, 1.1–6.7; P_{trend} = 0.06), but not in women (OR, 1.2; 95% CI, 0.5–2.8; P_{trend} = 0.64). The same comparison was statistically significant in men and women combined after the exclusion of participants who were younger than age 50 years at the end of the follow-up (RR, 2.0; 95% CI, 1.1–3.8; highest vs lowest intake). The relationship between red meat and colorectal cancer was not modified by *NAT1*, *NAT2*, and *GSTM1* genotypes. [The Working Group noted that a limited number of cancer cases were included in the study, and the assessment of meat intake was not comprehensive. A major source of meat intake – a mix of minced pork and beef – in the Dutch population was missed by the questionnaire. However, the authors indicated that meat consumption was estimated by the questionnaire, with acceptable reproducibility and validity when compared with a dietary history method (data were not given in the paper).]

A cohort study in Takayama, Japan, included 30 221 subjects aged 35 years or older who completed a general questionnaire and a 169–food item, validated food frequency questionnaire (FFQ) at baseline in 1992. Until 2000, 111 cases of colon cancer in men and 102 cases in women were identified through the medical records of two hospitals in Takayama, accounting for about 90% of the colon cancer cases registered in the city cancer registry (Oba et al., 2006). Red meat intake was unrelated to colon cancer risk. Multivariate-adjusted relative risks for the highest compared with the lowest tertile of intake were 1.03 (95% CI, 0.64–1.66; P_{trend} = 0.86) in men and 0.79 (95% CI, 0.49–1.28; P_{trend} = 0.20) in women. Rectal cancer cases were not included in the analysis. [The Working Group noted that a limited number of cancer cases were included in the study, and meat intake was low compared with meat intake in North American and European cohorts.]

In a 6-year follow-up of a cohort of 32 051 non-Hispanic, White members of the Adventist Health Study (AHS) in California, USA (1976–1982), 157 colon cancer cases were identified (Singh & Fraser, 1998). The participants completed at baseline a semiquantitative, 55–food item dietary questionnaire, in which six questions were on meat intake. Participants who consumed beef or pork ≥ 1 time/week were at increased risk of colon cancer compared with those who did not consume beef or pork (RR, 1.90; 95% CI, 1.16–3.11; P_{trend} = 0.02). White meat intake was also positively associated with colon cancer risk. [The Working Group noted that out of the 157 colon cancer cases identified, 42 cases were vegetarians and 40 cases were occasional meat eaters. The association with red meat remained significant in the analysis stratified by intake of white meat, and the analyses were adjusted for tobacco smoking and physical activity. Given the nature of the study population, and that residual confounding could not be ruled out, other lifestyle differences for low meat eaters and vegetarians could at least partially explain the association observed with both red and white meats. The exclusion of current or past smokers, and alcohol consumers did not substantially alter the association with red meat.]

In the Alpha-Tocopherol, Beta-Carotene Cancer Prevention (ATBC) Study, a randomized, double-blind, placebo-controlled trial on the prevention of incidence of lung cancer in Finnish male smokers, 185 colorectal cancer cases were identified during 8 years of follow-up (Pietinen et al., 1999). Usual diet at baseline was assessed using a self-administered questionnaire with 276 items, and total red meat was defined as beef, lamb, and pork and processed meat. Colorectal cancer was not associated with intake of beef, pork, and lamb (i.e. red meat), specifically; the relative risk for the highest compared with the lowest quartile was 0.8 (95% CI, 0.5–1.2; P_{trend} = 0.74) (Pietinen et al., 1999). Intake of fried meats (determined by adding up the frequency of intake of all dishes where the meat was prepared by frying) was not related to colorectal cancer risk (RR, 0.9; 95% CI, 0.6–1.3; for 204 vs 60 times/year). [The Working Group noted that fried meats may have included fried white meats. No other cooking methods were reported. A main limitation of this study was the low number of cases.]

In the Iowa Women's Health Study (IWHS), a study in postmenopausal women, 212 incident colon cancer cases were identified during 5 years of follow-up. Diet was assessed using a validated, 127–food item semiquantitative food frequency questionnaire (SQFFQ). Total red meat was defined as beef, lamb, or pork, and processed meat. Consumption of total red meat as defined was not associated with colon cancer, nor was consumption of beef, lamb, or pork as a main dish (RR, 1.21; 95% CI, 0.75–1.96; P_{trend} = 0.16; for > 3 vs < 1 serving/week) (Bostick et al., 1994). This lack of association was observed in women with or without a family history of colon cancer in first-degree relatives (Sellers et al., 1998).

Andersen et al. (2009) conducted a case–cohort study nested in the Danish Diet, Cancer and Health cohort study (372 cases, 765 controls), and reported a null association between intake of red meat and colorectal cancer risk. [Estimates were not adjusted for total energy intake, raising concerns about uncontrolled confounding. In addition,the Working Group noted that the study had a short follow-up (5 years), and cases identified in the first years of follow-up were not excluded from the analyses.]

In a case–cohort study in the Danish Diet, Cancer and Health cohort, including 379 colorectal cancer cases and 769 subcohort members, colorectal cancer was not significantly associated, although it was slightly increased, with intake of red meat (RR, 1.03; 95% CI, 0.97–1.09, per 25 g/day) or fried red meat (RR, 1.09; 95% CI, 0.96–1.23, per 25 g/day). A higher risk was observed in people who reported a preference for brown–dark pan-fried meat (any type of meat) compared with light–light brown meat (RR, 1.36; 95% CI, 1.04–1.77). This risk did not differ significantly between *NAT1* or *NAT2* genotype carriers ($P_{interaction}$ > 0.4) (Sørensen et al., 2008). [The Working Group noted that about 18% of the participants in this cohort were also included in the Danish component of the European Prospective Investigation into Cancer and Nutrition (EPIC).]

In another nested case–control study in the same cohort, a statistically significant increase (RR, 3.70; 95% CI, 1.70–8.04) in colorectal cancer risk per 100 g/day of red meat intake was observed among carriers of the homozygous variant *XPC* Lys939Gln, and no association among carriers of the wildtype allele was observed (Hansen et al., 2007). None of the other polymorphisms investigated (*XPA* A23G, *XPD* Lys751Gln, and *XPD* Asp312Asn) were related to colorectal cancer risk. [The Working Group noted that results regarding the association between *XPC* Lys939Gln and red meat intake on colorectal cancer risk might have been a chance finding, as multiple comparisons were made.]

The Shanghai Women's Health Study (SWHS) included 73 224 women aged 40–70 years at recruitment who completed an FFQ by interview at the baseline assessment beginning in 1997. Follow-up was through active surveys and periodic linkage to the Shanghai Cancer Registry. After a mean follow-up of 7.4 years, 394 incident cases of colorectal cancer (236 colon, 158 rectum) were identified (Lee et al., 2009). The risk of colorectal cancer was not related to the amount of red meat intake. The relative risks for the highest compared with the lowest quintile (> 67 g/day and < 24 g/day, respectively) were 0.8 (95% CI, 0.6–1.1; P_{trend} = 0.53) for colorectal cancer, 0.9 (95% CI, 0.6–1.5; P_{trend} = 0.31) for colon cancer, and 0.6 (95% CI, 0.3–1.1; P_{trend} = 0.79) for rectal cancer. When intakes of 90 g/day and 100 g/day were instead used as cut-points in a further analysis, the relative risk estimates for colorectal cancer were 1.29 (95% CI, 0.88–1.89) and 1.67 (95% CI, 1.11–2.52), respectively. [The Working Group noted that the association may not have been detected in the previous analyses due to an overall low level of meat consumption.] In an analysis of cooking methods, the risk of colon cancer was significantly associated with preparing food by smoking (RR, 1.4; 95% CI, 1.1–1.9; for ever vs never), but not with other cooking methods. [The Working Group noted that the definition of red meat was not given, but appeared to be unprocessed pork, beef, and lamb. Cooking methods were for all animal foods. The range of meat intake was low in the study.]

In the Melbourne Collaborative Cohort Study, the relative risk of colorectal cancer for consuming red meat more than 6.5 times/week compared with < 3 times/week was 1.4 (95% CI, 1.0–1.9; P_{trend} = 0.2; 451 cases). Red meat was defined as veal, beef, lamb, pork, and rabbit or other game. The association was mainly driven by a positive association with rectal cancer (RR for the same comparison, 2.3; 95% CI, 1.2–4.2; P_{trend} = 0.07; 169 cases). The relative risk for colon cancer was 1.1 (95% CI, 0.7–1.6; P_{trend} = 0.9; 283 cases) (English et al., 2004). In analyses with continuous variables for meat consumption, the relative risks for an increase of 1 time/week were 1.0 (95% CI, 0.94–1.07) for the colon and 1.08 (95% CI, 0.99–1.16) for the rectum.

In the Swedish Mammography Cohort (SMC), 733 incident cases of colorectal cancer were identified after completion of a 67-item, self-administered dietary questionnaire at baseline in 1987–1990. Consumption of unprocessed beef and pork was associated with almost a twofold risk of distal colon cancer for ≥ 4 servings/week, whereas there was no apparent association with risk of proximal colon or rectal cancers (Larsson et al., 2005a). The relative risks for consumption of beef and pork ≥ 4 times/week compared with < 2 times/week were 1.22 (95% CI, 0.98–1.53) for colorectal cancer, 1.10 (95% CI, 0.74–1.64) for proximal colon cancer (234 cases), 1.99 (95% CI, 1.26–3.14; P_{trend} = 0.01) for distal colon cancer (155 cases), and 1.08 (95% CI, 0.72–1.62) for rectal cancer (230 cases), respectively. [The Working Group noted that case ascertainment was virtually complete, and the analyses were controlled for main potential confounders.]

Singaporean Chinese aged 45–74 years who resided in government-built housing estates were enrolled in a prospective study in 1993–1998. At baseline, a 165-item quantitative FFQ, developed for and validated in this population, was administered to assess usual diet over the past year. After an average follow-up duration of nearly 10 years, 941 incident colorectal cancer cases were identified through record linkage to the population-based Singapore Cancer Registry (Butler et al., 2008 b). The adjusted hazard ratio (HR) for the highest compared with the lowest quartile of red meat intake was 1.01 (95% CI, 0.82–1.26; P_{trend} = 0.6). [The Working Group noted that the usual diet was mainly composed of mixed dishes. Red meat appeared to be unprocessed, but the definition was not given in the paper. The cut-off points of the quartiles were not given, and the 95th percentile of red meat intake in non-cases was 76 g/day.]

The EPIC study identified 1329 colorectal cancer cases during a mean follow-up of 4.8 years. Red meat included all fresh, minced, and frozen beef, veal, pork, and lamb. In the EPIC study (Norat et al., 2005), the relative risk for colorectal cancer was 1.17 (95% CI, 0.92–1.49; P_{trend} = 0.08) for an intake of red meat > 80 g/day compared with < 10 g/day. A significant association (RR, 1.21; 95% CI, 1.02–1.43, per 100 g/day; P_{trend} = 0.03) was observed when red meat was expressed as a continuous increment. The association with red meat was strengthened, but not significant, after calibration using 24-hour recall data. The calibrated relative risk for colorectal cancer per 100-g increment was 1.49 (95% CI, 0.91–2.43). The associations were similar for cancers of the colon and rectum, and of the proximal and distal colon. Analysis of specific meat types showed significant positive trends for intake of pork (highest vs lowest intake RR, 1.18; 95% CI, 0.95–0.48; P_{trend} = 0.02) and lamb (HR, 1.22; 95% CI, 0.96–1.55; P_{trend} = 0.03), but not for intake of beef/veal (HR, 1.03; 95% CI, 0.86–1.24; P_{trend} = 0.76). When mutually adjusted, only the trend for pork remained significant. [The Working Group noted that the strengths of the study were that participants were from 10 European countries with different dietary habits, and detailed validated dietary questionnaires were used. Dietary data were also calibrated using 24-hour recall in a subset of the population to partially correct the relative risk estimates for dietary measurement error. This study investigated red meat, processed meat, and specific meat types in relation to colorectal cancer risk. Follow-up was virtually complete, and the analyses were adjusted for main potential confounders. A potential limitation of the study was that different dietary questionnaires were used in the centres; however, the associations were strengthened after calibration of the dietary data, and no heterogeneity across centres was detected.]

The Nurses' Health Study (NHS) and the Health Professionals Follow-Up Study (HPFS) were among the first American cohorts to investigate the association between red and processed meat and colon cancer risk. The NHS included female, married nurses aged 30–55 years, and diet was assessed by a validated, 61-item SQFFQ. Self-reported cases were validated by medical or pathology records. The HPFS included men aged 40–75 years, and diet was assessed by a self-administered FFQ. Both studies had repeated measures of diet during follow-up (NHS, from 1980 to 2010; HPFS, from 1986 to 2010). Early reports from these cohorts, which included a small number of cases, showed significant positive associations between red and processed meat and colon cancer (age- and energy-adjusted) (Willett et al., 1990; Giovannucci et al., 1994). Several papers on the cohorts have since been published (Wei et al., 2004, 2009; Fung et al., 2010; Zhang et al., 2011; Bernstein et al., 2015), generally showing no association between beef, pork, or lamb as a main dish and colorectal cancer risk (Wei et al., 2004; Fung et al., 2010; Bernstein et al., 2015).

In the most recent analysis of the NHS and the HPFS (Bernstein et al., 2015), which included 2731 colorectal cancer cases (1151 proximal colon, 816 distal colon, and 589 rectum), the cumulative average intake of unprocessed red meat was not associated with colorectal cancer risk (RR per 1 serving/day increase, 0.99; 95% CI, 0.87–1.13; P_{trend} = 0.88). The results were similar when analysed in grams of intake. When analysed by tumour location, red meat consumption was inversely associated with risk of distal colon cancer (RR per 1 serving/day increase, 0.75; 95% CI, 0.68–0.82; P_{trend} < 0.001); a weak, non-significant positive association was observed with proximal colon cancer (RR, 1.14; 95% CI, 0.92–1.40; P_{trend} = 0.22)., and no association was observed with rectal cancer (RR, 1.14; 95% CI, 0.86–1.51; P = 0.37). The inverse associations with distal colon cancer were primarily seen after adjustment for specific nutrients, including fibre, folate, and calcium in men and calcium in women. [The Working Group noted that the analyses took into account long-term exposure and several potential risk factors simultaneously. Multiple sensitivity and effect modification analyses were conducted, and the results were robust.]

In a previous nested case–control study of 183 colorectal cancer cases and 443 controls enrolled in the NHS, women with the *NAT2* rapid acetylator genotype who consumed > 0.5 servings/day of beef, pork, or lamb as a main dish had an increased risk of colon cancer compared with women who consumed less red meat (OR, 3.01; 95% CI, 1.10–8.18). No association was observed in slow acetylators (multivariate OR, 0.87; 95% CI, 0.35–2.17; $P_{interaction}$ = 0.07) or in all women (OR, 1.21; 95% CI, 0.85–1.72) (Chan et al., 2005). [The Working Group noted that this study was large. Diet was estimated from repeated questionnaires, and there was a detailed selection of potential confounders.]

The Multiethnic Cohort Study identified 3404 incident cases of colorectal cancer up to 2007 among a sample of African Americans, Japanese Americans, Latinos, native Hawaiians, and Whites aged 45–75 years living in Hawaii and California, USA (Nöthlings et al., 2009; Ollberding et al., 2012). Red meat intake was not associated with colorectal cancer risk. The relative risk for the highest compared with the lowest quintile (34.86 and 4.59 g/1000 kcal, respectively) was 0.98 (95% CI, 0.87–1.10; P_{trend} = 0.58). For all types of meats considered together, the risk did not vary by doneness preference (cooked until dark brown or well done) or cooking method preference (pan-fried, oven-broiled, or grilled/barbecued); data were not reported by the authors. [The Working Group noted that this was a large study that sampled people from different ethnic groups for better generalizability of results. There was a strong attenuation of the effect estimates after multivariable adjustment.]

In a nested case–control in the United Kingdom Dietary Cohort Consortium, based on seven cohort studies in the United Kingdom (Spencer et al., 2010), diet was assessed using 4-, 5-, or 7-day food diaries. Red meat was defined as including beef, pork, lamb, and meat from burgers, and other non-processed meat items made with these meats. Red meat intake was not related to risk of colorectal cancer (579 cases). The relative risk estimate for an increase in intake of 50 g of red meat was 1.01 (95% CI, 0.84–1.22) for colorectal cancer. Similar relative risks were observed for colon and rectal cancers. [The Working Group noted that meat intake was relatively low in the overall consortium, as many participants were either vegetarians or low meat eaters. The use of food diaries may also have led to overestimation of the number of non-consumers of infrequently consumed food items.]

In a pooled analysis of the Genetics and Epidemiology of Colorectal Cancer Consortium (GECCO) and the Colon Cancer Family Registry (CCFR) (Kantor et al., 2014), which included 9160 cases of colorectal cancer and 9280 controls, the pooled relative risk estimate for colorectal cancer for each serving per day increase in intake of red meat was 1.33 (95% CI, 1.23–1.44) for all studies combined. The purpose of the study was to investigate gene–environment interactions, and the estimates of associations reported were controlled only for age, sex, and study centre. In another paper based on the same pooled study, Figueiredo et al. (2014) reported a relative risk of 1.23 (95% CI, 1.12–1.34) for red meat consumption above versus below the median and a relative risk of 1.15 per quartile of intake. In another publication based on GECCO and the CCFR that included data from case–control studies nested in five cohorts, red meat consumption was related to colorectal cancer risk only from retrospective case–control studies. The pooled odds ratio from four retrospective case–control studies was 1.75 (95% CI, 1.55–1.98). The relationship was not modified by NAT2 enzyme activity (based on polymorphism at rs1495741) (Ananthakrishnan et al., 2015). No interaction involving any gene and red meat was detected in a genome-wide diet–gene interaction analysis in GECCO or in a study on colorectal cancer susceptibility loci (Hutter et al., 2012). [The exact definition of red meat was not given in these studies.]

Five additional cohort studies did not investigate the overall association between colorectal cancer risk and red meat consumption, but did evaluate associations with specific red meat items (data not reported in Table).

In a prospective study conducted by the Norwegian National Health Screening Service (143 cases of colon cancer) among Norwegian men and women aged 20–54 years between 1977 and 1983 (Gaard et al., 1996), consumption of meatballs, meat stews, and fried or roasted meats was unrelated to colon cancer risk. [The Working Group noted that the analyses were only for specific red meat types and adjusted only for age.]

In the Women's Health Study (WHS), a randomized trial in the USA of low-dose aspirin and vitamin E in the primary prevention of cancer and cardiovascular disease, diet was assessed at study baseline using a 131-item FFQ that was previously validated in the NHS. Two hundred and two incident colorectal cancer cases were identified during 8.7 years of follow-up. The definition of red meat included hot dogs, bacon, and other processed meats. Data for consuming unprocessed red meat were limited to beef or lamb as a main dish and were stratified by cooking method. In comparison with beef or lamb cooked rare or medium–rare, the relative risks were 0.73 (95% CI, 0.47–1.11) for medium doneness, 1.02 (95% CI, 0.68–1.52) for medium well-done meat and 0.94 (95% CI, 0.63–1.41) for well-done meat (P_{trend} = 0.83) (Lin et al., 2004). Meat doneness was available only for beef or lamb as a main dish. This study also reported a positive association between white meats and colorectal cancer.]

In a case–cohort analysis including 448 colon and 160 rectal cancer cases and a subcohort of 2948 participants in the Netherlands Cohort Study (NLCS), intake of beef, pork, minced meat, or liver was not significantly associated with colon or rectal cancer risk, although a positive association was suggested for beef and colon cancer (RR for highest vs lowest category of beef intake, 1.28; 95% CI, 0.96–1.72; P_{trend} = 0.06) (Brink et al., 2005). In another analysis (434 colon cancer cases, 154 rectal cancer cases) (Lüchtenborg et al., 2005), beef consumption was associated with an increased risk of colon tumours without a truncating *APC* somatic mutation. The incidence rate ratio for the highest versus the lowest quartile of intake was 1.58 (95% CI, 1.10–2.25; P_{trend} = 0.01). [The Working Group noted that the follow-up period was short, and cases diagnosed in the first years of follow-up were excluded.]

A recent full cohort analysis of the Netherlands Cohort Study – Meat Investigation Cohort (NLCS-MIC), with all individuals reporting to be vegetarian or to consume meat only 1 day/week, was conducted with 20.3 years of follow-up (Gilsing et al., 2015). For red meat, defined as fresh meat without chicken, no clear association was observed with colon or rectal cancer.

In a cohort study in Japan, 47 605 residents aged 40–64 years from the Miyagi Prefecture completed a self-administered, 40-item FFQ in 1990. Four hundred and seventy-four colorectal cancer cases were identified after an average follow-up of 11 years through linkage to the Miyagi Prefectural Cancer Registry. Relative risk estimates for the highest compared with the lowest intake were 0.93 (95% CI, 0.67–1.30; P_{trend} = 0.63) for beef and 1.13 (95% CI, 0.79–1.74; P_{trend} = 0.31) for pork intake. No associations were observed with risk of cancers of the colon, proximal or distal colon, and rectum (Sato et al., 2006). [The Working Group noted that the number of categories in the questionnaire was low, and there was low variability in meat intake. The median intake in the top category was 7.4 g/week for beef and 26.3 g/week for pork (excluding ham and sausage). Beef and pork combined was not investigated.]

In the Japan Public Health Center-based Prospective Study (JPHC Study), men and women completed a self-administered questionnaire in 1995–1999 at age 45–74 years (Takachi et al., 2011), and 1145 cases of colorectal cancer were identified until the end of 2006. The category of red meat was defined as including processed products and chicken liver. In women, a significant association between beef intake and colon cancer was observed (RR for fifth vs first quintile, 1.62; 95% CI, 1.12–2.34; P_{trend} = 0.04), and a non-significant association was observed for pork (RR for fifth vs first quintile, 1.42; 95% CI, 0.99–2.04; P_{trend} = 0.05) (Takachi et al., 2011). No significant association between beef or pork intake and colon or rectal cancer was observed in men. [The Working Group noted that although red and processed meat consumption was lower in this cohort than in cohorts from Western countries, there was a sevenfold difference in the median intakes of the lowest and highest quintiles. Total consumption of red meat was not investigated.]

(b) Processed meat

Associations between colorectal cancer and consumption of processed meat have been examined in 18 informative cohort studies and two pooled analyses (see Table 2.2.2); some of these studies also reported data for red meat.

Intake of processed meat (ham and sausages) was not related to colorectal cancer risk in the NYUWHS (Kato et al., 1997). The relative risk for the highest compared with the lowest quartile was 1.09 (95% CI, 0.59–2.02; P_{trend} = 0.735; 100 cases). [The Working Group noted that this study had a small sample size. The analyses were adjusted only for energy intake, age, place, and education level.]

Colorectal cancer was not associated with intake of processed meat in the ATBC Study in Finnish male smokers (185 cases) (Pietinen et al., 1999). The relative risk for the highest compared with the lowest quartile (medians, 122 g/day and 26 g/day, respectively) was 1.2 (95% CI, 0.7–1.8; P_{trend} = 0.78). [The Working Group noted that a main limitation of this study was the low number of cases.]

In the WHS, processed meat intake was inversely, although not significantly, associated with colorectal cancer in the analysis including 202 cases (Lin et al., 2004). The relative risk for the highest compared with the lowest quintile was 0.85 (95% CI, 0.53–1.35; P_{trend} = 0.25; medians of the quintiles, 0.5 servings/day and 0 servings/day, respectively). Processed meat was defined as hot dogs, bacon, and other processed meats. [The Working Group noted that this study reported an inverse non-significant association between total red meat and colorectal cancer, and positive associations between white meat and colorectal cancer, in contrast with the results of other cohort studies.]

In the IWHS cohort (Bostick et al., 1994), which included 212 cases, the relative risk of colon cancer for consumption of > 3 servings/week of processed meat compared with none was 1.51 (95% CI, 0.72–3.17; P_{trend} = 0.45). In the same cohort, nitrate-treated meats were not related to colon cancer in women with or without a family history of colon cancer in first-degree relatives (Sellers et al., 1998). [The Working Group noted that this study had a small sample size, follow-up was 5 years, and cases identified in the first years of follow-up were not excluded from the analyses.]

In a community-based prospective study in Takayama, Japan, including 213 cases of colorectal cancer, there was a twofold, significant increased risk of colon cancer only in men who consumed a higher intake of processed meats (Oba et al., 2006). The relative risks for the highest compared with the lowest tertile of intake were 1.98 (95% CI, 1.24–3.16; P_{trend} < 0.01) in men and 0.85 (95% CI, 0.50–1.43; P_{trend} = 0.62) in women. Processed meat was defined as ham, sausage, bacon, and yakibuta (Chinese-style roasted pork). The results did not change after the exclusion of cases diagnosed in the first 3 years of follow-up.

Processed meat intake was associated with colorectal cancer in the Melbourne Collaborative Cohort Study (451 cases) (English et al., 2004). The relative risks were 1.5 (95% CI, 1.1–2.0; P_{trend} = 0.01) for the highest compared with the lowest intake and 1.07 (95% CI, 1.01–1.13) for an increase of 1 serving/week. Processed meat intake was more strongly associated with risk of rectal cancer than with risk of colon cancer in a categorical analysis. The relative risks for the highest compared with the lowest quartile were 1.3 (95% CI, 0.9–1.9) for the colon and 2.0 (95% CI, 1.1–3.4) for the rectum. The hazard ratios for each additional serving per week were similar; the hazard ratios were 1.07 (95% CI, 1.00–1.14) and 1.08 (95% CI, 0.99–1.18) for the colon and rectum, respectively (P = 0.8, test of homogeneity of trends).

In the Breast Cancer Detection Demonstration Project (BCDDP) in the USA (467 cases), women completed a 62-item National Cancer Institute (NCI)/Block FFQ. The Block FFQ defined processed meat as bacon, ham, lunchmeat, hot dogs, and sausage (Flood et al., 2003). The relative risk for the highest compared with the lowest quintile of processed meat intake was 0.97 (95% CI, 0.73–1.28; P_{trend} = 0.35; medians of the quintiles, 22.2 and 0.02 g/1000 kcal, respectively) after adjustment for age, energy, and total meat consumption. The inclusion of several other variables, including smoking, alcohol drinking, and BMI, did not materially change the estimates and were not kept in the final models. [The Working Group noted that colorectal cancer diagnosis was self-reported in most cases. Pathology reports were obtained for 79% of these cases, and the diagnosis confirmed in 94% of them, suggesting that case identification was not an issue.]

In the Miyagi Cohort Study in Japan, processed meat consumption was not related to risk of colorectal cancer (colorectum, colon, proximal colon, and distal colon and rectum); the analysis included 474 incident colorectal cancer cases (Sato et al., 2006). The relative risk for the highest compared with the lowest quartile was 0.91 (95% CI, 0.61–1.35; P_{trend} = 0.99). No associations were observed for cancers of the colon, rectum, or proximal and distal colon. [The Working Group noted that the number of categories in the questionnaires was low, and there was low variability in meat intake due to low frequency of consumption of some meat items.]

In the Danish Diet, Cancer and Health study (18% of the cases were included in the Danish component of the EPIC study), the relative risks per 25 g/day increase in intake of processed meats were 1.03 (95% CI, 0.94–1.13; 644 cases) for the colon and 0.93 (95% CI, 0.81–1.07; 345 cases) for the rectum (Egeberg et al., 2013). No significant associations were observed with intakes of sausages, cold cuts, or liver pâté. In addition, associations were not modified by four polymorphisms (*XPA* A23G, *XPC* Lys939Gln, *XPD* Lys751Gln, and *XPD* Asp312Asn) of enzymes involved in the nucleotide excision repair pathway in a case–control study nested in the cohort (405 colorectal cancer cases, 810 controls) (Hansen et al., 2007). Another analysis of 379 colorectal cancer cases and 769 subcohort members showed no association with consumption of processed meat when stratified by *NAT1* or *NAT2* genotypes (Sørensen et al., 2008).

In the SMC (Larsson et al., 2005a), processed meat intake was not related to risk of colorectal cancer or colorectal cancer subsites. The relative risk estimates for the highest compared with the lowest quartile of intake were 1.07 (95% CI, 0.85–1.33; P_{trend} = 0.23) for the colorectum (733 cases), 1.02 (95% CI, 0.69–1.52; P_{trend} = 0.97) for the proximal colon (234 cases), 1.39 (95% CI, 0.86–2.24; P_{trend} = 0.20) for the distal colon (155 cases), and 0.90 (95% CI, 0.60–1.34; P_{trend} = 0.88) for the rectum (230 cases). [The Working Group noted that the dietary questionnaire had 67 food items. Follow-up was long (13.9 years on average), and changes in dietary habits during follow-up were not taken into account. Case ascertainment was virtually complete, and the analyses were controlled for main potential confounders.]

In the Singapore Chinese Health Study (SCHS) (Butler et al., 2008b), the relative risk for the highest compared with the lowest quartile of processed meat intake was 1.16 (95% CI, 0.95–1.41; 941 incident colorectal cancer cases after an average follow-up of 10 years). Types of processed meats were not defined. [The Working Group noted that the cut-points of the quartiles were not given, and processed meat intake was low (the 95th percentile of processed meat intake in non-cases was 10 g/day).]

In the JPHC Study (Takachi et al., 2011) (1145 cases of cancer of the colorectum), processed meat included ham, sausage or wiener sausage, bacon, and luncheon meat. The relative risks of colon cancer for the highest compared with the lowest quintile were 1.27 (95% CI, 0.95–1.71; P_{trend} = 0.10) in men and 1.19 (95% CI, 0.82–1.74; P_{trend} = 0.64) in women. Similar results were observed for proximal and distal colon cancers. The relative risk for rectal cancer was 0.70 (95% CI, 0.45–1.09; P_{trend} = 0.10) in men and 0.98 (95% CI, 0.53–1.79;

P_{trend} = 1.00) in women. [The Working Group noted that the range of processed meat intake was low. The median intake in the top quintile was 16 g/day in men and 15 g/day in women.]

In the European EPIC study (1329 incident colorectal cancer cases), processed meats included mostly pork and beef preserved by methods other than freezing, such as salting (with and without nitrites), smoking, marinating, air-drying, or heating (i.e. ham, bacon, sausages, blood sausages, meat cuts, liver pâté, salami, bologna, tinned meat, luncheon meat, corned beef, and others). The relative risk of colorectal cancer for an intake of > 80 g/day of processed meat compared with < 10 g/day of processed meat was 1.42 (95% CI, 1.09–1.86; P_{trend} = 0.02) (Norat et al., 2005). The relative risk for an increase in intake of 100 g/day of processed meat was 1.32 (95% CI, 1.07–1.63; P_{trend} = 0.009). This was strengthened to 1.70 (95% CI, 1.05–2.76; P_{trend} = 0.03) after calibration using 24-hour recall data from a subset of the study population. The relative risks for the highest versus the lowest quintile were 1.62 (95% CI, 1.04–2.50), 1.48 (95% CI, 0.87–2.53), and 1.19 (95% CI, 0.70–2.01) for rectal, distal, and proximal colon cancer, respectively. No significant differences across cancer sites were observed ($P_{heterogeneity}$ = 0.87). Intake of ham (RR for highest vs lowest intake, 1.12; 95% CI, 0.90–1.37; P_{trend} = 0.44), bacon (HR, 0.96; 95% CI, 0.79–1.17; P_{trend} = 0.34), and other types of processed meats (HR, 1.05; 95% CI, 0.84–1.32; P_{trend} = 0.22) was not significantly related to colorectal cancer risk. [This was a large study in 10 European countries that used extensive dietary questionnaires. Follow-up is virtually complete, and the analyses were adjusted for main potential confounders.] In a substudy of the EPIC-Norfolk study, higher consumption of processed meat was associated with an increased risk of colorectal cancer harbouring a truncating *APC* mutation and, in particular, rectal tumours with GC→AT transitions compared with colorectal cancer without mutations (OR for increment of 19 g/day, 1.68; 95% CI, 1.03–2.75) (Gay et al., 2012).

A case–cohort analysis of the Netherlands Cohort Study (NLCS) included 1535 incident colorectal cancer cases identified after 9.3 years of follow-up through linkage to the Netherlands Cancer Registry (Balder et al., 2006). The relative risks for processed meats (meat items mostly cured, and sometimes smoked or fermented) and colorectal cancer (RR for highest vs lowest quartile) were 1.18 (95% CI, 0.84–1.64; P_{trend} = 0.25) in men and 1.05 (95% CI, 0.74–1.48; P_{trend} = 0.62) in women. No associations were observed for colon or rectal cancer in men or women. In another analysis in the same cohort, consumption of meat products (same definition as for processed meats) was significantly positively associated with risk of colon tumours with a wildtype *K-ras* gene (RR for highest vs lowest quartile of intake, 1.42; 95% CI, 1.00–2.03; P_{trend} = 0.03) (Brink et al., 2005) and *APC*-positive colon cancer (RR for highest vs lowest quartile of intake, 1.61; 95% CI, 0.96–2.71; P_{trend} = 0.04) (Lüchtenborg et al., 2005), but not with other types of colon or rectal tumours. These analyses included more than 430 colon and 150 rectal cancers occurring during 7.3 years of follow-up, excluding the first 2.3 years, and 2948 subcohort members. An analysis of the MIC embedded within the NLCS, which included individuals reporting to be vegetarian or to consume meat only 1 day/week, was conducted with 20.3 years of follow-up (Gilsing et al., 2015). For processed meat, a statistically significant association with rectal cancer was observed (RR, 1.36 for every 25 g/day of intake; 95% CI, 1.01–1.81; P_{trend} = 0.008). No significant association was observed with colon cancer, although a positive association with distal colon cancer was suggested.

The Cancer Prevention Study II (CPS-II) Nutrition Survey enrolled men and women in the USA who completed a mailed FFQ in 1992–1993 (1667 incident colorectal cancer cases) (Chao et al., 2005). The relative risk for the highest quintile compared with the lowest quintile of processed meat intake was

1.13 (95% CI, 0.91–1.41; P_{trend} = 0.02) in women and men combined. A significant trend was observed in men (P_{trend} = 0.03), but not in women (P_{trend} = 0.48). No significant associations were observed with proximal or distal colon cancer, and rectal cancer, although the relative risk estimates were higher for distal and rectal tumours. When long-term consumption of processed meat was considered, based on consumption reported in 1982 and at baseline in 1992–1993, participants in the highest tertile of consumption had an increased risk of distal colon cancer (RR, 1.50; 95% CI, 1.04–2.17). A non-significant 14% and 21% increased risk of cancers of the proximal colon, and rectosigmoid junction and rectum were observed. [The Working Group noted that the 1982 questionnaire did not assess the number of servings per day, and could not differentiate people who ate multiple servings from those who ate processed meat only once per day. It was also not possible to estimate total energy intake from the 1982 dietary questionnaire.]

In the NHS and the HPFS (Bernstein et al., 2015), using cumulative dietary intake data, the relative risk of colorectal cancer per 1 serving/day increment of processed meat was 1.15 (95% CI, 1.01–1.32; P_{trend} = 0.03), and it was 1.08 (95% CI, 0.98–1.18; P_{trend} = 0.13) when diet, as assessed at baseline, was analysed. Using cumulative dietary intake data, the relative risks were 0.99 (95% CI, 0.79–1.24) for proximal colon cancer (1151 cases), 1.36 (95% CI, 1.09–1.69; P_{trend} = 0.006) for distal colon cancer (817 cases), and 1.18 (95% CI, 0.89–1.57) for rectal cancer (589 cases). [The analyses were extensively adjusted for potential risk factors. The use of repeated questionnaires should have reduced dietary measurement error. Several sensitivity and stratified analyses showed the robustness of the results.] In an earlier nested case–control in the NHS including 197 cases identified by the year 2000 (Tranah et al., 2006), colorectal cancer risk was not related to consumption of > 1 slice/week of processed meat (OR, 1.06; 95% CI, 0.73–1.55), > 2 pieces/week of bacon (OR, 0.94; 95% CI, 0.56–1.58), or > 1 hot dog/week (OR, 1.06; 95% CI, 0.68–1.65). Compared with infrequent consumption of these items, no association with all types of processed meats combined was observed. There was no significant interaction on a multiplicative scale between the *MGMT* genotype and intake of processed meat, bacon, and hot dogs in women.

In the Multiethnic Cohort Study, the relative risk of colorectal cancer (n= 3404 cases) for the highest compared with the lowest quintile of processed meat intake was 1.06 (95% CI, 0.94–1.19; P_{trend} = 0.259) (Ollberding et al., 2012). Relative to the significant association that was observed in models adjusted only for age, ethnicity, and sex (HR, 1.25; 95% CI, 1.12–1.40; P < 0.001), this relative risk was attenuated after further adjustment for family history of colorectal cancer, history of colorectal polyps, BMI, pack-years of cigarette smoking, nonsteroidal anti-inflammatory drug use, alcohol consumption, vigorous physical activity, history of diabetes, hormone replacement therapy use (women only), total calories, and dietary fibre, calcium, folate, and vitamin D. [The main strengths of this study were its large size, the ethnic diversity of the study population, and the population-based sampling frame that was used, which allowed for better generalizability of the study results. As indicated in the section on red meats, the Working Group noted that there was a strong attenuation of the association estimates after multivariable adjustment.]

The National Institutes of Health – American Association of Retired Persons (NIH-AARP) Diet and Health Study was based on a cohort of over 500 000 men and women from eight states in the USA, aged 50–71 years at baseline (1995–1996), who completed a validated, 124-item FFQ. In an analysis of 5107 colorectal cancer cases, identified on average during 8.2 years of follow-up (Cross et al., 2007), processed meat consumption was significantly related to colorectal cancer risk. The relative risk for the fifth compared with the first quintile of intake was 1.20 (95% CI, 1.09–1.32;

P_{trend} < 0.001). The relative risks were similar for colon cancer and rectal cancer. Similar results were observed in another study in the same cohort that explored the mechanisms relating colorectal cancer and meat intake (Cross et al., 2010). The overall relative risk for the association between colorectal cancer and processed meat intake was 1.16 (95% CI, 1.01–1.32; P_{trend} = 0.017) for the highest compared with the lowest quintile. For colon and rectal cancer separately, the relative risks for the same comparison were 1.11 (95% CI, 0.95–1.29) and 1.30 (95% CI, 1.00–1.68), respectively. Nitrate and nitrite intake from processed meats was estimated using a database containing measured values of nitrate and nitrite from 10 types of processed meats. The relative risk of colorectal cancer for the highest compared with the lowest quintile of intake of nitrate from processed meat was 1.16 (95% CI, 1.02–1.32; P_{trend} = 0.001; medians of the quintiles, 289.2 μg/1000 kcal per day and 23.9 μg/1000 kcal per day, respectively). The association with nitrite from processed meat did not attain statistical significance (RR for highest vs lowest quintile, 1.11; 95% CI, 0.97–1.25; P_{trend} = 0.055; medians of the quintiles, 194.1 μg/1000 kcal per day and 11.9 μg/1000 kcal per day, respectively). In a lag analysis excluding the first 2 years of follow-up (1941 colorectal cancer cases), the association between processed meat intake and colorectal cancer remained significant (HR, 1.19, 95% CI, 1.02–1.39, P_{trend} = 0.013). Participants in the NIH-AARP study also completed a 37-item FFQ about diet 10 years before baseline. Participants in the highest intake category of processed meat 10 years before baseline had a higher risk of cancer of the colon (RR, 1.30; 95% CI, 1.13–1.51; P_{trend} < 0.01) and rectum (RR, 1.40; 95% CI, 1.09–1.81; P_{trend} = 0.02) than participants in the lower intake category (Ruder et al., 2011). [The Working Group noted that the questionnaire to assess diet 10 years before baseline was not validated, and did not allow for estimation of total energy intake.]

In the United Kingdom Dietary Cohort Consortium (Spencer et al., 2010), processed meat was assessed as ham, bacon, the meat component of sausages, and other items made with processed meat. For a 50 g/day increase in consumption of processed meat, the odds ratio for colorectal cancer was 0.88 (95% CI, 0.68–1.15). The odds ratios for colon and rectal cancer separately were also non-significantly different from unity.

In a pooled analysis of the GECCO study (Kantor et al., 2014), the pooled relative risk of colorectal cancer for each serving per day increase in intake of processed meats was 1.48 (95% CI, 1.30–1.70) for all studies combined. [The main strength of the study was the large number of cases included in the analysis.] In genome-wide diet–gene interaction analyses in GECCO, which included five retrospective case–control studies and five case–control studies nested in prospective studies, there was a positive interaction between rs4143094 (10p14/near *GATA3*) and processed meat consumption (OR, 1.17; 95% CI, 1.11–1.23; P = 8.7E−09), which was consistently observed across studies ($P_{heterogeneity}$ = 0.78) (Figueiredo et al., 2014). The risk of colorectal cancer associated with processed meat was increased among individuals with the rs4143094–TG (OR, 1.20; 95% CI, 1.13–1.26) and –TT genotypes (OR, 1.39; 95% CI, 1.22–1.59), and null among those with the –GG genotype (OR, 1.03; 95% CI, 0.98–1.07). In another study in GECCO on gene–environment interactions and colorectal cancer susceptibility loci, no interaction with processed meat was detected (all studies combined) (Hutter et al., 2012).

In the prospective study conducted by the Norwegian National Health Screening Service (Gaard et al., 1996), colon cancer risk was higher in women who consumed fried or poached sausages as their main meal ≥ 5 times/month compared with those who reported a consumption of < 1 time/month (RR, 3.50; 95% CI, 1.02–11.9; P_{trend} = 0.03). Among men, a similar, but not significant, association was observed

(RR, 1.98; 95% CI, 0.70–5.58; P_{trend} = 0.35). [The Working Group noted that only specific types of processed meats were investigated. The analyses were only adjusted for age. The 50 535 participants were relatively young (age, 20–54 years) at recruitment in 1977–1983, and only 143 cases of colon cancer were identified through linkage to the Norwegian Cancer Registry after 11.4 years of follow-up.]

(c) Red meat and processed meat combined

Several studies reported on the risk of colorectal cancer associated with measures of meat consumption, which included processed meats and unprocessed red meats, both red and white meats, or meats without a clear definition. The Working Group considered these data to be less informative than associations with red meat and processed meat considered separately. Key findings from this group of studies are summarized in this section and given in Table 2.2.1.

Several other studies reported data for specific red meat items, such as beef or pork, or for unprocessed red meat or processed meat separately, as well as for a broader category including both types of meats (e.g. Bostick et al., 1994; Pietinen et al., 1999; Lin et al., 2004; Larsson et al., 2005a; Norat et al., 2005; Spencer et al., 2010; Takachi et al., 2011; Ollberding et al., 2012; Bernstein et al., 2015). For these studies, the more informative data for red meat and for processed meat are reviewed in the preceding sections, but data for the combined category are not presented.

In the Finnish Mobile Clinic Health Examination Survey (109 colorectal cancer cases), the relative risks for the highest compared with the lowest quartile of red meat intake were 1.50 (95% CI, 0.77–2.94) for colorectal cancer, 1.34 (95% CI, 0.57–3.15) for colon cancer, and 1.82 (95% CI, 0.60–5.52) for rectal cancer (Järvinen et al., 2001). [The Working Group considered that the category of red meat may have included processed items. In contrast with other studies, there was a significant increase of colorectal cancer in participants consuming poultry compared with non-consumers. An important limitation of the study was the small size.]

In the Physicians' Health Study (PHS) (originally designed as a double-blind trial of aspirin and β-carotene as preventive measures for cardiovascular disease and cancer), diet at enrolment was assessed using an abbreviated FFQ, in which red and processed meat intake included beef, pork, lamb, and hot dogs. A case–control study nested in the PHS cohort (212 colorectal cancer cases) (Chen et al., 1998) found that combined red and processed meat intake was not significantly related to colorectal cancer risk (RR, 1.17; 95% CI, 0.68–2.02; for ≥ 1 vs ≤ 0.5 servings/day). There was no significant interaction with *NAT1*/*NAT2* genotypes (all $P_{interaction}$ > 0.16). [The Working Group noted that the definition of red meat included hot dogs, and analyses were not controlled for total energy intake, BMI, and other important confounders.]

A case–cohort study done within the CLUE II cohort (250 genotyped cases) (Berndt et al., 2006) reported a non-statistically significant positive association between red meat [including processed meat] intake and colorectal cancer risk (RR for highest vs lowest tertile, 1.32; 95% CI, 0.86–2.02), when adjusting for age, sex, and total energy. [The main focus of this paper was to explore gene–environment interactions with nucleotide excision repair genes; therefore, analyses of the main effects of meat were limited.]

A nested case–control study, the EPIC-Norfolk component of EPIC, investigated the effect of the variant genotype *MGMT* Ile143Val on colorectal cancer risk among 273 colorectal cancer cases and 2984 matched controls. The odds ratio was 1.43 (95% CI, 0.82–2.48; $P_{interaction}$ = 0.04) for the variant genotype carriers and red and processed meat intake above the median compared with common genotype carriers and red and processed meat intake below the median (Loh et al., 2010). The polymorphism was not related to colorectal cancer risk. [The Working Group noticed that red and processed meat intakes were assessed according to baseline 7-day food diary data.]

The Breast Cancer Detection Demonstration Project (BCDDP) (487 colorectal cancer cases) (Flood et al., 2003) reported a relative risk of 1.04 (95% CI, 0.77–1.41) for > 52.2 g/1000 kcal compared with < 6.1 g/1000 kcal (quintiles) of combined red and processed meat intake. [The Working Group noted that the associations became stronger after multiple adjustments.]

In a prospective study based on a trial of screening for breast cancer, the Canadian National Breast Screening Study (CNBSS), participants reported their diet in 1982 using an 86–food item SQFFQ (Kabat et al., 2007). Red meat intake, defined as beef, veal, pork, ham, bacon, and pork-based luncheon meats, was related to an increased risk of rectal cancer, but not colon cancer. For the highest compared with the lowest quintile (> 40.3 and < 14.2 g/day, respectively), the relative risks were 1.12 (95% CI, 0.86–1.46) for colorectal cancer (617 cases), 0.88 (95% CI, 0.64–1.21) for colon cancer (428 cases), and 1.95 (95% CI, 1.21–3.16; P_{trend} = 0.008) for rectal cancer (195 cases). No associations were observed with cancers of the proximal and distal colon (data were not shown).

In a study based on the Multiethnic Cohort, no clear evidence was found for an interaction with *NAT2* or *NAT1* acetylator genotypes on the association between colorectal cancer risk and red and processed meat intake, or meat doneness preference in 1009 cases and 1522 controls (Nöthlings et al., 2009).

In the CPS-II Nutrition Survey (1667 colorectal cancer cases) (Chao et al., 2005), red meat was defined as including bacon, sausage, liver, hot dogs, ham, bologna, salami, and lunchmeat, as well as unprocessed beef and pork. The relative risk for colon cancer and red meat (as defined above) consumption assessed at baseline was 1.15 (95% CI, 0.90–1.46; P_{trend} = 0.04) in men and women combined. Consumption of these meats was related to an increased risk of cancers of the rectosigmoid junction and rectum (RR, 1.71; 95% CI, 1.15–2.52; P_{trend} = 0.007; for highest vs lowest quintile), but not to cancers of the rectosigmoid junction only (numerical data were not shown). [The Working Group noted that an earlier questionnaire used to estimate long-term consumption assessed only frequency of intake; thus, estimation of total energy intake from that questionnaire was not possible.]

The NIH-AARP study defined red meat as beef, pork, and lamb, including bacon, cold cuts, ham, hamburger, hot dogs, liver, sausage, and steak. After an average follow-up of 7 years, 2719 colorectal cancer cases were identified. Red meat and processed meat were related to an increased risk of colon and rectal cancer. The relative risks for the highest compared with the lowest quintile of red and processed meat intake (61.6 and 9.5 g/1000 kcal, respectively) were 1.24 (95% CI, 1.09–1.42; P_{trend} < 0.001) for colorectal cancer, 1.21 (95% CI, 1.03–1.41; P_{trend} < 0.001) for colon cancer, and 1.35 (95% CI, 1.03–1.76; P_{trend} = 0.024) for rectal cancer (Cross et al., 2007, 2010). Significant associations were also observed when intake was analysed on a continuous scale. The relative risks were similar for proximal and distal colon cancer. The findings remained the same after exclusion of the first 2 years of follow-up. Study participants also completed a 37-item FFQ on dietary intake 10 years before baseline (Ruder et al., 2011). Participants in the highest intake category of red and processed meat 10 years before baseline (defined as ground beef, roast beef or steak, cold cuts, bacon or sausage, and hot dogs) had a higher risk of colon cancer (RR, 1.46; 95% CI, 1.26–1.69; P_{trend} = 0.01) than participants in the lowest intake category. A significant trend was observed for the rectum (RR, 1.24; 95% CI, 0.97–1.59; P_{trend} = 0.03). [The Working Group noticed that the FFQ to assess diet 10 years before baseline was not validated, and did not allow for estimation of total energy intake for adjustment of the analyses.]

(d) Haem iron

Data on the association between colorectal cancer risk and haem iron intake were available from five cohort studies reviewed in this section (Lee et al., 2004; Larsson et al., 2005b; Balder et al., 2006; Kabat et al., 2007; Cross et al., 2010). One study reported a statistically significant positive association with proximal, but not distal colon cancer (Lee et al., 2004), and another found a significant positive association with colon cancer after excluding 2 years of follow-up when registry data were believed to be incomplete (Balder et al., 2006). Relative risks were null or non-significantly increased (range, 0.99–1.31) in three other studies that reported data on colon cancer (Larsson et al., 2005b; Kabat et al., 2007; Cross et al., 2010), rectal cancer (Kabat et al., 2007; Cross et al., 2010), and colorectal cancer overall (Kabat et al., 2007; Cross et al., 2010). [The Working Group noted that the overall evidence on haem iron was limited by the possibility of publication bias and the few databases for estimating haem iron intake from dietary questionnaires.]

2.2.2 Case–control studies

Numerous case–control studies have examined the association between red or processed meat intake and risk of colorectal cancers. This section presents studies by how meat was defined in the following order: red meat and processed meat separately, red meat and processed meat combined, and then red meat, unclear whether fresh or processed.

In reviewing and interpreting the available literature, the Working Group considered for each of these categories the criteria summarized in Section 2.1 and the greatest weight was given to studies that met the following criteria:

- Had an unambiguous definition of red and processed meat (studies that reported data for unprocessed red and/or processed meat separately, and/or listed subtypes of meats included in each meat definition) (see criterion 1 in Section 2.1.1);
- Met the definition of a population-based study, or included hospital-based cases using approaches that ensured a representative sample of the underlying population (e.g. community hospitals that serve specific regions in a country) and population-based controls (see criterion 3 in Section 2.1.3);
- Used a previously validated dietary instrument (see criterion 4 in Section 2.1.4); and
- Considered detailed assessment for potential confounders, in particular total energy intake (see criterion 5 in Section 2.1.5).

The Working Group also considered as informative studies that met these criteria but showed limitations in criteria 3, 4, or 5 summarized above. Sample size was considered for informativeness (see criterion 2 in Section 2.1.2). The main limitations identified by the Working Group are noted between brackets in the description of each paper.

The Working Group gave less weight to other studies that showed important limitations in criterion 3, 4, or 5 above, and/or defined "total red meat" without further clarifying whether processed meat was included.

The Working Group excluded the following papers due to the reasons described below. None of the excluded studies are presented in the tables.

Studies with fewer than 100 cases were excluded because of limited statistical power (e.g. Phillips, 1975; Dales et al., 1979; Pickle et al., 1984; Tajima & Tominaga, 1985; Vlajinac et al., 1987; Wohlleb et al., 1990; Nashar & Almurshed, 2008; Guesmi et al., 2010; Ramzi et al., 2014).

Certain dietary patterns (e.g. traditional "Western-type" diet) are often characterized by a higher intake of red and processed meats, but these patterns also capture other foods that tend to be consumed with a diet high in red and processed meats, such as refined grains and a high intake of sugar. Thus, these studies are not specific enough to address the role of red meat and processed meats. Therefore, the Working Group also excluded from this review studies that reported on dietary patterns or dietary diversity, or only examined red meat in combination with other foods (e.g. McCann et al., 1994; Slattery et al., 1997, 2003; Rouillier et al., 2005; Satia et al., 2009; De Stefani et al., 2012b; Pou et al., 2012, 2014; Chen et al., 2015). In addition, the Working Group also excluded studies that reported on "meat" variables without a clear definition of what types of meats were included, making it impossible to rule out the inclusion of poultry and/or fish (e.g. Zaridze et al., 1992; Roberts-Thomson et al., 1996; Ping et al., 1998; Welfare et al., 1999; Zhang et al., 2002; Kim et al., 2003; Yeh et al., 2003, 2005; Kuriki et al., 2006; Little et al., 2006; Wakai et al., 2006; Skjelbred et al., 2007; Sriamporn et al., 2007; Jedrychowski et al., 2008; Arafa et al., 2011; Mahfouz et al., 2014; Pimenta et al., 2014), and studies that stated clearly that they had included poultry in their meat definition (e.g. Hu et al., 1991; Fernandez et al., 1996; Kuriki et al., 2005; Ganesh et al., 2009).

The Working Group also excluded studies that did not provide sufficient information to abstract risk estimates for red and processed meat intake per se or within strata defined by genotype (e.g. Gerhardsson de Verdier et al., 1990; Ghadirian et al., 1997; Keku et al., 2003; Forones et al., 2008; da Silva et al., 2011; Gialamas et al., 2011; Silva et al., 2012; Zhivotovskiy et al., 2012; Angstadt et al., 2013; Helmus et al., 2013). Studies were not described if they only reported on estimated amounts of carcinogens derived from meat, and not on meat variables. Of note, studies that reported on the same study population, published at different times, were generally summarized together, if applicable. The most recent, complete, or informative publication was included.

A few studies reported on selected red meat types (e.g. beef), groups of red meat types (e.g. beef/pork), or total processed meats, and presented estimates for total red meat variables, including processed meats. For these studies, the Working Group only summarized the estimates for red meat types and/or processed meat, but not the estimates for the combination of both, as the Working Group did not find these as informative.

Studies that unambiguously defined red meat as unprocessed only, or as unprocessed and processed combined, or did not provide an unambiguous definition and referred to "total red meat", are summarized in Table 2.2.3. Studies that unambiguously defined processed meat are summarized in Table 2.2.4.

(a) Red meat

See Table 2.2.3

(i) Studies considered to be informative

The case–control studies that follow reported results for red meat and were considered informative by the Working Group. These studies were given more weight in the evaluation. The studies are presented in order by sample size, from largest to smallest.

Joshi et al. (2015) (3350 cases, 3504 controls) presented results for colorectal cancer, and for colon and rectal cancer, and for subtypes of colorectal cancer defined by mismatch repair (MMR) proficiency from a population-based study done in Canada and the USA. They reported a non-statistically significant positive association with red meat (Q5 vs Q1 OR, 1.2; 95% CI, 1.0–1.4; P_{trend} = 0.085), with no associations for total beef or pork, and a marginal positive association for organ meats (Q5 vs Q1 OR, 1.2; 95% CI, 1.0–1.4; P_{trend} = 0.058). No differences were observed between colon and rectal cancer, and no other differences were observed between MMR-proficient and MMR-deficient tumours. When cooking methods were considered, stronger, statistically significant associations emerged; a positive association was observed for pan-fried beef steak (Q4 vs Q1 OR, 1.3; 95% CI, 1.1–1.5; $P_{trend} < 0.001$), which was stronger among MMR-deficient cases. A positive association was also observed with pan-fried hamburgers among MMR-deficient colorectal cancer cases (Q4 vs Q1 OR, 1.5; 95% CI, 1.0–2.1; $P_{trend} < 0.01$). Among oven-broiled meats, a statistically significant positive association was reported for short ribs or spare ribs (Q4 vs Q1 OR, 1.2; 95% CI, 1.0–1.5; $P_{trend} = 0.002$), which was restricted and stronger among MMR-deficient colorectal cancer cases (Q4 vs Q1 OR, 1.9; 95% CI, 1.12–3.00; $P_{trend} = 0.003$). No associations were reported for oven-broiled beef steak or hamburgers, grilled beef steak or short ribs or spare ribs; instead, an inverse association was reported for grilled hamburgers (Q4 vs Q1 OR, 0.8; 95% CI, 0.7–0.9; $P_{trend} = 0.002$). When use of marinades was considered ("Asian-style" vs "Western-style"), there was evidence that the use of "Asian-style" marinades (soy-based) was an effect modifier of the association with red meat, suggesting a stronger and statistically significant association among individuals who reported never using a soy-based marinade with their meats (Q5 vs Q1 OR, 1.3; 95% CI, 1.1.–1.6; $P_{trend} = 0.007$; $P_{interaction} = 0.008$). Overall, it was indicated that, given the many estimates obtained, if a Bonferroni correction was applied for multiple testing, the only statistically significant association would be the association between pan-fried beef steak and colorectal cancer risk, particularly for MMR-deficient tumours. The estimates for three different heterocyclic aromatic amines (HAAs), PhIP, DiMeIQx, and MeIQx were presented, and a positive association with increasing levels of DiMeIQx and MMR-deficient colorectal cancer was reported.

As part of a multicancer, population-based case–control study in Canada, which examined 18 cancer sites, Hu et al. (2007) (1723 cases, 3097 controls) reported that beef, pork, or lamb as a main dish and hamburger intake were positively associated with risk of proximal colon cancers in men only, but not in women. In men, the odds ratios for the highest versus the lowest tertile of intake (servings/week) were 1.5 (95% CI, 1.0–2.4; $P_{trend} = 0.05$) for beef, pork, or lamb as a main dish and 2.1 (95% CI, 1.3–3.5; $P_{trend} = 0.006$) for hamburger. A borderline positive association between hamburger intake in men and distal colon cancers was also observed. The odds ratio for the second tertile versus the lowest tertile was 1.4 (95% CI, 1.0–1.9), and the odds ratio for the highest tertile versus the lowest tertile was 1.4 (95% CI, 0.9–2.0; $P_{trend} = 0.11$).

Kampman et al. (1999) (1542 cases, 1860 controls) conducted a population-based case–control study in the USA, and reported that red meat intake was not associated with colon cancer in men (highest vs lowest intake OR, 0.9; 95% CI, 0.7–1.3) or women (OR, 1.0; 95% CI, 0.7–1.5). In both men and women, higher doneness was not significantly associated with risk of colon cancer (well-done vs rare OR, 1.2; 95% CI, 0.9–1.5). Further, no significant interactions between red meat and the examined *NAT2* and *GSTM1* gene variants were found.

In a companion paper, Slattery et al. (1998) examined associations separately by stage of disease. Some non-significant positive associations between red meat and colon cancer by stage were noted. In men, the odds ratios for > 7.9 oz/week versus ≤ 2.6 oz/week were 1.5 (95% CI, 0.9–2.3) for local, 1.2 (95% CI, 0.8–1.9) for regional, and 0.9 (95% CI, 0.4–1.8) for distant metastasis. In women, the odds ratios for > 5.4 oz/week versus ≤ 1.7 oz/week was 1.2 (95% CI, 0.7–2.1) for local, 1.1 (95% CI, 0.7–1.8) for regional, and 0.5 (95% CI, 0.2–1.2) for distant metastasis. Other papers by Slattery et al. (2000, 2002a, b) examined associations by the molecular characteristics of the tumours and borderline positive associations between red meat intake and colon cancers were observed among cancers with *p53* mutations.

In a related publication (Murtaugh et al., 2004) (952 rectal cancer cases, 1205 controls), no associations were observed between red meat intake and rectal cancers. The odds ratio for men consuming ≥ 6.1 servings/week versus < 2.9 servings/week was 1.08 (95% CI, 0.77–1.51). The odds ratio for women consuming ≥ 4.2 servings/week versus < 1.9 servings/week was 1.05 (95% CI, 0.72–1.53). A higher intake of well-done red meat was associated with a higher risk of rectal cancers in men compared with rare-done meat (OR, 1.33; 95% CI, 0.98–1.79; P_{trend} = 004). *NAT2*-phenotype and *GSTM1* did not consistently modify the rectal cancer risk associated with red meat intake. Follow-up papers combining the two aforementioned study populations reported no evidence for an interaction between red meat intake, cooking temperatures, use of red meat drippings red meat mutagen index or *CYP1A1* genotype and colorectal cancer . Nonetheless in men carrying the CYP1A1*1 allele, a higher intake of well-done red meat compared with rare-done meat intake was associated with a higher risk of colorectal cancer (OR, 1.37; 95% CI, 1.06–1.77; P_{trend} < 005). (Murtaugh et al., 2005). On the other hand, Murtaugh et al. (2006) found a higher risk of rectal cancer among those with a high intake of red meat and the vitamin D receptor gene FF genotype only. For high versus low intake of red meat for the FF genotype, the odds ratio was 1.45 (95% CI, 0.97–2.19), and for the Ff/ff genotypes combined, the odds ratio was 1.08 (95% CI, 0.74–1.58; $P_{interaction}$ = 0.06 additive, 0.09 multiplicative). [The Working Group noted that, in all these studies, the red meat variable included ham, likely baked ham, which is technically a processed meat.]

In a population-based case–control study in the USA (1192 colorectal cases, 1192 controls), Le Marchand et al. (1997) reported a positive association with beef/veal/lamb that was statistically significant among men (highest vs lowest quartile OR, 2.1; 95% CI, 1.4–3.1; P_{trend} < 0.0001), but not among women (highest vs lowest quartile OR, 1.3; 95% CI, 0.9–2.1; P_{trend} = 0.5). There was no association with pork. The odds ratio for the highest versus the lowest quartile in men was 1.2 (95% CI, 0.8–1.9; P_{trend} = 0.90), and the odds ratio in women was 0.7 (95% CI, 0.4–1.2; P_{trend} = 0.3). [The Working Group noted that the researchers also reported on a total red meat variable with more red meat items, but it also included processed meats. A positive statistically significant association was reported for this variable.]

Miller et al. (2013) (989 cases, 1033 controls) conducted a population-based study in the USA, and reported no association between red meat intake and colorectal cancer, and no differences between colon and rectal cancer. When considering cooking methods, they reported a positive association with pan-fried red meat (Q5 vs Q1 OR, 1.26; 95% CI, 0.93–1.70; P_{trend} = 0.044), but no associations with grilled/barbecued red meat, microwaved/baked red meat, broiled red meat, or red meat cooked rare/medium or well done/charred. A positive association was reported for estimated total PhIP and rectal cancer (Q5 vs Q1 OR, 1.33; 95% CI, 0.88–2.02; P_{trend} = 0.023). [The Working Group noted the somewhat low participation rate in cases and controls (57% cases, 51% controls), which raised concerns about possible bias introduced by the types of individuals who agreed to participate.]

The North Carolina Colon Cancer Study–Phase II, a population-based case–control study conducted in the USA (945 cases, 959 controls) in Whites and African Americans (Williams et al., 2010), reported that red meat was not significantly associated with risk of distal colorectal cancers. The odds ratios for the highest versus the lowest quartile were 0.66 (95% CI, 0.43–1.00; P_{trend} = 0.90) in Whites and 0.64 (95% CI, 0.27–1.50; P_{trend} = 0.94) in African Americans. [The Working Group noted that distal cancers included cancers of the sigmoid, rectosigmoid, and rectum. Controls had a lower response rate compared with cases (56% vs 74%).]

Chiu et al. (2003) reported on a population-based case–control study in Shanghai, China (931 colon cancer cases, 1552 controls).

Positive associations were observed between red meat and risk of colon cancer for both men and women; however, the associations were only statistically significant among men. The odds ratios for the highest versus the lowest quartile of intake (servings/month) were 1.5 (95% CI, 1.0–2.1; P_{trend} = 0.03) among men and 1.5 (95% CI, 1.0–2.2; P_{trend} = 0.08) among women. [The Working Group noted that a modified version of the validated Block FFQ was used, but no details regarding whether this modified FFQ was validated were provided. In addition, no reference was provided to confirm whether the modified FFQ captured the foods mostly eaten in that area.]

Using data from the Fukuoka Colorectal Cancer Study, Kimura et al. (2007) (840 hospital-based cases, 833 population-based controls) reported no significant associations between intake of beef/pork and colorectal cancer, regardless of the cancer subsite. There were some significant associations for the quintiles, but not for the highest quintile, and overall P_{trend} was not significant. [The Working Group noted that, even though the authors labelled the study as a population-based case–control study, the cases were recruited in hospitals, and the coverage of cases was not reported. The response rate of the controls (60%) was also considerably lower than that of the cases (80%).]

Tuyns et al. (1988) conducted a population-based study in Belgium (818 colorectal cases, 2851 controls). Higher beef consumption was associated with a higher risk of colon cancer (Q4 vs Q1 OR, 2.09; 95% CI, not reported; P_{trend} < 0.001), but not rectal cancer (Q4 vs Q1 OR, 0.71; P_{trend} = 0.14). Pork intake was not associated with risk of colon or rectal cancers, and a higher pork intake was associated with a lower risk of colon cancer (Q4 vs Q1 OR, 0.39; P_{trend} < 0.001). [The lack of adjustment for energy intake was noted as a limitation. A previous report stated that energy intake was similar between cases and controls, suggesting that it may not have been a confounder of meat in this study; however, data were not provided, and there was unclear validation of the questionnaire. The total pork variable included smoked pork.]

In another population-based case–control study by Le Marchand et al. (2001) (727 colorectal cancer cases, 727 controls), no association was observed between red meat intake and colorectal cancer risk when considering men and women combined. However, among participants with the *NAT2* genotype (rapid acetylators) and *CYP1A2* phenotype, an above the median, higher intake of well-done red meat was significantly associated with a higher risk of colorectal cancer (OR, 3.3; 95% CI, 1.3–8.1). In a subsequent paper (Le Marchand et al., 2002b) on the same study population (Le Marchand et al., 2001), associations with "total" red meat [not defined] intake appeared to be restricted to rectal cancer only (highest vs lowest tertile OR, 1.7; 95% CI, 1.0–3.0; P_{trend} = 0.16). No association was observed for colon cancer. Positive associations were reported for total HAAs, in particular DiMeIQx and MeIQx. Interactions were also reported, suggesting that smokers who preferred their red meat well done, and had a rapid metabolic phenotype for both NAT2 and CYP1A2 exhibited a risk that was almost nine times higher compared with those with low NAT2 and CYP1A2 activities and who preferred meat rare or medium done. Well-done red meat was not associated with risk among never-smokers or smokers with the slow or intermediate phenotype. A follow-up study on the same study population (Le Marchand et al., 2002a) reported that participants with a high consumption of red meat and the insert polymorphism in CYP2E1 had approximately a twofold increased risk of rectal cancers compared with those with no insert polymorphism who consumed a low intake of red meat (OR, 2.1; 95% CI, 1.2–3.7).

Gerhardsson de Verdier et al. (1991) conducted a population-based case–control in Stockholm, Sweden (559 colorectal cancer cases, 505 controls). For colon cancer, significant positive associations were observed with boiled beef/pork (OR, 1.8; 95% CI, 1.2-2.6 P_{trend} = 0.004), and for all cases with oven-roasted beef/pork (OR,1.8; 95% CI,, 1.1–2.9 P_{trend} = 0.02), and boiled beef/pork (OR, 1.9; 95% CI, 1.2–3.0 P_{trend} = 0.007). [The Working Group noted that the researchers did not provide an effect estimate for beef/pork without considering the cooking methods. They only asked about beef and pork, so it was unclear whether this was really representative of the subtypes of red meats consumed in that population. Information on validation of the dietary instrument was not provided.]

A hospital-based study done in the United Kingdom (Turner et al., 2004) (484 cases, 738 controls) reported that higher red meat intake was associated with a higher risk of colorectal cancer (highest vs lowest quartile, servings/month, OR, 2.3; 95% CI, 1.6–3.5; P_{trend} = 0.0001). A significant interaction between red meat intake and *GSTP1* ($P_{interaction}$ = 0.02, after adjustment for potential confounders) and *NQO1* predicted phenotype ($P_{interaction}$ = 0.01) on risk of colorectal cancer was reported. The original study (Barrett et al., 2003) reported no significant interaction between *NAT2* genotype and red meat intake. [The Working Group noted that the associations were reported after adjustment for total energy intake; however, lifestyle factors, such as physical activity, alcohol intake, or smoking, were not adjusted for.]

A hospital-based study done in Córdoba, Argentina (Navarro et al., 2003) (287 colorectal cases, 564 controls), reported that beef intake was inversely associated with colorectal cancer, particularly lean beef. The odds ratios for the highest versus the lowest tertile of intake (g/day) were 0.78 (95% CI, 0.51–1.18) for fatty beef and 0.67 (95% CI, 0.40–0.97) for lean beef. Pork (highest versus the lowest tertile) intake was not associated with risk of colorectal cancer (OR, 0.92; 95% CI, 0.62–1.36) (Navarro et al., 2003). A follow-up report on the same study (Navarro et al., 2004) (296 cases, 597 controls) reported that a higher intake of darkly browned red meat was associated with a higher risk of colorectal cancer, particularly for barbecued, iron pan–cooked, and fried red meat, but not roasted red meat. [Limitations noted by the Working Group included lack of report on the time between diagnosis and interview, lack of clarity whether total red meat included processed meat or not, and lack of adjustment for physical activity.]

Kampman et al. (1995) conducted a population-based study in the Netherlands (232 colon cancer cases, 259 controls), and reported no association between unprocessed red meat intake and colon cancer among men, but a positive association among women. For women consuming > 83 g/day versus < 38 g/day, the odds ratio was 2.35 (95% CI, 0.97–5.66; P_{trend} = 0.04), and for men consuming > 102 g/day versus < 60 g/day, the odds ratio was 0.89 (95% CI, 0.43–1.81; $P_{interaction}$ by sex = 0.02). The ratio of red meat to vegetables plus fruit was also positively associated with colon cancer in women. For the highest versus the lowest category, in men, the odds ratio was 1.18 (95% CI, 0.57–2.43; P_{trend} = 0.89), and in women, the odds ratio was 3.05 (95% CI, 1.39–6.17; P_{trend} = 0.0006; $P_{interaction}$ = 0.0001). [The Working Group noted that no information was provided about the validity of the FFQ.]

Steinmetz & Potter (1993) conducted a population-based case–control study in Australia (220 colon cases, 438 controls). Red meat intake was positively, but not significantly, associated with risk of colon cancer in both men and women. The odds ratios for the highest versus the lowest quartile were 1.48 (95% CI, 0.73–3.01) in women and 1.59 (95% CI, 0.81–3.13) in men. [The Working Group concluded that a key limitation was the lack of adjustment for energy intake.]

Juarranz Sanz et al. (2004) conducted a population-based study in Madrid, Spain (196 colorectal cases, 196 controls). They reported positive associations with red meat (g/day) (OR for red meat as a continuous variable, 1.026; 95% CI, 1.010–1.040; P_{trend} = 0.002) and organ meats (also considered as red meat) (OR, 1.122; 95% CI, 1.027–1.232; P_{trend} = 0.015). [The Working Group concluded that the main weakness was the lack of consideration of important confounders, such as total energy intake or BMI, although it was unclear whether the researchers did or did not find evidence of confounding.]

Boutron-Ruault et al. (1999) (171 colorectal cancer cases, 309 population-based controls) conducted a population-based study in France, and reported a non-statistically significant positive association with beef (OR for highest vs lowest quartile, g/day, 1.4; 95% CI, 0.8–2.4; P_{trend} = 0.31) and lamb (OR for high vs low, g/day, 1.3; 95% CI, 0.9–1.9; P = 0.2), and no association with pork (OR for highest vs lowest quartile, g/day, 1.0; 95% CI, 0.7–2.8). A statistically significant positive association was reported for offal (OR, 1.7; 95% CI, 1.1–2.8; P_{trend} = 0.04), which seemed stronger for rectal than colon cancer. [The Working Group noted that there was no consideration of additional potential confounders, such as BMI, alcohol, or smoking status. A difference in the response rates of cases and controls (80% vs 53%) was noted.]

(ii) Studies considered less informative

The following case–control studies that presented results for red meat were considered less informative by the Working Group. The studies are presented in order by sample size, from largest to smallest.

The hospital-based study by Di Maso et al. (2013) (2390 colorectal cases, 4943 controls) that included previous publications from the same group (i.e. Franceschi et al., 1997 and Levi et al., 1999), reported that a higher red meat intake was associated with a higher risk of colon and rectal cancers in men and women. The odds ratios per 50 g/day increase for colon cancer were 1.17 (95% CI, 1.08–1.26) in men and 1.11 (95% CI, 0.98–1.26) in women, and for rectal cancer, the odds ratios were 1.15 (95% CI, 1.02–1.29) in men and 1.32 (95% CI, 1.54–1.29) in women. Associations did not differ by cooking practice, except for rectal cancers, where the strongest associations were seen with fried/pan-fried red meat intake. The odds ratios per 50 g/day increase were 1.24 (95% CI, 1.07–1.45) for roasting/grilling, 1.32 (95% CI, 1.10–1.58) for boiling/stewing, and 1.90 (95% CI, 1.38–2.61) for frying/pan-frying ($P_{heterogeneity}$ = 0.06). [The Working Group concluded that the limitations included lack of adjustment for total caloric intake and physical activity. The researchers also did not assess the quantiles and differences in standard serving sizes between regions, which may have affected the calculated grams of intake per day.]

The hospital-based study by Tavani et al. (2000) (828 colorectal cases, 7990 controls) in Italy reported a positive association between the highest intake of red meat and both colon (highest vs lowest tertile OR, 1.9; 95% CI, 1.5–2.3; P_{trend} <0.01) and rectal cancer (highest vs lowest tertile OR, 1.7; 95% CI, 1.3–2.2; P_{trend} <0.01). [The Working Group concluded that the main weaknesses were lack of validation of the FFQ, which only included 40 food items, and lack of adjustment for total energy, BMI, and physical activity.]

A hospital-based case–control study was conducted in Harbin, China, by Guo et al. (2015) (600 colorectal cases, 600 controls), and reported a positive association between servings of red meat per week and colorectal cancer risk (> 7 vs < 7 servings/week OR, 1.5; 95% CI, 1.1–2.4; P_{trend} = 0.001). No evidence of interaction was observed for two polymorphisms in the *ADIPOQ* gene. [The Working Group concluded that the main weaknesses were lack of consideration of total energy intake and other dietary factors, and lack of information on whether the FFQ was validated.]

Muscat & Wynder (1994) conducted a hospital-based case–control study (511 colorectal cases, 500 controls) in the USA. No associations were observed between beef doneness and risk of colorectal cancer in men or women. The odds ratios for well-done versus rare beef were 1.15 (95% CI, 0.6–2.4) in men and 1.0 (95% CI, 0.6–1.5) in women. Estimates were only adjusted for matching variables. Results were only presented for beef doneness as exposure. [The Working Group concluded that the limitations included poor focus on red meat, by reporting only on well-done beef, and lack of validation of exposure survey tools.]

Kotake et al. (1995) conducted a hospital-based case–control study in Japan (363 colorectal cases, 363 controls). No significant associations between beef or pork intake and colon and rectal cancer were found. For an intake of > 3–4 times/week versus 1–2/week, the odds ratios for colon cancer were 1.7 (95% CI, 0.85–3.28) for beef and 0.8 (95% CI, 0.50–1.33) for pork, and the odds ratios for rectal cancer were 0.8 (95% CI, 0.38–1.52) for beef and 1.6 (95% CI, 0.95–2.73) for pork. [The Working Group concluded that the limitations were lack of use of quantiles for exposure variables, unclear validation status of the FFQ, lack of adjustment for energy intake, and inclusion of hospital controls with other tumours, including 49 cases with upper gastrointestinal tract cancers.]

A hospital-based study was done in Thailand (Lohsoonthorn & Danvivat, 1995) (279 colorectal cases, 279 controls), and reported null associations with either beef or pork intake. [The Working Group noted that the main weakness of this study was lack of consideration of any potential confounders.]

Freedman et al. (1996) reported on a hospital-based study in New York, USA (163 cases, 326 controls). They reported a positive association with beef (highest vs lowest tertile OR, 2.01; 95% CI, 0.96–4.20; P_{trend} = 0.03). They also subtyped tumours based on p53 expression and reported that the association with beef intake (highest vs lowest) was stronger among tumours that lacked overexpression of p53 (OR, 3.17; 95% CI, 1.83–11.28; P_{trend} = 0.006). The association was very modest and not statistically significant among p53+ tumours. [The Working Group concluded that the limitations of this study were lack of consideration of total energy adjustment, and lack of consideration of other dietary and lifestyle covariates.]

A population-based study in China (Chen et al., 2006) (140 colorectal cases, 343 controls) reported no association between red meat and colon cancer, but a non-significant association with rectal cancer (OR, 1.4; 95% CI, 0.7–2.82). Interactions with *SULT1A1* were also reported, without conclusive results. [The Working Group concluded that the limitations included lack of adjustment for total energy intake and other potential confounders, and unclear definition of red meat.]

A population-based case–control study in southern Italy (Centonze et al., 1994) (119 cases, 119 controls) reported a lack of association between beef intake and colorectal cancer risk; odds ratio for medium (>22 g/day) vs low (~21 g/day) intake of beef was, 0.95; 95% CI, 0.50–1.80. [The Working Group concluded that the use of a validated questionnaire was among the major strengths. The limitations were a small sample size, the fact that the researchers presented results for beef only, and the lack of total caloric intake adjustment.]

The study by Iscovich et al. (1992) (110 colon cancers, 220 controls) in Argentina reported a positive association with red meat intake, which was observed only in the second quartile (Q1 vs Q2 OR, 2.29; 95% CI, 1.03–5.08; Q1 vs Q3 OR, 0.82; 95% CI, 0.39–1.70; Q1 vs Q4, no estimates presented). [The Working Group concluded that the limitations of this study included lack of information about FFQ validation, lack of adjustment for energy intake, and limited distribution of red meat, given the very high consumption of red meat in Argentina, which limited the variability of red meat intake.]

Manousos et al. (1983) conducted a hospital-based case–control study of colorectal cancer

(100 cases, 100 controls) in Greece, and reported positive associations with beef (OR, 1.77) and lamb (OR, 2.61). [The Working Group concluded that the major limitations were lack of consideration of important confounders, such as total energy intake, among others, and small samples size.]

(b) Processed meat

(i) Studies considered informative

The following case–control studies reported results for processed meat separately and were considered informative by the Working Group (see Table 2.2.4). These studies were given more weight in the evaluation. The studies are presented in order by sample size, from largest to smallest. Many of these studies were described in the previous section.

Joshi et al. (2015) (3350 cases, 3504 controls), which was described as an informative study in Section 2.2.2(b), reported a positive association for processed meat (5th Quintile vs 1st quintile OR, 1.2; 95% CI, 1.0–1.4; P_{trend} = 0.054).; a similar positive association was reported for sausage and lunchmeats (Q5 vs Q1 OR, 1.2; 95% CI, 1.0–1.4; P_{trend} = 0.187). Analyses that considered subtypes of colorectal cancer defined by MMR status showed a statistically significant association with sausages and lunchmeats among MMR-proficient cases (Q5 vs Q1 OR, 1.3; 95% CI, 1.0–1.7; P_{trend} = 0.029). When cooking methods were considered, positive associations were noted for pan-fried sausage (4th quartile vs 1st quartile OR, 1.2; 95% CI, 1.0–1.3; P_{trend} = 0.041) and pan-fried spam or ham (Q4 vs Q1 OR, 1.2; 95% CI, 1.0–1.4; P_{trend} = 0.048). The latter seemed restricted and stronger among MMR-proficient cases. No associations were noted for pan-fried bacon and for grilled/barbecued sausages. No differences were noted for colon versus rectal cancers for any of these variables. [The limitations were the same as those described in Section 2.2.2(b).]

Hu et al. (2007) (1723 cases, 3097 controls), described as an informative study in Section 2.2.2(b),reported that processed meat intake was significantly positively associated with both proximal and distal colon cancers in both sexes, with risk estimates ranging between 1.5 and 1.6 for the highest compared with the lowest quartile of intake. Positive associations appeared to be stronger for bacon than for sausage intake, which was not significantly associated with proximal or distal cancers in men or women. For the highest tertile compared with the lowest tertile of bacon intake, the odds ratios for proximal cancer were 1.5 (95% CI, 1.0–2.2; P_{trend} = 0.04) in men and 2.2 (95% CI, 1.4–3.3; P_{trend} = 0.001) in women; andthe odds ratios for distal cancer were 1.4 (95% CI, 1.0–1.9; P_{trend} = 0.05) in men and 1.8 (95% CI, 1.2–2.8; P_{trend} = 0.01) in women. [It was unclear why associations were presented for bacon and sausage, but not for other types of processed meats.] A later published companion paper by the same group using the same study population confirmed their previous findings for processed meat and colon cancer (≥ 5.42 vs ≤ 0.94 servings/week OR, 1.5; 95% CI, 1.2–1.8; P_{trend} < 0.0001) (Hu et al., 2011). This publication also reported results for rectal cancer separately (≥ 5.42 vs ≤ 0.94 servings/week OR, 1.5; 95% CI, 1.2–2.0; P_{trend} = 0.001). [The limitations were the same as those noted for Hu et al. (2007).]

Kampman et al. (1999) (1542 cases, 1860 controls), an informative study described in Section 2.2.2(b), also reported on processed meats. They reported a statistically significant positive association with risk of colon cancers in men who consumed > 3.1 servings/week versus men who consumed ≤ 0.5 servings/week of processed meats (OR, 1.4; 95% CI, 1.0–1.9), but no significant associations were found in women. Moreover, stronger positive associations between processed meats and colon cancer were observed among those with the intermediate or rapid *NAT2* acetylator phenotype (albeit not a statistically significant interaction), while associations did not appear to differ by *GSTM1* genotype. A follow-up paper by this group (Slattery et al., 2000) reported that, among cases, higher processed meat intake was less likely to be associated with tumours with G→A transitions in the *KRAS* gene (OR, 0.4; 95% CI, 0.2–0.8; P_{trend} = 0.14). In a later publication by the same group focusing on rectal cancer (Murtaugh et al., 2004), processed meat intake was not significantly associated with risk of rectal cancer. For the highest versus the lowest intake, the odds ratios were 1.18 (95% CI, 0.87–1.61) in men and 1.23 (95% CI, 0.84–1.81) in women. [For the limitations, refer to Section 2.2.2(b).]

Le Marchand et al. (1997) (1192 cases, 1192 controls), an informative study described in Section 2.2.2(b),reported positive associations between processed meat intake and colorectal cancer; however, the associations appeared to be restricted to men only (highest vs lowest quartile of intake among men, OR, 2.3; 95% CI, 1.5–3.4; P_{trend} = 0.001; among women, OR, 1.2; 95% CI, 0.8–2.0; P_{trend} = 0.20; $P_{interaction}$ = 0.05). When considering processed meat subtypes, positive associations were reported for beef or pork luncheon meats, salami, sausage, and beef wieners among men only. In contrast, among women, a positive association was observed with spam (highest vs lowest quartile of intake among women OR, 1.8; 95% CI, 1.1–2.9; P_{trend} = 0.02). [The limitations were the same as those described in Section 2.2.2(b).]

Miller et al. (2013) (989 cases, 1033 controls), an informative study described in Section 2.2.2(b),reported a slight positive association between processed red meat and colorectal cancer; however, neither the estimates by intake category nor trend of association werestatistically significant. No differences were observed between colon and rectal cancer or between proximal and distal colon cancer. A statistically significant positive association between estimated levels of total nitrites and proximal cancer (Q5 vs Q1, OR, 1.57; 95% CI, 1.06–2.34; P_{trend} = 0.023) was reported. [For the limitations, refer to Section 2.2.2(b); additionally, processed red meat and processed poultry meat were considered separately and so total processed meat was not reported.]

In the study by Williams et al. (2010) (945 cases, 959 controls), described in Section 2.2.2(b), a positive association between processed meat intake and colon cancer was reported for the third quartile among Whites, but there was no evidence of a linear trend. No significant associations were observed among African Americans. [For the limitations, refer to Section 2.2.2(b).]

Kimura et al. (2007) (840 cases, 833 controls), described in Section 2.2.2(b), reported that processed meat was not associated with colorectal cancer, regardless of the cancer subsite. For Q5 versus Q1, the odds ratios were 1.15 (95% CI, 0.83–1.60) for colorectal cancer, 1.2 (95% CI, 0.72–2.03) for proximal colon cancer, 1.32 (95% CI, 0.82–2.11) for distal colon cancer, and 1.14 (95% CI, 0.73–1.77) for rectal cancer (all P_{trend} ≥ 0.27). [The Working Group concluded that a limitation was the lack of information on how processed meat was defined.]

A study by Tuyns et al. (1988) (818 cases, 2851 controls), described in Section 2.2.2(b), also reported data on "charcuterie", and reported no association with risk of colon or rectal cancers. [For the limitations, refer to Section 2.2.2(b).]

A study by Gerhardsson de Verdier et al. (1991) (559 cases, 505 controls), described in Section 2.2.2(b), also reported on individual processed meats and considered cooking methods. Significant positive associations were observed between intake of boiled sausage (P_{trend} = 0.04) and risk of colon cancer. Furthermore, positive associations were also found between bacon/smoked ham (P_{trend} = 0.025), oven-roasted sausage (P_{trend} = 0.038), and boiled sausage (P_{trend} < 0.001) and risk of rectal cancer. Associations did not appear to differ consistently by sex or colon subsites. [The Working Group noted that a limitation was the reduced number of processed meat items, as it was unclear whether the items were representative of the subtypes of processed meats consumed in this population. For other limitations, refer to Section 2.2.2(b).]

The study by Le Marchand et al. (2002a) (521 cases, 639 controls), described in Section 2.2.2(b), also reported that, among participants with a high intake of processed red meat and the *CYP2E1* insert polymorphism, a threefold risk was observed compared with those with low consumption and no insert polymorphism (OR, 3.1; 95% CI, 1.8–5.6; $P_{interaction} = 0.22$).

Squires et al. (2010) (518 cases, 688 controls) conducted a population-based case–control study in Canada. They reported that a higher consumption of pickled meat (food commonly eaten in Newfoundland) was significantly associated with an increased risk of colorectal cancer in both men and women (OR for men, 2.07; 95% CI, 1.37–3.15; OR for women, 2.51; 95% CI, 1.45–4.32).

Rosato et al. (2013) (329 cases, 1361 controls) conducted a hospital-based case–control study of young-onset colorectal cancer (diagnosis ≤ 45 years of age) in Italy. The study included individuals from three previously reported case–control studies on colorectal cancers – Levi et al. (1999), La Vecchia et al. (1991), and Negri et al. (1999). [Participants in these previous studies may have overlapped.] A statistically significant positive association was observed between processed meat intake and colorectal cancer (highest vs lowest tertile OR for processed meat, 1.56; 95% CI, 1.11–2.20; $P_{trend} = 0.008$). [The limitations of this study were lack of definition of meat types included in the processed meat variable, lack of clarity on the overlap with previous studies, and no consideration of alcohol and smoking as potential confounders.]

A study by Navarro et al. (2003) (287 cases, 564 controls), described in Section 2.2.2(b),reported that processed meat was positively associated with risk of colorectal cancer (highest vs lowest tertile OR, 1.47; 95% CI, 1.02–2.15). [For the limitations, refer to Section 2.2.2(b).]

Steinmetz & Potter (1993) (220 cases, 438 controls), described in Section 2.2.2(b), reported that processed meat intake was not associated with risk of colon cancer in either sex. For the highest compared with the lowest quartile, the odds ratios were 0.77 (95% CI, 0.35–1.68) in women and 1.03 (95% CI, 0.55–1.95) in men. [For the limitations, refer to Section 2.2.2(b).]

Juarranz Sanz et al. (2004) (196 cases, 196 controls), described in Section 2.2.2(b), reported positive associations between processed meat intake (12.9 ± 11.4 g/day vs 5.62 ± 7.6 g/day) and colorectal cancer (OR, 1.070; 95% CI, 1.035–1.107; $P_{trend} = 0.001$). [The Working Group noted that processed meat was not clearly defined. For other limitations, refer to Section 2.2.2(b).]

Boutron-Ruault et al. (1999) (171 cases, 309 controls), summarized in Section 2.2.2(b), reported that a higher intake of delicatessen (processed) meat was associated with a higher risk of colorectal cancer (highest vs lowest quartile, g/day, OR, 2.4; 95% CI, 1.3–4.5). [For the limitations, refer to Section 2.2.2(b).]

(ii) Studies considered less informative

The following case–control studies reported results for processed meat separately and were considered less informative by the Working Group. The studies are presented in order by sample size, from largest to smallest.

A hospital-based study was done by Franceschi et al. (1997) (1953 colorectal cancer cases, 4154 controls) in Italy. The study reported no statistically significant associations between processed meat and risk of colorectal cancer. Similarly, no associations were observed for colon or rectal cancer separately. [Processed meat was not defined.]

Macquart-Moulin et al. (1986) (399 colorectal cases, 399 controls) reported no statistically significant associations between a high intake of processed meats and colorectal cancer. [The

Working Group concluded that the main weaknesses of this study were lack of consideration of dietary fibre or total vegetables, and lack of details on the analytical models, such as confidence intervals.]

A hospital-based case–control study was done in Montevideo, Uruguay. De Stefani et al. (2012a) (361 colorectal cases, 2532 controls) reported that a higher intake of processed meat was associated with a higher risk of colon and rectal cancers in both sexes. For the highest tertile compared with the lowest tertile of intake (g/day), the odds ratios for colon cancer were 2.01 (95% CI, 1.07–3.76; P_{trend} = 0.03) in men and 3.53 (95% CI, 1.93–6.46; P_{trend} = 0.0001) in women, and the odds ratios for rectal cancer were 1.76 (95% CI, 1.03–3.01; P_{trend} = 0.03) in men and 3.18 (95% CI, 1.54–6.57; P_{trend} = 0.01) in women. A previous hospital-based study by the same group (De Stefani et al., 1997) (250 colorectal cases, 500 controls) had reported no statistically significant associations between processed meat and colorectal cancer, and no differences by cancer subsite (colon vs rectum) or by sex. [A major limitation of this study was that the control group may have included patients with diseases related to diet, increasing the likelihood of biased results. In addition, in the 1997 study, the researchers did not consider adjusting for energy intake.]

A hospital-based case–control study was done in the canton of Vaud, Switzerland, by Levi et al. (2004) (323 colorectal cases, 611 controls) and later included in the study by Di Maso et al. (2013), although the latter did not report on processed meat. A higher intake of processed meat was associated with a higher risk of colorectal cancer (OR for highest vs lowest category of intake, 2.35; 95% CI, 1.50-4.27; P_{trend} < 0.001).

A population-based case–control study in Majorca, Spain (Benito et al., 1990) (286 cases; 498 controls, which included some hospital-based), reported no significant associations with processed meat intake. [Lack of energy adjustment, lack of detailed analysis, use of a non-validated FFQ, and limited sample size were among the limitations of this study.]

Lohsoonthorn & Danvivat (1995) (279 colorectal cases, 279 controls), described in Section 2.2.2(b), reported positive associations with bacon (>10 vs ≤ 5 times/month OR, 12.49; 95% CI, 1.68–269) and with sausage (>10 vs ≤ 5 times/month OR, 1.26; 95% CI, 0.71–2.25), and a null association with salted beef. [The main weakness of this study was lack of consideration of any potential confounders.]

In a population-based study in France (Faivre et al., 1997) (171 colorectal cases, 309 controls) a positive association was reported between a high intake of processed meat and delicatessen and colorectal cancer risk (OR, 3.0; 95% CI, 2.1–4.8; P_{trend} < 0.001). [The key weaknesses included lack of information regarding how the processed meat estimate was obtained, and lack of consideration of smoking, BMI, dietary fibre, and alcohol.]

A population-based case–control study in Italy (Centonze et al., 1994) (119 cases, 119 controls), previously described in Section 2.2.2(b), reported that processed meat was not associated with colorectal cancer risk (OR for ≥ 3g/day vs < 2g/day processed meat, 1.01; 95% CI, 0.57–1.69). [For the limitations, refer to Section 2.2.2(b).]

Fernandez et al. (1997) (112 cases and 108 controls), based on data from a case–control study in northern Italy, focused on subjects with a family history of cancer and reported that some processed meats were positively associated with colorectal cancer. For the highest versus the lowest tertile, the odds ratios were 2.1 (95% CI, 0.9–4.9; P_{trend} > 0.05) for raw ham, 2.6 (95% CI, 1.0–6.8; P_{trend} > 0.05) for ham, and 1.9 (95% CI, 1.0–3.3; P_{trend} < 0.05) for canned meat. [The limitations of this study were the unclear definition of processed meats, the modest sample size, and the lack of adjustment for energy intake and other potential confounders.]

Iscovich et al. (1992) (110 cases, 220 controls), described in Section 2.2.2(b), reported that processed meat was inversely associated with risk of colon cancers, regardless of fat content (OR for highest vs lowest, 0.45; 95% CI, 0.23–0.90; P_{trend} = 0.017; for fat with skin; OR, 0.38; 95% CI, 0.19–0.75; for lean processed meat; P_{trend} = 0.002). [For the limitations, refer to Section 2.2.2(b).]

(c) Red meat and processed meat combined

In this subsection, the term "total red meat" as used in many studies refers to "unprocessed and processed red meats combined".

(i) Studies considered informative

The following case–control studies that reported results for red meat and processed meat combined were considered informative by the Working Group. The studies are presented in order by sample size, from largest to smallest.

A population-based colorectal case–control study conducted in Canada (Cotterchio et al., 2008) (1095 cases, 1890 controls) reported a positive association with total red meat (OR for highest vs lowest intake of total red meat, servings/week, 1.67; 95% CI, 1.36–2.05) and well-done total red meat (OR for > 2 servings/week of total well-done red meat vs ≤2 servings/week of rare total red meat, 1.57; 95% CI, 1.27–1.93). Polymorphisms in 15 xenobiotic-metabolizing enzymes (XMEs) were considered, and no statistically significant gene-environment interactions were observed, with two exceptions. In analyses stratified by genotypes, the relative risk of colorectal cancer for > 2 servings/week of "well-done" compared with ≤ 2 servings/week of "rare/regular" red meat was higher in *CYP1B1* wildtype variants compared with other genotypes with increased activity ($P_{interaction}$ = 0.04), and higher in the *SULT1A1* GG genotype compared with AA/GA genotypes ($P_{interaction}$ = 0.03). A follow-up study with a subset of the individuals (Mrkonjic et al., 2009) investigated gene-environment interactions, focusing on two single-nucleotide polymorphisms on the apolipoprotein E (*APOE*) gene and considering tumour subtypes with microsatellite instability (MSI). They reported that *APOE* isoforms might modulate the risk of MSI-high and MSI-low/normal colorectal cancers among high total red meat consumers. [The Working Group concluded that the major limitations of these studies were use of a dietary instrument that was not validated for red meat and lack of energy adjustment.]

Kune et al. (1987) reported on a population-based case–control study conducted in Melbourne, Australia (715 colorectal cases, 727 controls). They reported a positive association between high intake of beef, unprocessed and processed (> 360 g/week), and colorectal cancer risk for men and women combined (OR, 1.75; 95% CI, 1.26–2.44), and a positive association of similar magnitude for the colon and rectum. Results for men showed similar estimates. Estimates for women were not presented. In contrast, for pork, inverse associations were reported with colorectal cancer for men and women combined (OR, 0.55; 95% CI, 0.42–0.73) and similarly by sex and by cancer location (i.e. colon and rectum). [The lack of total energy adjustment and consideration of lifestyle risk factors were noted. The data analysis strategy and presentation were not sufficiently clear, and did not allow for proper interpretation of the findings.]

The North Carolina Colon Cancer Study (Butler et al., 2003), a population-based case–control study in the USA (620 colon cancer cases, 1038 controls), reported a twofold risk of colon cancer for total red meat intake (highest vs lowest intake OR, 2.0; 95% CI, 1.3–3.2). In addition, statistically significant associations between colon cancer risk and pan-fried red meat (OR, 2.0; 95% CI, 1.4–3.0) and well-done red meat (OR, 1.7; 95% CI, 1.2–2.5) were reported. In another paper (Satia-Abouta et al., 2004), differences by ethnic group were examined ("Caucasians" vs African Americans), and it was reported that the positive associations previously reported by Butler et al. (2003) for all individuals combined were no longer observed with ethnic stratification e (e.g. Q4 vs Q1 total red meat among Whites OR, 1.1;

95% CI, 0.7–1.8; P_{trend} = 0.61). Follow-up studies (Butler et al., 2005, 2008a) considered *UGT1A7* and *NAT1* polymorphisms in a subset of cases, and reported no significant gene–environment interactions. In a subset of cases (486 cases), Satia et al. (2005) observed that the positive association between total red meat intake and colon cancers seemed restricted to MSI-high cases (49 cases only), but was not statistically significant, and was null among MSI-low/MSI-stable tumours (total red meat intake T3 vs T1 OR for MSI-high cancers: 1.3; 95% CI, 0.6–3.0; P_{trend} = 0.42; and OR for MSI-low or MSI-stable cancers, 0.9; 95% CI, 0.7–1.3; P_{trend} = 0.90). A subsequent study conducted by Steck et al. (2014) considered gene-environment interactions between total red meat, pan-fried total red meat, and well-done or very well-done total red meat and seven single-nucleotide polymorphisms in five nucleotide excision repair genes (*XPD, XPF, XPG, XPC, RAD23B*). No significant interactions were reported. [Slightly lower response rates were noted for controls compared with cases, although this is not unusual for studies that include minority populations, and the response rates were still within an acceptable range.]

A population-based study of colorectal cancer was done by Joshi et al. (2009) (577 cases, 361 controls) and reported a positive association with total red meat (OR for > 3 vs ≤ 3 servings/week, 1.8; 95% CI, 1.3–2.5; P_{trend} = 0.001), which was restricted to colon cancer cases, and not rectal cases, and a similar association with total red meat cooked using high-temperature methods (pan-frying, broiling, grilling OR, 1.6; 95% CI, 1.1–2.2). No associations were reported for total red meat doneness (on the outside or inside of the meat) and colorectal cancer. Polymorphisms in five genes in the nucleotide excision repair pathway (*ERCC1, XPA, XPC, XPD, XPF, XPG*) and two genes in the MMR pathway (*MLH1, MSH2*) were considered. Overall, results suggested that a high intake of total red meat browned on the outside may increase the risk of colorectal cancer (especially rectal cancer) among carriers of the *XPD* codon 751 Lys/Lys genotype (OR, 3.8; 95% CI, 1.1–13; $P_{interaction}$ = 0.037). Two subsequent studies investigated additional interactions between these meat variables and polymorphisms in the base excision repair pathway (*APEX1, OGG1, PARP, XRCC1*) (Brevik et al., 2010) and carcinogen metabolism enzymes (*CYP1A2, CYP1B1, GSTP1, PTGS2, EPHX, NAT2*) (Wang et al., 2012). They reported a stronger association between a higher intake of total red meat cooked at high temperatures and colorectal cancer among carriers of one or two copies of the *PARP* codon 762 Ala allele (OR, 2.64; 95% CI, 1.54–4.51; $P \leq 0.0001$) than among carriers of two copies of the Val allele (OR, 1.17; 95% CI, 0.76–1.77; $P = 0.484$; $P_{interaction}$ = 0.012) (Brevik et al., 2010). They also reported that the *CYP1A2* −154 A > C single-nucleotide polymorphism may modify the association between intake of total red meat cooked using high-temperature methods ($P_{interaction} < 0.001$) and colorectal cancer risk, and the association between total red meat heavily browned on the outside and rectal cancer risk ($P_{interaction} < 0.001$) (Wang et al., 2012). [The Working Group concluded that a limitation of these studies was the use of sibling controls, which may have reduced power to detect associations with red meat variables; however, the use of a case-only design improved power for gene–environment interaction testing. Total energy intake was considered, but was obtained from a separate questionnaire than the ones used for meat assessment; therefore, residual confounding could not be excluded.]

A population-based case–control study of colorectal cancer was conducted in western Australia (Tabatabaei et al., 2011) (567 cases, 713 controls). The study reported that intake of total red meat cooked with different cooking methods (pan-fried, barbecued, stewed) was not significantly associated with risk of colorectal cancer, although a statistically significant inverse association with baked total red meat was observed.

For the highest versus the lowest intake, the odds ratios were 0.8 (95% CI, 0.57–1.13; $P_{trend} = 0.27$) for pan-fried, 0.89 (95% CI, 0.63–1.24; $P_{trend} = 0.17$) for barbecued, 0.73 (95% CI, 0.53–1.01; $P_{trend} = 0.04$) for baked, and 0.95 (95% CI, 0.67–1.33; $P_{trend} = 0.53$) for stewed. Results were not provided for red meat per se, only by cooking method. [The Working Group concluded that the main limitations were the lack of information regarding whether the FFQ was validated and the fact that the researchers inquired about meat intake 10 years before inclusion into the study, which may have increased the likelihood of misclassification of exposures.]

Squires et al. (2010) (518 cases, 686 controls) conducted a study in Newfoundland, Canada, summarized in Section 2.2.2(c), and reported a positive, but non-statistically significant, association between total red meat intake and colorectal cancer among women, but not among men. For the highest compared with the lowest category of intake (servings/day), the odds ratio among men was 0.75 (95% CI, 0.43–1.29), and among women, it was 1.81 (95% CI, 0.94–3.51; no $P_{interaction}$ by sex reported). In addition, a higher intake of well-done red meat was associated with a higher risk of colorectal cancer in women (> 2 servings well done vs < 2 servings rare/regular, OR, 3.1; 95% CI, 1.11–8.69).

Shannon et al. (1996) conducted a population-based study in Seattle, USA (424 colon cases, 414 controls), and reported no statistically significant associations between total red meat intake and colon cancer among women, but did report a statistically non-significant positive association among men (Q4 vs Q1 OR, 1.48; 95% CI, 0.82–2.66; $P_{trend} = 0.53$).

Nowell et al. (2002) conducted a hospital-based case–control study (155 cases, 380 population-based controls) in Arkansas and Tennessee, USA, and reported a positive association with total red meat cooked well/very well done (Q4 vs Q1 OR, 4.36; 95% CI, 2.08–9.60). They also reported a positive association with estimated levels of MeIQx (Q4 vs Q1 OR, 4.09; 95% CI, 1.94–9.08). Estimates for total red meat, without considering the cooking methods, were not provided. [A limitation was the lack of consideration of total energy adjustment, BMI, smoking, alcohol, and dietary fibre. Results reported on only one HAA, even though more exposure estimates were available.]

(ii) Studies considered less informative

The following case–control studies that reported results for red meat and processed meat combined were considered less informative by the Working Group. The studies are presented in order by sample size, from largest to smallest.

A case–control study was done in Scotland by Theodoratou et al. (2008) (1656 hospital-based cases, 2292 population-based controls). A validated FFQ was used to investigate gene–environment interactions between total red meat intake (minced meat, sausages, burgers, beef, pork, lamb, bacon, liver, gammon, liver sausage, liver pâté, haggis, black pudding) and two polymorphisms in the *APC* gene (Asp1822Val and Glu1317Gln). Overall, their findings suggested that, among carriers of the *APC* 1822 variant, diets high in total red meat may increase the risk of colorectal cancer. [No main effects were presented for total red meat.]

Bidoli et al. (1992) conducted a colorectal case–control study in Italy (248 cases, 699 controls), and reported that a higher intake of total red meat was associated with a higher risk of both colon and rectal cancers (highest vs lowest intake, colon cancer OR, 1.6; $P_{trend} = 0.07$; rectal cancer OR, 2.0; $P_{trend} = 0.01$). [Several limitations were noted, including lack of adjustment for caloric intake, use of a non-validated dietary instrument, and recruitment of cases and controls from different hospitals, which introduces potential selection bias.] A companion study (Fernandez et al., 1997), previously described in Section 2.2.2(c), focusing on subjects with a family history of cancer reported that, among participants with a positive family history, total red meat intake was positively associated with colorectal cancer (highest vs lowest tertile OR, 2.9; 95% CI, 1.4–6.0; $P_{trend} < 0.05$). [For the limitations, refer to Section 2.2.2(c).]

(d) Red meat – unclear if processed meat was included

The following studies were given little weight in the evaluation. The studies are presented in order by sample size, from largest to smallest.

A hospital-based case–control study by La Vecchia et al. (1996) in Italy (1326 colorectal cases, 2024 controls) reported a positive association with both colon and rectal cancer using a dichotomous variable for red meat (high vs low OR for colon cancer, 1.6; 95% CI, 1.3–1.9; OR for rectal cancer, 1.6; 95% CI, 1.3–2.0). [The limitations were the lack of clear definition of red meat, the use of a dichotomous variable, and the potential for partial overlap with studies that followed from this group; specifically, this study recruited from 1985 to 1992, and the follow-up study by Di Maso et al. (2013) was from 1991 to 2009.]

A hospital-based study in France (Pays de la Loire region) (1023 colorectal cancer cases with a family history and young onset, 1121 controls) (Küry et al., 2007) reported that an intake of red meat > 5 times/week was associated with a higher risk of colorectal cancers (OR, 2.81; 95% CI, 1.52–5.21; $P = 0.001$) compared with an intake of red meat < 5 times/week. They also examined gene–environment interactions between red meat intake and polymorphisms in cytochrome P450 genes (*CYP1A2, CYP2E1, CYP1B1, CYP2C9*) and colorectal cancer risk, with evidence of interaction for multiple combinations of polymorphisms; however, confidence intervals among high–red meat eaters were very wide, and no formal test of interaction was provided. [The Working Group concluded that the crude assessment of meat intake based on one question on a questionnaire and lack of detail on which covariates were added to the final model, including total energy intake, were among the limitations of this study.]

Morita et al. (2009) conducted a hospital-based study in Fukuoka, Japan (685 cases, 833 population-based controls), and reported a positive association between red meat and colon cancer, but only among carriers of one or two alleles for the 96-bp insertion for *CYP2E1* ($P_{interaction} = 0.03$). They did not report on the main effects of red meat, only on gene- interaction analyses between meat and these polymorphisms. [The Working Group concluded that the main weakness was the lack of presentation of the main effects of red meat.]

A study conducted in the Liverpool postcode area in the United Kingdom (Evans et al., 2002) (512 cases, 512 population-based controls) reported a positive association between red meat and colorectal cancer (highest vs lowest quartile OR, 1.51; 95% CI, 1.06–2.15). Associations appeared to be stronger for proximal cancers (OR for proximal cancer, 3.32; 95% CI, 1.42–7.73; OR for distal and rectal cancer, 1.38; 95% CI, 0.89–2.12). [The Working Group concluded that the key limitations of this study were lack of consideration of potential confounders, presentation of univariate analyses only, and unclear definition of red meat.]

Three papers on a matched, hospital-based case–control study from China (400 cases, 400 controls) (Hu et al., 2013, 2014, 2015) examined gene–environment interactions between red meat intake and different gene polymorphisms associated with insulin resistance pathways, focusing on adiponectin (*ADIPOQ)* rs2241766, uncoupling protein 2 (*UCP2*) rs659366, and fatty acid binding protein 2 (*FABP2*) rs1799883 (Hu et al., 2013); *ADIPOQ* rs2241766, *ADIPOQ* rs1501299, and calpain 10 (*CAPN-10)* rs3792267 (Hu et al., 2015); and *CAPN-10* SNP43 and SNP19 polymorphisms (Hu et al., 2014). A statistically significant positive association between red meat intake and colorectal cancer risk was observed (high vs low, > 7 vs ≤ 7 times/week, OR, 1.87; 95%

CI, 1.39–2.51) (Hu et al., 2013). [The Working Group concluded that lack of a validated dietary instrument, crude assessment of meat intake, lack of a clear definition of red meat, potential for residual confounding, and especially, lack of adjustment for total energy intake were among the main limitations of the study.]

The study by Rosato et al. (2013) (329 cases, 1361 controls), described in Section 2.2.2(c), also reported on red meat intake. They reported no association between red meat and risk of colorectal cancer (highest vs lowest tertile OR for red meat, 1.07; 95% CI, 0.79–1.64; P_{trend} = 0.63). [No definition was provided for red meat. For additional limitations, refer to Section 2.2.2(c).]

A hospital-based study conducted in Uruguay (De Stefani et al., 1997) (250 colorectal cases, 500 controls) reported positive associations between red meat and colorectal cancer (OR, 2.60; 95% CI, 1.64–4.13), with similar estimates for men and women. Similarly, a positive association was reported for beef (OR, 3.88; 95% CI, 2.34–6.45), but not for lamb. Estimates of HAAs were also provided, showing statistically significant associations with PhIP, MeIQx, and DiMeIQx. [The Working Group concluded that the limitations included concerns about hospital-based controls and lack of adjustment for energy intake.]

A hospital-based case–control study was done in Singapore (Lee et al., 1989) (203 colorectal cancer cases, 425 controls), and reported no statistically significant associations between red meat intake and risk of colorectal, colon, or rectal cancers. For the highest compared with the lowest tertile, the odds ratios were 1.29 (95% CI, 0.84–1.97) for colorectal cancer, 1.41 (95% CI, 0.87–2.31) for colon cancer, and 0.97 (95% CI, 0.48–1.92) for rectal cancer (all P_{trend} > 0.05). [The Working Group concluded that no adjustment for total energy intake and other potential confounders were among the limitations.]

A population-based study of colorectal cancer was done by Saebø et al. (2008) (198 cases, 222 controls), and reported a non-significant positive association between red meat and colorectal cancer (T3 vs T1 OR, 1.58; 95% CI, 0.71–3.47). No association was found when the doneness level was considered. Interactions with *CYP1A2* polymorphism were also examined, without conclusive results. [The Working Group concluded that the limitations included unclear details of the questionnaire used; lack of consideration of appropriate confounders, such as total energy intake; and unclear definition of red meat.]

A hospital-based study conducted in Jordan (Abu Mweis et al., 2015) (167 cases, 240 controls) reported a non-statistically significant inverse association between red meat and colorectal cancer risk (OR for ≥ 1 vs < 1 serving/week, 0.64; 95% CI, 0.37–1.11). [The Working Group concluded that the choice of the control population, limited sample size, lack of definition of the red meat variable, and crude categorization of exposure were among the limitations of this study.]

Seow et al. (2002) reported results from a hospital-based colorectal case–control study done in Singapore (121 cases, 222 population-based controls), and reported a positive association between red meat portions per year and colorectal cancer (highest vs first tertile OR, 2.2; 95% CI, 1.1–4.2). They also reported results stratified by total vegetable intake and reported that results for red meat were stronger among individuals with a low intake of vegetables; however, no test of heterogeneity was provided. [The Working Group concluded that the main weaknesses of this study were the limited dietary assessment and lack of proper consideration of total energy intake.]

(e) Cooking practices

Most meat products require cooking for consumption. In spite of this, only a subset of studies distinguished meat types by cooking method and/or doneness level, limiting the evaluation of more specific categories of meat.

When considering red meat, among the studies previously reviewed, there were four studies that reported on cooking practices in relation to colorectal cancer risk (Barrett et al., 2003; Navarro et al., 2004; Miller et al., 2013; Joshi et al., 2015), four studies on colon cancer risk (Gerhardsson de Verdier et al., 1991; Kampman et al., 1999; Miller et al., 2013; Joshi et al., 2015), and four studies on rectal cancer risk (Gerhardsson de Verdier et al., 1991; Murtaugh et al., 2004; Miller et al., 2013; Joshi et al., 2015). For colorectal cancer risk, data were available from two of the largest population-based case–control studies (Joshi et al., 2015; Miller et al., 2013), which reported on a combined total of 4312 cases ascertained from the USA and Canada. These two studies considered separate cooking methods (pan-frying, broiling, grilling/barbecuing), and both reported positive associations with pan-frying; pan-fried beef steak (Q4 vs Q1 OR, 1.3; 95% CI, 1.1–1.5) was reported by Joshi et al. (2015), and pan-fried red meat (Q5 vs Q1 OR, 1.26; 95% CI, 0.93–1.70) was reported by Miller et al. (2013). Overall, of the seven studies that reported on red meat cooking practices and colorectal, colon, or rectal cancer, six reported positive associations with red meat when high-temperature methods and/or doneness levels were considered.

There were additional studies that considered red meat and processed meats combined in relation to colorectal cancer risk (Le Marchand et al., 2002b; Nowell et al., 2002; Cotterchio et al., 2008; Joshi et al., 2009; Squires et al., 2010; Tabatabaei et al., 2011), colon cancer risk (Le Marchand et al., 2002b; Butler et al., 2003; Joshi et al., 2009), and rectal cancer risk (Joshi et al., 2009). Overall, of the seven studies that reported on cooking practices and colorectal cancer, colon cancer, or rectal cancer, five reported associations with high-temperature cooking methods and/or doneness levels. Of these studies, the only one that looked at cooking methods in detail was Butler et al. (2003), which was in agreement with the studies by Joshi et al. (2015) and Miller et al. (2013) previously described for red meat (only), and reported a positive association with pan-fried red meat (OR, 2.0; 95% CI, 1.4–3.0) in addition to well-done red meat (OR, 1.7; 95% CI, 1.2–2.5).

2.2.3 Meta-analyses

High intakes of red meat and processed meats were associated with a moderate, but significant, increase in colorectal cancer risk in several meta-analyses conducted before 2010 (Sandhu et al., 2001; Norat et al., 2002; Larsson et al., 2006; Huxley et al., 2009). The results of more recent meta-analyses of the associations between colorectal cancer and consumption of unprocessed red meat and processed meat, as well as specific meat types, haem iron, and genetic interactions with red and processed meat intake are described here.

In all meta-analyses, similar methods were used to derive summary estimates of dose–response and relative risks for the highest compared with the lowest intake categories. In most analyses, significant associations were observed for all prospective studies combined. However, because the magnitudes of the summary associations were moderate to small, the statistical significance was often lost in subgroup analyses with fewer studies. In addition, some inconsistencies in the results remained unexplained, as the relatively low number of studies in each subgroup did not allow for extensive exploration of all potential sources of heterogeneity.

Chan et al. (2011) summarized the results of prospective studies on red and processed meat and colorectal cancer risk for the World Cancer Research Fund/American Institute of Cancer Research (WCRF/AICR) Continuous Update Project. For red meat, the relative risks for the highest compared with the lowest intake were 1.10 (95% CI, 1.00–1.21; I^2 = 22%; 12 studies) for colorectal cancer, 1.18 (95% CI, 1.04–1.35; I^2 = 0%; 10 studies) for colon cancer, and 1.14 (95% CI, 0.83–1.56; I^2 = 38%; 7 studies) for rectal cancer. Within the colon, the summary risk for increase of cancer was 13% for proximal colon cancer and 57% for distal colon cancer, but the associations were not significant. The relative risk for an increase of 100 g/day of red meat was 1.17 (95% CI, 1.05–1.31; 8 studies) for colorectal cancer, 1.17 (95% CI, 1.02–1.33; 10 studies) for colon cancer, and 1.18 (95% CI, 0.98–1.42; 7 studies) for rectal cancer. For processed meats, the relative risk for the highest compared with the lowest intake was 1.17 (95% CI, 1.09–1.25; I^2 = 6%; 13 studies) for colorectal cancer, 1.19 (95% CI, 1.11–1.29; I^2 = 0%; 11 studies) for colon cancer, and 1.19 (95% CI, 1.02–1.39; I^2 = 20%; 9 studies) for rectal cancer. Within the colon, the summary risk for increase of cancer was 4% for proximal colon cancer and 20% for distal colon cancer, but the associations were not significant (five studies in the analyses). The relative risks for an increase of 50 g/day were 1.18 (95% CI, 1.10–1.28; I^2 = 12%; 9 studies) for colorectal cancer, 1.24 (95% CI, 1.13–1.35; I^2 = 0%; 10 studies) for colon cancer, and 1.12 (95% CI, 0.99–1.28; I^2 = 0%; 8 studies) for rectal cancer.

The most recent, comprehensive meta-analysis of colorectal cancer and meat consumption included data from 27 prospective cohort studies, published in the English language and identified through 2013 (Alexander et al., 2015). Statistical analyses were based on comparisons of the highest intake category with the lowest intake category. Intake levels in these categories varied across studies. Linear dose–response slopes were derived from categorical meta-analyses of two subgroups, based on the units of red meat intake reported by the studies (grams or servings). Random effect models were used. The summary relative risk of colorectal cancer for the highest compared with the lowest intake of red meat and processed meat was 1.11 (95% CI, 1.03–1.19; I^2 = 33.6%; P = 0.014). Heterogeneity was reduced when the analysis was restricted to studies on (unprocessed) red meat. The summary relative risk for those 17 studies was 1.05 (95% CI, 0.98–1.12; I^2 = 8.4%; P = 0.328).

In analyses by cancer site, the association was significant with no heterogeneity for the colon (RR, 1.11; 95% CI, 1.04–1.18; 16 studies), and not significant with high heterogeneity for the rectum (RR, 1.17; 95% CI, 0.99–1.39; I^2 = 51.97%; 13 studies). When the analyses were restricted to studies of (unprocessed) red meat, there was no evidence of heterogeneity across studies (RR, 1.06; 95% CI, 0.97–1.16; 11 studies) for colon cancer and 1.03 (95% CI, 0.88–1.21; 10 studies) for rectal cancer.

Stronger but more heterogeneous associations were observed in studies conducted in North America compared with studies published in other countries. The weakest associations were observed in Asian studies, where meat intake is lower than in North America and Europe.

In the dose–response analysis, the relative risks were 1.02 (95% CI, 1.00–1.14; 10 studies) for 1 serving/day increase, and heterogeneity was moderate to low (I^2 = 26.5%), and 1.05 (95% CI, 0.97–1.13; 13 studies) for each 70 g/day increase.

Alexander et al. (2015) did not investigate processed meats. However, in an earlier meta-analysis, Alexander et al. (2010) reported the relative risks for the highest compared with the lowest intake of processed meat as 1.16 (95% CI, 1.10–1.23; $P_{heterogeneity}$ = 0.556; 20 studies) for any colorectal cancer, 1.19 (95% CI, 1.10–1.28; 12 studies) for colon cancer, and 1.18 (95% CI, 1.03–1.36; 8 studies) for rectal cancer. The relative risk of any colorectal cancer was 1.10 (95% CI, 1.05–1.15; 9 studies) for an increase of 30 g of processed meat intake and 1.03 (95% CI, 1.01–1.05; 6 studies) for each serving per week intake.

[The Working Group noted that there was no significant evidence of publication bias. The pooled analyses of the GECCO study, which included some cohorts included in the meta-analysis, did not find an association between red and processed meats and colorectal cancer. The Danish Diet, Cancer and Health study (Egeberg et al., 2013), in which red and processed meats were not related to colorectal cancer risk, was published after the preparation of the meta-analysis, and therefore was not included. The Japanese study by Takachi et al. (2011) was included in Alexander et al. (2015), but was published after the end of the search for the meta-analysis by Chan et al. (2011).]

The statistical methods used by Alexander et al. (2015) and Chan et al. (2011) were similar. However, Chan et al. (2011) rescaled times consumed or servings to grams of intake using values reported in the studies, or standard portion sizes of 120 g for red meat and 50 g for processed meat, following the methodology of the WCRF/AICR second expert report. [The Working Group noted that the rescaling may have increased the measurement error of the diet in the rescaled studies, but allowed for the inclusion of all studies in the analyses. Chan et al. (2011) reported that the summary risk estimate in the studies using serving as the intake unit was lower than that in the studies using grams (same finding in Alexander et al. (2010) for processed meats). It is possible that the rescaling of the intake may have attenuated the observed association. Another difference between the meta-analyses is that Chan et al. (2011) grouped the studies according to exposure: red and processed meats, red meats (unprocessed), and processed meats.]

A meta-analysis of six Japanese cohort studies reported no significant associations between total and specific meat types and colorectal cancer risk (Pham et al., 2014). For red meat consumption, the summary relative risk estimates for the highest compared with the lowest intake in the studies were 1.20 (95% CI, 1.00–1.44; 4 cohort studies) for colon cancer and 0.95 (95% CI, 0.71–1.28; 3 studies) for rectal cancer. For processed meats, the summary relative risks for the same comparison were 1.18 (95% CI, 0.92–1.53; 4 studies) for colon cancer and 0.94 (95% CI, 0.72–1.21; 3 studies) for rectal cancer. When the authors combined the results of the cohort studies with those of 13 case–control studies, the summary relative risks for red meat were 1.16 (95% CI, 1.001–1.34) and 1.21 (95% CI, 1.03–1.43) for colorectal and colon cancer, respectively, and those for processed meat consumption were 1.17 (95% CI, 1.02–1.35) and 1.23 (95% CI, 1.03–1.47) for colorectal and colon cancer, respectively.

Another meta-analysis of prospective studies summarized the associations between types of red meats and risk of colorectal cancer (Carr et al., 2016). The meta-analysis included one study from the Netherlands, one from Denmark, two from Japan, and the 10 European cohorts participating in the EPIC study. For the highest compared with the lowest intake of beef, the summary relative risks were 1.11 (95% CI, 1.01–1.22), 1.24 (95% CI, 1.07–1.44), and 0.95 (95% CI, 0.78–1.16) for colorectal, colon, and rectal cancer, respectively. Higher consumption of lamb was also associated with an increased risk of colorectal cancer (RR, 1.24; 95% CI, 1.08–1.44). No association was observed for pork (RR, 1.07; 95% CI, 0.90–1.27).

Qiao & Feng (2013) summarized the results of eight prospective studies on haem iron intake. The summary relative risk of colorectal cancer for the highest versus the lowest intake was 1.14 (95% CI, 1.04–1.24). The observed associations were not significantly modified by cancer site or sex. In the dose–response analyses, the summary relative risk was 1.11 (95% CI, 1.03–1.18) for an increment of haem iron intake of 1 mg/day.

In another meta-analysis, people with the *NAT2* fast acetylator phenotype who consumed a high intake of total meat had a statistically non-significant increased risk of colorectal cancer compared with slow acetylators who consumed a low intake of total meat (4 cohorts; $P_{interaction} = 0.07$) (Andersen et al., 2013). No interaction with the *NAT1* phenotype was observed (cohort studies) on the multiplicative scale.

Table 2.2.1 Cohort studies: consumption of red meat or red meat & processed meat combined and cancer of the colorectum

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
Kato et al. (1997) USA 1985–1994 Cohort study	14 727; New York University Women's Health Study (NYUWHS) Exposure assessment method: questionnaire	Colon and rectum	Red meat intake (quartiles)			Total caloric intake, age, a place at enrolment and level of education
			Q1 (lowest quartile)	NR	1.00	
			Q2	NR	1.28 (0.72–2.28)	
			Q3	NR	1.27 (0.71–2.28)	
			Q4 (highest quartile)	NR	1.23 (0.68–2.22)	
			Trend-test *P* value: 0.545			
Chen et al. (1998) USA 1982–1995 Nested case–control study	Cases: 212; Physicians' Health Study (PHS); self-report, medical records, and death certificates Controls: 221; cohort, matched by age and smoking Exposure assessment method: questionnaire; abbreviated FFQ red meat included: beef, pork, or lamb as main dish, in sandwiches or hot dogs	Colon and rectum	Red meat/processed meat (servings/day)			Age, smoking status, BMI, physical activity, alcohol intake
			≤ 0.5	62	1.00	
			> 0.5–1.0	103	0.98 (0.64–1.52)	
			> 1.0	43	1.17 (0.68–2.02)	
			Trend-test *P* value: 0.59			
Singh and Fraser (1998) California, USA Enrolment, 1976–1982; follow-up, 1977–1982 Cohort study	32 051; non-Hispanic, White members of the Adventist Health Study (AHS), California, USA Exposure assessment method: questionnaire; mailed, 55-item SQFFQ; six questions on current consumption of specific meats; red meat included beef and pork	Colon and rectum	Red meat (times/wk)			Age, sex, BMI, physical activity, parental history of colorectal cancer, current smoking, past smoking, alcohol consumption, aspirin use
			Never	42	1.00	
			> 0 to < 1	40	1.40 (0.87–2.25)	
			≥ 1	45	1.90 (1.16 – 3.11)	
			Trend-test *P* value: 0.02			
Pietinen et al. (1999) Finland Enrolment, 1985 and 1988; follow-up to 1995 Cohort study	27 111; male smokers in the Alpha-Tocopherol, Beta-Carotene Cancer Prevention (ATBC) Study Exposure assessment method: questionnaire; self-administered, modified dietary history of usual diet 12 mo prior to baseline (276 food items)	Colon and rectum	Beef, pork, and lamb, quartile median (g/day)			Age, supplement group, years of smoking, BMI, alcohol, education, physical activity, calcium intake
			35	55	1.0	
			52	35	0.6 (0.4–1.1)	
			69	50	0.9 (0.6–1.3)	
			99	45	0.8 (0.5–1.2)	
			Trend-test *P* value: 0.74			

Table 2.2.1 Cohort studies: consumption of red meat or red meat & processed meat combined and cancer of the colorectum

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
Järvinen et al. (2001) Finland Enrolment, 1967–1972; follow-up until late 1999 Cohort study	9959; men and women participating in the population-based Finnish Mobile Clinic Health Examination Survey Exposure assessment method: questionnaire; structured questionnaires including more than 100 foods and mixed dishes; food models and real foods used in portion size estimation [red meat may have included processed meat]	Colon and rectum	Red meat/processed meat Quartiles of intake (g/day)			Age; sex; BMI; occupation; smoking; geographical area; total energy intake; consumption of vegetables, fruits, cereals
			< 94 in men and < 61 in women	NR	1.00	
			94–141 in men, 61–92 in women	NR	1.06 (0.67–2.01)	
			142–206 in men, 93–134 in women	NR	1.55 (0.88–2.73)	
			> 206 in men, > 134 in women	NR	1.50 (0.77–2.94)	
		Colon	Quartiles of intake (g/day)			
			< 94 in men, < 61 in women	NR	1.00	
			94–141 in men, 61–92 in women	NR	0.71 (0.33–1.51)	
			142–206 in men, 93–134 in women	NR	1.29 (0.63–2.66)	
			> 206 in men, > 134 in women	NR	1.34 (0.57–3.15)	
		Rectum	Quartiles of intake (g/day)			
			< 94 in men, < 61 in women	NR	1.00	
			94–141 in men, 61–92 in women	NR	2.18 (0.93–5.10)	
			142–206 in men, 93–134 in women	NR	2.11 (0.84–5.28)	
			> 206 in men, > 134 in women	NR	1.82 (0.60–5.52)	

Table 2.2.1 Cohort studies: consumption of red meat or red meat & processed meat combined and cancer of the colorectum

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
Tiemersma et al. (2002) The Netherlands 1987–1998 Nested case–control study	Cases: 102; national and regional cancer registries Controls: 537; cohort, frequency-matched by sex, age, and centre Exposure assessment method: questionnaire; short SQFFQ method, validated by a dietary history method; fresh red meat was beef and pork	Colon and rectum	0–3.0 times/wk	22	1.0	Age, sex, centre, total energy intake, alcohol consumption, body height
			3.1–4.5 times/wk	35	1.3 (0.7–2.3)	
			≥ 5.0 times/wk	45	1.6 (0.9–2.9)	
			Trend-test *P* value: 0.1			
			Women:			
			0–3.0 times/wk	15	1.0	
			3.1–4.5 times/wk	18	0.8 (0.4–1.8)	
			≥ 5.0 times/wk	15	1.2 (0.5–2.8)	
			Trend-test *P* value: 0.64			
			Men:			
			0–3.0 times/wk	7	1.0	
			3.1–4.5 times/wk	17	2.7 (1.1–6.9)	
			≥ 5.0 times/wk	30	2.7 (1.1–6.7)	
			Trend-test *P* value: 0.06			
			Slow and normal *NAT1*:			
			0–3.0 times/wk	NR	1.0	
			3.1–4.5 times/wk	NR	1.2 (0.6–2.4)	
			≥ 5.0 times/wk	NR	1.4 (0.7–2.9)	
			Fast *NAT1*: 0–3.0 times/wk	NR	0.7 (0.3–1.9)	
			3.1–4.5 times/wk	NR	0.9 (0.4–2.0)	
			≥ 5.0 times/wk	NR	1.4 (0.6–3.0)	
			Slow and normal *NAT2*:			
			0–3.0 times/wk	NR	1.0	
			3.1–4.5 times/wk	NR	1.0 (0.5–2.2)	
			≥ 5.0 times/wk	NR	1.4 (0.7–2.9)	
			Fast and intermediate *NAT2*:			
			0–3.0 times/wk	NR	0.7 (0.3–1.9)	
			3.1–4.5 times/wk	NR	1.1 (0.5–2.4)	
			≥ 5.0 times/wk	NR	1.4 (0.6–3.1)	

Table 2.2.1 Cohort studies: consumption of red meat or red meat & processed meat combined and cancer of the colorectum

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
Tiemersma et al. (2002) The Netherlands 1987–1998 Nested case–control study (cont.)			*GSTM1* genotype present:			
			0–3.0 times/wk	NR	1.0	
			3.1–4.5 times/wk	NR	1.5 (0.6–3.7)	
			≥ 5.0 times/wk	NR	2.0 (0.8–5.0)	
			GSTM1 genotype null:			
			0–3.0 times/wk	NR	1.7 (0.7–4.4)	
			3.1–4.5 times/wk	NR	1.7 (0.7–4.1)	
			≥ 5.0 times/wk	NR	2.2 (0.9–5.2)	
Flood et al. (2003) USA 1987–1998 Cohort study	61 431; Breast Cancer Detection Demonstration Project (BCDDP) Exposure assessment method: questionnaire; 62-item NCI Block FFQ; red meat was pork, beef, hamburger, processed meats, and liver in previous year	Colon and rectum	Red meat/processed meat (quintile median, g/1000 kcal)			Age, total energy intake by multivariate nutrient density method, total meat intake
			6.1	NR	1.00	
			14.6	NR	1.04 (0.79–1.36)	
			22.6	NR	0.95 (0.72–1.26)	
			32.7	NR	0.95 (0.71–1.27)	
			52.2	NR	1.04 (0.77–1.41)	
			Trend-test *P* value: 0.73			
English et al. (2004) Melbourne, Australia 1990–2002 Cohort study	41 528; residents of Melbourne aged 40–69 yr Exposure assessment method: FFQ; red meat was veal, beef, lamb, pork, rabbit, or other game; diet assessed through 121-item FFQ	Colon and rectum	< 3.0 times/wk	66	1.00	Age; sex; country of birth; intake of energy, fat, cereal products
			3.0–4.4 times/wk	123	1.40 (1.10–1.90)	
			4.5–6.4 times/wk	142	1.50 (1.10–2.10)	
			≥ 6.5 times/wk	120	1.40 (1.00–1.90)	
			Trend-test *P* value: 0.2			
			For increase of 1 time/wk	451	1.03 (0.98–1.08)	
			Trend-test *P* value: 0.9			
		Colon	< 3.0 times/wk	NR	1.00	
			3.0–4.4 times/wk	NR	1.20 (0.80–1.70)	
			4.5–6.4 times/wk	NR	1.30 (0.90–1.90)	
			≥ 6.5 times/wk	NR	1.10 (0.70–1.60)	
			Trend-test *P* value: 0.9			

Table 2.2.1 Cohort studies: consumption of red meat or red meat & processed meat combined and cancer of the colorectum

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
English et al. (2004) Melbourne, Australia 1990–2002 Cohort study (cont.)		Colon	For an increase of 1 time/wk	283	1.00 (0.94–1.07)	
		Rectum	< 3.0 times/wk	NR	1.00	
			3.0–4.4 times/wk	NR	2.20 (1.30–4.00)	
			4.5–6.4 times/wk	NR	2.20 (1.20–3.90)	
			≥ 6.5 times/wk	NR	2.30 (1.20–4.20)	
			Trend-test *P* value: 0.07			
			For an increase of 1 time/wk	169	1.08 (0.99–1.16)	
			Trend-test *P* value: 0.07			
Chao et al. (2005) USA 1992–2001 Cohort study	148 610; Cancer Prevention Study II (CPS-II) Nutrition Survey cohort Exposure assessment method: questionnaire; diet assessed through 68-item, modified Block FFQ; red meat included beef, pork, processed meats, and liver	Colon	Red meat/processed meat, quintile median (g/day)			Age; education; BMI; cigarette smoking; recreational physical activity; multivitamin use; aspirin use; intake of beer, wine, liquor, fruits, vegetables, high-fibre grain foods
			Men:			
			100	88	1.00	
			253	121	1.14 (0.86–1.50)	
			398	141	1.16 (0.88–1.53)	
			612	191	1.22 (0.92–1.61)	
			999	125	1.30 (0.93–1.81)	
			Trend-test *P* value: 0.08			
			Red meat/processed meat, quintile median (g/day)			
			Women:			
			43	76	1.00	
			168	154	0.98 (0.74–1.30)	
			278	72	0.94 (0.68–1.31)	
			416	144	0.98 (0.73–1.32)	
			712	86	0.98 (0.68–1.40)	
			Trend-test *P* value: 0.45			

Table 2.2.1 Cohort studies: consumption of red meat or red meat & processed meat combined and cancer of the colorectum

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
Chao et al. (2005) USA 1992–2001 Cohort study (cont.)		Colon	Red meat/processed meat Men and women (sex-specific quintiles):			
			Q1	164	1.00	
			Q2	275	1.07 (0.88–1.31)	
			Q3	213	1.07 (0.86–1.31)	
			Q4	335	1.11 (0.91–1.36)	
			Q5	210	1.15 (0.90–1.46)	
			Trend-test *P* value: 0.4			
		Proximal colon	Red meat/processed meat (sex-specific quintiles)			
			Q1	88	1.00	
			Q2	169	1.21 (0.93–1.58)	
			Q3	113	1.08 (0.81–1.44)	
			Q4	182	1.17 (0.89–1.53)	
			Q5	116	1.27 (0.91–1.76)	
			Trend-test *P* value: 0.05			
		Distal colon	Red meat/processed meat (sex-specific quintiles)			
			Q1	69	1.00	
			Q2	76	0.72 (0.52–1.00)	
			Q3	79	0.89 (0.64–1.24)	
			Q4	120	0.87 (0.63–1.21)	
			Q5	64	0.71 (0.47–1.07)	
			Trend-test *P* value: 0.92			
		Rectosigmoid junction and rectum	Red meat/processed meat (sex-specific quintiles)			
			Q1	57	1.00	
			Q2	118	1.43 (1.03–1.96)	
			Q3	85	1.26 (0.89–1.78)	
			Q4	114	1.18 (0.84–1.67)	
			Q5	96	1.71 (1.15–2.52)	
			Trend-test *P* value: 0.007			

Table 2.2.1 Cohort studies: consumption of red meat or red meat & processed meat combined and cancer of the colorectum

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
Larsson et al. (2005a) Sweden 1987–2003 Cohort study	61 433; Swedish women aged 40–76 yr Exposure assessment method: questionnaire; 67-item, 6-mo FFQ; red meat included bacon, ham, hot dogs, and lunchmeat; beef and pork as a main dish reported separately	Colon and rectum	Beef and pork (servings/wk), quartiles (quartile median)			Age; BMI; education level; intake of total energy, alcohol, saturated fat, calcium, folate, fruits, vegetables, whole-grain foods
			< 2.0 (1.5)	NR	1.00	
			2.0 to < 3.0 (2.5)	NR	1.13 (0.95–1.36)	
			3.0 to < 4.0 (4.0)	NR	0.90 (0.70–1.17)	
			≥ 4.0 (5.5)	NR	1.22 (0.98–1.53)	
			Trend-test *P* value: 0.32			
		Colon: proximal colon	Beef and pork (servings/wk), quartiles (quartile median)			
			< 2.0 (1.5)	NR	1.00	
			2.0 to < 3.0 (2.5)	NR	0.90 (0.65–1.24)	
			3.0 to < 4.0 (4.0)	NR	0.78 (0.45–1.17)	
			≥ 4.0 (5.5)	NR	1.10 (0.74–1.64)	
			Trend-test *P* value: 0.9			
		Colon: distal colon	Beef and pork (servings/wk), quartiles (quartile median)			
			< 2.0 (1.5)	NR	1.00	
			2.0 to < 3.0 (2.5)	NR	1.26 (0.84–1.90)	
			3.0 to < 4.0 (4.0)	NR	0.98 (0.55–1.75)	
			≥ 4.0 (5.5)	NR	1.99 (1.26–3.14)	
			Trend-test *P* value: 0.01			
		Rectum	Beef and pork (servings/wk), quartiles (quartile median)			
			< 2.0 (1.5)	NR	1.00	
			2.0 to < 3.0 (2.5)	NR	1.18 (0.86–1.62)	
			3.0 to < 4.0 (4.0)	NR	0.87 (0.55–1.37)	
			≥ 4.0 (5.5)	NR	1.08 (0.72–1.62)	
			Trend-test *P* value: 0.98			

Table 2.2.1 Cohort studies: consumption of red meat or red meat & processed meat combined and cancer of the colorectum

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
Norat et al. (2005) Europe 1992–2002 Cohort study	478 040; European Prospective Investigation into Cancer and Nutrition (EPIC) study Exposure assessment method: questionnaire; country-specific, validated dietary questionnaires (88–266 items), self-administered in most countries; second 24-h recall measurement from an 8% random sample to calibrate measurements across countries and correct for systematic error	Colon and rectum	Red meat (g/day)			Age, sex, energy from non-fat sources, energy from fat sources, height, weight, occupational physical activity, smoking status, dietary fibre, alcohol intake, stratified by centre
			< 10	132	1.00	
			10–20	138	1.00 (0.78–1.28)	
			20–40	323	1.03 (0.83–1.28)	
			40–80	486	1.16 (0.94–1.43)	
			> 80	250	1.17 (0.92–1.49)	
			Trend-test *P* value: 0.08			
		Colon	Red meat (g/day)			
			< 10	NR	1.00	
			10–20	NR	1.04 (0.77–1.41)	
			20–40	NR	1.02 (0.78–1.32)	
			40–80	NR	1.16 (0.90–1.51)	
			> 80	NR	1.20 (0.88–1.61)	
			Trend-test *P* value: 0.14			
		Colon: right colon	Red meat (g/day)			
			< 10	NR	1.00	
			10–20	NR	1.13 (0.70–1.84)	
			20–40	NR	1.00 (0.65–1.54)	
			40–80	NR	1.36 (0.90–2.07)	
			> 80	NR	1.18 (0.73–1.91)	
			Trend-test *P* value: 0.22			
		Colon: left colon	Red meat (g/day)			
			< 10	NR	1.00	
			10–20	NR	1.07 (0.68–1.68)	
			20–40	NR	1.10 (0.65–1.63)	
			40–80	NR	1.11 (0.75–1.64)	
			> 80	NR	1.24 (0.80–1.94)	
			Trend-test *P* value: 0.38			

Table 2.2.1 Cohort studies: consumption of red meat or red meat & processed meat combined and cancer of the colorectum

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
Norat et al. (2005) Europe 1992–2002 Cohort study (cont.)		Rectum	Red meat (g/day)			
			< 10	NR	1.00	
			10–20	NR	0.93 (0.60–1.44)	
			20–40	NR	1.07 (0.74–1.55)	
			40–80	NR	1.16 (0.80–1.66)	
			> 80	NR	1.13 (0.74–1.71)	
			Trend-test *P* value: 0.32			
		Colon and rectum	For an increase of 100 g/day (observed intake)	1329	1.21 (1.02–1.43)	
			Trend-test *P* value: 0.03			
		Colon and rectum	For an increase of 100 g/day (calibrated intake)	1329	1.49 (0.91–2.43)	
			Trend-test *P* value: 0.11			
		Colon	For an increase of 100 g/day (observed intake)	855	1.20 (0.96–1.48)	
			Trend-test *P* value: 0.1			
		Colon	For an increase of 100 g/day (calibrated intake)	855	1.36 (0.74–2.50)	
			Trend-test *P* value: 0.32			
		Rectum	For an increase of 100 g/day (observed intake)	474	1.23 (0.94–1.62)	
			Trend-test *P* value: 0.14			
		Rectum	For an increase of 100 g/day (calibrated intake)	474	1.75 (0.93–3.30)	
			Trend-test *P* value: 0.08			

Table 2.2.1 Cohort studies: consumption of red meat or red meat & processed meat combined and cancer of the colorectum

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
Berndt et al. (2006) Maryland, USA 1989–2003 Nested case–control study	Cases: 272; identified via population-based registry from participants in the CLUE II cohort Controls: 2224; 10% age-stratified sample of CLUE II cohort participants without cancer Exposure assessment method: FFQ; validated, administered by mail, and considered frequency and serving size; red meat was hamburgers, cheeseburgers, meatloaf, beef, beef stew, pork, hot dogs, bacon, sausage, ham, bologna, salami, and lunchmeats	Colon and rectum	Red meat/processed meat (g/day)			Age, ethnicity, total energy intake
			< 44	NR	1.00	
			44 to < 86.3	NR	1.16 (0.80–1.70)	
			≥ 86.3	NR	1.32 (0.86–2.02)	
Oba et al. (2006) Takayama, Japan 1992–2000 Cohort study	30 221; community-based cohort of men and women aged ≥ 35 yr in Takayama, Japan Exposure assessment method: questionnaire; self-administered, 169-item, validated SQFFQ; red meat defined as beef and pork	Colon	Men (tertile median, g/day):			Age, height, BMI, total pack-years of cigarette smoking, alcohol intake, physical activity
			18.7	40	1.00	
			34.4	39	1.14 (0.73–1.77)	
			56.6	32	1.03 (0.64–1.66)	
			Trend-test *P* value: 0.86			
			Women (tertile median, g/day):			
			10.7	50	1.00	
			25.2	25	0.64 (0.39–1.03)	
			42.3	27	0.79 (0.49–1.28)	
			Trend-test *P* value: 0.2			

Table 2.2.1 Cohort studies: consumption of red meat or red meat & processed meat combined and cancer of the colorectum

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
Kabat et al. (2007) Canada 1980–2000 Cohort study	49 654; Canadian National Breast Screening Study (CNBSS) Exposure assessment method: questionnaire; self-administered, 86-item FFQ with 22 meat items and two mixed dishes containing meat; red meat included ham, bacon, and pork-based luncheon meats	Colon and rectum	Red meat, processed meat (g/day)			Age; BMI; menopausal status; oral contraceptive use; hormone replacement use; pack-years of smoking; alcohol intake; education; physical activity; dietary intake of fat, fibre, folic acid, total calories
			< 14.25	NR	1.00	
			14.25 to < 21.02	NR	1.10 (0.85–1.42)	
			21.02 to < 28.74	NR	1.17 (0.90–1.50)	
			28.74–40.30	NR	0.97 (0.74–1.27)	
			≥ 40.30	NR	1.12 (0.86–1.46)	
			Trend-test *P* value: 0.66			
		Colon	Red meat/processed meat (g/day)			
			< 14.25	NR	1.00	
			14.25 to < 21.02	NR	1.06 (0.79–1.42)	
			21.02 to < 28.74	NR	0.97 (0.72–1.32)	
			28.74–40.30	NR	0.84 (0.61–1.15)	
			≥ 40.30	NR	0.88 (0.64–1.21)	
			Trend-test *P* value: 0.16			
		Rectum	Red meat/processed meat (g/day)			
			< 14.25	NR	1.00	
			14.25 to < 21.02	NR	1.25 (0.75–2.08)	
			21.02 to < 28.74	NR	1.79 (1.11–2.88)	
			28.74–40.30	NR	1.42 (0.85–2.35)	
			≥ 40.30	NR	1.95 (1.21–3.16)	
			Trend-test *P* value: 0.008			
Butler et al. (2008b) Singapore, China 1993–2005 Cohort study	61 321; Singaporean Chinese aged 45–74 yr Exposure assessment method: FFQ; validated, 165-item, 12-mo quantitative FFQ	Colon and rectum	Quartile 4 vs quartile 1	NR	1.01 (0.82–1.26)	Age, sex, total energy intake, dialect group, interview year, alcohol intake, BMI, diabetes, education, physical activity, smoking history, first-degree history of colorectal cancer
			Trend-test *P* value: 0.6			

Table 2.2.1 Cohort studies: consumption of red meat or red meat & processed meat combined and cancer of the colorectum

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
Sørensen et al. (2008) Denmark Enrolment, 1993–1997; follow-up to 2003 Cohort study	Case–cohort: 379 cases with colorectal cancer and 769 subcohort members; Danish men and women aged 50–64 yr free of cancer Exposure assessment method: questionnaire; FFQ with 192 foods and recipes, 63 meat items and meat dishes, and standard portion sizes; red meat was beef, veal, pork, lamb, and offal	Colon and rectum	Red meat, all (per 25 g/day increase)	105	1.03 (0.97–1.09)	Age; sex; intake of poultry, fish, alcohol, dietary fibre; BMI; HRT; smoking status
			Red meat for different polymorphisms (per 25 g/day increase)			
			NAT1 fast	NR	1.06 (0.97–1.17)	
			NAT1 slow	NR	1.02 (0.95–1.09)	
			NAT2 slow	NR	1.06 (0.97–1.14)	
			NAT2 fast	NR	1.01 (0.93–1.09)	
Andersen et al. (2009) Denmark 1994–1997 Nested case–control study	Cases: 372; case–cohort study within the Danish Diet, Cancer and Health cohort Controls: 765; subcohort members with DNA and questionnaire data available; frequency-matched to cases by sex Exposure assessment method: FFQ; mailed in, validated, 192-item FFQ; red meat was beef, veal, pork, lamb, and offal	Colon and rectum	Red meat (g/day)			Sex, age, tumour localization (proximal or distal colon, rectum, NOS), BMI, alcohol, processed meat, dietary fibre, smoking status, NSAID use, HRT use
			Per 25 g/day	NR	1.02 (0.94–1.12)	
Lee et al. (2009) Shanghai, China Enrolment, 1997–2000; follow-up to December, 2005 Cohort study	73 224; Shanghai Women's Health Study (SWHS), a population-based prospective cohort study of women aged 40–70 yr living in Shanghai, China Exposure assessment method: questionnaire; validated quantitative FFQ (including 19 food items/groups of animal origin)	Colon and rectum	Red meat (g/day), quintiles			Age, education, income, survey season, tea consumption, NSAID use, energy intake, fibre intake
			< 24	108	1.0	
			24–< 36	80	0.9	
			36–< 49	65	0.7	
			49–< 67	79	1.0	
			≥ 67	62	0.8 (0.6–1.1)	
			Trend-test *P* value: 0.53			
		Colon	Red meat (g/day), quintiles			
			< 24	63	1.0	
			24–< 36	49	0.9	
			36–< 49	40	0.8	
			49–< 67	43	0.9	
			≥ 67	41	0.9 (0.6–1.5)	
			Trend-test *P* value: 0.31			

Table 2.2.1 Cohort studies: consumption of red meat or red meat & processed meat combined and cancer of the colorectum

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
		Rectum	Red meat (g/day), quintiles			
			< 24	45	1.0	
			24–< 36	31	0.8	
			36–< 49	25	0.7	
			49–< 67	36	1.0	
			≥ 67	21	0.6 (0.3–1.1)	
			Trend-test *P* value: 0.79			
Cross et al. (2010) USA 1995–2003 Cohort study	300 948; National Institutes of Health – American Association of Retired Persons (NIH-AARP) Diet and Health Study in men and women aged 50–71 yr from six USA states and two metropolitan areas Exposure assessment method: FFQ; 124-item FFQ calibrated against two 24-h dietary recalls; red meat included beef, pork, lamb, bacon, cold cuts, ham, hamburger, hot dogs, liver, and sausage	Colon and rectum	Red meat/processed meat (median, g/1000 kcal)			Sex, BMI, dietary fibre intake, education level, smoking habits, dietary calcium intake, total energy intake, white meat intake
			9.5	451	1.00	
			20.9	484	1.00 (0.87–1.14)	
			30.7	502	0.99 (0.87–1.13)	
			42.1	614	1.18 (1.03–1.34)	
			61.6	668	1.24 (1.09–1.42)	
			Trend-test *P* value: 0.001			
		Colon and rectum	For an increase of 100 g/day	2719	1.23 (1.10–1.36)	
			Trend-test *P* value: 0.001			
		Colon	Red meat/processed meat (median, g/1000 kcal)			
			9.5	340	1.00	
			20.9	345	0.94 (0.81–1.09)	
			30.7	367	0.96 (0.82–1.12)	
			42.1	457	1.16 (1.00–1.36)	
			61.6	486	1.21 (1.03–1.41)	
			Trend-test *P* value: 0.001			
		Colon	For 100 g/day increase	1995	1.20 (1.05–1.36)	
			Trend-test *P* value: 0.024			

Table 2.2.1 Cohort studies: consumption of red meat or red meat & processed meat combined and cancer of the colorectum

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
Cross et al. (2010) USA 1995–2003 Cohort study (cont.)		Rectum	Red and processed meat (median, g/1000 kcal)			
			9.5	111	1.00	
			20.9	139	1.18 (0.91–1.52)	
			30.7	135	1.09 (0.84–1.42)	
			42.1	157	1.21 (0.93–1.58)	
			61.6	182	1.35 (1.03–1.76)	
			Trend-test *P* value: 0.024			
		Rectum	For 100 g/day increase	724	1.31 (1.07–1.61)	
			Trend-test *P* value: 0.024			
		Proximal colon	Red and processed meat intake, quintiles			
			Q5 vs Q1	1150	1.15 (0.94–1.41)	
			Trend-test *P* value: 0.024			
		Distal colon	Red and processed meat intake, quintiles			
			Q5 vs Q1	787	1.29 (1.00–1.66)	
			Trend-test *P* value: 0.018			
Ollberding et al. (2012) California or Hawaii, USA 1993–2007 Cohort study	131 763; multiethnic sample of African Americans, Japanese Americans, Latinos, native Hawaiians, and Whites aged 45–75 yr Exposure assessment method: questionnaire; validated quantitative FFQ that captured 85% of the intake of key nutrients	Colon and rectum	Red meat, excluding processed (quintile median, g/1000 kcal per day)			Age, ethnicity, family history of colorectal cancer, history of colorectal polyps, BMI, smoking, NSAID use, alcohol, physical activity, history of diabetes, HRT use (females), total calories, intake of dietary fibre, calcium, folate, vitamin D
			4.59	654	1.00	
			11.13	702	0.99 (0.89–1.11)	
			16.86	712	1.00 (0.90–1.12)	
			23.40	677	0.97 (0.87–1.09)	
			34.86	659	0.98 (0.87–1.10)	
			Trend-test *P* value: 0.58			

Table 2.2.1 Cohort studies: consumption of red meat or red meat & processed meat combined and cancer of the colorectum

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
Figueiredo et al. (2014) International – USA, Canada, and Europe NR Pooled case–control study and nested-case-control studies	Cases: 9287; identified from five case–control and five nested case–control studies within prospective cohorts from the Colon Cancer Family Registry (CCFR) and the Genetics and Epidemiology of Colorectal Cancer Consortium (GECCO) Controls: 9117; controls from the same population as cases Exposure assessment method: questionnaire; unclear harmonized red meat variable (in some studies, it included processed meats; in others, it did not)	Colon and rectum	Red meat intake			Age at the reference time, sex (when appropriate), centre (when appropriate), total energy consumption (if available), first three principal components from EIGENSTRAT to account for potential population substructure
			Per quartile of increasing intake (*P* = 1.63e–18)	NR	1.15	
Ananthakrishnan et al. (2015) USA, Canada, and Australia NR Pooled case–control study and nested case-control studies	Cases: 8290; cases were incident colorectal cancer patients enrolled in the Colon Cancer Family Registry (CCFR) and 10 different studies that were part of the Genetics and Epidemiology of Colorectal Cancer Consortium (GECCO) Controls: 9115; controls were enrolled as part of CCFR and as part of the 10 studies that were part of GECCO Exposure assessment method: questionnaire; red meat and other covariates were harmonized across all the 11 studies; therefore, the definition of red meat was heterogeneous, with some studies including processed meat and others not	Colon and rectum	Red meat/processed meat (servings/day)			Age, sex, study site, smoking status, aspirin use, NSAID use, BMI, dietary calcium, folate, servings of fruits and vegetables
			Q1	NR	1.00	
			Q2	NR	1.15 (1.03–1.28)	
			Q3	NR	1.17 (1.05–1.29)	
			Q4	NR	1.29 (1.15–1.44)	

Table 2.2.1 Cohort studies: consumption of red meat or red meat & processed meat combined and cancer of the colorectum

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
Bernstein et al. (2015) USA Nurses' Health Study, 1980–2010; Health Professionals Follow-Up Study, 1986– 2010 Cohort study	87 108 women and 47 389 men; Nurses' Health Study (NHS) and Health Professionals Follow-Up Study (HPFS) Exposure assessment method: FFQ; diet from FFQs collected about every 4 yr during follow-up (see Wei et al., 2004)	Colon and rectum	Red meat (1 serving/day)			Age, follow-up, family history, endoscopy, smoking, alcohol drinking, BMI, physical activity, medications and supplements, menopausal status, hormone use, total caloric intake, folate, calcium, vitamin D, fibre intake
			Baseline intake	2731	1.02 (0.94–1.12)	
			Trend-test *P* value: 0.61			
			Red meat (1 serving/day)			
			Cumulative average	2731	0.99 (0.87–1.13)	
			Trend-test *P* value: 0.88			
		Proximal colon	Red meat (1 serving/day)			
			Baseline intake	1151	1.13 (0.99–1.29)	
			Trend-test *P* value: 0.07			
			Red meat (1 serving/day)			
			Cumulative intake	1151	1.14 (0.92–1.40)	
			Trend-test *P* value: 0.22			
		Distal colon	Red meat (1 serving/day)			
			Baseline intake	817	0.88 (0.75–1.05)	
			Trend-test *P* value: 0.16			
			Red meat (1 serving/day)			
			Cumulative intake	817	0.75 (0.68–0.82)	
			Trend-test *P* value: < 0.01			
		Rectum	Processed red meat (1 serving/day)			
			Baseline intake	589	1.05 (0.84–1.32)	
			Trend-test *P* value: 0.64			
			Processed red meat (1 serving/day)			
			Cumulative intake	589	1.14 (0.86–1.51	
			Trend-test *P* value: 0.25			

BMI, body mass index; CI, confidence interval; FFQ, food frequency questionnaire; GWAS, genome-wide association study; h, hour; HRT, hormone replacement therapy; mo, month; NOS, not otherwise specified; NR, not reported; NSAID, nonsteroidal anti-inflammatory drug; SD, standard deviation; SQFFQ, semiquantitative food frequency questionnaire; wk, week; yr, year

Table 2.2.2 Cohort studies on consumption of processed meat and cancer of the colorectum

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
Bostick et al. (1994) USA Enrolment,1985; follow-up, 1986–1990 Cohort study	35 216; women aged 55–69 yr, mostly White, in the Iowa Women's Health Study (IWHS) Exposure assessment method: FFQ; 127-item, validated SQFFQ; processed meat was bacon, hot dogs, and other processed meats	Colon	Processed meats (servings/wk)			Age, total energy intake, height, parity, total vitamin E intake, interaction term vitamin E–age, vitamin A supplement
			0	91	1.00	
			0.5	67	1.00 (0.73–1.38)	
			1.0	32	1.07 (0.71–1.61)	
			2.0–3.0	14	0.81 (0.46–1.44)	
			> 3.0	8	1.51 (0.72–3.17)	
			Trend-test *P* value: 0.45			
Kato et al. (1997) USA Enrolment, 1985–1991; follow-up to 1994 Cohort study	14 727; women aged 34–65 yr in the New York University Women's Health Study (NYUWHS) enrolled at mammographic screening clinics in New York and Florida Exposure assessment method: FFQ; 70-item FFQ; processed meats were ham and sausages	Colon and rectum	Ham and sausage intake, quartiles			Total caloric intake, age, place at enrolment and level of education
			Q1 (lowest quartile)	NR	1.00	
			Q2	NR	1.39 (0.81–2.38)	
			Q3	NR	1.38 (0.79–2.42)	
			Q4 (highest quartile)	NR	1.09 (0.59–2.02)	
			Trend-test *P* value: 0.735			
Pietinen et al. (1999) Finland Enrolment, 1985 and 1988; follow-up, 30 April 1995 (average, 8 yr) Cohort study	27 111; male smokers aged 50 and 69 yr in the Alpha-Tocopherol, Beta-Carotene Cancer Prevention (ATBC) Study Exposure assessment method: FFQ; self-administered, modified, 12-mo dietary history method (276 food items); processed meat was mostly sausages	Colon and rectum	Processed meat (g/day)			Age, supplement group, smoking, BMI, alcohol, education, physical activity at work, calcium intake
			26	41	1.00	
			50	58	1.5 (1–2.2)	
			73	44	1.1 (0.7–1.8)	
			122	42	1.2 (0.7–1.8)	
			Trend-test *P* value: 0.78			
Flood et al. (2003) USA 1987–1998 Cohort study	45 496; follow-up of a subset of the women in the Breast Cancer Detection Demonstration Project (BCDDP) Exposure assessment method: FFQ; 62-item Block FFQ with 17 meat items; processed meats were bacon, ham, or other lunchmeats, hot dogs, and sausage	Colon and rectum	Processed meat (quintile median, g/1000 kcal)			Age, total energy intake by multivariate nutrient density method
			Q1 (0.02)	NR	1.00	
			Q2 (2.40)	NR	0.90 (0.68–1.18)	
			Q3 (5.90)	NR	0.83 (0.63–1.11)	
			Q4 (11.00)	NR	1.09 (0.84–1.43)	
			Q5 (22.20)	NR	0.97 (0.73–1.28)	
			Trend-test *P* value: 0.35			

Table 2.2.2 Cohort studies on consumption of processed meat and cancer of the colorectum

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
English et al. (2004) Melbourne, Australia 1990–2002 Cohort study	41 528; residents of Melbourne aged 40–69 yr Exposure assessment method: questionnaire; 121-item FFQ; processed meat was salami, sausages, bacon, ham, corned beef, and luncheon meats	Colon and rectum	Processed meat intake (times/wk)			Age; sex; country of birth; intake of energy, fat, cereal products
			< 1.0	80	1.00	
			1.5–1.9	105	1.30 (1.00–1.70)	
			2.0–3.9	129	1.00 (0.80–1.40)	
			≥ 4.0	137	1.50 (1.10–2.00)	
			Trend-test *P* value: 0.01			
			For an increase of 1 time/wk	451	1.07 (1.02–1.13)	
			Trend-test *P* value: 0.9			
		Colon	Processed meat intake (times/wk)			
			< 1.0	NR	1.00	
			1.5–1.9	NR	1.10 (0.80–1.60)	
			2.0–3.9	NR	0.80 (0.60–1.10)	
			≥ 4.0	NR	1.30 (0.90–1.90)	
			Trend-test *P* value: 0.06			
			For an increase of 1 time/wk	283	1.07 (1.00–1.14)	
		Rectum	Processed meat intake (times/wk)			
			< 1.0	NR	1.00	
			1.5–1.9	NR	1.90 (1.10–3.20)	
			2.0–3.9	NR	1.70 (1.00–2.90)	
			≥ 4.0	NR	2.00 (1.10–3.40)	
			Trend-test *P* value: 0.09			
			For an increase of 1 time/wk	169	1.08 (0.99–1.18)	

Table 2.2.2 Cohort studies on consumption of processed meat and cancer of the colorectum

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
Lin et al. (2004) USA 1993–2003 Cohort study	36 976; Women's Health Study (WHS) Exposure assessment method: FFQ; validated, 131-item SQFFQ; correlation ≥ 0.5 for most items	Colon and rectum	Processed meat (median, servings/day)			Age, random treatment assignment, BMI, family history of colorectal cancer, history of colorectal polyps, physical activity, cigarette smoking, alcohol consumption, postmenopausal hormone therapy, total energy intake
			0	51	1.00	
			0.07	45	1.18 (0.79–1.77)	
			0.13	42	1.27 (0.84–1.91)	
			0.21	32	0.95 (0.60–1.49)	
			0.50	32	0.85 (0.53–1.35)	
			Trend-test *P* value: 0.25			
Chao et al. (2005) USA Enrolment, 1992–1993; follow-up to 2001 Cohort study	148 610; adults in the Cancer Prevention Study II (CPS-II) aged 50–74 yr in 21 states Exposure assessment method: FFQ; 68-item, modified Block FFQ; processed meats were bacon, sausage, hot dogs, and ham, bologna, salami, or lunchmeat	Colon	Processed meat (g/wk) Men:			Age; total energy intake; education; BMI; cigarette smoking; recreational physical activity; multivitamin use; aspirin use; intake of beer, wine, liquor, fruits, vegetables, high-fibre grain foods
			0	64	1.00	
			< 60	125	0.75 (0.55–1.02)	
			61–160	225	1.02 (0.76–1.36)	
			161–240	108	1.11 (0.80–1.54)	
			> 240	143	1.11 (0.80–1.54)	
			Trend-test *P* value: 0.03			
			Processed meat (g/wk) Women:			
			0	89	1.00	
			< 30	125	1.11 (0.84–1.46)	
			31–60	96	0.95 (0.71–1.27)	
			61–120	104	0.94 (0.70–1.26)	
			> 120	118	1.16 (0.85–1.57)	
			Trend-test *P* value: 0.48			
			Processed meat, quintiles Men and women:			
			Q1	153	1.00	
			Q2	250	0.90 (0.74–1.11)	
			Q3	321	1.01 (0.83–1.23)	
			Q4	212	1.02 (0.82–1.27)	
			Q5	261	1.13 (0.91–1.41)	
			Trend-test *P* value: 0.02			

Table 2.2.2 Cohort studies on consumption of processed meat and cancer of the colorectum

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
Chao et al. (2005) USA Enrolment, 1992–1993; follow-up to 2001 Cohort study (cont.)		Proximal colon	Processed meat, quintiles			
			Men and women:			
			Q1	96	1.00	
			Q2	133	0.79 (0.61–1.03)	
			Q3	174	0.92 (0.71–1.19)	
			Q4	131	1.03 (0.78–1.35)	
			Q5	133	0.97 (0.72–1.29)	
			Trend-test *P* value: 0.17			
		Distal colon	Processed meat, quintiles			
			Men and women:			
			Q1	44	1.00	
			Q2	98	1.19 (0.83–1.70)	
			Q3	111	1.15 (0.80–1.65)	
			Q4	58	0.95 (0.63–1.43)	
			Q5	97	1.39 (0.94–2.05)	
			Trend-test *P* value: 0.11			
		Rectosigmoid and rectum	Processed meat, quintiles			
			Men and women:			
			Q1	50	1.00	
			Q2	106	1.14 (0.81–1.60)	
			Q3	134	1.24 (0.88–1.74)	
			Q4	86	1.31 (0.91–1.88)	
			Q5	94	1.26 (0.86–1.83)	
			Trend-test *P* value: 0.18			

Table 2.2.2 Cohort studies on consumption of processed meat and cancer of the colorectum

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
Larsson et al. (2005a) Sweden 1987–2003 Cohort study	61 433; Swedish women aged 40–76 yr Exposure assessment method: FFQ; 67-item, 6-mo FFQ (nine items on red and processed meats); processed meats were bacon, hot dogs, ham, or other lunchmeats and blood pudding	Colon and rectum	Processed meats (g/day), quartiles (quartile median)			Age; BMI; education level; intake of total energy, alcohol, saturated fat, calcium, folate, fruits, vegetables, wholegrain foods
			< 12 (6)	NR	1.00	
			12–21 (16)	NR	0.89 (0.72–1.90)	
			22–31 (26)	NR	1.01 (0.82–1.24)	
			≥ 32 (41)	NR	1.07 (0.85–1.33)	
			Trend-test *P* value: 0.23			
		Proximal colon	Processed meats (g/day), quartiles (quartile median)			
			< 12 (6)	NR	1.00	
			12–21 (16)	NR	0.92 (0.66–1.32)	
			22–31 (26)	NR	0.85 (0.58–1.24)	
			≥ 32 (41)	NR	1.02 (0.69–1.52)	
			Trend-test *P* value: 0.97			
		Distal colon	Processed meats (g/day), quartiles (quartile median)			
			< 12 (6)	NR	1.00	
			12–21 (16)	NR	1.05 (0.67–1.64)	
			22–31 (26)	NR	0.98 (0.61–1.58)	
			≥ 32 (41)	NR	1.39 (0.86–2.24)	
			Trend-test *P* value: 0.2			
		Rectum	Processed meats (g/day), quartiles (quartile median)			
			< 12 (6)	NR	1.00	
			12–21 (16)	NR	0.78 (0.52–1.12)	
			22–31 (26)	NR	1.02 (0.75–1.55)	
			≥ 31 (41)	NR	0.90 (0.60–1.34)	
			Trend-test *P* value: 0.88			

Table 2.2.2 Cohort studies on consumption of processed meat and cancer of the colorectum

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
Lüchtenborg et al. (2005) The Netherlands 1989–1994 Nested case–control study	Cases: 588; cases were identified from the subcohort of the Netherlands Cancer Study (NLCS); this was the same population described by Brink et al. (2005); incident cases with colorectal cancer, with available tumour tissue and FFQ data, were included in this study Controls: 2948; subcohort without colorectal cancer at the last follow-up Exposure assessment method: FFQ; self-administered; see description for Goldbohm et al. (1994); meat products were preserved meat, "sandwich fillings"	Colon	Meat products (g/day); *APC*– genotype			Age, sex, family history of colorectal cancer, smoking, BMI, energy intake
			Q1	71	1.00	
			Q2	62	0.90 (0.62–1.30)	
			Q3	71	0.97 (0.68–1.39)	
			Q4	70	1.07 (0.73–1.56)	
			Trend-test *P* value: 0.66			
			Meat products (g/day); *APC*+ genotype			
			Q1	26	1.00	
			Q2	23	0.87 (0.49–1.56)	
			Q3	33	1.15 (0.67–1.97)	
			Q4	45	1.61 (0.96–2.71)	
			Trend-test *P* value: 0.04			
		Rectum	Meat products (g/day); *APC*– genotype			
			Q1	20	1.00	
			Q2	12	0.57 (0.27–1.19)	
			Q3	19	0.85 (0.44–1.65)	
			Q4	22	1.02 (0.52–1.99)	
			Trend-test *P* value: 0.73			
			Meat products (g/day); *APC*+ genotype-			
			Q1	15	1.00	
			Q2	12	0.79 (0.36–1.74)	
			Q3	14	0.89 (0.41–1.92)	
			Q4	16	1.03 (0.47–2.27)	
			Trend-test *P* value: 0.88			

Table 2.2.2 Cohort studies on consumption of processed meat and cancer of the colorectum

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
Norat et al. (2005) Europe 1992–2002 Cohort study	478 040; European Prospective Investigation into Cancer and Nutrition (EPIC) study Exposure assessment method: questionnaire; country-specific, validated dietary questionnaires (88–266 items), self-administered in most countries; second 24-h recall measurement from an 8% random sample to calibrate measurements across countries and correct for systematic error	Colon and rectum	Processed meat (g/day)			Age, sex, energy from non-fat sources, energy from fat sources, height, weight, occupational physical activity, smoking status, dietary fibre, alcohol intake, stratified by centre
			<10	232	1.00	
			10–20	256	1.10 (0.91–1.32)	
			20–40	402	1.12 (0.94–1.35)	
			40–80	318	1.14 (0.94–1.40)	
			> 80	121	1.42 (1.09–1.86)	
			Trend-test *P* value: 0.02			
		Colon and rectum	For an increase of 100 g/day (observed intake)	1329	1.32 (1.07–1.63)	
			Trend-test *P* value: 0.009			
		Colon and rectum	For an increase of 100 g/day (calibrated intake)	1329	1.70 (1.05–2.76)	
			Trend-test *P* value: 0.03			
		Colon	Processed meat (g/day)			
			< 10	NR	1.00	
			10–20	NR	1.04 (0.77–1.41)	
			20–40	NR	1.02 (0.78–1.32)	
			40–80	NR	1.16 (0.90–1.51)	
			> 80	NR	1.20 (0.88–1.61)	
			Trend-test *P* value: 0.14			

Table 2.2.2 Cohort studies on consumption of processed meat and cancer of the colorectum

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
Norat et al. (2005) Europe 1992–2002 Cohort study (cont.)		Colon	For an increase of 100 g/day (observed intake)	855	1.39 (1.06–1.82)	
			Trend-test *P* value: 0.01			
		Colon	For an increase of 100 g/day (calibrated intake)	855	1.68 (0.87–3.27)	
			Trend-test *P* value: 0.12			
		Proximal colon	Processed meat (g/day)			
			< 10	NR	1.00	
			10–20	NR	1.04 (0.73–1.49)	
			20–40	NR	0.95 (0.67–1.34)	
			40–80	NR	1.17 (0.80–1.70)	
			> 80	NR	1.19 (0.70–2.01)	
			Trend-test *P* value: 0.22			
		Distal colon	Processed meat (g/day)			
			< 10	NR	1.00	
			10–20	NR	1.30 (0.92–1.83)	
			20–40	NR	1.32 (0.94–1.85)	
			40–80	NR	1.45 (1.00–2.11)	
			> 80	NR	1.48 (0.87–2.53)	
			Trend-test *P* value: 0.38			

Table 2.2.2 Cohort studies on consumption of processed meat and cancer of the colorectum

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
Norat et al. (2005) Europe 1992–2002 Cohort study (cont.)		Rectum	Processed meat (g/day)			
			< 10	NR	1.00	
			10–20	NR	1.13 (0.81–1.58)	
			20–40	NR	1.27 (0.93–1.74)	
			40–80 g/day	NR	1.05 (0.74–1.50)	
			> 80 g/day	NR	1.62 (1.04–2.50)	
			Trend-test *P* value: 0.2			
		Rectum	For an increase of 100 g/day (observed intake)	474	1.22 (0.87–1.71)	
			Trend-test *P* value: 0.25			
		Rectum	For an increase of 100 g/day (calibrated intake)	474	1.70 (0.83–3.47)	
			Trend-test *P* value: 0.14			
Balder et al. (2006) The Netherlands 1986–1996 Cohort study	152 852 men and women; case–cohort analysis of the Netherlands Cohort Study (NLCS) Exposure assessment method: FFQ; 150-item FFQ for 12 mo before enrolment	Colon and rectum	Processed meat (g/day)			Age, BMI, family history, smoking, alcohol intake, physical activity, vegetable consumption, total energy intake
			Men:			
			0	78	1.00	
			0.1–9.9	277	1.02 (0.74–1.41)	
			10.0–19.9	239	0.98 (0.71–1.36)	
			≥ 20.0	275	1.18 (0.84–1.64)	
			Trend-test *P* value: 0.25			
			Processed meat (g/day)			
			Women:			
			0	87	1.00	
			0.1–9.9	295	1.04 (0.78–1.39)	
			10.0–19.9	169	1.13 (0.82–1.55)	
			≥ 20.0	115	1.05 (0.74–1.48)	
			Trend-test *P* value: 0.62			

Table 2.2.2 Cohort studies on consumption of processed meat and cancer of the colorectum

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
Oba et al. (2006) Takayama, Japan 1992–2000 Cohort study	30221; community-based cohort with 13 894 men and 16 327 women in Takayama, Japan, aged 35 yr or older Exposure assessment method: FFQ; validated, self-administered, 169-item SQFFQ; processed meats were ham, sausage, bacon, and yakibuta (Chinese-style roasted pork)	Colon	Processed meat (tertile mean, g/day)			Age, height, BMI, total pack-years of cigarette smoking, alcohol intake, physical activity
			Men:			
			3.9	33	1.00	
			9.3	34	1.25 (0.75–1.95)	
			20.3	44	1.98 (1.24–3.16)	
			Trend-test *P* value: < 0.01			
			Processed meat (tertile mean, g/day)			
			Women:			
			3.0	42	1.00	
			7.3	37	1.13 (0.72–1.75)	
			16.3	23	0.85 (0.50–1.43)	
			Trend-test *P* value: 0.62			
Sato et al. (2006) Japan Enrolment, 1990; 11-yr follow-up to 2001 Cohort study	47 605; men and women aged 40–64 yr who were residents in Miyagi Prefecture Exposure assessment method: questionnaire; 40-item FFQ with five meat items; processed meat was ham or sausages	Colon and rectum	Median (g/day)			Sex; age; smoking status; alcohol consumption; BMI; education; family history of cancer; time spent walking; consumption of fat, calcium, dietary fibre; total energy intake
			0	75	1.00	
			1.1	118	0.98 (0.74–1.31)	
			4.5	128	1.02 (0.77–1.36)	
			15.8	37	0.91 (0.61–1.35)	
			Trend-test *P* value: 0.99			
		Colon	Median (g/day)			
			0	49	1.00	
			1.1	78	1.00 (0.70–1.42)	
			4.5	70	0.86 (0.60–1.25)	
			15.8	20	0.75 (0.45–1.27)	
			Trend-test *P* value: 0.25			
		Proximal colon	Median (g/day)			
			0	23	1.00	
			1.1	47	1.28 (0.78–2.11)	
			4.5	34	0.86 (0.50–1.46)	
			15.8	9	0.69 (0.32–1.51)	
			Trend-test *P* value: 0.2			

Table 2.2.2 Cohort studies on consumption of processed meat and cancer of the colorectum

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
Sato et al. (2006) Japan Enrolment, 1990; 11-yr follow-up to 2001 Cohort study (cont.)		Distal colon	Median (g/day)			
			0	21	1.00	
			1.1	22	0.86 (0.36–1.20)	
			4.5	26	0.79 (0.44–1.41)	
			15.8	7	0.65 (0.28–1.55)	
			Trend-test *P* value: 0.5			
		Rectum	Median (g/day)			
			0	22	1.00	
			1.1	57	0.87 (0.53–1.42)	
			4.5	62	0.90 (0.55–1.47)	
			15.8	16	0.97 (0.51–1.86)	
			Trend-test *P* value: 0.92			
Butler et al. (2008b) Singapore 1993–2005 Cohort study	61 321; Singaporean Chinese aged 45–74 yr Exposure assessment method: questionnaire; validated, 165-item, 12-mo quantitative FFQ	Colon and rectum	Quartile 4 vs quartile 1	NR	1.16 (0.95–1.41)	Age, sex, total energy intake, dialect group, interview year, alcohol intake, BMI, diabetes, education, physical activity, smoking history, first-degree history of colorectal cancer
			Trend-test *P* value: 0.1			
			Per 25 g/day	NR	1.00 (0.85–1.19)	
Cross et al. (2010) USA Enrolment, 1995–1996; follow-up until end of 2003 Cohort study	300 948; prospective cohort of men and women aged 50–71 yr in the National Institutes of Health – American Association of Retired Persons (NIH-AARP) Diet and Health Study Exposure assessment method: questionnaire; 124-item FFQ calibrated within the study population against two non-consecutive 24-h dietary recalls; processed meats were red and white meats	Colon and rectum	Processed meat (quintile median, g/1000 kcal)			Sex, education, BMI, smoking, total energy intake, dietary calcium, non-processed meat intake
			1.6	440	1.00	
			4.3	496	1.04 (0.91–1.18)	
			7.4	538	1.07 (0.94–1.23)	
			12.1	612	1.16 (1.02–1.32)	
			22.3	633	1.16 (1.01–1.32)	
			Trend-test *P* value: 0.017			
		Colon and rectum	For an increase of 100 g/day	2719	1.19 (0.96–1.48)	
			Trend-test *P* value: 0.001			

Table 2.2.2 Cohort studies on consumption of processed meat and cancer of the colorectum

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
Cross et al. (2010) USA Enrolment, 1995–1996; follow-up until end of 2003 Cohort study (cont.)		Colon	Processed meat (quintile median, g/1000 kcal)			
			1.6	334	1.00	
			4.3	357	0.98 (0.84–1.14)	
			7.4	393	1.03 (0.89–1.20)	
			12.1	453	1.14 (0.98–1.32)	
			22.3	458	1.11 (0.95–1.29)	
			Trend-test *P* value: 0.057			
			For an increase of 100 g/day	1995	1.13 (0.88–1.45)	
			Trend-test *P* value: 0.001			
		Rectum	Processed meat (quintile median, g/1000 kcal)			
			1.6	106	1.00	
			4.3	139	1.22 (0.94–1.58)	
			7.4	145	1.20 (0.93–1.56)	
			12.1	159	1.24 (0.95–1.61)	
			22.3	175	1.30 (1.00–1.68)	
			Trend-test *P* value: 0.145			
			For an increase of 100 g/day	724	1.38 (0.93–2.05)	
			Trend-test *P* value: 0.001			

Table 2.2.2 Cohort studies on consumption of processed meat and cancer of the colorectum

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
Takachi et al. (2011) Japan Follow-up, from 1995–1999 to December 2006 Cohort study	80 658; Japanese in the Japan Public Health Center-based Prospective Study (JPHC Study) Cohorts I and II, registered in 11 public health centre areas, who responded to a self-administered, 5-yr follow-up questionnaire at ages 45–74 yr Exposure assessment method: questionnaire; validated, self-administered, 138-item FFQ including 16 meat items Processed meat included ham, sausages, bacon, and luncheon meat	Colon	Processed meat (quintile median, g/day); in men			Age; area; BMI; smoking status; alcohol consumption; physical activity; medication use for diabetes; history of diabetes; screening examinations; intake of energy, calcium, vitamin D, vitamin B6, folate, dietary fibre, dried and salted fish
			0.2	106	1.00	
			1.9	106	1.11 (0.85–1.46)	
			3.9	81	0.91 (0.68–1.22)	
			7.3	89	1.05 (0.79–1.41)	
			16.0	99	1.27 (0.95–1.71)	
			Trend-test *P* value: 0.1			
		Proximal colon	Processed meat (quintile median, g/day); in men			
			0.2	36	1.00	
			1.9	51	1.60 (1.04–2.46)	
			3.9	37	1.20 (0.75–1.91)	
			7.3	39	1.31 (0.82–2.08)	
			16.0	37	1.38 (0.85–2.25)	
			Trend-test *P* value: 0.54			
		Distal colon	Processed meat (quintile median, g/day); in men			
			0.2	64	1.00	
			1.9	53	0.92 (0.64–1.33)	
			3.9	39	0.73 (0.49–1.10)	
			7.3	46	0.93 (0.63–1.38)	
			16.0	55	1.19 (0.80–1.77)	
			Trend-test *P* value: 0.19			
		Rectum	Processed meat (quintile median, g/day); in men			
			0.2	66	1.00	
			1.9	49	0.84 (0.58–1.21)	
			3.9	35	0.64 (0.42–0.97)	
			7.3	48	0.91 (0.62–1.33)	
			16.0	35	0.70 (0.45–1.09)	
			Trend-test *P* value: 0.25			

Table 2.2.2 Cohort studies on consumption of processed meat and cancer of the colorectum

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
Takachi et al. (2011) Japan Follow-up, from 1995–1999 to December 2006 Cohort study (cont.)		Colon	Processed meat (quintile median, g/day); in women			
			0.4	61	1.00	
			2.2	69	1.26 (0.89–1.79)	
			4.3	60	1.10 (0.76–1.58)	
			7.6	58	1.12 (0.77–1.62)	
			15.0	59	1.19 (0.82–1.74)	
			Trend-test *P* value: 0.64			
		Proximal colon	Processed meat (quintile median, g/day); in women			
			0.4	31	1.00	
			2.2	42	1.51 (0.95–2.42)	
			4.3	37	1.33 (0.82–2.16)	
			7.6	38	1.42 (0.87–2.31)	
			15.0	31	1.23 (0.73–2.07)	
			Trend-test *P* value: 0.87			
		Distal colon	Processed meat (quintile median, g/day); in women			
			0.4	26	1.00	
			2.2	23	0.98 (0.55–1.73)	
			4.3	19	0.79 (0.43–1.44)	
			7.6	18	0.77 (0.42–1.44)	
			15.0	24	1.03 (0.57–1.87)	
			Trend-test *P* value: 0.88			
		Rectum	Processed meat (quintile median, g/day); in women			
			0.4	27	1.00	
			2.2	27	1.09 (0.64–1.87)	
			4.3	21	0.85 (0.47–1.52)	
			7.6	27	1.19 (0.68–2.08)	
			15.0	22	0.98 (0.53–1.79)	
			Trend-test *P* value: 1.00			

Table 2.2.2 Cohort studies on consumption of processed meat and cancer of the colorectum

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
Ollberding et al. (2012) California and Hawaii, USA 1993–2007 Cohort study	15 717; multiethnic sample of African Americans, Japanese Americans, Latinos, native Hawaiians, and Whites aged 45–75 yr Exposure assessment method: FFQ; validated quantitative FFQ	Colon and rectum	Processed meat (quintile median, g/1000kcal per day)			Age, ethnicity, family history of colorectal cancer, history of colorectal polyps, BMI, smoking, NSAID use, alcohol, physical activity, history of diabetes, HRT use (females), total calories, intake of dietary fibre, calcium, folate, vitamin D
			1.70	599	1.00	
			4.48	626	0.98 (0.87–1.09)	
			7.28	706	1.04 (0.93–1.16)	
			10.86	704	1.00 (0.90–1.13)	
			17.98	769	1.06 (0.94–1.19)	
			Trend-test *P* value: 0.259			
Egeberg et al. (2013) Denmark 1993–2009 Cohort study	53 988; Danish men and women aged 50–64 yr free of cancer Exposure assessment method: FFQ; 192-item FFQ with 63 meat items and meat dishes, including specific processed meat products, mainly from pork; standard portion sizes	Colon	Processed meat (g/day)			Age, sex, waist circumference, schooling, smoking status, HRT use, sports activities, alcohol abstainer, alcohol intake, NSAID use, dietary fibre intake, total energy intake
			≤ 16	172	1.00	
			> 16 to ≤ 27	160	0.96 (0.77–1.20)	
			> 27 to ≤ 42	145	0.96 (0.75–1.22)	
			> 42	167	1.02 (0.78–1.34)	
			Continuous per 25 g/day	644	1.03 (0.94–1.13)	
			Trend-test *P* value: 0.53			
		Rectum	Processed meat (g/day)			
			< 16	75	1.00	
			> 16 to ≤ 27	96	1.21 (0.89–1.65)	
			> 27 to ≤ 42	93	1.18 (0.84–1.64)	
			> 42	81	0.88 (0.60–1.30)	
			Continuous, per 100 g/day	345	0.93 (0.81–1.07)	
			Trend-test *P* value: 0.32			

Table 2.2.2 Cohort studies on consumption of processed meat and cancer of the colorectum

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
Bernstein et al. (2015) USA Nurses' Health Study, 1980–2010; Health Professionals Follow-Up Study, 1986–2010 Cohort study	87 108 women and 47 389 men; Nurses' Health Study (NHS) and Health Professionals Follow-Up Study (HPFS) Exposure assessment method: FFQ; diet from FFQs collected about every 4 yr during follow-up (see Wei et al, 2004)	Colon and rectum	Processed red meat (1 serving/day)			Age, follow-up, family history, endoscopy, smoking, alcohol drinking, BMI, physical activity, medications and supplements, menopausal status, hormone use, total caloric intake, folate, calcium, vitamin D, fibre
			Baseline intake	2731	1.08 (0.98–1.18)	
			Trend-test *P* value: 0.13			
			Processed red meat (1 serving/day)			
			Cumulative average	2731	1.15 (1.01–1.32)	
			Trend-test *P* value: 0.03			
		Proximal colon	Processed red meat (1 serving/day)			
			Baseline intake	1151	0.98 (0.84–1.15)	
			Trend-test *P* value: 0.82			
			Processed red meat (1 serving/day)			
			Cumulative intake	1151	0.99 (0.79–1.24)	
			Trend-test *P* value: 0.93			
		Distal colon	Processed red meat (1 serving/day)			
			Baseline intake	817	1.23 (1.05–1.44)	
			Trend-test *P* value: 0.009			
			Processed red meat (1 serving/day)			
			Cumulative intake	817	1.36 (1.09–1.69)	
			Trend-test *P* value: 0.006			

Table 2.2.2 Cohort studies on consumption of processed meat and cancer of the colorectum

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
Bernstein et al. (2015) USA Nurses' Health Study, 1980–2010; Health Professionals Follow-Up Study, 1986–2010 Cohort study (cont.)		Rectum	Processed red meat (1 serving/day)			
			Baseline intake	589	1.05 (0.86–1.3)	
			Trend-test *P* value: 0.64			
			Processed red meat (1 serving/day)			
			Cumulative intake	589	1.18 (0.89–1.57)	
			Trend-test *P* value: 0.25			

BMI, body mass index; CI, confidence interval; FFQ, food frequency questionnaire; h, hour; HRT, hormone replacement therapy; mo, month; NOS, not otherwise specified; NR, not reported; NSAID, nonsteroidal anti-inflammatory drug; OR, odds ratio; SQFFQ, semiquantitative food frequency questionnaire; wk, week; yr, year

Table 2.2.3 Case–control studies on consumption of red meat and cancer of the colorectum

Reference, location, enrolment	Population size, description, exposure assessment method	Organ site	Exposure category or level	Exposed cases/ deaths	Risk estimate (95% CI)	Covariates controlled
Manousos et al. (1983) Athens, Greece 1974–1980	Cases: 100; hospital-based incident colorectal cancer cases Controls: 100; hospital-based patients seen at an orthopaedic clinic, matched to cases by age and sex Exposure assessment method: questionnaire; frequency questionnaire with 80 items, administered in person; individual red meats only were beef and lamb	Colon and rectum	Increase from 1 to 2 times/wk			Age, sex, vegetables
			Beef meat	NR	1.77	
			Lamb meat	NR	2.61	
Kune et al. (1987) Melbourne, Australia 1980–1981	Cases: 715; population-based cases Controls: 727; population-based controls matched to cases by age and sex Exposure assessment method: questionnaire; validated questionnaire with 300 items, administered in person; individual red meats were beef (steak, roast beef, ground beef, beef casserole, corned beef, beef sausages, canned beef meals) and pork (pork chops, roast pork, ham, bacon, pork sausages)	Colon and rectum	Beef (g/wk), men and women:			Age, sex, fibre, cruciferous vegetables, dietary vitamin C, pork, fish, other meat, fat, milk, supplements
			< 360	130	1.00	
			> 360	258	1.75 (1.26-2.44)	
		Colon	Beef (g/wk), men:			
			< 360	NR	1.00	
			> 360	NR	1.58	
		Rectum	Beef (g/wk), men:			
			< 360	NR	1.00	
			> 360	NR	1.88	
		Colon and rectum	Pork (g/wk), men and women:			
			≤ 58	370	1.00	
			> 58	332	0.55 (0.42–0.73)	
			Pork (g/wk), women:			
			≤ 58	212	1.00	
			> 58	115	0.52	
			Pork (g/wk), men:			
			≤ 58	159	1.00	
			> 58	217	0.59	
		Colon	Pork (g/wk), men:			
			≤ 58	NR	1.00	
			> 58	NR	0.73	
			Pork (g/wk), women:			
			≤ 58	159	1.00	
			> 58	217	0.62	

Table 2.2.3 Case–control studies on consumption of red meat and cancer of the colorectum

Reference, location, enrolment	Population size, description, exposure assessment method	Organ site	Exposure category or level	Exposed cases/ deaths	Risk estimate (95% CI)	Covariates controlled
Kune et al. (1987) Melbourne, Australia 1980–1981 (cont.)		Rectum	Pork (g/wk), men:			
			≤ 58	159	1.00	
			> 58	217	0.47	
			Pork (g/wk), women:			
			≤ 58	159	1.00	
			> 58	217	0.39	
		Colon and rectum	Beef (g/wk), men:			
			Q1 (≤ 250)	74	1.00	
			Q2 (> 250–360)	56	0.80	
			Q3: (> 260–500)	84	1.54	
			Q4 (> 500–720)	75	1.24	
			Q5: (> 720)	99	2.14	
		Colon and rectum	Pork (g/wk), men:			
			Q1 (≤ 15)	95	1.00	
			Q2 (> 15–58)	63	0.55	
			Q3 (> 58–106)	79	0.64	
			Q4 (> 106–174)	63	0.65	
			Q5 (> 174)	75	0.59	
		Colon and rectum	Pork (g/wk), women:			
			Q1 (≤ 0)	73	1.00	
			Q2 (> 0–27)	77	1.16	
			Q3 (> 27–58)	62	0.68	
			Q4 (> 58–114)	65	0.64	
			Q5 (> 114)	50	0.38	

Table 2.2.3 Case–control studies on consumption of red meat and cancer of the colorectum

Reference, location, enrolment	Population size, description, exposure assessment method	Organ site	Exposure category or level	Exposed cases/ deaths	Risk estimate (95% CI)	Covariates controlled
Tuyns et al. (1988) Belgium 1978–1982	Cases: 818; population-based cases, identified through treatment centres Controls: 2851; population-based Exposure assessment method: questionnaire; validated, administered in person, and captured frequency and serving size; individual red meat was beef (veal, lean beef, half-fat beef, and fat beef) or pork (lean and half-fat pork, fat pork, and smoked pork)	Colon	Beef consumption (g/wk)			Age (10-yr age groups), sex, province
			0	NR	1.00	
			>0– 226	NR	1.76	
			> 227 to ≤ 360	NR	1.60	
			> 361 to ≤ 538	NR	2.09	
			Trend-test *P* value: < 0.0001			
		Colon	Pork consumption (g/wk), quartiles			
			Level 1	NR	1.00	
			≤ 200	NR	0.85	
			> 200 to ≤ 330	NR	0.58	
			> 330 to ≤ 509	NR	0.39	
			Trend-test *P* value: < 0.0001			
		Rectum	Beef consumption (g/wk), quartiles			
			Level 1	NR	1.00	
			≤ 226	NR	1.20	
			> 227 to ≤ 360	NR	1.21	
			> 361 to ≤ 538	NR	0.71	
			Trend-test *P* value: 0.14			
		Rectum	Pork consumption (g/wk), quartiles			
			Level 1	NR	1.00	
			≤ 200	NR	0.89	
			> 200 to ≤ 330	NR	0.75	
			> 330 to ≤ 509	NR	0.70	
			Trend-test *P* value: 0.016			

Table 2.2.3 Case–control studies on consumption of red meat and cancer of the colorectum

Reference, location, enrolment	Population size, description, exposure assessment method	Organ site	Exposure category or level	Exposed cases/ deaths	Risk estimate (95% CI)	Covariates controlled
Lee et al. (1989) Singapore 1985–1987	Cases: 203; hospital-based colorectal cases, identified at Singapore General Hospital Controls: 425; hospital-based, identified from eye and orthopaedic wards in the same hospital as cases; frequency-matched by age and sex; GI disease excluded Exposure assessment method: questionnaire; validated, administered in person, and included 116 items; red meat was pork, beef, and mutton; unclear if red meat included processed meat	Colon and rectum	Total red meat intake (g/day), tertiles			Age, sex, dialect group, occupational group
			T1	NR	1.00	
			T2	NR	1.18 (0.77–1.81)	
			T3	NR	1.29 (0.84–1.97)	
			Trend-test: *P* value: NS			
		Rectum	Total red meat intake (g/day), tertiles			
			T1	NR	1.00	
			T2	NR	1.43 (0.75–2.74)	
			T3	NR	0.97 (0.48–1.92)	
			Trend-test *P* value: NS			
		Colon	Total red meat intake (g/day), tertiles			
			T1	NR	1.00	
			T2	NR	1.01 (0.60–1.70)	
			T3	NR	1.41 (0.87–2.31)	
			Trend-test *P* value: NS			
Gerhardsson de Verdier et al. (1991) Stockholm, Sweden 1986–1988	Cases: 559; population-based colorectal cases, identified through local hospitals and regional cancer registry Controls: 505; population-based, frequency-matched to cases by age and sex Exposure assessment method: questionnaire; unclear validation, self-administered, and included 55 items; red meat was beef and pork; assessed cooking methods	Colon	Red meat intake (Tertile 3 vs T1, i.e. > 1 time/wk vs more seldom)			Year of birth,sex, fat intake
			Beef/pork, fried	193	1.1 (0.7–1.8)	
			Trend-test *P* value: 0.353			
			Beef/pork, oven-roasted	57	1.2 (0.8–1.8)	
			Trend-test *P* value: 0.428			
			Beef/pork, boiled	104	1.8 (1.2–2.6)	
			Trend-test *P* value: 0.004			
		Rectum	Red meat intake (> 1 time/wk vs more seldom)			
			Beef/pork, fried	124	1.6 (0.9–3.0)	
			Trend-test *P* value: 0.073			
			Beef/pork, oven-roasted	47	1.8 (1.1–2.9)	
			Trend-test *P* value: 0.019			
			Beef/pork, boiled	69	1.9 (1.2–3.0)	
			Trend-test *P* value: 0.007			

Table 2.2.3 Case–control studies on consumption of red meat and cancer of the colorectum

Reference, location, enrolment	Population size, description, exposure assessment method	Organ site	Exposure category or level	Exposed cases/ deaths	Risk estimate (95% CI)	Covariates controlled
Bidoli et al. (1992) Province of Pordenone, Italy 1986–NR (possibly 1992)	Cases: 248; hospital-based Controls: 699; hospital-based, excluded patients with cancer, digestive-tract disorders, or any condition related to alcohol or tobacco consumption Exposure assessment method: questionnaire; not validated and administered in person; total red meat was beef and pork from all sources; assessed frequency	Colon	Total red meat consumption (frequency)			Age, sex, social status
			T1	35	1.0	
			T2	48	1.5	
			T3	40	1.6	
			Trend-test *P* value: 0.07			
		Rectum	Total red meat consumption (frequency)			
			T1	35	1.0	
			T2	50	1.5	
			T3	40	2.0	
			Trend-test *P* value: 0.01			
Iscovich et al. (1992) La Plata, Argentina 1985–1986	Cases: 110; hospital-based, identified through local hospitals Controls: 220; population-based, identified from neighbourhoods of cases and matched to cases by sex; controls with conditions that may have affected diet were excluded Exposure assessment method: questionnaire; unclear validation, administered in person, and included 140 items; red meat was beef, veal, pork, horse, red wild meat, goat, and hare	Colon	Red meat intake, quartiles			Matching variables
			Q1	NR	1.00	
			Q2	NR	2.29 (1.03–5.08)	
			Q3	NR	0.82 (0.39–1.70)	
			Q4	NR	NR	
			Trend-test *P* value: 0.076			
Steinmetz and Potter (1993) Adelaide, Australia 1979–1980	Cases: 220; population-based colon cases, identified via the South Australian Cancer Registry Controls: 438; population-based; two controls per case selected via the electoral roll; individually matched to cases by age and sex Exposure assessment method: questionnaire; validated, included 141 items, and self-administered; red meat was hamburger (with bread roll), grilled steak, fried steak, grilled pork chop, fried pork chop, grilled lamb chop, fried lamb chop, roast pork, roast beef, veal, crumbed veal (schnitzel), mince, and roast lamb	Colon	Red meat intake (servings/wk), quartiles Women:			Age at first live birth, Quetelet index, alcohol intake, the matching variable age
			Q1 (≤ 3.4)	NR	1.00	
			Q2 (3.5–5.0)	NR	1.44 (0.70–2.93)	
			Q3 (5.1–7.1)	NR	1.15 (0.57–2.32)	
			Q4 (≥ 7.2)	NR	1.48 (0.73–3.01)	
			Red meat intake (servings/wk), quartiles Men:			Occupation, Quetelet index, alcohol intake, the matching variable age
			Q1 (≤ 3.9)	NR	1.00	
			Q2 (4.0–5.5)	NR	1.80 (0.92–3.52)	
			Q3 (5.6–8.2	NR	1.64 (0.82–3.27)	
			Q4 (≥ 8.3)	NR	1.59 (0.81–3.13)	

Table 2.2.3 Case–control studies on consumption of red meat and cancer of the colorectum

Reference, location, enrolment	Population size, description, exposure assessment method	Organ site	Exposure category or level	Exposed cases/ deaths	Risk estimate (95% CI)	Covariates controlled
Centonze et al. (1994) Southern Italy 1987–1989	Cases: 119; population-based colorectal cases, identified from a population-based cancer registry Controls: 119; population-based, matched to cases by age, sex, and general practitioner Exposure assessment method: questionnaire; unclear validation, administered by in-person interview, and included 70 food items; red meat was beef, reported on individually	Colon and rectum	Beef intake (g/day)			Age , sex, level of education, smoking status, modifications of diet over the past 10 yr
			Low: 21	92	1.00	
			Medium (≥ 22)	27	0.95 (0.50–1.80)	
Muscat and Wynder (1994) USA 1989–1992	Cases: 511; hospital-based cases Controls: 500; hospital-based patients with disease unrelated to dietary fat or fibre intake; frequency-matched to cases by sex, race, hospital, and age Exposure assessment method: questionnaire; administered in person; red meat was beef, steaks, roasts, or hamburgers; assessed doneness level	Colon and rectum	Beef doneness, men:			Matching factors of sex, race, hospital, age, time of the case interview
			Rare	82	1.00	
			Medium	133	1.00	
			Well done	54	1.15 (0.6–2.4)	
			Beef doneness, women:			
			Rare	83	1.00	
			Medium	89	0.95 (0.6–1.5)	
			Well done	35	1.00	

Table 2.2.3 Case–control studies on consumption of red meat and cancer of the colorectum

Reference, location, enrolment	Population size, description, exposure assessment method	Organ site	Exposure category or level	Exposed cases/ deaths	Risk estimate (95% CI)	Covariates controlled
Kampman et al. (1995) The Netherlands 1989–1993	Cases: 232; population-based colon cases, identified from hospitals using a cancer registry Controls: 259; population-based, identified through rosters of general practitioners of participating cases; frequency-matched to cases by age, sex, and degree of urbanization Exposure assessment method: questionnaire; unclear validation, administered in person, included 289 items, and considered frequency and serving size; red meat was unprocessed red meat; no further details provided	Colon	Red meat intake (g/day), women:			Age, urbanization level, total energy intake, alcohol intake, family history of colon cancer, cholecystectomy
			< 38	12	1.00	
			38–59	25	1.82 (0.75–4.46)	
			60–83	36	2.71 (1.15–6.38)	
			> 83	29	2.35 (0.97–5.66)	
			Trend-test *P* value: 0.04			
			Red meat intake (g/day), men:			
			< 60	33	1.00	
			60–83	35	0.80 (0.39–1.61)	
			84–102	24	0.57 (0.27–1.30)	
			> 102	38	0.89 (0.43–1.81)	
			Trend-test *P* value: 0.62			
			Ratio of red meat: vegetables + fruit, men:			
			< 0.14	32	1.00	
			0.14–0.22	33	1.04 (0.51–2.13)	
			0.22–0.33	24	0.79 (0.38–1.64)	
			> 0.33	40	1.18 (0.57–2.43)	
			Trend-test *P* value: 0.69			
			Ratio of red meat: vegetables + fruit, women:			
			< 0.09	16	1.00	
			0.09–0.13	11	0.81 (0.30–2.17)	
			0.13–0.20	26	1.53 (0.67–3.51)	
			> 0.20	48	3.05 (1.39–6.17)	
			Trend-test *P* value: 0.0006			
Kotake et al. (1995) Japan 1992–1994	Cases: 363; hospital-based colorectal cases Controls: 363; hospital-based, individually matched to cases by sex and age group Exposure assessment method: questionnaire; unknown validation and administration; exposure definition for red meat was beef and pork, examined separately	Colon	Beef or pork intake (> 3–4 times/wk vs 1–2 times/wk)			Matching variables (other variables not reported)
			Beef	NR	1.70 (0.85–3.28)	
			Pork	NR	0.80 (0.50–1.33)	
		Rectum	Beef or pork intake (> 3–4 times/wk vs 1–2 times/wk)			
			Beef	NR	0.80 (0.38–1.52)	
			Pork	NR	1.60 (0.95–2.73)	

Table 2.2.3 Case–control studies on consumption of red meat and cancer of the colorectum

Reference, location, enrolment	Population size, description, exposure assessment method	Organ site	Exposure category or level	Exposed cases/ deaths	Risk estimate (95% CI)	Covariates controlled
Lohsoonthorn and Danvivat (1995) Bangkok, Thailand NR	Cases: 279; hospital-based colorectal cases Controls: 279; hospital-based, individually matched to cases by sex, age, admission period, hospital; included cancer patients with cancer in other organs Exposure assessment method: questionnaire; unclear validation and number of items asked; assessed frequency only; red meat (individual types only) was beef and pork	Colon and rectum	Beef consumption (times/mo)			None
			< 5	180	1.00	
			6– ≥ 10	99	1.00 (0.70–1.44)	
			Trend-test *P* value: 0.95			
			Pork consumption (times/mo)			
			< 5	29	1.00	
			6– ≥ 10	250	1.00 (0.56–1.78)	
			Trend-test *P* value: 0.95			
Freedman et al. (1996) New York, USA 1982–1992	Cases: 163; hospital-based Controls: 326; hospital-based, frequency-matched to cases by age and sex (2:1 ratio); 21.5% had non-malignant GI diseases Exposure assessment method: questionnaire; unclear validation, self-administered, and included 66 items; beef was hamburger, steak, roast, and stew; assessed frequency	Colon and rectum	Beef intake (times/mo)			Age, sex
			≤ 1	37	1.00	
			1–4	109	1.61 (1.03–2.52)	
			5–7	17	2.01 (0.96–4.20)	
			Trend-test *P* value: 0.03			
			Beef intake (times/mo); *p53+* genotype			
			≤ 1	22	1.00	
			1–4	45	1.12 (0.63–1.98)	
			5–7	6	1.25 (0.45–3.49)	
			Trend-test *P* value: 0.63			
			Beef intake (times/mo)); *p53–* genotype			
			≤ 1	15	1.00	
			1–4	64	2.35 (1.26–4.39)	
			5–7	11	3.17 (1.83–11.28)	
			Trend-test *P* value: 0.006			
La Vecchia et al. (1996) Northern Italy 1985–1992	Cases: 1326; hospital-based colorectal cases Controls: 2024; hospital-based, identified from same hospitals as cases for non-cancer, non-GI conditions Exposure assessment method: questionnaire; unclear validation, administered by in-person interview, and assessed frequency only; red meat was not defined	Colon	Red meat intake (portions/wk)			Age, sex, total caloric intake, β-carotene, vitamin C intake, meal frequency/day, major seasoning fat score, family history of colorectal cancer
			≥4 vs <4	NR	1.6 (1.3–1.9)	
		Rectum	Red meat intake (portions/wk)			
			≥4 vs <4	NR	1.6 (1.3–2)	

Table 2.2.3 Case–control studies on consumption of red meat and cancer of the colorectum

Reference, location, enrolment	Population size, description, exposure assessment method	Organ site	Exposure category or level	Exposed cases/ deaths	Risk estimate (95% CI)	Covariates controlled
Shannon et al. (1996) Seattle, USA 1985–1989	Cases: 424; population-based colon cancer cases, identified through the SEER Seattle–Puget Sound Registry Controls: 414; population-based controls, identified through random digit dialling; matched to cases by age, sex, and county of residence Exposure assessment method: questionnaire; validated, included 71 items, administered in person, and assessed frequency and portion sizes; total red meat was casserole dishes, beef, ham, lamb, veal, pork and beef roasts, hamburger, ribs, pot roast, bacon, liver, organ meats, wieners, sausages, and luncheon meats	Colon	Total red meat (servings/day), women:			Age, total energy intake
			Q1 (0–0.49)	46	1.00	
			Q2 (> 0.49–0.79)	44	0.90 (0.50–1.64)	
			Q3 (> 0.79–1.20)	49	1.03 (0.55–1.90)	
			Q4 (> 1.20)	47	0.72 (0.37–1.38)	
			Trend-test *P* value: 0.41			
			Total red meat (servings/day), men:			
			Q1 (0–0.78)	49	1.00	
			Q2 (> 0.78–1.20)	51	1.00 (0.58–1.74)	
			Q3 (> 1.20–1.70)	60	1.05 (0.61–1.83)	
			Q4 (> 1.70)	78	1.48 (0.82–2.66)	
			Trend-test *P* value: 0.53			
De Stefani et al. (1997) Montevideo, Uruguay 1993–1995	Cases: 250; hospital-based colorectal cases Controls: 500; hospital-based, identified at same hospitals as the cases and afflicted with a variety of disorders unrelated to tobacco smoking, alcohol, or diet Exposure assessment method: questionnaire; unclear validation, administered in person, and included 60 items; unclear what was included in red meat; assessed cooking methods and HAAS estimates	Colon and rectum	Red meat, quartiles			Age, residence, education, family history of colon cancer in a first-degree relative, BMI, vegetable and dessert intake
			Q1	NR	1.00	
			Q2	NR	1.22 (0.76 –1.94)	
			Q3	NR	1.44 (0.90–2.29)	
			Q4	NR	2.60 (1.64–4.13)	
			Trend-test *P* value: <0.001			
			Beef, tertiles			
			T1	NR	1.00	
			T2	NR	1.66 (1.16–2.38)	
			T3	NR	3.88 (2.34–6.45)	
			Trend-test *P* value: <0.001			
			Lamb, tertiles			
			T1	NR	1.00	
			T2	NR	1.15 (0.78–1.68)	
			T3	NR	1.46 (0.97–2.19)	
			Trend-test *P* value: 0.07			

Table 2.2.3 Case–control studies on consumption of red meat and cancer of the colorectum

Reference, location, enrolment	Population size, description, exposure assessment method	Organ site	Exposure category or level	Exposed cases/ deaths	Risk estimate (95% CI)	Covariates controlled
De Stefani et al. (1997) Montevideo, Uruguay 1993–1995 (cont.)			IQ intake estimates, quartiles			
			Q1	NR	1.00	
			Q2	NR	1.63 (1.02–2.62)	
			Q3	NR	2.30 (1.43 –3.72)	
			Q4	NR	3.08 (1.87 –5.07)	
			Trend-test *P* value: <0.001			
			MeIQx intake estimates, quartiles			
			Q1	NR	1.00	
			Q2	NR	1.21 (0.74–1.98)	
			Q3	NR	2.30 (1.44 –3.68)	
			Q4	NR	3.23 (2.02 –5.16)	
			Trend-test *P* value: <0.001			
			PhiP intake estimates, quartiles			
			Q1	NR	1.00	
			Q2	NR	1.43 (0.89 –2.29)	
			Q3	NR	2.12 (1.32 –3.41)	
			Q4	NR	3.01 (1.87 –4.83)	
			Trend-test *P* value: <0.001			
Fernandez et al. (1997) Province of Pordenone, Italy 1985–1992	Cases: 112; cases with a family history of colorectal cancer; see Bidoli et al. (1992) Controls: 108; controls with a family history of colorectal cancer; see Bidoli et al. (1992) Exposure assessment method: questionnaire; see Bidoli et al. (1992)	Colon and rectum	Total red meat intake, tertiles			Sex, age, area of residence
			T1	NR	1.0	
			T2	NR	0.9 (0.5–1.7)	
			T3	NR	2.9 (1.4–6.0)	
			Trend-test *P* value: <0.05			

Table 2.2.3 Case–control studies on consumption of red meat and cancer of the colorectum

Reference, location, enrolment	Population size, description, exposure assessment method	Organ site	Exposure category or level	Exposed cases/ deaths	Risk estimate (95% CI)	Covariates controlled
Le Marchand et al. (1997) Hawaii, USA 1987–1991	Cases: 1192; population-based cases, identified through the Hawaii Tumor Registry; cases included Japanese, Caucasian (White), Filipino, Hawaiian, and Chinese patients Controls: 1192; population-based, identified through the Hawaii State Department of Health; individually matched to each case by sex, race, and age Exposure assessment method: questionnaire; validated, administered in person, and included 280 items; red meat was beef, pork, and lamb	Colon and rectum	Total beef, veal, and lamb; quartiles			Age; family history of colorectal cancer; alcoholic drinks per wk; pack-years; lifetime recreational activity; BMI 5 yr ago; caloric, dietary fibre, calcium intakes
			Men:			
			Q1	NR	1.0	
			Q2	NR	1.3	
			Q3	NR	1.3	
			Q4	NR	2.1 (1.4–3.1)	
			Trend-test *P* value <0.0001			
			Total beef, veal, and lamb; quartiles			
			Women:			
			Q1	NR	1.0	
			Q2	NR	1.4	
			Q3	NR	0.8	
			Q4	NR	1.3 (0.9–2.1)	
			Trend-test *P* value: 0.5			
Boutron-Ruault et al. (1999) Burgundy, France 1985–1990	Cases: 171; population-based, identified from GI and surgery departments, in conjunction with the registry of digestive cancers Controls: 309; population-based, identified through a census list; frequency-matched to cases by age and sex Exposure assessment method: questionnaire; validated and administered in person; red meat was beef, pork, and lamb, reported individually	Colon and rectum	Beef intake (g/day), quartiles			Age, sex, caloric intake, sex-specific cut-offs for quartiless
			Q1	NR	1.0	
			Q2	NR	1.5 (0.9–2.6)	
			Q3	NR	1.7 (0.9–2.9)	
			Q4	NR	1.4 (0.8–2.4)	
			Trend-test *P* value: 0.31			
			Pork intake (g/day), quartiles			
			Q1	NR	1.0	
			Q2	NR	1.0 (0.6–1.7)	
			Q3	NR	1.5 (0.9–2.5)	
			Q4	NR	1.0 (0.6–2.8)	
			Trend-test *P* value: 0.61			
			Lamb intake			
			None	NR	1.0	
			Any	NR	1.3 (0.9–1.9)	
			Trend-test *P* value: 0.20			

Table 2.2.3 Case–control studies on consumption of red meat and cancer of the colorectum

Reference, location, enrolment	Population size, description, exposure assessment method	Organ site	Exposure category or level	Exposed cases/ deaths	Risk estimate (95% CI)	Covariates controlled
Kampman et al. (1999) California, Utah, and Minnesota, USA 1991–1994	Cases: 1542; cases identified through the Kaiser Permanente Medical Care Program of Northern California, Utah, and metropolitan twin cities area in Minnesota Controls: 1860; population-based, frequency-matched to cases by sex and age; identified using membership lists of the Kaiser Permanente Medical Care Program, random digit dialling, drivers' licence and identification lists, and Health Care Financing Administration forms Exposure assessment method: questionnaire; validated, administered by in-person interview, and included > 800 items; red meat was ground beef, hamburger, ground beef casseroles, hamburger helper, pot roast, steak, and ham; assessed cooking methods and mutagen index	Colon	Red meat, including ham (servings/wk), men			Age at diagnosis (cases) or selection (controls), BMI, lifetime physical activity, total energy intake, usual number of cigarettes smoked per day, intake of dietary fibre
			≤ 2.2	NR	1.0	
			2.3–3.7	NR	0.8 (0.6–1.0)	
			3.8–5.6	NR	1.1 (0.8–1.0)	
			5.7–8.8	NR	1.0 (0.7–1.4)	
			> 8.8	NR	0.9 (0.7–1.3)	
			Red meat, including ham (servings/wk), women			
			≤ 1.5	NR	1.0	
			1.6–2.5	NR	1.1 (0.8–1.5)	
			2.6–4.0	NR	1.3 (0.9–1.8)	
			4.1–6.2	NR	1.3 (0.9–1.8)	
			> 6.2	NR	1.0 (0.7–1.5)	
Tavani et al. (2000) Milan, Italy 1983–1991	Cases: 828; hospital-based colorectal cases Controls: 7990; hospital-based, admitted to the same network of hospitals as the cancer cases for acute non-neoplastic conditions, but excluded conditions that may have affected diet Exposure assessment method: questionnaire; non-validated but reproducible, 40 items, administered in person; red meat was beef, veal, and pork	Colon	Red meat (servings/wk)			Age, year of recruitment, sex, education, tobacco smoking, alcohol, fats in seasoning, fruits, vegetables
			≤ 3	206	1.0	
			>3 – ≤6	228	1.1 (0.9–1.3)	
			> 6	394	1.9 (1.5–2.3)	
			Per increment of 1 serving/day	828	1.5 (1.1–2.0)	
			Trend-test *P* value ≤ 0.01			
		Rectum	Red meat (servings/wk)			
			≤ 3	123	1.0	
			>3 – ≤6	150	1.1 (0.9–1.5)	
			> 6	225	1.7 (1.3–2.2)	
			Per increment of 1 serving/day	498	1.7 (1.2–2.4)	
			Trend-test *P* value ≤0.01			

Table 2.2.3 Case–control studies on consumption of red meat and cancer of the colorectum

Reference, location, enrolment	Population size, description, exposure assessment method	Organ site	Exposure category or level	Exposed cases/ deaths	Risk estimate (95% CI)	Covariates controlled
Le Marchand et al. (2001) Hawaii, USA 1994–1998	Cases: 727; population-based colorectal cases, identified through the Hawaii Tumor Registry; cases included Japanese, Caucasians, and native Hawaiians Controls: 727; population-based, selected through the Hawaii State Department of Health and the Health Care Financing Administration; individually matched to cases by sex, ethnicity, and age Exposure assessment method: questionnaire; validated, administered in person, and included 280 items; red meat was beef and pork; considered cooking methods, and interactions with *NAT2* and *CYP1A2* phenotypes, and *NAT* genotype	Colon and rectum	Red meat intake (g/day) in all interviewed participants (768 cases, 768 controls)			Pack-years of cigarette smoking; lifetime recreational physical activity; lifetime aspirin use; BMI 5 yr ago; years of schooling; intakes of non-starch polysaccharides from vegetables and calcium from foods and supplements; the matching variables age, sex, ethnicity
			≤ 18.9	162	1.0	
			19.0–37.4	170	1.0 (0.7–1.4)	
			37.5–68.5	209	1.1 (0.8–1.5)	
			> 68.6	186	1.0 (0.7–1.4)	
			Trend-test *P* value: 0.98			
			Red meat intake (g/day) in all phenotyped participants (349 cases, 467 controls)			
			≤ 18.9	68	1.0	
			19.0–37.4	74	1.0 (0.7–1.6)	
			37.5–68.5	108	1.2 (0.8–1.9)	
			> 68.6	99	1.0 (0.6–1.5)	
			Trend-test *P* value: 0.86			
			Red meat preference in all interviewed participants			
			Did not eat/rare/ medium–rare	328	1.0	
			Medium	188	1.0 (0.7–0.9)	
			Well done/very well done	211	1.2 (0.9–1.5)	
			Trend-test *P* value: 0.29			
			Red meat preference in all phenotyped participants			
			Did not eat/rare/ medium–rare	158	1.0	
			Medium	92	0.8 (0.6–1.1)	
			Well done/very well done	99	1.1 (0.8–1.6)	
			Trend-test *P* value: 0.73			

Table 2.2.3 Case–control studies on consumption of red meat and cancer of the colorectum

Reference, location, enrolment	Population size, description, exposure assessment method	Organ site	Exposure category or level	Exposed cases/ deaths	Risk estimate (95% CI)	Covariates controlled
Le Marchand et al. (2001) Hawaii, USA 1994–1998 (cont.)		Colon and rectum	Three-way interaction for *NAT2* genotype, *CYP1A2* phenotype, and red meat preference (well-done vs medium-rare red meat)			Age; sex; ethnicity; pack-years of cigarette smoking; number of cigarettes, cigars, pipes smoked during the 2 wk preceding the caffeine test; lifetime recreational physical activity; lifetime aspirin use; BMI 5 yr ago; yrs of schooling; intakes of non-starch polysaccharides from vegetables and calcium from foods and supplements
			NAT2 genotype (slow/intermediate); *CYP1A2* (≤ median)	31	1.2 (0.7–2.3)	
			NAT2 genotype (rapid); *CYP1A2* (≤ median)	19	1.0 (0.5–1.9)	
			NAT2 genotype (slow/intermediate); *CYP1A2* (> median)	28	1.0 (0.6–1.9)	
			NAT2 genotype (rapid); *CYP1A2* (> median)	21	3.3 (1.3–8.1)	
			P value for interaction = 0.12			
Evans et al. (2002) Liverpool, United Kingdom NR	Cases: 512; population-based colorectal cases, identified from the Merseyside and Cheshire Cancer Registry Controls: 512; population-based, identified from general primary care practice lists; matched by age, sex, postal code, and primary care practitioner Exposure assessment method: questionnaire; validated, administered by telephone interview, and included160 items; red meat was not defined; frequency and portion size were assessed	Colon and rectum	Red meat (servings/day)			Only presented univariate odds ratios in tables
			Q1: 0–3	NR	1.00	
			Q2: > 3–5	NR	0.96 (0.65–1.42)	
			Q3: > 5–6	NR	1.03 (0.64–1.66)	
			Q4: > 6–22	NR	1.51 (1.06–2.15)	
		Proximal colon	Red meat (servings/day)			
			Q1: 0–3	NR	1.00	
			Q2: > 3–5	NR	0.91 (0.39–2.09)	
			Q3: > 5–6	NR	1.30 (0.47–3.62)	
			Q4: > 6–22	NR	3.32 (1.42–7.73	
		Distal colon + rectum	Red meat (servings/day)			
			Q1: 0–3	NR	1.00	
			Q2: > 3–5	NR	1.02 (0.65–1.59)	
			Q3: > 5–6	NR	0.97 (0.62–1.52)	
			Q4: > 6–22	NR	1.38 (0.89–2.12)	

Table 2.2.3 Case–control studies on consumption of red meat and cancer of the colorectum

Reference, location, enrolment	Population size, description, exposure assessment method	Organ site	Exposure category or level	Exposed cases/ deaths	Risk estimate (95% CI)	Covariates controlled
Le Marchand et al. (2002b) Hawaii, USA 1994–1998	Cases: 727; see Le Marchand et al. (2001) Controls: 727; see Le Marchand et al. (2001) Exposure assessment method: other; see Le Marchand et al. (2001)	Colon	Red meat intake, tertiles			Pack-years of cigarette smoking, physical activity, aspirin use, BMI, education, non-starch polysaccharides from vegetables, total calcium, and the matching variables age and sex
			T1	NR	1.0	
			T2	NR	0.9 (0.6–1.3)	
			T3	NR	1.0 (0.7–1.5)	
			Trend-test *P* value: 0.8			
		Rectum	Red meat intake, tertiles			
			T1	NR	1.0	
			T2	NR	1.9 (1.1–3.3)	
			T3	NR	1.7 (1.0–3.0)	
			Trend-test *P* value: 0.16			
		Colon	Red meat preference			
			Rare	NR	1.0	
			Medium	NR	0.8 (0.6–1.1)	
			Well done	NR	1.0 (0.7–1.3)	
			Trend-test *P* value: 0.62			
		Rectum	Red meat preference			
			Rare	NR	1.0	
			Medium	NR	1.1 (0.7–1.7)	
			Well done	NR	1.5 (0.9–2.4)	
			Trend-test *P* value: 0.11			

Table 2.2.3 Case–control studies on consumption of red meat and cancer of the colorectum

Reference, location, enrolment	Population size, description, exposure assessment method	Organ site	Exposure category or level	Exposed cases/ deaths	Risk estimate (95% CI)	Covariates controlled
		Colon	Highest vs lowest tertile of HAAs from red meat			Pack-years of cigarette smoking; physical activity; aspirin use; BMI; education; non-starch polysaccharides from vegetables and total calcium; PhIP, MeIQx, and DiMeIQx models for rectal cancer were further adjusted for intake of other HAAs; the matching variables age, sex, ethnicity
			PhIP	NR	1.0 (0.6–1.6)	
			MeIQx	NR	1.0 (0.6–1.1)	
			DiMeIQx	NR	1.1 (0.7–1.7)	
			Total HAAs	NR	1.0 (0.6–1.6)	
		Rectum	Highest vs lowest tertile of HAAs from red meat			
			PhIP	NR	1.7 (0.3–3.8)	
			MeIQx	NR	3.1 (1.3–7.7)	
			Trend-test *P* value:0.01			
			DiMeIQx	NR	2.7 (1.1–6.3)	
			Total HAAs	NR	2.2 (1.0–4.7)	
Nowell et al. (2002) Arkansas and Tennessee, USA 1993–1999	Cases: 157; hospital-based Controls: 380; population-based, identified from Arkansas drivers' licence records; matched to cases by ethnicity, age, and county of residence Exposure assessment method: questionnaire; validated and administered in person; total red meat was burgers, steak, pork chops, bacon, and sausage; cooking methods were assessed using the CHARRED database to estimate HAAs	Colon and rectum	Total red meat cooked well/very well done (g/day)			Age, ethnicity, sex
			Q1	25	1.00	
			Q2	34	1.91 (0.85–4.41)	
			Q3	42	2.42 (1.11–5.47)	
			Q4	54	4.36 (2.08–9.60)	
			MeIQx (ng/day)			
			Q1	29	1.00	
			Q2	32	1.75 (0.78–4.05)	
			Q3	40	2.87 (1.32–6.52)	
			Q4	53	4.09 (1.94–9.08)	
Seow et al. (2002) Singapore 1999–2000	Cases: 121; hospital-based colorectal cases Controls: 222; population-based controls, identified using random sampling from electoral records Exposure assessment method: questionnaire; red meat was pork, beef, lamb, and mutton; unclear if red meat included processed meat	Colon and rectum	Red meat (portions/yr)			Age, family history of colorectal cancer, sex, smoking, education, physical exercise
			< 39	20	1.0	
			39 to < 117	34	1.1 (0.5–2.2)	
			≥ 117	66	2.2 (1.1–4.2)	
			Trend-test Pvalue <0.05			

Table 2.2.3 Case–control studies on consumption of red meat and cancer of the colorectum

Reference, location, enrolment	Population size, description, exposure assessment method	Organ site	Exposure category or level	Exposed cases/ deaths	Risk estimate (95% CI)	Covariates controlled
Butler et al. (2003) North Carolina, USA 1996–2000	Cases: 620; population-based colon cancer cases, identified through the North Carolina Central Cancer Registry; included White and African American cases Controls: 1038; population-based, identified through the Division of Motor Vehicles; frequency-matched to cases by race, age, and sex Exposure assessment method: questionnaire; unclear validation, administered in person, and included 150 items; red meat was hamburger, steak, pork chop, sausage, and bacon; cooking methods were assessed and HAAs estimated using the CHARRED database	Colon	Total red meat (g/day)			Age, race, sex, energy-adjusted fat intake, energy intake, fibre intake, total meat intake, offsets
			≤ 11.8	97	1.0	
			11.9–22.4	90	0.9 (0.6–1.3)	
			22.5–33.6	99	1.0 (0.7–1.5)	
			33.7–51.8	138	1.5 (1.0–2.2)	
			≥ 51.8	196	2.0 (1.3–3.2)	
			Total red meat intake by doneness (g/day), highest vs lowest intake category (number of cases)			
			Rare/medium done (> 22.7 vs 0)	93	1.2 (0.9–1.7)	
			Well/very well done (> 42.7 vs ≤ 5.9)	192	1.7 (1.2–2.5)	
			Baked (> 7.7 vs 0)	44	1.1 (0.7–1.7)	
			Pan-fried (> 25.2 vs 0)	199	2.0 (1.4–3.0)	
			Broiled (> 16.5 vs 0)	68	1.3 (0.9–1.9)	
			Grilled/barbecued (22.7 vs 0)	97	0.9 (0.6–1.3)	
Chiu et al. (2003) Shanghai, China 1990–1993	Cases: 931; population-based, identified through the Shanghai Cancer Registry Controls: 1552; population-based, frequency-matched to cases by age and sex Exposure assessment method: questionnaire; administered in person, included 86 items, and asked frequency and servings; red meat was pork, organ meats, beef, and mutton	Colon	Red meat (servings/mo of food group)			Age, total energy, education, BMI, income, occupational physical activity
			Men:			
			Q1	NR	1.0	
			Q2	NR	1.2 (0.8–1.6)	
			Q3	NR	1.3 (0.9–1.8)	
			Q4	NR	1.5 (1.0–2.1)	
			Trend-test *P* value: 0.03			
			Red meat (servings/mo of food group)			
			Women:			
			Q1	NR	1.0	
			Q2	NR	1.3 (0.9–1.8)	
			Q3	NR	1.0 (0.7–1.4)	
			Q4	NR	1.5 (1.0–2.2)	
			Trend-test *P* value: 0.08			

Table 2.2.3 Case–control studies on consumption of red meat and cancer of the colorectum

Reference, location, enrolment	Population size, description, exposure assessment method	Organ site	Exposure category or level	Exposed cases/ deaths	Risk estimate (95% CI)	Covariates controlled
Navarro et al. (2003) Córdoba, Argentina 1993–1998	Cases: 287; hospital-based colorectal cases, identified at hospitals in Córdoba Controls: 564; hospital-based control residents, identified at the same hospitals for acute non-neoplastic conditions unrelated to digestive tract diseases or long-term modifications Exposure assessment method: questionnaire; validated, administered in person, and evaluated frequency and portion size; individual red meats included fatty and lean beef, pork, and bovine viscera; unclear if total red meat included processed meats	Colon and rectum	Fatty beef intake (median, g/day)			Sex, age, BMI, social status, total energy intake, total lipids, proteins, glucids, and soluble and insoluble fibres
			T1	NR	1.00	
			T2 (37.3)	NR	0.80 (0.55–1.18)	
			T3 (76.71)	NR	0.78 (0.51–1.18)	
			Lean beef intake (median, g/day)			
			T1	NR	1.00	
			T2 (53.13)	NR	0.64 (0.43–0.94)	
			T3 (95.94)	NR	0.67 (0.40–0.97)	
			Pork intake (median, g/day)			
			T1	NR	1.00	
			T2 (0.05)	NR	0.98 (0.67–1.43)	
			T3 (2.02)	NR	0.92 (0.62–1.36)	
Juarranz Sanz et al. (2004) Madrid, Spain 1997–1998	Cases: 196; population-based colorectal cases, identified through a cancer registry Controls: 196; population-based, identified through health care rosters from the same districts of the identified cases; individually matched to cases by age, sex, and geographical region Exposure assessment method: questionnaire; validated, included 72 items, administered by phone, and asked about frequency and portion size; red meat was beef, pork, and lamb	Colon and rectum	Continuous variables (g/day)			Olives, processed meat, organ meat, cherries/strawberries, oranges, raw tomatoes, yogurt, fresh juice
			Red meat	NR	1.026 (1.010–1.040)	
			Trend-test *P* value: 0.002			
			Continuous variables (g/day)			
			Organ meat	NR	1.122 (1.027–1.232)	
			Trend-test *P* value: 0.015			

Table 2.2.3 Case–control studies on consumption of red meat and cancer of the colorectum

Reference, location, enrolment	Population size, description, exposure assessment method	Organ site	Exposure category or level	Exposed cases/ deaths	Risk estimate (95% CI)	Covariates controlled
Murtaugh et al. (2004) California and Utah, USA 1997–2001	Cases: 952; population-based rectal cancer cases, identified through a cancer registry and online pathology reports from the Kaiser Permanente Northern California Cancer Registry Controls: 1205; controls were randomly selected from membership lists, social security lists, drivers' licence lists; frequency-matched to cases by sex and 5-y age groups Exposure assessment method: questionnaire; validated, administered in person, and included > 800 items; red meat included ground beef, hamburger, ground beef casseroles, hamburger helper, pot roast, steak, and ham; cooking methods were assessed, and interactions with *NAT2* phenotype and *GSTM1* genotypes were assessed	Rectum	Red meat (servings/wk)			
			Men:			
			< 2.9	156	1.00	
			≥ 2.9 to < 6.1	188	1.10 (0.82–1.48)	
			≥ 6.1	212	1.08 (0.77–1.51)	
			Red meat (servings/wk)			
			Women:			
			< 1.9	112	1.00	
			≥ 1.9 to < 4.2	114	0.93 (0.65–1.31)	
			≥ 4.2	163	1.05 (0.72–1.53)	
			Red meat (servings/wk) by *NAT2* phenotype			
			Men: slow acetylator			
			< 2.9	NR	1.00	
			3.0–6.1r	NR	1.20 (0.77–1.87)	
			> 6.1	NR	0.92 (0.58–0.92)	
			Men: rapid or intermediate acetylator			
			< 2.9	NR	1.16 (0.73–1.84)	
			3.0–6.1	NR	0.86 (0.55–1.34)	
			> 6.1	NR	0.96 (0.57–1.60)	
			Red meat (servings/wk by *NAT2* phenotype)			
			Women: slow acetylator			
			< 1.9	NR	1.00	
			2.0–4.2	NR	0.55 (0.32–0.96)	
			> 4.2	NR	0.70 (0.40–1.23)	
			Women: rapid or intermediate acetylator			
			< 1.9	NR	0.53 (0.30–0.93)	
			2.0–4.2	NR	0.66 (0.38–1.16)	
			> 4.2	NR	0.76 (0.42–1.36)	
			P value for interaction on additive scale = significant			

Table 2.2.3 Case–control studies on consumption of red meat and cancer of the colorectum

Reference, location, enrolment	Population size, description, exposure assessment method	Organ site	Exposure category or level	Exposed cases/ deaths	Risk estimate (95% CI)	Covariates controlled
Murtaugh et al. (2004) California and Utah, USA 1997–2001 (cont.)			Highest vs lowest category			
			Men:			
			Red meat (≥ 6.1 vs < 2.9 servings/wk)	212	1.08 (0.77–1.51)	
			Use of red meat drippings (> 52 vs never frequency/yr)	135	1.03 (0.76–1.39)	
			Doneness of red meat (well done vs rare)	187	1.33 (0.98–1.79)	
			Red meat mutagen index (> 468 vs ≤ 104;	175	1.39 (1.00–1.94)	
			Trend-test *P* value for mutagen index: <0.05			
			Highest vs lowest category			Age, BMI, energy intake, dietary fibre, calcium, lifetime physical activity, usual number of cigarettes smoked
			Women:			
			Red meat (≥ 4.2 vs < 1.9 servings/wk)	163	1.05 (0.72–1.53)	
			Use of red meat drippings (> 52 vs never frequency/yr;	97	0.72 (0.51–1.01)	
			Trend-test *P* value: <0.05			
			Doneness of red meat (well done vs rare)	165	1.05 (0.74–1.50)	
			Red meat mutagen index (≥ 624 vs ≤ 104)	72	0.88 (0.57–1.35)	
			Use of red meat drippings (frequency/yr) by *NAT2* phenotype			
			Men: slow acetylator			
			Never	NR	1.00	
			1–52	NR	0.70 (0.47–1.05)	
			> 52	NR	1.12 (0.72–1.75)	
			Men: rapid or intermediate acetylator			
			Never	NR	1.00 (0.68–1.47)	
			1–52	NR	0.70 (0.46–1.07)	
			> 52	NR	0.93 (0.58–1.47)	

Table 2.2.3 Case–control studies on consumption of red meat and cancer of the colorectum

Reference, location, enrolment	Population size, description, exposure assessment method	Organ site	Exposure category or level	Exposed cases/ deaths	Risk estimate (95% CI)	Covariates controlled
Murtaugh et al. (2004) California and Utah, USA 1997–2001 (cont.)			Use of red meat drippings (frequency/yr) by *NAT2* phenotype			
			Women: slow acetylator			
			Never,	NR	1.00	
			1–52	NR	0.50 (0.30–0.84)	
			> 52	NR	0.40 (0.23–0.68)	
			Women: rapid or intermediate acetylator			
			Never	NR	0.60 (0.37–0.95)	
			1–52	NR	0.52 (0.31–0.85)	
			> 52	NR	0.62 (0.36–1.05)	
			P value for interaction on multiplicative scale < 0.05			
Navarro et al. (2004) Córdoba, Argentina 1994–2000	Cases: 296; hospital-based colorectal cases, identified at hospitals in Córdoba Controls: 597; hospital-based control residents, identified at the same hospitals for acute non-neoplastic conditions unrelated to digestive tract diseases or long-term modifications Exposure assessment method: questionnaire; validated, administered in person, and evaluated frequency and portion size; individual red meats included fatty and lean beef, pork, and bovine viscera; unclear if total red meat included processed meats	Colon and rectum	Red meat intake (g/day), darkly browned vs no preference			Sex, age, BMI, smoking habit, socioeconomic status
			Barbecued red meat	176	2.85 (1.97–4.10)	
			Trend-test *P* value: <0.05			
			Roasted red meat	110	1.08 (0.76–1.54)	
			Pan–cooked red meat	167	2.44 (1.71–3.47)	
			Trend-test *P* value: <0.05			
			Fried red meat	145	1.74 (1.23–2.45)	
			Trend-test *P* value: <0.05			

Table 2.2.3 Case–control studies on consumption of red meat and cancer of the colorectum

Reference, location, enrolment	Population size, description, exposure assessment method	Organ site	Exposure category or level	Exposed cases/ deaths	Risk estimate (95% CI)	Covariates controlled
Satia-Abouta et al. (2004) North Carolina, USA 1996–2000	Cases: 613; Controls: 996 see Butler et al. (2003); Exposure assessment method: questionnaire; see Butler et al. (2003); red meat was hamburger, cheeseburger, beef (roast, steak, sandwiches), beef stew, pot pie, liver (including chicken liver), pork, beef, veal, lamb, roast beef, meatloaf, pork roast, tacos or burritos, spaghetti meat sauce, hot dogs, bacon, ham, sausage, bologna, and lunchmeats	Colon	Total red meat intake (frequency/wk), quartiles; Caucasians			Potential confounders examined included age, sex, education, BMI, smoking history, physical activity, family history of colon cancer, NSAID use, fat, carbohydrates, dietary fibre, vitamin C, vitamin E, β-carotene, calcium, folate, fruits, vegetables; covariables ≥ 10% change in parameter coefficient included in model
			Q1	60	1.0	
			Q2	68	1.0 (0.7–1.6)	
			Q3	89	1.2 (0.8–1.9)	
			Q4	120	1.1 (0.7–1.8)	
			Trend-test *P* value: 0.61			
			Total red meat intake (frequency/wk), quartiles; African Americans			
			Q1	60	1.0	
			Q2	68	0.7 (0.4–1.1)	
			Q3	89	0.8 (0.5–1.4)	
			Q4	120	0.7 (0.4–1.3)	
			Trend-test *P* value: 0.61			
Barrett et al. (2003) Dundee, Perth, Leeds, and York, United Kingdom 1997–2001	Cases: 484; hospital-based, identified from hospitals in Dundee, Perth, Leeds, and York, United Kingdom Controls: 738; hospital-based, identified from the practice lists of the cases' general practitioners; matched to cases by age and sex Exposure assessment method: questionnaire; validated, administered in person, and included 132 items; red meat was beef (roast, steak, mince, stew or casserole), beef burgers, pork (roast, chops, stew, or slices), and lamb (roast, chops, or stew)	Colon and rectum	Red meat (servings/mo, quartiles) by *NAT2* genotype			Smoking status; BMI at age 40 yr; the main effects of fruits, vegetables, red meat, and the polymorphism of interest, plus the fruit–vegetable interaction, and the interaction between the polymorphism and the dietary factor of interest
			Men:			
			Slow acetylators			
			Q1	NR	1.00	
			Q2	NR	0.85 (0.42–1.74)	
			Q3	NR	1.22 (0.63–2.37)	
			Q4	NR	1.49 (0.77–2.90)	
			Fast acetylators			
			Q1	NR	1.00	
			Q2	NR	1.57 (0.71–3.44)	
			Q3	NR	1.73 (0.83–3.63)	
			Q4	NR	1.65 (0.77–3.55)	
			P value for interaction: 0.46			

Table 2.2.3 Case–control studies on consumption of red meat and cancer of the colorectum

Reference, location, enrolment	Population size, description, exposure assessment method	Organ site	Exposure category or level	Exposed cases/ deaths	Risk estimate (95% CI)	Covariates controlled
Barrett et al. (2003) Dundee, Perth, Leeds, and York, United Kingdom 1997–2001 (cont.)			Red meat (servings/mo, quartiles) by *NAT2* genotype			
			Women:			
			Slow acetylators			
			Q1	NR	1.00	
			Q2	NR	1.16 (0.55–2.42)	
			Q3	NR	1.02 (0.46–2.27)	
			Q4	NR	2.14 (0.99–4.66)	
			Fast acetylators			
			Q1	NR	1.00	
			Q2	NR	0.93 (0.30–2.87)	
			Q3	NR	2.22 (0.73–6.78)	
			Q4	NR	2.81 (1.00–7.89)	
			P value for interaction: 0.35			
Turner et al. (2004) Dundee, Perth, Leeds, and York, United Kingdom 1997–2001	Cases: 484; hospital-based, identified from hospitals in Dundee, Perth, Leeds, and York, United Kingdom Controls: 738; hospital-based, identified from the practice lists of the cases' general practitioners; matched to cases by age and sex Exposure assessment method: questionnaire; validated, administered in person, and included 132 items; red meat was beef (roast, steak, mince, stew, or casserole), beef burgers, pork (roast, chops, stew, or slices), and lamb (roast, chops, or stew)	Colon and rectum	Red meat (servings/mo), quartiles			The matching variables age, sex, energy intake
			Q1 (≤ 6)	88	1.0	
			Q2 (> 6 to ≤ 14)	87	1.0 (0.7–1.7)	
			Q3 (> 14 to ≤ 19)	146	1.7 (1.2–2.6)	
			Q4 (> 19)	153	2.3 (1.6–3.5)	
			Trend-test *P* value: 0.0001			
			Red meat (highest vs lowest intake by *GSTP1* Ile105Val			Smoking status; BMI at age 40 yr; the main effects of fruits, vegetables, red meat, and the polymorphism of interest, plus the fruit–vegetable interaction, and the interaction between the polymorphism and the dietary factor of interest
			Homozygous rare variant	103	1.0 (0.4–2.1)	
			Heterozygous	401	1.9 (1.3–2.8)	
			Homozygous common variant	367	2.3 (1.5–3.5)	
			Trend-test *P* value: 0.02			
			Red meat (highest vs lowest intake) by *NQO1*			
			Deficient	48	0.3 (0.1–1.0)	
			Intermediate	307	2.7 (1.7–4.3)	
			Fast	516	1.8 (1.2–2.5)	
			Trend-test *P* value: 0.04			

Table 2.2.3 Case–control studies on consumption of red meat and cancer of the colorectum

Reference, location, enrolment	Population size, description, exposure assessment method	Organ site	Exposure category or level	Exposed cases/ deaths	Risk estimate (95% CI)	Covariates controlled
Murtaugh et al. (2005) California and Utah, USA Colon, 1991–1994; rectum, 1997–2002	Cases: 2298; Controls: 2749; Exposure assessment method: questionnaire; see Murtaugh et al. (2004) and Kampman et al. (1999); interactions with *CYP1A1* and *GSTM1* genotypes were assessed	Colon and rectum	Highest vs lowest category for *CYP1A1*1* allele			Age, BMI, energy intake, dietary fibre, calcium, lifetime physical activity, usual number of cigarettes smoked
			Men:			
			Red meat (> 6.1 vs ≤ 3.1 servings/wk)	NR	0.95 (0.73–1.25)	
			Use of red meat drippings, (> 36 vs never frequency/yr)	NR	0.90 (0.72–1.12)	
			Doneness of red meat (well done vs rare)	NR	1.37 (1.06–1.77)	
			Red meat mutagen index (> 468 vs ≤ 104)	NR	1.05 (0.79–1.39)	
			Highest vs lowest category for *CYP1A1*1* allele			
			Women:			
			Red meat (> 4.2 vs < 1.9 servings/wk)	NR	1.05 (0.77–1.43)	
			Use of red meat drippings (> 36 vs never frequency/yr)	NR	0.72 (0.55–0.93)	
			Doneness of red meat (well done vs rare)	NR	0.90 (0.67–1.19)	
			Red meat mutagen index (> 624 vs ≤ 104)	NR	0.68 (0.47–0.99)	
			Highest vs lowest category for *CYP1A1* any *2 variant			
			Men:			
			Red meat (> 6.1 vs ≤ 3.1 servings/wk)	NR	0.87 (0.61–1.25)	
			Use of red meat drippings (> 36 vs never frequency/yr)	NR	0.84 (0.61–1.16)	
			Doneness of red meat (well done vs rare)	NR	1.22 (0.87–1.70)	
			Red meat mutagen index (> 468 vs ≤ 104)	NR	0.86 (0.58–1.27)	

Table 2.2.3 Case–control studies on consumption of red meat and cancer of the colorectum

Reference, location, enrolment	Population size, description, exposure assessment method	Organ site	Exposure category or level	Exposed cases/ deaths	Risk estimate (95% CI)	Covariates controlled
Murtaugh et al. (2005) California and Utah, USA Colon, 1991–1994; rectum, 1997–2002 (cont.)			Highest vs lowest category for *CYP1A1* any *2 variant			
			Women:			
			Red meat (> 4.2 vs < 1.9 servings/wk)	NR	1.24 (0.82–1.88)	
			Use of red meat drippings (> 36 vs never frequency/yr)	NR	0.79 (0.53–1.17)	
			Doneness of red meat (well done vs rare)	NR	1.05 (0.72–1.53)	
			Red meat mutagen index (> 624 vs ≤ 104)	NR	0.77 (0.44–1.33)	
Chen et al. (2006) China 1990–2002	Cases: 140; population-based colorectal cases Controls: 343; population-based Exposure assessment method: questionnaire; unclear validation, administered in person, and assessed portion size and frequency; red meat was pork, beef, and lamb; assessed genotypes in *SULT1A1*	Rectum	Red meat (kg/yr)			Age, sex, smoking, colorectal cancer history
			≤ 5	17	1.00	
			> 5	40	0.85 (0.40–1.80)	
		Colon	Red meat (kg/yr)			
			≤ 5	13	1.00	
			> 5	70	1.40 (0.70–2.82)	
Hu et al. (2007) Canada 1994–1997	Cases: 1723; cases identified via the National Enhanced Cancer Surveillance System (NECSS), including the provinces of British Columbia, Alberta, Saskatchewan, Manitoba, Ontario, Prince Edward Island, Nova Scotia, and Newfoundland Controls: 3097; population-based controls from each province, frequency-matched to cases by age and sex Exposure assessment method: questionnaire; validated FFQ with 70 items, administered by mail; red meat was beef, pork, or lamb; also reported on hamburger	Proximal colon	Beef, pork, and lamb intake as main dish (servings/wk), tertiles			10-yr age group, province, BMI (< 25.0, 25.0–29.9, ≥ 30.0), strenuous activity (h/mo), total energy intake.
			Men:			
			T1	141	1.0	
			T2	175	1.2 (0.9–1.6)	
			T3	58	1.5 (1.0–2.4)	
			Trend-test *P* value: 0.05			
			Hamburger intake (servings/wk), tertiles			
			Men:			
			T1	50	1.0	
			T2	257	2.3 (1.5–3.4)	
			T3	71	2.1 (1.3–3.5)	
			Trend-test *P* value: 0.006			

Table 2.2.3 Case–control studies on consumption of red meat and cancer of the colorectum

Reference, location, enrolment	Population size, description, exposure assessment method	Organ site	Exposure category or level	Exposed cases/ deaths	Risk estimate (95% CI)	Covariates controlled
Hu et al. (2007) Canada 1994–1997 (cont.)		Proximal colon	Beef, pork, and lamb intake as main dish (servings/wk), tertiles			
			Women:			
			T1	180	1.0	
			T2	130	1.1 (0.8–1.5)	
			T3	36	1.1 (0.7–1.8)	
			Trend-test *P* value: 0.45			
			Hamburger intake (servings/wk), tertiles			
			Women:			
			T1	61	1.0	
			T2	236	1.2 (0.8–1.6)	
			T3	44	1.2 (0.7–1.9)	
			Trend-test *P* value: 0.47			
		Distal colon	Beef, pork, and lamb intake as main dish (servings/wk), tertiles			
			Men:			
			T1	235	1.0	
			T2	241	0.9 (0.7–1.2)	
			T3	86	1.1 (0.8–1.6)	
			Trend-test *P* value: 0.94			
		Distal colon	Hamburger intake (servings/wk), tertiles			
			Men:			
			T1	91	1.0	
			T2	362	1.4 (1.0–1.9)	
			T3	110	1.4 (0.9–2.0)	
			Trend-test *P* value: 0.11			
		Distal colon	Beef, pork, and lamb intake as main dish (servings/wk), tertiles			
			Women:			
			T1	191	1.0	
			T2	163	1.3 (1.0–1.7)	
			T3	52	1.2 (0.8–1.9)	
			Trend-test *P* value: 0.16			

Table 2.2.3 Case–control studies on consumption of red meat and cancer of the colorectum

Reference, location, enrolment	Population size, description, exposure assessment method	Organ site	Exposure category or level	Exposed cases/ deaths	Risk estimate (95% CI)	Covariates controlled
Hu et al. (2007) Canada 1994–1997 (cont.)		Distal colon	Hamburger intake (servings/wk), tertiles			
			Women:			
			T1	76	1.0	
			T2	273	1.2 (0.8–1.7)	
			T3	57	1.2 (0.7–2.0)	
			Trend-test *P* value: 0.42			
Kimura et al. (2007) Fukuoka, Japan 2000–2003	Cases: 840; hospital-based cases admitted to hospitals in Fukuoka and three adjacent areas Controls: 833; population-based controls from 15 different areas, sampled based on frequency of age and sex of cases Exposure assessment method: questionnaire; validated, administered in person, and included 148 items; reported on beef and pork combined	Colon and rectum	Beef/pork, likely fresh meat (quintile median, g/day)			Age, sex, residential area, BMI 10 yr before, parental colorectal cancer, smoking, alcohol use, type of job, leisure-time physical activity, dietary calcium, dietary fibre
			Q1 (14.2)	142	1.00	
			Q2 (27.3)	188	1.35 (0.98–1.85)	
			Q3 (37.4)	161	1.28 (0.92–1.79)	
			Q4 (48.6)	140	0.03 (0.73–1.44)	
			Q5 (70.1)	151	1.13 (0.80–1.61)	
			Trend-test *P* value: 0.94			
		Proximal colon	Beef/pork (g/day), quintiles			
			Q1	23	1.00	
			Q2	48	2.21 (1.26–3.88)	
			Q3	41	2.00 (1.12–3.58)	
			Q4	35	1.67 (0.91–3.06)	
			Q5	30	1.44 (0.76–2.71)	
			Trend-test *P* value: 0.64			
		Distal colon	Beef/pork (g/day), quintiles			
			Q1	54	1.00	
			Q2	65	1.24 (0.80–1.94)	
			Q3	46	0.94 (0.58–1.52)	
			Q4	41	0.80 (0.49–1.31)	
			Q5	56	1.23 (0.75–2.00)	
			Trend-test *P* value: 0.97			

Table 2.2.3 Case–control studies on consumption of red meat and cancer of the colorectum

Reference, location, enrolment	Population size, description, exposure assessment method	Organ site	Exposure category or level	Exposed cases/ deaths	Risk estimate (95% CI)	Covariates controlled
Kimura et al. (2007) Fukuoka, Japan 2000–2003 (cont.)		Rectum	Beef/pork (g/day), quintiles			
			Q1	63	1.00	
			Q2	73	1.18 (0.78–1.79)	
			Q3	70	1.18 (0.77–1.81)	
			Q4	57	0.88 (0.56–1.38)	
			Q5	64	1.01 (0.64–1.60)	
			Trend-test *P* value: 0.64			
Küry et al. (2007) Pays de la Loire region, France 2002–2006	Cases: 1023; hospital-based colorectal cases with a family history of colorectal cancer, diagnosed at an age < 40 yr Controls: 1121; hospital-based, identified from health examination centres or the University Hospital of Nantes; matched to cases by sex, age, and geography Exposure assessment method: questionnaire; unclear validation and administered in person; red meat was beef and lamb; assessed genotypes in *CYP1A2*, *CYP2E1*, *CYP1B1*, and *CYP2C9*	Colon and rectum	Red meat intake (times/wk)			The matching variables age, sex, residence
			1– 4	NR	1.00	
			≥ 5	NR	2.81 (1.52–5.21)	
			Trend-test *P* value: 0.001			
Cotterchio et al. (2008) Ontario, Canada 1997–2000	Cases: 1095; population-based colorectal cases, identified through the Ontario Cancer Registry; familial cases were included Controls: 1890; population-based, identified through random digit dialling Exposure assessment method: questionnaire; not validated and self-administered; total red meat was beef, steak, hamburger, prime rib, ribs, beef hot dogs, beef-based processed meat, veal, pork, bacon, pork sausage, ham, lamb, and venison; assessed frequency only, cooking methods, and polymorphisms in 15 xenobiotic-metabolizing enzymes (CYPs, GSTs, UGTs, SULT, NATs, mEH, AHR), *CYP2C9*, and *NAT2*	Colon and rectum	Total red meat (servings/wk)			Age
			0–2.0	307	1.00	
			2.1–3.0	224	1.37 (1.10–1.70)	
			3.1–5.0	265	1.45 (1.18–1.78)	
			> 5.0	276	1.67 (1.36–2.05)	
			Total red meat doneness (servings/wk)			
			≤ 2 "rare/regular"	234	1.00	
			≤ 2 "well done"	278	1.23 (0.99–1.53)	
			> 2 "rare/regular"	211	1.24 (0.98–1.56)	
			> 2 "well done"	321	1.57 (1.27–1.93)	

Table 2.2.3 Case–control studies on consumption of red meat and cancer of the colorectum

Reference, location, enrolment	Population size, description, exposure assessment method	Organ site	Exposure category or level	Exposed cases/ deaths	Risk estimate (95% CI)	Covariates controlled
Cotterchio et al. (2008) Ontario, Canada 1997–2000 (cont.)			Total red meat doneness (servings/wk) *CYP1B1* combined variance (derived)			
			Wildtype (> 2 “well done” vs ≤ 2 “rare/ regular”)	NR	4.09 (2.17–7.71)	
			Increased activity (> 2 “well done” vs ≤ 2 “rare/regular”)	NR	1.52 (1.15–2.01)	
			P value for interaction = 0.04			
			Total red meat doneness (servings/wk) *SULT1A1*–638			
			GG (> 2 “well done” vs ≤ 2 “rare/regular”)	NR	2.43 (1.66–3.57)	
			AA/GA (> 2 “well done” vs ≤ 2 “rare/ regular”)	NR	1.39 (0.99–1.95)	
			P value for interaction = 0.03			
Saebø et al. (2008) Norway NR	Cases: 198; population-based colorectal cases, identified through a screening study Controls: 222; population-based, identified through a screening study and determined to be polyp-free by flexible sigmoidoscopy Exposure assessment method: questionnaire; unclear validation; red meat was not defined; assessed polymorphism in *CYP1A2*	Colon and rectum	Total red meat (g/day)			Age, sex, ever-smoking
			≤ 22.5	74	1.00	
			> 22.5 to ≤ 45.0	48	1.07 (0.54–2.14)	
			> 45.0	23	1.58 (0.71–3.47)	
			Doneness level			
			Rare/medium	45	1.00	
			Well done	73	0.69 (0.36–1.32)	

Table 2.2.3 Case–control studies on consumption of red meat and cancer of the colorectum

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. (2009) USA 1997–2002	Cases: 577; population-based colorectal cases, identified through cancer registries from California, North Carolina, Arizona, Minnesota, New Hampshire, and Colorado Controls: 361; unaffected siblings of cases who were older than cases Exposure assessment method: questionnaire; not validated and assessed frequency and cooking methods; total red meat was beef, steak, hamburger, prime rib, ribs, veal, lamb, bacon, pork, pork in sausages, or venison	Colon and rectum	Total red meat (servings/wk)			None
			≤ 3	131	1.00	
			> 3	177	1.8 (1.3–2.5)	
			Trend-test *P* value: 0.001			
		Colon	Total red meat (servings/wk)			
			≤ 3	79	1.00	
			> 3	106	1.8 (1.1–2.8)	
			Trend-test *P* value: 0.019			
		Rectum	Total red meat (servings/wk)			
			≤ 3	40	1.00	
			> 3	44	1.3 (0.6–2.5)	
			Trend-test *P* value: 0.517			
		Colon and rectum	Doneness of total red meat (estimated from outside colour).)			
			Light or medium browned	214	1.00	
			Heavily browned	94	1.1 (0.8–1.6)	
			Trend-test *P* value: 0.559			
			Test of heterogeneity, colon vs rectum (*P* = 0.613)			
		Colon and rectum	Doneness of red meat (estimated from insidecolour)			
			Red or pink	153	1.00	
			Brown	155	1.2 (0.8–1.6)	
			Trend-test *P* value: 0.362			
			Test of heterogeneity, colon vs rectum (*P* = 0.351)			
		Rectum	Doneness of red meat (estimated from outside colour); among carriers of XPD Lys751Lys			
			Light or medium browned	22	1.00	
			Heavily browned	13	3.8 (1.1–13.)	
			Trend-test *P* value = 0.037			

Table 2.2.3 Case–control studies on consumption of red meat and cancer of the colorectum

Reference, location, enrolment	Population size, description, exposure assessment method	Organ site	Exposure category or level	Exposed cases/deaths	Risk estimate (95% CI)	Covariates controlled
Morita et al. (2009) Fukuoka, Japan 2000–2003	Cases: 685; hospital-based colorectal cases Controls: 833; population-based Exposure assessment method: questionnaire; validated, administered by in-person interview, and included 148 items; red meat was beef and pork	Colon	Red meat intake (median, g/2000 kcal per day); among carriers of 0 alleles for *CYP2E1* 96-bp insertion			Sex, age, area, cigarette smoking, BMI, type of job, physical activity, parental colorectal cancer
			21	88	1.00	
			38	73	0.79 (0.52–1.18)	
			63	63	0.75 (0.48–1.16)	
			Trend-test *P* value: 0.18			
			Red meat intake (median, g/2000 kcal per day); among carriers of 1 or 2 alleles for *CYP2E1* 96-bp insertion			
			21	46	1.00	
			38	56	1.44 (0.85–2.42)	
			63	55	1.42 (0.82–2.43)	
			Trend-test *P* value: 0.21			
			P value for interaction = 0.03			
Squires et al. (2010) Newfoundland and Labrador, Canada 1999–2003	Cases: 518; population-based colorectal cases, identified through a cancer registry Controls: 686; population-based, identified through random digit dialling; frequency-matched to cases by age and sex Exposure assessment method: questionnaire; unclear validation of local foods, administered by mail, and included 169 items. Total red meat was beef, steak, hamburger, prime rib, ribs, beef hot dogs, beef-based processed meat, veal, pork, bacon, pork sausage, ham, lamb, and venison; assessed cooking methods	Colon and rectum	Total red meat intake (servings/day)			Age; BMI; smoking status; level of education; intake of vegetables, fruits, folic acid, cholesterol, dietary fibre, saturated fat, alcohol; caloric intake; level of physical activity; NSAID use; presence of inflammatory bowel disease
			Men:			
			≤ 2	125	1.00	
			> 2 to ≤ 3	74	0.96 (0.59–1.57)	
			> 3 to ≤ 5	49	0.95 (0.56–1.59)	
			> 5	53	0.75 (0.43–1.29)	
			Total red meat intake (servings/day)			
			Women:			
			≤ 2	81	1.00	
			> 2 to ≤ 3	41	1.14 (0.61–2.11)	
			> 3 to ≤ 5	40	1.46 (0.73–2.93)	
			> 5	39	1.81 (0.94–3.51)	
			Red meat doneness (servings/day)			
			Women:			
			≤ 2 "rare/regular"	17	1.00	
			≤ 2 "well-done"	106	1.94 (0.81–4.62)	
			> 2 "rare/regular"	10	3.95 (1.02–15.25)	
			> 2 "well-done"	32	3.1 (1.11–8.69)	

Table 2.2.3 Case–control studies on consumption of red meat and cancer of the colorectum

Reference, location, enrolment	Population size, description, exposure assessment method	Organ site	Exposure category or level	Exposed cases/ deaths	Risk estimate (95% CI)	Covariates controlled
Squires et al. (2010) Newfound-land and Labrador, Canada 1999–2003 (cont.)			Red meat doneness (servings/day)			
			Men:			
			≤ 2 “rare/regular”	71	1.00	
			≤ 2 “well-done”	132	1.23 (0.76–2.00)	
			> 2 “rare/regular”	18	1.42 (0.61-3.33)	
			> 2 “well-done”	42	1.44 (0.76-2.72)	
Williams et al. (2010) North Carolina, USA 2001–2006	Cases: 945; population-based distal colorectal cancer cases, identified through the North Carolina Central Cancer Registry; African Americans were oversampled Controls: 959; population-based, selected from the North Carolina Department of Motor Vehicles or Centers for Medicare and Medicaid Services Exposure assessment method: questionnaire; validated, administered in person, and included portion size and frequency; red meat was veal, lamb, beef steaks, beef roast, beef mixtures, burgers, ham (not luncheon meat), pork, and ribs	Distal colo-rectum	Red meat (quartile median, g/day) in Whites			Age, sex, education, BMI, family history, NSAID use, physical activity, calcium, fibre, total energy intake
			Q1 (16.2)	149	1.00	
			Q2 (32.9)	186	1.09 (0.78–1.52)	
			Q3 (53.6)	199	1.05 (0.74–1.49)	
			Q4 (94.8)	186	0.66 (0.43–1.00)	
			Trend-test *P* value: 0.90			
			Red meat (quartile median, g/day) in African Americans			
			Q1 (12.7)	58	1.00	
			Q2 (27.8)	39	0.54 (0.27–1.09)	
			Q3 (45.5)	65	0.83 (0.42–1.63)	
			Q4 (108.6)	63	0.64 (0.27–1.50)	
			Trend-test *P* value: 0.94			
Tabatabaei et al. (2011) Australia 2005–2007	Cases: 567; population-based colorectal cases, identified through the Western Australian Cancer Registry Controls: 713; population-based, identified from electoral rolls; frequency-matched to cases by age and sex Exposure assessment method: questionnaire; unclear validation, administered by mail, and included 74 items; total red meat included hamburger/cheeseburger, beef/veal, lamb/mutton, pork chops/ham steaks, bacon, and sausages; assessed cooking methods	Colon and rectum	Total red meat intake (highest vs lowest quartile, servings/wk) by cooking method			BMI, physical activity at ages 35–50 yr, smoking habits, alcohol consumption, fruit and vegetable consumption, supplemental vitamin intake, total energy, fat and fibre consumption, the matching variables age and sex
			Pan-fried	NR	0.80 (0.57–1.13)	
			Trend-test *P* value: 0.27			
			Barbecued	NR	0.89 (0.63–1.24)	
			Trend-test *P* value: 0.17			
			Baked	NR	0.73 (0.53–1.01)	
			Trend-test *P* value: 0.04			
			Stewed	NR	0.95 (0.67–1.33)	
			Trend-test *P* value: 0.53			

Table 2.2.3 Case–control studies on consumption of red meat and cancer of the colorectum

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 1991–2009	Cases: 2390; hospital-based colorectal cases, identified from hospitals as part of a network of case–control studies Controls: 4943; hospital-based, identified through the same network of hospitals as cases; frequency-matched to cases for variables not specified Exposure assessment method: questionnaire; validated, administered in person, included 77 items, and assessed frequency and serving size; 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); assessed cooking methods	Colon	Red meat intake (g/day) in men			Age, sex, education, BMI, tobacco use, alcohol drinking, vegetable consumption, fruit consumption, study centre
			< 60	446	1.00	
			60–89	443	1.19 (1.02–1.38)	
			≥ 90	554	1.22 (1.05–1.41)	
			Per 50 g/day increase	NR	1.17 (1.08–1.26)	
			Trend-test *P* value: 0.02			
		Rectum	< 60	268	1.00	
			60–89	279	1.25 (1.04–1.51)	
			≥ 90	380	1.35 (1.12–1.62)	
			Per 50 g/day increase	NR	1.22 (1.11–1.33)	
			Trend-test *P* value< 0.01			
		Rectum	For every 50 g/day increase in red meat by cooking practice			
			Roasting/ grilling	NR	1.24 (1.07–1.45)	
			Boiling/stewing	NR	1.32 (1.10–1.58)	
			Frying/ pan-frying	NR	1.90 (1.38–2.61)	
Hu et al. (2013) Sichuan, China 2010–2012	Cases: 400; hospital-based cases from the Sichuan Cancer Hospital Controls: 400; hospital-based, identified among individuals who underwent routine medical examinations at a health centre; individually matched by sex and age Exposure assessment method: questionnaire; unclear validation; red meat was beef, pork, and lamb; assessed frequency; genotypes for *ADIPOQ*, *UCP2*, and *FABP2* were assessed	Colon and rectum	Red meat (times/wk)			Family per capita annual income, family history of colorectal cancer, sitting (h/day), BMI, smoking habit, alcohol-drinking habit, tea-drinking habit
			≤ 7	144	1.00	
			> 7	256	1.87 (1.39–2.51)	
			Trend-test *P* value< 0.001			

Table 2.2.3 Case–control studies on consumption of red meat and cancer of the colorectum

Reference, location, enrolment	Population size, description, exposure assessment method	Organ site	Exposure category or level	Exposed cases/ deaths	Risk estimate (95% CI)	Covariates controlled
Miller et al. (2013) Pennsylvania, USA 2007–2011	Cases: 989; incident cases, identified through the Pennsylvania State Cancer Registry Controls: 1033; identified through random digit dialling; frequency-matched to cases by age, sex, and race Exposure assessment method: questionnaire; validated, in-person FFQ with 137 items; meat-cooking module was used with the CHARRED database to estimate carcinogens; red meat was beef and pork (hamburger, roast beef, pot roast, roast pork, steak, pork chops, pork or beef spare ribs, liver, meat added to mixed dishes)	Colon and rectum	Red meat intake (g/1000 kcal)			Age, sex, BMI, past NSAID use, total energy, total fruits and vegetables, total poultry
			Q1 (< 8.7)	184	1.00	
			Q2 (8.7–14.5)	217	1.24 (0.92–1.67)	
			Q3 (14.6–22.6)	184	1.05 (0.78–1.43)	
			Q4 (22.7–35.6)	231	1.38 (1.03–1.86)	
			Q5 (> 35.6)	173	1.02 (0.75–1.40)	
			Trend-test *P* value: 0.975			
		Colon	Red meat intake (g/1000 kcal)			
			Q1 (< 8.7)	139	1.00	
			Q2 (8.7–14.5)	146	1.12 (0.81–1.55)	
			Q3 (14.6–22.6)	127	1.00 (0.72–1.40)	
			Q4 (22.7–35.6)	162	1.34 (0.97–1.86)	
			Q5 (> 35.6)	119	1.00 (0.71–1.40)	
			Trend-test *P* value: 0.865			
		Rectum	Red meat intake (g/1000 kcal)			
			Q1 (< 8.7)	42	1.00	
			Q2 (8.7–14.5)	71	1.72 (1.10–2.68)	
			Q3 (14.6–22.6)	55	1.28 (0.81–2.03)	
			Q4 (22.7–35.6)	67	1.61 (1.02–2.52)	
			Q5 (> 35.6)	54	1.21 (0.76–1.94)	
			Trend-test *P* value: 0.997			
		Colon and rectum	Total DiMeIQx (ng/1000 kcal)			Age, sex, BMI, past NSAID use, total energy, total fruits and vegetables
			Q1 (< 0.23)	181	1.00	
			Q2 (0.23–0.67)	185	1.04 (0.77–1.40)	
			Q3 (0.68–1.23)	203	1.09 (0.81–1.47)	
			Q4 (1.24–2.20)	183	1.03 (0.77–1.39)	
			Q5 (> 2.20)	237	1.36 (1.02–1.82)	
			Trend-test *P* value: 0.027			

Table 2.2.3 Case–control studies on consumption of red meat and cancer of the colorectum

Reference, location, enrolment	Population size, description, exposure assessment method	Organ site	Exposure category or level	Exposed cases/ deaths	Risk estimate (95% CI)	Covariates controlled
Miller et al. (2013) Pennsylvania, USA 2007–2011 (cont.)		Colon and rectum	Total MeIQx (ng/1000 kcal)			
			Q1 (< 4.2)	194	1.00	
			Q2 (4.2–8.3)	170	0.90 (0.67–1.22)	
			Q3 (8.4–14.2)	185	0.96 (0.71–1.29)	
			Q4 (14.3–23.8)	197	1.05 (0.78–1.41)	
			Q5 (> 23.8)	243	1.22 (0.91–1.64)	
			Trend-test *P* value: 0.047			
			Total PhIP (ng/1000 kcal)			
			Q1 (< 7.2)	223	1.00	
			Q2 (7.2–17.4)	207	0.97 (0.73–1.29)	
			Q3 (17.4–33.7)	186	0.87 (0.65–1.16)	
			Q4 (33.8–68.3)	190	0.98 (0.73–1.31)	
			Q5 (> 68.3)	183	1.06 (0.79–1.43)	
			Trend-test *P* value: 0.439			
			Total BaP (ng/1000 kcal)			
			Q1 (< 0.32)	264	1.00	
			Q2 (0.32–2.20)	219	0.95 (0.72–1.25)	
			Q3 (2.30–6.60)	152	0.69 (0.52–0.93)	
			Q4 (6.70–19.00)	184	0.92 (0.69–1.23)	
			Q5 (> 19.00)	170	0.90 (0.67–1.21)	
			Trend-test *P* value: 0.906			
			Grilled/barbecued red meat (g/1000 kcal)			Age, sex, BMI, past NSAID use, total energy, total fruits and vegetables, total poultry
			T1 (0)	285	1.00	
			T2 (0.01–4.35)	352	0.84 (0.66–1.06)	
			T3 (> 4.36)	352	0.94 (0.74–1.20)	
			Trend-test *P* value: 0.808			
			Pan-fried red meat (g/1000 kcal)			
			Q1 (< 0.36)	178	1.00	
			Q2 (0.36–1.39)	181	0.97 (0.71–1.31)	
			Q3 (1.40–3.33)	183	0.99 (0.73–1.34)	
			Q4 (3.34–6.79)	188	0.93 (0.69–1.26)	
			Q5 (> 6.79)	259	1.26 (0.93–1.70)	
			Trend-test *P* value: 0.044			

Table 2.2.3 Case–control studies on consumption of red meat and cancer of the colorectum

Reference, location, enrolment	Population size, description, exposure assessment method	Organ site	Exposure category or level	Exposed cases/ deaths	Risk estimate (95% CI)	Covariates controlled
Miller et al. (2013) Pennsylvania, USA 2007–2011 (cont.)		Colon and rectum	Microwaved/baked red meat (g/1000 kcal)			
			Q1 (< 4.65)	213	1.00	
			Q2 (4.65–7.56)	194	0.89 (0.67–1.20)	
			Q3 (7.57–11.40)	196	0.93 (0.69–1.24)	
			Q4 (11.50–18.60)	204	0.97 (0.72–1.30)	
			Q5 (> 18.60)	182	0.87 (0.65–1.17)	
			Trend-test *P* value: 0.533			
			Broiled red meat (g/1000 kcal)			
			No consumption	727	1.00	
			Ever	262	0.99 (0.8–1.22)	
			Trend-test *P* value: 0.891			
			Red meat, rare/medium (g/1000 kcal)			
			T1 (0)	279	1.00	
			T2 (0.01–4.08)	362	0.94 (0.75–1.90)	
			T3 (> 4.08)	348	0.99 (0.79–1.26)	
			Trend-test *P* value: 0.844			
			Well-done/charred red meat (g/1000 kcal)			
			Q1 (< 0.89)	210	1.00	
			Q2 (0.89–2.41)	176	0.77 (0.57–1.03)	
			Q3 (2.42–4.70)	197	0.92 (0.69–1.24)	
			Q4 (4.71–8.96)	204	1.01 (0.75–1.35)	
			Q5 (> 8.96)	202	0.87 (0.64–1.16)	
			Trend-test *P* value: 0.857			
Rosato et al. (2013) Italy and Switzerland 1985–2009	Cases: 329; hospital-based cases with young-onset colorectal cancer (< 45 yr) Controls: 1361; hospital-based, identified from the same hospitals as cases; conditions unrelated to colorectal cancer risk factors or dietary modifications Exposure assessment method: questionnaire; validated and administered in person; red meat was not defined, and unclear if it included processed meat	Colon and rectum	Red meat intake			Age, sex, centre, study, year of interview, education, family history, alcohol, energy intake
			Low	101	1.00	
			Medium	88	0.93 (0.67–1.29)	
			High	140	1.07 (0.79–1.47)	
			Trend-test *P* value: 0.57			

Table 2.2.3 Case–control studies on consumption of red meat and cancer of the colorectum

Reference, location, enrolment	Population size, description, exposure assessment method	Organ site	Exposure category or level	Exposed cases/ deaths	Risk estimate (95% CI)	Covariates controlled
Abu Mweis et al. (2015) Jordan 2010–2012	Cases: 167; hospital-based colorectal cases recruited from five major Jordanian hospitals Controls: 240; hospital-based, identified from hospital personnel, outpatients, visitors, and accompanying individuals; matched by age, sex, occupation, and marital status Exposure assessment method: questionnaire; validated, administered in person, and included 109 items; red meat was not defined	Colon and rectum	Red meat intake (serving/wk)			Age, sex, total energy, metabolic equivalent, smoking, education level, marital status, work, income, family history of colorectal cancer
			< 1	103	1.00	
			≥ 1	51	0.64 (0.37–1.11)	
Guo et al. (2015) Harbin, China 2008–2013	Cases: 600; hospital-based colorectal cases Controls: 600; hospital-based, identified at the community health centre and individually matched to cases by age and sex Exposure assessment method: questionnaire; non-validated and administered in person; red meat was pork, beef, and lamb; unclear if processed meat was included	Colon and rectum	Red meat (times/wk)			BMI, family income, drinking, smoking, regular tea drinking, daily sedentary time, family history of cancer
			≤ 7	NR	1.00	
			> 7	NR	1.54 (1.114–2.424)	
			Trend-test *P* value: 0.001			

Table 2.2.3 Case–control studies on consumption of red meat and cancer of the colorectum

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. (2015) USA and Canada 1997–2002	Cases: 3350; population-based, identified through cancer registries in Ontario, Canada; Hawaii, California, Arizona, North Carolina, New Hampshire, Colorado, Minnesota, USA; cases with familial cases included Controls: 3504; cancer-free siblings of the cases (*n* = 1759), unaffected spouses of the cases (*n* = 138), and population-based controls (*n* = 1607) Exposure assessment method: questionnaire; validated, administered by mail, included 200 items, included portion size and frequency of intake, and used the CHARRED database to estimate carcinogens; red meat was beef, pork, veal, lamb, and game; cooking methods were considered	Colon and rectum	Red meat (g/1000 kcal per day)			Age, BMI, sex, race, saturated fat, dietary fibre, centre, vegetables, physical activity, total caloric intake
			Q1 (0–10.81)	633	1.0	
			Q2 (10.81–16.04)	644	1.0 (0.9–1.2)	
			Q3 (16.04–21.11)	707	1.2 (1.0–1.4)	
			Q4: 21.12–28.19	680	1.2 (1.0–1.4)	
			Q5 (28.19–102.43)	686	1.2 (1.0–1.4)	
			Trend-test *P* value: 0.085			
		Colon	Red meat (g/1000 kcal per day)			
			Q1 (0–10.81)	396	1.0	
			Q2 (10.81–16.04)	380	1.1 (0.9–1.3)	
			Q3 (16.04–21.11)	429	1.2 (1.0–1.5)	
			Q4 (21.12–28.19)	396	1.2 (1.0–1.4)	
			Q5 (28.19–102.43)	391	1.2 (0.9–1.4)	
			Trend-test *P* value: 0.152			
		Rectum	Red meat (g/1000 kcal per day)			
			Q1 (0–10.81)	171	1.0	
			Q2 (10.81–16.04)	152	0.8 (0.6–1.0)	
			Q3 (16.04–21.11)	201	1.0 (0.8–1.3)	
			Q4 (21.12–28.19)	179	0.8 (0.7–1.1)	
			Q5 (28.19–102.43)	173	0.8 (0.6–1.0)	
			Trend-test *P* value: 0.104			
		Colon and rectum	Beef (g/1000 kcal per day)			
			Q1 (0–7.69)	687	1.0	
			Q2 (7.70–11.49)	652	1.0 (0.9–1.2)	
			Q3 (11.49–15.08)	654	1.0 (0.9–1.2)	
			Q4 (12.09–20.06)	672	1.1 (0.9–1.3)	
			Q5 (20.08–83.77)	685	1.1 (0.9–1.3)	
			Trend-test *P* value: 0.289			

Table 2.2.3 Case–control studies on consumption of red meat and cancer of the colorectum

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. (2015) USA and Canada 1997–2002 (cont.)		Colon	Beef (g/1000 kcal per day)			
			Q1 (0–7.69)	426	1.0	
			Q2 (7.70–11.49)	377	9.0 (0.8–1.1)	
			Q3 (11.49–15.08)	396	1.0 (0.8–1.2)	
			Q4 (12.09–20.06)	400	1.1 (0.9–1.3)	
			Q5 (20.08–83.77)	383	1.0 (0.8–1.2)	
			Trend-test *P* value: 0.593			
		Rectum	Beef (g/1000 kcal per day)			
			Q1 (0–7.69)	155	1.0	
			Q2 (7.70–11.49)	185	1.2 (0.9–1.5)	
			Q3 (11.49–15.08)	174	1.1 (0.8–1.4)	
			Q4 (12.09–20.06)	184	1.1 (0.9–1.6)	
			Q5 (20.08–83.77)	209	1.2 (0.9–1.6)	
			Trend-test *P* value: 0.252			
			Test of heterogeneity, colon vs rectum (*P* = 0.292)			
		Colon and rectum	Pork (g/1000 kcal per day)			
			Q1 (0–1.32)	617	1.0	
			Q2 (1.32–3.01)	641	1.0 (0.9–1.2)	
			Q3 (3.01–4.84)	660	1.1 (0.9–1.2)	
			Q4 (4.85–7.44)	743	1.2 (1.0–1.4)	
			Q5 (7.44–49.62)	689	1.1 (1.0–1.3)	
			Trend-test *P* value: 0.069			

Table 2.2.3 Case–control studies on consumption of red meat and cancer of the colorectum

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. (2015) USA and Canada 1997–2002 (cont.)		Colon	Pork (g/1000 kcal per day)			
			Q1 (0–1.32)	383	1.0	
			Q2 (1.32–3.01)	388	1.0 (0.8–1.2)	
			Q3 (3.01–4.84)	383	1.0 (0.9–1.2)	
			Q4 (4.85–7.44)	440	1.2 (1.0–1.4)	
			Q5 (7.44–49.62)	398	1.1 (0.9–1.3)	
			Trend-test *P* value: 0.224			
		Rectum	Pork (g/1000 kcal per day)			
			Q1 (0–1.32)	154	1.0	
			Q2 (1.32–3.01)	163	1.0 (0.8–1.3)	
			Q3 (3.01–4.84)	178	1.1 (0.8–1.3)	
			Q4 (4.85–7.44)	207	1.2 (0.9–1.5)	
			Q5 (7.44–49.62)	205	1.1 (0.9–1.5)	
			Trend-test *P* value: 0.133			
		Colon and rectum	Organ meats (g/1000 kcal per day)			
			Q1 (0–0)	884	1.0	
			Q2 0–0)	282	1.2 (1.0–1.4)	
			Q3 (0–0)	650	1.1 (1–1.3)	
			Q4 (0–0.02)	755	1.0 (0.9–1.2)	
			Q5 (0.02–0.64)	779	1.2 (1.0–1.4)	
			Trend-test *P* value: 0.058			
		Colon and rectum	Pan-fried beef steak (g/1000 kcal per day)			
			Q1 (0–0)	1692	1.0	
			Q2 (0.01–0.02)	506	1.0 (0.8–1.1)	
			Q3 (0.02–0.04)	511	1.0 (0.9–1.2)	
			Q4 (0.04–0.99)	619	1.3 (1.1–1.5)	
			Trend-test *P* value: <0.001			

Table 2.2.3 Case–control studies on consumption of red meat and cancer of the colorectum

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. (2015) USA and Canada 1997–2002 (cont.)		Colon and rectum	Pan-fried beef steak(g/1000 kcal per day); MMR proficient			
			Q1	469	1.0	
			Q2	129	0.9 (0.7–1.1)	
			Q3	119	0.9 (0.7–1.1)	
			Q4	155	1.0 (1.0–1.5)	
			Trend-test *P* value:0.098			
			Pan-fried beef steak(g/1000 kcal per day); MMR deficient			
			Q1	121	1.0	
			Q2	33	1.0 (0.7–1.5)	
			Q3	35	1.1 (0.8–1.7)	
			Q4	54	1.7 (1.2–2.4)	
			Trend-test *P* value:0.002			
			Test of heterogenicity MMR-deficient vs MMR-proficient (*P*=0.059)			
			Pan-fried hamburger (g/1000 kcal per day)			
			Q1 (0–0)	1297	1.0	
			Q2 (0.01–0.02)	627	0.9 (0.8–1.1)	
			Q3 (0.02–0.05)	707	1.0 (0.9–1.2)	
			Q4 (0.05–0.99)	697	1.1 (0.9–1.2)	
			Trend-test *P* value: 0.209			
			Pan-fried hamburger (g/1000 kcal per day); MMR-proficient			
			Q1 (0–0)	381	1.0	
			Q2 (0.01–0.02)	164	0.8 (0.7–1.0)	
			Q3 (0.02–0.05)	178	1.0 (0.8–1.2)	
			Q4 (0.05–1.37)	150	0.9 (0.7–1.1)	
			Trend-test *P* value: 0.516			

Table 2.2.3 Case–control studies on consumption of red meat and cancer of the colorectum

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. (2015) USA and Canada 1997–2002 (cont.)		Colon and rectum	Pan-fried hamburger (g/1000 kcal per day); MMR-deficient			
			Q1 (0–0)	89	1.0	
			Q2 (0.01–0.02)	34	0.8 (0.5–1.2)	
			Q3 (0.02–0.05)	56	1.3 (0.9–1.9)	
			Q4 (0.05–0.99)	63	1.5 (1.0–2.1)	
			Trend-test *P* value: 0.01			
			Test of heterogeneity, MMR-deficient vs MMR-proficient (*P* = 0.026)			
			Oven-broiled beef steak (g/1000 kcal per day)			
			Q1 (0–0)	2145	1.0	
			Q2 (0.01–0.02)	399	1.0 (0.8–1.2)	
			Q3 (0.02–0.04)	397	1.1 (0.9–1.3)	
			Q4 (0.04–1.37)	346	0.9 (0.8–1.1)	
			Trend-test *P* value: 0.742			
			Oven-broiled hamburger (g/1000 kcal per day)			
			Q1 (0–0)	2506	1.0	
			Q2 (0.01–0.02)	241	0.8 (0.7–1.0)	
			Q3 (0.02–0.04)	279	1.0 (0.8–1.2)	
			Q4 (0.04–0.99)	283	1.0 (0.9–1.2)	
			Trend-test *P* value: 0.989			
			Oven-broiled short ribs or spare ribs (g/1000 kcal per day)			
			Q1 (0–0)	2389	1.0	
			Q2 (0.01–0.02)	319	1.2 (1.0–1.5)	
			Q3 (0.02–0.03)	299	1.3 (1.1–1.6)	
			Q4 (0.03–0.99)	306	1.2 (1.0–1.5)	
			Trend-test *P* value: 0.002			

Table 2.2.3 Case–control studies on consumption of red meat and cancer of the colorectum

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. (2015) USA and Canada 1997–2002 (cont.)		Colon and rectum	Oven-broiled short ribs or spare ribs (g/1000 kcal per day); MMR-proficient			
			Q1 (0–0)	656	1.0	
			Q2 (0.01–0.02)	91	1.3 (1.0–1.7)	
			Q3 (0.02–0.04)	64	1.1 (0.8–1.5)	
			Q4 (0.04–0.99)	58	1.0 (0.8–1.4)	
			Trend-test *P* value: 0.415			
			Oven-broiled short ribs or spare ribs (g/1000 kcal per day); MMR-deficient			
			Q1 (0–0)	178	1.0	
			Q2 (0.01–0.02)	15	0.9 (0.5–1.5)	
			Q3 (0.02–0.04)	21	1.5 (0.9–2.4)	
			Q4 (0.04–0.99)	26	1.9 (1.2–3.0)	
			Trend-test *P* value: 0.003			
			Test of heterogeneity, MMR-proficient vs MMR-deficient (*P* = 0.052)			
			Grilled beef steak (g/1000 kcal per day)			
			Q1 (0–0)	1314	1.0	
			Q2 (0.01–0.02)	726	0.9 (0.8–1.1)	
			Q3 (0.02–0.04)	677	1.0 (0.8–1.1)	
			Q4 (0.04–0.99)	582	0.9 (0.8–1.0)	
			Trend-test *P* value: 0.212			

Table 2.2.3 Case–control studies on consumption of red meat and cancer of the colorectum

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. (2015) USA and Canada 1997–2002 (cont.)		Colon and rectum	Grilled hamburger (g/1000 kcal per day)			
			Q1 (0–0)	1401	1.0	
			Q2 (0.01–0.02)	690	0.9 (0.7–1.0)	
			Q3 (0.02–0.05)	686	0.9 (0.8–1.1)	
			Q4 (0.05–0.99)	542	0.8 (0.7–0.9)	
			Trend-test *P* value: 0.002			
			Grilled short ribs or spare ribs (g/1000 kcal per day)			
			Q1 (0–0)	2239	1.0	
			Q2 (0.01–0.02)	360	0.9 (0.8–1.1)	
			Q3 (0.02–0.03)	344	1.1 (0.9–1.3)	
			Q4 (0.03–0.99)	361	1.1 (0.9–1.3)	
			Trend-test *P* value: 0.166			

AHR, aryl hydrocarbon receptor; BaP, benzo[*a*]pyrene; BMI, body mass index; CHARRED, Computerized Heterocyclic Amines Resource for Research in Epidemiology of Disease; CI, confidence interval; CYP, cytochrome P450; DiMeIQx, 2-amino-3,4,8-trimethylimidazo[4,5-*f*]quinoxaline; FFQ, food frequency questionnaire; GI, gastrointestinal; GST, glutathione S-transferase; h, hour; HAA, heterocyclic aromatic amine; HRT, hormone replacement therapy; kg, kilogram; mEH, microsomal epoxide hydrolase; MeIQx, 2-amino-3,8-dimethylimidazo[4,5-*f*]quinoxaline; min, minute; MMR, mismatch repair; mo, month; NAT, *N*-acetyltransferase; NOS, not otherwise specified; NR, not reported; NS, not significant; NSAID, nonsteroidal anti-inflammatory drug; PhIP, 2-amino-1-methyl-6-phenylimidazo[4,5-*b*]pyridine; SEER, Surveillance, Epidemiology, and End Results; SULT, sulfotransferase; UGT, UDP glucuronosyltransferase; wk, week; yr, year

Table 2.2.4 Case–control studies on consumption of processed meat and cancer of the colorectum

Reference, location, enrolment	Population size, description, exposure assessment method	Organ site	Exposure category or level	Exposed cases/ deaths	Risk estimate (95% CI)	Covariates controlled
Macquart-Moulin et al. (1986) Marseille, France 1979–1984	Cases: 399; hospital-based colorectal cases Controls: 399; hospital-based, identified from centres treating injuries or trauma; no GI disease, no alcohol-related diseases, and matched to cases by sex and age Exposure assessment method: questionnaire; unknown validation, administered in person, included 158 items, and considered frequency and portion size; processed meat was ham, salami, sausages, and pâté	Colon and rectum	Processed meats (percentiles)			Age, sex, weight, total calories
			Q1	112	1.00	
			Q2 (25th)	109	1.31	
			Q3 (50th)	90	0.88	
			Q4 (75th)	88	0.89	
			Trend-test *P* value: 0.22			
Tuyns et al. (1988) Belgium 1978–1982	Cases: 818; population-based cases, identified through treatment centres Controls: 2851; population-based Exposure assessment method: questionnaire; validated, administered in person, and captured frequency and serving size; processed meat was "charcuterie"	Colon	"Charcuterie" (g/wk)			Age, sex, province
			0	NR	1.00	
			>0–50	NR	1.16	
			>50–125	NR	0.83	
			>125	NR	0.90	
			Trend-test *P* value: 0.26			
		Rectum	"Charcuterie" (g/wk)			
			0	NR	1.00	
			>0–50	NR	1.38	
			>50–125	NR	0.94	
			>125	NR	0.98	
			Trend-test *P* value: 0.63			
Benito et al. (1990) Majorca, Spain 1984–1988	Cases: 286; population-based colorectal cases in a case–control study Controls: 498; population-based, identified from the electoral census and frequency-matched to cases by age and sex; hospital-based, selected from ophthalmology and orthopaedic clinics from hospitals where the majority of cases were identified; Exposure assessment method: questionnaire; not validated, included 99 items, and administered in person; exposure definition was processed meat including all types of cured meat and meats processed with other animal products, such as blood and fats	Colon and rectum	Processed meat (intake per mo), quartiles			Age, sex, weight 10 yr before interview
			Q1	22	1.00	
			Q2	89	1.35	
			Q3	94	1.42	
			Q4	81	1.36	
			Trend-test *P* value: 0.4			

Table 2.2.4 Case–control studies on consumption of processed meat and cancer of the colorectum

Reference, location, enrolment	Population size, description, exposure assessment method	Organ site	Exposure category or level	Exposed cases/ deaths	Risk estimate (95% CI)	Covariates controlled
Gerhardsson de Verdier et al. (1991) Stockholm, Sweden 1986–1988	Cases: 559; population-based colorectal cases, identified through local hospitals and a regional cancer registry Controls: 505; population-based, frequency-matched to cases by age and sex Exposure assessment method: questionnaire; unclear validation, self-administered, and included 55 items; processed meat was bacon/smoked ham and sausage assessed separately; assessed cooking methods	Colon	Processed meat intake (Tertile 3 vs T1, i.e. > 1 time/wk vs more seldom)			Year of birth, sex, fat intake
			Bacon/smoked ham	84	1.3 (0.8–1.9)	
			Trend-test *P* value = 0.34			
			Sausage, fried	90	1.0 (0.6–1.4)	
			Trend-test *P* value = 0.91:			
			Sausage, oven-roasted	12	1.2 (0.5–2.8)	
			Trend-test *P* value = 0.36			
			Sausage, boiled	57	1.4 (0.9–2.2)	
			Trend-test *P* value = 0.04			
		Rectum	Processed meat intake (> 1 time/wk vs more seldom)			
			Bacon/smoked ham	53	1.7 (1.1–2.8)	
			Trend-test *P* value = 0.025			
			Sausage, fried	71	1.5 (0.9–2.4)	
			Trend-test *P* value = 0.093			
			Sausage, oven-roasted	13	2.1 (0.9–4.9)	
			Trend-test *P* value = 0.038			
			Sausage, boiled	53	3.0 (1.8–4.9)	
			Trend-test *P* value: <0.001			
Iscovich et al. (1992) La Plata, Argentina 1985–1986	Cases: 110; hospital-based, identified through local hospitals Controls: 220; population-based, identified from neighbourhoods of cases and matched to cases by sex; controls with conditions that may have affected diet were excluded Exposure assessment method: questionnaire; unclear validation, administered in person, and included 140 items; processed meat was sausage, mortadella, salami (with skin), ham, and cooked skinless meat	Colon	Processed meat intake (fat with skin), quartiles			Matching variables
			Q1	NR	1.00	
			Q2	NR	0.76 (0.38–1.52)	
			Q3	NR	0.63 (0.28–1.41)	
			Q4	NR	0.45 (0.23–0.90)	
			Trend-test *P* value: 0.017			
			Processed meat intake (lean), quartiles			
			Q1	NR	1.00	
			Q2	NR	0.73 (0.36–1.49)	
			Q3	NR	0.50 (0.20–1.24)	
			Q4	NR	0.38 (0.19–0.75)	
			Trend-test *P* value: 0.002			

Table 2.2.4 Case–control studies on consumption of processed meat and cancer of the colorectum

Reference, location, enrolment	Population size, description, exposure assessment method	Organ site	Exposure category or level	Exposed cases/ deaths	Risk estimate (95% CI)	Covariates controlled
Steinmetz and Potter (1993) Adelaide, Australia 1979–1980	Cases: 220; population-based colon cases, identified via the South Australian Cancer Registry Controls: 438; population-based; two controls per case selected via the electoral roll and individually matched to cases by age and sex Exposure assessment method: questionnaire; validated, self-administered, and included 141 items; processed meat was grilled bacon, fried bacon, grilled pork sausage, fried pork sausage, grilled beef sausage, fried beef sausage, sausage roll, cold meat (e.g. ham, “fritz”), and spicy meat (e.g. salami)	Colon	Processed meat intake (servings/wk), quartiles			Age at first live birth, Quetelet index, alcohol intake, the matching variable age
			Women:			
			Q1 (≥ 1.4)	NR	1.00	
			Q2 (1.5–2.8)	NR	0.54 (0.25–1.23)	
			Q3 (2.9–4.3)	NR	0.81 (0.37–1.77)	
			Q4 (≥ 4.3)	NR	0.77 (0.35–1.68)	
			Processed meat intake (servings/wk), quartiles			Occupation, Quetelet index, alcohol intake for males, the matching variable age
			Men:			
			Q1 (≤ 2.2)	NR	1.00	
			Q2 (2.3–4.3)	NR	0.69 (0.35–1.37)	
			Q3 (4.4–7.6)	NR	0.68 (0.35–1.34)	
			Q4 (≥ 7.7)	NR	1.03 (0.55–1.95)	
Centonze et al. (1994) Southern Italy 1987–1989	Cases: 119; population-based colorectal cases, identified from a population-based cancer registry Controls: 119; population-based, matched to cases by age, sex, and general practitioner Exposure assessment method: questionnaire; unclear validation, administered by in-person interview, and included 70 food items; processed meat was sausage, ham, and tinned meat	Colon and rectum	Processed meat (g/day)			Age, sex, level of education, smoking status, modifications of diet in the past 10 yr
			<2	66	1.00	
			≥3	53	1.01 (0.57–1.69)	
Lohsoonthorn and Danvivat (1995) Bangkok, Thailand NR	Cases: 279; hospital-based colorectal cases Controls: 279; hospital-based, individually matched to cases by sex, age, admission period, and hospital; included cancer patients with cancer in other organs Exposure assessment method: questionnaire; unclear validation and number of items asked; assessed frequency only; processed meat (individual types only) was bacon, salted beef, and sausage	Colon and rectum	Bacon consumption (times/mo)			Not specified
			< 5	267	1.00	
			6– ≥ 10	12	12.49 (1.68–269)	
			Trend-test *P* value: 0.82			
			Salted beef consumption (times/mo)			
			< 5	184	1.00	
			6– ≥ 10	95	0.97 (0.67–1.39)	
			Trend-test *P* value: 0.93			
			Sausage consumption (times/mo)			
			< 5	247	1.00	
			6– ≥ 10	32	1.26 (0.71–2.25)	
			Trend-test *P* value: 0.79			

Table 2.2.4 Case–control studies on consumption of processed meat and cancer of the colorectum

Reference, location, enrolment	Population size, description, exposure assessment method	Organ site	Exposure category or level	Exposed cases/ deaths	Risk estimate (95% CI)	Covariates controlled
De Stefani et al. (1997) Montevideo, Uruguay 1993–1995	Cases: 250; hospital-based colorectal cases Controls: 500; hospital-based, identified at the same hospitals as the cases and had a variety of disorders unrelated to tobacco smoking, alcohol, or diet Exposure assessment method: questionnaire; unclear validation, administered in person, and included 60 items; unclear what was included in processed meat; assessed cooking methods	Colon and rectum	Processed meat, quartiles			Age, residence, education, family history of colon cancer in a first-degree relative, BMI, vegetable and dessert intake
			Men:			
			Q1	NR	1.00	
			Q2	NR	1.19 (0.65–2.15)	
			Q3	NR	0.70 (0.39–1.25)	
			Q4	NR	0.75 (0.40–1.37)	
			Trend-test *P* value: 0.17			
			Processed meat, quartiles			
			Women:			
			Q1	NR	1.00	
			Q2	NR	0.81 (0.39–1.65)	
			Q3	NR	0.93 (0.44–1.95)	
			Q4	NR	1.35 (0.65–2.82)	
			Trend-test *P* value: 0.37			
		Colon	Processed meat, quartiles			
			Men:			
			Q1	NR	1.00	
			Q2	NR	1.68 (0.77–3.66)	
			Q3	NR	1.09 (0.50–2.39)	
			Q4	NR	1.21 (0.55–2.66)	
			Trend-test *P* value: 0.99			
			Processed meat, quartiles			
			Women:			
			Q1	NR	1.00	
			Q2	NR	0.64 (0.27–1.49)	
			Q3	NR	0.87 (0.37–2.03)	
			Q4	NR	1.37 (0.59–3.19)	
			Trend-test *P* value: 0.36			

Table 2.2.4 Case–control studies on consumption of processed meat and cancer of the colorectum

Reference, location, enrolment	Population size, description, exposure assessment method	Organ site	Exposure category or level	Exposed cases/ deaths	Risk estimate (95% CI)	Covariates controlled
De Stefani et al. (1997) Montevideo, Uruguay 1993–1995 (cont.)		Rectum	Processed meat, quartiles			
			Men:			
			Q1	NR	1.00	
			Q2	NR	0.98 (0.47–2.04)	
			Q3	NR	0.51 (0.24–1.09)	
			Q4	NR	0.54 (0.25–1.17)	
			Trend-test *P* value: 0.04			
			Processed meat, quartiles			
			Women:			
			Q1	NR	1.00	
			Q2	NR	1.10 (0.36–3.33)	
			Q3	NR	0.90 (0.26–3.09)	
			Q4	NR	1.19 (0.36–3.92)	
			Trend-test *P* value: 0.85			
Faivre et al. (1997) Burgundy, France 1985–1990	Cases: 171; population-based colorectal cases, identified through a registry Controls: 309; population-based; no more information was provided Exposure assessment method: questionnaire; validated, administered in person, included 39 items, and queried frequency and portion sizes; no details were provided for processed meat and delicatessen; pâtés and meat spreads were included	Colon and rectum	Processed meat and delicatessen			Age, sex, caloric intake
			NR	NR	3.0 (2.1–4.8)	
			Trend-test *P* value: <0.001			
Fernandez et al. (1997) Province of Pordenone, Italy 1985–1992	Cases: 112; cases with a family history of colorectal cancer; Controls: 108 controls; controls with a family history of colorectal cancer; Exposure assessment method: questionnaire; data on salami/sausage, raw ham and ham intake	Colon and rectum	Processed meat intake (highest vs lowest tertile, times/wk)			Age, sex, area of residence
			Raw ham	NR	2.1 (0.9–4.9)	
			Trend-test *P* value: < 0.05			
			Ham	NR	2.6 (1.0–6.8)	
			Trend-test *P* value: < 0.05			
			Canned meat	NR	1.9 (1.0–3.3)	
			Trend-test *P* value: <0.05			

Table 2.2.4 Case–control studies on consumption of processed meat and cancer of the colorectum

Reference, location, enrolment	Population size, description, exposure assessment method	Organ site	Exposure category or level	Exposed cases/ deaths	Risk estimate (95% CI)	Covariates controlled
Franceschi et al. (1997) Italy 1992–1996	Cases: 1953; hospital-based colorectal cases, identified at multiple sites Controls: 4154; hospital-based, identified in the same catchment areas of cases; included acute non-neoplastic, non-gynaecological conditions unrelated to hormonal or digestive tract diseases or to long-term modifications of diet Exposure assessment method: questionnaire; validated, administered in person, and included 79 items; processed meat was not defined	Colon and rectum	Processed intake (servings/wk), quintiles			Age, sex, centre, education, physical activity, total energy intake
			Q1	NR	1.00	
			Q2	NR	1.21 (1.03–1.42)	
			Q3	NR	1.06 (0.89–1.26)	
			Q4	NR	1.24 (1.02–1.49)	
			Q5	NR	1.02 (0.84–1.24)	
			Trend-test *P* value: 0.13			
		Colon	Processed meat intake			
			Increase of 1 serving/day	NR	1.08 (0.87–1.36)	
		Rectum	Processed meat intake			
			Increase of 1 serving/day	NR	0.78 (0.57–1.06)	
		Colon and rectum	Processed meat intake			
			Increase of 1 serving/day	NR	0.97 (0.79–1.18)	
Norat et alt al. (1997) Hawaii, USA 1987–1991	Cases: 1192; population-based cases, identified through the Hawaii Tumor Registry; cases included Japanese, Caucasian (White), Filipino, Hawaiian, and Chinese patients Controls: 1192; population-based, identified through the Hawaii State Department of Health and individually matched to each case by sex, ethnicity, and age Exposure assessment method: questionnaire; validated, administered in person, and included 280 items; processed meat was luncheon meat, salami, wieners, sausage, spam, and bacon	Colon and rectum	Processed meat intake, quartiles			Age; family history of colorectal cancer; alcoholic drinks per wk; pack-years; lifetime recreational activity; BMI 5 yr ago; caloric, dietary fibre, calcium intakes
			Men:			
			Q1	NR	1.0	
			Q2	NR	1.7	
			Q3	NR	2.2	
			Q4	NR	2.3 (1.5–3.4)	
			Trend-test *P* value: 0.001			
			Processed meat intake, quartiles			
			Women: Q1	NR	1.0	
			Q2	NR	0.8	
			Q3	NR	1.1	
			Q4	NR	1.2 (0.8–2.0)	
			Trend-test *P* value: 0.2			

Table 2.2.4 Case–control studies on consumption of processed meat and cancer of the colorectum

Reference, location, enrolment	Population size, description, exposure assessment method	Organ site	Exposure category or level	Exposed cases/ deaths	Risk estimate (95% CI)	Covariates controlled
Boutron-Ruault et al. (1999) Burgundy, France 1985–1990	Cases: 171; population-based, identified from GI and surgery departments in conjunction with a registry of digestive cancers Controls: 309; population-based, identified from a census list and frequency-matched to cases by age and sex Exposure assessment method: questionnaire; validated and administered in person; processed meat was "delicatessen"	Colon and rectum	Intake of delicatessen (g/day), quartiles			Age, sex, caloric intake
			Q1	NR	1.0	
			Q2	NR	1.6 (0.9–2.9)	
			Q3	NR	1.2 (0.6–2.2)	
			Q4	NR	2.4 (1.3–4.5)	
			Trend-test *P* value: 0.01			
Kampman et al. (1999) California, Utah, and Minnesota, USA 1991–1994	Cases: 1542; cases identified through the Kaiser Permanente Medical Care Program of Northern California, Utah, and metropolitan twin cities area in Minnesota Controls: 1860; population-based, frequency-matched to cases by sex and age; identified using membership lists of the Kaiser Permanente Medical Care Program, random digit dialling, drivers' licence and identification lists, and Health Care Financing Administration forms Exposure assessment method: questionnaire; exposure definition, validated, in-person interview, and > 800 items; processed meat was bacon, sausages, and cold cuts; assessed cooking methods and mutagen index	Colon	Processed meat (servings/wk) Men:			Age at diagnosis (cases) or selection (controls), BMI, lifetime physical activity, total energy intake, usual number of cigarettes smoked per day, intake of dietary fibre
			≤ 0.5	NR	1.0	
			0.6–1.0	NR	1.1 (0.8–1.6)	
			1.1–1.8	NR	1.2 (0.9–1.8)	
			1.9–3.1	NR	1.3 (1.0–1.8)	
			> 3.1	NR	1.4 (1.0–1.9)	
			Processed meat (servings/wk) Women:			
			≤ 0.2	NR	1.0	
			0.3–0.5	NR	1.3 (1.0–1.9)	
			0.6–0.9	NR	1.2 (0.9–1.7)	
			1.0–1.7	NR	1.3 (0.9–1.8)	
			> 1.7	NR	1.1 (0.8–1.6)	
Navarro et al. (2003) Córdoba, Argentina 1993–1998	Cases: 287 colorectal cancer cases (163 men, 124 women); hospital-based colorectal cases identified at hospitals in Córdoba Controls: 564 (309 men, 255 women); hospital-based control residents identified at the same hospitals for acute non-neoplastic conditions unrelated to digestive tract diseases or long-term modifications Exposure assessment method: questionnaire; validated, administered in person, and evaluated frequency and portion size; processed meats were cold cuts (ham, bologna, salami, cured meat of pork, etc.) and sausages	Colon and rectum	Processed meat ("cold cuts/sausages", g/day)			Sex, age, BMI, social status, energy, total lipids, proteins, carbohydrates, soluble and insoluble fibre intake
			T1	NR	1.00	
			T2 (median intake, 7.39 g/day)	NR	1.07 (0.72–1.59)	
			T3 (median intake, 16.52 g/day)	NR	1.47 (1.02–2.15)	

Table 2.2.4 Case–control studies on consumption of processed meat and cancer of the colorectum

Reference, location, enrolment	Population size, description, exposure assessment method	Organ site	Exposure category or level	Exposed cases/ deaths	Risk estimate (95% CI)	Covariates controlled
Juarranz-Sanz et al. (2004) Madrid, Spain 1997–1998	Cases: 196; population-based colorectal cases, identified through a cancer registry Controls: 196; population-based, identified through a health care roster from the same districts of the identified cases; individually matched to cases by age, sex, and geographical region Exposure assessment method: questionnaire; validated, included 72 items, administered by phone, and asked about frequency and portion size; processed meats were not defined	Colon and rectum	Processed meats (g/day), continuous variables			Olives, red meat, organ meat, cherries/ strawberries, oranges, raw tomatoes, yogurt, fresh juice
			Processed meat	NR	1.070 (1.035–1.107)	
			Trend-test *P* value: 0.001			
Levi et al. (2004) Canton of Vaud, Switzerland 1992– 2002	Cases: 323; hospital-based colorectal cancer cases Controls: 611; hospital-based, identified at same hospitals of cases, with conditions unrelated to smoking or alcohol and long-term modification of diet Exposure assessment method: questionnaire; validated, administered in person, and included 79 items; processed meat was raw ham, boiled ham, salami, and sausages	Colon and rectum	Processed meat intake (servings/wk), quartiles			Education, tobacco smoking, alcohol drinking, total energy intake, fruit and vegetable intake, BMI, physical activity
			< 0.8	36	1.00	
			0.8–1.5	46	1.03 (0.61–1.75)	
			1.6–3.9	111	1.82 (1.12–2.95)	
			> 4.0	130	2.53 (1.50–4.27)	
			Trend-test *P* value: < 0.001			
Murtaugh et al. (2004) California and Utah, USA 1997–2001	Cases: 952; population-based rectal cancer cases, identified through a cancer registry and online pathology reports from the Kaiser Permanente Northern California Cancer Registry Controls: 1205; controls were randomly selected from membership lists, social security lists, drivers' licence lists; frequency-matched to cases by sex and 5-y age groups Exposure assessment method: Questionnaire; validated, administered in person, and included >800 items; processed meat was bacon, sausages, and cold cuts; cooking methods were assessed, and interactions with *NAT2* phenotype and *GSTM1* genotypes were assessed	Rectum	Processed meat (servings/wk), men:			Age, BMI, energy intake, dietary fibre, calcium, lifetime physical activity, usual number of cigarettes smoked
			< 0.6	172	1.00	
			≥ 0.6 to < 1.6	149	0.95 (0.71–1.28)	
			≥ 1.6	235	18 (0.87–1.61)	
			Trend-test *P* value: < 0.05			
			Processed meat (servings/wk), women:			
			< 0.2	87	1.00	
			≥ 0.2 to < 0.9	140	1.21 (0.85–1.72)	
			≥ 0.9	162	1.23 (0.84–1.81)	
			Trend-test *P* value: < 0.05			

Table 2.2.4 Case–control studies on consumption of processed meat and cancer of the colorectum

Reference, location, enrolment	Population size, description, exposure assessment method	Organ site	Exposure category or level	Exposed cases/ deaths	Risk estimate (95% CI)	Covariates controlled
Hu et al. (2007) Canada 1994–1997	Cases: 1723; identified via the National Enhanced Cancer Surveillance System (NECSS), including the provinces of British Columbia, Alberta, Saskatchewan, Manitoba, Nova Scotia, Newfoundland, Ontario, Prince Edward Island Controls: 3097; population-based controls from each province, frequency-matched to cases by age and sex Exposure assessment method: questionnaire; validated FFQ with 70 items, administered by mail; processed meat was hot dogs, lunch meat, smoked meat, bacon, and sausage	Proximal colon	Processed meat intake (servings/wk), quartiles; men			10-yr age group, province, BMI, strenuous activity, total energy intake
			Q1	68	1.0	
			Q2	92	1.4 (0.9–2.0)	
			Q3	121	1.9 (1.3–2.7)	
			Q4	99	1.6 (1.0–2.4)	
			Trend-test *P* value: 0.01			
			Processed meat intake (servings/wk), quartiles; women			
			Q1	70	1.0	
			Q2	108	1.3 (0.9–1.9)	
			Q3	68	1.2 (0.8–1.8)	
			Q4	105	1.5 (1.0–2.3)	
			Trend-test *P* value: 0.06			
		Distal colon	Processed meat intake (servings/wk), quartiles; men:			
			Q1	112	1.0	
			Q2	130	1.4 (0.9–2.0	
			Q3	177	1.9 (1.3–2.7)	
			Q4	159	1.6 (1.0–2.4)	
			Trend-test *P* value: 0.01			
			Processed meat intake (servings/wk), quartiles; women:			
			Q1	80	1.0	
			Q2	126	1.5 (1.0–2.3)	
			Q3	98	1.8 (1.2–2.7)	
			Q4	110	1.5 (1.0–2.2)	
			Trend-test *P* value: 0.08			
		Proximal colon	Bacon intake (highest vs lowest tertile, servings/wk); men:			
			T1	95	1.0	
			T2	190	1.5 (1.1–2.1)	
			T3	56	1.5 (1.0–2.2)	
			Trend-test *P* value: 0.04			

Table 2.2.4 Case–control studies on consumption of processed meat and cancer of the colorectum

Reference, location, enrolment	Population size, description, exposure assessment method	Organ site	Exposure category or level	Exposed cases/ deaths	Risk estimate (95% CI)	Covariates controlled
Hu et al. (2007) Canada 1994–1997 (cont.)		Proximal colon	Bacon intake (highest vs lowest tertile, servings/wk); women:			
			T1	NR	1.0	
			T2	NR	1.3 (1.0–1.8)	
			T3	NR	2.2 (1.4–3.3)	
			Trend-test *P* value: 0.001			
		Distal colon	Bacon intake (highest vs lowest tertile, servings/wk); men:			
			T1	NR	1.0	
			T2	NR	1.3 (1.0–1.6)	
			T3	NR	1.4 (1.0–1.9)	
			Trend-test *P* value: 0.05			
			Bacon intake (highest vs lowest tertile, servings/wk); women:			
			T1	NR	1.0	
			T2	NR	(0.9–1.6)	
			T3	NR	(1.2–2.8)	
			Trend-test *P* value: 0.01			
Kimura et al. (2007) Fukuoka, Japan 2000–2003	Cases: 840; hospital-based, cases admitted to hospitals in Fukuoka and three adjacent areas Controls: 833; population-based controls from 15 different areas, sampled based on frequency of age and sex of cases Exposure assessment method: questionnaire; validated, administered in person, and included 148 items; definition of processed meat was not provided	Colon and rectum	Processed meat quintiles (median, g/day)			Age, sex, residential area, BMI, smoking, alcohol use, type of job, leisure-time physical activity, dietary calcium, dietary fibre
			Q1 (0.4)	152	1.00	
			Q2 (2.5)	149	1.03 (0.74–1.43)	
			Q3 (4.9)	160	1.09 (0.79–1.52)	
			Q4 (8.2)	151	1.07 (0.77–1.49)	
			Q5 (14.9)	170	1.15 (0.83–1.60)	
			Trend-test *P* value: 0.40			
		Proximal colon	Processed meat (g/day), quintiles			
			Q1	40	1.00	
			Q2	27	0.82 (0.47–1.44)	
			Q3	35	1.12 (0.65–1.92)	
			Q4	33	1.04 (0.60–1.80)	
			Q5	42	1.20 (0.72–2.03)	
			Trend-test *P* value: 0.33			

Table 2.2.4 Case–control studies on consumption of processed meat and cancer of the colorectum

Reference, location, enrolment	Population size, description, exposure assessment method	Organ site	Exposure category or level	Exposed cases/ deaths	Risk estimate (95% CI)	Covariates controlled
Kimura et al. (2007) Fukuoka, Japan 2000–2003 (cont.)		Distal colon	Processed meat (g/day), quintiles			
			Q1	48	1.00	
			Q2	49	1.10 (0.68–1.78)	
			Q3	57	1.30 (0.81–2.08)	
			Q4	49	1.15 (0.71–1.86)	
			Q5	59	1.32 (0.82–2.11)	
			Trend-test *P* value: 0.27			
		Rectum	Processed meat (g/day), quintiles			
			Q1	59	1.00	
			Q2	70	1.20 (0.78–1.84)	
			Q3	64	1.08 (0.69–1.67)	
			Q4	68	1.21 (0.78–1.87)	
			Q5	66	1.14 (0.73–1.77)	
			Trend-test *P* value: 0.61			
Squires et al. (2010) Newfoundland and Labrador, Canada 1999–2003	Cases: 518; population-based colorectal cases, identified through a cancer registry Controls: 686; population-based, identified through random digit dialling; frequency-matched to cases by age and sex Exposure assessment method: questionnaire; unclear validation of local foods, administered by mail, and included 169 items. Pickled meat was meats preserved in brine solution (e.g. trimmed navel beef, cured pork riblets); assessed cooking methods	Colon and rectum	Pickled meat (g/day), tertiles, men:			Age; BMI; smoking status; level of education; intake of vegetables, fruits, folic acid, cholesterol, dietary fibre, saturated fat, alcohol; caloric intake; level of physical activity; NSAID use; presence of inflammatory bowel disease
			T1 (< 1)	139	1.00	
			T2 (1–3)	37	1.64 (0.89–3.02)	
			T3 (> 3)	132	2.07 (1.37–3.15)	
			Pickled meat (g/day), tertiles, women:			
			T1 (< 1)	96	1.00	
			T2 (1–3)	24	1.03 (0.49–2.17)	
			T3 (> 3)	90	2.51 (1.45–4.32)	

Table 2.2.4 Case–control studies on consumption of processed meat and cancer of the colorectum

Reference, location, enrolment	Population size, description, exposure assessment method	Organ site	Exposure category or level	Exposed cases/ deaths	Risk estimate (95% CI)	Covariates controlled
Williams et al. (2010) North Carolina, USA 2001–2006	Cases: 945; population-based distal colorectal cancer cases, identified through the North Carolina Central Cancer Registry; African Americans were oversampled Controls: 959; population-based, selected from the North Carolina Department of Motor Vehicles or Centers for Medicare and Medicaid Services Exposure assessment method: questionnaire; validated, administered in person, and included portion size and frequency; processed meat was sausage, bacon, hot dogs, and all cold cuts (i.e. luncheon meats made from beef, veal, ham, pork, chicken, and turkey)	Distal colon and rectum	Processed meat (quartile median, g/day) in Caucasians			Age, sex, education, BMI, family history, NSAID use, physical activity, calcium, fibre, total energy
			Q1 (3.4)	131	1.00	
			Q2 (9.6)	178	1.15 (0.82–1.62)	
			Q3 (19.1)	208	1.43 (1.02–2.02)	
			Q4 (37.7)	203	1.16 (0.80–1.68)	
			Trend-test *P* value: 0.57			
			Processed meat (quartile median, g/day) in African Americans			
			Q1 (12.2)	44	1.00	
			Q2 (12.2)	85	1.47 (0.76–2.85)	
			Q3 (24.9)	42	0.54 (0.24–1.18)	
			Q4 (42.7)	54	0.86 (0.38–1.96)	
			Trend-test *P* value: 0.94			
De Stefani et al. (2012a) Montevideo, Uruguay 1996–2004	Cases: 361; hospital-based colorectal cases; patients with low socioeconomic status Controls: 2532; Hospital-based from the same hospitals as cases, with conditions unrelated to smoking and drinking Exposure assessment method: questionnaire; not validated, included 64 items, and administered in person; processed meat was bacon, sausage, mortadella, salami, saucisson, hot dog, ham, and air-dried and salted lamb	Colon	Processed meat (g/day), tertiles, men:			Age; residence; BMI; smoking status; smoking cessation; number of cigarettes smoked per day among current smokers; alcohol drinking; mate consumption; total energy, total vegetables and fruits, total white meat, red meat intakes
			≤ 11.4	NR	1.00	
			11.5–28.2	NR	1.76 (0.94–3.28)	
			≥ 28.3	NR	2.01 (1.07–3.76)	
			Trend-test *P* value: 0.03			
			Processed meat (g/day), tertiles, women:			
			≤ 11.4	NR	1.00	
			11.5–28.2	NR	2.25 (1.19–4.23)	
			≥ 28.3	NR	3.53 (1.93–6.46)	
			Trend-test *P* value: <0.0001			
		Rectum	Processed meat (g/day), tertiles, men:			
			≤ 11.4	NR	1.00	
			11.5–28.2	NR	1.47 (0.85–2.54)	
			≥28.3	NR	1.76 (1.03–3.01)	
			Trend-test *P* value: 0.03			
			Processed meat (g/day), tertiles, women:			
			≤ 11.4	NR	1.00	
			11.5–28.2	NR	2.44 (1.17–5.09)	
			≥ 28.3	NR	3.18 (1.54–6.57)	
			Trend-test *P* value: 0.001			

Table 2.2.4 Case–control studies on consumption of processed meat and cancer of the colorectum

Reference, location, enrolment	Population size, description, exposure assessment method	Organ site	Exposure category or level	Exposed cases/ deaths	Risk estimate (95% CI)	Covariates controlled
Miller et al. (2013) Pennsylvania, USA 2007–2011	Cases: 989; incident cases, identified through the Pennsylvania State Cancer Registry Controls: 1033; identified through random digit dialling; frequency-matched to cases by age, sex, and ethnicity Exposure assessment method: questionnaire; validated, in-person FFQ with 137 items; meat-cooking module was used with the CHARRED database to estimate carcinogens; processed red meat was bacon, sausage, cold cuts, beef jerky, corned beef, hot dogs, ham, and processed meats added to mixed dishes [There were no data for processed meat including processed poultry.]	Colon and rectum	Processed red meat intake (g/1000 kcal)			Age, sex, BMI, past NSAID use, total energy, total fruits and vegetables, total poultry
			Q1 (< 2.8)	170	1.00	
			Q2 (2.8–5.5)	181	0.99 (0.73–1.34)	
			Q3 (5.6–9.4)	195	1.09 (0.81–1.49)	
			Q4 (9.5–17.6)	218	1.18 (0.87–1.61)	
			Q5 (> 17.6)	225	1.18 (0.87–1.62)	
			Trend-test *P* value: 0.223			
		Colon	Processed red meat intake (g/1000 kcal)			
			Q1 (< 2.8)	125	1.00	
			Q2 (2.8–5.5)	120	0.91 (0.65–1.28)	
			Q3 (5.6–9.4)	142	1.13 (0.81–1.57)	
			Q4 (9.5–17.6)	149	1.15 (0.82–1.61)	
			Q5 (> 17.6)	157	1.21 (0.86–1.70)	
			Trend-test *P* value: 0.157			
		Rectum	Processed red meat intake (g/1000 kcal)			
			Q1 (< 2.8)	42	1.00	
			Q2 (2.8–5.5)	59	1.28 (0.81–2.01)	
			Q3 (5.6–9.4)	53	1.12 (0.70–1.79)	
			Q4 (9.5–17.6)	68	1.35 (0.86–2.13)	
			Q5 (> 17.6)	67	1.22 (0.77–1.95)	
			Trend-test *P* value: 0.613			
		Proximal colon	Total nitrites plus nitrates (µg/1000 kcal)			
			Q1 (< 114.6)	77	1.00	
			Q2 (114.6–197.0)	75	1.05 (0.71–1.56)	
			Q3 (197.1–310.2)	86	1.25 (0.85–1.86)	
			Q4 (310.3–496.6)	76	1.06 (0.71–1.58)	
			Q5 (> 496.6)	102	1.57 (1.06–2.34)	
			Trend-test *P* value: 0.023			

Table 2.2.4 Case–control studies on consumption of processed meat and cancer of the colorectum

Reference, location, enrolment	Population size, description, exposure assessment method	Organ site	Exposure category or level	Exposed cases/ deaths	Risk estimate (95% CI)	Covariates controlled
Rosato et al. (2013) Italy and Switzerland 1985–2009	Cases: 329; hospital-based cases with young-onset colorectal cancer (< 45 yr) Controls: 1361; hospital-based, identified from the same hospitals as cases; conditions unrelated to colorectal cancer risk factors or dietary modifications Exposure assessment method: questionnaire; validated and administered in person; processed meat was not defined	Colon and rectum: young-onset colorectal cancer	Processed meat			Age, sex, centre, study, year of interview, education, family history, alcohol, energy intake
			Low	69	1.00	
			Medium	115	1.18 (0.84–1.65)	
			High	145	1.56 (1.11–2.20)	
			Trend-test *P* value: 0.008			
Joshi et al. (2015) USA and Canada 1997–2002	Cases: 3350; population-based, identified through cancer registries in Ontario, Canada; Hawaii, California, Arizona, North Carolina, New Hampshire, Colorado, Minnesota, USA; cases with familial cases included Controls: 3504; cancer-free siblings of the cases (*n* = 1759), unaffected spouses of the cases (*n* = 138), and population-based controls (*n* = 1607) Exposure assessment method: questionnaire; validated, administered by mail, included 200 items, included portion size and frequency of intake, and used the CHARRED database to estimate carcinogens; considered cooking methods Processed meat was reported as total processed meat (including processed red meat and poultry)	Colon and rectum	Processed meat (g/1000 kcal per day)			Age, BMI, sex, ethnicity, saturated fat, dietary fibre, centre, vegetables, physical activity, total caloric intake
			Q1 (0–4.43)	593	1.0	
			Q2 (4.43–7.35)	643	1.1 (0.9–1.2)	
			Q3 (7.36–10.62)	640	1.0 (0.9–1.2)	
			Q4 (10.63–15.29)	654	1.0 (0.8–1.2)	
			Q5 (15.29–152.04)	820	1.2 (1.0–1.4)	
			Trend-test *P* value: 0.054			
			Sausages and lunchmeats (g/1000 kcal per day)			
			Q1 (0–0.08)	582	1.0	
			Q2 (0.08–0.14)	657	1.1 (0.9–1.3)	
			Q3 (0.14–0.22)	706	1.2 (1.0–1.4)	
			Q4 (0.22–0.32)	654	1.0 (0.9–1.2)	
			Q5 (0.32–3.86)	751	1.2 (1.0–1.4)	
			Trend-test *P* value: 0.187			
			Sausages and lunchmeats (g/1000 kcal per day); MMR-proficient			
			Q1 (0–0.08)	138	1.0	
			Q2 (0.08–0.14)	148	1.0 (0.7–1.3)	
			Q3 (0.14–0.22)	194	1.2 (1.0–1.6)	
			Q4 (0.22–0.32)	179	1.1 (0.8–1.4)	
			Q5 (0.32–3.86)	217	1.3 (1.0–1.7)	
			Trend-test *P* value: 0.029			

Table 2.2.4 Case–control studies on consumption of processed meat and cancer of the colorectum

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. (2015) USA and Canada 1997–2002 (cont.)		Colon and rectum	Sausages and lunchmeats (g/1000 kcal per day); MMR-deficient			
			Q1 (0–0.08)	44	1.0	
			Q2 (0.08–0.14)	58	1.3 (0.8–1.9)	
			Q3 (0.14–0.22)	56	1.2 (0.8–1.9)	
			Q4 (0.22–0.32)	40	0.9 (0.6–1.4)	
			Q5 (0.32–3.86)	45	1.0 (0.6–1.6)	
			Trend-test *P* value: 0.408			
			Test of heterogeneity, MMR-proficient vs MMR-deficient (*P* = 0.069)			
			Pan-fried sausage (g/1000 kcal per day)			
			Q1 (0–0)	1271	1.0	
			Q2 (0.01–0.02)	643	1.1 (1.0–1.3)	
			Q3 (0.020–0.04)	619	1.1 (0.9–1.2)	
			Q4 (0.04–1.32)	781	1.2 (1.0–1.3)	
			Trend-test *P* value: 0.041			
		Colon	Pan-fried sausage (g/1000 kcal per day)			
			Q1 (0–0)	789	1.0	
			Q2 (0.01–0.02)	371	1.1 (0.9–1.3)	
			Q3 (0.20–0.04)	356	1.0 (0.8–1.2)	
			Q4 (0.04–1.32)	456	1.1 (0.9–1.3)	
			Trend-test *P* value: 0.371			
		Rectum	Pan-fried sausage (g/1000 kcal per day)			
			Q1 (0–0)	302	1.0	
			Q2 (0.01–0.02)	204	1.3 (1.1–1.6)	
			Q3 (0.20–0.04)	177	1.2 (1.0–1.5)	
			Q4 (0.04–1.32)	213	1.4 (1.1–1.7)	
			Trend-test *P* value: 0.004			
			Test of heterogeneity, colon vs rectum (*P* = 0.053)			

Table 2.2.4 Case–control studies on consumption of processed meat and cancer of the colorectum

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. (2015) USA and Canada 1997–2002 (cont.)		Colon and rectum	Pan-fried spam or ham (g/1000 kcal per day)			
			Q1 (0–0)	2097	1.0	
			Q2 (0.01–0.02)	395	1.0 (0.9–1.2)	
			Q3 (0.20–0.04)	403	1.1 (0.9–1.3)	
			Q4 (0.04–0.99)	425	1.2 (1.0–1.4)	
			Trend-test *P* value: 0.048			
			Pan-fried spam or ham (g/1000 kcal per day); MMR-proficient			
			Q1 (0–0)	524	1.0	
			Q2 (0.01–0.02)	106	1.3 (1.0–1.7)	
			Q3 (0.20–0.04)	110	1.4 (1.1–1.8)	
			Q4 (0.04–0.99)	128	1.6 (1.2–2.0)	
			Trend-test *P* value: <0.001			
			Pan-fried spam or ham (g/1000 kcal per day); MMR-deficient			
			Q1 (0–0)	173	1.0	
			Q2 (0.01–0.02)	18	0.6 (0.4–1.0)	
			Q3 (0.20–0.04)	30	1.1 (0.7–1.6)	
			Q4 (0.04–0.99)	19	0.8 (0.5–1.3)	
			Trend-test *P* value: 0.461			
			Test of heterogeneity, MMR-proficient vs MMR-deficient (*P* = 0.026)			

Table 2.2.4 Case–control studies on consumption of processed meat and cancer of the colorectum

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. (2015) USA and Canada 1997–2002 (cont.)		Colon and rectum	Pan-fried bacon (g/1000 kcal per day)			
			Q1 (0–0)	1094	1.0	
			Q2 (0.01–0.03)	664	1.0 (0.8–1.1)	
			Q3 (0.03–0.05)	720	1.0 (0.9–1.2)	
			Q4 (0.05–1.43)	841	1.0 (0.9–1.2)	
			Trend-test *P* value: 0.61			
			Grilled sausage (g/1000 kcal per day)			
			Q1 (0–0)	2222	1.0	
			Q2 (0.01–0.02)	410	1.1 (0.9–1.3)	
			Q3 (0.02–0.03)	327	0.9 (0.8–1.1)	
			Q4 (0.03–0.99)	357	1.0 (0.9–1.2)	
			Trend-test *P* value: 0.903			

BaP, benzo[*a*]pyrene; BMI, body mass index; CHARRED, Computerized Heterocyclic Amines Resource for Research in Epidemiology of Disease; CI, confidence interval; FFQ, food frequency questionnaire; GI, gastrointestinal; h, hour; HAA, heterocyclic aromatic amine; ICD, International Classification of Diseases; MMR, mismatch repair; mo, month; NR, not reported; NSAID, nonsteroidal anti-inflammatory drug; OR, odds ratio; wk, week; yr, year

References

Abu Mweis SS, Tayyem RF, Shehadah I, Bawadi HA, Agraib LM, Bani-Hani KE et al. (2015). Food groups and the risk of colorectal cancer: results from a Jordanian case-control study. *Eur J Cancer Prev*, 24(4):313–20. doi:10.1097/CEJ.0000000000000089 PMID:25415835

Alexander DD, Miller AJ, Cushing CA, Lowe KA (2010). Processed meat and colorectal cancer: a quantitative review of prospective epidemiologic studies. *Eur J Cancer Prev*, 19(5):328–41. doi:10.1097/CEJ.0b013e32833b48fa PMID:20495462

Alexander DD, Weed DL, Miller PE, Mohamed MA (2015). Red meat and colorectal cancer: a quantitative update on the state of the epidemiologic science. *J Am Coll Nutr*, 34(6):521–43. doi:10.1080/07315724.2014.992553 PMID:25941850

Ananthakrishnan AN, Du M, Berndt SI, Brenner H, Caan BJ, Casey G et al. (2015). Red meat intake, NAT2, and risk of colorectal cancer: a pooled analysis of 11 studies. *Cancer Epidemiol Biomarkers Prev*, 24(1):198–205. doi:10.1158/1055-9965.EPI-14-0897 PMID:25342387

Andersen V, Holst R, Vogel U (2013). Systematic review: diet-gene interactions and the risk of colorectal cancer. *Aliment Pharmacol Ther*, 37(4):383–91. doi:10.1111/apt.12180 PMID:23216531

Andersen V, Ostergaard M, Christensen J, Overvad K, Tjønneland A, Vogel U (2009). Polymorphisms in the xenobiotic transporter Multidrug Resistance 1 (MDR1) and interaction with meat intake in relation to risk of colorectal cancer in a Danish prospective case-cohort study. *BMC Cancer*, 9(1):407. doi:10.1186/1471-2407-9-407 PMID:19930591

Angstadt AY, Berg A, Zhu J, Miller P, Hartman TJ, Lesko SM et al. (2013). The effect of copy number variation in the phase II detoxification genes UGT2B17 and UGT2B28 on colorectal cancer risk. *Cancer*, 119(13):2477–85. doi:10.1002/cncr.28009 PMID:23575887

Arafa MA, Waly MI, Jriesat S, Al Khafajei A, Sallam S (2011). Dietary and lifestyle characteristics of colorectal cancer in Jordan: a case-control study. *Asian Pac J Cancer Prev*, 12(8):1931–6. PMID:22292627

Balder HF, Vogel J, Jansen MC, Weijenberg MP, van den Brandt PA, Westenbrink S et al. (2006). Heme and chlorophyll intake and risk of colorectal cancer in the Netherlands cohort study. *Cancer Epidemiol Biomarkers Prev*, 15(4):717–25. doi:10.1158/1055-9965.EPI-05-0772 PMID:16614114

Barrett JH, Smith G, Waxman R, Gooderham N, Lightfoot T, Garner RC et al. ; Colorectal Cancer Study Group(2003). Investigation of interaction between N-acetyltransferase 2 and heterocyclic amines as potential risk factors for colorectal cancer. *Carcinogenesis*, 24(2):275–82. doi:10.1093/carcin/24.2.275 PMID:12584178

Benito E, Obrador A, Stiggelbout A, Bosch FX, Mulet M, Muñoz N et al. (1990). A population-based case-control study of colorectal cancer in Majorca. I. Dietary factors. *Int J Cancer*, 45(1):69–76. doi:10.1002/ijc.2910450114 PMID:2298506

Berndt SI, Platz EA, Fallin MD, Thuita LW, Hoffman SC, Helzlsouer KJ (2006). Genetic variation in the nucleotide excision repair pathway and colorectal cancer risk. *Cancer Epidemiol Biomarkers Prev*, 15(11):2263–9. doi:10.1158/1055-9965.EPI-06-0449 PMID:17119055

Bernstein AM, Song M, Zhang X, Pan A, Wang M, Fuchs CS et al. (2015). Processed and unprocessed red meat and risk of colorectal cancer: analysis by tumor location and modification by time. *PLoS One*, 10(8):e0135959. doi:10.1371/journal.pone.0135959 PMID:26305323

Bidoli E, Franceschi S, Talamini R, Barra S, La Vecchia C (1992). Food consumption and cancer of the colon and rectum in north-eastern Italy. *Int J Cancer*, 50(2):223–9. doi:10.1002/ijc.2910500211 PMID:1730516

Bostick RM, Potter JD, Kushi LH, Sellers TA, Steinmetz KA, McKenzie DR et al. (1994). Sugar, meat, and fat intake, and non-dietary risk factors for colon cancer incidence in Iowa women (United States). *Cancer Causes Control*, 5(1):38–52. doi:10.1007/BF01830725 PMID:8123778

Boutron-Ruault MC, Senesse P, Faivre J, Chatelain N, Belghiti C, Méance S (1999). Foods as risk factors for colorectal cancer: a case-control study in Burgundy (France). *Eur J Cancer Prev*, 8(3):229–35. doi:10.1097/00008469-199906000-00011 PMID:10443952

Brevik A, Joshi AD, Corral R, Onland-Moret NC, Siegmund KD, Le Marchand L et al. (2010). Polymorphisms in base excision repair genes as colorectal cancer risk factors and modifiers of the effect of diets high in red meat. *Cancer Epidemiol Biomarkers Prev*, 19(12):3167–73. doi:10.1158/1055-9965.EPI-10-0606 PMID:21037106

Brink M, Weijenberg MP, de Goeij AF, Roemen GM, Lentjes MH, de Bruïne AP et al. (2005). Meat consumption and K-ras mutations in sporadic colon and rectal cancer in The Netherlands Cohort Study. *Br J Cancer*, 92(7):1310–20. doi:10.1038/sj.bjc.6602491 PMID:15812479

Butler LM, Duguay Y, Millikan RC, Sinha R, Gagné J-F, Sandler RS et al. (2005). Joint effects between UDP-glucuronosyltransferase 1A7 genotype and dietary carcinogen exposure on risk of colon cancer. *Cancer Epidemiol Biomarkers Prev*, 14(7):1626–32. doi:10.1158/1055-9965.EPI-04-0682 PMID:16030093

Butler LM, Millikan RC, Sinha R, Keku TO, Winkel S, Harlan B et al. (2008a). Modification by N-acetyltransferase 1 genotype on the association between dietary heterocyclic amines and colon cancer in a multiethnic study. *Mutat Res*, 638(1-2):162–74. doi:10.1016/j.mrfmmm.2007.10.002 PMID:18022202

Butler LM, Wang R, Koh WP, Yu MC (2008b). Prospective study of dietary patterns and colorectal cancer among Singapore Chinese. *Br J Cancer*, 99(9):1511–6. doi:10.1038/sj.bjc.6604678 PMID:18813309

Butler LM, Sinha R, Millikan RC, Martin CF, Newman B, Gammon MD et al. (2003). Heterocyclic amines, meat intake, and association with colon cancer in a population-based study. *Am J Epidemiol*, 157(5):434–45. doi:10.1093/aje/kwf221 PMID:12615608

Carr PR, Walter V, Brenner H, Hoffmeister M (2016). Meat subtypes and their association with colorectal cancer: Systematic review and meta-analysis. *Int J Cancer*, 138(2):293–302. doi:10.1002/ijc.29423 PMID:25583132

Centonze S, Boeing H, Leoci C, Guerra V, Misciagna G (1994). Dietary habits and colorectal cancer in a low-risk area. Results from a population-based case-control study in southern Italy. *Nutr Cancer*, 21(3):233–46. doi:10.1080/01635589409514322 PMID:8072877

Chan AT, Tranah GJ, Giovannucci EL, Willett WC, Hunter DJ, Fuchs CS (2005). Prospective study of N-acetyltransferase-2 genotypes, meat intake, smoking and risk of colorectal cancer. *Int J Cancer*, 115(4):648–52. doi:10.1002/ijc.20890 PMID:15700302

Chan DS, Lau R, Aune D, Vieira R, Greenwood DC, Kampman E et al. (2011). Red and processed meat and colorectal cancer incidence: meta-analysis of prospective studies. *PLoS One*, 6(6):e20456. doi:10.1371/journal.pone.0020456 PMID:21674008

Chao A, Thun MJ, Connell CJ, McCullough ML, Jacobs EJ, Flanders WD et al. (2005). Meat consumption and risk of colorectal cancer. *JAMA*, 293(2):172–82. doi:10.1001/jama.293.2.172 PMID:15644544

Chen J, Stampfer MJ, Hough HL, Garcia-Closas M, Willett WC, Hennekens CH et al. (1998). A prospective study of N-acetyltransferase genotype, red meat intake, and risk of colorectal cancer. *Cancer Res*, 58(15):3307–11. PMID:9699660

Chen K, Fan CH, Jin MJ, Song L, Xu H, He HQ et al. (2006). [A case-control study on the association between the genetic polymorphism of sulfotransferase 1A1, diet and susceptibility of colorectal cancer] *Zhonghua Zhong Liu Za Zhi*, 28(9):670–3. PMID:17274372

Chen Z, Wang PP, Woodrow J, Zhu Y, Roebothan B, Mclaughlin JR et al. (2015). Dietary patterns and colorectal cancer: results from a Canadian population-based study. *Nutr J*, 14(1):8. doi:10.1186/1475-2891-14-8 PMID:25592002

Chiu BC, Ji BT, Dai Q, Gridley G, McLaughlin JK, Gao YT et al. (2003). Dietary factors and risk of colon cancer in Shanghai, China. *Cancer Epidemiol Biomarkers Prev*, 12(3):201–8. PMID:12646508

Cotterchio M, Boucher BA, Manno M, Gallinger S, Okey AB, Harper PA (2008). Red meat intake, doneness, polymorphisms in genes that encode carcinogen-metabolizing enzymes, and colorectal cancer risk. *Cancer Epidemiol Biomarkers Prev*, 17(11):3098–107. doi:10.1158/1055-9965.EPI-08-0341 PMID:18990750

Cross AJ, Ferrucci LM, Risch A, Graubard BI, Ward MH, Park Y et al. (2010). A large prospective study of meat consumption and colorectal cancer risk: an investigation of potential mechanisms underlying this association. *Cancer Res*, 70(6):2406–14. doi:10.1158/0008-5472.CAN-09-3929 PMID:20215514

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):e325. doi:10.1371/journal.pmed.0040325 PMID:18076279

da Silva TD, Felipe AV, de Lima JM, Oshima CT, Forones NM (2011). N-Acetyltransferase 2 genetic polymorphisms and risk of colorectal cancer. *World J Gastroenterol*, 17(6):760–5. doi:10.3748/wjg.v17.i6.760 PMID:21390146

Dales LG, Friedman GD, Ury HK, Grossman S, Williams SR (1979). A case-control study of relationships of diet and other traits to colorectal cancer in American blacks. *Am J Epidemiol*, 109(2):132–44. doi:10.1093/oxfordjournals.aje.a112668 PMID:425952

De Stefani E, Boffetta P, Ronco AL, Deneo-Pellegrini H, Correa P, Acosta G et al. (2012a). Processed meat consumption and risk of cancer: a multisite case-control study in Uruguay. *Br J Cancer*, 107(9):1584–8. doi:10.1038/bjc.2012.433 PMID:23011480

De Stefani E, Ronco AL, Boffetta P, Deneo-Pellegrini H, Correa P, Acosta G et al. (2012b). Nutrient-derived dietary patterns and risk of colorectal cancer: a factor analysis in Uruguay. *Asian Pac J Cancer Prev*, 13(1):231–5. doi:10.7314/APJCP.2012.13.1.231 PMID:22502675

Destefani E, Deneopellegrini H, Mendilaharsu M, Ronco A (1997). Meat intake, heterocyclic amines and risk of colorectal cancer. *Int J Oncol*, 10(3):573–80. PMID:21533415

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

Egeberg R, Olsen A, Christensen J, Halkjær J, Jakobsen MU, Overvad K et al. (2013). Associations between red meat and risks for colon and rectal cancer depend on the type of red meat consumed. *J Nutr*, 143(4):464–72. doi:10.3945/jn.112.168799 PMID:23427329

English DR, MacInnis RJ, Hodge AM, Hopper JL, Haydon AM, Giles GG (2004). Red meat, chicken, and fish consumption and risk of colorectal cancer. *Cancer Epidemiol Biomarkers Prev*, 13(9):1509–14. PMID:15342453

Evans RC, Fear S, Ashby D, Hackett A, Williams E, Van Der Vliet M et al. (2002). Diet and colorectal cancer: an investigation of the lectin/galactose hypothesis. *Gastroenterology*, 122(7):1784–92. doi:10.1053/gast.2002.33659 PMID:12055585

Faivre J, Boutron MC, Senesse P, Couillault C, Belighiti C, Meny B (1997). Environmental and familial risk factors in relation to the colorectal adenoma–carcinoma sequence: results of a case-control study in Burgundy (France). *Eur J Cancer Prev*, 6(2):127–31. PMID:9237060

Fernandez E, D'Avanzo B, Negri E, Franceschi S, La Vecchia C (1996). Diet diversity and the risk of colorectal cancer in northern Italy. *Cancer Epidemiol Biomarkers Prev*, 5(6):433–6. PMID:8781738

Fernandez E, La Vecchia C, D'Avanzo B, Negri E, Franceschi S (1997). Risk factors for colorectal cancer in subjects with family history of the disease. *Br J Cancer*, 75(9):1381–4. doi:10.1038/bjc.1997.234 PMID:9155063

Figueiredo JC, Hsu L, Hutter CM, Lin Y, Campbell PT, Baron JA et al.; CCFR; GECCO (2014). Genome-wide diet-gene interaction analyses for risk of colorectal cancer. *PLoS Genet*, 10(4):e1004228. doi:10.1371/journal.pgen.1004228 PMID:24743840

Flood A, Velie EM, Sinha R, Chaterjee N, Lacey JV Jr, Schairer C et al. (2003). Meat, fat, and their subtypes as risk factors for colorectal cancer in a prospective cohort of women. *Am J Epidemiol*, 158(1):59–68. doi:10.1093/aje/kwg099 PMID:12835287

Forones NM, de Lima JM, de Souza LG, da Silva ID (2008). Cyclin D1 A870G polymorphism in Brazilian colorectal cancer patients. *J Gastrointest Cancer*, 39(1-4):118–23. doi:10.1007/s12029-009-9057-z PMID:19373442

Franceschi S, Favero A, La Vecchia C, Negri E, Conti E, Montella M et al. (1997). Food groups and risk of colorectal cancer in Italy. *Int J Cancer*, 72(1):56–61. doi:10.1002/(SICI)1097-0215(19970703)72:1<56::AID-IJC8>3.0.CO;2-3 PMID:9212223

Freedman AN, Michalek AM, Marshall JR, Mettlin CJ, Petrelli NJ, Black JD et al. (1996). Familial and nutritional risk factors for p53 overexpression in colorectal cancer. *Cancer Epidemiol Biomarkers Prev*, 5(4):285–91. PMID:8722220

Fung TT, Hu FB, Wu K, Chiuve SE, Fuchs CS, Giovannucci E (2010). The Mediterranean and Dietary Approaches to Stop Hypertension (DASH) diets and colorectal cancer. *Am J Clin Nutr*, 92(6):1429–35. doi:10.3945/ajcn.2010.29242 PMID:21097651

Gaard M, Tretli S, Løken EB (1996). Dietary factors and risk of colon cancer: a prospective study of 50,535 young Norwegian men and women. *Eur J Cancer Prev*, 5(6):445–54. PMID:9061275

Ganesh B, Talole SD, Dikshit R (2009). A case-control study on diet and colorectal cancer from Mumbai, India. *Cancer Epidemiol*, 33(3-4):189–93. doi:10.1016/j.canep.2009.07.009 PMID:19717354

Gay LJ, Mitrou PN, Keen J, Bowman R, Naguib A, Cooke J et al. (2012). Dietary, lifestyle and clinicopathological factors associated with APC mutations and promoter methylation in colorectal cancers from the EPIC-Norfolk study. *J Pathol*, 228(3):405–15. doi:10.1002/path.4085 PMID:22864938

Gerhardsson de Verdier M, Hagman U, Peters RK, Steineck G, Overvik E (1991). Meat, cooking methods and colorectal cancer: a case-referent study in Stockholm. *Int J Cancer*, 49(4):520–5. doi:10.1002/ijc.2910490408 PMID:1917152

Gerhardsson de Verdier M, Hagman U, Steineck G, Rieger A, Norell SE (1990). Diet, body mass and colorectal cancer: a case-referent study in Stockholm. *Int J Cancer*, 46(5):832–8. doi:10.1002/ijc.2910460514 PMID:2172171

Ghadirian P, Lacroix A, Maisonneuve P, Perret C, Potvin C, Gravel D et al. (1997). Nutritional factors and colon carcinoma: a case-control study involving French Canadians in Montréal, Quebec, Canada. *Cancer*, 80(5):858–64. doi:10.1002/(SICI)1097-0142(19970901)80:5<858::AID-CNCR5>3.0.CO;2-H PMID:9307184

Gialamas SP, Petridou ET, Tseleni-Balafouta S, Spyridopoulos TN, Matsoukis IL, Kondi-Pafiti A et al. (2011). Serum adiponectin levels and tissue expression of adiponectin receptors are associated with risk, stage, and grade of colorectal cancer. *Metabolism*, 60(11):1530–8. doi:10.1016/j.metabol.2011.03.020 PMID:21632074

Gilsing AM, Schouten LJ, Goldbohm RA, Dagnelie PC, van den Brandt PA, Weijenberg MP (2015). Vegetarianism, low meat consumption and the risk of colorectal cancer in a population based cohort study. *Sci Rep*, 5(1):13484. doi:10.1038/srep13484 PMID:26316135

Giovannucci E, Rimm EB, Stampfer MJ, Colditz GA, Ascherio A, Willett WC (1994). Intake of fat, meat, and fiber in relation to risk of colon cancer in men. *Cancer Res*, 54(9):2390–7. PMID:8162586

Goldbohm RA, van den Brandt PA, van 't Veer P, Brants HA, Dorant E, Sturmans F et al. (1994). A prospective cohort study on the relation between meat consumption and the risk of colon cancer. *Cancer Res*, 54(3):718–23. PMID:8306333

Guesmi F, Zoghlami A, Sghaiier D, Nouira R, Dziri C (2010). [Alimentary factors predisposing to colorectal cancer risk: a prospective epidemiologic study] *Tunis Med*, 88(3):184–9. PMID:20415192

Guo X, Liu J, You L, Li G, Huang Y, Li Y (2015). Association between adiponectin polymorphisms and the risk of colorectal cancer. *Genet Test Mol Biomarkers*, 19(1):9–13. doi:10.1089/gtmb.2014.0238 PMID:25489716

Hansen RD, Sørensen M, Tjønneland A, Overvad K, Wallin H, Raaschou-Nielsen O et al. (2007). XPA A23G, XPC Lys939Gln, XPD Lys751Gln and XPD Asp312Asn polymorphisms, interactions with smoking, alcohol and dietary factors, and risk of colorectal cancer. *Mutat Res*, 619(1-2):68–80. doi:10.1016/j.mrfmmm.2007.02.002 PMID:17363013

Helmus DS, Thompson CL, Zelenskiy S, Tucker TC, Li L (2013). Red meat-derived heterocyclic amines increase risk of colon cancer: a population-based case-control study. *Nutr Cancer*, 65(8):1141–50. doi:10.1080/01635581.2013.834945 PMID:24168237

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

Hu J, Morrison H, Mery L, DesMeules M, Macleod M, Group CCRER; Canadian Cancer Registries Epidemiology Research Group (2007). Diet and vitamin or mineral supplementation and risk of colon cancer by subsite in Canada. *Eur J Cancer Prev*, 16(4):275–91. doi:10.1097/01.cej.0000228411.21719.25 PMID:17554200

Hu JF, Liu YY, Yu YK, Zhao TZ, Liu SD, Wang QQ (1991). Diet and cancer of the colon and rectum: a case-control study in China. *Int J Epidemiol*, 20(2):362–7. doi:10.1093/ije/20.2.362 PMID:1917235

Hu X, Feng F, Li X, Yuan P, Luan R, Yan J et al. (2015). Gene polymorphisms related to insulin resistance and gene-environment interaction in colorectal cancer risk. *Ann Hum Biol*, 42(6):560–8. PMID:26203767

Hu X, Yuan P, Yan J, Feng F, Li X, Liu W et al. (2013). Gene polymorphisms of ADIPOQ +45T>G, UCP2 -866G>A, and FABP2 Ala54Thr on the risk of colorectal cancer: a matched case-control study. *PLoS One*, 8(6):e67275. doi:10.1371/journal.pone.0067275 PMID:23826253

Hu XQ, Yuan P, Luan RS, Li XL, Liu WH, Feng F et al. (2014). Calpain-10 SNP43 and SNP19 polymorphisms and colorectal cancer: a matched case-control study. *Asian Pac J Cancer Prev*, 14(11):6673–80. doi:10.7314/APJCP.2013.14.11.6673 PMID:24377587

Hutter CM, Chang-Claude J, Slattery ML, Pflugeisen BM, Lin Y, Duggan D et al. (2012). Characterization of gene-environment interactions for colorectal cancer susceptibility loci. *Cancer Res*, 72(8):2036–44. doi:10.1158/0008-5472.CAN-11-4067 PMID:22367214

Huxley RR, Ansary-Moghaddam A, Clifton P, Czernichow S, Parr CL, Woodward M (2009). The impact of dietary and lifestyle risk factors on risk of colorectal cancer: a quantitative overview of the epidemiological evidence. *Int J Cancer*, 125(1):171–80. doi:10.1002/ijc.24343 PMID:19350627

Iscovich JM, L'Abbé KA, Castelleto R, Calzona A, Bernedo A, Chopita NA et al. (1992). Colon cancer in Argentina. I: Risk from intake of dietary items. *Int J Cancer*, 51(6):851–7. doi:10.1002/ijc.2910510603 PMID:1639534

Järvinen R, Knekt P, Hakulinen T, Rissanen H, Heliövaara M (2001). Dietary fat, cholesterol and colorectal cancer in a prospective study. *Br J Cancer*, 85(3):357–61. doi:10.1054/bjoc.2001.1906 PMID:11487265

Jedrychowski W, Maugeri U, Pac A, Sochacka-Tatara E, Galas A (2008). Protective effect of fish consumption on colorectal cancer risk. Hospital-based case-control study in Eastern Europe. *Ann Nutr Metab*, 53(3-4):295–302. doi:10.1159/000195770 PMID:19169007

Joshi AD, Corral R, Siegmund KD, Haile RW, Le Marchand L, Martínez ME et al. (2009). Red meat and poultry intake, polymorphisms in the nucleotide excision repair and mismatch repair pathways and colorectal cancer risk. *Carcinogenesis*, 30(3):472–9. doi:10.1093/carcin/bgn260 PMID:19029193

Joshi AD, Kim A, Lewinger JP, Ulrich CM, Potter JD, Cotterchio M et al. (2015). Meat intake, cooking methods, dietary carcinogens, and colorectal cancer risk: findings from the Colorectal Cancer Family Registry. *Cancer Med*, 4(6):936–52. doi:10.1002/cam4.461 PMID:25846122

Juarranz Sanz M, Soriano Llora T, Calle Purón ME, Martínez Hernández D, González Navarro A, Domínguez Rojas V (2004). Influencia de la dieta en la aparición del cáncer colorrectal en una población de Madrid. *Rev Clin Esp*, 204(7):355–61. doi:10.1016/S0014-2565(04)71484-8 PMID:15274780

Kabat GC, Miller AB, Jain M, Rohan TE (2007). A cohort study of dietary iron and heme iron intake and risk of colorectal cancer in women. *Br J Cancer*, 97(1):118–22. doi:10.1038/sj.bjc.6603837 PMID:17551493

Kampman E, Slattery ML, Bigler J, Leppert M, Samowitz W, Caan BJ et al. (1999). Meat consumption, genetic susceptibility, and colon cancer risk: a United States multicenter case-control study. *Cancer Epidemiol Biomarkers Prev*, 8(1):15–24. PMID:9950235

Kampman E, Verhoeven D, Sloots L, van 't Veer P (1995). Vegetable and animal products as determinants of colon cancer risk in Dutch men and women. *Cancer Causes Control*, 6(3):225–34. doi:10.1007/BF00051794 PMID:7612802

Kantor ED, Hutter CM, Minnier J, Berndt SI, Brenner H, Caan BJ et al. (2014). Gene-environment interaction involving recently identified colorectal cancer susceptibility Loci. *Cancer Epidemiol Biomarkers Prev*, 23(9):1824–33. doi:10.1158/1055-9965.EPI-14-0062 PMID:24994789

Kato I, Akhmedkhanov A, Koenig K, Toniolo PG, Shore RE, Riboli E (1997). Prospective study of diet and female colorectal cancer: the New York University Women's Health Study. *Nutr Cancer*, 28(3):276–81. doi:10.1080/01635589709514588 PMID:9343837

Keku TO, Millikan RC, Martin C, Rahkra-Burris TK, Sandler RS (2003). Family history of colon cancer: what does it mean and how is it useful? *Am J Prev Med*, 24(2):170–6. doi:10.1016/S0749-3797(02)00590-1 PMID:12568823

Kim JI, Park YJ, Kim KH, Kim JI, Song BJ, Lee MS et al. (2003). hOGG1 Ser326Cys polymorphism modifies the significance of the environmental risk factor for colon cancer. *World J Gastroenterol*, 9(5):956–60. doi:10.3748/wjg.v9.i5.956 PMID:12717837

Kimura Y, Kono S, Toyomura K, Nagano J, Mizoue T, Moore MA et al. (2007). Meat, fish and fat intake in relation to subsite-specific risk of colorectal cancer:

The Fukuoka Colorectal Cancer Study. *Cancer Sci*, 98(4):590–7. doi:10.1111/j.1349-7006.2007.00425.x PMID:17425596

Kotake K, Koyama Y, Nasu J, Fukutomi T, Yamaguchi N (1995). Relation of family history of cancer and environmental factors to the risk of colorectal cancer: a case-control study. *Jpn J Clin Oncol*, 25(5):195–202. PMID:7474407

Kune S, Kune GA, Watson LF (1987). Case-control study of dietary etiological factors: the Melbourne Colorectal Cancer Study. *Nutr Cancer*, 9(1):21–42. doi:10.1080/01635588709513908 PMID:3027675

Kuriki K, Hamajima N, Chiba H, Kanemitsu Y, Hirai T, Kato T et al. (2005). Increased risk of colorectal cancer due to interactions between meat consumption and the CD36 gene A52C polymorphism among Japanese. *Nutr Cancer*, 51(2):170–7. doi:10.1207/s15327914nc5102_7 PMID:15860439

Kuriki K, Hirose K, Matsuo K, Wakai K, Ito H, Kanemitsu Y et al. (2006). Meat, milk, saturated fatty acids, the Pro12Ala and C161T polymorphisms of the PPARgamma gene and colorectal cancer risk in Japanese. *Cancer Sci*, 97(11):1226–35. doi:10.1111/j.1349-7006.2006.00314.x PMID:16965392

Küry S, Buecher B, Robiou-du-Pont S, Scoul C, Sébille V, Colman H et al. (2007). Combinations of cytochrome P450 gene polymorphisms enhancing the risk for sporadic colorectal cancer related to red meat consumption. *Cancer Epidemiol Biomarkers Prev*, 16(7):1460–7. doi:10.1158/1055-9965.EPI-07-0236 PMID:17627011

La Vecchia C, D'Avanzo B, Negri E, Franceschi S (1991). History of selected diseases and the risk of colorectal cancer. *Eur J Cancer*, 27(5):582–6. doi:10.1016/0277-5379(91)90223-Z PMID:1828966

La Vecchia C, Ferraroni M, Mezzetti M, Enard L, Negri E, Franceschi S et al. (1996). Attributable risks for colorectal cancer in northern Italy. *Int J Cancer*, 66(1):60–4. doi:10.1002/(SICI)1097-0215(19960328)66:1<60::AID-IJC11>3.0.CO;2-F PMID:8608968

Larsson SC, Adami HO, Giovannucci E, Wolk A (2005b). Re: Heme iron, zinc, alcohol consumption, and risk of colon cancer. *J Natl Cancer Inst*, 97(3):232–3, author reply 233–4. doi:10.1093/jnci/dji032 PMID:15687367

Larsson SC, Orsini N, Wolk A (2006). Processed meat consumption and stomach cancer risk: a meta-analysis. *J Natl Cancer Inst*, 98(15):1078–87. doi:10.1093/jnci/djj301 PMID:16882945

Larsson SC, Rafter J, Holmberg L, Bergkvist L, Wolk A (2005a). Red meat consumption and risk of cancers of the proximal colon, distal colon and rectum: the Swedish Mammography Cohort. *Int J Cancer*, 113(5):829–34. doi:10.1002/ijc.20658 PMID:15499619

Le Marchand L, Donlon T, Seifried A, Wilkens LR (2002a). Red meat intake, CYP2E1 genetic polymorphisms, and colorectal cancer risk. *Cancer Epidemiol Biomarkers Prev*, 11(10 Pt 1):1019–24. PMID:12376502

Le Marchand L, Hankin JH, Pierce LM, Sinha R, Nerurkar PV, Franke AA et al. (2002b). Well-done red meat, metabolic phenotypes and colorectal cancer in Hawaii. *Mutat Res*, 506-507:205–14. doi:10.1016/S0027-5107(02)00167-7 PMID:12351160

Le Marchand L, Hankin JH, Wilkens LR, Pierce LM, Franke A, Kolonel LN et al. (2001). Combined effects of well-done red meat, smoking, and rapid N-acetyltransferase 2 and CYP1A2 phenotypes in increasing colorectal cancer risk. *Cancer Epidemiol Biomarkers Prev*, 10(12):1259–66. PMID:11751443

Le Marchand L, Wilkens LR, Hankin JH, Kolonel LN, Lyu LC (1997). A case-control study of diet and colorectal cancer in a multiethnic population in Hawaii (United States): lipids and foods of animal origin. *Cancer Causes Control*, 8(4):637–48. doi:10.1023/A:1018406716115 PMID:9242481

Lee DH, Anderson KE, Harnack LJ, Folsom AR, Jacobs DR Jr (2004). Heme iron, zinc, alcohol consumption, and colon cancer: Iowa Women's Health Study. *J Natl Cancer Inst*, 96(5):403–7. doi:10.1093/jnci/djh047 PMID:14996862

Lee HP, Gourley L, Duffy SW, Estève J, Lee J, Day NE (1989). Colorectal cancer and diet in an Asian population–a case-control study among Singapore Chinese. *Int J Cancer*, 43(6):1007–16. doi:10.1002/ijc.2910430609 PMID:2731998

Lee SA, Shu XO, Yang G, Li H, Gao YT, Zheng W (2009). Animal origin foods and colorectal cancer risk: a report from the Shanghai Women's Health Study. *Nutr Cancer*, 61(2):194–205. doi:10.1080/01635580802419780 PMID:19235035

Levi F, Pasche C, La Vecchia C, Lucchini F, Franceschi S (1999). Food groups and colorectal cancer risk. *Br J Cancer*, 79(7-8):1283–7. doi:10.1038/sj.bjc.6690206 PMID:10098773

Levi F, Pasche C, Lucchini F, Bosetti C, La Vecchia C (2004). Processed meat and the risk of selected digestive tract and laryngeal neoplasms in Switzerland. *Ann Oncol*, 15(2):346–9. doi:10.1093/annonc/mdh060 PMID:14760132

Lin J, Zhang SM, Cook NR, Lee IM, Buring JE (2004). Dietary fat and fatty acids and risk of colorectal cancer in women. *Am J Epidemiol*, 160(10):1011–22. doi:10.1093/aje/kwh319 PMID:15522858

Little J, Sharp L, Masson LF, Brockton NT, Cotton SC, Haites NE et al. (2006). Colorectal cancer and genetic polymorphisms of CYP1A1, GSTM1 and GSTT1: a case-control study in the Grampian region of Scotland. *Int J Cancer*, 119(9):2155–64. doi:10.1002/ijc.22093 PMID:16823842

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

Lohsoonthorn P, Danvivat D (1995). Colorectal cancer risk factors: a case-control study in Bangkok. *Asia Pac J Public Health*, 8(2):118–22. doi:10.1177/101053959500800211 PMID:9037809

Lüchtenborg M, Weijenberg MP, de Goeij AF, Wark PA, Brink M, Roemen GM et al. (2005). Meat and fish consumption, APC gene mutations and hMLH1 expression in colon and rectal cancer: a prospective cohort study (The Netherlands). *Cancer Causes Control*, 16(9):1041–54. doi:10.1007/s10552-005-0239-0 PMID:16184469

Macquart-Moulin G, Riboli E, Cornée J, Charnay B, Berthezène P, Day N (1986). Case-control study on colorectal cancer and diet in Marseilles. *Int J Cancer*, 38(2):183–91. doi:10.1002/ijc.2910380207 PMID:3015806

Mahfouz EM, Sadek RR, Abdel-Latief WM, Mosallem FA-H, Hassan EE (2014). The role of dietary and lifestyle factors in the development of colorectal cancer: case control study in Minia, Egypt. *Cent Eur J Public Health*, 22(4):215–22. doi:10.21101/cejph.a3919 PMID:25622477

Manousos O, Day NE, Trichopoulos D, Gerovassilis F, Tzonou A, Polychronopoulou A (1983). Diet and colorectal cancer: a case-control study in Greece. *Int J Cancer*, 32(1):1–5. doi:10.1002/ijc.2910320102 PMID:6862688

McCann SE, Randall E, Marshall JR, Graham S, Zielezny M, Freudenheim JL (1994). Diet diversity and risk of colon cancer in western New York. *Nutr Cancer*, 21(2):133–41. doi:10.1080/01635589409514311 PMID:8058524

Miller PE, Lazarus P, Lesko SM, Cross AJ, Sinha R, Laio J et al. (2013). Meat-related compounds and colorectal cancer risk by anatomical subsite. *Nutr Cancer*, 65(2):202–26. doi:10.1080/01635581.2013.756534 PMID:23441608

Morita M, Le Marchand L, Kono S, Yin G, Toyomura K, Nagano J et al. (2009). Genetic polymorphisms of CYP2E1 and risk of colorectal cancer: the Fukuoka Colorectal Cancer Study. *Cancer Epidemiol Biomarkers Prev*, 18(1):235–41. doi:10.1158/1055-9965.EPI-08-0698 PMID:19124503

Mrkonjic M, Chappell E, Pethe VV, Manno M, Daftary D, Greenwood CM, Gallinger S, Zanke BW, Knight JA, Bapat B. (2009). Association of apolipoprotein E polymorphisms and dietary factors in colorectal cancer 100(12):1966–1974.

Murtaugh MA, Ma KN, Sweeney C, Caan BJ, Slattery ML (2004). Meat consumption patterns and preparation, genetic variants of metabolic enzymes, and their association with rectal cancer in men and women. *J Nutr*, 134(4):776–84. doi:10.1093/jn/134.4.776 PMID:15051825

Murtaugh MA, Sweeney C, Ma KN, Caan BJ, Slattery ML (2005). The CYP1A1 genotype may alter the association of meat consumption patterns and preparation with the risk of colorectal cancer in men and women. *J Nutr*, 135(2):179–86. doi:10.1093/jn/135.2.179 PMID:15671210

Murtaugh MA, Sweeney C, Ma KN, Potter JD, Caan BJ, Wolff RK et al. (2006). Vitamin D receptor gene polymorphisms, dietary promotion of insulin resistance, and colon and rectal cancer. *Nutr Cancer*, 55(1):35–43. doi:10.1207/s15327914nc5501_5 PMID:16965239

Muscat JE, Wynder EL (1994). The consumption of well-done red meat and the risk of colorectal cancer. *Am J Public Health*, 84(5):856–8. doi:10.2105/AJPH.84.5.856 PMID:8179063

Nashar RM, Almurshed KS (2008). Colorectal cancer: a case control study of dietary factors, king faisal specialist hospital and researh center, riyadh, saudi arabia. *J Family Community Med*, 15(2):57–64. PMID:23012168

Navarro A, Díaz MP, Muñoz SE, Lantieri MJ, Eynard AR (2003). Characterization of meat consumption and risk of colorectal cancer in Cordoba, Argentina. *Nutrition*, 19(1):7–10. doi:10.1016/S0899-9007(02)00832-8 PMID:12507631

Navarro A, Muñoz SE, Lantieri MJ, del Pilar Diaz M, Cristaldo PE, de Fabro SP et al. (2004). Meat cooking habits and risk of colorectal cancer in Córdoba, Argentina. *Nutrition*, 20(10):873–7. doi:10.1016/j.nut.2004.06.008 PMID:15474875

Negri E, Bosetti C, La Vecchia C, Levi F, Tomei F, Franceschi S (1999). Allergy and other selected diseases and risk of colorectal cancer. *Eur J Cancer*, 35(13):1838–41. doi:10.1016/S0959-8049(99)00209-9 PMID:10674000

Norat T, Bingham S, Ferrari P, Slimani N, Jenab M, Mazuir M et al. (2005). Meat, fish, and colorectal cancer risk: the European Prospective Investigation into cancer and nutrition. *J Natl Cancer Inst*, 97(12):906–16. doi:10.1093/jnci/dji164 PMID:15956652

Norat T, Lukanova A, Ferrari P, Riboli E (2002). Meat consumption and colorectal cancer risk: dose-response meta-analysis of epidemiological studies. *Int J Cancer*, 98(2):241–56. doi:10.1002/ijc.10126 PMID:11857415

Nöthlings U, Yamamoto JF, Wilkens LR, Murphy SP, Park SY, Henderson BE et al. (2009). Meat and heterocyclic amine intake, smoking, NAT1 and NAT2 polymorphisms, and colorectal cancer risk in the multiethnic cohort study. *Cancer Epidemiol Biomarkers Prev*, 18(7):2098–106. doi:10.1158/1055-9965.EPI-08-1218 PMID:19549810

Nowell S, Coles B, Sinha R, MacLeod S, Luke Ratnasinghe D, Stotts C et al. (2002). Analysis of total meat intake and exposure to individual heterocyclic amines in a

case-control study of colorectal cancer: contribution of metabolic variation to risk. *Mutat Res*, 506-507:175–85. doi:10.1016/S0027-5107(02)00164-1 PMID:12351157
Oba S, Shimizu N, Nagata C, Shimizu H, Kametani M, Takeyama N et al. (2006). The relationship between the consumption of meat, fat, and coffee and the risk of colon cancer: a prospective study in Japan. *Cancer Lett*, 244(2):260–7. doi:10.1016/j.canlet.2005.12.037 PMID:16519996
Ollberding NJ, Wilkens LR, Henderson BE, Kolonel LN, Le Marchand L (2012). Meat consumption, heterocyclic amines and colorectal cancer risk: the Multiethnic Cohort Study. *Int J Cancer*, 131(7):E1125–33. doi:10.1002/ijc.27546 PMID:22438055
Pham NM, Mizoue T, Tanaka K, Tsuji I, Tamakoshi A, Matsuo K et al.; Research Group for the Development and Evaluation of Cancer Prevention Strategies in Japan (2014). Meat consumption and colorectal cancer risk: an evaluation based on a systematic review of epidemiologic evidence among the Japanese population. *Jpn J Clin Oncol*, 44(7):641–50. doi:10.1093/jjco/hyu061 PMID:24842864
Phillips RL (1975). Role of life-style and dietary habits in risk of cancer among seventh-day adventists. *Cancer Res*, 35(11 Pt. 2):3513–22. PMID:1192416
Pickle LW, Greene MH, Ziegler RG, Toledo A, Hoover R, Lynch HT et al. (1984). Colorectal cancer in rural Nebraska. *Cancer Res*, 44(1):363–9. PMID:6690049
Pietinen P, Malila N, Virtanen M, Hartman TJ, Tangrea JA, Albanes D et al. (1999). Diet and risk of colorectal cancer in a cohort of Finnish men. *Cancer Causes Control*, 10(5):387–96. doi:10.1023/A:1008962219408 PMID:10530608
Pimenta CA, Latini FR, DE Lima JM, DA Silva TD, Felipe AV, DE Lima Pazine VM et al. (2014). Study of the polymorphisms of cyclooxygenase-2 (-765G>C) and 5-lipoxygenase (1708G>A) in patients with colorectal cancer. *Oncol Lett*, 7(2):513–8. doi:10.3892/ol.2013.1732 PMID:24396479
Ping Y, Ogushi Y, Okada Y, Haruki Y, Okazaki I, Ogawa T (1998). Lifestyle and colorectal cancer: A case-control study. *Environ Health Prev Med*, 3(3):146–51. doi:10.1007/BF02931705 PMID:21432494
Pou SA, Díaz MP, Osella AR (2012). Applying multilevel model to the relationship of dietary patterns and colorectal cancer: an ongoing case-control study in Córdoba, Argentina. *Eur J Nutr*, 51(6):755–64. doi:10.1007/s00394-011-0255-7 PMID:21990003
Pou SA, Niclis C, Aballay LR, Tumas N, Román MD, Muñoz SE et al. (2014). [Cancer and its association with dietary patterns in Córdoba (Argentina)] *Nutr Hosp*, 29(3):618–28. PMID:24559007
Qiao L, Feng Y (2013). Intakes of heme iron and zinc and colorectal cancer incidence: a meta-analysis of prospective studies. *Cancer Causes Control*, 24(6):1175–83. doi:10.1007/s10552-013-0197-x PMID:23568532
Ramzi NH, Chahil JK, Lye SH, Munretnam K, Sahadevappa KI, Velapasamy S et al. (2014). Role of genetic & environment risk factors in the aetiology of colorectal cancer in Malaysia. *Indian J Med Res*, 139(6):873–82. PMID:25109722
Roberts-Thomson IC, Ryan P, Khoo KK, Hart WJ, McMichael AJ, Butler RN (1996). Diet, acetylator phenotype, and risk of colorectal neoplasia. *Lancet*, 347(9012):1372–4. doi:10.1016/S0140-6736(96)91012-0 PMID:8637343
Rosato V, Bosetti C, Levi F, Polesel J, Zucchetto A, Negri E et al. (2013). Risk factors for young-onset colorectal cancer. *Cancer Causes Control*, 24(2):335–41. doi:10.1007/s10552-012-0119-3 PMID:23224326
Rouillier P, Senesse P, Cottet V, Valléau A, Faivre J, Boutron-Ruault MC (2005). Dietary patterns and the adenomacarcinoma sequence of colorectal cancer. *Eur J Nutr*, 44(5):311–8. doi:10.1007/s00394-004-0525-8 PMID:15316829
Ruder EH, Thiébaut AC, Thompson FE, Potischman N, Subar AF, Park Y et al. (2011). Adolescent and mid-life diet: risk of colorectal cancer in the NIH-AARP Diet and Health Study. *Am J Clin Nutr*, 94(6):1607–19. doi:10.3945/ajcn.111.020701 PMID:22071715
Saebø M, Skjelbred CF, Brekke Li K, Bowitz Lothe IM, Hagen PC, Johnsen E et al. (2008). CYP1A2 164 A–>C polymorphism, cigarette smoking, consumption of well-done red meat and risk of developing colorectal adenomas and carcinomas. *Anticancer Res*, 28:4C:2289–95. PMID:18751408
Sandhu MS, White IR, McPherson K (2001). Systematic review of the prospective cohort studies on meat consumption and colorectal cancer risk: a meta-analytical approach. *Cancer Epidemiol Biomarkers Prev*, 10(5):439–46. PMID:11352852
Satia JA, Keku T, Galanko JA, Martin C, Doctolero RT, Tajima A et al. (2005). Diet, lifestyle, and genomic instability in the North Carolina Colon Cancer Study. *Cancer Epidemiol Biomarkers Prev*, 14(2):429–36. doi:10.1158/1055-9965.EPI-04-0486 PMID:15734969
Satia JA, Tseng M, Galanko JA, Martin C, Sandler RS (2009). Dietary patterns and colon cancer risk in Whites and African Americans in the North Carolina Colon Cancer Study. *Nutr Cancer*, 61(2):179–93. doi:10.1080/01635580802419806 PMID:19235034
Satia-Abouta J, Galanko JA, Martin CF, Ammerman A, Sandler RS (2004). Food groups and colon cancer risk in African-Americans and Caucasians. *Int J Cancer*, 109(5):728–36. doi:10.1002/ijc.20044 PMID:14999782
Sato Y, Nakaya N, Kuriyama S, Nishino Y, Tsubono Y, Tsuji I (2006). Meat consumption and risk of colorectal cancer in Japan: the Miyagi Cohort Study. *Eur J Cancer Prev*, 15(3):211–8. doi:10.1097/01.cej.0000197455.87356.05 PMID:16679863
Sellers TA, Bazyk AE, Bostick RM, Kushi LH, Olson JE, Anderson KE et al. (1998). Diet and risk of colon

cancer in a large prospective study of older women: an analysis stratified on family history (Iowa, United States). *Cancer Causes Control*, 9(4):357–67. doi:10.1023/A:1008886715597 PMID:9794167
Seow A, Yuan JM, Sun CL, Van Den Berg D, Lee HP, Yu MC (2002). Dietary isothiocyanates, glutathione S-transferase polymorphisms and colorectal cancer risk in the Singapore Chinese Health Study. *Carcinogenesis*, 23(12):2055–61. doi:10.1093/carcin/23.12.2055 PMID:12507929
Shannon J, White E, Shattuck AL, Potter JD (1996). Relationship of food groups and water intake to colon cancer risk. *Cancer Epidemiol Biomarkers Prev*, 5(7):495–502. PMID:8827352
Silva TD, Felipe AV, Pimenta CA, Barão K, Forones NM (2012). CYP2E1 RsaI and 96-bp insertion genetic polymorphisms associated with risk for colorectal cancer. *Genet Mol Res*, 11(3):3138–45. doi:10.4238/2012.September.3.2 PMID:23007992
Singh PN, Fraser GE (1998). Dietary risk factors for colon cancer in a low-risk population. *Am J Epidemiol*, 148(8):761–74. doi:10.1093/oxfordjournals.aje.a009697 PMID:9786231
Skjelbred CF, Saebø M, Hjartåker A, Grotmol T, Hansteen IL, Tveit KM et al. (2007). Meat, vegetables and genetic polymorphisms and the risk of colorectal carcinomas and adenomas. *BMC Cancer*, 7(1):228. doi:10.1186/1471-2407-7-228 PMID:18093316
Slattery ML, Berry TD, Potter J, Caan B (1997). Diet diversity, diet composition, and risk of colon cancer (United States). *Cancer Causes Control*, 8(6):872–82. doi:10.1023/A:1018416412906 PMID:9427430
Slattery ML, Curtin K, Anderson K, Ma KN, Edwards S, Leppert M et al. (2000). Associations between dietary intake and Ki-ras mutations in colon tumors: a population-based study. *Cancer Res*, 60(24):6935–41. PMID:11156393
Slattery ML, Curtin K, Ma K, Edwards S, Schaffer D, Anderson K et al. (2002a). Diet activity, and lifestyle associations with p53 mutations in colon tumors. *Cancer Epidemiol Biomarkers Prev*, 11(6):541–8. PMID:12050095
Slattery ML, Curtin K, Ma K, Schaffer D, Potter J, Samowitz W (2002b). GSTM-1 and NAT2 and genetic alterations in colon tumors. *Cancer Causes Control*, 13(6):527–34. doi:10.1023/A:1016376016716 PMID:12195642
Slattery ML, Edwards SL, Samowitz W (1998). Stage of colon cancer at diagnosis: implications for risk factor associations? *Int J Epidemiol*, 27(3):382–7. doi:10.1093/ije/27.3.382 PMID:9698124
Slattery ML, Levin TR, Ma K, Goldgar D, Holubkov R, Edwards S (2003). Family history and colorectal cancer: predictors of risk. *Cancer Causes Control*, 14(9):879–87. doi:10.1023/B:CACO.0000003840.94591.76 PMID:14682445
Sørensen M, Autrup H, Olsen A, Tjønneland A, Overvad K, Raaschou-Nielsen O (2008). Prospective study of NAT1 and NAT2 polymorphisms, tobacco smoking and meat consumption and risk of colorectal cancer. *Cancer Lett*, 266(2):186–93. doi:10.1016/j.canlet.2008.02.046 PMID:18372103
Spencer EA, Key TJ, Appleby PN, Dahm CC, Keogh RH, Fentiman IS et al. (2010). Meat, poultry and fish and risk of colorectal cancer: pooled analysis of data from the UK dietary cohort consortium. *Cancer Causes Control*, 21(9):1417–25. doi:10.1007/s10552-010-9569-7 PMID:20437091
Squires J, Roebothan B, Buehler S, Sun Z, Cotterchio M, Younghusband B et al. (2010). Pickled meat consumption and colorectal cancer (CRC): a case-control study in Newfoundland and Labrador, Canada. *Cancer Causes Control*, 21(9):1513–21. doi:10.1007/s10552-010-9580-z PMID:20506038
Sriamporn S, Wiangnon S, Suwanrungruang K, Rungsrikaji D, Sukprasert A, Thipsuntornsak N et al. (2007). Risk factors for colorectal cancer in northeast Thailand: lifestyle related. *Asian Pac J Cancer Prev*, 8(4):573–7. PMID:18260731
Steck SE, Butler LM, Keku T, Antwi S, Galanko J, Sandler RS et al. (2014). Nucleotide excision repair gene polymorphisms, meat intake and colon cancer risk. *Mutat Res*, 762:24–31. doi:10.1016/j.mrfmmm.2014.02.004 PMID:24607854
Steinmetz KA, Potter JD (1993). Food-group consumption and colon cancer in the Adelaide Case-Control Study. II. Meat, poultry, seafood, dairy foods and eggs. *Int J Cancer*, 53(5):720–7. doi:10.1002/ijc.2910530503 PMID:8449595
Tabatabaei SM, Fritschi L, Knuiman MW, Boyle T, Iacopetta BJ, Platell C et al. (2011). Meat consumption and cooking practices and the risk of colorectal cancer. *Eur J Clin Nutr*, 65(6):668–75. doi:10.1038/ejcn.2011.17 PMID:21364608
Tajima K, Tominaga S (1985). Dietary habits and gastro-intestinal cancers: a comparative case-control study of stomach and large intestinal cancers in Nagoya, Japan. *Jpn J Cancer Res*, 76(8):705–16. PMID:3930448
Takachi R, Tsubono Y, Baba K, Inoue M, Sasazuki S, Iwasaki M et al.; Japan Public Health Center-Based Prospective Study Group (2011). Red meat intake may increase the risk of colon cancer in Japanese, a population with relatively low red meat consumption. *Asia Pac J Clin Nutr*, 20(4):603–12. PMID:22094846
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
Theodoratou E, Campbell H, Tenesa A, McNeill G, Cetnarskyj R, Barnetson RA et al. (2008). Modification of the associations between lifestyle, dietary

factors and colorectal cancer risk by APC variants. *Carcinogenesis*, 29(9):1774–80. doi:10.1093/carcin/bgn082 PMID:18375958

Tiemersma EW, Kampman E, Bueno de Mesquita HB, Bunschoten A, van Schothorst EM, Kok FJ et al. (2002). Meat consumption, cigarette smoking, and genetic susceptibility in the etiology of colorectal cancer: results from a Dutch prospective study. *Cancer Causes Control*, 13(4):383–93. doi:10.1023/A:1015236701054 PMID:12074508

Tranah GJ, Bugni J, Giovannucci E, Ma J, Fuchs C, Hines L et al. (2006). O6-methylguanine-DNA methyltransferase Leu84Phe and Ile143Val polymorphisms and risk of colorectal cancer in the Nurses' Health Study and Physicians' Health Study (United States). *Cancer Causes Control*, 17(5):721–31. doi:10.1007/s10552-006-0005-y PMID:16633920

Turner F, Smith G, Sachse C, Lightfoot T, Garner RC, Wolf CR et al. (2004). Vegetable, fruit and meat consumption and potential risk modifying genes in relation to colorectal cancer. *Int J Cancer*, 112(2):259–64. doi:10.1002/ijc.20404 PMID:15352038

Tuyns AJ, Kaaks R, Haelterman M (1988). Colorectal cancer and the consumption of foods: a case-control study in Belgium. *Nutr Cancer*, 11(3):189–204. doi:10.1080/01635588809513986 PMID:3405870

Vlajinac H, Adanja B, Jarebinski M (1987). Case-control study of the relationship of diet and colon cancer. *Arch Geschwulstforsch*, 57(6):493–8. PMID:3435228

Wakai K, Hirose K, Matsuo K, Ito H, Kuriki K, Suzuki T et al. (2006). Dietary risk factors for colon and rectal cancers: a comparative case-control study. *J Epidemiol*, 16(3):125–35. doi:10.2188/jea.16.125 PMID:16710081

Wang J, Joshi AD, Corral R, Siegmund KD, Marchand LL, Martinez ME et al. (2012). Carcinogen metabolism genes, red meat and poultry intake, and colorectal cancer risk. *Int J Cancer*, 130(8):1898–907. doi:10.1002/ijc.26199 PMID:21618522

Wei EK, Colditz GA, Giovannucci EL, Fuchs CS, Rosner BA (2009). Cumulative risk of colon cancer up to age 70 years by risk factor status using data from the Nurses' Health Study. *Am J Epidemiol*, 170(7):863–72. doi:10.1093/aje/kwp210 PMID:19723749

Wei EK, Giovannucci E, Wu K, Rosner B, Fuchs CS, Willett WC et al. (2004). Comparison of risk factors for colon and rectal cancer. *Int J Cancer*, 108(3):433–42. doi:10.1002/ijc.11540 PMID:14648711

Welfare M, Monesola Adeokun A, Bassendine MF, Daly AK (1999). Polymorphisms in GSTP1, GSTM1, and GSTT1 and susceptibility to colorectal cancer. *Cancer Epidemiol Biomarkers Prev*, 8(4 Pt 1):289–92. PMID:10207630

Willett WC, Stampfer MJ, Colditz GA, Rosner BA, Speizer FE (1990). Relation of meat, fat, and fiber intake to the risk of colon cancer in a prospective study among women. *N Engl J Med*, 323(24):1664–72. doi:10.1056/NEJM199012133232404 PMID:2172820

Williams CD, Satia JA, Adair LS, Stevens J, Galanko J, Keku TO et al. (2010). Associations of red meat, fat, and protein intake with distal colorectal cancer risk. *Nutr Cancer*, 62(6):701–9. doi:10.1080/01635581003605938 PMID:20661817

Wohlleb JC, Hunter CF, Blass B, Kadlubar FF, Chu DZ, Lang NP (1990). Aromatic amine acetyltransferase as a marker for colorectal cancer: environmental and demographic associations. *Int J Cancer*, 46(1):22–30. doi:10.1002/ijc.2910460107 PMID:2365498

Yeh CC, Hsieh LL, Tang R, Chang-Chieh CR, Sung FC (2003). Risk factors for colorectal cancer in Taiwan: a hospital-based case-control study. *J Formos Med Assoc*, 102(5):305–12. PMID:12874668

Yeh CC, Hsieh LL, Tang R, Chang-Chieh CR, Sung FC (2005). MS-920: DNA repair gene polymorphisms, diet and colorectal cancer risk in Taiwan. *Cancer Lett*, 224(2):279–88. doi:10.1016/j.canlet.2005.01.029 PMID:15914278

Zaridze D, Filipchenko V, Kustov V, Serdyuk V, Duffy S (1992). Diet and colorectal cancer: results of two case-control studies in Russia. *Eur J Cancer*, 29A(1):112–5. PMID:1445726

Zhang B, Li X, Nakama H, Zhang X, Wei N, Zhang X et al. (2002). A case-control study on risk of changing food consumption for colorectal cancer. *Cancer Invest*, 20(4):458–63. doi:10.1081/CNV-120002145 PMID:12094540

Zhang X, Giovannucci EL, Smith-Warner SA, Wu K, Fuchs CS, Pollak M et al. (2011). A prospective study of intakes of zinc and heme iron and colorectal cancer risk in men and women. *Cancer Causes Control*, 22(12):1627–37. doi:10.1007/s10552-011-9839-z PMID:21909950

Zhivotovskiy AS, Kutikhin AG, Azanov AZ, Yuzhalin AE, Magarill YA, Brusina EB (2012). Colorectal cancer risk factors among the population of South-East Siberia: a case-control study. *Asian Pac J Cancer Prev*, 13(10):5183–8. doi:10.7314/APJCP.2012.13.10.5183 PMID:23244132