Meat, dairy, and cancer[1–4]

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ABSTRACT
In 2007 the World Cancer Research Fund and American Institute for Cancer Research (WCRF/AICR) report judged that the evidence for an association between red and processed meat consumption and colorectal cancer was convincing. In addition, the effect of other animal products on cancer risk has been studied, and the WCRF/AICR report concluded that milk probably decreases the risk of colorectal cancer but diets high in calcium probably increase the risk of prostate cancer, whereas there was limited evidence for an association between milk and bladder cancer and insufficient evidence for other cancers. There are several potential mechanisms relating meat to cancer, including heterocyclic amines, polycyclic aromatic hydrocarbons, *N*-nitroso compounds, and heme iron. Although the evidence in favor of a link between red and processed meat and colorectal cancer is convincing, the relations with other cancers are unclear. In this review, we summarize cohort studies conducted by the National Cancer Institute on meat and dairy intake in relation to cancer since the 2007 WCRF/AICR report. We also report the findings of meta-analyses published since 2007. *Am J Clin Nutr* 2014;100(suppl):386S–93S.

INTRODUCTION

The Diet and Cancer Report published by the World Cancer Research Fund and American Institute for Cancer Research (WCRF/AICR)[5] in 2007 concluded that the positive association between red and processed meat and colorectal cancer was convincing on the basis of the results of 16 cohort studies and 71 case-control studies (1). The WCRF/AICR Continuous Update Project on colorectal cancer in 2011 only served to strengthen the evidence in favor of a link between red and processed meat intake and colorectal cancer (2). The 2007 panel also concluded that cancers of the esophagus, lung, pancreas, prostate, stomach, and endometrium may be linked to red and processed meat consumption; however, the evidence at the time was limited and inconsistent. In addition to meat, the association between dairy products and cancer has been investigated. The WCRF/AICR report concluded that milk probably decreases the risk of colorectal cancer, whereas the evidence in favor of a decreased risk of bladder cancer was limited. Diets high in calcium—including foods that naturally contain calcium and those fortified with calcium—were reported to probably increase the risk of prostate cancer, although there was limited evidence for milk and dairy products increasing the risk of prostate cancer (1). There was insufficient evidence to draw conclusions about milk or dairy products and other cancers. Since the publication of the WCRF/AICR report, researchers at the National Cancer Institute (NCI) have conducted a considerable number of large prospective analyses on the intake of meat, meat-related compounds, and dairy in relation to cancer. Other researchers have conducted meta-analyses on these topics. These publications have added new insight into the mechanistic role of heterocyclic amines (HCAs), polycyclic aromatic hydrocarbons (PAHs), *N*-nitroso compounds (NOCs), and heme iron from meat in the etiology of various cancers. This review summarizes the NCI's studies since 2007. Because of the large number of prospective studies published during this time period, case-control studies are not included unless otherwise stated. A particular emphasis is placed on the relation of meat and dairy with colorectal cancer, and other cancer sites are also discussed.

In addition to meta-analyses, we focused on data obtained from 2 large prospective studies carried out at the NCI: the NIH-AARP Diet and Health Study and the Prostate, Lung, Colorectal, and Ovarian (PLCO) Cancer Screening Trial. We chose to highlight data from these 2 studies because of the large number of published articles on the relation between animal products and cancer from these 2 studies, our personal involvement and familiarity with these studies, and to maintain focus and achieve appropriate brevity. The NIH-AARP study has been described in detail elsewhere (3). Briefly, in 1995–1996, 566,401 AARP members completed a comprehensive baseline questionnaire assessing diet and lifestyle, including a 124-item food-frequency questionnaire. Through linkage with state cancer registries, participants have been followed from baseline and follow-up is ongoing, with current follow-up through 2006. The PLCO trial, a large, randomized

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[5] Abbreviations used: AICR, American Institute for Cancer Research; DiMeIQx, 2-amino-3,4,8-trimethylimidazo(4,5-f)quinoxaline; HCA, heterocyclic amine; MeIQx, 2-amino-3,8-dimethylimidazo(4,5-f)quinoxaline; NCI, National Cancer Institute; NHL, non-Hodgkin lymphoma; NOC, *N*-nitroso compound; PAH, polycyclic aromatic hydrocarbon; PhIP, 2-amino-1-methyl-6-phenylimidazo(4,5-b)pyridine; PLCO, Prostate, Lung, Colorectal, and Ovarian (Cancer Screening Trial); SRR, summary RR; WCRF, World Cancer Research Fund.

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controlled trial designed to test the efficacy of cancer screening and to investigate early markers and etiology of cancer, has also been described previously (4). Briefly, from 1993 to 2001, ∼155,000 participants aged 55–74 y were enrolled from 10 US centers. Participants completed a 137-item food-frequency questionnaire at baseline and were sent annual questionnaires that asked whether they had been diagnosed with cancer by a health care provider. These 2 large cohorts have provided data to study the effects of animal products on cancer incidence as well as mortality.

RED MEAT

Red meat is commonly defined as flesh from animals that have a higher proportion of red muscle fibers than white muscle fibers (eg, beef, goat, lamb, pork). With the use of food availability data from the FAO and the USDA, Daniel et al (5) reported that overall meat consumption has continued to increase in the United States and in the rest of the developed world; red meat represents the largest proportion of meat consumed in the United States at 58%. Furthermore, beef consumption is increasing in China and other middle- and low-income countries (6).

Colorectal cancer

Red meat intake was positively associated with incident colorectal adenomas in the PLCO trial (OR for individuals in the highest compared with the lowest quartile of intake: 1.59; 95% CI: 1.02, 2.49) (7) as well as with colorectal cancer in the NIH-AARP study (HR for the highest compared with the lowest quintile of intake: 1.24; 95% CI: 1.12, 1.36) (8). Xu et al (9) found an increased risk of colorectal adenomas in their meta-analysis of red meat intake in 5 cohort and nested case-control studies [summary RR (SRR) per 100-g/d increment in red meat intake: 1.22; 95% CI: 1.04, 1.42], and Smolińska et al (10) found a positive association for colon cancer (SRR for red meat intake >50 g/d: 1.21; 95% CI: 1.07, 1.37) in a meta-analysis of 22 cohort and case-control studies; the findings from both of these analyses lend support to the conclusions of the WCRF/AICR report (1). In another meta-analysis evaluating the same relation in 24 prospective studies, Chan et al (11) concluded that a significantly increased risk of colorectal cancer was associated with high intakes of red meat (SRR for high compared with low intakes: 1.22; 95% CI: 1.11, 1.34). A 2011 meta-analysis of red meat consumption and colorectal cancer concluded that "an independent and unequivocal" positive association cannot be established on the basis of the available evidence, despite a significant SRR of 1.12 (95% CI: 1.04, 1.21) for high compared with low intakes among the 34 prospective studies included (12). The SRRs for these 2 meta-analyses are comparable and both are significant; the inclusion criteria and statistical analyses were also similar. Unlike Chan et al, Alexander et al (12) also explored the relation across subgroups and tumor sites, the findings of which contributed to their overall assessment of inadequate evidence.

Other cancers

In an analysis across a range of malignancies in the NIH-AARP study, individuals in the highest quintile of red meat intake, compared with those in the lowest quintile, had a significantly increased risk of cancers of the lung, esophagus, and liver (13). Further detailed site-specific analyses in the NIH-AARP study found significant associations between red meat intake and cancers of the kidney (14), esophagus (squamous cell) (15), liver (16), lung (17), pancreas (in men) (18), and prostate (19). In contrast, red meat intake was not associated with cancers of the bladder (20), stomach (15), or breast (21) or with glioma (22) or non-Hodgkin lymphoma (NHL) (23). In other cohort studies, including the PLCO trial and the Agricultural Health Study, which is an NCI cohort of US farmers and their spouses, red meat intake was not associated with either lung (24) or prostate cancer (25), but it was positively associated with breast cancer (26). In summary, the results from these 3 cohorts are conflicting for lung, prostate, and breast cancer. In addition to the positive associations observed for the incidence of various cancers, men and women in the highest categories of red meat intake also had an increased risk of dying of cancer in the NIH-AARP study (27). A summary of the NCI studies on red meat and cancer risk is provided in **Table 1**.

Since 2007, there have been a number of meta-analyses of studies on meat and cancer. In a meta-analysis of red meat and kidney cancer, Alexander and Cushing (28) found no association when only cohort studies were analyzed (n = 3), with a reported SRR of 1.02 (95% CI: 0.91, 1.15). Given the limited number of prospective studies, and the nonsignificant relation observed when case-control studies were included, no independent relation between red meat and kidney cancer can be surmised (28). A recently published meta-analysis of red meat and esophageal adenocarcinomas did not find significant SRRs among 3 cohort studies (29). A meta-analysis of red meat and pancreatic cancer conducted by scientists in Sweden concluded that the association between red meat and pancreatic cancer was significant in men (SRR: 1.29; 95% CI: 1.08, 1.53) among the 11 prospective studies (30); this association in men is consistent with Stolzenberg-Solomon et al's (18) findings from the NIH-AARP cohort. In a meta-analysis of 15 cohort studies of red meat and prostate cancer, no association was observed for total prostate cancer or advanced prostate cancer (31). A meta-analysis of red meat and breast cancer with the use of 18 cohort studies showed a significant association among postmenopausal women, but the included studies were not sufficiently homogeneous for the statistical pooling to be valid (32). Finally, Wallin et al's (33) meta-analysis of 8 cohort studies evaluating the relation between red meat and ovarian cancer showed no evidence of a significant link.

WHITE MEAT

White meat, including fish and poultry, has more white than red muscle fibers. Evaluating the relation between white meat consumption and health outcomes can be problematic, given that the relation may be confounded by the replacement of red meat in the diet with white meat. If, in an addition model, red meat consumption is held constant, will white meat still show protective health benefits or is the decreased risk primarily attributable to reduced intake of red meat when white meat consumption is increased in the diet (ie, a substitution model in which total meat consumption is kept constant)? Based on the recent literature, the answer to this question is unclear, because the majority of studies on cancer do not adequately evaluate the addition compared with the substitution of red meat by white meat. Previous studies observed different results when red meat was substituted with other protein sources such as poultry and fish (34, 35) and evaluated

TABLE 1
Summary of findings from NCI studies on meat and cancer risk since 2007[1]

Meat type	Risk of cancer incidence and mortality: Increase	Decrease	Null
Red meat	Colorectal adenoma (7), colorectum (8), lung[2] (17), prostate[2] (19), breast[2] (26), esophagus (15), liver (16), pancreas (men) (18), kidney (14), cancer mortality (27)	—	NHL (23), bladder (20), lung[2] (24), prostate[2] (25), breast[2] (21), glioma (22)
White meat	—	Colorectum (8), liver (16), chronic liver disease mortality (16), cancer mortality (27), total mortality (27)	Colorectal adenoma (36), breast (21), NHL (23)
Processed meat	Colorectal adenoma (36), colorectum (8), lung[2] (17), prostate (19), chronic liver disease mortality (16)	—	Liver (16), pancreas (18), breast (21, 26), lung[2] (24), glioma (22), NHL (23)

[1] Numbers in parentheses correspond to references for the noted association. NCI, National Cancer Institute; NHL, non-Hodgkin lymphoma; —, no significant associations observed.
[2] Denotes inconsistent findings.

with respect to heart disease and stroke, but these models have not yet been applied to cancer endpoints.

Colorectal cancer

White meat intake was inversely associated with colorectal cancer incidence in the NIH-AARP study using an addition model (8), but no association was observed for incident distal colorectal adenoma in the PLCO trial also using an addition model (36). As of this writing, we did not identify any relevant meta-analyses on white meat intake and cancer.

Other cancers

In a study that specifically addressed the question of addition or substitution of red meat by white meat, Daniel et al (37) found that a significant inverse relation between poultry intake and cancers of the lung, liver, and esophagus in the NIH-AARP study was "largely due to the substitution of red meat" in the diet. Furthermore, Freedman et al (16) found a decreased risk of hepatocellular carcinoma and chronic liver disease mortality with white meat intake with the use of an addition model. Daniel et al (23) reported that there was no association between poultry or fish intake and NHL, and Kabat et al (21) found no association between white meat intake and breast cancer in the NIH-AARP study. In addition, white meat intake was associated with a decreased risk of total mortality and cancer mortality in both men and women in the NIH-AARP study (27). Each of these latter 3 studies (21, 23, 27) used an addition model and did not evaluate the substitution of red meat by white meat. We summarize the NCI data on white meat and cancer risk in Table 1.

PROCESSED MEAT

There is currently no universally accepted definition for processed meat. The term generally refers to meats that have been preserved by smoking, curing, salting, or by adding chemical preservatives such as sodium nitrite (eg, ham, bacon, pastrami, salami). Some studies also define certain types of ground meat as processed (38).

Colorectal cancer

Processed meat intake was positively associated with colorectal adenomas in the PLCO trial (36) and with incident colorectal cancer in the NIH-AARP study (8). Alexander et al's (39) meta-analysis of 28 prospective studies (representing 20 independent nonoverlapping study populations) reported significant associations between processed meat intake and colorectal cancer (SRR for high compared with low intake: 1.16; 95% CI: 1.10, 1.23) but concluded that the current epidemiologic evidence is not sufficient to support an association given the weak magnitudes, varying processed meat definitions between studies, and potential confounding factors. Xu et al's (9) meta-analysis of 5 prospective studies showed an increased risk of colorectal adenomas (SRR for those in the highest compared with the lowest category of processed meat intake: 1.17; 95% CI: 1.08, 1.26) as did Chan et al's (11) meta-analysis of 21 prospective studies (SRR for every 50-g/d increase in processed meat intake: 1.18; 95% CI: 1.10, 1.28), which led the respective authors to conclude that the current evidence is largely supportive of a relation between processed meat and colorectal cancer.

Other cancers

With the use of data from the NIH-AARP study and the PLCO trial, processed meat intake was positively associated with lung cancer in some (13, 17), but not all (24), analyses; in addition, positive associations were reported for chronic liver disease, although not for hepatocellular carcinoma (16). A positive association was also reported for prostate cancer in the NIH-AARP study (19). In contrast, processed meat intake was not associated with cancers of the pancreas (18) or breast (21, 26) or with glioma (22) or NHL (23). The NCI studies on processed meat and cancer risk are summarized in Table 1.

There have been several meta-analyses of processed meat intake and a number of cancer sites. With regard to kidney cancer, many of the summary risk estimates were positive, and a significant association was observed among 3 cohort studies (SRR for high compared with low intakes: 1.19; 95% CI: 1.03, 1.37) (28). A meta-analysis of esophageal adenocarcinomas using 3 cohort studies (29) showed no associations. A meta-analysis of 11 studies showed a significant association between processed meat intake and pancreatic cancer (RR for a 50-g/d increase in processed meat consumption: 1.19; 95% CI: 1.04, 1.36) (30). Larsson et al (40) reported a significant positive association between processed meat consumption and stomach cancer (SRR for an increase in processed meat consumption of 30 g/d: 1.15; 95% CI: 1.04, 1.27) in a meta-analysis of 6 prospective studies. As with red meat, a meta-analysis for processed meat and breast cancer that used 18 prospective studies found that, whereas some significant associations were observed (SRR for high compared with low intakes: 1.08; 95% CI: 1.01, 1.16), these estimates were highly dependent on the choice of analytic model (fixed effects compared with random effects) and publication biases were likely in effect according to the authors (32). A meta-analysis of processed meat and ovarian cancer that used 8 cohort studies (33) found no associations.

COOKING BYPRODUCTS FOUND IN MEAT

The formation of HCAs and PAHs is dependent on cooking time and temperature, with the highest amounts found in meats cooked well done at high temperatures. When meat is cooked over an open flame, pyrolysis of the fats in the meat will generate PAHs, which then become deposited on the meat (41). HCAs are formed from the reaction between creatine or creatinine, amino acids, and sugars (found in muscle meats) at high cooking temperatures (42). As of 2007, there were 17 identified HCAs formed during the meat-cooking process (1). In 1993 the International Agency for Research on Cancer concluded that the evidence from animal studies was sufficient to claim that 2-amino-3,8-dimethylimidazo(4,5-f)quinoxaline (MeIQx) and 2-amino-1-methyl-6-phenylimidazo(4,5-b)pyridine (PhIP) are carcinogenic (43). PhIP is the most abundant HCA detected in the human diet, followed by MeIQx and 2-amino-3,4,8-trimethylimidazo(4,5-f)quinoxaline (DiMeIQx) (44). There are 7 PAH compounds designated by the Environmental Protection Agency as probable human carcinogens, including benzo(a)pyrene, which is often used as a surrogate for total PAH exposure. Amounts of HCAs and benzo(a)pyrene from meat can be estimated in epidemiologic studies by using the NCI's CHARRED database (http://charred.cancer.gov/).

Colorectal cancer

Both MeIQx and DiMeIQx were positively associated with colorectal cancer in the NIH-AARP study (8) but not with colorectal adenoma incidence in the PLCO trial (36). PhIP intake was linked to colorectal adenomas in the PLCO trial (36) but not to colorectal cancer in the NIH-AARP study (8). However, these compounds can be highly correlated and it may not be possible to separate their effects.

The diets of those with high intakes of grilled and barbecued meat, as well as breads, cereals, and grains, will contribute substantially to their overall PAH exposure, as described in Kazerouni et al's (45) analysis of 200 food items for benzo(a)pyrene content. The PAH content of grains, cereals, and vegetables is not attributable to the method of cooking but is believed to be the result of crop contamination by atmospheric deposition of small particles containing PAHs, and to a lesser extent by uptake from the soil (41). Among a control population of men and women at the National Naval Medical Center, bread/cereal/grains and grilled/barbecued meat contributed 29% and 21%, respectively, to mean daily intakes of benzo(a)pyrene (45). Just as with PhIP, increased benzo(a)pyrene intake from meats has been associated with colorectal adenomas (36), but not colorectal cancer (8), in NCI studies.

Other cancers

MeIQx intake was positively associated with lung (17) and pancreatic (46) cancer in the NIH-AARP study and the PLCO trial, respectively, but not with liver (16), breast (21, 26), or prostate (19, 25, 45) cancer. DiMeIQx was positively associated with pancreatic (18, 46) and gastric cardia (15) cancer but not with lung (17, 24), liver (16), breast (21, 26), or prostate (19, 25) cancer. In contrast, both MeIQx and DiMeIQx were associated with a decreased risk of chronic lymphocytic leukemia and small lymphocytic lymphoma in the NIH-AARP study (23). In the NCI studies, PhIP was linked to an increased risk of renal cell carcinoma (14) but not to cancers of the lung (17, 24), bladder (20), pancreas (41), liver (16), breast (21, 26), or prostate (19, 25, 47). Benzo(a)pyrene intake from meats was positively associated with cancers of the kidney (14) and prostate (19) but not with those of the pancreas (18, 44), lung (17, 24), stomach (15), esophagus (15), or breast (21, 26). Data from the NCI cohorts on these byproducts formed in cooked meat are summarized in **Table 2**.

OTHER COMPOUNDS IN MEAT

Nitrite is often added to processed meat as an antibacterial agent against *Clostridium botulinum* and also to produce the characteristic red-pink color of cured meats (48). Nitrates and nitrites found in processed meats and smoked cheeses can lead to the formation of NOCs, which are produced when nitrites and nitrogen oxides react with secondary amines and *N*-alkylamides, a process that can occur endogenously (49). In 2006 the International Agency for Research on Cancer concluded that nitrate and nitrite ingested under conditions that cause endogenous nitrosation are "probable human carcinogens (2A)" (50). To explore this hypothesis, the NCI developed a detailed questionnaire

TABLE 2
A summary of the findings from NCI studies on meat-cooking–related compounds and cancer risk since 2007[1]

Meat-cooking carcinogens	Cancer risk: Increase	Decrease	Null
Heterocyclic amines			
DiMeIQx	Colorectum (8), pancreas (18, 46), gastric cardia (15)	CLL/SLL (23)	Colorectal adenoma (36), lung (17, 24), breast (21, 26), liver (16), prostate (19, 25)
MeIQx	Colorectum (8), lung (17), pancreas (46)	CLL/SLL (23)	Colorectal adenoma (36), breast (21, 26), prostate (19, 25, 47), liver (16)
PhIP	Colorectal adenoma (36), kidney (14)	—	Colorectum (8), lung (17, 24), breast (21, 26), prostate (19, 25, 47), bladder (20), pancreas (46), liver (16)
Polycyclic aromatic hydrocarbons			
Benzo(a)pyrene	Colorectal adenoma (36), kidney (14), prostate (19)	—	Colorectum (8), breast (21, 26), pancreas (18, 46), lung (17, 24), stomach (15), esophagus (15)

[1] Numbers in parentheses correspond to references for the noted association. CLL, chronic lymphocytic leukemia; DiMeIQx, 2-amino-3,4,8-trimethylimidazo(4,5-f)quinoxaline; MeIQx, 2-amino-3,8-dimethylimidazo(4,5-f)quinoxaline; NCI, National Cancer Institute; PhIP, 2-amino-1-methyl-6-phenylimidazo(4,5-b)pyridine; SLL, small lymphocytic lymphoma; —, no significant associations observed.

and database for estimating nitrate and nitrite intake from meat (51).

The formation of NOCs, however, may be altered by other dietary factors. Heme iron, of which red meats are a rich source, can act as a catalyst in the formation of NOCs in the gut (50). There is also evidence to suggest that heme iron increases cell proliferation in the mucosa (49). Heme iron intake is commonly estimated by applying a standard factor to the meat consumed (eg, 40%) or sometimes meat-specific percentages are used, such as 65% for beef, 39% for pork, and 26% for chicken or fish (51). More recently, the NCI has developed a heme iron database, which is based on measured values from meat samples cooked by different methods and to varying doneness levels (52).

Colorectal cancer

Since the WCRF/AICR report in 2007, nitrate and nitrite intakes from processed meats have been positively associated with colorectal adenomas in the PLCO trial (36) and with colorectal cancer in the NIH-AARP study (8), as has consumption of heme iron from meat (8, 36). In a meta-analysis of 5 prospective studies, the SRR for colon cancer was 1.18 (95% CI: 1.06, 1.32) for those in the highest compared with the lowest category of heme iron intake (53). Although this analysis is suggestive of a significant but modest increased risk, the measurement of heme iron intake differed in each of the studies included.

Other cancers

In the NIH-AARP study, nitrate and nitrite from processed meats were positively associated with gastric (15), esophageal (15), bladder (20), pancreatic (54), thyroid (in men only) (55), advanced prostate (19), and ovarian (56) cancer, as well as with chronic liver disease mortality (16), but not hepatocellular carcinoma (16), glioma (22), or NHL (23). In the NIH-AARP study, individuals in the highest category of heme iron intake also had an increased risk of cancers of the lung (17) and prostate (19), as well as an increased risk of chronic liver disease mortality (16), but not hepatocellular carcinoma (16), NHL (23), or breast cancer (57); heme iron intake was also not associated with breast cancer in the PLCO trial (26). The data on nitrite, nitrate, and heme iron intake from meat in the NCI cohorts are summarized in **Table 3**. No relevant meta-analyses on the relation between nitrate, nitrite, or heme iron and other cancers were identified in the literature.

DAIRY

In the 2007 WCRF/AICR report, a panel of experts reported that milk probably protects against colorectal cancer and that there is limited evidence to suggest that milk protects against bladder cancer and insufficient evidence for other cancers (1). Diets high in calcium, however, were reported to probably increase the risk of prostate cancer, although milk and dairy products showed limited evidence of increasing the risk of prostate cancer (1). Likewise, the panel concluded that limited evidence exists in support of an inverse relation between cheese intake and colorectal cancer. In general, the association between dairy foods and cancer, if it exists, tends to be observed with low-fat dairy foods but not with high-fat dairy foods.

TABLE 3
A summary of the findings from NCI studies on other meat-related compounds and cancer risk since 2007[1]

	Cancer risk		
Meat-related compounds	Increase	Decrease	Null
Heme iron	Colorectal adenoma (36), colorectum (8), lung (17), prostate (19), chronic liver disease mortality (16)	—	Breast (26, 57), liver (16), NHL (23)
Nitrate/nitrite	Colorectal adenoma (36), colorectum (8), prostate (19), thyroid (men) (55), ovarian (56), gastric (15), esophagus (15), bladder (20), pancreas (54), chronic liver disease mortality (16)	—	Liver (16), glioma (22), NHL (23)

[1] Numbers in parentheses correspond to references for the noted association. NCI, National Cancer Institute; NHL, non-Hodgkin lymphoma; —, no significant associations observed.

Colorectal cancer

In 2009 Park et al (58) reported a decreased risk of colorectal cancer for those with a high intake of dairy food [HRs (95% CIs) for the highest compared with the lowest quintile for men and women, respectively: 0.85 (0.76, 0.94) and 0.72 (0.61, 0.84)] in the NIH-AARP study. This finding is consistent with the WCRF/AICR conclusion that milk intake is probably inversely associated with colorectal cancer. A more recent meta-analysis of 19 cohort studies also found that milk and total dairy products decreased the risk of colorectal cancer (SRR per 200 g of milk intake/d: 0.91; 95% CI: 0.85, 0.94; SRR per 400 g of total dairy products/d: 0.83; 95% CI: 0.78, 0.88) but cheese did not (59). The inverse association between dairy foods and colorectal cancer may be largely attributable to the protective effect of calcium on colorectal cancer.

Other cancers

Park et al (58) observed that increasingly higher intakes of dairy foods were associated with a decreased risk of bladder cancer in men (P-trend = 0.03), although the risk estimate was not significant for the highest quintile of intake (HR: 0.86; 95% CI: 0.72, 1.02). Similarly, a meta-analysis of 16 cohort studies and 13 case-control studies found a decreased risk of bladder cancer associated with high milk intake (SRR: 0.84; 95% CI: 0.71, 0.97; P-heterogeneity < 0.001) (60). However, another meta-analysis of 2 cohort studies and 4 case-control studies on dairy consumption and bladder cancer found no association (SRR: 0.95; 95% CI: 0.71, 1.27), but significant heterogeneity was observed among the studies included (ie, the different effect sizes across studies cannot be explained by chance alone, thereby decreasing the credibility of the results; P-heterogeneity = 0.001). This finding remained the same, however, even when the cohort studies were evaluated separately (SRR: 0.95; 95% CI: 0.80, 1.13) and appropriate study homogeneity was observed (P-heterogeneity = 0.413) (61).

A high intake of dairy foods was positively associated with prostate cancer (HR: 1.06; 95% CI: 1.01, 1.12; P-trend = 0.01) in the NIH-AARP cohort, which is consistent with the findings from the 2007 WCRF/AICR report (58). A meta-analysis of 4 cohort studies showed no evidence of an association between calcium-adjusted dairy and the risk of prostate cancer (SRR: 1.06; 95% CI: 0.92, 1.22) (62). Furthermore, no association was observed between milk intake and the risk of prostate cancer in 11 homogeneous cohort studies (SRR: 1.06; 95% CI: 0.91, 1.23) (62). Dairy foods have also been hypothesized to increase the risk of ovarian cancer; however, a pooled analysis of 12 prospective cohort studies found no association (63). A recent meta-analysis by Dong et al (64) showed that total dairy food intake was inversely associated with breast cancer in 12 prospective cohort studies (SRR: 0.85; 95% CI: 0.76, 0.95; P-heterogeneity = 0.012), with stronger associations for low-fat dairy intake and for premenopausal women.

CONCLUSIONS

The epidemiologic studies reviewed in this article provide data to support a role of red and processed meat in colorectal cancer, as well as some evidence for other cancers sites, including esophagus, liver, kidney, and prostate. Variation in effects across anatomic sites may be attributed to mechanistic variability, including direct, local contact with the lumen in the case of gastrointestinal cancers; differential expression of activating/deactivating enzymes across organ sites, which may either promote or suppress carcinogenesis; and the hormone-like properties of certain heterocyclic amines, which may differentially affect target organs (13, 37, 65–67). Recent publications on dairy products and cancer risk have been generally consistent with the 2007 WCRF/AICR report, but the breadth of research in this area is far less than that for meat. With regard to cooking byproducts and other potential carcinogens, the literature is growing, and although some studies show a significant link between meat mutagens and some specific cancer types, more research in large prospective studies is needed to show consistency of findings. The question of addition or substitution of red meat by white meat requires further study, and meta-analyses of studies on white meat intake and cancer are warranted. Studies with more detailed exposure assessment are also needed, including questionnaires with detailed cooking methods and doneness levels. The development of biomarkers of intake and metabolism is necessary to fully understand the associations between these food items and cancer risk, to obtain more accurate exposure estimates, and to understand mechanisms related to carcinogenesis.

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