Meta-analysis of animal fat or animal protein intake and colorectal cancer1–4

Dominik D Alexander, Colleen A Cushing, Kimberly A Lowe, Bonnie Sceurman, and Mark A Roberts

ABSTRACT
Background: In the recent World Cancer Research Fund/American Institute for Cancer Research report of diet and cancer, it was concluded that there is limited but suggestive evidence that animal fat intake increases the risk of colorectal cancer.

Objective: To clarify this potential relation, we conducted meta-analyses across a variety of subgroups, incorporating data from additional studies.

Design: Analyses of high compared with low animal fat intakes and categorical dose-response evaluations were conducted. Subgroup analyses, consisting of evaluations by study design, sex, and tumor site were also performed.

Results: Six prospective cohort studies with comprehensive dietary assessments, contributing 1070 cases of colorectal cancer and ≈1.5 million person-years of follow-up, were identified. The summary relative risk estimate (SRRE) for these studies was 1.04 (95% CI: 0.83, 1.31; P for heterogeneity = 0.221) on the basis of high compared with low intakes. When data from case-control studies were combined with the cohort data, the resulting SRRE was 1.15 (95% CI: 0.93, 1.42) with increased variability (P for heterogeneity = 0.015). In our dose-response analysis of the cohort studies, no association between a 20-g/d increment in animal fat intake and colorectal cancer was observed (SRRE: 1.02; 95% CI: 0.95, 1.09). In a separate analysis of 3 prospective cohort studies that reported data for animal protein or meat protein, no significant association with colorectal cancer was observed (SRRE: 0.90; 95% CI: 0.70, 1.15).

Conclusion: On the basis of the results of this quantitative assessment, the available epidemiologic evidence does not appear to support an independent association between animal fat intake or animal protein intake and colorectal cancer.


INTRODUCTION

The association between total dietary fat, including fat constituents such as saturated fat, monounsaturated fat, polyunsaturated fat, and cholesterol, and risk of colorectal cancer has been evaluated in numerous epidemiologic studies. Results from these analytic investigations have generally been mixed. Whereas some studies have reported positive associations, several studies have observed null and inverse associations. In a pooled analysis of data from 13 case-control studies, risk of colorectal cancer was found to increase significantly with increasing categories of total daily energy intake (1). In the same analysis, and after adjustment for total energy intake, the authors observed no evidence of an energy-independent effect of total dietary fat or specific fat components other than cholesterol. In fact, many of the associations among men and women were in the inverse direction (1). In the Women’s Health Initiative, a randomized controlled dietary modification trial of ≈50,000 postmenopausal women, a low-fat dietary pattern intervention did not reduce the risk of colorectal neoplasia (2). Moreover, results for total dietary fat across several prospective cohort studies have not been supportive of a significant positive association with colorectal cancer (3–7), although a statistically significant 2-fold association for total fat was found in an analysis of women in the Nurses’ Health Study (8).

Animal foods and meat products contain both saturated and unsaturated fats; however, similar to analyses of total fat intake, several studies have not observed any consistent epidemiologic evidence of an association between saturated fat or polyunsaturated fat intake and risk of colorectal cancer. Although some studies (8–10) reported positive associations for consumption of saturated fat, nonsignificant associations at or near the null value or inverse associations have been observed in numerous cohort studies (3–5, 7, 11, 12) and case-control studies (1, 13, 14). For saturated fat, associations for polyunsaturated and monounsaturated fats are variable, and no consistent patterns of associations have been observed across the epidemiologic literature (1, 3, 5, 6, 8, 13–16).

Although data for total dietary fat or isolated components of fat and colorectal cancer are relatively abundant in the epidemiologic literature, considerably fewer studies have categorized and assessed animal fat as a unique analytic variable. Nevertheless, consumption of animal fat has been implicated as possibly

1 From Exponent Health Sciences, Wood Dale, IL (DDA, CAC, and MAR); Exponent Health Sciences, Washington, DC (BS); and Exponent Health Sciences, Bellevue, WA (KAL).

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4 Address reprint requests and correspondence to DD Alexander, Managing Epidemiologist Exponent Inc, 185 Hansen Court, Suite 100, Wood Dale, IL 60191. E-mail: dalexander@exponent.com.


contributing to colorectal carcinogenesis, and this hypothesis originated >4 decades ago. In a 1965 symposium (17, 18), Ernst Wynder, using international food and cancer mortality data, reported that age-adjusted mortality from colon cancer increases concurrently in countries with increasing per capita fat and oil consumption. Similarly, in a 1975 ecologic study of animal consumption, international per capita animal fat and animal protein intakes were correlated with incidence and mortality rates of colon cancer and rectal cancer among men and women (19). In the 2007 World Cancer Research Fund/American Institute for Cancer Research report (WCRF/AICR) Food, Nutrition, Physical Activity, and the Prevention of Cancer: a Global Perspective (20), it was concluded that there was a limited suggestive association with increased risk of colorectal cancer with intake of foods containing animal fat.

It has been hypothesized that the bile acids required to digest animal fat in humans may promote the development of colorectal cancer (21). Specifically, the metabolism of secondary bile acids from primary bile acids by anaerobic bacteria in the large bowel is known to be toxic to cellular systems and may cause damage to intercolonial membranes or intracellular mitochondrial function (21). In addition, it has also been hypothesized that elevated concentrations of transforming growth factor-β1 (TGF-β1), a cytokine fundamentally responsible for regulating the growth of epithelial cells in the intestine, may aid in the progression of colorectal cancer cells (22). Inflammation and animal fat have been shown to increase TGF-β1, and neoplastic cells are known to be less sensitive to the effects of this cytokine than are normal cells (22).

To clarify the potential association between animal fat intake and colorectal cancer, we conducted a meta-analysis of prospective cohort studies in which data for animal fat were available. In addition, we identified case-control studies that reported results for animal fat intake and combined data from these studies with the prospective cohort data in separate analyses. Because the primary macronutrients in the consumption of animals include protein and fat, we also conducted a separate meta-analysis of prospective cohort studies in which data categorized as animal protein or meat protein were available.

METHODS

Literature search and study identification
We conducted a MEDLINE literature search using the PubMed interface to identify articles eligible for review. Our search included all articles indexed by PubMed that were published through December 2007. We used unqualified keywords, which are searched as text words in the title, abstract, and full journal article. The unqualified terms were also matched against a MeSH (Medical Subject Headings) Translation Table, a Journals Translation, a Phrase List, and an Author Index. Our cancer literature search string included a variety of terms for colorectal cancer (eg, colon cancer, rectal cancer, and colorectal carcinoma). Our dietary search string component included terms for total dietary fat, constituents of fat, animal fat, animal protein, and meat protein. In addition to our PubMed literature search, we examined the bibliographies of review articles and quantitative assessments pertaining to dietary fat consumption and colorectal cancer in an effort to identify all available literature that may not have been identified by our database searches. All data considered for inclusion in our meta-analysis originated from peer-reviewed published articles written in English language.

For this meta-analysis, we included epidemiologic cohort and case-control studies that reported results for the association between animal fat intake and colorectal cancer, colon cancer, or rectal cancer. We excluded ecologic assessments, correlation studies, and other publications of aggregate-level analyses. In addition, experimental animal studies and mechanistic studies were excluded. To be included in the meta-analyses of animal fat intake, studies were required to report data for a variable categorized and analyzed as animal fat. Thus, we did not include data categorized as saturated or unsaturated fat because nonanimal food sources may have contributed to these exposure variables. Studies that reported results for these dietary fat variables were ascertained, however, and patterns of associations across studies were reviewed but not meta-analyzed. For inclusion in this meta-analysis, studies were also required to report point estimates (ie, rate ratios, odds ratios) and measures of variability (ie, 95% CIs) for increasing categories of animal fat intake compared with a lower intake reference category. Our primary meta-analysis consisted of 6 prospective cohort studies (3, 5, 6, 8, 11, 23), and 3 case-control studies (13, 15, 24) that reported data for animal fat were included in our sensitivity analyses. We identified a Belgian case-control study (25) that reported nonsignificant inverse associations between “fats of animal origin” and cancer of the colon and the rectum, but data from this study could not be meta-analyzed because a measure of variability was not available. Another case-control study, conducted in Thailand, reported data for a variable labeled as “animal fatty foods”; however, we did not include this study in our meta-analysis because the exposure categorization did not analytically isolate animal fat intake (26).

Because fat and protein are the primary macronutrients in animal foods, we also conducted a separate meta-analysis of studies that reported results for variables categorized as animal protein or meat protein. Our literature search for these variables yielded 3 cohort studies and 3 case-control studies that met our criteria for inclusion. Two cohort studies (4, 11) reported data for a variable labeled as meat protein, whereas one cohort study (5) analyzed animal protein as well as red meat protein. The 3 case-control studies (13, 15, 27) included in our meta-analysis all reported data for a variable categorized as animal protein. Three case-control studies (27–29) were identified that analyzed the same population; therefore, we extracted data only from the most recent publication (27). Data for animal protein from 2 additional case-control studies could not be meta-analyzed because measures of variability were not available; one of these studies (30) reported a positive association and the other study (31) reported an inverse association.

Data extraction and statistical analysis
We extracted qualitative information and quantitative data from each study that met our criteria for inclusion. Specifically, we extracted information pertaining to the year of the study, study population, geographic location of the study, methods of dietary exposure ascertainment, definitions of animal fat and animal protein, analytic comparison (ie, the exposure contrast), duration
of follow-up, number of exposed cases, relative risk estimates, 95% CIs for each incremental category of intake, and factors that were adjusted or controlled for in the analysis. Two reviewers (DDA and CAC) ascertained individual study information independently as part of our quality-control process. As mentioned previously, we extracted data for a variable categorized and analyzed as animal fat or fat from animal/meat sources, and we did not extract data for variables categorized as saturated fat or unsaturated fat. This was done to ensure homogeneity within the primary exposure variable.

Our primary meta-analyses included animal fat or meat fat intake data from 6 prospective cohort studies. We conducted analyses comparing the highest intake category with the lowest (or referent) intake category. Heterogeneity was assessed in our sensitivity analyses by generating meta-analysis models by sex and anatomic tumor site (ie, colorectal cancer and colon cancer). In addition, we conducted a meta-analysis for which data from 3 case-control studies that analyzed animal fat were combined with the prospective cohort data. We generated separate meta-analysis models that included animal protein and/or meat protein data from 3 cohort studies and 3 case-control studies.

Additionally, we conducted a meta-analysis of dose-response categorical data for animal fat and colorectal cancer across the cohort studies. For this analysis, we used the method proposed by Greenland and Longnecker (32), in which the linear intake-response slope is calculated for each study while accounting for the correlation across intake categories within a study (33). The coefficient b with its associated measure of variance for each study was calculated in a linear logistic regression model as

$$\ln \text{RR} = bx,$$

where lnRR is the natural log of the relative risk, and the coefficient b represents the change (slope) in the lnRR for each unit change in the value of X (exposure) (33). For the current analysis, we used a 20-g/d increment of animal fat intake because this exposure category best represented the actual intake categories. For an open-ended upper category of intake, the intake amount was estimated on the basis of the difference between the median or midpoint of the penultimate category and the lower bound of the highest category of intake (ie, assuming the same amplitude as the previous category).

Our data extraction and analytic procedure was compared with that of the aforementioned WCRF/AICR report. Virtually the same studies were identified; however, the WCRF/AICR only conducted a dose-response meta-analysis for animal fat in 3 cohort studies (6, 8, 11). We conducted several additional analyses, including high intakes compared with low intakes, and evaluations by sex, study design, and tumor site. In addition, we rescaled data in a grams-per-day format from all 6 prospective studies and conducted a dose-response meta-analysis. Although the same studies were identified, the WCRF/AICR did not conduct a quantitative assessment for animal protein intake because data were not suitable for a per-unit analysis. Indeed, we performed a high compared with low intake analysis and evaluations by sex and study design, and we did not conduct a dose-response analysis for animal protein.

Random-effects models were used to calculate summary relative risk estimates (SRREs), 95% CIs, and corresponding P values for heterogeneity. The estimates of the individual studies were weighted based on the inverse of the variance, which is related to the sizes of the study populations. In our “one study removed” sensitivity analyses, the relative influence of each study on the model-specific SRRE was examined by generating an SRRE based on all studies in a particular model, followed by the removal of one study at a time to compare the overall SRRE with SRREs from models that had one study removed. The presence of publication bias for studies of animal fat intake and colorectal cancer was assessed visually by examining a funnel plot measuring the SE as a function of effect size, as well as performing Begg and Mazumdar’s rank correlation test and Egger’s regression method (34). These tests for publication bias, however, are not particularly powerful in an assessment of relatively few studies, such as in the present analysis. All statistical analyses were performed by using STATA (version 10.0; StataCorp, College Station, TX), Comprehensive Meta-Analysis (version 2.2.046; Biostat, Englewood, NJ), and Episheet (35). Use of independent analytic programs allowed for the verification of calculations.

RESULTS

The characteristics of the prospective cohort studies of animal fat and colorectal cancer are summarized in Table 1. No statistically significant associations were observed in any of the animal fat and colorectal cancer meta-analyses (Table 2). The SRREs for the meta-analysis model that included data from the prospective cohort studies was 1.04 (95% CI: 0.83, 1.31; P for heterogeneity = 0.221), on the basis of comparisons between the highest and lowest categories of intake (Table 2, Figure 1). Individual study associations were between 0.83 and 1.07 in 5 of the 6 studies. In contrast, the association for the Nurses’ Health Study cohort was 1.89 (8), with the lower bound of the CI (ie, 1.13) being higher than all relative risks in the other studies. In our sensitivity analysis with this study removed from the model, the SRRE was 0.94 (95% CI: 0.76, 1.15), and the model became much more homogeneous (P for heterogeneity = 0.952). In the overall model, no single study contributed a disproportionate amount of statistical influence: the relative weights ranged from 11.29% to 19.52% (Figure 1).
Only 2 cohort studies analyzed and/or reported data specifically for men; the SRRE for these studies was 0.96 (95% CI: 0.67, 1.38; Table 2). In the meta-analysis of 4 cohort studies of women, the summary association was in the positive direction, although weakly elevated and not statistically significant (SRRE: 1.10; 95% CI: 0.77, 1.57). Four cohort studies reported data specifically for colon cancer, and 2 studies reported data for colorectal cancer. Summary associations from tumor site subgroup meta-analyses were not significantly different from unity (SRRE for colon cancer: 1.11; 95% CI: 0.81, 1.52; SRRE for colorectal cancer = 0.91; 95% CI: 0.63, 1.30; Table 2). The summary association among the 3 case-control studies (SRRE: 1.34; 95% CI: 0.90, 1.98) was stronger in magnitude than the cohort studies, but the model was more variable (P for heterogeneity = 0.009). When data from the case-control studies were combined with the cohort studies, the SRRE became 1.15 (95% CI: 0.93, 1.42) and heterogeneity was indicated (P for heterogeneity = 0.015; Table 2).

### TABLE 1
Summary of prospective cohort studies of animal fat and colorectal cancer

<table>
<thead>
<tr>
<th>Author and year</th>
<th>Study location</th>
<th>Follow-up</th>
<th>Exposure ascertainment</th>
<th>Analytic comparison</th>
<th>Relative risk estimate</th>
<th>95% CI</th>
<th>Statistical adjustment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bostick et al, 1994 (6)</td>
<td>United States (Iowa Women’s Health Study)</td>
<td>1986–1990</td>
<td>Food-frequency questionnaire (127-item)</td>
<td>Women, colon</td>
<td>&lt;24.5 g/d (49) 1.00 — Age, total energy intake, height, parity, total vitamin E intake, interaction of total vitamin E intake and age, and vitamin A intake</td>
<td>0.67, 1.38</td>
<td></td>
</tr>
<tr>
<td>Giovannucci et al, 1994 (5)</td>
<td>United States (Health Professionals Follow-Up Study)</td>
<td>1986–1992</td>
<td>Food-frequency questionnaire (131-item)</td>
<td>Men, colon</td>
<td>25 g/d (42) 1.0 — Age and total energy intake</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Goldbohm et al, 1994 (11)</td>
<td>Netherlands (Netherlands Cohort Study)</td>
<td>1986–1989</td>
<td>Food-frequency questionnaire (150-item)</td>
<td>Men and women, colon</td>
<td>8.5 g/d² (47) 1.00 — Age, sex, and dietary fiber intake</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lin et al, 2004 (3)</td>
<td>United States (Women’s Health Study)</td>
<td>1993–2003</td>
<td>Food-frequency questionnaire (131-item)</td>
<td>Women, CRC</td>
<td>10% energy (48) 1.00 — Age, random treatment assignment, BMI, history of colorectal cancer, history of polyps, physical activity, smoking, alcohol intake, postmenopausal hormone therapy, and total energy intake</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sanjoaquin et al, 2004 (23)</td>
<td>United Kingdom (Oxford Vegetarian Study)</td>
<td>1982–1999</td>
<td>Food-frequency questionnaire</td>
<td>Men and women, CRC</td>
<td>24.8 g/d (23) 1.00 — Age, sex, alcohol intake, and smoking</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Willett et al, 1990 (8)</td>
<td>United States (Nurses’ Health Study)</td>
<td>1980–1986</td>
<td>Food-frequency questionnaire (61-item)</td>
<td>Women, colon</td>
<td>&lt;39 g/d (24) 1.0 — Age and total energy intake</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

1 The number of cases is provided in parentheses. CRC, colorectal cancer.
2 Intake categories for combined sexes were not reported. These values are the average of men’s and women’s intake.
The relative risk estimates for each category of animal fat intake, as reported in the 6 cohort studies, are presented in Figure 2. Only the Nurses’ Health Study analysis by Willett et al (8) indicated an increasing pattern of relative risk with increasing consumption of animal fat. No increase in risk was found for each incremental increase of 20 g of animal fat intake per day (SRRE: 1.02; 95% CI: 0.95, 1.09). We used various combinations of other incremental intakes in our sensitivity analyses; however, the SRRE was not markedly modified.

As with our analyses of animal fat intake, none of the analyses for animal protein intake and colorectal cancer were significantly elevated (Table 2). The SRRE for the model that included 3 cohort studies that reported data for animal protein or meat protein was 0.90 (95% CI: 0.70, 1.15; P for heterogeneity = 0.554) (Table 2). When data for red meat protein from Giovannucci et al (5) were used instead of data for animal protein, the SRRE became 1.15 (95% CI: 0.84, 1.58; data not shown). Results specifically for men were reported in all 3 cohort studies, but results for women were reported in just one cohort study. The SRRE for the animal protein model that included data for men only was 0.86 (95% CI: 0.65, 1.13; P for heterogeneity = 0.753). When data for red meat protein from Giovannucci et al were substituted for the values for animal protein from the same study, the SRRE became 1.14, but was not statistically significant (95% CI: 0.79, 1.64). The SRRE for the animal protein model that included data from cohort and case-control studies was 1.05 (95% CI: 0.89, 1.22; Table 2).

We observed no asymmetry in our funnel plot assessment of publication bias among studies that analyzed animal fat consumption, although the study by Willett et al (8) was not located within the funnel (data not shown). Furthermore, Begg and Mazumdar’s correlation technique (P = 0.35) and Egger’s regression test (P = 0.42) did not indicate the presence of publication bias. This assessment, however, was based on only 6 studies.

DISCUSSION

In this meta-analysis, no consistent evidence of a positive association between consumption of animal fat and colorectal cancer was observed (Table 2). Specifically, we found no association between the highest animal fat intake category and colorectal cancer. Furthermore, none of the subgroup analyses (ie, sex, anatomic tumor site, and study design) indicated positive patterns of associations. Although the summary association among the case-control studies (ie, 1.34) was stronger in

### Table 2

<table>
<thead>
<tr>
<th>Model</th>
<th>SRRE</th>
<th>95% CI</th>
<th>P for heterogeneity</th>
</tr>
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<tbody>
<tr>
<td><strong>Animal fat</strong></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Prospective cohort studies, high compared with low intake (n = 6)</td>
<td>1.04</td>
<td>0.83, 1.31</td>
<td>0.221</td>
</tr>
<tr>
<td>Men (n = 2)</td>
<td>0.96</td>
<td>0.67, 1.38</td>
<td>0.490</td>
</tr>
<tr>
<td>Women (n = 4)</td>
<td>1.10</td>
<td>0.77, 1.57</td>
<td>0.096</td>
</tr>
<tr>
<td>Colon (n = 4)</td>
<td>1.11</td>
<td>0.81, 1.52</td>
<td>0.120</td>
</tr>
<tr>
<td>Colorectal (n = 2)</td>
<td>0.91</td>
<td>0.63, 1.30</td>
<td>0.510</td>
</tr>
<tr>
<td>Case-control studies (n = 3)</td>
<td>1.34</td>
<td>0.90, 1.98</td>
<td>0.009</td>
</tr>
<tr>
<td>Cohort and case-control studies (n = 9)</td>
<td>1.15</td>
<td>0.93, 1.42</td>
<td>0.015</td>
</tr>
<tr>
<td><strong>Prospective cohort studies, relative risk of an incremental increase of 20 g/d (n = 6)</strong></td>
<td>1.02</td>
<td>0.95, 1.09</td>
<td>0.001</td>
</tr>
<tr>
<td><strong>Animal protein</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Prospective cohort studies, high compared with low intake (n = 3)</td>
<td>0.90</td>
<td>0.70, 1.15</td>
<td>0.554</td>
</tr>
<tr>
<td>Men (n = 3)</td>
<td>0.86</td>
<td>0.65, 1.13</td>
<td>0.753</td>
</tr>
<tr>
<td>Case-control studies (n = 3)</td>
<td>1.16</td>
<td>0.94, 1.41</td>
<td>0.702</td>
</tr>
<tr>
<td>Cohort and case-control studies (n = 6)</td>
<td>1.05</td>
<td>0.89, 1.22</td>
<td>0.550</td>
</tr>
</tbody>
</table>

1. SRRE, summary relative risk estimate.
2. Meta-analysis is based on data from cohort studies.
magnitude than in the cohort studies (ie, 1.04), the association for the case-control studies was not statistically significant; the analysis was based on only 3 studies, and the model was heterogeneous. No positive trends of increasing risks with increasing animal fat intakes were observed in our intake-response meta-analysis. Specifically, we examined risk of colorectal cancer for each 10-, 20-, 30-, and 40-g/d increment in animal fat consumption and found no evidence of positive patterns of associations. Relative risk estimates for each category of animal fat intake, as reported in the individual studies, are presented in Figure 2. Visually and quantitatively, only the study by Willett et al (8), an evaluation of the Nurses’ Health cohort, showed a monotonic pattern of intake-response, ie, an increasing risk of colon cancer with increasing categories of animal fat consumption.

Dietary fat plays an important role in a nutritionally balanced diet. Fats (ie, lipids) are a very concentrated energy source, and they act as a vehicle for energy storage and form essential components of cell membranes (36). Over the past several decades, the total fat available in the US food supply has increased; during this period, the availability of specific types of dietary fat has changed (37). A comparison of the fat availability data between the first 2 decades of the 1900s with the last decade showed that fat available from vegetable sources more than tripled, whereas fat from animal sources decreased by $\approx 27\%$ (37). The downward trend in the proportion of fat from animal sources is largely due to changes in livestock feeding and fat trimming practices, resulting in the production of leaner animals (38). Despite changes over time in the amount and type of fatty acid constituents available in the public food supply, no trends of associations for colorectal cancer with respect to total dietary fat, specific fatty acid components, or sources of fat, such as that from animals, are evident across the epidemiologic literature.

The present analysis is limited to data from relatively few countries; thus, we could not assess whether associations differed by geographic study location or by cultural and/or culinary differences across populations. Different geographic locations or cultures can have distinct patterns of sources of fat in the diet, and the ratio of fatty acid composition varies by source. In addition, the amount and nature of fat from animal sources depends on the methods of rearing, processing, and preparation as well as the type of animal (20). Plant fats have higher concentrations of unsaturated fatty acids and tend to be oils, whereas animal fats consist of larger amounts of saturated fatty acids as well as

![Figure 2](image_url)

**FIGURE 2.** Dose-response for animal fat intake and colon or colorectal cancer. *Estimated grams per day are based on reported values of fat as percentage of energy. *For combined sex data, the intake in grams per day was estimated as the average of women’s and men’s intake.
unsaturated fats. Fish and marine mammals, however, are more likely to contain unsaturated fatty acids (36). It was concluded in the WCRF/AICR report on diet and cancer that there was some evidence, albeit limited, suggesting a decreased risk of colorectal cancer among consumers of fish (20). In a large systematic review of omega-3 fatty acids and cancer across studies published through 2005, no consistent evidence of a reduced risk of colorectal cancer was indicated (39). In the current evaluation, the specific origins of animal fat (eg, dairy products, red meat, processed meat, poultry, and fish) were not reported consistently across studies, thereby, precluding an assessment of animal fat and colorectal cancer by food source. Although there may be geographic or cultural disparities in the nature of consumption of plant and animal sources of dietary fat, epidemiologic investigations of individual fat components and colorectal cancer have yielded little evidence of potential positive associations (1, 3, 4, 7, 14).

Relatively few epidemiologic studies have reported findings specifically for animal protein. As with the analyses of animal fat intake, no significant associations were observed in the meta-analyses of animal protein or meat protein and colorectal cancer. Our analysis was restricted to studies that classified and analytically isolated dietary variables labeled as animal protein or meat protein. Evaluation of broader animal food categories (eg, total meat intake, red meat intake, processed meat intake, and dairy consumption) or other constituents of animal products (eg, iron, beef, pork, or poultry intake) are beyond the scope of the present analysis.

An epidemiologic assessment of dietary factors and cancer outcomes at the individual study level is a challenging undertaking. Thus, the aggregation of secondary data using meta-analysis methodology is susceptible to the same potential limitations (eg, bias, confounding) of the studies analyzed herein. In addition, a meta-analysis must use the quantitative and qualitative information pertaining to the specific factors of interest that is readily available in the individual publications. Indeed, several studies have reported data for dietary fat intake or broad categories of animal foods across the epidemiologic literature, but relatively fewer studies isolated animal fat or animal protein as analytic variables. Consequently, additional information may exist beyond that which is available to meta-analyze. For example, Chyou et al (16) reported similar mean daily animal protein intakes between colorectal cancer cases and controls; however, data were not in a format to facilitate a meta-analysis assessment. Despite this potential limitation, we were able to meta-analyze data for >1000 cases of colorectal cancer and ≈1.5 million person-years of study population follow-up across 6 prospective cohort studies. Another potential limitation was that data regarding associations by anatomic site (ie, colon, rectum) or subsite within the colon (ie, proximal or distal) are insufficient to summarize across studies. There may be disparate underlying etiologies for different anatomic sections of the colorectum, and diet-related factors may influence colorectal carcinogenesis differently depending on subsite (40). In addition, the ability to comprehensively meta-analyze other factors (eg, study design) or subgroups (eg, sex) is relatively limited because of the small number of studies.

Similar to numerous epidemiologic assessments of dietary fat and specific constituents of fat intake, the results of this meta-analysis do not support an independent association between animal fat consumption and colorectal carcinogenesis. However, it is unclear whether patterns of associations vary by factors such as anatomic tumor site within the colorectum, cultural and/or international differences in consumption patterns, or specific sources of animal fat. Thus, additional prospective cohort studies with comprehensive and detailed dietary assessments are needed to explore potential associations between these factors.

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