REVIEW

Problems with the Assessment of Dietary Fat in Prostate Cancer Studies

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The authors conducted a detailed review of studies on the association between prostate cancer and total dietary fat along with specific fatty acids. Overall, the 29 studies reporting actual dietary fat levels in grams of fat were heterogeneous, suggesting that pooling of the relative risks may be inappropriate. Heterogeneity was also seen by study design. More specifically, although the pooled estimate for prostate cancer and an increase of 45 g in total fat consumption per day was small (relative risk = 1.2), heterogeneity between studies was large, and the association was not supported by specific fatty acids. The strongest association was found among the five extremely inconsistent studies of alpha-linolenic fatty acid. The associations with advanced prostate cancer were more homogeneous and suggest a relation with total and saturated fat but none with specific fatty acids. This review highlights the inconsistent way in which total dietary fat and specific fatty acids have been measured and reported across epidemiologic studies of prostate cancer. The heterogeneity between studies was large, possibly because of the variation in the dietary instruments used and the corresponding databases (nondifferential misclassification), recall bias, differing case definitions, residual confounding, or potential selection bias in different studies.

dietary fats; meta-analysis; prostatic neoplasms; review literature

Abbreviations: FFQ, food frequency questionnaire; lnRR, natural log of the relative risk estimate.

Ecologic studies of prostate cancer, including correlational studies and migration studies, suggest diet as a potential risk factor (1, 2). Intake of fat in countries with a typically lower incidence of prostate cancer tends to be lower than in countries with higher rates (3). Cohort and case-control studies of prostate cancer and dietary fat have tried to examine the relation; inconsistent findings are reported (4).

We conducted a detailed review in an attempt to carry out a meta-analysis of studies of prostate cancer associated with aspects of dietary fat intake, including total fat, saturated fat, monounsaturated fat, and polyunsaturated fat, along with intake of linoleic acid, alpha-linolenic acid, eicosapentaenoic acid, and docosahexaenoic acid. Our initial aim was to examine both the strength and the consistency of the observed associations between aspects of dietary fat and prostate cancer. However, because of the large amount of heterogeneity we found, we explored details on the measurement of dietary fat.

MATERIALS AND METHODS

Literature search

In identifying studies that assessed the relation between dietary fat and prostate cancer, we used the following strategy. First, we searched MEDLINE automated citation
files (National Library of Medicine, Bethesda, Maryland) by using Medical Subject Headings (MeSH) headings, keywords, and text words for “prostate cancer” or “Prostatic Neoplasms” and dietary fat in articles published from 1966 through the end of October 2003. Dietary fat subject headings and keywords that we searched on included “Dietary Fats/ae, et [Adverse Effects, Etiology]”, “alpha-Linolenic Acid/”, “5,8,11,14,17-Eicosapentaenoic Acid/”, and “Docosahexaenoic Acids/”. We excluded studies of animals and of therapy after reviewing the article title and abstract. We gathered articles found through literature searches and then checked the references listed in each article for additional relevant studies. We found additional publications by using references and by searching on authors who presented preliminary reports. Non-English-language publications were included. We found several such publications and translated and abstracted relevant information. However, none of the non-English-language studies reported on specific fatty acids.

More than 100 articles were abstracted and reviewed. Many had no relevant dietary intake data, or several appeared to include populations already reported on and thus were excluded. Studies that concentrated on the percentage of fatty acids in adipose tissue or serum rather than on intake were also excluded (5–7). In addition, ecologic studies were excluded: one was a correlational study of cancers and food consumption suggesting an association of prostate cancer with milk and animal fat consumption (8); another correlated incidence and fat consumption by racial groups (9).

We reviewed studies for information on intake of fatty acids along with reports of meat, red meat, animal fat, and dairy consumption. However, studies did not define these other intake groups consistently; thus, we omitted such sub-analyses. Several such studies that we reviewed in detail were excluded from the tables presented in this review because they did not report on one or more specific fatty acids (10–27). A study that discussed adolescent consumption of total fat and meat was excluded because such consumption was not comparable to adult intake (28). A few studies reported on “unsaturated fats” rather than presenting data on monounsaturated fats and polyunsaturated fats. Thus, they were not included in our analyses.

These exclusions left 29 studies from 37 publications that reported on at least one of the following in association with prostate cancer: total fat, saturated fat, monounsaturated fat, polyunsaturated fat, linoleic acid, alpha-linolenic acid, eicosapentaenoic acid, and docosahexaenoic acid. For completeness, we included in Web table 1, in parentheses, studies that reported quartiles, quintiles, or similar categories of fat without reporting the median or range in grams of fat; however, we excluded these studies from analyses. (This information is described in the first of two supplementary tables; each is referred to as “Web table” in the text and is posted on the Journal’s website (http://aje.oupjournals.org/).) Again for completeness in Web table 1, we included studies reporting dichotomous data (noted in brackets), but they did not provide enough information to calculate a dose response for their study.

For each study and level of a factor, the natural log of the relative risk estimate (lnRR) and its variance were needed. For case-control studies, the relative risks were estimated by using odds ratios. We calculated the variances based on the reported confidence intervals, if available (29). When such information was not provided, we calculated the lnRR and its variance from the reported data. Two of three independent reviewers (L. K. D., R. E. S., and L. G. S.) abstracted data from each article. We reevaluated inconsistencies until agreement was achieved and used third-party resolution of disagreements when needed. Reviewers were blinded to the authors, journal of publication, introduction, and discussion of each article. For case-control studies that used both population-based and other types of controls, we used only those risk estimates based on the population-based controls to obtain pooled estimates for this meta-analysis. Such studies are reported under population-based studies in Web table 1.

Studies that reported results for advanced or metastatic prostate cancer were pooled separately. The authors of some studies stated that they reexamined the data by excluding either latent or local disease and found similar results, but they did not report the data. Therefore, these studies could not be included in the analyses of advanced prostate cancer.

Statistical analysis

For each study, we examined relative risks, where available, across multiple ordinal categories of the exposures. In pooling data across studies, we assumed that individual studies properly adjusted for potential confounders. If multiple relative risks were presented, we examined the ones adjusted for the greatest number of potential confounders. We also reviewed adjustment factors by study. We looked for a reduction in heterogeneity by restricting the analyses to studies that adjusted their results for energy and age. The linear regression model of Greenland and Longnecker (30) was used to compute study-specific slopes (linear betas) from the correlated log relative risk estimates across exposure categories. Pooled estimates of risk were then obtained from random-effects models applied to the study-specific slopes (31). As suggested by Greenland and Longnecker, for grams of fat we used the midpoint for each category range in calculating an overall linear beta for each study. Iterations required for estimating the linear beta for each study were performed by using S-Plus software (Insightful Corporation, Seattle, Washington).

The linear model was most appropriate when categories of fats were reported in grams. In such analyses, the linear model was based on a unit change of a gram. Each category was weighted by the mean number of grams of fat per day. However, many studies reported relative risks associated with differences in quartiles or quintiles of fat only. These relative risks were excluded from our analyses. Data were stratified into subgroups based on study design (cohort or case-control) and type of controls (population-based, non-population-based controls).

Heterogeneity

Statistical tests of heterogeneity were performed by using Cochran’s chi-square test ($Q$) to assess the consistency of associations (29, 30, 32):
Homogeneity was assessed overall and by study design. To quantify the extent of heterogeneity in this collection of studies, we estimated the between-study variance (33). $I^2$ was calculated as the relative difference between the $Q$ statistic and its expected value $(k – 1)$ in the absence of heterogeneity. Thus, the $I^2$ statistic describes the proportion of total variation in estimates of the relative risk due to the heterogeneity between studies (33). Homogeneous studies should have an $I^2$ value of 0.

**RESULTS**

Web table 1 describes 29 independent studies from 37 publications reporting actual dietary fat levels in grams of fat in association with prostate cancer (28, 34–69). Of the five cohort studies that included information relevant to these analyses, only four reported on total fat intake. Of the relevant case-control studies, 13 used population-based controls and 10 used other types, including cancer, benign prostatic hyperplasia, and other hospital-based controls. Population-based controls included neighborhood controls, community controls, and general population-based controls. Web table 1 describes the study design, number of study subjects, location of the study population, measures of dietary fat, and adjustment for potential confounders. Reported measurements of fat intake are listed in parentheses or brackets for those studies not reporting usable information on grams of fat (e.g., quartiles). Web table 1 also lists the confounders reported to be adjusted for in each study. We considered reports of adjustment for calories, energy, or total energy as adjustment for energy intake.

Web table 2 describes the dietary instrument used to assess fat. The only standard food frequency questionnaires (FFQs) we encountered in our review were two available from the United States—the Willett FFQ (70) and the Block FFQ (71, 72)—and one from Canada—the Jain et al. FFQ (73). Both the Willett FFQ and the Block FFQ were designed in the 1980s, with 61 and 109 items, respectively. The Canadian FFQ, designed by the National Cancer Institute of Canada, had 200 items, more than most other FFQs. Only two of the 29 studies (44, 53, 54) used a modified Willett FFQ and validated the modifications. One study (74) reported modifying a combination of the Willett and the Block FFQs but did not validate the modification. Three studies (34, 36, 37) used the validated Canadian FFQ. An additional study (46, 47) used a modification of the Canadian FFQ but did not validate it. The remaining studies varied in how they ascertained dietary fat, ranging from asking about 14 food items to 276 items. Three studies (35, 43, 55) did not report the number of items, and another study (38) reported measuring 20 food groups.

We examined two models: 1) a linear estimate across quartiles or quintiles (not shown) and 2) an estimate across grams of fat per day in studies reporting such information (table 1). Slightly more than half of the studies specified the cutpoints used for quartiles, quintiles, or similar categories. In 23 studies, data were presented for total fat. Only 15 of these studies reported the range or midpoint for each category in grams, five reported quartiles only (37, 38, 40, 46, 69), and three others reported data that could not be used to calculate a linear trend (43, 49, 55). Similarly, the range or midpoint of grams of fat was reported in 14 of 18 studies that included saturated fat analyses, whereas one study reported quartiles (46) and three others contained unusable data (52, 55, 58). For monounsaturated fat, nine of 13 studies were used (one reported quartiles (46) and three were unusable (52, 58, 63, 64)). Eight of 11 studies reporting on polyunsaturated fat were pooled (one reported quartiles (46) and two were unusable (52, 58)). Studies pooled across categories or quartiles were generally heterogeneous ($p < 0.05$); thus, relative risks are not reported on these subsets. No clear pattern was seen across study designs when we examined quartiles without ranges.

Table 1 presents pooled relative risks for different measurements of dietary fat intake in grams, including total fat, saturated fat, monounsaturated fat, and polyunsaturated fat, by study design along with n-3 and n-6 fatty acids. This table also describes the pooled relative risks and the large amount of heterogeneity seen, making pooling of the data questionable. As described previously in this review, heterogeneity was examined through testing and by presenting the percentage of the variation between studies ($I^2$). The between-study variation ranged from 0 percent to 88 percent. The overall pooled estimates for total fat based on categories of grams of fat per day were significant. However, these data were heterogeneous and not consistent by study design. No association was found across four cohort studies reporting total fat intake, three of which controlled for age and energy intake. The strongest association for total fat was seen in the studies with hospital controls. No associations with saturated fat or polyunsaturated fat were suggested. An increased risk of prostate cancer with increasing monounsaturated fat intake was seen in three cohort studies but was not supported in other study designs. An unexplained, increased risk with alpha-linolenic acid fatty acid intake was seen in five heterogeneous studies (table 1). Increased risk was also suggested for eicosapentaenoic acid.

In an attempt to reduce heterogeneity, we reanalyzed the data from only those studies adjusting for energy intake. Doing so showed reduced-heterogeneity $p$ values and increased or decreased variation ($I^2$). All of the studies of linoleic acid, alpha-linolenic acid, eicosapentaenoic acid, and docosahexaenoic acid reported age- and energy-adjusted relative risks.

A few studies reported relative risks for fatty acids and advanced prostate cancer as well. When data for advanced prostate cancer were pooled, similar associations were seen with the exception of a significant increased relative risk for saturated fat and the removal of a positive association with alpha-linolenic acid (table 1 and figure 1). These associations were more homogeneous than those for all-stage cancers. Advanced prostate cancer was associated with intake of total and saturated fat but not with polyunsaturated fat, linoleic acid, alpha-linolenic acid, eicosapentaenoic acid, or docosahexaenoic acid fatty acids. We also examined total
### TABLE 1. Pooled meta-analyses estimates of the effects of dietary fat on the relative risk of prostate cancer

| Type of fat and types of studies combined for analysis | Unit change in fat | No. of studies (no. of groups*) | RR† | 95% CI† | Between-study variation (P²) (%) | Heterogeneity p value | No. of studies (no. of groups) | RR† | 95% CI | Between-study variation (P²) (%) | Heterogeneity p value |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Total fat | All 45 g/day | 15 (17) | 1.17 | 1.10, 1.25 | 56 | 0.003 | 10 (10) | 1.11 | 1.01, 1.22 | 58 | 0.01 |
| Cohort | 4 (4) | 1.00 | 0.86, 1.16 | 0 | 0.55 | 3 (3) | 1.04 | 0.87, 1.24 | 0 | 0.46 |
| Population case-control | 8 (9) | 1.20 | 1.11, 1.30 | 67 | 0.002 | 5 (5) | 1.10 | 0.96, 1.27 | 76 | 0.002 |
| Hospital case-control | 3 (4) | 1.26 | 1.07, 1.50 | 25 | 0.26 | 2 (2) | 1.21 | 1.01, 1.45 | 43 | 0.19 |
| Saturated fat | All 25 g/day | 14 (15) | 1.09 | 0.99, 1.20 | 65 | <0.001 | 10 (10) | 1.03 | 0.89, 1.19 | 65 | 0.002 |
| Cohort | 4 (4) | 1.00 | 0.87, 1.16 | 0 | 0.81 | 3 (3) | 1.03 | 0.73, 1.46 | 0 | 0.63 |
| Population case-control | 8 (9) | 1.19 | 1.03, 1.36 | 78 | <0.001 | 5 (5) | 1.02 | 0.85, 1.24 | 83 | <0.001 |
| Hospital case-control | 2 (2) | 1.04 | 0.77, 1.40 | 15 | 0.28 | All adjusted for energy |
| Monounsaturated fat | All 20 g/day | 9 (10) | 1.04 | 0.94, 1.15 | 30 | 0.17 | 8 (8) | 1.01 | 0.90, 1.13 | 27 | 0.21 |
| Cohort | 3 (3) | 1.61 | 1.00, 2.59 | 0 | 0.41 | All adjusted for energy |
| Population case-control | 5 (6) | 1.01 | 0.89, 1.15 | 35 | 0.18 | 4 (4) | 0.96 | 0.82, 1.11 | 18 | 0.30 |
| Hospital case-control | 1 (1) | 1.02 | 0.85, 1.23 | All adjusted for energy |
| Polyunsaturated fat | All 20 g/day | 8 (9) | 1.06 | 0.88, 1.27 | 13 | 0.32 | 7 (7) | 1.00 | 0.82, 1.22 | 0 | 0.62 |
| Cohort | 2 (2) | 0.93 | 0.69, 1.26 | 24 | 0.25 | All adjusted for energy |
| Population case-control | 5 (6) | 1.20 | 0.94, 1.54 | 0 | 0.45 | 4 (4) | 1.12 | 0.85, 1.49 | 0 | 0.79 |
| Hospital case-control | 1 (1) | 0.62 | 0.27, 1.44 | All adjusted for energy |
| Linoleic acid | All 10 g/day | 5 (5) | 0.96 | 0.85, 1.09 | 21 | 0.39 | All adjusted for energy |
| Alpha-linolenic acid | All 1.5 g/day | 5 (5) | 1.26 | 1.10, 1.45 | 88 | <0.001 | All adjusted for energy |
| Eicosapentaenoic acid | All 0.5 g/day | 2 (2) | 1.11 | 1.00, 1.24 | 0 | 0.55 | All adjusted for energy |
| Docosahexaenoic acid | All 0.5 g/day | 2 (2) | 1.05 | 0.99, 1.11 | 0 | 0.76 | All adjusted for energy |
| Advanced cancers only | Total fat | All 45 g/day | 5 (5) | 1.12 | 1.01, 1.25 | 0 | 0.97 | 4 (4) | 1.14 | 0.97, 1.34 | 0 | 0.92 |
| Saturated fat | All 25 g/day | 5 (5) | 1.38 | 1.13, 1.70 | 43 | 0.14 | 4 (4) | 1.13 | 0.88, 1.46 | 0 | 0.91 |
| Monounsaturated fat | All 20 g/day | 4 (4) | 1.25 | 0.97, 1.62 | 0 | 0.96 | All adjusted for energy |
| Polyunsaturated fat | All 20 g/day | 2 (2) | 0.96 | 0.66, 1.38 | 0 | 0.97 | All adjusted for energy |
| Linoleic acid | All 10 g/day | 4 (4) | 0.93 | 0.78, 1.11 | 53 | 0.09 | All adjusted for energy |
| Alpha-linolenic acid | All 1.5 g/day | 4 (4) | 1.03 | 0.77, 1.38 | 74 | 0.01 | All adjusted for energy |
| Eicosapentaenoic acid | All 0.5 g/day | 1 (1) | 1.05 | 0.92, 1.21 | All adjusted for energy |
| Docosahexaenoic acid | All 0.5 g/day | 2 (2) | 0.99 | 0.95, 1.04 | 49 | 0.16 | All adjusted for energy |

* Some studies reported multiple groups, usually by race.
† RR, relative risk estimates based on a change in grams of fat per day; CI, confidence interval.
‡ The percentage variation due to heterogeneity between studies.
fat stratified by study location (United States, Canada, Asia, or Europe); few differences were seen except for a much larger linear relative risk for a 45-g change in fat per day in the one Asian study that reported on total fat (57). However, heterogeneity remained when this study was excluded. This study had similarly high relative risks for saturated fat.

**DISCUSSION**

This review found wide heterogeneity in the relative risk estimates describing the association between prostate cancer and intake of dietary fat. More specifically, although the pooled estimates suggested a small, significant association between prostate cancer and an increase of 45 g in total fat consumption per day, the heterogeneity between studies was large, and the association was not supported by specific fatty acids. No clear patterns across related types of fatty acid intake were found. The strongest association was for alpha-linolenic acid, but the five studies that examined this fatty acid were extremely inconsistent. However, few studies reported on specific fatty acids (linoleic acid, alpha-linolenic acid, eicosapentaenoic acid, and docosahexaenoic acid).
Results for alpha-linolenic, eicosapentaenoic acid, and docosahexaenoic acid suggested that such fatty acids are risk factors rather than protective. Variations by study design did not highlight clear bias by study design method used. When heterogeneity was not significant, typically only a few studies were available. Nevertheless, the associations with advanced prostate cancer were more homogeneous and suggested an association with total and saturated fat and no associations with polyunsaturated fat, linoleic acid, alpha-linolenic acid, eicosapentaenoic acid, or docosahexaenoic acid fatty acids. These conditions imply that pooled relative risks should be interpreted with great caution and that dietary fat has been measured or reported differently across studies.

Web table 1 describes the adjustment factors in each study. Confounders varied across studies, as might be expected. It is unclear to what extent residual confounding in studies may have on the between-study variation (heterogeneity). However, studies may have examined other potential confounders but not found them to affect the data. Overall, pooled analyses of the most extensively adjusted relative risks from each study assume that the original investigators understood how to conduct their analyses and properly adjusted their study estimates for confounders. Without the full, original data sets, we could not examine all available variables in each original study. We did conduct additional analyses by pooling only those studies that adjusted for energy intake, which are reported in table 1. These analyses tended to have similar pooled relative risks with wider confidence intervals. This process reduced heterogeneity slightly in some analyses and increased it slightly in others (because of a smaller number of pooled studies).

In general, these analyses highlight the inconsistent way in which dietary fat intake has been measured and reported across studies. Many studies reported data only in quartiles without providing the cutpoints of the quartiles, making the pooling of such data uninterruptible. Some heterogeneity may be due to the use of different cutpoints for quartiles. However, the heterogeneity persisted when we pooled across studies that did report levels of fat consumption. Studies failed to include details related to their dietary assessment. Only 8 percent reported pretesting their FFQ, and only 32 percent reported a validated FFQ (75). Quality control measures were described in 19 percent of the studies, and 22 percent did not report the number of food items surveyed.

The large heterogeneity observed between studies may be due to the variation in dietary instruments used and their corresponding databases (Web table 2). An important consideration in meta-analyses involving dietary intake is the type of instrument used to collect data. Food frequency instruments vary in the types of nutrients emphasized as a result of the kinds of foods listed, instructions given to respondents about estimating serving sizes, definitions of food groups, nutrients listed in databases, format for completing the questionnaire (self-administered or clinician administered), methodology for food selection, and methodology for quality control (method of contacting the respondent to resolve items left blank). Because of these factors, comparison is difficult in a meta-analysis of diet studies.

Only two studies (44, 53, 54) used a modified Willett (70) questionnaire. None used Block’s (71, 72) questionnaire. One study reported using a combined Willett and Block survey (74), and four (34, 36, 37, 46) used a modified Canadian diet questionnaire (73). The Block and Willett FFQs have similar attributes in that both inquire about food and supplement intake, both use scannable forms, and both have a database. They differ in the nutrient values they provide and in the way in which the foods and nutrients are chosen. Block et al. (71, 72) chose foods to include by referring to National Health and Nutrition Examination Survey consumption figures, whereas Willett et al. (70) chose foods most likely to distinguish high and low consumers by using regression methods from their own data. Willett et al. describe their questionnaire as semiquantitative, which means that portion sizes are stated but subjects have no way to indicate that they consume more or less than the stated amount, only how often they consume this amount. The Block FFQ asks whether the subject had a small, medium, or large serving or allows the subject to choose among three stated portion sizes. Servings sizes offered by the Block FFQ were determined by referring to intake data from the National Health and Nutrition Examination Survey. The remaining studies varied in how they ascertained dietary fat, ranging from 14 food items to 276 items.

Often, FFQs are designed to focus on specific nutrients. Controversy exists concerning the importance of collecting additional data on portion sizes. The methodology for food selection can vary from compiling a food list to starting with a long list of foods that are potentially important nutrient sources and then systematically reducing the list. Even in those studies using similar methods to select foods, we found variations. Food group definitions often vary from one questionnaire to another. For example, meat may mean red meat, red meat and poultry, or red meat, poultry, and fish. The nutrients in the database associated with the questionnaire also varied and thus would result in differences in overall nutrient intakes. A questionnaire may be formatted to be totally self-administered, or a clinician may ask each question in person, potentially resulting in different data. The level of quality control when questionnaire responses are reviewed can have major implications in terms of the validity of dietary data. Some studies reviewed for this meta-analysis included an in-person interview, while other questionnaires were mailed to participants. In some instances, instruments included questions about fats added to foods. While many foreign studies used instruments especially formulated for dietary intakes in those countries, ensuring that ethnic high-fat foods were included, these instruments tended not to be validated and may have contributed to the variation among studies. Additional problems with the studies reviewed included an insufficient definition of foods in certain categories.

In addition to dietary measurement, other factors are likely to have contributed to the heterogeneity seen between studies. When the data were stratified by study design, minimal heterogeneity was observed in the few cohort studies. In the population-based case-control studies, we found a large amount of heterogeneity. The heterogeneity may reflect different biases related to study design, including
recall bias in case-control studies, overall reporting bias or nondifferential misclassification of exposures, or potential selection bias in different studies. Studies differed in the assumed lag times between exposure and disease, or they assumed a constant diet over time. Furthermore, the case groups examined were likely different because of the variety of age ranges studied, the inconsistency of including cancer detected via prostate-specific antigen versus non-prostate-specific antigen, and the inconsistent definition of localized or latent cancer. Some studies clearly described their case groups whereas others did not, making it unclear whether all stages of disease were included in all studies. There may also have been residual confounding due to uncontrolled factors in some studies. However, since little is known about risk factors for prostate cancer, it is uncertain which factors may be related to both prostate cancer and dietary fat. Almost all studies adjusted for age. Many studies adjusted for the positive association between energy intake and fat intake, generally distorting the results toward the null value. It is debated whether energy intake is truly independent of dietary fat intake or whether it may be adjusting some of the “true” fat association away. Overall, general misclassification of dietary fat would bias these results toward the null value, whereas confounding, recall bias, and selection bias could bias pooled estimates in either direction. Thus, these associations between dietary fat and prostate cancer remain unclear.

The role of dietary fat in prostate cancer remains controversial. As discussed above, this controversy reflects inconsistencies in the assessment of dietary fat intake (using unvalidated, retrospective FFQs), case definitions, and adjustment for confounding factors. The tendency to determine fat intake in terms of saturated fat alone has led to an inability to identify whether the clear role of specific fats, namely, polyunsaturated fatty acids observed in experimental studies of tumor growth, is translatable to the clinical situation. The many problems encountered when determining dietary intake by using survey methods have prompted the use of biomarkers. Biomarkers provide quantitative measures of the relative availability of individual fats irrespective of food source, reflecting an integrated measure of diet over time and the genetic factors that may influence metabolism of particular fatty acids. Plasma, erythrocyte membranes, and subcutaneous adipose tissue have all been used as biomarkers. Biomarkers do not provide a quantitative estimate of intake; rather, they provide only relative proportions of the various fatty acids stored. Adipose tissue fatty acid content would appear to be a long-term marker of dietary intake of fatty acid composition; however, only the relative proportions of fatty acids can be determined (76–81). The prostate is more likely to be affected by fat stored in tissue than by fat intake.

It is imperative that journals describing dietary data include as reviewers experts in the field of nutrition. Journals and reviewers should require investigators to accurately describe the design of their dietary assessment instruments, any efforts at validation, and the development of their food composition databases. A better description of the dietary assessment may help eliminate the pitfalls identified in this meta-analysis.

In conclusion, although the pooled estimates suggest a small, significant association between prostate cancer and total fat consumption, the heterogeneity between studies was large, and the association was not supported by specific fatty acids. The strongest association was seen for alpha-linolenic acid; however, the five studies that examined this fatty acid were extremely inconsistent. Only two studies examined either eicosapentaenoic acid or docosahexaenoic acid. The associations with advanced prostate cancer were more homogeneous and suggest an association with total and saturated fat but no associations with polyunsaturated fat, linoleic acid, alpha-linolenic acid, eicosapentaenoic acid, or docosahexaenoic acid fatty acids. These associations between dietary fatty acids and prostate cancer remain unclear.

Consistency in dietary instruments and their corresponding nutrient databases is lacking. Lack of detail reported in publications also adds to the confusion. Future studies of prostate cancer and fatty acids should use well-described and validated instruments. When appropriate biologic markers are available, studies of biologic markers should eliminate potential recall or reporting bias possible in case-control studies dependent on reporting of exposures in the distant past and on variations in dietary instruments.

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