Dietary fats and cancer

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The present review addresses the evidence for a possible link between dietary fat and cancer. International comparisons suggest that a high-fat diet may increase cancer risk, and this hypothesis is supported by animal experiments. However, epidemiological studies within populations show little or inconsistent associations. Taken together, the available evidence for a relation between dietary fat and cancer is weak.

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Abbreviations

CLA	conjugated linoleic acid
COMA	Committee on Medical Aspects of Food and Nutrition Policy (UK)
AICR	American Institute for Cancer Research
WCRF	World Cancer Research Fund

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Introduction

The present review addresses the existing evidence on the possible link between dietary fat and cancer, with emphasis on epidemiological studies of cancers of the breast, colorectum and prostate.

The evidence for a relation between fat and cancer is derived mainly from international comparisons between populations, from animal experiments and from epidemiological studies within populations. There are only very few data from randomized clinical trials on dietary fat and cancer. When judging the possible relation between fat and cancer, evidence from some study types should be given more emphasis than that from others. Population comparisons have major limitations, and evidence from such studies can at best be seen as suggestive. More weight should be given to evidence from epidemiological studies within populations, in particular prospective cohort studies. Meta-analyses and pooled analyses can help to consolidate the findings from such studies. Experimental studies in animal models can support human evidence, but by themselves can only suggest a link. Thus, in the absence of direct data from randomized controlled trials, most reliance must be placed on aggregate evidence from high-quality cohort studies.

Diet is an important lifestyle determinant of common cancers; it has been estimated that dietary factors may account for up to 80% of cancers of the breast, large bowel and prostate [1]. The 1982 National Academy of Sciences report on diet and health [2] concluded that, of all of the dietary components it reviewed, the evidence was most suggestive for a causal relationship between dietary fat and cancer. However, much research on this issue has been done since then. In 1997, the World Cancer Research Fund (WCRF) and the American Institute for Cancer Research (AICR) published a comprehensive report [3], in which an expert panel judged the evidence for relationships between diet and cancers, including dietary fats (Table 1). In the same year, a Working Group of the UK Committee on Medical Aspects of Food and Nutrition Policy (COMA) published a more concise report on nutritional aspects of cancer [4]. The WCRF/AICR report [3] denoted four levels of the strength of evidence of causal relationships: convincing, probable, possible and insufficient. None of the evidence for links between total fat or classes of fats and cancers was judged to be convincing (conclusive) or probable (likely), indicating that none of the evidence for any of the cancers was regarded as providing a

Table 1. Relationships between dietary fats and cancers

Cancer site	Total fat	Saturated/animal fat	Monounsaturated fat	Polyunsaturated/ vegetable fat	n-3 fatty acids/fish
Breast	↑ (?) a	↑ (?)	= (?)	= (?)	↓ (??)
Colon and rectum	↑ (?)	↑ (?)	X	X	0 ?
Prostate	↑ (?)	↑ (?)	X	X	X
Lung	↑ (?)	↑ (?)	X	X	X
Ovary	↑ (??)	↑ (??)	X	X	↓ (??)
Endometrium	↑ (??)	↑ (?)	X	X	–
Bladder	↑ (??)	X	–	–	–

Relationships between dietary fats and cancers as judged in 1997 by an expert panel for the World Cancer Research Fund and the American Institute for Cancer Research [3]. One question mark (?) indicates 'possible', meaning that a causal relationship may exist, but that the evidence is not strong enough to make recommendations. Two question marks (??) indicate 'insufficient', meaning that there is suggestive evidence, but that it is too scanty or imbalanced. None of the relationships was judged by this panel as 'probable' (likely) or 'convincing' (conclusive). [a]Not in accord with the conclusion by this Panel, the UK Working Group of the Committee on Medical Aspects of Food and Nutrition Policy [4] concluded that 'there is moderate evidence to conclude that total fat intake does not influence the risk of breast cancer independently of body mass index.' ↑, increases risk; =, no relationship; ↓, decreases risk; X, no judgement possible.

sufficiently strong basis for dietary recommendations. Similarly, the COMA working group [4] concluded that the evidence that higher fat intake increases cancer risk is insufficient or weak, and that no specific recommendation on total fat intake should be made.

Breast cancer

Fat intake is the most studied and the most debated dietary component in relation to breast cancer risk. An often proposed mechanism is that dietary fat raises breast cancer risk by raising blood levels of oestrogens and related hormones [5].

Early international correlation studies [6] suggested that high intakes of total fat and of animal or saturated fat may increase the risk of breast cancer. These findings were supported by animal studies [7], which found that saturated and n-6 polyunsaturated fats promoted mammary tumour growth in some, but not all models. However, epidemiological studies within populations generally do not support this hypothesis. Although case–control studies produced somewhat inconsistent results [8,9], most prospective cohort studies [10] do not show a relationship for total fat and saturated fat. The most recent epidemiological analyses [11•,12–14] also showed no strong associations between intake of total fat breast cancer risk (Table 2). A recent case–control study [15] suggested that total fat intake could affect risk in populations on low-fat diets in Indonesia. However, large prospective studies [10,11•] have found no lower risk among women with very-low-fat diets (20% of energy or less) in Western populations.

The evidence for monounsaturated fat is largely the same as for total fat and saturated fat. Nevertheless, there are some suggestions from animal experiments [22,23] and epidemiological studies [24,25] that high intakes of olive oil may decrease breast cancer risk, independently of its high monounsaturated fat content. Monounsaturated trans-fatty acids in adipose tissue were positively associated with breast cancer risk in one case–control study [26], but not in two others [27,28]. In recent prospective analyses, intake of trans-fatty acids was either weakly inversely [11•] or positively [13] associated with breast cancer risk (Table 2). Thus, there is no consistent evidence for a role of trans-fatty acids in breast cancer.

A high intake of n-6 polyunsaturated fatty acids and a low intake of n-3 polyunsaturated fatty acids increase breast cancer in certain animal models [29]. However, epidemiological studies [30–32] do not show associations between polyunsaturated fat or linoleic acid (C18:2n-6) and breast cancer in humans. N-3 fatty acids have barely been studied, but several case–control studies and a few prospective cohort studies reported on fish intake, the dietary source of very-long-chain n-3 fatty acids (mainly C20:5n-3 and C22:6n-3). Most of those studies did not find significant associations [32]. In the European Community Study on Antioxidants, Myocardial Infarction, and Breast Cancer (EURAMIC) case–control study [33], the ratio of n-3 to n-6 fatty acids in adipose tissue, but not n-3 fatty acids or n-6 fatty acids alone, was associated with a lower breast cancer risk. Another case–control study [34] found an inverse association for α-linolenic acid (C18:3n-3), but not for very-long-chain n-3 fatty acids in breast tissue. Conjugated linoleic acid (CLA) is a trans-fatty acid (cis-9,trans-11,C18:2 and trans-10,cis-12C18:2) from dairy and beef fat, for which anticarcinogenic properties have been suggested by experimental studies [35]. A preliminary report from a French case–control study [36] suggests a protective effect of CLA in humans, whereas The Netherlands Cohort Study [13] found increased breast cancer risk with higher CLA intake (Table 2). Thus, the epidemiological evidence does not support any important association between intake of specific polyunsaturated fatty acids and breast cancer risk.

Table 2. Recent analyses of relationships between dietary fats and cancers in individually based epidemiological studies

Reference; study type	Number of cases and population	End-point	Total fat[a]	Saturated or animal fat[a]	Unsaturated fat[a]	Comments
[11•]; prospective cohort	2956 US Nurses	Breast cancer	0.96	Saturated: 0.94 (NS)[b] Animal: 0.98 (NS)[b]	Vegetable: 0.97 (NS)[b] Polyunsaturated: 0.91 (NS)[b] Monounsaturated: 0.94 (NS)[b] Trans-unsaturated: 0.92[b] N-3 unsaturated: 1.09[b]	Overall trend was higher risk with lower fat intake (P = 0.03)
[12]; prospective cohort	996 US women	Breast cancer	1.07 (NS)	1.12 (NS)	1.13 (NS)	Significant association for total and unsaturated fat in women with no history of benign breast disease
[13]; prospective cohort	939 Dutch women	Breast cancer	Not related	1.40 (NS)	Monounsaturated: 0.61 Cis-unsaturated: 0.79 Trans-unsaturated: 1.30 CLA: 1.24	
[14]; case–control	2569 Italian women	Breast cancer		1.16	Monounsaturated: 0.99 (NS) Polyunsaturated: 0.72	
[15]; case–control	226 Indonesian women	Breast cancer	8.47			
[14]; case–control	1953 Italian persons	Colorectal cancer		1.12 (NS)	Monounsaturated: 1.00 Polyunsaturated: 0.89 (NS)	
[16]; prospective cohort	642 Dutch men	Prostate cancer	1.10 (NS)	1.19 (NS)	Oleic acid: 1.38 (NS) Linoleic acid: 0.78 (NS) Trans-unsaturated: 0.99 (NS) C18:3n-3: 0.76 (NS) Other n-3: no association	
[17]; case–control	932 US men: Blacks (n = 449) Whites (n = 483)	Prostate cancer	1.4 1.9 1.1 (NS)	1.5 1.9 1.2 (NS)		
[18]; case–control	133 Chinese men	Prostate cancer	3.6	2.9	3.3	
[19]; case–control	217 men from Uruguay	Prostate cancer	1.33 (NS)	1.44 (NS)	Monounsaturated: 1.38 (NS) Linoleic acid: 0.71 (NS) α-Linolenic: 1.91	Association with C18:3 for animal as well as vegetable sources
[20]; prospective cohort	139 Women from Iowa, USA	Epithelial ovarian cancer	0.80 (NS)	Saturated: 1.17 (NS) Animal: 0.98 (NS)	Monounsaturated: 0.65 (NS) Polyunsaturated: 0.63 (NS) Vegetable: 0.75 (NS)	
[21•]; prospective cohort	3190 Male US health professionals	Basal cell carcinoma	0.80	1.03 (NS)	Monounsaturated: 0.79 Polyunsaturated: 1.07 (NS) N-3 unsaturated: 1.13	Association with n-3 was weaker after exclusion of nonwhites

[a]Figures are relative risks (odds ratios) for highest versus lowest quintile or quartile of intake. [b]Relative risks for a 5%-of-energy increase in intake. CLA, conjugated linoleic acid; NS, not significant.

The WCRF/AICR report [3] concluded that breast cancer risk possibly increases with higher intakes of total and saturated fat, but not with increased monounsaturated and polyunsaturated fat intake (Table 1). This conclusion was partly based on the idea that high-fat diets may increase obesity, and in this way raise the risk of breast cancer. Although obesity and weight gain are risk factors for breast cancer, such an indirect mechanism can certainly be questioned because there is no strong evidence that the percentage of dietary energy from fat causes obesity [37]. The COMA working group [4] concluded that there is now moderate evidence to conclude that total fat intake in adult life does not influence the risk of breast cancer independently of body mass index. This conclusion is in my view more appropriate than that of the WCRF/AICR.

A few large clinical trials on diet and breast cancer are underway, of which the Women's Health Initiative [38] is the largest. However, it is doubtful whether these trials will be able to detect an independent effect of dietary fat [39]. Taken together, existing data provide little support for the notion that reducing fat intake, even to levels as low as 20% of energy, reduces the risk of breast cancer.

Colorectal cancer

The hypothesis that high fat intake may be linked to colorectal cancer has, like that for breast cancer, a long history. The most proposed mechanism is that dietary fat enhances secretion of primary bile acids, which are converted to more cytotoxic secondary and tertiary bile acids by colonic bacteria.

Differences in colorectal cancer incidence among different populations are highly correlated with per-capita consumptions of fat, in particular of saturated fat [6]. Animal experiments generally support a link between

dietary fat and colorectal cancer [40]. Colorectal cancer rates sharply increase in people who migrate from low-incidence areas to countries with a high fat consumption [41].

Although case–control and cohort studies quite consistently show that a low intake of vegetables, low level of physical activity, and a high intake of red meat and alcohol increase colorectal cancer risk, the evidence from these types of study for a role of fat intake is much weaker [3]. Case–control studies have often reported a positive association between colorectal cancer risk and total dietary fat, but in most of those studies the effect was not distinguished from that of energy intake, an important confounder. A combined analysis of 13 case–control studies that adjusted for energy intake [42] showed no association between intake of total fat or saturated fat and colorectal cancer risk. In the individual case-control studies that showed a positive association between fat intake and colon cancer risk [43], the relation was generally attributable to animal or saturated fat, and not to unsaturated fats. Most prospective cohort studies did not find significant associations between total fat and colorectal cancer risk, but the results are less consistent for saturated and animal fats. One early study [44] showed a lower risk with high saturated fat intake among Japanese men in Hawaii, whereas the Nurses Health Study [45] showed a higher risk in women with a high intake of animal fat. Results from studies on diet and the risk of colonic adenomatous polyps [43] (which are well-established precursors of colon cancer) are in accord with findings from prospective cohort studies.

In comparison with breast cancer, few epidemiological studies have addressed the link between colorectal cancer and monounsaturated or polyunsaturated fat, and hardly any epidemiological data exist for specific types of fatty acids. Studies on monounsaturated fatty acids [3,43] found no or inconsistent associations, and studies on polyunsaturated fat or linoleic acid [30,31] showed essentially no association. Some of the prospective cohort studies [45,46] and a number of case–control studies [43,47] reported weak inverse associations for colorectal cancer and fish intake, but taken together there is not much evidence for a possible protective effect of n-3 fatty acids [3].

There are only a few recent epidemiological analyses of colorectal cancer and diet that focused on fat intake (Table 2). A recent Italian case–control study [14] found no significant associations between different types of fat and colorectal cancer, although the association for saturated fat was in the positive direction. Data from that study also suggested lower risk of colon and rectum cancer with higher intakes of fish [48]. An analysis of the Iowa Women's Health Study cohort [49] did not report a relative risk estimate for total fat. However, in that study low fat as well as high fat dairy products were associated with lower risk of colon cancer, suggesting that dietary fat, in particular saturated fat, did not affect risk. In the Polyp Prevention Trial [50•], a diet that was low in fat and high in fibre and vegetables failed to prevent the recurrence of colorectal adenomas over a period of 4 years. The absence of an effect in this one trial cannot provide definitive proof, but it does not support the hypothesis that lowering fat intake reduces colorectal cancer risk.

The WCFR/AICR report [3] concluded that higher intakes of total fat and saturated fat possibly increase colorectal cancer risk (Table 1). This is in accord with the conclusion of the COMA working group [4], who judged the evidence that total fat intake increases colorectal cancer risk to be weak. Taken together, epidemiological studies within populations do not indicate an independent role of dietary total or saturated fat in colorectal cancer.

Prostate cancer

The hypothesis that a high fat intake could promote prostate cancer also originates from international correlations and migrant studies [6,41]. Like for breast cancer, an often proposed underlying mechanism involves effects of fat and fatty acids through sex hormones.

The number of epidemiological studies on fat and prostate cancer is much lower than that on breast or colorectal cancer (for review [51]). A large proportion of case–control studies reported positive associations between incidence of prostate cancer and intake of fat, in particular animal fat, but most did not attempt to adjust these effects for energy intake. The case–control studies that did adjust for energy intake found no significant associations [3,51], increased risk [52], or decreased risk [53] with higher saturated fat intake. Three case-control studies [17–19] were recently reported; two of these [17,18] showed positive associations between saturated fat intake and risk of prostate cancer (Table 2). Some prospective cohort studies [3,54] also pointed to an increased risk with high intake of animal fat products. However, a recent prospective analysis [16] found no associations for prostate cancer and intake of total fat and saturated fat (Table 2).

The associations between monounsaturated fat and prostate cancer have been examined in only a few studies, and results are inconsistent [3]. Trans-fatty acids were not associated with prostate cancer in a recent cohort study [16]. Polyunsaturated or vegetable fat, mainly linoleic acid, has also not been associated with

prostate cancer incidence in epidemiological studies [30,31]. However, several studies [19,54–56], but not all [16], suggest that α-linolenic acid may increase risk. This finding warrants further examination. Human studies of body tissue levels of very-long-chain n-3 fatty acids and fish intake [54–56] showed no association with prostate cancer risk, with one exception [57].

The WCFR/AICR report [3] concluded that total fat and saturated fat possibly increase prostate cancer risk (Table 1). The Working Group of COMA [4] concluded that, although the epidemiological data are weakly consistent, there is not enough evidence that total fat intake influences risk of prostate cancer. The possible link between prostate cancer, fat intake and specific fatty acids deserves attention in further studies.

Other cancers

Other cancers for which a link with dietary fat has been implicated are those of the lung, ovary, endometrium and bladder, and nonmelanoma skin carcinoma. For lung cancer, the WCRF/AICR report [3] judged that high fat diets possibly increase risk (Table 1), with results from case–control and cohort studies being inconsistent. For ovary, endometrium and bladder cancer, the evidence for a link with dietary fat was judged to be insufficient (Table 1). A recent prospective analysis of the Iowa Women's Health Study [20] showed no associations between ovary cancer incidence and intake of total fat or classes of fatty acids (Table 2). A protective effect of a low fat diet on basal cell skin carcinoma was suggested by a 2-year trial with 100 patients [58]. However, the number of cases in that trial was very small and the intervention was not blinded. A recent analysis from the Health Professionals Follow-up Study [21•] found that a high intake of total and monounsaturated was associated with a lower, rather than a higher risk of basal cell carcinoma.

Conclusion

For cancers of the breast and colorectum, the associations in international comparisons and effects in animal experiments seen with intake of total and saturated fat are not supported by large cohort studies. Although small increases in risk cannot be excluded, it is unlikely that dietary fat or specific fatty acids have important effects on the risk of breast and colon cancer. Some epidemiological studies suggest that intake of animal fats might increase the risk of prostate cancer. The possible role of specific fatty acids in relation to prostate cancer warrants further investigation.

Taken together, the evidence that dietary fat is linked with cancers in humans is at best weak, and is not strong enough to justify dietary recommendations or health claims.

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References and recommended reading

Papers of particular interest, published within the annual period of review, have been highlighted as:

- • of special interest
- •• of outstanding interest

1 Doll R, Peto R. The causes of cancer: quantitative estimates of the avoidable risks of cancer in the United States today. J Natl Cancer Inst 1981; 66:1191–1308.

2 Committee on Diet of the National Academy of Sciences. Diet, nutrition, and cancer. Washington, DC: National Acadamy Press; 1982.

3 World Cancer Research Fund/American Institute of Cancer Research. Food, nutrition and the prevention of cancer: a global perspective, 1st ed. Washington, DC: American Institute for Cancer Research; 1997.

4 Department of Health. Nutritional aspects of the development of cancer, 1st ed. Norwich: HMSO; 1998.

5 Wu AH, Pike MC, Stram DO. Meta-analysis: dietary fat intake, serum estrogen levels, and the risk of breast cancer. J Natl Cancer Inst 1999; 91:529–534.

6 Armstrong B, Doll R. Environmental factors and cancer incidence and mortality in different countries, with special reference to dietary practices. Int J Cancer 1974; 15:617–631.

7 Welsch CW. Relationship between dietary fat and experimental mammary tumorigenesis: a review and critique [Suppl]. Cancer Res 1992; 52:2040s–2048s.

8 Howe GR, Hirohata T, Hislop TG, *et al.* Dietary factors and risk of breast cancer: combined analysis of 12 case–control studies. J Natl Cancer Inst 1990; 82:561–569.

9 Boyd NF, Martin LJ, Noffel M, *et al.* A meta-analysis of studies of dietary fat and breast cancer risk. Br J Cancer 1993; 68:627–636.

10 Hunter DJ, Spiegelman D, Adami H-O, *et al.* Cohort studies of fat intake and the risk of breast cancer: a pooled analysis. N Engl J Med 1996; 334:356–361.

11 • Holmes MD, Hunter DJ, Colditz GA, *et al.* Association of dietary intake of fat and fatty acids with risk of breast cancer. JAMA 2000; 281:914–920.
This is the largest prospective cohort study on diet in women. No evidence was found that lower intake of total fat or of specific types of fat reduces the risk of breast cancer.

12 Velie E, Kulldorff M, Schairer C, *et al.* Dietary fat, fat subtypes, and breast cancer in postmenopausal women: a prospective cohort study. J Natl Cancer Inst 2000; 92:833–839.

13 Voorrips LE, Brants HAM, Goldbohm RA, *et al.* Intake of conjugated linoleic acid and other fatty acids in relation to postmenopausal breast cancer: the Netherlands cohort study on diet and cancer [abstract]. Am J Epidemiol 2000; 151:S62.

14 Francheschi S, Favero A. The role of energy and fat in cancers of the breast and colon-rectum in southern European population. Ann Oncol 1999; 10(suppl 6):61–63.

15 Wakai K, Dillon DS, Ohno Y, *et al.* Fat intake and breast cancer risk in an area where fat intake is low: a case–control study in Indonesia. Int J Epidemiol 2000; 29:20–28.

16 Schuurman AG, van-den-Brandt PA, Dorant E, *et al.* Association of energy and fat intake with prostate carcinoma risk: results from The Netherlands Cohort Study. Cancer 1999; 86:1019–1027.

17 Hayes RB, Ziegler RG, Gridley G, *et al.* Dietary factors and risks for prostate cancer among blacks and whites in the United States. Cancer Epidemiol Biomarkers Prev 1999; 8:25–34.

18 Lee MM, Wang RT, Hsing AW, *et al.* Case–control study of diet and prostate cancer in China. Cancer Causes Control 1998; 9:545–552.

19 De-Stefani E, Deneo PH, Boffetta P, *et al.* Alpha-linolenic acid and risk of prostate cancer: a case–control study in Uruguay. Cancer Epidemiol Biomarkers Prev 2000; 9:335–338.

20 Kushi LH, Mink PJ, Folsom AR, *et al.* Prospective study of diet and ovarian cancer. Am J Epidemiol 1999; 149:21–31.

21 van-Dam RM, Huang Z, Giovannucci E, *et al*. Diet and basal cell carcinoma of • the skin in a prospective cohort of men. Am J Clin Nutr 2000; 71:135–141.
This prospective cohort study of more than 40 000 male health professionals showed that total fat consumption was associated with a lower rather than a higher risk of basal cell carcinoma.

22 Newmark HL. Squalene, olive oil, and cancer risk. Review and hypothesis. Ann NY Acad Sci 1999; 889:193–203.

23 Bartoli R, Fernandez BF, Navarro E, *et al*. Effect of olive oil on early and late events of colon carcinogenesis in rats: modulation of arachidonic acid metabolism and local prostaglandin E(2) synthesis. Gut 2000; 46:191–199.

24 Trichopoulou A, Katsouyanni K, Stuver S, *et al*. Consumption of olive oil and specific food groups in relation to breast cancer risk in Greece. J Natl Cancer Inst 1995; 87:110–116.

25 Simonsen N, Fernandez-Crehuet Navajas J, Martin-Moreno JM, *et al*. Monounsaturated fatty acids and breast cancer: the EURAMIC Study. Am J Clin Nutr 1998; 68:134–141.

26 Kohlmeier L, Simonsen N, van 't Veer P, *et al*. Adipose tissue trans fatty acids and breast cancer in the European Community Multicenter Study on Antioxidants, Myocardial Infarction, and Breast Cancer. Cancer Epidemiol Biomarkers Prev 1997; 6:705–710.

27 London SJ, Sacks FM, Stampfer MJ, *et al*. Fatty acid composition of the subcutaneous adipose tissue and risk of proliferative benign breast disease and breast cancer. J Natl Cancer Inst 1993; 85:785–793.

28 Petrek JA, Hudgins LC, Levine B, *et al*. Breast cancer risk and fatty acids in the breast and abdominal adipose tissues. J Natl Cancer Inst 1994; 86:53–56.

29 Bartsch H, Nair J, Owen RW. Dietary polyunsaturated fatty acids and cancers of the breast and colorectum: emerging evidence for their role as risk modifiers. Carcinogenesis 1999; 20:2209–2218.

30 Zock PL, Katan MB. Linoleic acid intake and cancer risk. A review and meta-analysis. Am J Clin Nutr 1998; 68:142–153.

31 Bakker N, van 't Veer P, Zock PL, EURAMIC Study Group. Adipose fatty acids and cancer of the breast, prostate, and colon: an ecological study. Int J Cancer 1997; 72:587–591.

32 Willett WC. Specific fatty acids and risks of breast and prostate cancer: dietary intake [Suppl]. Am J Clin Nutr 1997; 66:1557S–1563S.

33 Simonsen N, van 't Veer P, Strain JJ, *et al*. Adipose tissue omega-3 and omega-6 fatty acid content and breast cancer in the EURAMIC Study. Am J Epidemiol 1998; 147:342–352.

34 Klein V, Chajes V, Germain E, *et al*. Low alpha-linolenic acid content of adipose breast tissue is associated with an increased risk of breast cancer. Eur J Cancer 2000; 36:335–340.

35 Kritchevsky D. Antimutagenic and some other effects of conjugated linoleic acid. Br J Nutr 2000; 83:459–465.

36 Bougnoux P, Germain E, Lavillonniere F, *et al*. Polyunsaturated fatty acids and breast cancer [Suppl]. Lipids 1999; 34:S99.

37 Willett WC. Is dietary fat a major determinant of body fat? [Suppl]. Am J Clin Nutr 1998; 67:556S–562S.

38 The Women's Health Initiative Study Group. Design of the Women's Health Initiative clinical trial and observational study. Control Clin Trials 1998; 19:61–109.

39 Byers T, Gieseker K. Issues in the design and interpretation of studies of fatty acids and cancer in humans [Suppl]. Am J Clin Nutr 1997; 66:S1541–S1547.

40 Reddy BS. Dietary fat and colon cancer: animal model studies. Lipids 1992; 27:807–813.

41 Haenszel W, Kurihara M. Studies of Japanese migrants. I. Mortality from cancer and other diseases among Japanese in the United States. J Natl Cancer Inst 1968; 40:43–68.

42 Howe GR, Aronson KJ, Benito E, *et al*. The relationship between dietary fat intake and risk of colorectal cancer: evidence from the combined analysis of 13 case–control studies. Cancer Causes Control 1997; 8:215–228.

43 Giovannucci E, Goldin B. The role of fat, fatty acids, and total energy intake in the etiology of human colon cancer [Suppl]. Am J Clin Nutr 1997; 66:1564S–1571S.

44 Stemmermann GN, Nomura AM, Heilbrun LK. Dietary fat and the risk of colorectal cancer. Cancer Res 1984; 44:4633–4637.

45 Willett WC, Stampfer MJ, Colditz GA, *et al*. Relation of meat, fat, and fiber intake to the risk of colon cancer in a prospective study among women. N Engl J Med 1990; 323:1664–1672.

46 Bostick RM, Potter JD, Kushi LH, *et al*. Sugar, meat, and fat intake, and non-dietary risk factors for colon cancer incidence in Iowa women. Cancer Causes Control 1994; 5:38–52.

47 de-Deckere EA. Possible beneficial effect of fish and fish n-3 polyunsaturated fatty acids in breast and colorectal cancer. Eur J Cancer Prev 1999; 8:213–221.

48 Fernandez E, Chatenoud L, La-Vecchia C, *et al*. Fish consumption and cancer risk. Am J Clin Nutr 1999; 70:85–90.

49 Sellers TA, Bazyk AE, Bostick RM, *et al*. Diet and risk of colon cancer in a large prospective study of older women: an analysis stratified on family history (Iowa, United States). Cancer Causes Control 1998; 9:357–367.

50 Schatzkin A, Lanza E, Corle D, *et al*. Lack of effect of a low-fat, high-fiber diet on • the recurrence of colorectal adenomas. Polyp Prevention Trial Study Group. N Engl J Med 2000; 342:1149–1155.
In this randomized trial, a diet that was low in fat and high in fibre, fruits and vegetables did not reduce the recurrence of adenomatous polyps over a period of 4 years.

51 Kolonel LN, Nomura AM, Cooney RV. Dietary fat and prostate cancer: current status. J Natl Cancer Inst 1999; 91:414–428.

52 Whittemore AS, Kolonel LN, Wu AH, *et al*. Prostate cancer in relation to diet, physical activity, and body size in Blacks, Whites, and Asians in the United States and Canada. J Natl Cancer Inst 1995; 87:652–661.

53 Rohan TE, Howe GR, Burch JD, Jain M. Dietary factors and risk of prostate cancer: a case–control study in Ontario, Canada. Cancer Causes Control 1995; 6:145–154.

54 Giovannucci E, Rimm EB, Colditz GA, *et al*. A prospective study of dietary fat and risk of prostate cancer. J Natl Cancer Inst 1993; 85:1571–1579.

55 Gann PH, Hennekens CH, Sacks FM, *et al*. Prospective study of plasma fatty acids and risk of prostate cancer. J Natl Cancer Inst 1994; 86:281–286.

56 Harvei S, Bjerve KS, Tretli S, *et al*. Prediagnostic level of fatty acids in serum phospholipids: omega-3 and omega-6 fatty acids and the risk of prostate cancer. Int J Cancer 1997; 71:545–551.

57 Norrish AE, Skeaff CM, Arribas GL, *et al*. Prostate cancer risk and consumption of fish oils: a dietary biomarker-based case–control study. Br J Cancer 1999; 81:1238–1242.

58 Black HS. Influence of dietary factors on actinically-induced skin cancer. Mutat Res 1998; 422:185–190.