Fruit and Vegetables in Cancer Prevention

Harri Vainio and Elisabete Weiderpass

Abstract: Our aim was to review the epidemiological literature on possible cancer-preventive effects of the consumption of fruits and vegetables in humans, to quantify the effect of high versus low consumption of fruits and vegetables, and to give an overall assessment of the existing evidence. We based our work on an expert meeting conducted by the International Agency for Research on Cancer in 2003. A qualitative reading and evaluation of relevant articles on the cancer-preventive effect of the consumption of fruits and vegetables was made followed by the calculation of the mean relative risk and range for cohort and case-control studies separately. The possible population-preventable fraction for modifying diet in relation to fruit and vegetable consumption was calculated as well as an overall statement about the degree of evidence for the cancer-preventive effect of fruit and vegetable consumption for each cancer site. There is limited evidence for a cancer-preventive effect of the consumption of fruits and vegetables for cancer of the mouth and pharynx, esophagus, stomach, colon-rectum, larynx, lung, ovary (vegetables only), bladder (fruit only), and kidney. There is inadequate evidence for a cancer-preventive effect of the consumption of fruits and vegetables for all other sites. Applying this range of risk difference to the range of prevalence of low intake, the preventable fraction for low fruit and vegetable intake would fall into the range of 5–12%. It is important to recognize that this is only a crude range of estimates and that the proportion of cancers that might be preventable by increasing fruit and vegetable intake may vary beyond this range for specific cancer sites and across different regions of the world.

Methods

Definition of Fruits and Vegetables

Although culinary definitions are less precise than botanical definitions, they are commonly used by researchers and subjects in epidemiological surveys.

The culinary definition of fruits and vegetables refers to edible parts of plant foods with the exclusion of cereal grains, nuts, and seeds. The culinary term for fruit refers to the part of a plant that contains the seeds and pulpy surrounding tissue. Plant parts used as vegetables include stems and stalks, roots, tubers, bulbs, leaves, flowers, some fruits, and pulses. The definition and classification of fruits and vegetables are...
not precise and differ between dietary assessment instruments depending on the purposes of the study and dietary patterns of the population being evaluated.

**Measuring Intake of Fruits and Vegetables**

Questionnaire methods such as food-frequency questionnaires (FFQs) and diet history (DH) have been the most commonly used methods to assess individuals’ diets in case-control and cohort studies. These methods are designed to estimate usual intake, allowing classification of subjects in epidemiological studies. Twenty-four-hour recalls were mostly used to validate FFQ and DH. Given the large intra-individual variation in food intake, measurement errors are an important source of potential misclassification and bias. The estimation of fruit and vegetable intake using FFQ and DH largely differs in epidemiological studies, depending on the way the questionnaire is structured, the amount of specific questions, the method of assessing portion size, and the types of fruits and vegetables assessed. In the following, we present information from studies on fruit and vegetable intake as a group; no subgroup classification was used.

**Integration of the Evidence: Cancer-Preventive Effects of Fruit and Vegetable Consumption in Humans**

In reviewing the evidence, inclusion criteria were used. Case reports were not considered, and ecological studies were not used in the evaluation. Cohort and case-control studies were always considered unless they were inadequate in conception, design, conduct, or analysis. There have been several instances of sequential or multiple publications of analyses of the same or overlapping datasets. When the reports clearly related to the same or overlapping datasets, only data from the largest or most recent publication were included.

The data considered are presented in detail elsewhere (3). The data used in the evaluations also appear as plots (Figs. 1–36). Only those studies on total fruit or vegetable consumption reporting confidence intervals and adjusted for the main confounders for the relevant sites are included in the plots. An estimate of the overall effect across all the evaluated studies, calculated as explained subsequently, is presented, taking the size of the study (as reflected in the confidence interval) into account when weighing the individual study findings. The result of applying a test for heterogeneity is given as a footnote to each plot. The reader is cautioned that these summary estimates do not constitute the result of a formal meta-analysis, and they should not be interpreted as such.

The summary estimates in the plots were calculated as follows. Using the log of the relative risks for the highest versus lowest exposure categories in the individual studies, designated as $\beta_i$, the pooled estimate (summary value, $\beta_p$) was obtained, separately for cohort and case-control studies, as

$$\beta_p = \frac{\Sigma \beta_i / \text{var}(\beta_i)}{\Sigma 1 / \text{var}(\beta_i)}$$

with estimated standard error

$$\text{SE}(\beta_p) = \left[ \Sigma 1 / \text{var}(\beta_i) \right]^{-1/2}$$

The $\chi^2$ for heterogeneity was calculated as

$$\chi^2 = \Sigma (\beta_i - \beta_p)^2 / \text{var}(\beta_i)$$

with $(N – 1)$ degrees of freedom, where $N$ is the total number of studies.

Analyses and generation of the plots were performed using R Language and Environment for Statistical Computing (R Foundation for Statistical Computing, Vienna, Austria) (4). Individual studies are presented in the plot in chronological order, with the “box size” proportional to the inverse of their variance.

For some studies, results are reported for subcategories of the population under study, for example, males and females, pre- and postmenopausal women, and colon and rectal cancer. In the calculation of the overall effect and in the final plot, the subgroups counted as individual studies; however, when counting the number of evaluable studies for different cancer sites, subgroups were considered as coming from a single study.

**Overall Evaluation of the Evidence**

The group of experts who met at IARC made judgments concerning the evidence that fruits and vegetables prevent cancer in humans. In making the judgment, several criteria are considered. Findings that are replicated in several studies of the same design or using different approaches are more likely to provide evidence of a true protective effect than isolated observations from single studies. The results of studies judged to be of high quality are given more weight. In summarizing the data, evaluations of the strength of the evidence for cancer-preventive activity and carcinogenic effects from studies in humans are made, using standard terms, knowing that the evaluations may change as new information becomes available. The categories in which the potential cancer-preventive agent is classified are

- **Sufficient evidence of cancer-preventive activity:** A causal relationship has been established between the agent or intervention and the prevention of human cancer in studies in which chance, bias, and confounding could be ruled out with reasonable confidence.
- **Limited evidence of cancer-preventive activity:** The data suggest a reduced risk for cancer with use of the agent or intervention but are limited for making a definitive evaluation either because chance, bias, or confounding could not be ruled out with reasonable confidence or because the data are restricted to intermediary biomarkers or uncertain validity in the putative pathway to cancer.
- **Inadequate evidence of cancer-preventive activity:** The available studies are of insufficient quality, consistency, or statistical power to permit a conclusion regarding a can-
cer-preventive effect of the agent or intervention, or no data on the prevention of cancer in humans are available.

- Evidence suggesting lack of cancer-preventive activity: Several adequate studies of use or exposure to the agent or intervention are mutually consistent in not showing a preventive effect.

The evaluations refer to fruits and vegetables as whole classes, without consideration of separate subcategories.

**Results**

**Oral Cavity and Pharynx**

No cohort study on fruit consumption and risk of oral or oropharyngeal cancer was identified. Most studies were hospital-based case-control studies. For the 10 evaluated case-control studies of fruit consumption (5–14) the mean relative risk for high versus low consumption was 0.45 and the range was 0.10–0.70 (Fig. 1).

In the large cohort study of Hirayama in Japan (15), the frequency of intake of green-yellow vegetables was inversely associated with risk of oropharyngeal cancer nonsignificantly in men and significantly in women. Seven case-control studies were evaluated for vegetable intake (5–8,11–13), and the mean relative risk for high versus low consumption was 0.49 and the range was 0.19–0.80 (Fig. 2). Concerns about residual confounding by cigarette smoking, alcohol consumption, and socioeconomic status as well as recall bias among cases and selection bias among control subjects may at least partially explain these results. There are no consistent findings of an inverse association of salivary gland and nasopharynx cancer with fruit and vegetable consumption.

**Esophagus**

An inverse association between fruit consumption and mortality for esophageus cancer was found in one cohort study (16). Among the 16 evaluated case-control studies (7,9,17–30), the mean relative risk for high versus low fruit consumption was 0.54 and the range was 0.14–1.50 (Fig. 3).

For vegetable consumption, no cohort studies were identified, and the results of 10 case-control studies that were evaluated (7,17–21,23,25,31,32) entailed a mean relative risk for

![Figure 1](image_url). Case-control studies of oral and pharyngeal cancer and fruit consumption. (Reproduced with permission from the IARC Handbook of Cancer Prevention, vol 8. Lyon, France: IARC Press, 2003.)
high versus low consumption of 0.64 and a range of 0.10–0.97 (Fig. 4). The studies evaluated did not indicate gender-specific effects and were underpowered to detect effect modification by smoking and alcohol consumption. Selection and recall bias or residual confounding cannot be ruled out from the evaluated studies.

Stomach

For fruit consumption, 10 cohort (16,33–41) and 28 case-control studies (28,42–68) were evaluated. In the cohort studies, the mean relative risk for high versus low consumption was 0.85 and the range was 0.55–1.92 (Fig. 5). In the case-control studies the mean was 0.63 and the range was 0.31–1.39 (Fig. 6).

For vegetable consumption, 5 cohort studies (33,35,39,41,69) and 20 case-control studies (31,42,43,45,48,51,52,55–58,60,61,63,64,66,70–73) were evaluated. For the cohort studies, the mean relative risk for high versus low consumption was 0.94 and the range was 0.72–1.78 (Fig. 7); for the case-control studies, the mean relative risk for high versus low consumption was 0.66 and the range was 0.30–1.70 (Fig. 8).

Colon and Rectum

For fruit consumption, 11 cohort studies (16,74–83) were evaluated, and the mean relative risk for high versus low consumption was 1.0 and the range was 0.50–1.60 (Fig. 9). For the nine evaluated case-control studies (84–92), the mean relative risk for high versus low fruit consumption was 0.87 and the range was 0.30–1.74 (Fig. 10).

For vegetable consumption, there were 10 evaluated cohort studies (74–83), and the mean relative risk for high versus low consumption was 0.94 and the range was 0.72–1.78 (Fig. 11). For the 13 evaluated case-control studies (84–90,92–97), the mean relative risk for high versus low consumption was 0.63 and the range was 0.18–1.29 (Fig. 12). Recall and selection bias in case-control studies and confounding in both case-control and cohort studies may have affected the results.

The reason that case-control studies tended to show inverse associations and cohorts did not is unclear. Recall bias as well as changes in dietary patterns at early stages of disease may at least partially explain the discrepancy between case-control and cohort studies mean results.
Liver

Only one cohort study (16) and three case-control studies (98–101) were evaluated, and none found evidence of an association between fruit consumption and liver cancer risk.

For vegetable consumption, the cohort study of Sauvaget et al. (16) found a significant inverse association with green-yellow vegetables, whereas Hirayama et al. (15) did not. The cohort study by Yu et al. (102) reported a significant reduced risk. For the case-control studies, La Vecchia et al. (100) found no effect of all vegetables but an effect for fruit and vegetables combined (103). Hadziyannis et al. (98), Fukuda et al. (104), and Kuper et al. (101) found no association for vegetable consumption and risk of liver cancer.

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Heterogeneity test: $\chi^2$ (18 df) = 82; $p < 0.001$

Biliary Tract

One cohort study (16) found no association between fruit consumption and risk of gallbladder cancer. One case-control study (105) showed a significant protective effect of consumption of fruit and vegetables combined, whereas two other case-control studies on green-yellow vegetables (15, 16) found no association.

Pancreas

In the four evaluated cohort studies that also considered smoking as a confounding factor in the analysis (16, 106–108), all found inverse, nonsignificant associations for pancreas cancer with increased fruit consumption. In six case-control studies (109–114) the mean relative risk for high versus low consumption was 0.72, and the range was 0.07–0.92 (Fig. 13).

Nonsignificant inverse associations were found in the two evaluated cohort studies of vegetable consumption (106, 108). For the five evaluated case-control studies (109, 111–114), the mean relative risk for high versus low consumption of vegetables was 0.80 and the range was 0.32–1.03 (Fig. 14).

Figure 3. Case-control studies of esophageal cancer and fruit consumption. S, squamous cell carcinoma; A, adenocarcinoma. (Reproduced with permission from the IARC Handbook of Cancer Prevention, vol 8. Lyon, France: IARC Press, 2003.)
In studies where the proxies of patients were interviewed, as well as those studies that excluded deceased cases, reporting bias is a serious concern. Many of the inverse associations were found in studies where the response rates among controls were low.

**Larynx**

Four case-control studies (7,115–117) were evaluated for fruit consumption, and the mean relative risk for high versus low consumption was 0.63 and the range was 0.38–0.80 (Fig. 15).

For vegetable consumption, the four evaluated case-control studies (7,115–117) had a mean relative risk of 0.49 and a range of 0.17–1.1 (Fig. 16).

The majority of the studies were hospital based, with the exception of one large population-based study. Control for smoking was rather crude in earlier studies. One study presented results for fruit and vegetable consumption according to smoking and alcohol consumption history, and the effect of fruit and vegetable consumption among smokers and among drinkers was weaker than among nonsmokers and among nondrinkers. This indicates that the possibility of recall and selection bias in earlier studies cannot be ruled out.

**Lung**

For the 13 evaluated cohort studies of fruit consumption (16,74,118–128), the mean relative risk for high versus low consumption was 0.77 and the range was 0.33–2.04 (Fig. 17).

For the 21 evaluated case-control studies (57,129–148), the mean relative risk for high versus low consumption of fruit was 0.70 and the range was 0.33–2.04 (Fig. 18).

For 11 cohort studies on vegetable consumption (74,119–128), the mean relative risk was 0.80 and the range was 0.47–1.37 (Fig. 19).
For 18 evaluated case-control studies on vegetable consumption, (129–133,135,137,139,140,143,145,147,149–154) the mean relative risk was 0.69 and the range was 0.30–1.49 (Fig. 20). There were no clear differences in the results for men and women, hospital- and population-based studies, nor between morphological categories on lung cancer. The strength of the inverse association was smaller in cohort than in case-control studies, leaving the possibility of recall and selection bias in the case-control studies.

Although the newer cohort studies have attempted to carefully control for confounding by smoking, residual confounding cannot be excluded, and cohort studies usually fail to capture changes in smoking and diet after cohort enrollment. Studies that did subanalysis among nonsmokers usually found a weaker effect, although the results are not entirely consistent.

**Breast**

For fruit consumption, there were six evaluated cohort studies (16,74,155–158), and the mean relative risk for high versus low consumption was 0.94 and the range was 0.64–1.43 (Fig. 21). For the 12 evaluated case-control studies (9,159–169), the mean relative risk for high versus low fruit consumption was 0.66 and the range was 0.09–1.40 (Fig. 22).

For five evaluated cohort studies of vegetable consumption (74,155–158), the mean relative risk for high versus low consumption was 0.94 and the range was 0.64–1.43 (Fig. 23). For 12 evaluated case-control studies (159–161,163–167,170–173), the mean relative risk for high versus low vegetable consumption was 0.66 and the range was 0.09–1.40 (Fig. 24).

After the meeting, a large cohort study on the association between fruits and vegetables and breast cancer risk has been published with null results (174).

**Cervix**

No cohort studies on fruit and vegetable consumption and cervix cancer risk were identified. For the case-control studies, there was no consistent effect and very little evidence of an effect of either fruit or vegetable consumption (175–180). Given the very strong effect of human papillomavirus (HPV) with the disease, there is concern about the appropriate con-
trol for possible confounding or modifying effect by the infection. One study examined the risk restricted to HPV-positive women, and the results were similar when both HPV-positive and -negative controls were included or when controls were limited to women with HPV infection.

**Endometrium**

The association between fruit and vegetable consumption has been studied only in case-control studies. For seven evaluated case-control studies (180–186), the mean relative risk for high versus low fruit consumption was 1.03 and the range was 0.67–1.97 (Fig. 25). For five evaluated case-control studies on vegetable consumption (181–185), the relative risk for high versus low consumption was 0.75 and the range was 0.65–1.00 (Fig. 26). The combined effect of fruit and vegetable consumption was inversely associated with endometrial cancer risk in one cohort and three case-control studies. Body mass index, as a proxy of obesity, an established risk factor for endometrial cancer, has been adjusted in several but not all of the previous studies.

**Ovary**

For fruit consumption, the number of studies available was limited: two cohort (187,188) and four case-control studies...
Figure 7. Cohort studies of stomach cancer and vegetable consumption. M, males; F, females. (Reproduced with permission from the *IARC Handbook of Cancer Prevention*, vol 8. Lyon, France: IARC Press, 2003.)

Figure 8. Case-control studies of stomach cancer and vegetable consumption. I, intestinal type; D, diffuse type; M, males; F, females; C, cardia; N, noncardia; *, not applicable. (Reproduced with permission from the *IARC Handbook of Cancer Prevention*, vol 8. Lyon, France: IARC Press, 2003.)
studies (189–192), and the results were inconsistent but in general indicating no association. For vegetable consumption, an inverse association was found in two cohort (nonsignificant results) (187,188) and five (189,190,192–194) of six case-control (191) studies. In one case-control study there was an inverse association for the combined consumption of fruits and vegetables (190).

Prostate

For eight evaluated cohort studies of fruit consumption (74,195–201), the mean relative risk for high versus low consumption was 1.11 and the range was 0.84–1.57 (Fig. 27). For nine evaluated case-control studies (9,202–209), the mean relative risk was 1.08 and the range was 0.40–1.70 (Fig. 28).

The results for fruit are consistent and suggest that high fruit consumption does not reduce prostate cancer risk. The increased risk found in some studies may be due to bias associated with prostate cancer screening and detection in health-conscious men.

For vegetable consumption, the mean relative risk for high versus low consumption in six evaluated cohort studies (74,197–201) was 0.95 and the range was 0.7–1.04 (Fig. 29). For nine evaluated case-control studies (202–204,206–211), the mean relative risk for high versus low consumption was 0.90 and the range was 0.6–1.39 (Fig. 30).

Thus, for vegetables, the majority of studies have reported a slight, nonsignificant lower risk for higher consumption.

Testis

There were no cohort studies on testis cancer, and two case-control studies are available (212,213).

Bladder

There were five cohort studies evaluated (214–218), and the mean relative risk for high versus low consumption of fruit was 0.87 and the range was 0.63–1.12 (Fig. 31).
For the four available case-control studies (219–222), the mean relative risk for high versus low intake was 0.74 and the range was 0.53–0.95 (Fig. 32).

Three cohort studies evaluated vegetable consumption (215,217,218), and the mean relative risk for high versus low consumption was 0.94 and the range was 0.72–1.16 (Fig. 33).

For the three case-control studies evaluated (219,220,222), the mean relative risk for low vegetable consumption was 0.89 and the range was 0.66–1.14 (Fig. 34).

Kidney

Two cohort studies were evaluated: one did not show an association with total fruit consumption (223) and the other one had too few cases to be informative (224). Seven case-control studies were evaluated (9,225–230), and the mean relative risk for high versus low fruit consumption was 0.76 and the range was 0.20–1.20 (Fig. 35).

Four case-control studies (and no cohort studies) were evaluated for vegetable consumption (226,227,229,230). The mean relative risk for high versus low intake was 0.86 and the range was 0.30–1.60 (Fig. 36).

All evaluated case-control studies presented results adjusted for body mass index and smoking, and most studies used population-based controls. However, recall bias cannot be completely excluded as an explanation for the results.

Brain

Three case-control studies of adult (231–233) and five for childhood brain cancers (234–238) considered fruit and vegetable consumption usually as one among many study hypotheses. All adult studies and three childhood studies showed inverse associations with fruit and/or vegetable consumption. Only one of the three childhood studies showed a statistically significant inverse association (234); in the other two the associations were nonsignificant (235,237).
Thyroid

No cohort studies were available, and none of the three case-control studies evaluated found a significant association with total fruit or vegetable consumption (239–241).

Non-Hodgkin Lymphoma

A nonsignificant inverse association was found in both of the two cohort studies of fruit consumption (242,243). The only case-control study evaluated showed no evidence of association with fruit consumption (244).

For vegetable consumption, one (243) of three cohort studies evaluated (15,242,243) showed an inverse association. The only case-control study evaluated for vegetable consumption showed no association (245).

Leukemia

The only cohort study available evaluated green-yellow vegetables only (and no fruit) and found no association (15).

Overall Evaluation

After the evaluating the evidence presented previously, it has been concluded that there is limited evidence for a cancer-preventive effect of the consumption of fruits and vegetables for cancer of the mouth and pharynx, esophagus, stomach, colon-rectum, larynx, lung, ovary (vegetables only), bladder (fruit only), and kidney in humans.

There is inadequate evidence for a cancer-preventive effect of the consumption of fruits and vegetables for all other sites.
Preventable Fraction

The proportion of any disease potentially preventable by modification of a risk factor in a population is determined by both the strength of the risk factor, as represented by the relative risk, and the prevalence of the risk factor. This proportion is commonly known as the “preventable fraction” (also sometimes called the “population attributable risk”) (246). The certainty in any estimate of preventable fraction, including that for the fraction of cancers that is due to low intake of fruits and vegetables, is dependent on the precision of both the relative risk associated with low intake and the proportion of the population consuming low levels. It is clear that many of the relative risk estimates are uncertain and that the prevalence of exposure to low intake varies widely across studies and cancer sites. Therefore, confidence in an estimate of any particular cancer’s preventable fraction for low fruit and vegetable intake must be low.

Nevertheless, we calculated the preventable fractions for cancer sites for which there was at least limited support for a causal association to estimate the approximate extent of the potential prevention that could be linked to increasing fruit and vegetable intake. Although the relative risks and prevalences of low intake vary widely between studies, in many of the studies reviewed, the levels of fruit and vegetable intake being compared were the highest versus lowest quartiles or tertiles (that is, range of prevalence of low intake of 25–33%), and the relative risk estimates were generally in the range of 20–30% lower risk for subjects in the highest category of intake. Applying this range of risk difference to

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Figure 12. Case-control studies of colorectal cancer and vegetable consumption. M, males; F, females; CR, colorectal; C, colon; R, rectum. (Reproduced with permission from the IARC Handbook of Cancer Prevention, vol 8. Lyon, France: IARC Press, 2003.)
Figure 13. Case-control studies of pancreas cancer and fruit consumption. M, males; F, females. (Reproduced with permission from the *IARC Handbook of Cancer Prevention*, vol 8. Lyon, France: IARC Press, 2003.)

Figure 14. Case-control studies of pancreas cancer and vegetable consumption. M, males; F, females. (Reproduced with permission from the *IARC Handbook of Cancer Prevention*, vol 8. Lyon, France: IARC Press, 2003.)
Figure 15. Case-control studies of larynx cancer and fruit consumption. (Reproduced with permission from the *IARC Handbook of Cancer Prevention*, vol 8. Lyon, France: IARC Press, 2003.)

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Heterogeneity test: $\chi^2 (3df) = 5; p = 0.17$

Figure 16. Case-control studies of larynx cancer and vegetable consumption. (Reproduced with permission from the *IARC Handbook of Cancer Prevention*, vol 8. Lyon, France: IARC Press, 2003.)

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</table>

Heterogeneity test: $\chi^2 (3df) = 30; p < 0.0001$
the range of prevalence of low intake, the preventable fraction for low fruit and vegetable intake would fall into the range of 5–12%. It is important to recognize that this is only a crude range of estimates and that the proportion of cancers that might be preventable by increasing fruit and vegetable intake may vary beyond this range for specific cancer sites and across different regions of the world.

There have been many estimates of the fraction of cancer preventable by increasing fruit and vegetable intake based on individual case-control studies but only two based on meta-analyses. van’t Veer et al. (247) reviewed published studies and estimated the population attributable risks for all cancer sites due to consumption of 250 g of fruits and vegetables per day compared with the recommended 400 g/day. They made three estimates based on different assumptions of the size of the relative risks: a “best guess” estimate (19%), an “optimistic” estimate (28%), and a “conservative” estimate (6%). Riboli and Norat (248) estimated the preventable fractions for esophageal, stomach, and colorectal cancers in various populations around the world using relative risks derived from a meta-analysis of published studies (largely from developed countries) coupled with regional prevalence estimates derived from sources including FAO data. This approach led to estimates of the proportion of cancers preventable by increasing fruit and vegetable intake from current levels to 350 g/day in the range of 8–16% for colorectal cancer and 20–30% for esophageal and gastric cancers; these estimates varied substantially in different regions of the world.

The preventable fraction estimates of 5–12% for the groups of cancers evaluated here as having limited evidence for an inverse association with fruit and vegetable consumption are similar to the estimates for all cancer sites made by van’t Veer et al. (247) and to the estimates for colorectal cancer by Riboli and Norat (248), but they are lower than the Riboli and Norat (248) estimates for esophageal and stomach cancers. The range of estimates of the fraction of selected cancers preventable by increasing intake of fruits and vegetables is only an approximation. The true relative risk for low intake is quite uncertain given limitations in dietary assessment and in study designs. In addition, the mix of various cancers as well as the prevalence of low intake can vary substantially across different populations.

The present estimates for the fraction of selected cancers preventable by increasing fruit and vegetable intake could be either high or low. They would be too high if the relative...
risk estimates on which the measure is based are inflated by biases in study design and/or uncontrolled confounding by other factors. On the other hand, they would be too low if the relative risks were underestimated because of misclassification arising from random errors in estimating dietary intake. In addition, benefits of increasing fruit and vegetable intake may well extend beyond those at the lowest levels of intake. Shifting the diets of entire populations over long periods to lower levels of risk can have a greater impact on population health than reducing risk only for a subgroup at highest risk (249). Increasing fruit and vegetable intake in populations is likely also to be accompanied by other beneficial changes in diet composition and in other chronic diseases.

Acknowledgments and Notes

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Figure 18. Case-control studies of lung cancer and fruit consumption. B, blacks; W, whites; M, males; F, females; A, adenocarcinoma; S, squamous and small cell carcinoma; Sm, smokers; NonSm, nonsmokers; *, not applicable. (Reproduced with permission from the IARC Handbook of Cancer Prevention, vol 8. Lyon, France: IARC Press, 2003.)
Figure 19. Cohort studies of lung cancer and vegetable consumption. M, males; F, females; I, intervention arm; P, placebo arm. (Reproduced with permission from the IARC Handbook of Cancer Prevention, vol 8. Lyon, France: IARC Press, 2003.)

Figure 20. Case-control studies of lung cancer and vegetable consumption. B, blacks; W, whites; M, males; F, females; Sm, smokers; NonSm, nonsmokers; *, not applicable. (Reproduced with permission from the IARC Handbook of Cancer Prevention, vol 8. Lyon, France: IARC Press, 2003.)
Figure 21. Cohort studies of breast cancer and fruit consumption. pre, premenopausal; post, postmenopausal; I, incidence. (Reproduced with permission from the IARC Handbook of Cancer Prevention, vol 8. Lyon, France: IARC Press, 2003.)

Figure 22. Case-control studies of breast cancer and fruit consumption. pre, premenopausal; post, postmenopausal; *, not applicable. (Reproduced with permission from the IARC Handbook of Cancer Prevention, vol 8. Lyon, France: IARC Press, 2003.)
Figure 23. Cohort studies of breast cancer and vegetable consumption. pre, premenopausal; post, postmenopausal; I, incidence. (Reproduced with permission from the IARC Handbook of Cancer Prevention, vol 8. Lyon, France: IARC Press, 2003.)

Figure 24. Case-control studies of breast cancer and vegetable consumption. pre, premenopausal; post, postmenopausal; *, not applicable. (Reproduced with permission from the IARC Handbook of Cancer Prevention, vol 8. Lyon, France: IARC Press, 2003.)
Figure 25. Case-control studies of endometrial cancer and fruit consumption. (Reproduced with permission from the *IARC Handbook of Cancer Prevention*, vol 8. Lyon, France: IARC Press, 2003.)

Figure 26. Case-control studies of endometrial cancer and vegetable consumption. (Reproduced with permission from the *IARC Handbook of Cancer Prevention*, vol 8. Lyon, France: IARC Press, 2003.)
Figure 27. Cohort studies of prostate cancer and fruit consumption. *, not applicable. (Reproduced with permission from the *IARC Handbook of Cancer Prevention*, vol 8. Lyon, France: IARC Press, 2003.)

Figure 28. Case-control studies of prostate cancer and fruit consumption. (Reproduced with permission from the *IARC Handbook of Cancer Prevention*, vol 8. Lyon, France: IARC Press, 2003.)
Figure 29. Cohort studies of prostate cancer and vegetable consumption. *, not applicable. (Reproduced with permission from the IARC Handbook of Cancer Prevention, vol 8. Lyon, France: IARC Press, 2003.)

Figure 30. Case-control studies of prostate cancer and vegetable consumption. (Reproduced with permission from the IARC Handbook of Cancer Prevention, vol 8. Lyon, France: IARC Press, 2003.)
Figure 31. Cohort studies of bladder cancer and fruit consumption. (Reproduced with permission from the *IARC Handbook of Cancer Prevention*, vol 8. Lyon, France: IARC Press, 2003.)

<table>
<thead>
<tr>
<th>Cohort studies</th>
<th>No. of categ.</th>
<th>OR</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chyou <em>et al.</em>, 1993</td>
<td>3</td>
<td>0.63</td>
<td>0.37–1.08</td>
</tr>
<tr>
<td>Michaud <em>et al.</em>, 1999</td>
<td>5</td>
<td>1.12</td>
<td>0.70–1.78</td>
</tr>
<tr>
<td>Nagano <em>et al.</em>, 2000</td>
<td>3</td>
<td>0.75</td>
<td>0.46–1.22</td>
</tr>
<tr>
<td>Zeegers <em>et al.</em>, 2001</td>
<td>5</td>
<td>0.74</td>
<td>0.53–1.04</td>
</tr>
<tr>
<td>Michaud <em>et al.</em>, 2002</td>
<td>5</td>
<td>1.10</td>
<td>0.77–1.57</td>
</tr>
<tr>
<td>SUMMARY VALUE</td>
<td></td>
<td>0.87</td>
<td>0.72–1.04</td>
</tr>
</tbody>
</table>

Heterogeneity test: $\chi^2 (4 df)=5.4; p=0.25$

Figure 32. Case-control studies of bladder cancer and fruit consumption. (Reproduced with permission from the *IARC Handbook of Cancer Prevention*, vol 8. Lyon, France: IARC Press, 2003.)

<table>
<thead>
<tr>
<th>Case-control studies</th>
<th>No. of categ.</th>
<th>OR</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Riboli <em>et al.</em>, 1991</td>
<td>4</td>
<td>0.95</td>
<td>0.67–1.35</td>
</tr>
<tr>
<td>Bruemmer <em>et al.</em>, 1996</td>
<td>4</td>
<td>0.53</td>
<td>0.30–0.93</td>
</tr>
<tr>
<td>Wakai <em>et al.</em>, 2000</td>
<td>4</td>
<td>0.65</td>
<td>0.40–1.06</td>
</tr>
<tr>
<td>Balbi <em>et al.</em>, 2001</td>
<td>3</td>
<td>0.65</td>
<td>0.40–1.04</td>
</tr>
<tr>
<td>SUMMARY VALUE</td>
<td></td>
<td>0.74</td>
<td>0.59–0.92</td>
</tr>
</tbody>
</table>

Heterogeneity test: $\chi^2 (3 df)=3.8; p=0.28$
Figure 33. Cohort studies of bladder cancer and vegetable consumption. (Reproduced with permission from the *IARC Handbook of Cancer Prevention*, vol 8. Lyon, France: IARC Press, 2003.)

<table>
<thead>
<tr>
<th>Cohort studies</th>
<th>No. of categ.</th>
<th>OR</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Michaud et al., 1999</td>
<td>5</td>
<td>0.72</td>
<td>0.47–1.09</td>
</tr>
<tr>
<td>Zeegers et al., 2001</td>
<td>5</td>
<td>0.91</td>
<td>0.65–1.27</td>
</tr>
<tr>
<td>Michaud et al., 2002</td>
<td>5</td>
<td>1.16</td>
<td>0.82–1.63</td>
</tr>
<tr>
<td>SUMMARY VALUE</td>
<td></td>
<td>0.94</td>
<td>0.76–1.16</td>
</tr>
</tbody>
</table>

Heterogeneity test: $\chi^2 (2 df)=3; p=0.22$

Figure 34. Case-control studies of bladder cancer and vegetable consumption. (Reproduced with permission from the *IARC Handbook of Cancer Prevention*, vol 8. Lyon, France: IARC Press, 2003.)

<table>
<thead>
<tr>
<th>Case-control studies</th>
<th>No. of categ.</th>
<th>OR</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Riboli et al., 1991</td>
<td>4</td>
<td>1.04</td>
<td>0.73–1.48</td>
</tr>
<tr>
<td>Bruemmer et al., 1996</td>
<td>4</td>
<td>0.87</td>
<td>0.52–1.45</td>
</tr>
<tr>
<td>Balbi et al., 2001</td>
<td>3</td>
<td>0.66</td>
<td>0.40–1.09</td>
</tr>
<tr>
<td>SUMMARY VALUE</td>
<td></td>
<td>0.89</td>
<td>0.69–1.14</td>
</tr>
</tbody>
</table>

Heterogeneity test: $\chi^2 (2 df)=2.1; p=0.35$
Figure 35. Case-control studies of renal cell cancer and fruit consumption. M, males; F, females. (Reproduced with permission from the IARC Handbook of Cancer Prevention, vol 8. Lyon, France: IARC Press, 2003.)

Figure 36. Case-control studies of renal cell cancer and vegetable consumption. M, males; F, females; NonSm, nonsmokers. (Reproduced with permission from the IARC Handbook of Cancer Prevention, vol 8. Lyon, France: IARC Press, 2003.)
References


