Intake of Fruits and Vegetables and Risk of Breast Cancer

A Pooled Analysis of Cohort Studies

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Context Some epidemiologic studies suggest that elevated fruit and vegetable consumption is associated with a reduced risk of breast cancer. However, most have been case-control studies in which recall and selection bias may influence the results. Additionally, publication bias may have influenced the literature on associations for specific fruit and vegetable subgroups.

Objective To examine the association between breast cancer and total and specific fruit and vegetable group intakes using standardized exposure definitions.

Data Sources/Study Selection Eight prospective studies that had at least 200 incident breast cancer cases, assessed usual dietary intake, and completed a validation study of the diet assessment method or a closely related instrument were included in these analyses.

Data Extraction Using the primary data from each of the studies, we calculated study-specific relative risks (RRs) that were combined using a random-effects model.

Data Synthesis The studies included 7377 incident invasive breast cancer cases occurring among 351 825 women whose diet was analyzed at baseline. For comparisons of the highest vs lowest quartiles of intake, weak, nonsignificant associations were observed for total fruits (pooled multivariate RR, 0.93; 95% confidence interval [CI], 0.86-1.00; *P* for trend=.08), total vegetables (RR, 0.96; 95% CI, 0.89-1.04; *P* for trend=.54), and total fruits and vegetables (RR, 0.93; 95% CI, 0.86-1.00; *P* for trend=.12). No additional benefit was apparent in comparisons of the highest and lowest deciles of intake. No associations were observed for green leafy vegetables, 8 botanical groups, and 17 specific fruits and vegetables.

Conclusion These results suggest that fruit and vegetable consumption during adulthood is not significantly associated with reduced breast cancer risk.

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THE ASSOCIATION BETWEEN FRUIT and vegetable consumption and breast cancer risk has been examined in more than 25 case-control studies, but relatively few cohort studies.[1] A recent summary of 19 case-control and 3 cohort studies concluded that elevated fruit and vegetable consumption probably reduces breast cancer risk. Approximately half of the reported associations for all types of fruit and vegetable groups combined showed at least a 25% reduction in breast cancer risk, whereas few associations showed more than a 50% elevation in risk.[2] A meta-analysis of 14 case-control and 3 cohort studies reported that breast cancer risk was reduced by 25% for vegetables (relative risk [RR], 0.75; 95% confidence interval [CI], 0.66-0.85) and by 6% for fruits (RR, 0.94; 95% CI, 0.79-1.11) for comparisons of high vs low consumption.[3] Besides the 2 main groups, total fruits and total vegetables, associations for specific food groups or individual foods have been reported sporadically and the associations that have been reported may be subject to publication bias. To gain a better understanding of how total and specific fruit and vegetable

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intakes are associated with breast cancer risk, we examined these relationships in the Pooling Project of Prospective Studies of Diet and Cancer (referred to as the Pooling Project) that was established to evaluate associations between dietary factors and cancer risk using a standardized approach. Using the primary data from each of the cohort studies, we standardized exposure categories and covariate definitions across studies, controlled for other dietary and nondietary variables, and evaluated potential effect modification of dietary variables by nondietary risk factors.

METHODS

The Pooling Project has been described previously.[4,5] The following inclusion criteria were formulated: (1) a published prospective study with at least 200 incident breast cancer cases; (2) assessment of usual dietary intake; and (3) a validation study of the diet assessment method or a closely related instrument. Eight studies[6-13] were identified that met these criteria (TABLE 1). The Nurses' Health Study was divided into 2 studies because it had repeated assessments of dietary intake and a longer follow-up period than the other studies. The 1980-1986 follow-up period is referred to as Nurses' Health Study (a) and the 1986-1996 follow-up period is referred to as Nurses' Health Study (b). Following the underlying theory of survival data, blocks of person-time in different periods are statistically independent, regardless of the extent that they are derived from the same people,[14] so pooling the estimates from these 2 periods is equivalent to using a single period but takes advantage of the enhanced exposure assessment in 1986 compared with 1980.

Dietary Assessment

Diet was measured at baseline in each study using a food frequency questionnaire designed for that particular study. The number of fruit and vegetable questions ranged from 9 in the Sweden Mammography Cohort to 54 in the Nurses' Health Study (b). Intake data were obtained for the foods listed on the food frequency questionnaire. Missing responses for items were coded as never consumed. To take into account the varying portion sizes among participants within some cohorts and between study populations, the food intake data were analyzed as grams consumed per day. For the Iowa Women's Health Study, Nurses' Health Study (a), and Nurses' Health Study (b), the frequency data for each food item were converted to grams per day using standard gram weights[15] for the serving sizes listed on the questionnaire. For the Adventist Health Study and New York State Cohort, serving sizes were not mentioned on the food frequency questionnaire; thus, the most common serving size specified on the questionnaires in the other cohorts in the Pooling Project was used to estimate the portion consumed.

We examined fruits without juice (referred to as fruits); fruit juice; fruits and fruit juice (total fruits); vegetables and vegetable juice (total vegetables); and fruits, vegetables, and juice (total fruits and vegetables). In addition, several fruit and vegetable groups were evaluated based on botanical taxonomy.[16] These groups were examined as a potential method of identifying groups of fruits and vegetables that may be rich sources of bioactive phytochemicals for which adequate food composition data are not available. We could not examine associations with the Liliaceae family because garlic, onions, and leeks were asked about on the questionnaires in only 2 studies. Associations also were examined for individual fruits and vegetables for which intake was assessed in at least 5 studies. The studies that were included in the analyses of the botanical groups and individual foods varied based on whether the relevant food(s) was included on their food frequency questionnaires. Potatoes and mature beans were not included in the total vegetable or total fruit and vegetable groups because of their high starch and protein content, respectively, compared with other fruits and vegetables.[17] However, they were included in estimates of the relevant botanically defined groups.

Table 1. Characteristics of the Cohort Studies Included in the Pooled Analysis of Fruit and Vegetable Intake and Breast Cancer*

					Total Fruits		Total Vegetables	
Study	Years of Follow-up	Baseline Cohort, No.	Age Range at Baseline, y	No. of Cases†	No. of Questions	Median Intake, g/d	No. of Questions	Median Intake, g/d
Adventist Health Study[6]	1976-1982	15 172	28-90	160	7	355	6	162
Canadian National Breast Screening Study[7]	1982-1987	56 837	40-59	419	6	327	15	226
Iowa Women's Health Study[8]	1986-1995	34 406	55-69	1130	15	342	31	196
Netherlands Cohort Study[9]	1986-1992	62 412	55-69	937	12	206	25	164
New York State Cohort[10]	1980-1987	18 475	50-93	367	8	297	23	189
New York University Women's Health Study[11]	1985-1994	14 006	34-65	385	11	293	17	198
Nurses' Health Study (a)[12]	1980-1986	89 046	34-59	1023	6	284	13	155
Nurses' Health Study (b)[12]	1986-1996	68 817	40-65	1638	21	336	33	262
Sweden Mammography Cohort[13]	1987-1997	61 471	40-76	1318	4	164	5	77

*The total number of women in the baseline cohort is 351 825 and the total number of cases is 7377. As a result of additional exclusion criteria specifically applied for the Pooling Project analyses (see "Statistical Methods" for details) and expanded follow-up in some studies, the baseline cohort size and number of cases included in these analyses may differ from original study-specific publications.
†Cases indicate women diagnosed with invasive breast cancer.

Statistical Methods

For each data set, after applying the exclusion criteria used by that study, we excluded participants if they reported energy intakes greater or less than 3 SDs from the study-specific log-transformed mean energy intake of the baseline population or reported a history of cancer (except nonmelanoma skin cancer) at baseline.

To reduce computational burden with little loss of statistical efficiency,[18] the Adventist Health Study, Iowa Women's Health Study, New York State Cohort, New York University Women's Health Study, Nurses' Health Study (a), Nurses' Health Study (b), and Sweden Mammography Cohort were each analyzed as nested case-control studies. For each participant diagnosed as having invasive breast cancer, 10 controls were randomly selected from the subset of participants who had the same year of birth and who were alive, were not known to have migrated from the study area, and had not been diagnosed as having breast cancer before the year in which the case was diagnosed. A nested case-control design also was used in the Canadian National Breast Screening Study; the investigators of that study selected 2 controls for each case.[7] The Netherlands Cohort Study used a case-cohort design.[19]

For the nested case-control studies, incidence rate ratios were estimated by conditional logistic regression using SAS PROC PHREG[20]; for the Netherlands Cohort Study, Epicure software was used.[21] The RRs were adjusted for several breast cancer risk factors (TABLE 2). An indicator variable for missing responses for measured covariates within a study was created when applicable. Two-sided 95% CIs were calculated. We used the random-effects model developed by DerSimonian and Laird[22] to combine the $\log_e$ RRs; the study-specific RRs were weighted by the inverse of their variance. We tested for heterogeneity among studies using the asymptotic DerSimonian and Laird Q statistic.[22]

We analyzed the effects of fruits, fruit juice, total fruits (corresponding to fruits plus fruit juice), total vegetables, and total fruits and vegetables as continuous variables (increment of 100 g/d) and as quartiles. Study-specific quartiles were assigned based on the distributions of the control populations for the nested case-control data sets and the subcohort in the Netherlands Cohort Study. To calculate the *P* for trend across quartiles, participants were assigned the median value of their quartile of intake and this variable was entered as a continuous term in the conditional logistic regression model. Intakes of botanical groups and individual foods were modelled as continuous variables (increment of 100 g/d).

Effect Modification

We evaluated whether menopausal status at follow-up modified the association between breast cancer risk and each food group or individual food. Because most studies collected information at baseline only, we assigned menopausal status at follow-up in each study to women who were premenopausal at baseline using an algorithm based on an analysis of 42 531 Nurses' Health Study participants who were premenopausal in 1976 and remained premenopausal or had natural menopause by 1992 (see Smith-Warner et al[5] for more details). Breast cancer cases and their age-matched controls whose age at follow-up was 51 years or younger were considered to be premenopausal, between 51 and 55 years were considered as having an uncertain menopausal status, and 55 years or older were considered to be postmenopausal. For these analyses, the Iowa Women's Health Study, New York State Cohort, and Neth-

Table 2. Study-Specific and Pooled Multivariate Relative Risks of Breast Cancer by Categories of Fruit and Vegetable Consumption*

	Relative Risk (95% Confidence Interval) for 100 g/d Intake Increment†				
Study‡	Total Fruits	Fruits	Fruit Juice	Total Vegetables	Total Fruits and Vegetables
Adventist Health Study	0.97 (0.87-1.08)	0.97 (0.85-1.11)	0.92 (0.78-1.10)	1.10 (0.88-1.38)	0.99 (0.91-1.09)
Canadian National Breast Screening Study	0.98 (0.92-1.05)	0.95 (0.87-1.04)	1.03 (0.92-1.16)	0.98 (0.89-1.07)	0.98 (0.94-1.03)
Iowa Women's Health Study	1.01 (0.98-1.04)	1.02 (0.98-1.06)	1.00 (0.96-1.05)	0.98 (0.93-1.03)	1.00 (0.98-1.02)
Netherlands Cohort Study	0.97 (0.91-1.04)	0.98 (0.91-1.05)	0.94 (0.79-1.12)	0.90 (0.81-1.00)	0.96 (0.91-1.01)
New York State Cohort	1.01 (0.94-1.08)	1.02 (0.94-1.11)	0.96 (0.82-1.14)	1.04 (0.93-1.15)	1.01 (0.96-1.06)
New York University Women's Health Study	1.00 (0.95-1.05)	0.98 (0.90-1.07)	1.00 (0.94-1.07)	0.97 (0.90-1.04)	0.99 (0.95-1.03)
Nurses' Health Study (a)	0.98 (0.95-1.02)	0.98 (0.93-1.02)	0.99 (0.94-1.04)	1.01 (0.95-1.07)	0.99 (0.96-1.02)
Nurses' Health Study (b)	0.98 (0.95-1.01)	0.97 (0.94-1.01)	0.98 (0.95-1.02)	1.01 (0.98-1.05)	0.99 (0.97-1.01)
Sweden Mammography Cohort	0.99 (0.94-1.03)	0.97 (0.92-1.02)	1.02 (0.94-1.12)	1.01 (0.93-1.11)	0.99 (0.96-1.03)
Pooled	**0.99 (0.98-1.00)**	**0.99 (0.97-1.00)**	**0.99 (0.97-1.02)**	**1.00 (0.97-1.02)**	**0.99 (0.98-1.00)**
P value					
Pooled relative risk	.14	.13	.54	.67	.18
Test for heterogeneity	.90	.77	.96	.50	.92

*Incident rate ratios were estimated using conditional logistic regression and were adjusted for age at menarche (≤11, 12, 13, 14, ≥15 years), interaction between parity (0, 1-2, ≥3) and age at birth of first child (≤20, 21-25, 26-30, ≥30 years), oral contraceptive use (ever, never), history of benign breast disease (no, yes), menopausal status at follow-up (premenopausal, postmenopausal, uncertain), postmenopausal hormone use (ever, never), family history of breast cancer (no, yes), smoking status (ever, never), education (<high school graduation, high school graduation, >high school graduation), body mass index (weight in kilograms divided by the square of the height in meters; continuous), body mass index–menopausal status interaction, height (<1.60, 1.60 to <1.65, 1.65 to <1.70, 1.70 to <1.75, ≥1.75 m), alcohol intake (0, <15, ≥15 g/d), and energy intake (continuous).
†Approximate weights for common servings of specific fruits and vegetables are provided in Table 6.
‡We calculated the study-specific relative risks.

erlands Cohort Study were excluded because these studies only included postmenopausal women. Participants with uncertain menopausal status also were excluded from these analyses.

We also examined whether associations with total fruit, total vegetable, and total fruit and vegetable intakes and breast cancer risk were modified by baseline measures of family history of breast cancer, age at menarche, parity, age at first birth, oral contraceptive use, hormone replacement therapy use, history of benign breast disease, body mass index (<21, 21 to <23, 23 to <25, 25 to <29, ≥29 kg/m^2), height, smoking, education, total fat consumption (quintiles), and alcohol consumption. The potential effect modifiers were categorized using the same groups as specified in Table 2, unless otherwise noted. For each factor of interest, a cross-product term of the ordinal score for the level of each factor and intake of a specific food group or food expressed as a continuous variable was included in the multivariate model. Participants with missing values of the factor of interest were excluded from these analyses. The pooled *P* value for the test for effect modification was obtained using squared Wald statistics by pooling the study-specific interaction coefficients and dividing by the square of the SE of the pooled interaction term, and referring the resulting statistics to a χ^2 distribution with 1 *df*.

RESULTS

Reported fruit and vegetable intakes differed across studies and were positively correlated with the number of fruit and vegetable questions on the food frequency questionnaires (Spearman correlation coefficients comparing intakes with the number of questions were 0.41 for fruits and 0.70 for vegetables). Reported total fruit consumption was highest in the Adventist Health Study and total vegetable consumption was highest in the Nurses' Health Study (b) (Table 1).

Fruit, fruit juice, total fruit (fruit plus fruit juice), total vegetable, and total fruit and vegetable intakes were not associated with breast cancer risk when modeled as continuous variables (Table 2). These results were not substantially different from those obtained from models not including the additional covariates (results not shown). Despite the differences in the number of items included on the food frequency questionnaires and the absolute intakes across studies, no association was observed for any of the 5 groups in any study except for total vegetable consumption in the Netherlands Cohort Study. Similarly, the *P* for heterogeneity exceeded .40 for each food group, indicating that there was no statistically significant heterogeneity in the results across studies. Simultaneous adjustment for total fruit and total vegetable intakes on a continuous scale (results not shown) did not materially alter the results observed when each group was included in a separate model. There was no evidence of an interaction by menopausal status at follow-up for any of these groups (TABLE 3). Similar associations were observed for total fruits, total vegetables, and total fruits and vegetables for postmenopausal breast cancer diagnosed prior to age 62 years compared with cancers diagnosed at 62 years and older (results not shown).

When fruit and vegetable intakes were modeled as quartiles, the RRs comparing the highest vs lowest quartiles for fruit, fruit juice, total fruit, total vegetable, and total fruit and vegetable intakes were compatible with a reduced risk; however, none of the associations was statistically significant (TABLE 4). In these analyses, reported median total fruit and vegetable intakes for quartile 1 ranged from 110 g/d in the Sweden Mammography Cohort to 331 g/d in the Nurses' Health Study (b) and for quartile 4 ranged from 462 g/d in the Sweden Mammography Cohort to 1007 g/d in the Nurses' Health Study (b).

To investigate whether there was an effect of very high fruit and vegetable consumption, we categorized total fruit, total vegetable, and total fruit and vegetable intakes into deciles. The RRs for the uppermost vs lowermost deciles of intake were 0.97 (95% CI, 0.87-1.10) for total fruits, 0.91 (95% CI, 0.81-1.02) for total vegetables, and 0.96 (95% CI, 0.83-1.10) for total fruits and vegetables. Additional adjustment for total fat consumption or saturated, monounsaturated, and polyunsaturated fat intakes separately did not materially change the continuous, quartile, or decile results for total fruit, total vegetable, and total fruit and vegetable intakes; however, the RRs for the

Table 3. Pooled Multivariate Relative Risks of Breast Cancer by Menopausal Status and Categories of Fruit and Vegetable Consumption*

	Premenopausal (n = 1052)†		Postmenopausal (n = 5447)†		*P* Value for Interaction by Menopausal Status‡
	RR (95% CI) for 100 g/d	*P* Value for Heterogeneity	RR (95% CI) for 100 g/d	*P* Value for Heterogeneity	
Total fruits	0.98 (0.94-1.02)	.83	0.99 (0.98-1.01)	.89	.80
Fruits	0.95 (0.90-1.00)	.95	1.00 (0.97-1.02)	.69	.53
Fruit juice	1.00 (0.95-1.06)	.91	0.99 (0.97-1.02)	.99	.85
Total vegetables	0.99 (0.93-1.06)	.34	1.00 (0.97-1.02)	.31	.54
Total fruits and vegetables	0.99 (0.96-1.02)	.78	1.00 (0.98-1.01)	.85	.57

*RR indicates relative risk; CI, confidence interval. Menopausal status at follow-up was assigned using an algorithm (see "Methods" for details). See asterisk footnote for Table 2, which describes how relative risks were adjusted. For both premenopausal and postmenopausal breast cancer, menopausal status and the body mass index–menopausal status interaction terms are not included in the model. For premenopausal breast cancer, postmenopausal hormone use also is not included.
†The values designate the number of cases.
‡The *P* value for effect modification by menopausal status was calculated using data for only those studies including premenopausal and postmenopausal women at baseline. The Netherlands Cohort Study, Iowa Women's Health Study, and New York State Cohort were excluded from these analyses.

Table 4. Pooled Multivariate Relative Risks of Breast Cancer According to Quartiles of Fruit and Vegetable Consumption*

	Pooled Relative Risk (95% Confidence Interval)				*P* Value	
	Quartile 1	Quartile 2	Quartile 3	Quartile 4	Heterogeneity for Quartile 4	Trend
Total fruits	1.00	0.94 (0.87-1.01)	0.92 (0.86-0.99)	0.93 (0.86-1.00)	.94	.08
Fruits	1.00	0.98 (0.90-1.07)	0.95 (0.88-1.02)	0.93 (0.84-1.02)	.15	.08
Fruit juice	1.00	0.96 (0.87-1.06)	1.00 (0.92-1.08)	0.93 (0.86-1.00)	.64	.27
Total vegetables	1.00	0.99 (0.90-1.08)	0.97 (0.90-1.05)	0.96 (0.89-1.04)	.73	.54
Total fruits and vegetables	1.00	0.94 (0.88-1.01)	0.92 (0.86-0.99)	0.93 (0.86-1.00)	.99	.12

*See asterisk footnote for Table 2, which describes how relative risks were adjusted.

highest vs lowest quartile of total fruit and total fruit and vegetable consumption were marginally significant ($P=.04$) in the analyses that controlled for total fat intake. For these 3 groups, excluding the 1125 cases diagnosed during the first year of follow-up did not substantially change the continuous results, but did attenuate the quartile and decile results (results not shown).

Green leafy vegetable consumption (ie, spinach, lettuce, mustard/collard greens, kale) was not associated with breast cancer risk (RR, 0.99 for a 100-g/d increment, 95% CI, 0.92-1.06). The Rosaceae family was the only botanical group for which an inverse association was suggested (TABLE 5). Intakes of Compositae, Cruciferae, Cucurbitaceae, Leguminosae, Rutaceae, Solanacea, and Umbelliferae were not associated with breast cancer risk. Likewise, none of the specific fruits or vegetables examined was significantly associated with breast cancer risk (TABLE 6). Menopausal status at follow-up did not modify the associations for green leafy vegetables, the botanical groups, or the specific fruits and vegetables evaluated (results not shown).

We evaluated whether associations for total fruit, total vegetable, and total fruit and vegetable intakes were modified by several breast cancer risk factors. The only significant pooled interactions occurred for height and total fruit intakes, for oral contraceptive use and total fruit intakes, and for oral contraceptive use and total fruit and vegetable consumption. The RR for a 100-g/d increment of total fruit consumption was 1.01 (95% CI, 0.99-1.04) for women with heights less than 160 cm and 0.96 (95% CI, 0.88-1.04) for women with heights of 175 cm or more; however, the relationship was not monotonic across the 5 height categories (P for interaction=.01). For the analyses evaluating whether oral contraceptive use modified the association with total fruit consumption, the RR for a 100-g/d increment of total fruit consumption was 0.97 (95% CI, 0.95-0.99) for participants who had never used oral contraceptives and 1.01 (95% CI, 0.97-1.04) for participants who reported ever using oral contraceptives (P for interaction=.05). Likewise, the RR for a 100-g/d increment of total fruit and vegetable consumption was 0.98 (95% CI, 0.97-1.00) for participants who had never used oral contraceptives and 1.01 (95% CI, 0.99-1.02) for participants who reported ever using oral contraceptives (P for interaction=.02).

Table 5. Pooled Multivariate Relative Risks of Breast Cancer by Consumption of Botanically Defined Fruit and Vegetable Groups*

Botanical Group	Example Foods	Relative Risk (95% Confidence Interval)	*P* Value for Heterogeneity
Compositae	Lettuce, endive	0.93 (0.84-1.02)†	.83
Cruciferae	Broccoli, cabbage	0.96 (0.87-1.06)‡	.95
Cucurbitaceae	Melons, squash	1.03 (0.88-1.21)§	.02
Leguminosae	Beans, peas	0.97 (0.87-1.08)	.36
Rosaceae	Apples, peaches	0.97 (0.94-1.00)‡	.72
Rutaceae	Grapefruits, oranges	0.99 (0.97-1.01)	.98
Solanacea	Potatoes, tomatoes	1.02 (0.99-1.05)	.75
Umbelliferae	Carrots, celery	0.97 (0.87-1.09)‡	.46

*The values are based on a 100-g/d intake increment. See asterisk footnote for Table 2, which describes how relative risks were adjusted.
†The Nurses' Health Study (a) was not included in this analysis.
‡The Adventist Health Study was not included in this analysis.
§The Adventist Health Study, Canadian National Breast Screening Study, and Sweden Mammography Cohort were not included in this analysis.

COMMENT

These results suggest that fruit and vegetable consumption is not associated with breast cancer risk when analyzed as total fruits and vegetables, fruits, fruit juice, total fruits, total vegetables, green leafy vegetables, 8 botanically defined fruit and vegetable groups, or 17 specific fruits and vegetables. Our results are similar to those of the 2 cohort studies not included in the Pooling Project, which reported weak, nonsignificant associations for various fruit and vegetable groups.[23,24] However, a recent summary[2] of associations between several fruit and vegetable groups and breast cancer risk from 19 case-control and 3 cohort studies was more suggestive of an inverse association than our results. Overall, of the 70 risk estimates reported in the summary, 53% of the estimates showed at least a 25% reduction in breast cancer risk for the highest vs lowest consumers; whereas only 4% of the associations showed a 50% or more elevation in risk. The evidence was more consistent for vegetables than fruits. Identifying whether specific types of fruits and vegetables

vs overall exposure to fruits and vegetables have more cancer preventive potential is difficult because of the multitude of fruit and vegetable categories that have been reported. Besides the total fruit and total vegetable groups, few fruit and vegetable food groups have been reported consistently and reviews of published results are likely to be subject to publication bias.[1,2] Furthermore, different analytic approaches have been used across studies even when the same exposures have been examined, which makes summarizing the data difficult. In contrast, in the Pooling Project, common food group and covariate definitions were applied across studies, uniform comparisons were made, and summary estimates were generated for those comparisons. Another potential explanation for the discrepancy could be related to differences in study design. The majority of studies in the summaries of the published literature were case-control studies, which are susceptible to recall and selection bias. Our analyses used data from prospective cohort studies that are less susceptible to these biases. Further clarification of the association between fruit and vegetable consumption and breast cancer risk may be forthcoming from ongoing diet intervention trials.

One of the advantages of the Pooling Project is the large sample size and, therefore, the enhanced statistical power to examine potential interactions with dietary factors. Several studies have evaluated whether the association between fruit and vegetable consumption is modified by menopausal status[7,12,25-32] or by age group.[32-34] Although 3 studies have suggested that the association with fruit and vegetable consumption is stronger for premenopausal compared with postmenopausal breast cancer,[12,31,34] most studies have found no evidence of an interaction by menopausal status.[7,25-30,32,33] Like these studies, we also found no evidence of an interaction by menopausal status for any of the fruit and vegetable groups examined; however, we had limited power to evaluate associations in premenopausal women. Of the remaining interactions tested, only 3 were statistically significant and these were probably due to chance as they were not hypothesized a priori.

The number of fruit and vegetable questions included on the food frequency questionnaires varied over 4-fold across the studies. As reported previously,[35] reported fruit and vegetable servings increased with the number of fruit and vegetable items on the questionnaires. As a result, differences in estimates of absolute fruit and vegetable consumption across the studies in the Pooling Project may be due to differences in questionnaire design, as well as differences in true intakes. Therefore, we did not calculate risk estimates for categories of intakes that were defined using identical absolute cut points across the individual studies. Instead, we formed study-specific quartiles and pooled the RRs for each quartile. This type of analysis would reduce our ability to detect an association if breast cancer risk was lower only above a threshold of intake, and if only a subset of the studies had a substantial number of women consuming above this threshold. However, we observed little evidence that the risk estimates for comparisons of the highest vs lowest quartiles, or even deciles, of intakes was different among the studies. Furthermore, for most groupings, a slight reduction in risk was evident for the second compared with the lowest quartile, with little additional reduction in risk in comparisons of the third or fourth quartiles with the lowest quartile. This again suggests that while very low intakes may be adversely associated with breast cancer risk, very high intakes are not likely to be associated with a large reduction in risk.

Table 6. Pooled Multivariate Relative Risks of Breast Cancer for Specific Fruits and Vegetables*

Foods	Portion Size (Weight, g)†	Relative Risk (95% Confidence Interval)	*P* Value for Heterogeneity
Fruits			
Apples, pears	1 (138)	0.97 (0.93-1.01)‡	.54
Bananas	1 (114)	1.00 (0.93-1.08)‡	.30
Oranges, tangerines	1 (121)	0.98 (0.92-1.05)‡§#††	.94
Peaches, apricots, plums, nectarines	1 (87)	1.00 (0.91-1.09)‡‖††	.59
Vegetables			
Broccoli	1/2 cup (78)	0.86 (0.72-1.02)‡‖††	>.99
Brussels sprouts	1/2 cup (30)	0.67 (0.35-1.27)‡#**††	.12
Cabbage	1/2 cup (75)	1.05 (0.85-1.29)‡§**	.97
Carrots	1/2 cup (78)	0.95 (0.81-1.12)‡††	.70
Corn	1/2 cup (82)	1.25 (0.99-1.58)‡‖¶††	>.99
Lettuce, salad	1 cup (56)	0.93 (0.84-1.02)**	.83
Peas, lima beans	1/2 cup (80)	1.03 (0.78-1.37)‡‖#††	.26
Potatoes			
Total		1.03 (0.98-1.08)‡	.50
Baked, boiled, or mashed	1 (202)	1.02 (0.97-1.08)‡¶	.30
Fried	10 pieces (50)	1.00 (0.76-1.33)‡¶	.90
Spinach	1/2 cup cooked	0.61 (0.33-1.15)‡§**††	.02
String beans	1/2 cup (62)	0.85 (0.66-1.09)‡¶#††	.25
Tomatoes	1 (123)	1.04 (0.96-1.12)#**	.31

*The values are based on a 100-g/d intake increment. See asterisk footnote for Table 2, which describes how relative risks were adjusted.
†Based on Pennington, 1998.[17]
‡The Adventist Health Study was not included in the analysis.
§The Canadian National Breast Screening Study was not included in the analysis.
‖The Netherlands Cohort Study was not included in the analysis.
¶The New York State Cohort was not included in the analysis.
#The New York University Women's Health Study was not included in the analysis.
**The Nurses' Health Study (a) was not included in the analysis.
††The Sweden Mammography Cohort was not included in the analysis.

We could only analyze most fruit and vegetable subgroups and individual foods as continuous variables, rather than as quartiles, because intakes within a study tended to be described in a limited number of discrete categories. Another limitation due to differences in questionnaire design is that the number of studies included in the fruit and vegetable subgroup analyses varied depending on whether the foods comprising a particular subgroup were asked on a study's questionnaire. Consequently, the power to examine associations for some subgroups and specific foods is more limited compared with that for analyses of the main fruit and vegetable groups.

In conclusion, our results suggest that fruit and vegetable consumption during adulthood is not significantly associated with breast cancer risk. Breast cancer risk was only 3% to 9% lower in women in the highest decile of fruit or vegetable consumption compared with the lowest decile. We did not identify any fruit and vegetable subgroups or specific fruits or vegetables that had stronger and statistically significant associations with breast cancer risk compared with the associations observed for total fruit and total vegetable consumption. Although fruits and vegetables may offer protection against other types of cancer[2] and heart disease,[36,37] other types of interventions are needed to reduce the risk of breast cancer.

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> Remember, then, that it [science] is the guide of action; that the truth which it arrives at is not that which we can ideally contemplate without error, but that which we may act upon without fear; and you cannot fail to see that scientific thought is not an accompaniment or condition of human progress, but human progress itself.
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> —William Kingdon Clifford (1845-1879)