

# What is the relationship between glycemic index or glycemic load and cancer?

## Conclusion

Abundant, strong epidemiological evidence demonstrates that there is no association between glycemic index or load and cancer.

## Grade: Strong

Overall strength of the available supporting evidence: Strong; Moderate; Limited; Expert Opinion Only; Grade not assignable For additional information regarding how to interpret grades, [click here](#).

## Overall Evidence Summary

The epidemiological evidence for an association between glycemic index (GI) or glycemic load (GL) and cancer is overwhelmingly negative. Twenty-eight reports have been published since 2005. Of these, 20 are prospective longitudinal observation studies, one is a cross-sectional observation study, five are case-control studies and two are case-cohort studies.

Of the 20 prospective longitudinal observational studies, 18 studied the association between GI and cancer. One showed a very weak positive association between GI and total cancer risk (George, 2009), while thirteen studies found no association between GI and specific types of cancer including pancreatic (Heinen, 2008; Johnson, 2005; Nothlings, 2007; Patel, 2007; Silvera, 2005), breast (Giles, 2006; Lajous, 2008; Sieri, 2007; Silvera, 2005), endometrial (Cust, 2007; Larsson and Friberg, 2007) stomach (Larsson, 2006) and ovarian (Silvera, 2007) cancers. Varying results were found for colorectal cancer with no association reported in three studies (Larsson, 2007; McCarl, 2006; Michaud, 2005) and an inverse association reported by Strayer et al (2007).

Of the 20 prospective longitudinal observational studies, all studied the association between GL and cancer. Two showed a positive association for total cancer (George, 2009) and ovarian cancer (Silvera, 2007). However, most studies reported no association between GL and cancer, including pancreatic (Heinen, 2008; Johnson, 2005; Nothlings, 2007; Patel, 2007; Silvera, 2005), breast (Giles, 2006; Lajous, 2008; Sieri, 2007; Silvera, 2005), endometrial (Cust, 2007; Larsson and Friberg, 2007), and stomach (Larsson, 2006) cancers. Similar to glycemic index, there were mixed results regarding the relationship between GL and colorectal cancer, with five studies finding no association (Kabat, 2008; Larsson, 2007; McCarl, 2006; Michaud, 2005; Strayer, 2007) and one study reporting an inverse association (Howarth, 2008).

The two case-cohort studies reported no association of either GI or GL with pancreatic (Kabat, 2008) or colorectal (Weijenberg, 2008) cancers. Similarly, one cross-sectional observational study showed no association between either GI or GL and colorectal adenomas (Flood, 2006a).

The five available case-control reports reported mixed results. Of these, three found GI to be significantly associated with prostate (Augustin, 2004), gastric (Bertuccio, 2009) and thyroid (Randi, 2008) cancers, and two found no association with breast cancer (Lajous, 2005; McCann, 2007). Similarly, three found glycemic load to be significantly associated with cancer of the breast (Lajous, 2005), prostate (Bertuccio, 2009) or thyroid (Randi, 2008) and found no association for

breast (McCann, 2007) and prostate (Augustin, 2004) cancers.

### Evidence Summary Paragraphs

**Augustin, 2004** (neutral quality), a case-control study conducted in Italy, investigated the association of dietary glycemic index (GI) and glycemic load (GL) with prostate cancer risk in 1,204 male cases and 1,352 male controls (aged 46 to 74 years). Compared to the lowest quintile of GI, odds ratios (OR) for developing prostate cancer were 1.23, 1.24, 1.47 and 1.57 for subsequent levels of GI, and the corresponding values for GL were 0.91, 1.00, 1.20, 1.41. The authors concluded that direct relations between dietary GI and GL and prostate risk were found. Correcting for potential confounding factors did not substantially modify these associations.

**Bertuccio, 2009** (positive quality), a case-control study conducted in Italy, assessed the relationship between glycemic load (GL), glycemic index (GI) and gastric cancer in patients admitted to major teaching and general hospitals in Italy. 230 patients had incident, histologically confirmed gastric cancer and 547 patients served as matched controls (mean age for both groups of 63 years, range 22 to 80 years). The OR in the highest vs. lowest quintile were 1.9 (95% CI: 1.0 to 3.3) for GI and 2.5 (95% CI: 1.3 to 4.9) for GL. The OR rose across strata of high GL and low fruit and vegetable intake to reach 5.0 (95% CI: 2.2 to 11.5) for those reporting high GL and low fruit and vegetable intake, compared with participants reporting low GL and high fruit and vegetable intake. The authors concluded that GL may have an independent role in gastric cancer formation and they noted lack of information on *H. pylori* infection and hospital dietary habits differing from the general population as possible limitations.

**Cust, 2007** (positive quality), the European Prospective Investigation into Cancer and Nutrition cohort study (prospective cohort study), examined the association of endometrial cancer risk with dietary total carbohydrates, glycemic index (GI) and glycemic load (GL) in 288,428 women recruited between 1992 and 2000 throughout 10 western European countries. During a mean 6.4 years and 1,842,995 person-years of follow-up, 710 incident endometrial cancer cases were diagnosed. Data suggest no association of overall GI, total starch and total fiber with endometrial cancer risk; however, multivariable RR were 1.61 (95% CI: 1.06 to 2.45) per 100g per day of total carbohydrates, 1.40 (95% CI: 0.99 to 1.99) per 50g per day of total dietary GL, and 1.36 (95% CI: 1.05 to 1.76) per 50g per day of total sugars. These associations were stronger among women who had never used post-menopausal hormone therapy.

**Flood, 2006** (positive quality), a multi-center cross-sectional study conducted in the US, determined if glycemic index (GI) or load (GL) was associated with risk of distal adenomas in 44,572 participants from the Prostate, Lung, Colorectal and Ovarian screening trial. A total of 3,696 participants were diagnosed with at least one distal adenoma. There were no significant (NS) associations between GI and risk of distal adenomas for men or women; after multivariate adjustment, there was a significant inverse association between GL and risk of distal adenomas in men, but not in women.

**George, 2009** (positive quality), a prospective cohort study conducted in the US, investigated whether glycemic index (GI) and glycemic load (GL) were related to increased risk of developing a primary cancer in 262,642 male and 183,535 female participants from the National Institutes of Health-American Association of Retired Persons (NIH-AARP) Diet and Health Study (average age approximately 60 years). The RR for total cancer for high vs. low GI were 1.03 for women (P=0.217) and 1.04 for men (P=0.012), and for high vs. low GL, were 0.90 for men (P=0.024) and 0.93 for women (P=0.01), suggesting that GI and GL are not strong predictors of cancer incidence.

**Giles, 2006** (neutral quality), a prospective cohort study conducted in Australia, investigated

associations between dietary carbohydrates (CHO), dietary fiber, glycemic index (GI) and glycemic load (GL), and risk of invasive breast cancer in female participants (aged 40 to 69 years at baseline) of the Melbourne Collaborative Cohort Study. During an average of 9.1 years follow-up, 324 breast cancers were diagnosed in 12,273 post-menopausal women. Although an increase of one standard deviation (SD) in CHO intake was marginally associated with risk of breast cancer (RR=1.31, 95% CI: 0.98, 1.75), there were NS associations with fiber, GI, GL or CHO foods.

**Heinen, 2008** (neutral quality), a prospective cohort study in the Netherlands, examined pancreatic cancer risk in a subcohort of the Netherlands Cohort Study. After 13.3 years of follow-up, the final subcohort included 4,438 subjects (2,191 men, 2,247 women) and 408 exocrine pancreatic cancer cases (217 men, 191 women) (subcohort aged 55 to 69 years at baseline). Dietary glycemic load, glycemic index or intake of CHO and mono- and disaccharides were not associated with pancreatic cancer risk.

**Howarth, 2008** (neutral quality), a prospective cohort study conducted in the US, determined the risk of colorectal cancer associated with glycemic load (GL), CHO and sucrose, and ascertained whether this risk was modified by sex and ethnicity in 191,004 men and women participating in the Multiethnic Cohort Study. Over eight years of follow-up, 2,379 incident cases of colorectal adenocarcinoma occurred in 1,293 men and 1,086 women. In multivariate models, relative risks (RR) for colorectal cancer decreased significantly with increasing GL in women (RR for the highest vs. lowest quintile = 0.75, 95% CI: 0.57, 0.97; P=0.02) but not in men (RR=1.15, 95% CI: 0.89, 1.48; P=0.19); results for CHO and sucrose were similar. The inverse association was found in women of all ethnic groups. The authors concluded that GL and CHO intake appeared to be protective against colorectal cancer in women after adjustment for potential confounders.

**Johnson, 2005** (neutral quality), a prospective cohort study conducted in the US, examined the hypothesis that high dietary glycemic index (GI) and glycemic load (GL) were associated with increased risk of pancreatic cancer in 33,551 women from the Iowa Women's Health Study (aged 55 to 69 at baseline). Participants were followed from 1986 until 2002. Incidence of pancreatic cancer was higher in subjects aged 65 to 69 vs. aged 55 to 64, diabetic vs. non-diabetic, current smokers vs. non-smokers, and multivitamin non-users vs. users, but there was no increased hazard of pancreatic cancer associated with high dietary GI or GL. The authors did not find evidence to support the hypothesis that high dietary GI or GL increases the risk of pancreatic cancer.

**Kabat, 2008** (neutral quality), using data from the Observational Study and Clinical Trial cohorts of the Women's Health Initiative (prospective cohort study) in the US, examined the association of intake of CHO, glycemic index (GI), glycemic load (GL) and related dietary factors in relation to colorectal cancer and subsites within the colorectum in 158,800 post-menopausal women (aged 50 to 79 at baseline). Over an average of 7.8 years of follow-up, 1,476 incident cases of colorectal cancer were identified. When data were analyzed separately as well as combined, total carbohydrate intake, GI and GL, plus intake of sugars and fiber showed no association with colorectal cancer and there were no trends over increasing quintiles. This study provides no evidence that a diet characterized by high GI or GL, or by a high intake of CHO or sugars, increases the risk of colorectal cancer in generally healthy post-menopausal women.

**Lajous, 2005** (neutral quality), a case-control study conducted in Mexico, compared dietary glycemic load (GL) and overall glycemic index (GI) with breast cancer risk in 475 women with biopsy-confirmed breast cancer and 1,391 controls. The multivariate adjusted OR for all women comparing the highest and lowest tertiles of dietary GL was 1.62 (95% CI: 1.13 to 2.32, P=0.02), and the association was stronger in post-menopausal women [multivariate adjusted OR was 2.18 (95% CI: 1.34 to 3.55; P=0.005)]. Glycemic index was NS associated with risk of breast cancer. The

authors concluded that high intake of rapidly absorbed CHO may play a role in the risk of breast cancer in Mexican women.

**Lajous, 2008** (neutral quality), a prospective cohort study in France, evaluated CHO intake, glycemic index (GI), glycemic load (GL) and fiber intake and the subsequent risk of overall and hormone receptor-defined breast cancer among 62,739 post-menopausal women (aged 42 to 72 years at baseline) participating in the E3N French Study, the French component of the European Prospective Investigation into Cancer and Nutrition. During nine years of follow-up, 1,812 cases of pathology-confirmed breast cancer were documented. Dietary carbohydrate intakes, GI and GL were not associated with overall breast cancer risk. However, among overweight women, there was an association between GI and breast cancer (RR=1.35, 95% CI: 1.00, 1.82, P=0.04); this association was absent for women with body mass index (BMI) <25kg/m<sup>2</sup>. The authors concluded that rapidly absorbed CHO may be associated with post-menopausal breast cancer risk among overweight women and women with large waist circumference. In addition, carbohydrate intake may be associated with estrogen receptor-negative breast cancer.

**Larsson, Giovannucci et al, 2007** (neutral quality), a prospective cohort study in Sweden, examined the associations between CHO intake, glycemic index (GI) and glycemic load (GL) and the risk of colorectal cancer in 61,433 women participating in the Swedish Mammography Cohort Study who completed a baseline questionnaire in 1987 to 1990. Over 963,426 person-years of follow-up (mean = 15.7 years), there were 870 cases of colorectal cancer, but CHO intake, GI and GL had NS association with colorectal, colon or rectal cancer, regardless of BMI and alcohol consumption. The authors concluded that this study does not support the hypothesis that high carbohydrate intake, high GI and high GL increase the risk of colorectal cancer.

**Larsson, Friberg et al, 2007** (neutral quality), a prospective cohort study in Sweden, examined the associations between CHO intake, glycemic index (GI) and glycemic load (GL) and the risk of endometrial cancer in 61,226 women participating in the Swedish Mammography Cohort Study. Over 952,629 person-years of follow-up, 608 cases of endometrial cancer developed, but there was no overall association between carbohydrate intake, GI or GL and incidence of endometrial cancer. However, carbohydrate intake and GL were positively related to endometrial cancer risk among overweight women (BMI higher than 25kg/m<sup>2</sup>) with low physical activity in a subanalysis of these data; multivariate RRs comparing extreme quartiles were 1.90 (95% CI: 0.84 to 4.31) for CHO intake and 2.99 (95% CI: 1.17 to 7.67) for GL. The authors concluded that they found no overall associations between CHO intake, GI or GL and the incidence of endometrial cancer. However, among overweight women with low physical activity, we observed a NS 1.9-fold increase in risk of endometrial cancer for those who had a high CHO intake and a statistically significant three-fold increase in risk for those who had a high GL.

**Larsson, 2006** (neutral quality), a prospective cohort study in Sweden, examined the associations between dietary glycemic load (GL), overall glycemic index (GI) and CHO intake in relation to the incidence of stomach cancer among 61,433 women in the Swedish Mammography Cohort. Diet was assessed at baseline (1987 to 1990) with a 67-item food-frequency questionnaire (FFQ) and again in 1997 with a 96-item FFQ. Stomach cancer incidence was obtained by linkage to national and regional Swedish Cancer registers with follow up through 2004. During 903,586 person-years of follow-up, there were 156 incident cases of stomach cancer. There was no association between CHO intake, GI or GL and incidence of stomach cancer using any of the dietary intake data. The multivariate hazard ratios (HR) for the highest vs. the lowest quintile were 0.76 (95% CI: 0.46, 1.25) for GL, 0.77 (95% CI: 0.46, 1.30) for overall GI and 0.85 (95% CI: 0.50, 1.43) for CHO intake. The study did not provide evidence of a positive association between GI, GL or CHO intake among middle-aged and elderly women and they noted lack of information on *H. pylori* infection.

**McCann, 2007** (positive quality), a case-control study in the US, examined the associations between glycemic index (GI) and glycemic load (GL) and the risk of breast cancer in 1,166 women with incident, primary, histologically confirmed breast cancer and 2,105 matched controls in the Western New York Exposure and Breast Cancer Study (WEB). Participants were predominantly white (90%), and approximately 40% were pre-menopausal. In pre-menopausal women, breast cancer was not related to GI or GL. There was a NS trend toward a decrease in the risk of breast cancer for post-menopausal women in the highest vs. lowest quartile of GI (OR: 0.80; 95% CI: 0.61, 1.03) and GL (OR: 0.74; 95% CI: 0.53, 1.03). The authors concluded that they observed little association between breast cancer and GI or GL.

**McCarl, 2006** (neutral quality), a prospective cohort study in the US, examined the associations between glycemic index (GI) and glycemic load (GL) and the risk of colorectal cancer in 35,197 women from the Iowa Women's Health Study (99% Caucasian, aged 55 to 69 years at baseline). Over 15 years of follow-up, 757 cases of colon cancer and 209 cases of rectal cancer (954 CRC cases) were observed. Overall, GI and GL were NS associated with incident colorectal cancer. However, when stratified by BMI, among obese women, colorectal cancer incidence was increased in the highest vs. lowest quintiles of GI (RR=1.66; 95% CI: 1.13 to 2.43; P=0.02) and GL (RR=1.79; 95% CI: 1.19 to 2.70; P<0.01). Similar results were observed for colon and rectal cancer. No significant associations between GI and GL and colorectal cancer risk were observed for non-obese women (BMI <30kg/m<sup>2</sup>). The authors concluded that high GI or GL are not major colorectal cancer risk factors among older women in general, but may increase risk among women who are categorized as obese.

**Michaud, 2005** (positive quality), a prospective cohort studies in the US, examined the associations between glycemic index (GI) and glycemic load (GL) and the risk of colorectal cancer in 47,422 male participants from the Health Professionals Follow-Up Study and 83,927 women from the Nurses' Health Study. During 20 years of follow-up, 1,809 incidence colorectal cancer cases were available for analyses. A slight increase in colorectal cancer risk for dietary GL was observed in men, but not women. The associations were slightly stronger among men with higher BMI, but there were still no associations observed after stratifying by BMI, physical activity or hormone use among women. The authors concluded that the glycemic response to diet may not play a major role in colorectal cancer.

**Nöthlings, 2007** (neutral quality), a prospective cohort study in the US, examined the associations between dietary glycemic load (GL), dietary CHO, sucrose, fructose, total sugars and added sugars and pancreatic cancer risk among 162,150 men (N=72,966) and women (N=89,184) participating in the Multiethnic Cohort Study. Between 1993 and 1996 and 2002, 434 incident pancreatic cancer cases occurred in the cohort. Glycemic load was not associated with pancreatic cancer risk in the overall cohort (P=0.65). Non-significantly higher risks of pancreatic cancer were seen in the overweight and obese group (BMI ≥25kg/m<sup>2</sup>) than in the normal weight group (BMI ≤25kg/m<sup>2</sup>) in the top quartiles of GL. The authors concluded that dietary GL may not add important information about the quality of CHO in the diet of their cohort participants.

**Patel, 2007** (positive quality), a prospective cohort study in the US, examined the association between glycemic load (GL), glycemic index (GI), CHO intake and pancreatic cancer risk among 124,907 men and women in the American Cancer Society Cancer Prevention Study II (CPS-II) Nutrition Cohort. During nine years of follow-up, 401 incident pancreatic cancer cases were identified. No association between GL or GI and risk of pancreatic cancer was observed. No factors examined (including being overweight or sedentary) modified the association between these dietary measures and pancreatic cancer risk. The authors concluded that their data do not support the

hypothesis that GI or GL are associated with a substantial increase in pancreatic cancer risk.

**Randi, 2008** (neutral quality), a case-control study in Italy, examined the association between glycemic index (GI) and glycemic load (GL) and risk of thyroid cancer. Cases (N=399, median age 44 years, 73% women) had histologically confirmed and incident cases of thyroid cancer. Controls (N=617, median age 46 years, 69% women) were patients admitted to the same network of hospitals as cases for acute non-neoplastic diseases unrelated to known or potential risk factors for thyroid carcinoma, and unrelated to long-term diet modification. Compared with the lowest tertile, the multivariate ORs in subsequent tertiles were 1.68 and 1.73 for GI (P=0.0047) and 1.76 and 2.17 for GL (P<0.0001). The authors concluded that GI and GL are associated with thyroid cancer risk.

**Sieri, 2007** (neutral quality), a prospective cohort study in Italy, examined the association between glycemic index (GI) and glycemic load (GL) and risk of breast cancer in 8,926 women from the Hormones and Diet in the Etiology of Breast Tumors Study (ORDET Study). After a mean follow-up of 11.5 years, 289 breast cancers were identified. The adjusted RR of breast cancer in the highest vs. lowest quintiles of GI and GL was 1.57 (95% CI: 1.04, 2.36; P=0.040) and 2.53 (95% CI: 1.54, 4.16; P=0.001), respectively. When categorized by baseline menopausal status and BMI, the increased risk of dietary GL was confined to those who were pre-menopausal (RR=3.89; 95% CI: 1.81, 8.34) and who had normal BMI (i.e., <25kg/m<sup>2</sup>) (RR=5.79; 95% CI: 2.60, 12.90; P=0.001 for both). The authors concluded that high dietary GL and, to a lesser extent, high dietary GI were significantly associated with a greater risk of breast cancer, particularly for pre-menopausal women and those with BMI <25kg/m<sup>2</sup>.

**Silvera, 2005** (positive quality), a prospective cohort study in Canada, examined the association between glycemic index (GI) and glycemic load (GL) and risk of breast cancer in 49,111 women from the Canadian National Breast Screening Study (NBSS). During a mean follow-up of 16.6 years, 1,450 incident breast cancer cases were observed. Dietary GL was not associated with risk of breast cancer. Overall GI was not associated with risk of breast cancer in the total study population. However, there was evidence of effect modification of the association between GI and breast cancer risk by menopausal status (P=0.01), the hazard ratio (HR) for the highest vs. the lowest quintile level of GI being 0.78 (95% CI: 0.52, 1.16; P=0.12) in pre-menopausal women and 1.87 (95% CI: 1.18, 2.97; P=0.01) in post-menopausal women. The associations between GI and GL were not modified by BMI or by vigorous physical activity among pre- or post-menopausal women. The associations between GI and GL and risk in post-menopausal women were not modified by BMI, vigorous physical activity or ever use of hormone replacement therapy (HRT), although the associations were slightly stronger among those who reported no vigorous physical activity (P=0.02), among those who reported ever using HRT (P=0.02) and among normal weight women (BMI <25kg/m<sup>2</sup>; P=0.03). The authors concluded that dietary GL was not associated with risk of breast cancer. However, a relatively high overall GI might be associated with increased risk among women who are post-menopausal, possibly more so among subgroups defined by participation in vigorous physical activity, ever used HRT and those with BMI >25kg/m<sup>2</sup>.

**Silvera, 2005** (neutral quality), a prospective cohort study in Canada, examined the association between glycemic index (GI) and glycemic load (GL) and risk of endometrial cancer in 34,391 women from the Canadian National Breast Screening Study (NBSS). During a mean of 16.4 years of follow-up, 426 incident cases of endometrial cancer were observed. Adjusted hazard ratios (HR) for the highest vs. the lowest quartile of overall GI and GL were 1.47 (95% CI: 0.90, 2.41; P=0.14) and 1.36 (95% CI: 1.01, 1.84; P=0.21), respectively. When quartiles of GI and GL and risk of endometrial cancer were stratified by categories of BMI (<25, 25 to 29, 30kg/m<sup>2</sup> or more), participation in vigorous physical activity (none vs. some), menopausal status and use of HRT (never vs. ever), NS trends were observed. However, the authors concluded that dietary GL and

overall GI may be associated with risk of endometrial cancer overall. They also stated that a relatively high dietary GL might be associated with increased risk among obese women and pre-menopausal women. Finally, they concluded that GL may be positively associated with endometrial cancer risk among post-menopausal women who have used HRT.

**Silvera, 2005** (positive quality), a prospective cohort study in Canada, examined the association between glycemic index (GI) and glycemic load (GL) and risk of pancreatic cancer in 49,111 women from the Canadian National Breast Screening Study (NBSS). During a mean 16.5 years of follow-up, 112 incident pancreatic cancer cases were observed. No association between overall GI or GL and pancreatic cancer risk was observed. In multivariate adjusted models, the hazard ratio (HR) for the highest vs. lowest quartile levels of overall GI and GL were 1.43 (95% CI: 0.56, 3.65; P=0.58) and 0.80 (95% CI: 0.45, 1.41; P=0.41), respectively. The authors concluded that overall GI and GL were not associated with pancreatic cancer risk.

**Silvera, 2007** (positive quality), a prospective cohort study in Canada, examined the association between glycemic index (GI) and glycemic load (GL) and risk of ovarian cancer in 48,776 women from the Canadian National Breast Screening Study (NBSS). During a mean 16.4 years of follow-up, 264 incident cases of ovarian cancer were observed. Glycemic index was not associated with risk of ovarian cancer in the total cohort. Glycemic load was positively associated with a 72% increase in risk of ovarian cancer (HR=1.72, 95% CI: 1.13, 2.62; P=0.01). The magnitude of the association was slightly greater among post-menopausal (HR=1.89, 95% CI: 0.98, 3.65, P=0.03) than among pre-menopausal women (HR=1.64, 95% CI: 0.95, 2.88; P=0.07); however, there was no statistical evidence of effect modification by baseline menopausal status (P for interaction = 0.54). The authors concluded that high GL may be associated with increased risk of ovarian cancer.

**Strayer, 2007** (positive quality), a prospective cohort study in the US, examined the association between glycemic index (GI) and glycemic load (GL) and risk of colorectal cancer in 41,133 women from the Breast Cancer Detection Demonstration Project (BCDDP). During an average of 8.5 years of follow-up, 490 incident cases of colorectal cancer were observed. Reduction in colorectal cancer risk was observed for diets high in GI (RR for Q5 vs. Q1 = 0.75, 95% CI: 0.56, 1.00, P=0.03). There was NS association for GL (RR = 0.91, 95% CI: 0.70, 1.20; P=0.32). The authors concluded that the BCDDP cohort did not support the hypothesis that diets high in GI or GL increase the risk of colorectal cancer.

**Weijenbergh, 2008** (neutral quality), a case-cohort study in the Netherlands, examined the association between glycemic index (GI) and glycemic load (GL) and risk of colorectal cancer in participants in the Netherlands Cohort Study on Diet and Cancer. After 11.3 years of follow-up, 1,225 colon and 418 rectal cancer cases were identified. A case-cohort approach was used for data analysis. Case subjects were enumerated from the entire cohort, whereas the person-years at risk were estimated from a random sample of 5,000 subjects, taken from the cohort at baseline in 1987. The RR for colorectal cancer comparing the highest to the lowest quintile levels of GL and GI were 0.83 (95% CI: 0.64, 1.08; P=0.37) and 0.81 (95% CI: 0.61, 1.08, P=0.27) for men and 1.00 (95% CI: 0.73, 1.36, P=0.81) and 1.20 (95% CI: 0.85, 1.67; P=0.53) for women. In men, GI was associated with a reduced risk of distal colon cancer (P=0.03). The authors concluded that a diet with a high GL or GI was not associated with an increased risk of colorectal cancer in men or women in the Netherlands Cohort Study on Diet and Cancer.

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Author, Year,	Population/Subjects	Methodology	Significant Outcomes
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Study Design, Class, Rating			
<p>Augustin et al 2004</p> <p>Study Design: Case-Control Study</p> <p>Class: C</p> <p>Rating: </p>	<p>N=1,204 male cases and 1,352 male controls.</p> <p>Median age: 66 years cases, 63 years controls.</p>	<p>Cases and controls recruited between 1991 and 2002 in network of major teaching and general hospitals in four Italian areas.</p> <p>Cases were men admitted for incident, histologically confirmed prostate cancer.</p> <p>Controls were men admitted for acute, non-malignant conditions unrelated to long-term modifications of diet.</p> <p>Interviewer-administered 78-item FFQ utilized to assess usual diet for the two years preceding diagnosis for cases or hospital admission for controls.</p>	<p>Compared to the lowest quintile of GI, OR for developing prostate cancer were 1.23, 1.24, 1.47 and 1.57 for subsequent levels of GI and the corresponding values for GL were 0.91, 1.00, 1.20, 1.41.</p>
<p>Bertuccio et al 2009</p> <p>Study Design: Case-Control Study</p> <p>Class: C</p> <p>Rating: </p>	<p>Total N: 787 (429 males, 348 females).</p> <ul style="list-style-type: none"> <li>• Study group: 230 (143 males, 87 females)</li> <li>• Control group: 547 (286 males, 261 women).</li> </ul> <p>Median age: 63 years for both study group and control group.</p> <p>Location: Italy.</p>	<p>230 patients had incident, histologically confirmed gastric cancer between 1997 and 2007 and 547 patients who had non-neoplastic conditions served as matched controls.</p> <p>Researchers assessed subjects' usual diet from the two years prior to hospital admission and diagnosis using a valid FFQ.</p>	<p>OR in the highest vs. lowest quintile were 1.9 (95% CI: 1.0 to 3.3) for GI and 2.5 (95% CI: 1.3 to 4.9) for GL.</p> <p>OR rose across strata of high GL and low fruit and vegetable intake to reach 5.0 (95% CI: 2.2 to 11.5) for those reporting high GL and low fruit and vegetable intake, compared with participants reporting low GL and high fruit and vegetable intake.</p>

<p>Cust et al 2007</p> <p>Study Design: Prospective cohort study</p> <p>Class: B</p> <p>Rating: </p>	<p>N=288,428 women from the European Prospective Investigation into Cancer and Nutrition cohort study.</p> <p>Age: 54.1±8.7 years endometrial cancer cases; 49.9±11.6 years non-cases.</p> <p>Location: Europe.</p>	<p>Participants enrolled between 1992 and 2000 in 23 centers throughout 10 western European countries .</p> <p>During a mean 6.4 years and 1,842,995 person-years of follow-up, 710 incident endometrial cancer cases were diagnosed.</p> <p>Cancer diagnosis microscopically verified for 89.3% of cases and by clinical examination for 8.5%; the remaining 2.2% verified by self-report, tomography scan, surgery, autopsy or death certificate.</p> <p>Overall GI or GL: Usual diet during the previous 12 months was assessed with country-specific, validated dietary assessment instruments.</p>	<p>Data suggest no association of overall GI, total starch and total fiber with endometrial cancer risk; however, multivariable RR were 1.61 (95% CI: 1.06 to 2.45) per 100g per day of total CHOs, 1.40 (95% CI: 0.99 to 1.99) per 50g per day of total dietary GL, and 1.36 (95% CI: 1.05 to 1.76) per 50g per day of total sugars.</p> <p>Associations were stronger among women who had never used post-menopausal hormone therapy.</p>
<p>Flood et al. 2006</p> <p>Study Design: Cross-sectional Study</p> <p>Class: D</p> <p>Rating: </p>	<p>N=44,572 participants from the Prostate, Lung, Colorectal and Ovarian Screening Trial.</p> <p>N=24,017 men and 20,555 women.</p> <p>Age: 55 to 74 years.</p> <p>Location: United States.</p>	<p>Participants completed a flexible sigmoidoscopy exam.</p> <p>N=34,817 had no lesions and 3,696 had at least one distal adenoma.</p> <p>137-item FFQ used to assess usual dietary intake for each participant over the 12 months before enrollment. FFQ provided information for ascertainment of portion size for all food items except fruit and vegetables.</p>	<p>GI was NS associated with risk for distal adenomas in men or women.</p> <p>Among men, GL had significant inverse association with distal adenomas (OR for quintile five compared with quintile one in multivariate-adjusted models for men: 0.79; 95% CI: 0.68, 0.93; P=0.003).</p> <p>Among women, GL was NS associated with risk</p>

			for distal adenomas (OR for women: 0.98; 95% CI: 0.81, 1.19; P=0.70).
<p>George et al 2009</p> <p>Study Design: Prospective Cohort Study</p> <p>Class: B</p> <p>Rating: </p>	<p>N=262,642 male and 183,535 female participants from the NIH-AARP Diet and Health Study.</p> <p>Age: 50 to 71 years at baseline.</p> <p>Location: United States.</p>	<p>Participants followed from 1995 to 2003.</p> <p>Cancer cases identified through probabilistic linkage with 11 state cancer registry databases.</p> <p>Dietary intake assessed at baseline using a self-administered 124-item FFQ.</p>	<p>15,215 cancer cases identified in women; 33,203 cases identified in men.</p> <p>RR for total cancer for high vs. low GI were 1.03 for women (P=0.217) and 1.04 for men (P=0.012), and for high vs. low GL, were 0.90 for women (P=0.024) and 0.93 for men (P=0.01), suggesting that GI and GL are not strong predictors of cancer incidence.</p>
<p>Giles et al 2006</p> <p>Study Design: Prospective Cohort Study</p> <p>Class: B</p> <p>Rating: </p>	<p>N=12,273 post-menopausal women in the Melbourne Collaborative Cohort Study (MCCS).</p> <p>Age: 40 to 69 years at baseline.</p> <p>Location: Australia.</p>	<p>Participants recruited in 1990 to 1994 and followed until 2002.</p> <p>Breast cancers ascertained by the Victorian Cancer Registry.</p> <p>Dietary intake assessed at baseline using 121-item, self-administered FFQ, specifically developed for the MCCS.</p>	<p>During an average of 9.1 years follow-up, 324 breast cancers were diagnosed.</p> <p>Although an <math>\uparrow</math> of one SD in CHO intake was marginally associated with risk of breast cancer (RR=1.31, 95% CI: 0.98, 1.75), there were NS associations with fiber, GI, GL or CHO foods.</p>
<p>Heinen et al 2008</p> <p>Study Design: Prospective</p>	<p>Subcohort of the Netherlands Cohort Study.</p> <p>Final N: 4,438</p>	<p>Baseline questionnaire completed in 1986 and participants followed to 1999.</p>	<p>13.3 years of follow-up, 408 pancreatic cancer cases were detected (66% microscopically confirmed).</p>

<p>Cohort Study</p> <p>Class: B</p> <p>Rating: </p>	<p>subjects (2,191 men, 2,247 women) and 408 exocrine pancreatic cancer cases (217 men, 191 women).</p> <p>Age: 55 to 69 years at baseline.</p> <p>Location: Netherlands.</p>	<p>Pancreatic cancer occurrence by annual record linkage to the Netherlands Cancer Registry and the Netherlands Pathology Registry.</p> <p>150-item validated FFQ completed at baseline and used to calculate CHO and mono- and disaccharide intake and GI and GL of the diet.</p>	<p>Dietary GL, GI or intake of CHO and mono- and disaccharides were not associated with pancreatic cancer risk.</p>
<p>Howarth et al 2008</p> <p>Study Design: Prospective Cohort Study</p> <p>Class: B</p> <p>Rating: </p>	<p>Total N=191,004 men (N=85,898) and women (N=105,106) participating in the Multiethnic Cohort Study.</p> <p>Age: 45 to 75 years at baseline.</p> <p>From five ethnic groups: African American, White, Latino, Native Hawaiian or Japanese American.</p> <p>Location: United States.</p>	<p>Baseline measurements conducted between 1993 and 1996 and participants followed through 2002.</p> <p>Incident colorectal cancer cases identified by record linkage to the Hawaii Tumor Registry, the Cancer Surveillance Program for Los Angeles County and the California State Cancer Registry; all registries are members of the Surveillance, Epidemiology and End Results Program (SEER) of the National Cancer Institute.</p> <p>Quantitative FFQ data with over 180 food items used to assess usual dietary intake over preceding year.</p> <p>Quantitative FFQ was developed specifically for study population and based on 3-day measured food records from each ethnic group</p>	<p>Over eight years of follow-up, 2,379 incident cases of colorectal adenocarcinoma occurred in 1,293 men and 1,086 women.</p> <p>In multivariate models, RR for colorectal cancer ↓ significantly with ↑ GL in women (RR for the highest vs. lowest quintile = 0.75, 95% CI: 0.57, 0.97; P=0.02), but not in men (RR=1.15, 95% CI: 0.89, 1.48; P=0.19).</p> <p>Inverse association with GL found in women of all ethnic groups (P for interaction = 0.58).</p> <p>In men, interaction found between ethnicity and GL (P&lt;0.01) in that white men had positive association with ↑ GL (RR=1.69, 95% CI: 0.98, 2.92, P=00.01), but men of other ethnic groups did not.</p>

Note: GI not included in analyses.

<p>Johnson et al 2005</p> <p>Study Design: Prospective Cohort Study</p> <p>Class: B</p> <p>Rating: </p>	<p>N=33,551 women from the Iowa Women's Health Study.</p> <p>Age: 55 to 69 years at baseline.</p> <p>Location: United States.</p>	<p>Baseline data collected in 1986 and followed to 2002.</p> <p>Incidence of pancreatic cancer as measured by Iowa death records, the National Death Index and the Iowa Cancer Registry.</p> <p>Dietary intake assessed using a 126-item FFQ.</p>	<p>Incidence of pancreatic cancer was higher in subjects aged 65 to 69 vs. aged 55 to 64, diabetic vs. non-diabetic, current smokers vs. non-smokers and multivitamin non-users vs. users, but there was no ↑ hazard of pancreatic cancer associated with ↑ dietary GI or GL.</p>
<p>Kabat et al 2008</p> <p>Study Design: Prospective Cohort Study</p> <p>Class: B</p> <p>Rating: </p>	<p>N=158,800 post-menopausal women from the Observational Study and Clinical Trial cohorts of the Women's Health Initiative.</p> <p>Age: 50 to 79 years at baseline, average 63 years.</p> <p>Location: United States.</p>	<p>Participants recruited between 1993 and 1998.</p> <p>Colorectal cancer diagnosis obtained using mail or telephone questionnaires; self-reports verified by trained physician adjudicators; all cancer diagnoses confirmed by blinded review.</p> <p>Dietary intake in past three months assessed using self-administered FFQ with 122 food items, 19 “adjustment” questions and three summary questions.</p>	<p>Over an average of 7.8 years of follow-up 1,476 incident cases of colorectal cancer were identified.</p> <p>Total CHO intake, GI, GL and intake of sugars and fiber showed no association with colorectal cancer.</p>
<p>Lajous et al 2005</p> <p>Study Design: Population-based</p>	<p>N=475 women with breast cancer and 1,391 controls.</p> <p>Age:</p>	<p>Participants recruited between 1990 and 1995.</p> <p>Breast cancer confirmed by biopsy.</p>	<p>Multivariate adjusted OR for all women comparing the highest and lowest tertiles of dietary GL was 1.62 (95% CI: 1.13 to</p>

<p>Case Control Study</p> <p>Class: C</p> <p>Rating: </p>	<ul style="list-style-type: none"> <li>• &lt;40 years: 16% of cases, 25% of controls</li> <li>• 40 to 49 years: 24% of cases, 27% of controls</li> <li>• 50 to 59 years: 27% of cases, 22% of controls</li> <li>• ≥60 years: 33% of cases, 26% of controls.</li> </ul> <p>Location: Mexico.</p>	<p>Diet assessed with validated, semi-quantitative FFQ adapted to Mexican population.</p>	<p>2.32, P=0.02); the association was stronger in post-menopausal women, where the multivariate adjusted OR comparing the extreme quartiles was 2.18 (95% CI: 1.34 to 3.55; P=0.005).</p> <p>Overall, GI was NS associated with risk of breast cancer.</p>
<p>Lajous et al 2008</p> <p>Study Design: Prospective Cohort Study</p> <p>Class: B</p> <p>Rating: </p>	<p>N=62,739 post-menopausal women participating in the E3N French Study (French component of the European Prospective Investigation into Cancer and Nutrition).</p> <p>Age: Mean 53±7 years (range 42 to 72 years).</p> <p>Location: France.</p>	<p>Diet history questionnaires completed in 1993. Follow-up questionnaires sent in 1994, 1997, 2000 and 2002.</p> <p>Incidental cases of breast cancer were initially identified by self-report .</p> <p>Physicians contacted to obtain pathology reports and information on estrogen receptor and progesterone receptor status.</p> <p>Deaths in cohort were identified by reports from family members, postal service and MGEN health insurance database.</p> <p>Dietary intake during past year assessed using 208-item FFQ.</p>	<p>During nine years of follow-up, 1,812 cases of pathology-confirmed breast cancer documented.</p> <p>Dietary CHO intakes, GI and GL not associated with overall post-menopausal breast cancer risk.</p> <p>However, among overweight women (BMI &gt;25kg/m<sup>2</sup>), there was an association between GI and breast cancer (RR=1.35, 95% CI: 1.00, 1.82, P=0.04); this association was absent for women with BMI &lt;25kg/m<sup>2</sup>.</p> <p>For women in the highest category of WC, the RR (Q1-Q4) was 1.28 (95% CI: 0.98, 1.67; P for trend = 0.10) for CHO, 1.35 (95% CI: 1.04, 1.75; P for trend = 0.01) for GI and</p>

			<p>1.37 (95% CI: 1.05, 1.77; P for trend = 0.003) for GL.</p> <p>They also reported a direct association between CHO intake, GL and estrogen receptor-negative breast cancer risk.</p>
<p>Larsson et al 2006</p> <p>Study Design: Prospective Cohort Study</p> <p>Class: B</p> <p>Rating: </p>	<p>N=61,433 women participating in the Swedish Mammography Cohort Study.</p> <p>Diet was assessed at baseline (1987–1990) and again in 1997.</p>	<p>Follow-up through 2004.</p> <p>Stomach cancer incidence obtained by linkage to national and regional Swedish Cancer registers</p> <p>Subjects completed a 67-item FFQ at baseline and a 96-item FFQ in 1997.</p>	<p>During 903,586 person-years of follow-up, there were 156 incident cases of stomach cancer.</p> <p>No association between CHO intake, GI or GL and incidence of stomach cancer using any of the dietary intake data.</p> <p>Multivariate HR for highest vs. lowest quintile were 0.76 (95% CI: 0.46, 1.25) for GL, 0.77 (95% CI: 0.46, 1.30) for overall GI and 0.85 (95% CI: 0.50, 1.43) for CHO intake.</p> <p>Associations did not vary according to BMI.</p>
<p>Larsson et al 2007 Am J Epidemiol</p> <p>Study Design: Prospective Cohort Study</p> <p>Class: B</p> <p>Rating: </p>	<p>N=61,433 women participating in the Swedish Mammography Cohort Study.</p> <p>Age: 40 to 76 years.</p> <p>Location: Sweden.</p>	<p>Baseline questionnaire in 1987 to 1990. Follow-up through 2005.</p> <p>Incidence of colorectal cancers ascertained by computerized record linkage of the study population with the national and regional Swedish Cancer registers.</p> <p>Subjects completed a</p>	<p>Analysis with first FFQ (1987 to 1990):</p> <p>1) Over 963,426 person-years of follow-up (mean = 15.7 years), there were 870 cases of colorectal adenocarcinoma</p> <p>2) CHO intake, GI and GL had NS association with risk of</p>

		<p>67-item FFQ at baseline.</p> <p>N=36,616 women completed a 96-item FFQ in 1997.</p>	<p>colorectal, colon or rectal cancer regardless of BMI and alcohol intake.</p> <p>Analysis with second FFQ (1997):</p> <ol style="list-style-type: none"> <li>1) Over 266,022 person-years of follow-up (mean 7.3 years), there were 297 incident colorectal cancer cases</li> <li>2) No association between CHO intake or GL and risk of colorectal cancer</li> <li>3) GI positively associated with colorectal cancer risk (multivariate HR comparing highest and lowest quintile was 1.95; 95% CI: 1.19, 3.20; P=0.01) even after adjustment for confounders, but was attenuated when first three years of follow-up excluded (HR=1.58; 95% CI: 1.17, 3.16).</li> </ol>
<p>Larsson et al 2007 Int J Cancer</p> <p>Study Design: Prospective Cohort Study</p> <p>Class: B</p> <p>Rating: </p>	<p>N=61,226 women participating in the Swedish Mammography Cohort Study.</p> <p>Age: 40 to 76 years.</p> <p>Location: Sweden.</p>	<p>Baseline questionnaire in 1987 to 1990. Follow-up through 2005.</p> <p>Incidence of endometrial cancers ascertained by computerized record linkage of the study population with the national and regional Swedish Cancer registers.</p> <p>Subjects completed a 67-item FFQ at baseline.</p>	<p>Analysis with second FFQ (1997):</p> <ol style="list-style-type: none"> <li>1) Over 262,993 person-years of follow-up, 214 incidence endometrial cancer cases available</li> <li>2) No overall association between CHO intake, GI or GL and endometrial cancer risk</li> </ol>

		<p>N=36,369 women completed 96-item FFQ in 1997.</p> <p>Analysis with first FFQ (1987 to 1990): Over 952,629 person-years of follow-up (mean 15.6 years), there were 608 cases of endometrial cancer, but no overall association between CHO intake, GI or GL and incidence of endometrial cancer.</p>	<p>3) CHO intake and GL were positively related to endometrial cancer risk among overweight women (BMI &gt;25kg/m<sup>2</sup>) with ↓ physical activity; multivariate RRs comparing extreme quartiles were 1.90 (95% CI: 0.84 to 4.31) for CHO intake and 2.99 (95% CI: 1.17 to 7.67) for GL.</p>
<p>McCann SE, McCann WE et al, 2007</p> <p>Study Design: Case Control Study</p> <p>Class: C</p> <p>Rating: </p>	<p>N=1,166 cases and 2,105 matched controls in the Western New York Exposure and Breast Cancer Study (WEB).</p> <p>Age: 35 to 79 years.</p> <p>Predominantly white (90%).</p> <p>40% pre-menopausal (30% of cases pre-menopausal).</p> <p>Location: United States.</p>	<p>Data collected between 1996 and 2001.</p> <p>Cases were incident, primary, histologically confirmed breast cancer.</p> <p>Participants were randomly selected from either New York State Department of Motor Vehicles drivers' license list (participants under 65 years) or from the Health Care Finance Administration rolls (participants age ≥65 years).</p> <p>Diet 12 to 24 months before diagnosis assessed with FFQ in cases or an interview in controls.</p>	<p>In pre-menopausal women, breast cancer was not related to GI or GL.</p> <p>NS trend toward a ↓ in risk of breast cancer for post-menopausal women in the highest vs. lowest quartile of GI (OR: 0.80; 95% CI: 0.61, 1.03) and GL (OR: 0.74; 95% CI: 0.53, 1.03).</p>
<p>McCarl M, Harnack L et al, 2006</p> <p>Study Design: Prospective Cohort Study</p>	<p>N=35,197 women from the Iowa Women's Health Study.</p> <p>Age: 55 to 69 years at baseline (mean of 61.7 years).</p>	<p>Baseline assessments in 1986 and followed through 2000.</p> <p>Colorectal cancer incidence and deaths ascertained by computer linkage with the State Health Registry of</p>	<p>Over 15 years of follow-up, 757 cases of colon cancer and 209 cases of rectal cancer (954 CRC cases) were observed.</p> <p>When adjusted for age</p>

Class: B

Rating: 

99% Caucasian.

Location: United States.

Iowa, which includes a Surveillance, Epidemiology, and End Results cancer registry.

Dietary intake over previous year assessed with validated 127-item FFQ at baseline.

and energy, no association between either GI or GL and incident colorectal cancer.

Adjustment for other risk factors or adding other dietary variables to the model did not appreciably  $\Delta$  results.

Separate analyses based on colon and rectal subsites were similarly unremarkable.

Analyses stratified by BMI (<25, 25 to 30, >30kg/m<sup>2</sup>) showed that GI and GL positively associated with colorectal cancer in highest BMI category (P for interaction = 0.04 for GI; 0.05 for GL).

GL, but not GI, positively associated with colon cancer in highest BMI category (P<0.01), whereas GL and GI were both positively associated with rectal cancer in highest BMI category (P=0.04 and 0.02, respectively).

NS relations between GI or GL and CRC among subjects whose baseline BMI was <30 kg/m<sup>2</sup> were observed.

<p>Michaud DS, Fuchs CS et al, 2005</p> <p>Study Design: Prospective Cohort Study</p> <p>Class: B</p> <p>Rating: </p>	<p>N=131,349 participants from the Health Professionals Follow-Up Study (47,422 men aged 40 to 75 years) and the Nurses' Health Study (83,927 women aged 30 to 55 years).</p> <p>Location: United States.</p>	<p>Health Professionals Follow-up Study: Initiated in 1986 and followed through January 2000.</p> <p>Nurses' Health Study: Initiated in 1976 and followed through May 2000.</p> <p>Colorectal cancer, colon cancer, rectal cancer: Participants asked to report specified cancers that were diagnosed in the two-year period between each follow-up questionnaire. Confirmation attempted with medical record review or additional questioning of the participant.</p> <p>Nurses' Health Study: Diet assessed with a 61-item FFQ in 1980; a 116-item FFQ assessed intake in 1984, 1986 and every four years thereafter.</p> <p>Health Professionals Follow-Up Study: Diet assessed with a 131-item FFQ in 1986 and every four years thereafter.</p>	<p>During 20 years of follow-up, 1,809 incidence colorectal cancer cases were available for analysis.</p> <p>Among women, no associations were observed for dietary CHO, GL or GI and risk of colorectal cancer.</p> <p>No associations identified after stratifying by BMI or physical activity.</p> <p>Among men, a small ↑ in risk was observed with high GL (multivariate RR, 1.32; 95% CI, 0.98 to 1.79; highest vs. lowest quintile) and associations were slightly stronger among men with ↑ BMI (<math>\geq 25\text{kg/m}^2</math>).</p>
<p>Nothlings U, Murphy SP et al, 2007</p> <p>Study Design: Prospective Cohort Study</p> <p>Class: B</p> <p>Rating: </p>	<p>N=162,150 men (N=72,966) and women (N=89,184) participating in the Multiethnic Cohort Study.</p> <p>Age: 45 to 75 years at baseline.</p> <p>Ethnic groups:</p>	<p>Baseline measurements conducted between 1993 and 1996 and participants followed through 2002.</p> <p>Incident exocrine pancreatic cancer cases identified by record linkage to Hawaii Tumor Registry, Cancer Surveillance Program of</p>	<p>During follow-up, 434 incident pancreatic cancer cases occurred in cohort.</p> <p>GL not associated with pancreatic cancer risk in the overall cohort (P=0.65).</p> <p>Higher (but NS higher)</p>

<p>Rating: —</p>	<p>African American, White, Latino, Native Hawaiian or Japanese American.</p> <p>Location: United States.</p>	<p>Los Angeles County and California State Cancer Registry.</p> <p>Dietary intake assessed with quantitative FFQ especially designed and validated for use in this multiethnic population.</p>	<p>risks of pancreatic cancer were seen in the overweight and obese group (BMI <math>\geq 25\text{kg/m}^2</math>) than in normal-weight group (BMI <math>\leq 25\text{kg/m}^2</math>) in the top quartiles of GL.</p> <p>Note: GI not included in analyses.</p>
<p>Patel AV, McCullough ML et al, 2007</p> <p>Study Design: Prospective Cohort Study</p> <p>Class: B</p> <p>Rating: </p>	<p>N=124,907 men and women from the American Cancer Society Cancer Prevention Study II (CPSII) Nutrition Cohort.</p> <p>Mean age at study entry: 62.7 years (<math>\pm 6.35</math> SD).</p> <p>Location: United States.</p>	<p>Baseline in 1992 and follow-up through August 2001.</p> <p>78% of pancreatic cancer cases identified initially as interval deaths for which pancreatic cancer was listed as cause of death on death certificate; additional cases identified by self-report with verification by medical records or linkage with state registries.</p> <p>Dietary intake over past year assessed at baseline using a semi-quantitative 68-item FFQ.</p>	<p>During nine years of follow-up, 401 incident pancreatic cancer cases were identified.</p> <p>No association between GL or GI and risk of pancreatic cancer observed.</p> <p>Hazard rate ratio (RR) was 1.01 (95% CI: 0.75, 1.37, P=0.80) for GL and 0.92 (95% CI: 0.68, 1.24) for GI among men and women in the highest quintile vs. the lowest quintile.</p> <p>NS association between these measures and pancreatic cancer risk observed among individuals who were overweight or more sedentary.</p>
<p>Randi G, Ferraroni M et al, 2008</p> <p>Study Design: Case Control Study</p>	<p>N=399 cases (291 women, 108 men, aged 16 to 72 years, median age 44 years).</p> <p>N=617 controls (427 women, 190 men,</p>	<p>Study conducted from 1986 to 1992 in major teaching and university hospitals in three areas of Northern Italy.</p> <p>Cases: Histologically confirmed and incident</p>	<p>Multivariate ORs of thyroid cancer according to GI: Compared with the lowest tertile, the ORs in subsequent tertiles were 1.68 and 1.73 for GI (P=0.0047).</p>

<p>Class: C</p> <p>Rating: </p>	<p>aged 16 to 74 years, median age 46 years).</p> <p>Location: Italy.</p>	<p>cases of thyroid cancer.</p> <p>Controls: Patients admitted to same network of hospitals as cases for acute non-neoplastic diseases unrelated to known or potential risk factors for thyroid carcinoma and unrelated to long-term diet modification.</p> <p>Dietary intake assessed by trained interviewer.</p> <p>Weekly frequency of consumption of 29 food items during the two years before the onset of symptoms that led to the diagnosis were recorded.</p>	<p>Multivariate ORs of thyroid cancer according to GL: Compared with the lowest tertile, the ORs in subsequent tertiles were 1.76 and 2.17 for GL (P&lt;0.0001).</p>
<p>Sieri S, Pala V et al, 2007</p> <p>Study Design: Prospective Cohort Study</p> <p>Class: B</p> <p>Rating: </p>	<p>N=8,926 women from the Hormones and Diet in the Etiology of Breast Tumors Study (ORDET Study).</p> <p>Age: 34 to 70 years at baseline.</p> <p>Location: Italy.</p>	<p>Baseline enrollment between 1987 and 1992 and follow-up to December 2001.</p> <p>Breast cancer cases from cancer registry (Varese Cancer Registry).</p> <p>Dietary intake over previous year assessed with 107-item semi-quantitative FFQ at baseline.</p>	<p>After a mean follow-up of 11.5 years, 289 breast cancers identified.</p> <p>Adjusted RR of breast cancer in highest vs. lowest quintiles of GI and GL was 1.57 (95% CI: 1.04, 2.36; P=0.040) and 2.53 (95% CI: 1.54, 4.16; P=0.001), respectively.</p> <p>When categorized by baseline menopausal status and BMI, the ↑ risk of dietary GL was confined to those who were pre-menopausal (RR=3.89; 95% CI: 1.81, 8.34) and who had normal BMI (i.e., &lt;25kg/m<sup>2</sup>) (RR=5.79; 95% CI: 2.60, 12.90)</p>

(P=0.001 for both).

Silvera SA, Jain M et al, 2005

Study Design:  
Prospective  
Cohort Study

Class: B

Rating: 

N=49,111 women from the Canadian National Breast Screening Study (NBSS).

Age: 40 to 59 years at baseline.

Location: Canada.

Baseline between 1980 and 1985 and follow-up ending between 1998 and 2000.

Linkages to national mortality and cancer databases yielded data on deaths and breast cancer incidence.

Dietary intake assessed with self-administered 86-item FFQ.

During a mean follow-up of 16.6 years, 1,450 incident breast cancer cases observed.

GI and GL not associated with breast cancer risk in the total cohort.

There was evidence of effect modification of the association between GI and breast cancer risk by menopausal status (P=0.01), the HR for the highest vs. the lowest quintile level of GI being 0.78 (95% CI: 0.52, 1.16; P=0.12) in pre-menopausal women and 1.87 (95% CI: 1.18, 2.97; P=0.01) in post-menopausal women.

Associations between GI and GL were not modified by BMI or by vigorous physical activity among pre- or post-menopausal women.

Associations between GI and GL and risk in post-menopausal women were not modified by BMI, vigorous physical activity or ever use of HRT, although associations were slightly stronger among those who reported no vigorous physical activity (P=0.02), among those

who reported ever using HRT (P=0.02) and among normal weight women (BMI <25kg/m<sup>2</sup>; P=0.03).

			<p>who reported ever using HRT (P=0.02) and among normal weight women (BMI &lt;25kg/m<sup>2</sup>; P=0.03).</p>
<p>Silvera SA, Jain M et al, 2007</p> <p>Study Design: Prospective Cohort Study</p> <p>Class: B</p> <p>Rating: </p>	<p>N=48,776 women from the Canadian National Breast Screening Study (NBSS).</p> <p>Age: 40 to 59 years at baseline.</p> <p>Location: Canada.</p>	<p>Baseline between 1980 and 1985 and follow-up ending between 1998 and 2000.</p> <p>Linkages to Canadian Cancer Database and National Mortality Database yielded data on deaths and ovarian cancer incidence.</p> <p>Dietary intake assessed with self-administered 86-item FFQ.</p>	<p>During a mean 16.4 years of follow-up, 264 incident cases of ovarian cancer observed.</p> <p>GI not associated with risk of ovarian cancer in total cohort.</p> <p>GI positively associated with a 72% ↑ in risk of ovarian cancer (HR=1.72, 95% CI: 1.13, 2.62; P=0.01).</p> <p>Magnitude of association was slightly greater among post-menopausal (HR=1.89, 95% CI: 0.98, 3.65, P=0.03) than among pre-menopausal women (HR=1.64, 95% CI: 0.95, 2.88; P=0.07); however, no statistical evidence of effect modification by baseline menopausal status (P for interaction = 0.54).</p>
<p>Silvera SA, Rohan TE et al, 2005 (endometrial)</p> <p>Study Design: Prospective Cohort Study</p> <p>Class: B</p>	<p>N=34,391 women from the Canadian National Breast Screening Study (NBSS).</p> <p>Age: 40 to 59 years at baseline.</p> <p>Location: Canada.</p>	<p>Baseline between 1980 and 1985 and follow-up ending between 1998 and 2000.</p> <p>Linkages to national mortality and cancer databases yielded data on deaths and endometrial cancer incidence.</p>	<p>During a mean of 16.4 years of follow-up, 426 incident cases of endometrial cancer observed.</p> <p>Adjusted HR for the highest vs. the lowest quartile of overall GI and GL were 1.47 (95% CI;</p>

<p>Rating: </p>		<p>Dietary intake assessed with self-administered 86-item FFQ.</p>	<p>0.90, 2.41; P=0.14) and 1.36 (95% CI: 1.01, 1.84; P=0.21), respectively.</p> <p>When quartiles of GI and GL and risk of endometrial cancer were stratified by categories of BMI (&lt;25, 25 to 29, ≥30kg/m<sup>2</sup>), participation in vigorous physical activity (none vs. some), menopausal status and use of HRT (never vs. ever), NS trends were observed.</p>
<p>Silvera SA, Rohan TE et al, 2005 (pancreatic)</p> <p>Study Design: Prospective Cohort Study</p> <p>Class: B</p> <p>Rating: </p>	<p>N=49,111 women from the Canadian National Breast Screening Study (NBSS).</p> <p>Age: 40 to 59 years at baseline.</p> <p>Location: Canada.</p>	<p>Baseline between 1980 and 1985 and follow-up ending between 1998 and 2000.</p> <p>Linkages to Canadian Cancer Database and National Mortality Database yielded data on deaths and pancreatic cancer incidence.</p> <p>Dietary intake assessed with self-administered 86-item FFQ.</p>	<p>During a mean 16.5 years of follow-up, 112 incident pancreatic cancer cases observed.</p> <p>No association between overall GI and GL and pancreatic cancer risk.</p> <p>In multivariate adjusted models, the HR for the highest vs. lowest quartile levels of overall GI and GL were 1.43 (95% CI: 0.56, 3.65; P=0.58) and 0.80 (95% CI: 0.45, 1.41; P=0.41), respectively.</p>
<p>Strayer L, Jacobs DR Jr et al, 2007</p> <p>Study Design: Prospective Cohort Study</p>	<p>N=41,133 women from the Breast Cancer Detection Demonstration Project (BCDDP).</p> <p>Mean age: 61.9 years.</p>	<p>Dietary assessment completed between 1987 and 1989. Follow-up continued through 1995 and 1998.</p> <p>Colorectal cancer cases identified from self-reports</p>	<p>During an average of 8.5 years of follow-up, 490 incident cases of colorectal cancer observed.</p> <p>↓ in colorectal cancer risk observed for diets high in</p>

<p>Class: B</p> <p>Rating: </p>	<p>Location: United States.</p>	<p>on questionnaires in 1992 to 1995 and 1995 to 1998 (79% confirmed by pathology), statewide cancer registries and the National Death Index (through 1997).</p> <p>62-item validated FFQ used to assess usual dietary intake over the previous year.</p>	<p>GI (RR for Q5 vs. Q1 = 0.75, 95% CI: 0.56, 1.00, P=0.03).</p> <p>NS association for GL (RR=0.91, 95% CI: 0.70, 1.20; P=0.32).</p>
<p>Weijenberg MP, Mullie PF et al, 2008</p> <p>Study Design: Prospective Cohort Study</p> <p>Class: B</p> <p>Rating: </p>	<p>N=120,852 men and women from the Netherlands Cohort Study.</p> <p>Age: 55 to 69 years at baseline (53% women).</p> <p>Location: Netherlands.</p>	<p>Case-cohort approach used for data analysis. Case subjects enumerated from entire cohort, whereas person-years at risk estimated from random sample of 5,000 subjects, taken from cohort at baseline in 1987.</p> <p>Colon and rectal cancers identified by using combination of computerized linkage system to nine cancer registries in the Netherlands and a nationwide pathology database.</p> <p>A semi-quantitative FFQ that included 150 food items covered habitual food habits during the year before the start of the study.</p>	<p>After 11.3 years of follow-up, 1,225 colon and 418 rectal cancer cases available for analysis.</p> <p>RR for colorectal cancer comparing the highest vs. the lowest quintile levels of GL and GI were 0.83 (95% CI: 0.64, 1.08; P=0.37) and 0.81 (95% CI: 0.61, 1.08, P=0.27) for men and 1.00 (95% CI: 0.73, 1.36, P=0.81) and 1.20 (95% CI: 0.85, 1.67; P=0.53) for women.</p> <p>In men, GI associated with a ↓ risk of distal colon cancer (P=0.03).</p>

### Research Design and Implementation Rating Summary

For a summary of the Research Design and Implementation Rating results, [click here](#).

### Worksheets

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