The Benefits of Dietary Fiber Intake on Reducing the Risk of Cancer: An Umbrella Review of Meta-analyses

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ABSTRACT

Objective: The purpose of this study was to review previously published meta-analyses on the effectiveness of dietary fiber on reducing the incidence of cancer.

Methods: An umbrella review of all published meta-analyses was performed. A PubMed search from January 1, 1980 to June 30, 2017 was conducted using the following search strategy: (fiber OR fibre) AND (meta-analysis OR systematic review) AND (cancer OR carcinoma). Only English-language publications that provided quantitative statistical analysis on cancer were retrieved.

Results: Nineteen meta-analyses comparing highest vs lowest dietary fiber intake were retrieved for inclusion in this umbrella review. There was a statistically significant reduction in the relative risk (RR) of colorectal, esophageal, gastric, and pancreatic cancer (RR = 0.52-0.88); however, statistically significant heterogeneity was observed in the meta-analyses on esophageal, gastric, and pancreatic cancer. There was a statistically significant reduction in the RR of breast cancer (RR = 0.85-0.93).

Conclusion: This review suggests that those consuming the highest amounts of dietary fiber may benefit from a reduction in the incidence of developing colorectal cancer, and there also appears to be a small reduction in the incidence of breast cancer. (J Chiropr Med 2018;17:90-96)

Key Indexing Terms: *Dietary Fiber; Meta-analysis; Neoplasms*

INTRODUCTION

In 2017, in the United States, it is estimated that there will be approximately 1.67 million new cases of cancer diagnosed, and 600 000 deaths from this disease are projected to occur.[1] Epidemiologic studies show that dietary factors are believed to play an important role in the prevention of cancer, among which dietary fiber has received considerable interest.[2] Increased intake of dietary fibers has been associated with decreased risk of several cancers, such as colorectal and breast cancer.[3-7] However, the results of many epidemiologic studies have shown conflicting results, with some showing a weak or null association.[8-12] Furthermore, the 2007 World Cancer Research Fund's second expert report concluded that the data were too inconsistent to draw a conclusion on the association between dietary fiber and cancer risk.[13]

Given the inconsistency of the existing literature, a pooling of information from individual trials could provide a more precise and accurate estimate of dietary fibers role in reducing the incidence of cancer. To achieve this result, many investigators have turned to performing a powerful statistical method known as meta-analysis. Meta-analyses are fundamental to provide the highest level of evidence to best inform health care decision making. Because of the current inconsistency in the literature on the benefits of dietary fiber's ability to reduce cancer incidence, the purpose and objective of this paper is to summarize the evidence from previously published meta-analyses regarding the effectiveness of dietary fiber in reducing the incidence of cancer.

METHODS

An umbrella review was selected for this study. An umbrella review provides a summary of existing published meta-analyses and systematic reviews and determines whether authors addressing similar review questions independently observe similar results and arrive at similar conclusions.[14] Inclusion criteria for assessing the

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effectiveness of dietary fiber to reduce cancer incidence will have to include meta-analyses that surveyed cancer incidence within normal populations (with no geographic, race, or sex restrictions) while comparing the relative rates (RRs) or odds ratios (ORs) of those with the highest vs lowest dietary fiber intakes.

As meta-analyses started appearing in medical literature in the early 1980s, a systematic literature search of PubMed and CINAHL from January 1, 1980 to June 30, 2017 was conducted using the following search strategy: (fiber OR fibre) AND (meta-analysis OR systematic review) AND (cancer OR carcinoma OR adenoma).

Abstracts, conference proceedings, and gray literature were not included as the focus of this umbrella review; it was restricted to peer-reviewed, full-length papers indexed only in PubMed and CINAHL. The titles and abstracts from the literature search were scanned, and only English-language publications that provided quantitative statistical analysis (RRs and ORs) on cancer incidence were retrieved. Meta-analyses or systematic reviews that did not present study-specific summary data using a minimum of 4 randomized controlled trials were excluded.

For the published meta-analyses that were accepted into this review, the following information was extracted and entered into a Microsoft Excel spreadsheet: number of publications included in the meta-analysis, number of total participants, and pooled treatment effects for RRs or ORs. Although not always present, the meta-analyses were also analyzed for their disclosure of quality assessment, statistical heterogeneity (Cochran's Q test and I^2 statistic), and publication bias (visual inspection of funnel plots and Egger or Begg regression test). A methodological quality appraisal was conducted for all meta-analyses using the Critical Appraisal Checklist for Systematic Reviews, which was developed by the Umbrella Review Methodology Working Group.[14] This checklist consists of 10 items, in which each item within the instrument can receive 1 point for an overall quality score that could range from 0 to 10. Meta-analyses with quality scores ranging from 0 to 4 were labeled as low quality, those with scores between 5 and 7 were labeled as medium quality, and those with scores of 8 to 10 were labeled as high quality. Because this is a descriptive summary review of meta-analyses, no statistical analyses were performed.

Results

The initial search strategy identified 88 articles; after careful review, 19 meta-analyses were retrieved for inclusion into this umbrella review.[15-33] A flow chart of the meta-analyses selection process is provided in Figure 1. The 2 meta-analyses by Hajishafiee et al[34] and Kim and Je[35] were not included in the umbrella review because they used only 2 and 3 clinical studies, respectively, to calculate their effect size on cancer mortality RR.

In regard to the methodological quality of the 19 meta-analyses in this umbrella review, the mean quality appraisal score was 8 of 10, where 14 (74%) meta-analyses scored as high quality; 2 (10%) satisfied medium quality; and 3 (16%) satisfied low quality. These 3 low quality meta-analyses included a paper by Trock et al[15] and 2 papers by Howe et al.[16,25] Although these 3 meta-analyses have been deemed lower quality, they were still included in this umbrella review because they provide useful information regarding the role dietary fiber has for reducing the incidence of colorectal cancer and breast cancer.

The meta-analyses presented in Tables 1 and 2 are based on dietary surveys, which compare the highest vs lowest daily dietary fiber consumption on the incidence of developing gastrointestinal related cancers (Table 1) and nongastrointestinal cancers, such as breast, prostate, endometrial, and renal cancer (Table 2). However, the meta-analysis by Liu et al[33] was not entered into either table because this was the only meta-analysis that investigated the impact of fiber consumption on cancer mortality and not cancer incidence. This particular meta-analysis assessed 5 clinical studies with a total population of 640,482 participants and provided a hazard ratio of 0.83, which was statistically significant ($P < .05$). There was no statistically significant observation of either heterogeneity or publication bias in this particular meta-analysis.

For populations that consumed the highest dietary fiber intake, the incidence of colorectal cancer was significantly reduced in 4 of the 5 meta-analyses, with the RR ranging between 0.53 and 0.88 for those that were statistically significant (Table 1). However, for 2 of these 4 meta-analyses, statistically significant heterogeneity was observed. The only nonsignificant meta-analysis, by Asano and McLeod,[17] had an RR of 1.04.

Esophageal, gastric, and pancreatic cancers were also significantly reduced in all 5 meta-analyses, with the OR ranging between 0.52 and 0.66 (Table 1). However, statistically significant heterogeneity was observed in 4 of the 5 of these meta-analyses.

The incidence of breast cancer was significantly reduced in all 3 meta-analyses, with the RR ranging between 0.85 and 0.93 (Table 2). Although the incidence of endometrial cancer was significantly reduced (OR = 0.71), the reduction in the incidence of prostate cancer was not statistically significant. Finally, the incidence of renal cell cancer was significantly reduced with an RR of 0.84.

Discussion

When comparing participants with the highest intakes of total dietary fiber to those with the lowest intakes relative to the incidence of developing colorectal cancer, 4 of the 4 meta-analyses in this umbrella review presented statistically significant reductions that ranged between 12% and

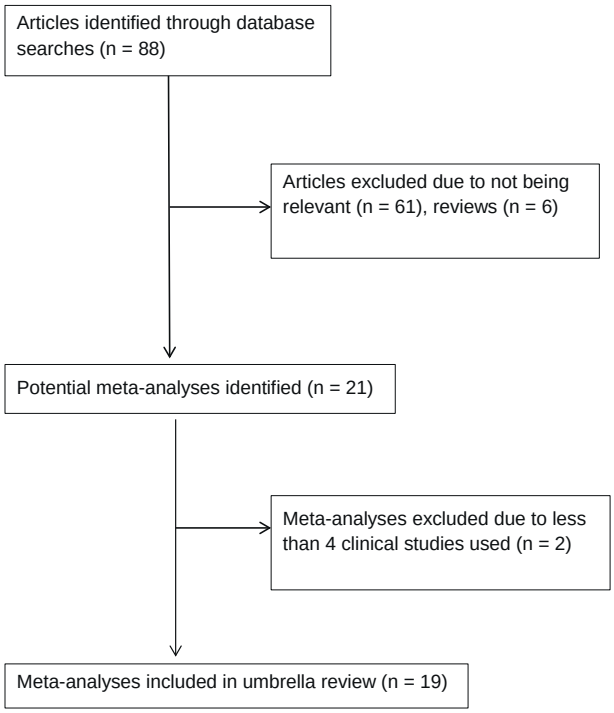

Fig 1. *Flow chart of meta-analysis selection.*

Table 1. *High vs Low Dietary Fiber Intake on the Incidence of Developing Gastrointestinal Related Cancers*

Meta-analysis Authors and Date	Cancer Type	No. of Studies in Meta-analysis	No. of Participants in Meta-analysis	Main Findings of Meta-analysis	Q Test *P* Value	I^2 Statistic	Egger or Begg Test *P* Value	Quality Assessment and Outcome
Trock et al. 1990[15]	Colorectal	16	15 379	OR = 0.57, $P < .001$	$P < .001$			
Howe et al. 1992[16]	Colorectal	13	15 574	RR = 0.53, $P < .001$				
Asano and McLeod 2002[17]	Colorectal	5	3641	RR = 1.04, NS	NS	5		Cochrane 5/5 high quality
Aune et al. 2011[18]	Colorectal	18	200 066	RR = 0.88, $P < .05$	NS	0	NS	
Ben et al. 2014[19]	Colorectal	20	132 102	RR = 0.72, $P < .05$	$P = .002$	55	NS	NOS 14/20 high quality
Coleman et al. 2013[20]	Esophageal	8	9688	OR = 0.66, $P < .05$	$P < .001$	83	NS	
Sun et al. 2015[21]	Esophageal	15	16 885	OR = 0.52, $P < .05$	$P < .001$	72	NS	NOS 9/15 high quality
Zhang et al. 2013[22]	Gastric	21	580 064	OR = 0.58, $P < .05$	$P = .001$	62	NS	NOS 14/21 high quality
Wang et al. 2015[23]	Pancreatic	14	38 141	OR = 0.54, $P < .05$	$P = .043$	41	NS	NOS NR
Mao et al. 2017[24]	Pancreatic	14	38 141	OR = 0.52, $P < .05$	NS	7	NS	NOS 10/14 high quality

NOS, Newcastle-Ottawa Scale; *NR*, not reported; *NS*, not significant; *OR*, odds ratio; *RR*, relative risk.

Table 2. *High vs Low Dietary Fiber Intake on the Incidence of Developing Nongastrointestinal Cancers*

Meta-analysis Authors and Date	Cancer Type	No. of Studies in Meta-analysis	No. of Participants in Meta-analysis	Main Findings of Meta-analysis	Q Test *P* Value	I^2 Statistic	Egger or Begg Test *P* Value	Quality Assessment and Outcome
Howe et al. 1990[25]	Breast	12	10 522	RR = 0.85, *P* = .001				
Dong et al. 2011[26]	Breast	10	712 195	RR = 0.89, *P* < .05	NS	0	NS	
Aune et al. 2012[27]	Breast	16	999 271	RR = 0.93, *P* < .05	NS	0	NS	
Chen et al. 2016[28]	Breast	24	3 662 421	RR = 0.88, *P* < .05	*P* = .001	59	NS	Jadad 18/24 high quality
Bandera et al. 2007[29]	Endometrial	8	12 312	OR = 0.71, *P* < .05	NS	21		Intentionally not performed
Sheng et al. 2015[30]	Prostate	17	140 179	OR = 0.89, NS	*P* = .005	54	NS	NOS 9/17 high quality
Wang et al. 2015[31]	Prostate	16	136 979	RR = 0.94, NS	NS	40	NS	NOS 5/16 high quality
Huang et al. 2014[32]	Renal Cell	6	938 664	RR = 0.84, *P* < .05	NS	24	NS	NOS 2/6 high quality

NOS, Newcastle-Ottawa Scale; *NS*, not significant; *OR*, odds ratio; *RR*, relative risk.

47%.[15,16,18,19] However, we must appreciate these positive results with some caution because statistically significant heterogeneity was observed in 2 of these 4 meta-analyses.[15,19] There was 1 meta-analysis published by Asano and McLeod that did not report a statistical significant reduction but instead reported an RR of 1.04.[17] This finding may be accounted for by the fact that the 5 clinical trials used in this particular meta-analysis were solely randomized clinical controlled trials, whereas the 4 previous meta-analyses, which observed statistically significant reductions, used clinical studies that were observational case-controlled or cohort studies. This paradoxical finding has been noted in many other dietary interventions, in which randomized controlled trials of diet-related factors have not yet shown any conclusive associations between diet and cancer incidence.[2]

In regard to the gastrointestinal system beyond the colon and rectum, 5 separate meta-analyses found statistically significant reductions in the RR for developing esophageal, gastric, and pancreatic cancer with reductions ranging between 34% and 48%.[20-24] However, we must appreciate these positive results with some caution because statistically significant heterogeneity was observed in 4 of these 5 meta-analyses.[24] Curiously, the I^2 statistic and the Q-test's *P* values were very different for the pancreatic cancer meta-analyses, considering they were designed using the same 14 clinical trials and observed nearly identical OR (0.54 vs 0.52).[23,24]

In 2017, in the United States, it is estimated that colorectal cancer will be only the fourth most common cancer diagnosis in men and women combined, but unfortunately it will be the second most common cause of cancer mortality, second only to lung cancer in cancer-related deaths.[1] In regard to the mechanism of action for reducing the incidence of colorectal cancer, it is possible that dietary fiber increases stool bulk, and this dilutes carcinogen concentrations in the colonic lumen. Coupled with a shortened fecal transit time, the time during which luminal carcinogens may be in contact with gastrointestinal epithelial cells decreases.[36] Dietary fiber may also bind to both carcinogens and primary and secondary bile acids to promote their excretion in the feces. Bacterial fermentation of fibers to short chain fatty acids such as acetate, propionate and butyrate decreases luminal pH, which helps decrease the conversion of primary bile acids to carcinogenic secondary bile acids.[37] Butyrate, a 4-carbon short chain fatty acid, also provides 70% of energy for healthy normal colonic epithelial cells and has been shown to have antineoplastic actions by inhibiting cancer cell proliferation and inducing apoptosis and cell cycle arrest, as well as increasing cell differentiation in colon cancer tissue.[36,37] It is well established that inflammation is directly associated with cancer progression, and it has been observed that butyrate also plays an anti-inflammatory role by inhibiting the transcription factor NF-κB, which results in a reduced concentration of the proinflammatory cytokines interleukin-6 and tumor necrosis factor-α.[38,39] Butyrate's beneficial effects are mediated at the epigenetic level through the inhibition of histone deacetylases (HDACs), which consequently regulates the expression of downstream genes such as NF-κB and p53.[39,40] The HDACs are important for gene expression,

and the levels of these enzymes are increased in tumor cells; thus, a decrease in HDAC activity is associated with the suppression of tumor cell growth.[41] In regard to esophageal and gastric cancer, dietary fiber has been shown to scavenge nitrites, which are the precursors of the gastrointestinal cancer causing N-nitroso compounds.[20]

When comparing participants with the highest intakes of total dietary fiber to those with the lowest intakes relative to the incidence of developing breast cancer, 4 of the 4 meta-analyses in this umbrella review presented with statistically significant reductions that ranged between 7% and 15%.[25-28] The meta-analysis on endometrial cancer also observed a statistically significant reduction of 29%.[29] However, although the range in reduction for prostate cancer was between 6% and 11%, the observations from both of these 2 meta-analyses were not statistically significant.[30,31]

In 2017, it is estimated that, in the United States, breast cancer will be the most common cancer diagnosis overall and the second leading cause of death from cancer in women.[1] Dietary fiber effects on reducing the incidence of breast cancer was not as strong as compared to effects observed with colorectal cancer, and this may be attributed to dietary fibers' different mechanisms of action at these 2 very different sites. Prolonged exposure to estrogen is a strong risk factor for breast and endometrial cancer, and reductions in circulating estrogens have been observed in participants who are consuming larger quantities of dietary fiber.[42] It has been proposed that dietary fibers can bind to estrogens in the lumen of colon and increase their fecal excretion.[27] In addition, dietary fiber may also reduce intestinal enzymatic activity of β-glucuronidase, which is responsible for the hydrolysis of conjugated estrogens prior to their absorption by colonic epithelial cells.[43] Other components in dietary fiber, such as antioxidants, phenolic acids, and lignans, may also be protective against breast and endometrial cancer. Lignans such as enterodiol and enterolactone are phytoestrogens that are derived from the noncarbohydrate dietary fibers called lignins, and they possess weak estrogenic-inhibiting effects.[44] Dietary fiber may also promote weight loss, and because adipocytes produce estrogen at a proportional amount relative to their size, there would be a subsequent reduction in the levels of estrogen.[27]

The Dietary Guidelines for Americans states that the adequate intake value of dietary fiber consumption is 25 to 38 g/day, but the 2009 to 2010 National Health and Nutrition Examination Survey shows that the daily intake of fiber in the United States is only 17 g/d.[45] Therefore, emphasizing fiber consumption for health promotion and disease prevention is a critical public health goal, and by aggressively promoting the Dietary Guidelines for Americans recommendation of at least 25 to 38 g/d of total dietary fiber, this may prevent a significant number of new cancer cases. Although the evidence in this umbrella review supports the beneficial association of dietary fiber on reducing the incidence of colorectal and breast cancer, too few long-term, large-population, randomized controlled trials have undertaken the goal to analyze this potential causal relationship between dietary fiber and cancer incidence. Finally, while no Tolerable Upper Intake Level has been established for total fiber intake, it should be noted that minor side effects have been observed, such as flatulence, abdominal bloating, loose stools or diarrhea, and abdominal cramping.[46]

Limitations

This umbrella review has several limitations that should be acknowledged. First, confounding factors are always a potential threat to the validity of any meta-analysis. For instance, people who have high dietary fiber intakes tend to have other healthy behaviors, such as being more physically active, having lower dietary intakes of saturated fat and processed meats, and avoiding smoking and excessive alcohol intake. Fortunately, the majority of studies included in the meta-analyses that were involved in this umbrella review did adjust for potential confounding factors, but the possibility of residual confounders cannot be excluded. Second, self-reported dietary fiber intake is most often assessed using food frequency questionnaires; because these dietary assessment tools were not specifically developed for dietary fiber intake, it is possible that misclassifications and measurement errors regarding fiber doses and types are quite likely. This problem may also be compounded by the fact that dietary fiber may be defined differently by the various food frequency questionnaire databases in use.[46] A third limitation is that the meta-analyses reviewed here represent a heterogeneous group of clinical studies composed from a diverse group of participants of different ages, sexes, races, and ethnic groups: therefore, readers are cautioned against specifying these results to any specific sociodemographic group. Finally, as in all literature reviews, the quality of this umbrella review is directly related to the quality of the included meta-analyses, which are dependent upon the design and reporting quality of the individual meta-analysis itself, as well as on the quality of the individual studies used to conduct the meta-analysis. Fortunately, the majority (84%) of the meta-analyses in this umbrella review were apprised as having moderate to high methodological quality.

Conclusion

This umbrella review suggests that those consuming the highest amounts of dietary fiber may benefit from a reduction in the incidence of developing colorectal cancer, as well as a small reduction in developing breast cancer. These findings have important public health implications, especially in light of the finding by Liu et al,[33] who determined that individuals with the highest dietary fiber consumption reduced their cancer mortality by 17%.

Unfortunately, the mean dietary fiber intake in the United States is 17 g/d, which is considerably less than the recommended intake of 25 to 38 g/d.[45] Future well-designed, large, multicenter, randomized controlled studies are required to confirm these associations.

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No funding sources or conflicts of interest were reported for this study.

Contributorship Information

Concept development (provided idea for the research): M.P.M.
Design (planned the methods to generate the results): M.P.M.
Supervision (provided oversight, responsible for organization and implementation, writing of the manuscript): M.P.M.
Data collection/processing (responsible for experiments, patient management, organization, or reporting data): M.P.M.
Analysis/interpretation (responsible for statistical analysis, evaluation, and presentation of the results): M.P.M.
Literature search (performed the literature search): M.P.M.
Writing (responsible for writing a substantive part of the manuscript): M.P.M.
Critical review (revised manuscript for intellectual content, this does not relate to spelling and grammar checking): M.P.M.

Practical Applications

- Dietary fiber consumption has been postulated to reduce the incidence of cancer, but unfortunately there is much discrepancy when it comes to individual cohort and case-controlled studies.
- By combining the meta-analyses on these clinical outcomes as an umbrella review, we can show that increased dietary fiber intake may help reduce the incidence of gastrointestinal and breast cancers. More high-quality research is needed regarding the association between use of chiropractic services and risk of adverse drug events.

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