

Commentary

# Does Dietary Fiber Reduce the Risk of Rheumatoid Arthritis?

Zhaoli Dai <sup>1,\*</sup> and Yuqing Zhang <sup>1,2</sup>

<sup>1</sup> Clinical Epidemiology Research & Training Unit, Department of Medicine, Boston University School of Medicine, 650 Albany Street, X200 Boston, MA 02118, USA; yuqing@bu.edu

<sup>2</sup> Division of Rheumatology, Allergy, and Immunology, Massachusetts General Hospital, Harvard Medical School, Boston, MA 02114, USA

\* Correspondence: joyzdai@bu.edu; Tel.: +1-617-638-5180; Fax: +1-617-638-5239

Received: 22 February 2018; Accepted: 16 March 2018; Published: 27 March 2018



**Abstract:** Accumulating evidence has suggested the effects of a higher dietary fiber intake on weight loss and reduced inflammation. In line with this, recent observations presented higher consumption of dietary fiber in relation to the lower risks of symptomatic knee osteoarthritis and worsening knee pain. Because both obesity and inflammation are commonly linked with knee osteoarthritis and rheumatoid arthritis, and preliminary results have suggested a role of microbiome in both joint disorders, we hypothesized that increased dietary fiber intakes might confer benefits in reducing the risk of rheumatoid arthritis and/or delaying disease progression. In this commentary, we sought to provide rationales regarding fiber's physiological characteristics and its influence in the gut microbiome to postulate a potential link between fiber intake and the risk of rheumatoid arthritis. Verification of these hypotheses requires data from observational and experimental studies.

**Keywords:** dietary fiber; knee osteoarthritis; rheumatoid arthritis

---

Dietary fibers are carbohydrates that are non-digestible or non-absorbable in the small intestine but are partially or fully fermented in the colon. These physiological characteristics are in part responsible for the health benefits of dietary fiber. Observational studies have shown that fiber intakes are related to lowered risks of cardiovascular diseases, type-2 diabetes, and all-cause mortality [1,2]. Such beneficial effects of fiber in cardiometabolic health are thought in part due to fiber's effects on body weight regulation, lowered inflammation and serum lipids, and glycemic control [1]. Recent evidence on the desirable impacts of fiber on these metabolic factors has further extended to fiber's bifidogenic property in gut health [3].

Obesity is one strong risk factor for knee osteoarthritis (OA) and has been considered as a major target for the prevention of OA. It is hypothesized that obesity not only increases loadings of the joint but also augments serum and tissue levels of pro-inflammatory cytokines and adipokines [4], which accelerate disease development and induce joint pain [5]. This is supported by accumulating evidence which suggests that inflammation both systemically and locally plays an important role in the pathogenesis of OA and pain in the knees. Based on these hypotheses, we observed a potential protective association between a high dietary intake of fiber and lower risks of severe knee pain patterns [6] and incident symptomatic knee OA [7]. In the latter study, we found a significantly lower risk of incident symptomatic knee OA in individuals who consumed the most dietary fiber (at 75th percentile and above) as compared with those who consumed the least fiber (at 25th percentile and below) in a population-based cohort and a cohort of persons at risk or with knee OA [7]. This observation suggests a potentially independent role of dietary fiber in lowering the risk of symptomatic knee OA after adjustment for potential confounders including dietary quality. The observed associations between a high fiber intake and a lower risk of symptomatic knee OA,

as we speculate, are in part due to the weight-control effect of dietary fiber and fiber's prebiotic function, both of which might further reduce inflammation. Although dietary fiber is associated with lower body weight, weight loss associated with a higher fiber intake is usually modest [8,9] and may not be detectable regarding the improvement of OA symptoms.

Rheumatoid arthritis (RA) is an inflammatory autoimmune arthritis, where abnormal activation of B cells, T cells, and innate immune effectors occurs and leads to the development of both acute and chronic inflammatory proliferation of the synovial linings [10]. Symptoms of RA include aggressive cartilage destruction and progressive bony erosions accompanying with flare, swelling and high levels of pain [10]. Risk factors for RA include being female, older age and a complex set of genetic predisposition and environmental factors. However, genetic heritability only accounts for 60% of the disease development; therefore, it does not account for RA sufficiently [11]. Additionally, heavy body weight might have an adverse effect in RA, where increased occurrence, reduced chance of remission, and lowered responses to treatments have been reported in obesity-induced RA [11]. Mechanistically, it is thought that macrophage infiltration activates abnormal B cells and T cells in the adipose tissue, which in turn promotes immune responses and increases pro-inflammatory markers in such obesity-induced inflammation [12]. Recent research paradigm has shifted with increasing interests in the role of gut flora in human health including joint disorders [13]. One hypothesis has been proposed that increased permeability of the gut wall lumen may lead to an exposure of the immune system to microorganisms, resulting in a local inflammatory process within the joints: It is possible that the imbalance of microbiota modifies the local mucosal immune responses through innate signaling pathways to trigger local joint inflammatory processes. Supporting this theory, evidence from animal models has suggested that injection or feeding microbes affects the inflammatory joints [14]. In humans, *Prevotella copri*, an intestinal microbe, has been found to induce antibody responses in both new onset and chronic RA patients [15]. In another study, patients with RA had over-represented pathogenic *Lactobacillus salivarius* as compared with the healthy controls [16]. Further, patients with chronic inflammatory bowel disease also have been found to have recurrent episodes of peripheral arthritis [17].

Because diet plays an essential role in shaping the composition of microbiota, dietary interventions have the potential to target certain microbes to play an adjunctive role in the prevention and treatment of RA. In light with our recent findings in dietary fiber with lowering the risk of symptomatic knee OA, two potential mechanisms are postulated: On one hand, the weight loss effect of fiber is in part due to satiation and satiety from the low energy value of high fiber consumption. This is because for some fibers, they are metabolically inert and provide a bulking effect to increase satiety to control weight gain, which may further reduce obesity-related systemic inflammation. On the other hand, the prebiotic function of fiber is fermented by the gut microbes, which in turn further stimulate the growth of bifidobacteria and produce healthful metabolites such as short-chain fatty acids. As a result, these processes improve immune responses, inhibit pathogenesis and reduce inflammation systemically and locally [3]. Mounting evidence has been suggested that increased fiber intakes are correlated with the growth of gut bifidobacteria and lactic acid bacteria [18], which contribute to the regulation of the epithelial cells to maintain immune homeostasis. Connecting obesity, inflammation and immune responses with RA, we postulate that increased intakes of dietary fiber may have a potential to confer benefits in reducing the risk of RA and/or delaying disease progression as an adjunctive therapeutic treatment option for RA.

As RA can occur at different age groups and has a high heritability compared with OA, we raised a further research question whether dietary fiber may reduce the risk of RA depend on age groups or serostatus. Although fiber can be found in many plant-based foods and has been shown to have health benefits in obesity and cardiometabolic health, the average intake of dietary fiber is far below the recommended level. As a result, the general public may not have achieved to the optimal health benefits through fiber intakes. Such dietary variance provides an opportunity in observational studies to assess the etiologic association with incidence and progression of RA. If the preliminary results are promising, data in experimental settings in animal models and human subjects can further assess

causal effects and the underlying mechanisms to provide insights into the link between fiber intakes and rheumatoid arthritis.

**Author Contributions:** Zhaoli Dai and Yuqing Zhang both conceived and designed the study concept, had access to the data, and had a substantial contribution to the development of the manuscript and approved the final version of the manuscript.

**Conflicts of Interest:** The authors declare no conflict of interest.

## References

1. Anderson, J.W.; Baird, P.; Davis, R.H., Jr.; Ferreri, S.; Knudtson, M.; Koraym, A.; Waters, V.; Williams, C.L. Health benefits of dietary fiber. *Nutr. Rev.* **2009**, *67*, 188–205. [[CrossRef](#)] [[PubMed](#)]
2. Yang, Y.; Zhao, L.G.; Wu, Q.J.; Ma, X.; Xiang, Y.B. Association between dietary fiber and lower risk of all-cause mortality: A meta-analysis of cohort studies. *Am. J. Epidemiol.* **2015**, *181*, 83–91. [[CrossRef](#)] [[PubMed](#)]
3. Kuo, S.M. The interplay between fiber and the intestinal microbiome in the inflammatory response. *Adv. Nutr.* **2013**, *4*, 16–28. [[CrossRef](#)] [[PubMed](#)]
4. Thijssen, E.; van Caam, A.; van der Kraan, P.M. Obesity and osteoarthritis, more than just wear and tear: Pivotal roles for inflamed adipose tissue and dyslipidaemia in obesity-induced osteoarthritis. *Rheumatology* **2015**, *54*, 588–600. [[CrossRef](#)] [[PubMed](#)]
5. Jin, X.; Beguerie, J.R.; Zhang, W.; Blizzard, L.; Otahal, P.; Jones, G.; Ding, C. Circulating C reactive protein in osteoarthritis: A systematic review and meta-analysis. *Ann. Rheum. Dis.* **2015**, *74*, 703–710. [[CrossRef](#)] [[PubMed](#)]
6. Dai, Z.; Lu, N.; Niu, J.; Felson, D.T.; Zhang, Y. Dietary intake of fiber in relation to knee pain trajectories. *Arthritis Care Res.* **2017**, *69*, 1331–1339. [[CrossRef](#)] [[PubMed](#)]
7. Dai, Z.; Niu, J.; Zhang, Y.; Jacques, P.; Felson, D.T. Dietary intake of fibre and risk of knee osteoarthritis in two US prospective cohorts. *Ann. Rheum. Dis.* **2017**, *76*, 1411–1419. [[CrossRef](#)] [[PubMed](#)]
8. Kim, S.J.; de Souza, R.J.; Choo, V.L.; Ha, V.; Cozma, A.I.; Chiavaroli, L.; Mirrahimi, A.; Blanco Mejia, S.; Di Buono, M.; Bernstein, A.M.; et al. Effects of dietary pulse consumption on body weight: A systematic review and meta-analysis of randomized controlled trials. *Am. J. Clin. Nutr.* **2016**, *103*, 1213–1223. [[CrossRef](#)] [[PubMed](#)]
9. Mukai, J.; Tsuge, Y.; Yamada, M.; Otori, K.; Atsuda, K. Effects of resistant dextrin for weight loss in overweight adults: A systematic review with a meta-analysis of randomized controlled trials. *J. Pharm. Health Care Sci.* **2017**, *3*, 15. [[CrossRef](#)] [[PubMed](#)]
10. Allan, C.; Gelber, S.M.L.; Rosen, A. Inflammatory Rheumatic Diseases. In *Pathophysiology of Disease: An Introduction to Clinical Medicine, 7e*; Hammer, G.D., McPhee, S.J., Eds.; McGraw-Hill: New York, NY, USA, 2013.
11. Deane, K.D.; Demoruelle, M.K.; Kelmenson, L.B.; Kuhn, K.A.; Norris, J.M.; Holers, V.M. Genetic and environmental risk factors for rheumatoid arthritis. *Best Pract. Res. Clin. Rheumatol.* **2017**, *31*, 3–18. [[CrossRef](#)] [[PubMed](#)]
12. Frasca, D.; Blomberg, B.B.; Paganelli, R. Aging, Obesity, and Inflammatory Age-Related Diseases. *Front. Immunol.* **2017**, *8*, 1745. [[CrossRef](#)] [[PubMed](#)]
13. Pisetsky, D.S. How the gut inflames the joints. *Ann. Rheum. Dis.* **2018**. [[CrossRef](#)] [[PubMed](#)]
14. Baharav, E.; Mor, F.; Halpern, M.; Weinberger, A. Lactobacillus GG bacteria ameliorate arthritis in Lewis rats. *J. Nutr.* **2004**, *134*, 1964–1969. [[CrossRef](#)] [[PubMed](#)]
15. Pianta, A.; Arvikar, S.; Strle, K.; Drouin, E.E.; Wang, Q.; Costello, C.E.; Steere, A.C. Evidence of the Immune Relevance of *Prevotella copri*, a Gut Microbe, in Patients with Rheumatoid Arthritis. *Arthritis Rheumatol.* **2017**, *69*, 964–975. [[CrossRef](#)] [[PubMed](#)]
16. Zhang, X.; Zhang, D.; Jia, H.; Feng, Q.; Wang, D.; Liang, D.; Wu, X.; Li, J.; Tang, L.; Li, Y. The oral and gut microbiomes are perturbed in rheumatoid arthritis and partly normalized after treatment. *Nat. Med.* **2015**, *21*, 895–905. [[CrossRef](#)] [[PubMed](#)]

17. Lichtman, S.N.; Wang, J.; Sartor, R.B.; Zhang, C.; Bender, D.; Dalldorf, F.G.; Schwab, J.H. Reactivation of arthritis induced by small bowel bacterial overgrowth in rats: Role of cytokines, bacteria, and bacterial polymers. *Infect. Immun.* **1995**, *63*, 2295–2301. [[PubMed](#)]
18. Singh, R.K.; Chang, H.W.; Yan, D.; Lee, K.M.; Ucmak, D.; Wong, K.; Abrouk, M.; Farahnik, B.; Nakamura, M.; Zhu, T.H.; et al. Influence of diet on the gut microbiome and implications for human health. *J. Transl. Med.* **2017**, *15*, 73. [[CrossRef](#)] [[PubMed](#)]



© 2018 by the authors. Licensee MDPI, Basel, Switzerland. This article is an open access article distributed under the terms and conditions of the Creative Commons Attribution (CC BY) license (<http://creativecommons.org/licenses/by/4.0/>).