Supplement Article

Evidence mapping to assess the available research on fiber, whole grains, and health

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Evidence mapping is a useful methodology for characterizing existing research on a broad topic and identifying gaps in the scientific literature. Evidence mapping entails conducting a systematic literature search and extracting information on study details, often in the form of a database. Researchers at Tufts University and the North American branch of the International Life Sciences Institute created the Diet-Related Fibers & Human Health Outcomes Database, which is publicly available and updated annually. The database captures intervention studies examining dietary fiber and 10 predefined physiological health outcomes, including weight/adiposity, blood pressure, gut microbiota, and bone health. The database and subsequent potential for evidence mapping may be particularly useful in light of new food labeling requirements by the US Food and Drug Administration that require fibers to have accepted scientific evidence of a physiological health benefit in order to be labeled as "dietary fiber." Following the success of the fiber database, Tufts University and the General Mills Bell Institute of Health and Nutrition collaborated to develop a whole grain database and evidence map. This work successfully highlighted the need for better consistency in how whole grains are reported with respect to amount and type of whole grains and intervention compliance.

INTRODUCTION

Dietary fiber database

In the United States, the Food and Drug Administration (FDA) adopted a new definition of "dietary fiber" for food labeling. The Nutrition Facts Label Final Rule defines *dietary fiber* as "non-digestible soluble and insoluble carbohydrates (with 3 or more monomeric units), and lignin that are intrinsic and intact in plants; isolated or synthetic non-digestible carbohydrates (with 3 or more monomeric units) determined by FDA to have physiological effects that are beneficial to human health."[1] These fibers must have accepted scientific evidence of some physiological health benefit in order to be considered "dietary fiber." As a result, the FDA began the process of assessing whether individual fibers from the isolated and synthetic category are linked to clinical evidence demonstrating a physiological benefit.

The Technical Committee on Dietary Carbohydrates of the North American branch of the International Life Sciences Institute (ILSI NA), in collaboration with researchers at the Jean Mayer USDA

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Human Nutrition Research Center on Aging at Tufts University, with Dr. Nicola McKeown as principal investigator, developed the "Diet-Related Fibers & Human Health Outcomes Database," which captured published data generated from intervention research studies examining the effect of a wide range of dietary fibers on selected health endpoints. This research database was developed to streamline the process of identifying relevant research on dietary fiber that may be of benefit to the FDA, as well as other scientists, to expedite the review process. The fiber database was completed and made publicly available on the ILSI website (http://ilsina.org/our-work/research-tools-open-data/dietary-fiber-database/), as well as on the Agency for Healthcare Research and Quality's SRDR (Systematic Review Data Repository) website (https://srdr.ahrq.gov/projects/1464). A user manual is available to download with the data, and a recent publication provides background information on how the database was developed and the methodology used.[2]

The database, which is updated annually to incorporate new literature, contains data extracted from over 1,000 research papers detailing human intervention studies. Observational studies were excluded. The database was targeted specifically at literature examining one or more of the 9 physiological health outcomes attributed to dietary fiber intake at the Ninth Vahouny Fiber Symposium[3] and, more recently, bone-related outcomes. In addition to identifying the relevant publications and authors, the database includes PICO information—population (age, gender), intervention (fiber types, dose), comparator (control diet), and outcomes (endpoints and health markers). A detailed list of all variables collected as part of the database is available as part of the codebook on the ILSI website, available at: http://ilsina.org/wp-content/uploads/sites/6/2019/04/Fiber-Database-user-manual-04012019.pdf. The database is searchable, allowing users the flexibility to restrict their searches to dietary fibers and/or health outcomes of interest based on their own research needs.

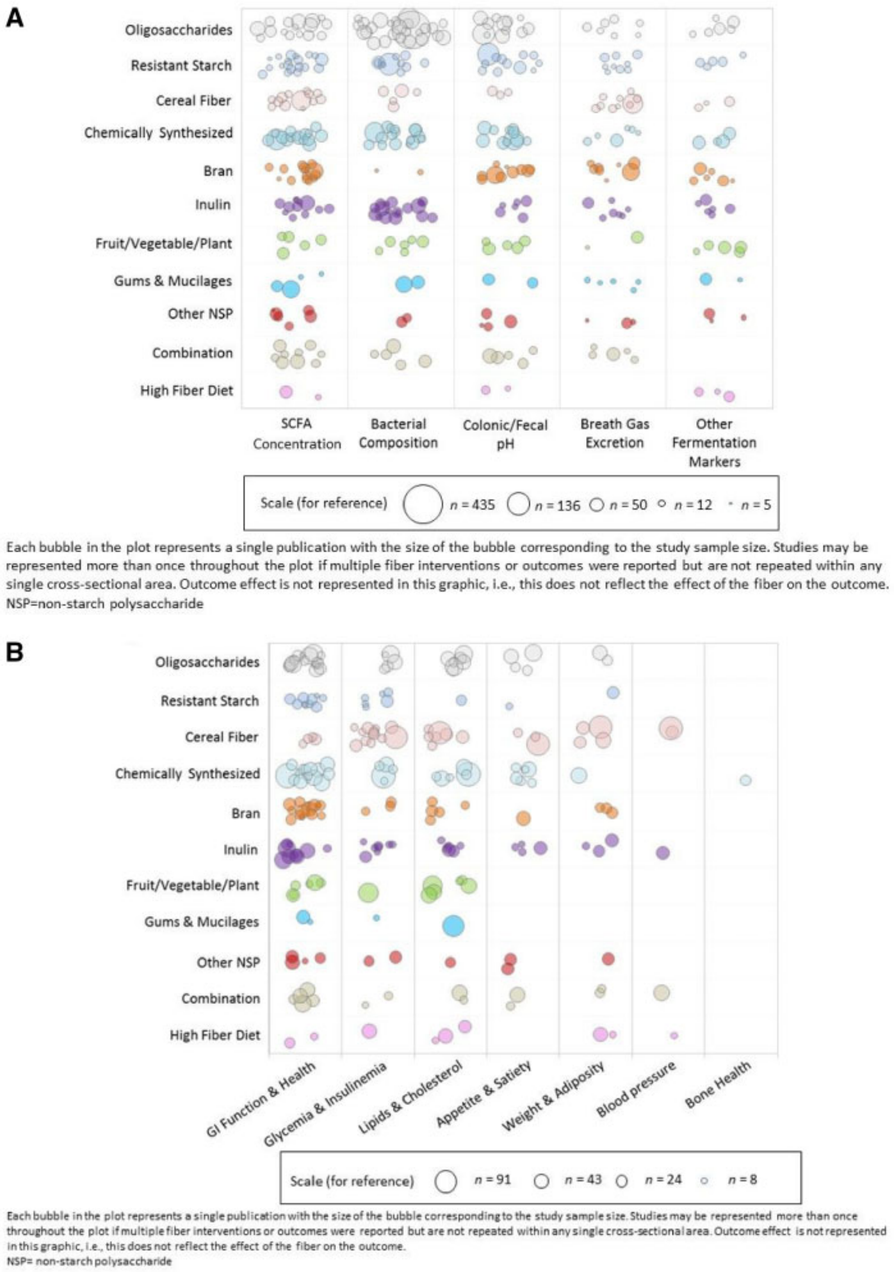
Evidence mapping is a technique used in various fields, including nutritional epidemiology, to help drive evidence-based decision-making, and it exemplifies the utility of this database. This technique provides a fast and cost-effective way to summarize published research across broad topics of interest, in particular through the identification of major research gaps.[4] Rather than addressing a targeted question, evidence maps help scientists to understand the research "landscape" of a specific topic area. The methods required for evidence mapping, described in greater detail below, represent the initial steps of a systematic review; however, evidence mapping does not typically include information on results such as direction and size of effect.

Evidence mapping can include descriptive and visual representations of the data, such as weighted scatter plots. The weighted scatter plots, created using Microsoft Excel, represent three components of information (x-axis, y-axis, and bubble size). For example, Figure 1a depicts outcome on the x-axis and fiber type on the y-axis, and the bubble size represents the sample size of the study. Figure 1a shows that several intervention studies focused on microbiota-related outcomes have also included data on gastrointestinal (GI) function and health, with a greater body of research involving larger sample sizes focused on oligosaccharides, chemically synthesized fibers, and inulin. This evidence map, however, does not indicate whether oligosaccharides have a positive or negative effect, or no effect, on GI function. Future work may focus on a meta-analysis examining the effects of oligosaccharides on various health benefits. Alternatively, future research may also focus on studying an area in which little research has been conducted, such as on bone health outcomes among studies examining dietary fiber and microbiota. Meta-analyses from systematic reviews may be at the top of the hierarchy of scientific evidence, but evidence mapping is a particularly useful technique for visualizing the broader research landscape in fast-paced or rapidly developing areas of research.

Evidence mapping involves three major steps: (1) clearly defining a topic area and setting criteria around the questions of interest; (2) systematically searching for and selecting relevant studies based on predefined criteria; and (3) extracting and reporting on study characteristics, such as study design and outcomes of interest, thereby creating a "map" outlining the extent of existing research. Below, evidence maps generated using the Diet-Related Fibers & Human Health Outcomes Database and the General Mills Bell Institute of Health & Nutrition (BIHN) Whole Grain Database are presented and described.

Dietary fiber evidence map

Version 5.0 of the Diet-Related Fibers & Human Health Outcomes Database has recently been made available. However, the dietary fiber evidence map presented here includes descriptive analyses detailing study design types (ie, randomized crossover trials, randomized parallel trials), fiber interventions, and outcomes examined using version 3.0. Since this evidence map is meant to capture the wider landscape of evidence and is, therefore, more inclusive and heterogeneous than a meta-analysis, results are not represented. Owing to the large variety of fiber interventions identified, fiber intervention exposures were classified in the database as they were reported in the original publication. For example,



Each bubble in the plot represents a single publication with the size of the bubble corresponding to the study sample size. Studies may be represented more than once throughout the plot if multiple fiber interventions or outcomes were reported but are not repeated within any single cross-sectional area. Outcome effect is not represented in this graphic, i.e., this does not reflect the effect of the fiber on the outcome.
NSP=non-starch polysaccharide

Each bubble in the plot represents a single publication with the size of the bubble corresponding to the study sample size. Studies may be represented more than once throughout the plot if multiple fiber interventions or outcomes were reported but are not repeated within any single cross-sectional area. Outcome effect is not represented in this graphic, i.e., this does not reflect the effect of the fiber on the outcome.
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Figure 1 (**a**) **Weighted scatter plot of other health outcomes captured within interventions examining type or source of dietary fiber and microbiota-related outcomes.** (**b**) **Weighted scatter plot of microbiota outcomes by type or source of dietary fiber intake.** *Abbreviations*: GI, gastrointestinal; SCFA, short-chain fatty acid; NSP, non-starch polysaccharide.

although psyllium and ispaghula are different names for the same fiber, they could be reported by either name in the database depending on how they were described in each individual publication.

Weighted scatter plots were used to visualize the current evidence on different fiber types by outcome groups and sample size. One example includes a weighted scatter plot that highlights the research on dietary fiber and microbiota-related outcomes (Figure 1b), from a study conducted by Sawicki et al.[4] From this scatter plot, it is clear that oligosaccharides, relative to other fibers, have been well studied for their effect on short-chain fatty acid production and bacterial composition in the gut. As presented in that published paper, researchers interested in a specific topic can refine their search to specific fibers and/or endpoints, such as oligosaccharides and bacterial composition, to review those publications in further detail in order to draw conclusions about the direction of the evidence. Figure 1a shows another example of a weighted scatter plot, which

¹Mixed WG group includes combinations of 2 or more WG, WG diets, and unspecified WG foods (ex: WG bread); ²Other outcomes include exercise performance, micronutrient status, clinical blood and urine measures, and other metabolites.

Each bubble in the plot represents a single publication with the size of the bubble corresponding to the study sample size. Studies may be represented more than once throughout the plot if multiple whole grain interventions or outcomes were reported but are not repeated within any single cross-sectional area. Outcome effect is not represented in this graphic, i.e., this does not reflect the effect of the grain on the outcome.

Figure 2 **Weighted scatter plot of published studies on whole grain interventions and outcome categories examined**.
Abbreviations: GI, gastrointestinal; WG, whole grain.

presents a visualization of the other outcomes reported on among those studies restricted to having microbiota-related outcomes. It is evident from Figure 1a that these studies also frequently included outcome data on GI function and health, glycemia and insulinemia, and blood lipids and cholesterol.

Whole grain database and evidence map

Based on the success and value of the fiber database, a whole grain database was developed in a collaboration between Tufts University and the General Mills BIHN. Similar to dietary fiber, whole grains are heterogeneous and comprise many different varieties, including oat, wheat, rice, and corn. Scientific evaluation of whole grains on markers of health is additionally challenging because studies on “whole grains” often represent meals or diets that include a variety of whole grains in contrast to simply examining the effect of an individual whole grain, such as whole grain oats. While each whole grain has an endosperm, germ, and bran, each species of grain has a unique composition of carbohydrates, proteins, fats, micronutrients, and other phytochemicals. For this reason, the health benefits significantly associated with one type of whole grain (eg, reduced blood cholesterol linked to whole grain oats) may not be highly associated with other grains (eg, whole grain rice).

The whole grain database and evidence map also help to highlight the lack of standardized reporting practices for the amount and type of whole grains and degree of study compliance. There is no universal consensus around how to define whole grain, and definitions vary by different organizations.[5–8] More consistent definitions for whole grain ingredients and whole grain foods would contribute greatly to improving consistency in nutrition research. Efforts to standardize study protocols and reporting practices will allow for effective synthesis of study results in meta-analyses, and thereby provide a stronger foundation to better inform nutrition scientists and public health policy.

A systematic search to identify published intervention studies examining the effect of whole grains on health identified more than 1700 publications. However, approximately 1500 publications were eliminated during abstract and full-text screening, leaving just over 200 eligible publications for inclusion in the final database. Inclusion and exclusion criteria are discussed in detail in a 2018 study by Sawicki et al.[8]

A weighted scatter plot – a visual component of the evidence map – for whole grains and health outcomes is shown in Figure 2. In contrast to the weighted scatter plots shown previously, an additional fraction of the data was included to highlight the duration of the individual studies. Each circle represents a trial, and the color of the circle indicates whether the duration of the trial was acute (1 day or less), mid-term (more than 1 day and up to 6 weeks), or long-term (more than 6 weeks). The plot illustrates that the majority of studies were mid- to long-term trials exploring the effect of oats on cardiometabolic endpoints. The fully updated evidence map and weighted scatter plot are available in the report of Sawicki et al.[8]

Unlike the dietary fiber database, supported by ILSI NA's Technical Committee on Dietary Carbohydrates the whole grain database was developed in collaboration with General Mills BIHN and is not currently available to the public. However, the General Mills BIHN recognizes the value that the whole grain database and evidence mapping offer to parties interested in studying the effect of whole grains on health. The database is a unique resource that can be used to inform new intervention studies and facilitate meta-analyses. As a result, the General Mills BIHN encourages regulatory and health authorities to request access to the database. The corresponding author of the present article may be contacted for more information.

CONCLUSION

Nutrition research is constantly evolving and, thus, summarizing fiber and whole grain research is complex. Evidence maps are a useful tool for areas of fast-paced research, as they can help to highlight gaps in the literature and identify study design considerations that can be used to inform future work. For example, Figure 1a provides an efficient visual depiction of the fact that few studies have examined whether dietary fibers that modulate gut microbiota may be implicated in changes in bone health parameters.[9] While many meta-analyses have been published on whole grains, the majority are based on observational data. Databases and evidence maps support developing questions regarding intervention studies, especially with the less-well-studied whole grains such as millet, sorghum, quinoa, amaranth, teff, and triticale. Moving forward, research studies examining the health benefits of whole grains should examine a variety of whole grains beyond whole wheat, including those mentioned above, to determine whether longer study intervention periods would yield different results, such as greater improvement in cardiometabolic risk factors, satiety, and weight loss among whole grain consumers.

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Author contributions. N.M.M. and K.B.M. drafted the manuscript. K.A.L. managed the creation and ongoing development of the Diet-Related Fibers & Human Health Outcomes Database. C.M.S. managed the creation and ongoing development of the whole grain database. K.A.L. and C.M.S. generated the descriptive statistics used to create the evidence maps and weighted scatter plots. N.M.M. oversaw the creation of the databases and interpretation of the results with respect to the evidence maps. All authors critically reviewed, revised, and approved the manuscript.

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