Commentary

Commentary on whole-grain intake and pancreatic cancer risk-the danish, diet, cancer and health cohort by Schacht *et al.*

Rick J. Jansen

Department of Public Health, Genomics, Phenomics, and Bioinformatics Program, Center for Immunization Research and Education (CIRE), Center for Diagnostic and Therapeutic Strategies in Pancreatic Cancer, North Dakota State University, Fargo, ND, USA

Correspondence to: Rick J. Jansen. Department of Public Health, North Dakota State University, Fargo, ND 58105, USA. Email: rick.jansen@ndsu.edu.

Comment on: Schacht SR, Olsen A, Dragsted LO, *et al.* Whole-Grain Intake and Pancreatic Cancer Risk-The Danish, Diet, Cancer and Health Cohort. J Nutr 2021;151:666-74.

Submitted Jul 13, 2021. Accepted for publication Aug 19, 2021.
doi: 10.21037/hbsn-21-286
View this article at: https://dx.doi.org/10.21037/hbsn-21-286

Summary of study results

In their manuscript, "*Whole-Grain Intake and Pancreatic Cancer Risk-The Danish, Diet, Cancer and Health Cohort*", Schacht *et al.* (1) report that total whole-grain product (per 50 g/d serving) intake was significantly associated with lower incidence of pancreatic cancer (HR: 0.93; 95% CI: 0.86, 1.00). A sex-specific analysis revealed that this association only held among men. However, neither total whole-grain (per 16-g serving) or specific individual whole-grain products and cereals were significantly associated with lower pancreatic cancer risk. In this commentary, I will describe some of the assumptions and biases associated with assessing dietary intake and attempting to find associations with disease.

Issues with dietary data collection and analysis

Abundant literature exists highlighting the limitations of current dietary assessment methods (2). These limitations become even more pronounced when the dietary assessment is for diseases, like cancer, with long lag times (e.g., decades between biological disease onset and clinical diagnosis). One of the biggest problems is the issue of recall bias. For example, we know that in general women pay attention to food choices more than men. There are additional characteristics where we could see differential recall by categories such as with type 2 diabetes, BMI, or based on the number of calories consumed in a day (all factors adjusted for in different models in the manuscript). Unfortunately, because recall varies from individual to individual and is not necessarily systematic, standard regression adjustments cannot be used to fully "adjust away" these types of bias.

Attempts at solutions to this issue have been investigated and include performing sensitivity analyses (3), combining multiple forms of dietary assessments (e.g., 24 hours recall and FFQ) (4), using new adjustment methods (5), and using technology assisted capture of consumed dietary items (6).

In a cohort study, we also have the issue of temporal bias, where those who report on their diet close to a diagnosis are more likely to have that diet influenced by their disease making the diet less reflective of the diet that contributed to their disease in the first place. This could be helpful if the objective was to develop a way to detect disease earlier, but not as a way to understand the functional importance of diet in the development of a specific disease. In a disease like pancreatic cancer where the digestive system is impacted by disease, the metabolism of what a person eats may change as well. For example, many recent studies have linked different types of cancers with altered microbiomes.

Attempts at solutions to this issue could be longitudinal or continuous diet collections (3,7), integration of collection of microbiome profiles longitudinally (8), or sensitivity analyses looking at exclusion of those who are diagnosed with disease within a few years of the start of the cohort study (9).

Several assumptions are associated with the FFQ including that the person ate a standard amount (serving

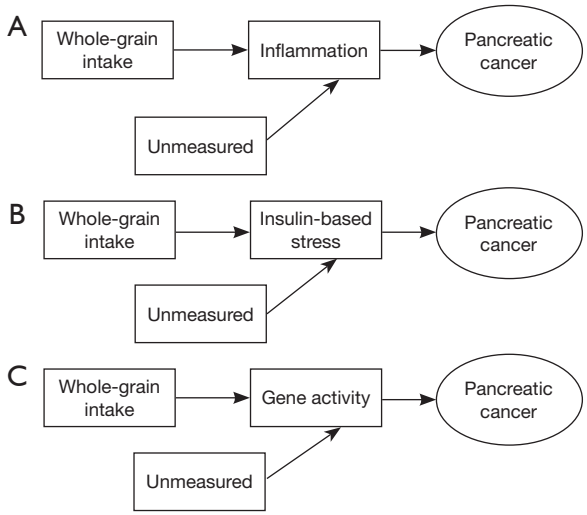

Figure 1 Directed acyclic graphs representing the three proposed functional connections between whole-grains and pancreatic cancer. The unmeasured box here represents unmeasured variables that may also influence the mediator. An important note is that the mediator in these models could be measured within dietary studies to further understand these proposed biological relationships.

size of an item is the same for everyone) and that all food products of one type contain the same proportion of nutrients and other components. We can see that these assumptions have flaws in that a hamburger could be different sizes (1/4 pound, 1/3 pound, 1/2 pound, double patty, etc.) and contain different amount of toppings (ketchup, mustard, mayo, tomato, lettuce, pickles) and that the hamburger could be made from ground beef, ground sirloin, or ground chuck. These types of assessments also cannot identify what a person actually ate of the food.

Attempts at solutions to this issue could be image/picture based collection methods which can provide an objective capture of a person's plate before and after a meal (7,10).

Biologically functional and available components of whole-grains

The authors propose that whole-grains could reduce inflammation, lower insulin-based "stress" of pancreas tissue, or the metabolites or alkylresorcinols of the whole-grain could reduce oncogene activities or induce tumor-suppressor activity. The causal models illustrate the authors' proposed pathways (*Figure 1*). In all these proposed pathways, whole-grains are upstream of the biological mechanism and incorporating a measurement of the biological mechanism would provide important information.

Conclusions

There is no doubt that diet plays a significant role in many diseases and conditions, however, our methods for dietary collection and measurement need to continue to be improved. With so much variation across geographic location, population, and individual, it is no surprise that significant dietary study associations are hard to find consistently. As technology-based solutions continue to be developed and explored, our biological understanding and public health guidance will improve. It will be essential for funding agencies to value this type of research and support researchers advancing dietary knowledge and methods.

Acknowledgments

Funding: This work was supported through NIH funds from the NDSU COBRE Center for Diagnostic and Therapeutic Strategies in Pancreatic Cancer (P20GM109024).

Footnote

Provenance and Peer Review: This article was commissioned by the editorial office of *Hepatobiliary Surgery and Nutrition*. The article did not undergo external peer review.

Conflicts of Interest: The author has completed the ICMJE uniform disclosure form (available at https://hbsn.amegroups.com/article/view/10.21037/hbsn-21-286/coif). The author has no conflicts of interest to declare.

Ethical Statement: The author is accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

References

1. Schacht SR, Olsen A, Dragsted LO, et al. Whole-Grain Intake and Pancreatic Cancer Risk-The Danish, Diet, Cancer and Health Cohort. J Nutr 2021;151:666-74.
2. Bailey RL. Overview of dietary assessment methods for measuring intakes of foods, beverages, and dietary supplements in research studies. Curr Opin Biotechnol 2021;70:91-6.
3. Siddique J, Daniels MJ, Carroll RJ, et al. Measurement error correction and sensitivity analysis in longitudinal dietary intervention studies using an external validation study. Biometrics 2019;75:927-37.
4. Looman M, Boshuizen HC, Feskens EJ, et al. Using enhanced regression calibration to combine dietary intake estimates from 24 h recall and FFQ reduces bias in diet-disease associations. Public Health Nutr 2019;22:2738-46.
5. Lankester J, Perry S, Parsonnet J. Comparison of two methods - regression predictive model and intake shift model - for adjusting self-reported dietary recall of total energy intake of populations. Front Public Health 2014;2:249.
6. Boushey CJ, Spoden M, Zhu FM, et al. New mobile methods for dietary assessment: review of image-assisted and image-based dietary assessment methods. Proc Nutr Soc 2017;76:283-94.
7. Shoneye CL, Dhaliwal SS, Pollard CM, et al. Image-Based Dietary Assessment and Tailored Feedback Using Mobile Technology: Mediating Behavior Change in Young Adults. Nutrients 2019;11:435.
8. Yammine A, Namsi A, Vervandier-Fasseur D, et al. Polyphenols of the Mediterranean Diet and Their Metabolites in the Prevention of Colorectal Cancer. Molecules 2021;26:3483.
9. Baker CF, Overvad K, Dahm CC. Lean body mass and risk of type 2 diabetes - a Danish cohort study. J Diabetes Metab Disord 2019;18:445-51.
10. Kirkpatrick SI, Guenther PM, Douglass D, et al. The Provision of Assistance Does Not Substantially Impact the Accuracy of 24-Hour Dietary Recalls Completed Using the Automated Self-Administered 24-H Dietary Assessment Tool among Women with Low Incomes. J Nutr 2019;149:114-22.

Cite this article as: Jansen RJ. Commentary on whole-grain intake and pancreatic cancer risk-the danish, diet, cancer and health cohort by Schacht *et al.* HepatoBiliary Surg Nutr 2021;10(5):702-704. doi: 10.21037/hbsn-21-286

