HHS Public Access

Author manuscript

Ann Intern Med. Author manuscript; available in PMC 2021 June 04.

Published in final edited form as:

Ann Intern Med. 2020 March 03; 172(5): 354–355. doi:10.7326/M19-3290.

Dietary Assessment and Opportunities to Enhance Nutritional Epidemiology Evidence

Ross L. Prentice, PhD

Fred Hutchinson Cancer Research Center and University of Washington

Dietary guidelines are promulgated periodically by the US government (e.g., 1), as well as by other authoritative bodies, with content substantially based on expert review of pertinent biological considerations and the world nutritional epidemiology literature. These contribute to widely held beliefs that adherence to dietary guidelines will reduce the risk of major chronic diseases, including cardiovascular diseases, cancers, and diabetes. However, when systematic reviews of specific recommended dietary behaviors have been conducted, the conclusion is often that evidence for chronic disease benefits is of low certainty and that any benefits are likely to be small. Recent examples are provided by systematic reviews of sodium (2), eggs (3), and red and processed meat (4). Vigorous debate typically ensues, with differing opinions expressed concerning the reliability of epidemiologic data underlying dietary recommendations.

There is usually much to agree with on both sides of these arguments. One can agree that systematic reviews have been well-conducted generally and under the criteria applied, which weight randomized controlled trials much more heavily than observational studies, that evidence for chronic disease risk benefits from recommended dietary consumption can be classified as being of low certainty, and then only for modest benefits. At the same time one can ask how such weak and uncertain data can support any related dietary recommendations by systematic review authors (e.g., 4), especially if these contradict dietary guidelines.

On the other side of the argument, one can acknowledge that dietary guidelines developed by multidisciplinary groups over many years are eminently sensible, and worthy of notice. However, one can ask also whether dietary guidelines have been developed from a convincing body of scientific evidence?

The last question gets to the heart of the nutritional epidemiology research agenda, which for the past 50 years has relied primarily on observational studies in conjunction with self-reported diet. A substantial reliance on observational studies may be justified, given the many important hypotheses related to the health benefits and risks of foods, nutrients and dietary patterns, and the cost and logistical challenges of carrying out long-term randomized, controlled dietary intervention trials to test such hypotheses. However, observational studies, including the carefully conducted cohort studies that have been central to nutritional

Corresponding Author: Ross L. Prentice, PhD, Fred Hutchinson Cancer Research Center, Room M3-A410, 1100 Fairview Ave. N, Seattle WA 98104; rprentic@whi.org.

Disclosure: Author has no conflict of interest.

epidemiology reporting, can never be certain about the extent of confounding control, and there may be challenges to ensuring equal outcome ascertainment across dietary exposure categories in the absence of a clinical context.

Furthermore, in the author's opinion the biggest impediment to reliable disease association information from observational studies, and one that merits greater emphasis in systematic reviews, is that of measurement error in dietary assessment. The random component of measurement error may substantially attenuate estimated associations, so that a recommended consumption of a nutrient or food that appears to convey a small health benefit, may reflect a much stronger disease prevention potential. Importantly, concurrent systematic bias in dietary assessment can fundamentally distort disease association results. Hence, while one may accept a central role for observational studies in nutritional epidemiology, there is no compelling argument for accepting self-reported dietary data.

To amplify, while many epidemiologic reports claim the use of 'validated' dietary assessment tools, predominantly food frequency questionnaires, these claims almost universally arise from repeatability, based on positive correlations between intake estimates when the same or different assessment tools are applied to individual study participants. In contrast, a validity claim requires a close correspondence with actual intake.

Intake biomarkers (5), based on measures in urine, blood or other biospecimens, can provide the opportunity for a stronger assessment of diet. Such biomarkers may be able to be applied directly in disease association analyses (e.g., 6), or may be used to calibrate self-report assessments to reduce systematic and random measurement error influences. An important special case of the latter is provided by the doubly-labeled water (DLW) assessment of total energy consumption. The DLW method accurately assesses energy intake over a two-week period among weight-stable study participants (7). Comparisons of DLW energy with self-reported energy in Women's Health Initiative (WHI) cohorts reveal weak associations and strong systematic biases, with energy intake substantially underestimated among overweight and obese participants (8). Moreover, these measurement issues are evident whether using food frequency questionnaires, dietary recalls, or dietary records (9). However, these weak assessments may combine with body mass index and other participant characteristics to yield measurement error-corrected energy intake estimates having strong positive estimated associations with major chronic diseases (10).

The set of established nutritional biomarkers is small, primarily including DLW (for energy), urinary nitrogen (for protein), 24-hour urinary sodium and potassium, and recently proposed serum concentration based micronutrient biomarkers (6). There is a great need for the development of additional intake biomarkers, perhaps using metabolomics, microbiomics, or other high-dimensional platforms. Doing so can help ensure that the dietary assessment limitations do not imply another 50 years of disease associations of uncertain interpretation.

There are other research initiatives that merit exploration for strengthening nutritional epidemiology evidence. For example, small-scale intervention trials of promising dietary changes in conjunction with a broad array of intermediate outcomes and nutritional biomarkers, may be able to be paired with cohort studies having these same measurements

from stored biospecimens in cases and controls, to usefully project intervention influences on health outcomes, in studies having acceptable cost and duration.

Nutritional epidemiology research is not at all easy. Even without the measurement error issue it would be a statistical challenge to sort out the contribution of specific dietary factors to health outcomes given the complex mixture of nutrients, foods, patterns and practices that constitute the human diet. Add to that, major systematic and random biases in intake assessment, and the challenge may seem overwhelming. However, there are available research avenues that can be expected to lead to a fresh perspective on a broad range of diet and disease association topics, including the health implications of sodium, eggs, and red meat, if the considerable capabilities of the multidisciplinary nutrition science community, especially those able to conduct human feeding studies and small-scale human intervention trials, are directed to current opportunities.

Acknowledgments

Funding: This work was supported by US National Institutes of Health grants R01 CA119171 and R01 CA210921.

References:

1. United States Department of Agriculture (USDA) United States Department of Health and Human Services (HHS). 2015–2010 Dietary Guidelines for Americans, 8th Edition: United States Department of Agriculture, United States Department of Health and Human Services; 2015.
2. Sodium and Potassium Intake: Effects on Chronic Disease Outcomes and Risks. Comparative Effectiveness Review Number 206. Agency for Healthcare Research and Quality. U.S. Department of Health and Human Services. Rockville, MD 6 2018.
3. Shin JY, Xun P, Nakamura Y, He K. Egg consumption in relation to risk of cardiovascular disease and diabetes: a systematic review and meta-analysis. Am J Clin Nutr. 2013;98:146–59. [PubMed: 23676423]
4. Johnston BC, Zeraatkar D, Han MA, Vernooij RWM, Valli C, El Dib R, et al. Unprocessed red meat and processed meat consumption: dietary guideline recommendations from the nutritional recommendations (NutriRECS) consortium. Ann Intern Med. 2019 10 1; doi:10.7326/M19-1621. (Published on-line at Annals.org on Oct 1, 2019)
5. Brennan L. The nutritional metabolomics crossroads: how to ensure success for dietary biomarkers. Am J Clin Nutr. 2017;105:293–294. [PubMed: 28100510]
6. Prentice RL, Pettinger M, Neuhouser ML, Tinker LF, Huang Y, Zheng C, et al. Application of blood concentration biomarkers in nutritional epidemiology: example of carotenoid and tocopherol intake in relation to chronic disease risk. Am J Clin Nutr. 2019;109:1189–1196. [PubMed: 30915444]
7. Schoeller DA. Recent advances from application of doubly labeled water to measurement of human energy expenditure. J Nutr. 1999;129:1765–1768. [PubMed: 10498745]
8. Neuhouser ML, Tinker L, Shaw PA, Schoeller D, Bingham SA, Van Horn L, Beresford SAA, Caan B, Thompson C, Satterfield S, Kuller L, Heiss G, Smit E, Sarto G, Ockene J, Stefanick ML, Assaf A, Runswick S, Prentice RL. Use of recovery biomarkers to calibrate nutrient consumption self-reports in the Women's Health Initiative. Am J Epidemiol. 2008;167(10):1247–1259. [PubMed: 18344516]
9. Prentice RL, Mossavar-Rahmani Y, Huang Y, Van Horn L, Beresford SAA, Caan B, et al. Evaluation and comparison of food records, recalls, and frequencies for energy and protein assessment by using recovery biomarkers. Am J Epidemiol. 2011;174:591–603. [PubMed: 21765003]
10. Zheng C, Beresford SA, Van Horn L, Tinker LF, Thomson CA, Neuhouser ML, et al. Simultaneous association of total energy consumption and activity-related energy expenditure with risks of cardiovascular disease, cancer, and diabetes among postmenopausal women. Am J Epidemiol. 2014;180: 526–535. [PubMed: 25016533]

TABLE 1.

Systematic bias in relation to body mass index in energy intake self-report as adapted from (8), and measurement error implications for association of energy intake and activity-related energy expenditure (AREE) with chronic disease incidence as adapted from (10), in Women's Health Initiative cohorts of postmenopausal U.S. women

(A) Energy intake (kcal/day) by a doubly-labeled water (DLW) biomarker, and by food frequency questionnaire (FFQ) without and with measurement error correction (n=544)

TOTAL ENERGY						
Body Mass Index	**DLW**		**FFQ**		**Corrected[a] FFQ**	
Category	**Geometric Mean**	**IQR**	**Geometric Mean**	**IQR**	**Geometric Mean**	**IQR**
Normal (< 25.0)	1,894	1,714 – 2,083	1,407	1,157 – 1,759	1,912	1,853 – 1,980
Overweight (25.0 – 29.9)	2,043	1,904 – 2,232	1,462	1,196 – 1,837	2,028	1,962 – 2,103
Obese (≥ 30)	2,213	2,034 – 2,415	1,454	1,161 – 1,897	2,247	2,156 – 2,338

(B) Hazard ratios (HRs) and 95% confidence intervals (CIs) for 20% increments in energy intake and activity-related energy expenditures (AREE) jointly[b], without and with measurement error correction (n=55,000 – 73,000)

Disease Risk	**No Measurement Error Correction**				**Measurement Error Corrected**			
Category (cases)	**Energy**		**AREE**		**Energy**		**AREE**	
	HR[c]	**95% CI**	**HR**	**95% CI**	**HR[d]**	**95% CI**	**HR**	**95% CI**
Total Invasive Cancer (9227)	1.01	1.00 – 1.02	0.99	0.99 – 1.00	1.43	1.17 – 1.73	0.84	0.73 – 0.96
Total Cardiovascular (2967)[e]	0.99	0.97 – 1.00	0.99	0.98 – 1.00	1.49	1.18 – 1.88	0.80	0.69 – 0.92
Diabetes Mellitus (6494)	1.06	1.04 – 1.07	1.01	1.00 – 1.02	4.17	2.68 – 6.49	0.60	0.44 – 0.83

[a] Corrected FFQ energy based on regression of log DLW energy on logFFQ energy and various participant characteristics in a biomarker subcohort (n=544).

[b] Energy intake from FFQ, AREE from a Women's Health Initiative Personal habits questionnaire.

[c] HRs from Cox regression either using self-reported energy and AREE or using calibrated energy and AREE following measurement error correction.

[d] Hazard ratio calculations allow body mass index to facilitate energy and AREE exposure assessments, but not to be included in disease risk models. See (10) for discussion.

[e] Coronary heart disease and stroke.