Best (but oft-forgotten) practices: *AJCN* series overview & updated introduction

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"Sapere Aude," dare to know. So wrote Immanuel Kant and before him, Horace (1).

In religion, knowledge is sought through faith and divine inspiration. In mathematics, knowledge is obtained by proof. In science, we obtain knowledge from empirical evidence. Through empirical evidence, we have learned much about nutrition.

We know that if one does not eat enough, one starves to death. We know that without certain vitamins and minerals one dies or has grossly impaired health. We know that consuming particular mushrooms leads to imminent death (2). We know that human beings must consume some protein. Because we know these things so well, we may tend to trivialize that knowledge. But we learned them through empirical evidence.

In modern day nutrition research circles, we do not spend a great deal of time talking about what we learned fairly definitively long ago, and so we may take such knowledge for granted. We instead tend to focus on what we are still trying to learn, topics that are often the subject of debate, confusion, and frequently changing opinions and recommendations. This may lead some persons to the impression that nutrition science is not making progress (3, 4). Yet, a different way to look at this is that nutrition scientists struggle because we are working on difficult problems that require far more rigorous and precise methods of inquiry to obtain valid knowledge than that required for the more "obvious" nutrition findings of earlier times that we now take for granted.

We struggle with questions such as whether gluten or wheat has some deleterious effects for some as-yet-to-be-identified subset of the population who do not have celiac disease, while at the same time separating out placebo and other expectancy effects (5). We struggle to determine whether school-based intervention and prevention strategies for childhood obesity are effective (6, 7). We struggle to determine whether the body adapts by lowering energy expenditure after weight loss even when taking into account one's lower body mass (8, 9). We struggle to determine the effects, and not just the associations, of body weight, body fatness, and changes thereof on mortality rate (10, 11). These are just a few examples. Many of our current questions involve postulated causes that, if they do have effects, likely have relatively small effects in a sea of many other background causes. The knowledge we obtain in such situations is not the definitive proof of mathematics. Rather, like all empirical knowledge, it is provisional upon current evidence and subject to revision. In generating and evaluating the evidence we bring to bear on such questions involving small effects, postulated causes to which we cannot regularly randomly assign subjects, variables that can only be measured with error, factors whose effects vary by person and circumstance, mitigating and quantifying our uncertainty is vital. The tools we have for making scientific conclusions in such circumstances are sound study designs, sound statistical analyses, and sound inferential logic.

There was perhaps a time when most nutrition scientists might have been expected to conduct their own statistical analysis, and many still do. Yet whether one conducts one's analyses oneself or enlists the aid of a professional statistician, what is clear is several-fold: (a) the pallet of available statistical procedures is ever-broadening; (b) the complexity of the statistical procedures is ever-increasing; and (c) study design and analysis errors of a sufficient magnitude to invalidate studies in their conclusions are not difficult to find in nutrition-related research (12–15). At the same time, there is growing recognition in science in general, and in nutrition and obesity research in particular, that there is increasing need for rigor, reproducibility, and transparency in research, and many societies, journals, investigators, and government funding agencies are stepping up to help address this need (16–20).

As one way of helping to play its part, *The American Journal of Clinical Nutrition* (*AJCN*) began a series titled "Best (but oft-forgotten) practices." The purpose of the series is to offer tutorials on existing and established statistical methods for the design and analysis of nutrition-related research of the type published in *AJCN* (21). The first article in the series (22) addressed the design and analysis of cluster randomized trials, randomized controlled trials in which *sets* of individuals, rather than individuals, are randomly assigned to experimental conditions. Such studies are becoming increasingly popular; yet it is clear that they are often designed poorly and analyzed incorrectly in research in general and in nutrition and obesity-related research as well. This is a serious issue, because studies have been published that drew conclusions and made recommendations that cannot be supported based on the observed data. The initial article in the series was well

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received, and since then 8 more articles have been published (see **Text Box 1**). Feedback is quite positive, and a resulting symposium is being presented at the American Society for Nutrition annual meeting in June 2018.

Text Box 1 Additional published articles in the series

•Barker LE, Shaw KM. Best (but oft-forgotten) practices: checking assumptions concerning regression residuals. Am J Clin Nutr 2015;102:533–9.
•Streiner DL. Best (but oft-forgotten) practices: the multiple problems of multiplicity---whether and how to correct for many statistical tests. Am J Clin Nutr 2015;102:721–8.
•de Souza RJ, Eisen RB, Perera S, Bantoto B, Bawor M, Dennis BB, Samaan Z, Thabane L. Best (but oft-forgotten) practices: sensitivity analyses in randomized controlled trials. Am J Clin Nutr 2016;103:5–17.
•McLeod LD, Cappelleri JC, Hays RD. Best (but oft-forgotten) practices: expressing and interpreting associations and effect sizes in clinical outcome assessments. Am J Clin Nutr 2016;103:685–93.
•Haycock PC, Burgess S, Wade KH, Bowden J, Relton C, Dave Smith G. Best (but oft-forgotten) practices: the design, analysis, and interpretation of Mendelian randomization studies. Am J Clin Nutr 2016;103:965–78.
•Ali MS, Groenwold RHH, Klungel OH. Best (but oft-forgotten) practices: propensity score methods in clinical nutrition research. Am J Clin Nutr 2016;104:247–58.
•Johnston BC, Guyatt GH. Best (but oft-forgotten) practices: intention-to-treat, treatment adherence, and missing participant outcome data in the nutritional literature. 2016;104:1197–201.
•Fairchild AJ, McDaniel HL. Best (but oft-forgotten) practices: mediation analysis. Am J Clin Nutr 2017;105:1259–71.

Papers in the series cover existing methods and do not present new methodologic inquiries or new methods that have not yet been vetted in the scientific and statistical communities. Papers in the series address only statistically related design and analysis issues and not all methodologic issues related to nutrition research. There is no definitive number of additional papers or timeframe in which they will be published. Review papers for the series are invited, and all such papers undergo rigorous peer review. Occasionally, potential authors contact us to volunteer to write a paper on a particular topic for the series. We welcome such suggestions, though we cannot and do not accept them all. Authors with strong track records of publishing cogent tutorial writings on statistical methods for sophisticated nonstatistician scientists are given priority as authors, and prioritized topics are those for which there has been insufficient writing within *AJCN*, but which relate to many papers published or received by *AJCN*. We also welcome suggestions from readers for topics even if they themselves do not wish to author the papers on such topics.

We hope that the series continues to be seen as valuable by the nutrition science community and thank you for the positive reception to date.

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