

## The A, B, C, D's of dietary trials

Dear Editor:

We read with interest the article by Bayes et al. (1) reporting a randomized controlled trial (RCT) of a Mediterranean diet compared with a social befriending control in 72 males with moderate to severe depression. We commend the authors for conducting this 12-week trial of an RCT that adds to 3 others demonstrating the positive effects of a Mediterranean-style diet (2, 3) and a combined intervention of a Mediterranean diet and an omega-3 supplement for improving depressive symptoms (4). In the study by Bayes et al. (1), the Mediterranean diet intervention led to large changes to diet based on the Mediterranean Diet Adherence score (MEDAS) and impressive depressive symptom reduction based on the Beck Depression Inventory II. This trial adds significant value to the existing evidence in nutritional psychiatry.

In terms of advances, this trial recruited young men, an understudied group in this field. That individuals with lived experience were involved in the trial design should also be commended. Previous work by the authors investigating nutrition knowledge in 384 young men with depression showed most of this group would change their diet if it were to improve their symptoms (5). These data, together with evidence that males are less likely to access mental health treatment, provide strong impetus for testing uptake and efficacy of dietary treatment in this group. Although a similar age group has previously been targeted in a 3-week Mediterranean-style diet intervention (3), nearly two-thirds of participants in that study were female; this may reflect the greater motivation of females in seeking help for their symptoms, or the greater prevalence of mood disorders in this group.

The authors maximized the chances of dietary changes by including participants with a poor baseline diet, as scored by the Commonwealth Scientific and Industrial Research Organisation (CSIRO) healthy diet score (mean, 35 points; possible score range, 0–100 points). In fact, diet was much poorer among the participants than among Australians in a population survey of 145,000 individuals (mean, 59 individuals; SD, 13 individuals) (6). Incorporating a baseline low-diet-quality threshold is common (2–4) and, here, the very low baseline diet quality left ample room for substantial dietary improvements: an 8-point change in mean Mediterranean diet score (score range, 0–15 points) at 12 weeks. Although an advantage for maximizing efficacy, this has disadvantages for generalizability of findings.

In order to now move the field forward, we would like to discuss some aspects of this study with the aim of providing guidance for future trials in this field. Adherence, blinding, composition, and mode of diet delivery (A, B, C, D's) are some factors of key importance when reporting and interpreting findings of dietary trials to support reproducibility and future syntheses of the literature, as well as for external validity (7).

With regards to assessing adherence to the dietary intervention, there are 2 issues that could have potentially reduced measurement precision. Firstly, the MEDAS was modified from the original.

Changes to a validated questionnaire have the potential to introduce significant measurement bias; a more detailed justification of the modifications would be helpful. Secondly, an online daily diet diary was recorded over 12 weeks of intervention. This was a worthy attempt to capture dietary information but carries the risk of prompting misreporting. Misreporting is an enormous challenge in nutrition research, and an extended diet diary may compound this issue: most trials using food diaries record for no more than 7 days. Prolonged recording and diet feedback (a MEDAS score was calculated daily) could potentially enhance response set bias (overestimation of dietary adherence) (8), as well as expectation bias. How to accurately assess dietary adherence is an ongoing challenge, and best practices for dietary trials in nutritional psychiatry are still unclear. However, over-monitoring adherence should be avoided, and adequate adherence should ideally be defined *a priori*.

Blinding (B) participants in trials of whole-diet interventions is also immensely challenging. Inadequate blinding is problematic, particularly where outcomes are subjectively reported. In this trial, blinding was not possible, but the authors report 2 ways in which they attempted to address this: 1) presenting both interventions as potentially beneficial; and 2) withholding information about the research hypothesis. Reporting the proportion of individuals that guessed which was the active intervention may have shed light on the success of these attempts. Future trials will need to employ more sophisticated designs (e.g., placebo diets or interventions) to aid blinding and reduce the risk of expectation bias (7).

The composition (C) of the intervention diet was described in detail, which is a strength of the study. It was a Mediterranean-style diet based on Greek and Spanish guidelines, and the food group recommendations fit parameters of a traditional Mediterranean diet, except for fish consumption, which was at the lower end of that recommended in the guidelines referenced (references 35–37) and slightly lower than that recommended in the Mediterranean diet trial of young adults (3) and the seminal PREDIMED trial (9).

Dietary advice was delivered (D) by a nutritionist using a standard approach (1:1 appointments, written information, food hamper). Trials thus far have incorporated 6–7 appointments with a dietitian to provide education, set dietary goals, and follow up to identify barriers for change (2, 4). Using only 3 appointments to achieve a significant dietary behavior change is a promising development, and we encourage the authors of the study to share details of their approach to enhance translation in clinical practice. Involvement of a trained, accredited dietitian or nutritionist in diet delivery is key to efficacy for improving mental health in individuals with mental illness (10). Dietitians play a pivotal role in mental health-care teams, have the skill and expertise to deliver effective personalized dietary interventions, and are integral to the delivery of nutritional psychiatry interventions in research and practice.

The coming years will see continued interest in utilizing dietary approaches to manage mood disorders. Blinded RCTs that clearly describe diet compositions, modes of diet delivery, and adherence are necessary to fully evaluate what interventions work and how they should be applied in practice, as well as to facilitate synthesis of the literature. Further research in young men is needed to consolidate

this evidence from Bayes et al. (1) and to understand whether dietary interventions are efficacious, effective, and cost-effective in men with depression.

HMS is supported by an Alfred Deakin Postdoctoral Research Fellowship and has previously received research funding from the Guy's & St Thomas' NHS Foundation Trust, British Dietetic Association, NIHR, VSL Pharmaceuticals, Deakin University Institute for Mental and Physical Health and Clinical Translation Institute, Rome Foundation, and DSM Pharmaceuticals; and has previously received nonfinancial support from VSL pharmaceuticals.; TR is supported by the Wilson Foundation and Roberts Family Foundation and has received grants, fellowships and research support from University of the Sunshine Coast, Australian Postgraduate Awards, Fernwood Foundation, Roberts Family Foundation, Wilson Foundation and Be Fit Food; and received consultancy, honoraria, and travel funds from Oxford University Press, the University of Melbourne, the University of Sydney, Bond University, Victoria University, University of Southern Queensland, Dietitians Australia, Nutrition Society of Australia, The Royal Australian and New Zealand College of Psychiatrists, Academy of Nutrition and Dietetics, Black Dog Institute, Australian Rotary Health, Australian Disease Management Association, Drug and Alcohol Nurses Australasia, Department of Health and Human Services, Primary Health Networks, Barwon Health, West Gippsland Healthcare Group, Central West Gippsland Primary Care Partnership, Parkdale College, City of Greater Geelong, and Global Age. FNJ is supported by a National Health and Medical Research Council Investigator Grant (#1194982); has received competitive grant/research support from the Brain and Behaviour Research Institute, the National Health and Medical Research Council, Australian Rotary Health, the Geelong Medical Research Foundation, the Ian Potter Foundation, and the University of Melbourne; has received industry support for research from Meat and Livestock Australia, Woolworths Limited, the A2 Milk Company, and Be Fit Foods; has received philanthropic support from the Fernwood Foundation, Wilson Foundation, the JTM Foundation, the Serp Hills Foundation, the Roberts Family Foundation, the Waterloo Foundation; has received travel support and speakers honoraria from Sanofi-Synthelabo, Janssen Cilag, Servier, Pfizer, Network Nutrition, Angelini Farmaceutica, Eli Lilly, Metagenics, and The Beauty Chef; and has written 2 books for commercial publication.

Heidi M Staudacher  
Tetyana Rocks  
Felice N Jacka

From the Food & Mood Centre, The Institute for Mental and Physical Health and Clinical Translation (IMPACT), School of Medicine, Deakin University, Geelong, Australia (HMS, e-mail: [heidi.staudacher@deakin.edu.au](mailto:heidi.staudacher@deakin.edu.au); TR; FNJ); the Centre for Adolescent Health, Murdoch Children's Research Institute, Parkville, Australia (FNJ); and Black Dog Institute, Sydney, Australia (FNJ)

## References

1. Bayes J, Schloss J, Sibbritt D. The effect of a Mediterranean diet on the symptoms of depression in young males (the "AMMEND: A Mediterranean Diet in Men with Depression" study): A randomized controlled trial. *Am J Clin Nutr* 2022;116(2):572–80.
2. Jacka FN, O'Neil A, Opie R, Itsiopoulos C, Cotton S, Mohebbi M, et al. A randomised controlled trial of dietary improvement for adults with major depression (the 'SMILES' trial). *BMC Med* 2017;15(1):23.
3. Francis HM, Stevenson RJ, Chambers JR, Gupta D, Newey B, Lim CK. A brief diet intervention can reduce symptoms of depression in young adults - A randomised controlled trial. *PLoS One* 2019;14(10):e0222768.
4. Parletta N, Zarnowiecki D, Cho J, Wilson A, Bogomolova S, Villani A, et al. A Mediterranean-style dietary intervention supplemented with fish oil improves diet quality and mental health in people with depression: A randomized controlled trial (HELFIMED). *Nutr Neurosci* 2019;22(7):474–87.
5. Bayes J, Schloss J, Sibbritt D. Investigation into the diets and nutritional knowledge of young men with depression: The MENDDS survey. *Nutrition* 2020;78:110946.
6. Hendrie GA, Baird D, Golley RK, Noakes M. The CSIRO Healthy Diet Score: An online survey to estimate compliance with the Australian Dietary Guidelines. *Nutrients* 2017;9(1):47.
7. Staudacher HM, Irving PM, Lomer MCE, Whelans K. The challenges of control groups, placebos and blinding in clinical trials of dietary interventions. *Proc Nutr Soc* 2017;76(4):628.
8. Kristal AR, Andrilla CH, Koepsell TD, Diehr PH, Cheadle A. Dietary assessment instruments are susceptible to intervention-associated response set bias. *J Am Diet Assoc* 1998;98(1):40–3.
9. Estruch R, Ros E, Salas-Salvadó J, Covas MI, Corella D, Arós F, et al. Primary prevention of cardiovascular disease with a Mediterranean diet. *N Engl J Med*. 2013;368(14):1279–90.
10. Firth J, Marx W, Dash S, Carney R, Teasdale S, Solmi M, et al. The effects of dietary improvement on symptoms of depression and anxiety: A meta-analysis of randomised controlled trials. *Psychosom Med* 2019;81(3):265–80.

doi: <https://doi.org/10.1093/ajcn/nqac274>.