

Implausible discussions in saturated fat 'research'; definitive solutions won't come from another million editorials (or a million views of one)

David Nunan,¹ Duane Mellor,² Nicola Guess,³ Ian M Lahart⁴

The *British Journal of Sports Medicine* published an opinion editorial advocating a revision of public health guidance on saturated fat.¹ Here, we offer a rebuttal, incorporating evidence-based principles absent

¹Centre for Evidence-Based Medicine, Nuffield Department of Primary Care Health Sciences, University of Oxford, Oxford, UK

²Coventry University, Coventry, UK

³Division of Diabetes and Nutritional Sciences, Kings College London, London, UK

⁴Faculty of Education, Health and Wellbeing, University of Wolverhampton, Walsall, UK

Correspondence to Dr David Nunan, Centre for Evidence-Based Medicine, Nuffield Department of Primary Care Health Science, University of Oxford, Oxford OX2 6GG, UK; david.nunan@phc.ox.ac.uk

in the original editorial, focusing on the quality of the evidence presented and we discuss contradictory evidence in relation to saturated fat, low-density lipoprotein cholesterol (LDL-C), specific dietary interventions and cardiovascular disease (CVD) alongside future directions.

EFFECTS OF REDUCING SATURATED FAT INTAKE ON CVD

The authors cite a 2015 'landmark' meta-analysis of observational studies showing a lack of an association between saturated fat consumption and both all-cause mortality and cardiovascular outcomes.² According

to best practice evidence-based methods, these types of studies provide low-quality evidence.³ Indeed, the authors of the cited meta-analysis reported that the likelihood of the reported associations was 'very low',² meaning we can have very little confidence in the findings.

The authors have also overlooked a 2015 Cochrane meta-analysis of 17 randomised controlled trials (RCTs; ~59 000 participants) which showed moderate quality evidence that long-term reduction of dietary saturated fat lowered the risk of cardiovascular events (number needed to treat=14) but had no statistical effect on all-cause mortality or cardiovascular outcomes.⁴ In pre-planned subgroup analyses, cardiovascular events were reduced when saturated fat was replaced by polyunsaturated fat (but not by carbohydrates, proteins or monounsaturated fat).⁴ This is a caveat that has been observed and emphasised by others and is well acknowledged in the field.⁵

To further support their view, the editorial authors turn to data from a 2004 post hoc observational study (low quality evidence) of postmenopausal women with established coronary heart disease, which showed an

inverse relation between self-reported saturated fat intake and progression of atherosclerosis.⁶ Methodological weaknesses of this study include assessment of dietary intake only at baseline, with no information on changes in diet over the duration of follow-up and residual confounding. The authors of that observational study concluded: 'this was a post hoc analysis among participants in a randomised trial, and our findings may not be generalisable to all postmenopausal women'.⁶

Thus, the consensus viewpoint of a beneficial effect of reduced dietary saturated fat and replacement with polyunsaturated fat in the general population appears to be underpinned by a higher quality evidence base.

BENEFITS OF A MEDITERRANEAN DIET ON PRIMARY AND SECONDARY CVD

The PREDIMED⁷ (Prevención con Dieta Mediterránea) and the Lyon Diet Heart⁸ studies are cited by the authors as evidence of a protective effect from a 'high-fat' diet. However, the dietary interventions in both of these trials were designed to increase intake of unsaturated fats. The Lyon Heart study specifically aimed to reduce saturated fat intake, and in both studies the diets had a saturated fat content lower than UK recommendations. The PREDIMED study investigated the effects of a Mediterranean diet, including fish, whole grain cereals and fruits and supplemented with extra-virgin olive oil versus the same Mediterranean diet supplemented with only mixed nuts versus a control diet (which aimed for low fat intake) on primary prevention of CVD. Whereas the Lyon Diet Heart study compared a Mediterranean-style diet that was rich in alpha-linolenic acid-rich omega-3 polyunsaturated fat but low in total fat (30% dietary energy), saturated fat, cholesterol and linolenic acid (omega-6 polyunsaturated fat), with a control group (standard French diet). The findings from both these studies support the current consensus to increase intakes of unsaturated dietary fats instead of saturated fat. These findings also suggest that placing a limit on the percentage of calories from unsaturated fats may be unwarranted, as has been acknowledged in a recent consensus.⁹

LDL-C AND CARDIOVASCULAR MORTALITY

The authors claim that the cardiovascular risk of LDL-C has been exaggerated and support this contention with the 1973 data from the Minnesota Coronary Experiment (MCE)¹⁰ and a systematic review of observational studies.¹¹ However, the authors have not addressed documented limitations of the MCE study, including discrepant event

rates and selective outcome reporting, over 80% attrition (with lack of intention-to-treat analysis) and a small event rate difference (n=21), plausibly driven by a higher unexplained dropout rate in the control group.¹²

The cited systematic review reports a lack of an association between LDL-C and CVD and some evidence of an inverse association with all-cause mortality in elderly populations.¹⁰ However, the methodological quality of this review has been rated poor, because of, among other limitations, a non-uniform application of inclusion/exclusion criteria, a lack of quality assessment of the included studies (low quality observational studies), failure to account for multifactorial analysis (ie, lack of control for confounders) and not considering statin use (see EatZ letter in response to Ramsden *et al*¹⁰ and CEBM¹³).

Moreover, any evidence-based discussion on LDL-C cannot omit large-scale RCT evidence showing that in people at high risk of CVD or those who have established heart disease, LDL-C-reducing statin therapy reduces the risk of coronary deaths, myocardial infarction, strokes and coronary revascularisation procedures by ~25% for each mmol/L reduction in LDL-C during each year it is taken, after the first.¹⁴

Therefore, given the flaws of the referenced trial⁹ and the systematic review of observational studies¹¹ and evidence in support of benefits of LDL-C therapy, it appears to be too early to dismiss LDL-C as a risk factor for CVD and mortality.

TIME TO MOVE THE DISCUSSION FORWARD

The authors choose a binary and simplistic approach that gives little regard to the complex narrative regarding saturated fats, as this is not a biologically homogeneous group of compounds. The triglyceride composition, fatty acid chain length, food source and nutrients and non-nutritive compounds in the foods all determine the effects of saturated fat on health. This is a key point that is not considered in the editorial. We therefore encourage a move to food-based guidelines that takes these nuances into account.

Similarly, it appears from the Lyon Heart Study and PREDIMED that the reduced risk of death associated with a diet higher in unsaturated and lower in saturated fat may not be simply via LDL-C dependent mechanisms. It is likely that there are multiple pathways by which different dietary factors may modify risk alongside classical risk factors, including modulation of inflammatory pathways.¹⁵ Insulin sensitivity,¹⁵ insulin concentrations¹⁶ and altered lipid metabolism¹⁷ are also probably important factors.

Biological pathways are not a zero-sum game and over-simplified editorials that ignore their complexities do not serve science or the public. Good research and evidence-based practice demands that such discussions consider the totality of the evidence base and the inherent uncertainty in nutritional epidemiological studies and trials.¹⁸ Journal editors play a pivotal role in ensuring that such balanced discussions take place.

Finally, arbitrary concepts such as 'real food' are unlikely to offer a simple message for most people and their use risks manipulation according to personal, cultural or societal values and morals and not scientific evidence. It is time to shift the narrative to a discussion of dietary patterns over and above individual macronutrients that considers collaborative efforts for improving the evidence base and our understanding of the complex relation between diet and health.

Acknowledgements The authors thank Dr Jeffrey Aronson for comments on the manuscript.

Contributors DN and IL drafted the first version with equal contribution from all authors to the drafting and editing of the final manuscript.

Funding The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

Disclaimer The views expressed are those of the authors and not necessarily those of the NHS, the NIHR, the RCGP, the Department of Health, the BDA, Nestec, Barry Callebaut, Diet Chef, the MRC, the Winston Churchill Memorial Trust, the American Overseas Dietetic Association, Oviva or Swim England.

Competing interests DN is a member of the Royal College of General Practitioners (RCGP) steering committee to support the new Physical Activity and Lifestyle clinical priority. He has received funding for research from the NHS National Institute for Health Research School for Primary Care Research (NIHR SPCR) and the RCGP for independent research projects related to physical activity and dietary interventions. DM is a company director of the British Dietetic Association (BDA) and has received research funding from Nestec, Barry Callebaut and Diet Chef along with honorariums from ISA. NG has received funding from Diabetes UK, the National Obesity Forum/Weight Watchers (joint grant), the Medical Research Council (MRC), the Winston Churchill Memorial Trust and the American Overseas Dietetic Association for independent research projects. She has done consultancy work for Fixing Dad (low-carb app for management of type 2 diabetes) and is currently funded by Oviva on an effectiveness evaluation of a digital programme for management of type 2 diabetes. IML has received funding from Swim England to write a review of the evidence for the physiological effects of swimming.

Patient consent Not required.

Provenance and peer review Not commissioned; internally peer reviewed.

© Author(s) (or their employer(s)) 2019. No commercial re-use. See rights and permissions. Published by BMJ.



To cite Nunan D, Mellor D, Guess N, *et al.*
Br J Sports Med 2019;**53**:1512–1514.

Accepted 9 July 2018

Published Online First 31 August 2018

Br J Sports Med 2019;**53**:1512–1514.

doi:10.1136/bjsports-2018-099799

REFERENCES

- 1 Malhotra A, Redberg RF, Meier P. Saturated fat does not clog the arteries: coronary heart disease is a chronic inflammatory condition, the risk of which can be effectively reduced from healthy lifestyle interventions. *Br J Sports Med* 2017;**51**:1111–2.
- 2 de Souza RJ, Mente A, Maroleanu A, *et al.* Intake of saturated and trans unsaturated fatty acids and risk of all cause mortality, cardiovascular disease, and type 2 diabetes: systematic review and meta-analysis of observational studies. *BMJ* 2015;**351**:h3978.
- 3 Atkins D, Best D, Briss PA, *et al.* Grading quality of evidence and strength of recommendations. *BMJ* 2004;**328**:1490.
- 4 Hooper L, Martin N, Abdelhamid A, *et al.* Reduction in saturated fat intake for cardiovascular disease. In: *Cochrane Database of Systematic Reviews*. 330: John Wiley & Sons, Ltd, 2015.
- 5 Siri-Tarino PW, Chiu S, Bergeron N, *et al.* Saturated fats versus polyunsaturated fats versus carbohydrates for cardiovascular disease prevention and treatment. *Annu Rev Nutr* 2015;**35**:517–43.
- 6 Mozaffarian D, Rimm EB, Herrington DM. Dietary fats, carbohydrate, and progression of coronary atherosclerosis in postmenopausal women. *Am J Clin Nutr* 2004;**80**:1175–84.
- 7 Estruch R, Ros E, Salas-Salvadó J, *et al.* Primary prevention of cardiovascular disease with a Mediterranean diet. *N Engl J Med* 2013;**368**:1279–90.
- 8 de Lorgeril M, Renaud S, Mamelle N, *et al.* Mediterranean alpha-linolenic acid-rich diet in secondary prevention of coronary heart disease. *Lancet* 1994;**343**:1454–9.
- 9 U.S. Department of Health and Human Services and U.S. Department of Agriculture. *2015–2020 Dietary guidelines for Americans*. 8th edn, 2015.
- 10 Ramsden CE, Zamora D, Majchrzak-Hong S, *et al.* Re-evaluation of the traditional diet-heart hypothesis: analysis of recovered data from minnesota coronary experiment (1968-73). *BMJ* 2016;**353**:i1246.
- 11 Ravnkov U, Diamond DM, Hama R, *et al.* Lack of an association or an inverse association between low-density-lipoprotein cholesterol and mortality in the elderly: a systematic review. *BMJ Open* 2016;**6**:e010401.
- 12 Beinortas T, Mahtani KR, Nunan D. Revisiting the diet-heart hypothesis: critical appraisal of the Minnesota Coronary Experiment. *BMJ* 2017;**357**:j2108.
- 13 CEBM. CEBM response: "Lack of an association or an inverse association between low-density-lipoprotein cholesterol and mortality in the elderly: a systematic review" – a post publication peer review. 2016 <http://www.cebm.net/cebm-response-lack-association-inverse-association-low-density-lipoprotein-cholesterol-mortality-elderly-systematic-review-post-publication-peer/> (accessed 24 Apr 2017).
- 14 Collins R, Reith C, Emberson J, *et al.* Interpretation of the evidence for the efficacy and safety of statin therapy. *Lancet* 2016;**388**:2532–61.
- 15 Martínez-González MA, Salas-Salvadó J, Estruch R, *et al.* Benefits of the mediterranean diet: insights from the PREDIMED study. *Prog Cardiovasc Dis* 2015;**58**:50–60.
- 16 DECODE Insulin Study Group. Plasma insulin and cardiovascular mortality in non-diabetic European men and women: a meta-analysis of data from eleven prospective studies. *Diabetologia* 2004;**47**:1245–56.
- 17 Blaak EE. Characterisation of fatty acid metabolism in different insulin-resistant phenotypes by means of stable isotopes. *Proc Nutr Soc* 2017;**19**:419–24.
- 18 Ioannidis JP. Implausible results in human nutrition research. *BMJ* 2013;**347**:f6698.