effects (e.g. adverse effects of both over- and underweight). Perhaps the most compelling approach to interpreting research findings is to triangulate findings across multiple methods. If all approaches provide consistent evidence, stronger conclusions can be drawn. However, in this case, the genomic evidence consistently suggests that meaningful effects of BMI on risk of Alzheimer's disease are unlikely. This evidence, in addition to the limited number of interventions that have been shown to reduce BMI over the long term, suggests that it is probably not an efficacious target for intervention to reduce the rates of dementia.

However, as a positive, this would indicate that the obesity epidemic is unlikely to increase the incidence of dementia in the coming years.

Conflict of interest

None declared.

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Authors' response to comments on: Higher risk of dementia in English older individuals who are overweight or obese

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Dorina Cadar ^{1*}, Yixuan Ma,¹ Olesya Ajnakina^{1,2} and Andrew Steptoe¹

¹Department of Behavioural Science and Health, University College London, London, UK and ²Department of Biostatistics & Health Informatics, Institute of Psychiatry, Psychology and Neuroscience, King's College London, London, UK

*Corresponding author: Department of Behavioural Science and Health, University College London, 1-19 Torrington Place, London WC1E 6BT, UK. E-mail: d.cadar@ucl.ac.uk

In their comments on our study,¹ Davies *et al.* suggest that weight reduction is unlikely to be a plausible intervention target for reducing the incidence of dementia.² Although we did not claim a causal link between obesity and dementia risk, the relationship reported in our study is observational, based on a longitudinal analysis of a large representative population sample of English adults aged 50 years or older,³ and our findings are not in isolation.⁴ One meta-analysis found that mid-life obesity was associated with an increased dementia risk [risk ratio (RR) = 1.91; 95% confidence interval (CI), 1.4–2.62] across populations from both the USA and China.⁵

Whereas obesity is a complex issue, with a high degree of genetic heritability,⁶ substantial reductions in caloric intake, increases in physical activity and tailored psychological interventions could be beneficial for many health outcomes. As we have seen from one of the first randomized controlled trials (CALERIE: Comprehensive Assessment of the Long-term Effects of Reducing Intake of Energy), cutting caloric intake by 15% for 2 years decreased systemic oxida-

tive stress,⁷ which has also been tied to age-related neurological conditions such as dementia and Alzheimer's disease (AD).

Moreover, the link between obesity and dementia is supported by underlying biological mechanisms that are part of the hallmarks of the cardiometabolic profile (e.g. diabetes, hyperinsulinaemia and raised glycosylated haemoglobin levels)⁸ and associated inflammatory response.⁹ Some evidence indicates that these mechanisms are also influenced by the hormonal changes occurring after mid-life, with increased levels of estrogen and sex hormone-binding globulin affecting dementia risk.¹⁰ Therefore, weight reduction may well be a plausible intervention target for reducing the incidence of dementia, although we acknowledge that more research is needed, with more attention given to the type of dementia investigated (e.g. dementia, vascular dementia or AD) and the specific periods across mid-life when obesity is particularly detrimental.

The argument that the rise in obesity is inconsistent with the fall in AD incidence assumes that adiposity acts independently of these cardiometabolic processes, but we also need to consider the current

challenges in diagnosing AD. The Mendelian randomization studies are important but are based on diagnosed AD, which may underestimate true population prevalence.

Irrespective of the arguments made around causality, weight loss interventions are certainly needed, considering the sharp increase in levels of obesity in recent years and their long-term consequences. However, such interventions should not be considered in isolation but within the appropriate economic and political context driving the relevant policy infrastructure. Public health efforts to prevent and manage health issues related to body weight should be strengthened for healthy ageing. At the same time, the relationship between obesity and dementia, in particular, is worthy of future study.

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Conflict of interest

None declared.

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