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Animal protein intake and hepatic steatosis in the elderly – Authors' response

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Gut. 2020 Jan;69(1):189

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Response

We would like to thank *Tang and Mann* for their interest in our study in which we showed that animal protein intake was independently associated with higher prevalence of non-alcoholic fatty liver disease (NAFLD) in an overweight, predominantly aged Caucasian population.[344,458]

Rightfully so, the authors express their concerns regarding the generalisability of our findings towards younger patients with clinically significant non-alcoholic steatohepatitis (NASH).[458] Indeed, our results only pertain to our study population, consisting of an elderly and presumably healthy population in which the vast majority will have NAFLD, not NASH. Nonetheless, we believe that aiming for a healthy lifestyle, such as adherence to a healthy diet, is key across the entire spectrum of NAFLD and is not reserved for advanced disease only.[13] Also, *Tang et al.* question the clinical significance of NAFLD as a liver disease at the age of 70 years, but patients with NAFLD are, in fact, twice as likely to die from cardiovascular disease than from liver disease itself.[17] As cardiovascular disease is a clinically relevant disease in the elderly, we do believe that NAFLD embodies a relevant trait in our population with a mean age of 70 years.

Other remarks that are put forward in the letter were, in fact, already elaborated on in the discussion of our paper.[344,458] Briefly, energy intake as assessed by a semi-quantitatively food-frequency questionnaire is not reliable because it is known to be underreported.[278] This under-reporting does generally not affect the energy-adjusted macronutrient composition of the diet. In addition, we extensively adjusted for energy intake in various ways[457] to account for extraneous variation and potential measurement error. Second, we have not studied mechanistic pathways underlying our findings. We have merely discussed two already established hypotheses to explain the association between animal protein and NAFLD. Future studies are needed to explore these hypotheses in depth before conclusions can be drawn. Finally, in contrast to the impression by *Tang and Mann,* our main findings are not that surprising at all. Mounting evidence from other large population studies (with an average age of about 55 years) support our results on animal protein being associated with higher prevalence of NAFLD.[247,352] Also, the presumable detrimental effect of mono and disaccharides is thought to be only true in presence of excess caloric intake or related to specific food sources such as sugar-containing beverages, for which we already corrected in our analyses.[459]

In conclusion, our population-based study gives insight into the correlation between macronutrients and NAFLD. However, mechanistic and (randomised) intervention studies are ultimately needed to explore causality before recommendations can be made.