



Published in final edited form as:

*Stroke*. 2017 September ; 48(9): e269. doi:10.1161/STROKEAHA.117.018603.

## Response by Pase et al. to Letter Regarding Article on Sweetened Beverages and the Risks of Incident Stroke and Dementia

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We thank Dr. Fenton and Dr. Bellman for their letter regarding our recent article concerning sugar and artificially sweetened beverage consumption and the risks of stroke and dementia.<sup>1</sup> There are two main issues raised by Fenton and Bellman. The first relates to our examination of mediation and the second relates to the fact that we did not adjust for multiple comparisons. We address each point in turn.

Following mediation analysis, we examined the associations between artificially sweetened beverage (ASB) intake and both all dementia and Alzheimer's disease dementia after excluding persons with prevalent diabetes, as well as the association between ASB intake and stroke after excluding subjects with prevalent hypertension. Whereas we adjusted these analyses for model 1 covariates, including age, sex, education (for the outcome of dementia), and total caloric intake, Fenton and Bellman suggest that we should have included additional adjustments for the potential confounders of diet quality, physical activity, smoking status and the cardiometabolic factors that were not tested as mediators. To address this concern, we have re-examined the associations between ASB intake and the risk of both all dementia and Alzheimer's disease dementia after the exclusion of participants with diabetes mellitus and after adjusting for age, sex, education, total caloric intake, diet quality, physical activity, smoking status, atrial fibrillation, left ventricular hypertrophy, and Apolipoprotein E ε4 allele status. In these updated analyses, daily intake of ASBs, relative to no intake, remained a predictor of all-cause dementia (HR, 3.17; 95% confidence interval [CI], 1.32–7.62, p =0.01) and Alzheimer's disease dementia (HR, 4.45; 95% confidence interval [CI], 1.57–12.61, p =0.005). In other words, the approach suggested by Fenton and Bellman yielded similar results to those already reported in our paper. We did not re-examine the association between ASB intake and stroke after exclusion of participants with prevalent hypertension given that our original results did not reach statistical significance.

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**Disclosures** – None.

As we did not adjust our findings for multiple comparisons, our article noted that some of the observed associations might have been due to chance. Consequently, we agree with Fenton and Bellman in that our results should be interpreted cautiously. We also agree with Fenton and Bellman's conclusion that our paper does not prove a causal link between artificially-sweetened beverage (ASB) intake and stroke or dementia. Indeed, this is something explicitly noted in our paper. Whereas our abstract focuses on our primary models, our article includes extensive discussion about the fact that we cannot determine whether ASB intake leads to stroke or dementia or whether persons who are unhealthier simply favor ASBs to begin with. Overall, we thank Fenton and Bellman for reiterating the main caveats of our study and for emphasizing the need for caution in interpreting our findings.

## References

1. Pase MP, Himali JJ, Beiser AS, Aparicio HJ, Satizabal CL, Vasan RS, et al. Sugar- and Artificially Sweetened Beverages and the Risks of Incident Stroke and Dementia. A Prospective Cohort Study. *Stroke*. 2017; 48:1139–1146. [PubMed: 28428346]