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Author Response to Dr. Aziz – Statin Use and Delayed Onset of Huntington Disease

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We greatly appreciate the thoughtful commentary and review provided by Dr. Aziz¹ and agree that confounders, such as body mass index (BMI), are very important to consider when interpreting the results of this study.² First, the propensity score matching procedures implemented utilized maximum execution performance with a maximum difference in propensity scores of 0.005 (0.5%). As suggested by Dr. Aziz¹, we have performed a double-adjustment in our propensity score matched analysis and included baseline BMI as a covariate in the Cox regression survival analysis. While baseline BMI did significantly contribute to this model ($\beta = -0.059$, $p = 0.018$), inclusion of this covariate did not significantly change the results of the statin analysis (Hazard Ratio = 0.20, 95% CI [0.11 – 0.36], $p < 0.0001$). Additionally, inclusion of all variables that were used for the original matching procedure in the survival analysis (CAG, baseline age, baseline CAP score, baseline BMI, sex, region, and history of tobacco abuse) did not alter the results of the statin analysis (Hazard Ratio = 0.18, 95% CI [0.10 – 0.36], $p < 0.0001$), and baseline BMI did not significantly contribute to this enhanced model ($\beta = -0.030$, $p = 0.238$), nor did any other

included covariates. Again, we agree that body weight is an important consideration when modeling disease progression of Huntington Disease (HD), but the mean difference in baseline BMI that is observed between the groups did not seem to significantly confound the results of this study.² It is also important to consider that the participants included in our present study differ from participants in the study cited by Dr. Aziz³ in which their group demonstrated that body weight is a predictor of disease progression. In that study, participants from the Enroll-HD study were included who had already received a motor diagnosis and were being followed after their clinical diagnosis. However, in our present study², only participants who had a diagnostic confidence level of less than four at their baseline visit were included.⁴ This is important because the relationship between BMI and disease progression prior to motor diagnosis of HD is not well-established.

As Dr. Aziz mentions¹, it is important to understand if statins themselves are neuroprotective or if they are a marker for some other neuroprotective state, such as hyperlipidemia. While we agree with these concerns, the lipid profiles of participants is not immediately available within the Enroll-HD database⁵ making it difficult to comment on the association between hyperlipidemia and disease progression. This limitation is outlined in more detail in the discussion section of our manuscript.² Overall, we agree with Dr. Aziz that the results of the present study should be interpreted with caution until further follow-up studies are conducted to help us better understand the mechanisms underlying these findings.²

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REFERENCES

1. Aziz NA. Reader Response: Statin Use and Delayed Onset of Huntington disease. *Movement disorders : official journal of the Movement Disorder Society* 2019, in press.
2. Schultz JL, Nopoulos PC, Killoran A, Kamholz JA. Statin use and delayed onset of Huntington's disease. *Movement disorders : official journal of the Movement Disorder Society* 2018 (10.1002/mds.27591)
3. van der Burg JMM, Gardiner SL, Ludolph AC, Landwehrmeyer GB, Roos RAC, Aziz NA. Body weight is a robust predictor of clinical progression in Huntington disease. *Ann Neurol* 2017;82:479–483. [PubMed: 28779551]
4. Huntington Study Group. Unified Huntington's Disease Rating Scale: reliability and consistency. *Mov Disord* 1996;11:136–142. [PubMed: 8684382]
5. Landwehrmeyer GB, Fitzer-Attas CJ, Giuliano JD, et al. Data Analytics from Enroll-HD, a Global Clinical Research Platform for Huntington's Disease. *Mov Disord Clin Pract* 2017;4:212–224. [PubMed: 30363395]