Reviewer's report

Title: The effect of changes in IOP on the risk of developing POAG in patients with ocular hypertension: an application of latent class analysis

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Reviewer: Gui-shuang Ying

Reviewer's report:

This is a very nice paper to answer a very important clinical question: the impact of IOP fluctuation over time on POAG development, using the modern latent class analysis. The statistical methods are appropriate and well described. The data used in paper were from two large clinical trials of glaucoma, and are high quality. The following are a few comments for consideration to improve the manuscript.

1. In the conditional LCA analysis, total of 13 variables on demographic and clinical characteristics were included. It is not clear how these 13 variables were selected, were they selected based on its statistical significant association with POAG or statistical significant association with IOP in the OHTS, EGPS, or other studies? This should be clarified.

2. In the OHTS, 24.8% were Black, but only 0.1% were Black in EGPS. Latent class analysis on POAG and EGPS provided different number of latent classes. It is possible that this difference in the Black proportion may contribute this difference in the number of latent classes, because the IOP fluctuation and its effect on POAG may be different in Blacks. Probably a LCA analysis (at least as a sensitivity analysis) should be performed by excluding Black, so that OHTS and EGPS are more comparable, to see whether both data provided the same latent classes.

3. It will be useful to add the observed proportion of patient with POAG for each latent class determined from LCA in OHTS and EGPS. This information can be added into either Table 3, or Figures 2 &3.

4. The treatment of ocular hypertension has substantial impact on the IOP change over time, and this can distort the relationship of natural IOP fluctuation with POAG development. It is clinically important to evaluate the effect of natural IOP fluctuation on POAG development. This can be done by performing LCA on the data only from untreated group.

Level of interest: An article of outstanding merit and interest in its field

Quality of written English: Acceptable

Statistical review: Yes, and I have assessed the statistics in my report.