

In this work, the author presents a comprehensive derivation of asymptotic detection boundaries for a variety of risks composed of combinations of FWER, FWRN, FDR, and FNR. In addition, the focus on categorical outcomes in GWAS settings is important and compelling. The manuscript is well written and, importantly, the theoretical results are provided in very practical contexts. Therefore, this manuscript provides a good contribution to both the asymptotic theory as well as its application in GWAS contexts. My substantive comments below primarily focus on some aspects of the proofs (in particular in theorem 3.1) which led to some counterintuitive results, particularly when considered next to the empirical results:

1. Throughout the manuscript  $\nu$  is considered fixed. This is a natural assumption for many situations and has general applicability. However, there may be an opportunity to extend these results to cases of increasing  $n$ . One example of categorical variables that increase in the number of categories as  $n$  increases occurs in a network context. In particular, when community membership (as obtained through community detection) of a network of  $n$  individuals is the outcome variable in GWAS settings, it is common to assume the number of communities increases with  $n$ . This would correspond with an increase in  $\nu$ . So long as the rate of increase in  $\nu$  is well controlled, I believe the author's results could be easily extended to this case. Take, for example, Theorem 3.1. The distribution of the  $\chi_\nu^2(\Delta)$  term was bounded from above by ignoring the  $\nu - 1$  central chi-squared terms (see equation immediately following (B.3)). If  $\nu$  is allowed to increase, a smaller effect size  $\Delta$  may be possible by not ignoring the first  $\nu - 1$  central chi-square terms, potentially leading to a change in the detection boundary. I mention this idea because, although fixed- $\nu$  situations are more standard in GWAS settings, it may be straightforward to adapt the current proof to this alternative case.
2. Again, with regard to Theorem 3.1, it would follow that increasing  $\nu$  would make the bound on  $P(\hat{S}_p \subset S_p)$  sharper, because the difference between  $\chi_\nu^2(\Delta)$  and  $(Z_\nu + \sqrt{\Delta})^2$  increases with increased  $\nu$  and so the inequality in (B.4) also becomes less tight. This would intuitively suggest that FWRN, or at least its lower bound, increases in  $\nu$ . However, your empirical results showed that for increased  $\nu$ , the detection boundary increased. Obviously this detection boundary is a function of both FWRN and FWER, and there is no discussion on how changing  $\nu$  may impact FWER, so there could be another reason driving the empirical results aside from FWRN. It would help if the author could help provide an intuition that matches this aspect of the proof with their empirical results.
3. In example 4.2, the asymptotic power result evaluated at the smallest detectable effect size led to a required sample size of 153,509. Equation 4.11 led to a larger sample size of 165,035. I would expect a very conservative asymptotic result, particularly considering it is evaluated at the smallest

feasible effect size. Perhaps the author can provide some intuition on why this may have occurred.

4. In Figure 4, why are the empirical results anti-conservative in the  $\nu = 1$  and large  $p$  ( $p = 10000$ ) case? The author commented on how increasing  $\nu$  led to a higher detection boundary, but it would be good to address this apparently lower detection boundary in this case. I particularly mention the large  $p$ , small  $\nu$  case because we should expect asymptotic results to hold better here, and if anything the detection boundary should be conservative due to the fact that some of the inequalities in the proof may not be tight.

Minor grammatical edits:

1. pg.19 "In a typically GWAS, a pair of alleles...": "typically" should be "typical".
2. pg.21 "...this indicates vanishing difference in the...": should be "...this indicates a vanishing difference in the..."