Reviewer’s report

Title: Dissecting genetic factors affecting phenylephrine infusion rates during anesthesia: a genome-wide association study employing EHR data

Version: 1 Date: 22 Jul 2019

Reviewer: Matthew Zawistowski

Reviewer’s report:

The authors have clarified several aspects of the GWAS, making the analysis clearer to the reader. The GWAS is methodologically valid yet yielded no genome-wide significant results. Indicated risk variants are speculative but do provide candidates for additional research. Given the small sample size and complex nature of this trait, it is not surprising that no SNP achieved genome-wide significance. I remain skeptical of the supposed sub-phenotypes identified through k-means clustering. The machine learning method is applied correctly, but I interpret the results differently. The phenotype appears to me to be a continuous spectrum of response, rather than distinct sub-phenotypes. The clustering was not used in the GWAS however and therefore does not affect the primary GWAS results.

Are the methods appropriate and well described?
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Yes

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