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LETTER

Pathway to Ascertain the Role of Pharmacogenomics in Healthcare Utilization Outcomes [Letter]

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Dear editor

I read with great interest and excitement the findings published in your journal by Takahashi[1] and colleagues investigating the association between select pharmacogenetic variants and hospitalization and emergency department (ED) visits. However, I would like to share some comments regarding the study that have not been addressed in the original manuscript.

Very important pharmacogenes, including *UGT1A1, CYP2B6, NUDT15, VKORC1, CYP4F2, HLA-B1502, G6PD*, were not ascertained in this analysis. These genes have been strongly associated with drug toxicity and adverse drug events. The same genes have been supported by the clinical implementation of pharmacogenetics consortium guidelines.[2] Nonetheless, the authors only included a limited number of alleles in a limited number of genes. This approach could have significantly underpowered the analysis of achieving a statistical significance regarding the clinical utility of pharmacogenomics in reducing healthcare utilization.

The authors reported no association between pharmacogenomics phenotype and disease burden. To date, we expect that pharmacogenomics phenotypes, independent of drugs used, have no to little effect on disease burden or disease complications. A crude example, a patient that is a carrier for the *CYP2C19*3* is unlikely to have an ED visit just because of being a poor metabolizer for CYP2C19. However, if the same patient had a percutaneous intervention, requiring a stent and clopidogrel, there is a higher chance for an ED visit than an individual with normal CYP2C19 activity status.

The ultimate goal of pharmacogenetic testing is to achieve greater precision in selecting the right drug for the right patient and reduce the overall burden on the healthcare system.[3] To generate this level of evidence, investigators could use a more targeted approach to assess the effect of select drug-gene pairs on specific patient-centered outcomes or select healthcare utilization outcomes.[4] This approach allows for a robust and adequately powered assessment to delineate the role of pharmacogenomics in predicting outcomes. Unfortunately, using a limited number of pharmacogenetic variants to ascertain their effect on healthcare utilization could have significantly underpowered the study to show an association between the predictors and the outcomes.

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A limitation of observational studies involving non-random allocation of treatment is selection bias confounded by indication.[5] Specifically, underlying patient characteristics associated with specific treatment may influence the outcome of the study. Propensity scores are a statistical method to address bias from confounding by indication. Simply, propensity scoring is a prediction model that predicts the likelihood of treatment based on a specified set of patient characteristics. Propensity scoring aims to balance two non-equivalent groups on observed characteristics to minimize biased estimates of treatment effects. Therefore, using the propensity score in this published analysis would have been a more robust assessment tool for the role of pharmacogenetic variants in predicting the primary outcomes.

In summary, this published analysis confirms the role of non-genetic risk factors in predicting healthcare utilization. However, the study had major limitations to draw a premature conclusion and too-soon to rule out the clinical utility of pharmacogenetics in reducing healthcare utilization.

Disclosure

The author reports no conflicts of interest in this communication.

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