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

Dear editor

We appreciate the thoughts of Dr. Roman and his comments. We understand that the number of identified pharmacogenomic genes continues to increase with time, and the clinical utility also increases with time and expert opinion. We chose these selected pharmacogenes because of their strong clinical practice recommendations and the data available at the time of the gene selection. Due largely to the efforts associated with other initiatives within the RIGHT study, our clinical practice set up specific electronic medical record best practice alerts for these pharmacogenes, and it was believed that there was the potential for change in clinical care for patients with extreme phenotypes. We did not design the study to specifically look at all pharmacogenomic genes.

We agree that the ideal goal would be to study specific drug/gene pairs. In our limitation section, we described the problems of not including specific drug/gene pairs and specific causes of hospitalizations or ED visits. In this real-world pharmacogenomic implementation study, we did not have a sufficient number of patients with the specific drug exposures, the high-risk genotypes, and clearly recorded electronic record documentation of side effects and lack of effectiveness. We also had to rely upon medication prescriptions rather than medications dispensed. Therefore, our alternate goal was to determine if PGx genes could be used as potential biomarkers for adverse health outcomes. In our previous pilot study, we found that patients with ultrarapid metabolizer of CYP 2D6 had higher risk of hospital utilization. Thus, we had hope that potentially expanding the number of pharmacogenomic genes would continue to show an effect. We agree and hope that as pharmacogenomics becomes more widespread, the ability to look at specific drug/gene pairing will be more feasible.

Lastly, we agree that there are practical limitations to the use of observational cohort studies to study pharmacogenomics. As described above, this includes the need for a very large sample size to compensate for the low likelihood of medication usage among those carrying the extreme phenotypes (those most likely to demonstrate a clinical effect), as well as inconsistent documentation of lack of efficacy and side effects. There is also the potential for bias and confounding in any observational design. However, there are also high costs involved with conducting clinical trials of pharmacogenomics which also limit the utility of this design for
addressing many important questions. We look forward to seeing data from larger observational cohorts that may address some of the limitations inherent to our study.

Disclosure
We have nothing to disclose.

References
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