Meaningful, Actionable Pharmacogenomic Patient Results

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What might the attendee be able to do after being in your session?
After this session, attendees should have an understanding of the importance of pharmacogenomic (PGx) testing and the implications of preemptive testing for a targeted set of patients using our developed method.

Description of the Problem or Gap
An estimated 90% of patients have at least one actionable variant allele with PGx importance in their genome[1], providing the foundation for the benefits of PGx testing. Ideally there are adequate resources to immediately generate PGx test results for all patients in order to identify which patients have an actionable drug-gene variant . However, limitations on the throughput of PGx testing, along with associated costs, require a more thorough evaluation of which patients would be most likely to benefit from this type of testing, leading to expedited testing for this vulnerable group.

Methods: What did you do to address the problem or gap?
In order to identify time sensitive relevance of PGx testing for patients, we developed a tool named Meaningful, Actionable Pharmacogenomic Patient Results (MAPPeR) that can predict the relevance of pharmacogenomic testing for patients. This method takes in information in the form of prescribed medications and diagnosed diseases to identify the likelihood that they would benefit from PGx testing. Medications have direct mapping to PGx alleles based on Clinical Pharmacogenetic Implementation Consortium (CPIC) guidelines[2] and the FDAs Table of Pharmacogenomic Biomarkers in Drug Labeling[3]. Disease status also provides valuable insight into a patient's likelihood of being prescribed medications affected by their genetics and subsequently benefit from PGx testing. To incorporate this information, we constructed a mapping system based on a Bayesian network generated from 3,977,249 prescribed medications and 1,013,204 disease diagnoses from 741,023 individual patients from the Sanford Health system over the course of 12 months. Of the 741,023 patient records, 207,694 patients had been prescribed a medication with PGx significance, resulting in 2,382,389 medication prescriptions and 366,184 disease codes being used to develop the model. The input for this method is prescribed medication generic names and ICD-10 diagnostic codes. Using a probabilistic framework, prescribed medications are assigned a probability of 1, with all other non-prescribed PGx-relevant medications having probabilities determined by our mapping infrastructure. Considering disease status, the generated Bayesian network determines the probability that the patient will be prescribed the medication, given their set of disease status codes. For an operational threshold, we have defined 0.5 as the minimum probability to consider this patient relevant for PGx testing.

In order to validate our method, we considered the similarity of our Bayesian network mappings to what is observed in real world data. To do so, we validated using an 80/20 train/test split of the Sanford Health data, as well as using external data from the VA Precision Oncology Cohort A. This analysis showed consistency of over 99% of the mappings from the internal data and over 97% of the mappings for the external data using a binomial hypothesis test. Additionally, we established a ROC curve to estimate the model's performance, which resulted in an AUC of 0.746.

Results: What was the outcome(s) of what you did to address the problem or gap?
The resulting method allows for a concise prioritization of patients likely to benefit from PGx testing, based on their medication and disease history. Embedded within this framework is the Bayesian network that determines the likelihood that a patient will be prescribed a medication, given that they have a certain disease status. Our validation of the mapping system identified over 99% of conditional probabilities as consistent with the internal Sanford Health data and over 97% of conditional probabilities as consistent with the proportions observed in the external VA data.

Discussion of Results
The internal and external consistency of Bayesian probability demonstrates the overall reliability of the Bayesian network used for mapping between disease status and medications. Additionally, consideration of more data, from both within and external to the Sanford Health system, will enable a more robust set of probabilities for a wider number of disease statuses.

Conclusion
MAPPeR provides a framework for clinicians and administrators to prioritize which patients would be likely to benefit from PGx testing by using their medication and disease histories. Through the integration of prescribed medications and prediction of future medications based on disease status, prioritized patients can be informed of the benefits of and consented for PGx testing preemptively. This will enable actionable drug-gene variant alleles to be documented and indicated within the EMR so that providers can make more informed decisions when it comes to prescribing medications with PGx relevance. Future considerations include integration of more preemptive methodologies, such as disease risk prediction and consideration of the likelihood that a given patient will actually carry an actionable variant. In addition to more predictive methods, we plan to integrate consideration of how soon a patient can be expected to benefit from the PGx testing. By prospecting a 3- or 5-year window, our model would flag patients who would be likely to be prescribed a PGx associated medication within this window.

Attendee's Take-away Tool
Both the concept of preemptive PGx testing based on predictive modeling from patient data and the MAPPeR tool itself are intended as take-aways from this session.

Use of Knowledge Acquired at Previous AMIA Events
Not Applicable

References

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