Medical Benefit of Preemptive Reporting of Pharmacogenomic Information From Whole Exome Sequencing

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Abstract

The effectiveness of utilizing individual patient's whole exome sequencing (WES) genetic information to influence patient care by predicting and preventing possible adverse drug reactions (ADRs) is investigated. Pharmacogenomically relevant variants from WES studies collected into two databases were analyzed to determine the expected medical benefit of reporting the incidental findings when WES studies are performed. One dataset was from UNC Chapel Hill as part of the NCGENES project database; the other was from Columbia University Medical Center's Whole Exome Research Database. The frequency of possible drug exposure for individuals in the US population was approximated by using data gathered from a database of outpatient drug prescribing, www.imshealth.org using the new prescription number data for 2014. Results were calculated to determine the aggregate number needed to screen (ANNS) to determine need for a change in medical management (different drug prescribing, monitoring, etc).

The NCGENES data utilized in this analysis included data from 672 individuals' genomes. The projected ANNS for this data set was 54.02. The calculated mean ANNS for the simulated data was 54.11, with a 95% confidence interval from 53.94 to 54.30 using Monte Carlo simulation (based on 1000 simulated points). CUMC data utilized in this analysis included data from 2,983 individuals' genomes. The projected ANNS for this data set was 46.15. Using Monte Carlo simulation, the calculated mean ANNS was 46.00 and the projected 95% confidence interval was from 45.93 to 46.08. Monte Carlo simulation of the error in these values was used to compute a 95% confidence interval, because of the complexity of estimating errors in these calculations.

Based on this analysis, the pharmacogenomically relevant impact of using WES based screening is in the range of 46 to 52 persons needed to screen when using incidental findings to dictate an expected change in management. A model implementation plane for incorporating pharmacogenomic information into patient care within a healthcare system is provided and discussed.