The potential cost-effectiveness of warfarin pharmacogenomic testing

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Background and objectives: Warfarin is a commonly used anticoagulant that has high inter- and intra-patient variability and is associated with serious adverse bleeding events of 5-10% per patient per year. Recent studies have identified variants in two genes that are significantly associated with warfarin dosing requirements. *CYP2C9* codes for the enzyme primarily responsible for warfarin metabolism, and *VKORC1* codes for the molecular target of warfarin, vitamin K epoxide reductase. The FDA has recently added information about pharmacogenomic testing to the warfarin label and smaller clinical trials are ongoing, but the longer-term clinical and economic outcomes of warfarin pharmacogenomic testing are unclear.

Methods: We conducted a retrospective database analysis to evaluate the relationship between genetic variants and anticoagulation status (INR) and bleeding risk. We performed a survey of clinicians involved in managing warfarin therapy regarding their perceptions of testing. Lastly, we conducted a cost-utility study of warfarin pharmacogenomic testing based on the results of our database analysis and a recently completed pilot randomized controlled trial.

Results: We found in our database analysis that variants of *VKORC1*, in contrast to *CYP2C9,* were not significantly associated with anticoagulation status or bleeding risk. However, the relationship between observed INR and bleeding risk appears to differ between *CYP2C9* variants and wildtypes. Initial surveys were sent to 200 clinicians; to date, the response rate is approximately 25%, and follow-up telephone reminders and interviews are underway. Preliminary evaluation of the potential cost-effectiveness of warfarin pharmacogenomic testing indicates that testing may result in an overall increase in medical care costs, but in a cost-effective manner. Incremental cost-effectiveness ratios varied from approximately cost-neutral to $54,000 per quality-adjusted life year (QALY) gained, up to over $100,000/QALY, depending on assumptions. Analyses based on the results of the randomized clinical trial are currently ongoing.

Discussion/Conclusion: Warfarin pharmacogenomic testing offers significant potential to reduce the risk of serious adverse events that lead to significant morbidity, mortality, and costs. Evidence-based cost-utility studies can be used to assess potential clinical and economic outcomes of pharmacogenomic testing, identify critical data gaps, and help inform policy decisions.