The Hospital for Sick Children
Technology Assessment at SickKids (TASK)

EXECUTIVE SUMMARY

UPDATED

A MICROCOSTING AND COST-CONSEQUENCE ANALYSIS OF GENOMIC TESTING STRATEGIES IN AUTISM SPECTRUM DISORDER

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TASK Technology Assessment at SickKids

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Executive Summary

Background

Chromosomal microarray analysis (CMA) is currently the first-tier clinical genetic test for individuals with autism spectrum disorder (ASD). Clinical genome and exome sequencing (CGES) technologies are promising tools for demonstrating genetic causality, due to their higher diagnostic yield compared with CMA for cases presenting with positive phenotypes for autism spectrum disorder. It is not yet clear whether genomic technologies can add value for money invested or how best to translate these technologies from research to clinical care. An economic evaluation of CGES technologies requires a comprehensive and accurate estimation of all costs involved in the sequencing workflow.

Objectives

The primary objective of this study is to estimate costs associated with CMA, whole exome sequencing (WES) and whole genome sequencing (WGS) tests for a targeted patient population consisting of children with ASD from an institutional payer perspective over 5 years. The secondary objective is to compare the incremental costs and diagnostic yields of CMA, WES and WGS in hypothetical clinical testing scenarios in a cost-consequence analysis.

Methods

Using a bottom-up microcosting approach, the opportunity cost per sample excluding mark-ups, fees and charges for CMA, for WES on the Illumina HiSeq® 2500 platform and for WGS on the Illumina HiSeq® 2500 and HiSeq X™ platforms for patients with ASD were estimated from an institutional payer perspective based on the laboratory practices at the Hospital for Sick Children (SickKids), Toronto, Canada. As these tests are currently mainly done in research, a clinical application was simulated for WES and WGS. The cost per sample was determined for each year of a five-year program. Total program costs to service the ASD patient population were also estimated over five years. A probabilistic sensitivity analysis (PSA) was conducted to incorporate parameter uncertainty in the model. Three one-way deterministic sensitivity analyses (DSA) were conducted to examine the effects of changing the inputs for the overhead cost, the total volume of CGES tests in the institution, and the number of primary variants found by CGES tests, while other inputs remained the same. To calculate incremental diagnostic yields associated with clinical scenarios, a review of published studies that reported diagnostic yields for CMA, WES or WGS for patients with ASD was undertaken.

Results

The cost per ASD sample in Year 1 was $1655 (95% CI: 1611, 1699) for WES, $2851 (95% CI: 2750, 2956) for WGS on the HiSeq X™ platform and $5519 (95% CI: 5244, 5785) for WGS on the HiSeq® 2500 platform, compared to $744 (95% CI 714, 773) for CMA. Reagent supply costs accounted for the largest proportion of costs for each type of CGES. Estimated five-year program CMA costs were $1.05 million (95% CI: 1.01, 1.09) based on 300 ASD cases. Estimated program costs for WES and WGS tests were also based on 300 ASD cases each. WES program costs were $2.31 million (95% CI: 2.25, 2.37) over five years. Estimated WGS five-year program costs were $7.78 million (95% CI: 7.39, 8.15) for the HiSeq® 2500 platform and $3.98 million (95% CI: 3.84, 4.13) for the HiSeq X™ platform. Based on the literature review, the diagnostic yield for ASD used in the cost consequence analysis was 9.3% for CMA and 15.8% for a combination of CMA and WES (CMA+WES). A hypothetical diagnostic yield for WGS was calculated to be 17.8%. The cost per additional ASD patient with a positive genetic diagnosis was $25459 when substituting CMA alone with CMA+WES. The cost per additional positive genetic diagnosis was $26020 or $58959 when replacing CMA with the WGS HiSeq X™ or WGS HiSeq® 2500 platforms, respectively. The substitution of CMA+WES with WGS resulted in the ratio of incremental cost to incremental diagnostic yield of $28300 in using the HiSeq X™ platform and $195056 using the HiSeq® 2500 platform.

Conclusions

This study is the first to estimate the cost of clinical exome and genome sequencing using a bottom-up microcosting approach in a clinical paradigm. The WGS using older technology (HiSeq® 2500) was the most expensive test, costing almost three times as much as WES and seven times as much as CMA. The new technology using the HiSeq X™ platform reduced the cost of WGS test by 48%. Labour costs were reduced for HiSeq X™ due to improved automation and streamlining of sample processing. Overall, supplies, followed by equipment and labour, constituted the largest proportion of total cost for all three tests. A cost-consequence analysis revealed a cost of over $25000 per additional patient with a pathologic variant if CMA were to be replaced by CMA+WES or by WGS. Additional research is required to assess the impact of CGES on the pathway of care for children with ASD and to measure ultimate improvements in health outcomes as a result of testing. This study provides comprehensive cost data for use in future economic evaluations of clinical genome and exome sequencing in ASD and allows for a costing model that can be easily adapted to other pediatric patient populations.