Value for money? Array genomic hybridization for diagnostic testing for genetic causes of intellectual disability

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Record Status
This is a critical abstract of an economic evaluation that meets the criteria for inclusion on NHS EED. Each abstract contains a brief summary of the methods, the results and conclusions followed by a detailed critical assessment on the reliability of the study and the conclusions drawn.

CRD summary
This study examined the cost-effectiveness of array genomic hybridisation (AGH) compared with conventional cytogenetic testing to identify chromosomal imbalance causing intellectual disability in children aged five to 10 years, from the perspective of the third-party payer. AGH provided good value for money compared with cytogenetic testing, when used as a first-line test. The cost-effectiveness framework was conventional and key areas of uncertainty were satisfactorily investigated, enhancing the validity of the authors’ conclusions, despite limited reporting of the clinical data sources.

Type of economic evaluation
Cost-effectiveness analysis

Study objective
This study examined the cost-effectiveness of array genomic hybridisation (AGH) compared with conventional cytogenetic testing to identify chromosomal imbalance causing intellectual disability in children aged from five to 10 years.

Interventions
Cytogenetic testing uses a karyotype (complete chromosome assessment under a microscope) to assay the entire genome to detect chromosomal rearrangements that are greater than five to 10 million base pairs. AGH can identify sub-microscopic chromosomal imbalances that are 100 or more times smaller than this. With cytogenetic testing, if the karyotype did not provide a diagnosis, either targeted fluorescence in situ hybridisation (FISH) or subtelomeric FISH was conducted. With AGH, children who were suspected of having a trisomy 21, 18, or 13 were assessed by a karyotype, followed by the AGH if a diagnosis was not established, otherwise they received the AGH.

Location/setting
Canada/secondary care, laboratory.

Methods
Analytical approach:
The analysis was based on a decision-analytic model with a one-year time horizon and a hypothetical cohort of children with idiopathic intellectual disability. The authors stated that the perspective of the third-party payer, namely the British Columbia Ministry of Health Services, was adopted.

Effectiveness data:
The clinical data were from published literature and a review of the patient records from the Provincial Medical Genetics Programme at the Children’s & Women’s Hospital in Vancouver, Canada. This chart review included 162 families and provided data on the accuracy of karyotyping, which was a key model parameter. Some assumptions were needed for the accuracy of AGH.

Monetary benefit and utility valuations:
Not considered.

Measure of benefit:
The number of diagnoses for children with intellectual disability was the benefit measure.

Cost data:
The economic analysis included the costs of karyotyping, FISH, AGH, and laboratory testing (before cytogenetic testing and after cytogenetic testing with or without a diagnosis). The resource use was based on data from the chart review. The unit costs were from the Medical Services Plan fee schedule of the Ministry of Health, and the Cytogenetics Laboratory at the British Columbia Children’s Hospital. The costs were in Canadian dollars (CAD) and the price year was 2007.

Analysis of uncertainty:
Various alternative scenarios were considered: the use of a multiplex ligation-dependent probe amplification instead of subtelomeric FISH; AGH after a normal karyotype for children without suspected trisomy 21, 18, or 13; and AGH compared with cytogenetic testing only in those without suspected trisomy 21, 18, or 13. A probabilistic sensitivity analysis was conducted using conventional probability distributions for the sets of inputs and a Monte Carlo simulation; cost-effectiveness acceptability curves were generated.

Results
AGH led to a gain of 0.082 (95% CI 0.044 to 0.119) in the rate of diagnosis at an additional cost of CAD 217 (95% CI 172 to 261), resulting in an incremental cost per additional diagnosis of CAD 2,646 (95% CI 1,619 to 5,296).

The probabilistic analysis showed that there was a 95% probability of AGH being cost-effective at a willingness-to-pay threshold of CAD 4,550.

Using the preferences of parents who had a child with an intellectual disability, the willingness-to-pay for a diagnosis was calculated to be CAD 12,792. At this threshold, the probability of AGH being cost-effective was 99%.

The sensitivity analysis showed that using multiplex ligation-dependent probe amplification instead of subtelomeric FISH gave an incremental cost per diagnosis of CAD 4,463 (95% CI 2,962 to 8,446), while the use of AGH solely for those individuals without suspected trisomy 21, 18, or 13 had an incremental cost per diagnosis of CAD 2,766 (95% CI 1,543 to 5,267).

Authors’ conclusions
The authors concluded that AGH provided good value for money compared with cytogenetic testing, when used as a first-line test.

CRD commentary
Interventions:
The rationale for the selection of the comparators was clear. The authors compared the standard clinical approach for identifying chromosomal abnormalities against the more costly, but more accurate proposed strategy.

Effectiveness/benefits:
No systematic review was reported to identify the relevant sources of data. The authors did not justify their selection of the published studies and did not report the study methods, patient populations, and other key details for them. This makes it difficult to judge the validity of the clinical inputs. Limited information about the primary data was given. The benefit measure was disease specific and a natural outcome of a diagnostic programme, but it might not be comparable with the benefits of other health care interventions. The authors stated that quality-adjusted life-years (QALYs) were not used because of methodological concerns about the use of preference-based quality of life instruments in children.

Costs:
The economic analysis was consistent with the perspective adopted. The unit costs were reported for most items, but some were presented as category totals. The data sources were explicitly reported and reflected the local setting, based on reimbursement rates. The price year and the currency were clearly reported. The resource consumption was from a sample of patients at the authors’ institution, but appears to be generalisable to other settings. Some resource use was varied in the scenario analyses to reflect alternative diagnostic pathways.
Analysis and results:
The expected costs and benefits of the two strategies were clearly presented and appropriately synthesised, using an incremental approach. The uncertainty was satisfactorily investigated, using various approaches, which were appropriate, and the findings were clearly presented and discussed. The key details of the decision model were given. The authors acknowledged some limitations of their analysis, such as the use of a short time horizon that did not include the future costs of intellectual disability, and the use of an intermediate outcome for the benefits that did not have an established cost-effectiveness threshold. They also stated that the cost of AGH was likely to be lower than their estimate, which could be considered to be conservative.

Concluding remarks:
The cost-effectiveness framework was conventional and key areas of uncertainty were satisfactorily investigated, enhancing the validity of the authors' conclusions, despite limited reporting of the clinical data sources.

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