Key Summary of Published Article

Cost-Effectiveness of Karyotyping, Chromosomal Microarray Analysis, and Targeted Next-Generation Sequencing of Patients with Unexplained Global Developmental Delay or Intellectual Disability

Background

- Global developmental delay and intellectual disability (GDD/ID) affect 1% to 3% of children.[1] A substantial proportion of GDD/ID is caused by genetic abnormalities that can be identified by karyotyping, chromosomal microarray analysis (CMA), and targeted next-generation sequencing (NGS).[2-4]
- Many US organizations recommend CMA as a first-tier test for diagnosis of unexplained GDD/ID.[2-4] However, CMA is often used as a second-tier test in the United States, because it costs more than karyotyping.
- Studies of populations in the United Kingdom and Canada indicate CMA is cost-effective compared to karyotyping.
- **Objective:** To compare the cost-effectiveness of genetic testing methods for the diagnosis of GDD/ID from a US healthcare perspective.

Methods

- Two decision-tree models were used to evaluate the incremental cost-effective ratios (ICERs) of genetic testing scenarios for GDD/ID diagnosis. (The ICER is the average cost of additional diagnoses provided by one scenario relative to diagnoses provided by a reference scenario: difference in costs ÷ difference in number of diagnoses.)
- Model parameters included rates and probabilities of testing outcomes and costs to US payers for genetic testing. The time horizon was 1 year.
- One model compared 4 testing scenarios: 1) karyotyping only; 2) CMA only; 3) karyotyping then CMA; and 4) CMA then karyotyping.
- The other model compared scenarios related to the detection of a variant of unknown significance (VUS) using CMA and follow-up testing:
  - CMA and parental CMA: patient is tested by CMA; if a VUS is identified, parents are also tested by CMA
  - CMA and parental CMA/NGS: same as CMA-and-parental-CMA scenario, plus NGS testing if parents are not available or if CMA results are normal

Results

- On average, a karyotyping-only scenario cost $11,033 per genetic diagnosis of GDD/ID. Compared to karyotyping-only, the CMA-only approach improved diagnostic yield 3.9-fold; the ICER was $2,692 per additional genetic diagnosis.
- Compared to a karyotyping-only scenario, both the CMA-then-karyotyping and the karyotyping-then-CMA scenarios improved diagnostic yield with the same number of genetic diagnoses. However, the CMA-then-karyotyping scenario cost less than the karyotyping-then-CMA scenario.
- Compared to the CMA-alone scenario, the CMA-and-parental-CMA scenario improved diagnostic yield 11.6%; the ICER was $4,220 per additional genetic diagnosis.
- Compared to the CMA-and-parental-CMA scenario, the CMA-and-parental-CMA/NGS scenario improved diagnostic yield 60%; the ICER was $12,295 per additional genetic diagnosis.

Conclusions

- Use of CMA as the first-tier genetic test is cost-effective for diagnosis of unexplained GDD/ID for US payers. Testing parents of patients with a VUS identified by CMA is also cost-effective.

Article published in the journal *Molecular Diagnosis & Therapy*

Authors
Yonghong Li,[1] Lori A Anderson,[1] Edward I Ginns,[2] James J Devlin[1]

Affiliations
[1] Quest Diagnostics, San Juan Capistrano, CA
[2] Quest Diagnostics, Marlborough, MA

Citation
Li Y, Anderson, LA, Ginns EI, Devlin JJ. *Mol Diagn Ther*. 2017 Dec 5. doi: 10.1007/s40291-017-0309-5

Webpage
https://link.springer.com/article/10.1007/s40291-017-0309-5

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