Economic Evaluation of Next-Generation Sequencing Technologies in Paediatric Patient Groups With Rare Diseases: a Systematic Review

"What is the evidence for the economic evaluation of next generation sequencing technologies in paediatric patient populations with rare diseases?"

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Background

Next-Generation Sequencing (NGS) for newborn screening can lead to cost savings through early treatment initiation and reduced long-term severe disability.

Economic evaluation helps to inform policy decisions on upscaled adoption of NGS into clinical practice.

Results of studies vary widely (technology comparison, diseases, outcomes, findings) with majority of reviews not reflecting newer evidence.

Study aim was to consolidate and synthesise existing evidence addressing restrictions in previous reviews, to highlight best practices and derive implications for future research and policy.

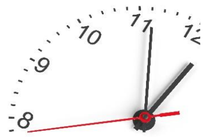
Review procedure and eligibility criteria

- Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) and CHEERS 2022 statement.
- Database search (Cochrane, EconLit, Embase, Global Health, Medline, Scopus and Web of Science).
- Further screening of articles identified in relevant systematic literature reviews.
- Two researchers independently assessing inclusion with a third reviewer for conflicting cases.

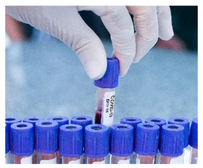
	Inclusion criteria	Exclusion criteria
Population	Paediatrics (persons aged ≤ 18)	Persons aged > 18 (not combined with persons aged ≤ 18)
Intervention	NGS technologies (WGS, WES, TS) for detection of rare disease	Interventions other than NGS technologies
Comparator	Standard / traditional diagnostic methods or other NGS methods	No comparator
Outcome	Full economic evaluation measures such as QALYs, DALYs, ICER, number of positive cases, NPV, etc.	Studies comparing only costs without health outcomes or outcomes related to effectiveness only
Study design	Full economic evaluations (CEA, CUA and CBA) Primary, peer-reviewed literature and full text available	Cost analysis, cost comparison analysis, cost minimisation, etc. Non-primary literature, full text not available
Context	OECD and EU countries	Countries not part of the OECD or EU
Timespan	Studies published between January 2015 and May 2024	Studies published outside inclusion criteria dates
Language	English	Studies written in other languages

Study characteristics

Majority of studies were conducted in Australia (14/24), only two in Europe.



Variation across sample sizes (32 – 1'259 individuals), health conditions (monogenic most common) and time horizon (3 months to lifetime).



Majority take healthcare sector perspective (16/24) (2 taking a societal perspective) and most frequent strategy was comparison of WES vs. standard care (10/24).

Key findings (24 articles)

More than half of studies concluded NGS dominated the traditional diagnostic pathway (14/24).

Less than a third of studies found NGS to be a more expensive option but proved cost-effective due to significantly higher diagnostic yield (7/24).

ICER most reported outcome, with diagnostic yield most popular measure for effectiveness (23/24), followed by QALYs (6/24).

Optimal timing for introducing NGS into diagnostic pathway (6/24) – early implementation most cost-effective strategy.

Reporting quality: 15 studies reported 75% or more of CHEERS 2022 items

Implications, focus of future research and limitations

Drawing high-level conclusions

- Significant variability makes it difficult to draw general conclusions about cost-effectiveness of NGS, need for standardisation in study methodology and reporting.
- Policy implications treated with caution for certain geographic regions where research is lacking (e.g. Asia, South America and Africa).

Target population

- Current focus on symptomatic paediatric populations, excluding "healthy" population based newborn screening initiatives.
- From a policy perspective, early implementation of NGS could potentially enhance cost-effectiveness by identifying rare disease patients at the earliest stage of life.

Lack of use of quality adjusted life years (QALYs)

- Difficult to measure QALYs in the context of rare disease and paediatric patient groups.
- Need to focus on development of child-specific HRQoL measures within the context of rare disease to reduce uncertainty in decision-making and policy for adoption of new technologies in paediatric populations.

Lack of consideration of societal perspective and indirect costs

- Inclusion of indirect costs could improve cost-effectiveness of NGS technologies as rare disease have significant societal costs.

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