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CADTH RAPID RESPONSE REPORT: SUMMARY OF ABSTRACTS

Rapid Genome-wide Testing: Clinical Utility and Cost-Effectiveness

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About CADTH: CADTH is an independent, not-for-profit organization responsible for providing Canada's health care decision-makers with objective evidence to help make informed decisions about the optimal use of drugs, medical devices, diagnostics, and procedures in our health care system.

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Research Questions

1. What is the clinical utility of providing rapid turnaround for genome-wide testing for patients in intensive care?
2. What is the cost-effectiveness of providing rapid turnaround for genome-wide testing for patients in intensive care?
3. What are the evidence-based guidelines of providing rapid turnaround for genome-wide testing for patients in intensive care?

Key Findings

One randomized controlled trial and three non-randomized studies were identified regarding the clinical utility of providing rapid turnaround for genome-wide testing for patients in intensive care. No relevant economic evaluations or evidence-based guidelines were identified.

Methods

A limited literature search was conducted by an information specialist on key resources including PubMed, the Cochrane Library, the University of York Centre for Reviews and Dissemination (CRD) databases, the websites of Canadian and major international health technology agencies, as well as a focused Internet search. The search strategy was comprised of both controlled vocabulary, such as the National Library of Medicine's MeSH (Medical Subject Headings), and keywords. The main search concepts were rapid genome testing and intensive care units. No filters were applied to limit the retrieval by study type. Where possible, retrieval was limited to the human population. The search was also limited to English language documents published between January 1, 2014 and August 13, 2019. Internet links were provided, where available.

Selection Criteria

One reviewer screened citations and selected studies based on the inclusion criteria presented in Table 1.

Table 1: Selection Criteria

Population	Patients of all ages in an intensive care setting (i.e., neonatal, pediatric, or adults) Exclusion: pre-natal patients (i.e., in utero)
Intervention	Rapid genome-wide testing [e.g., rapid/expedited/express whole exome sequencing, broad panel of multiple genes (e.g., neonatal crisis panel)] Rapid or expedited turnaround time = 1 to 4 weeks
Comparator	No testing; Genome-wide testing with routine turnaround time (i.e., 6 to 12 weeks)

Outcomes	Q1: Clinical utility, clinical outcome (e.g., mortality, change in active patient management) Q2: Cost-effectiveness Q3: Evidence-based guidelines
Study Designs	Health technology assessments, systematic reviews, meta-analyses, randomized controlled trials, non-randomized studies, economic evaluations, evidence-based guidelines

Results

Rapid Response reports are organized so that the higher quality evidence is presented first. Therefore, health technology assessment reports, systematic reviews, and meta-analyses are presented first. These are followed by randomized controlled trials, non-randomized studies, economic evaluations, and evidence-based guidelines.

One randomized controlled trial[1] and three non-randomized studies[2-4] were identified regarding the clinical utility of providing rapid turnaround for genome-wide testing for patients in intensive care. No health technology assessments, systematic reviews, meta-analyses, economic evaluations, or evidence-based guidelines were identified regarding rapid turnaround for genome-wide testing for patients in intensive care.

Additional references of potential interest are provided in the appendix.

Overall Summary of Findings

One randomized controlled trial[1] and three non-randomized studies[2-4] were identified regarding the clinical utility of providing rapid turnaround for genome-wide testing for patients in intensive care.

The authors of one randomized controlled trial[1] concluded that infants in neonatal and pediatric intensive care units who were tested using trio rapid whole-genome sequencing received more timely diagnoses compared to the control group. Similarly, the authors of one non-randomized study[2] reported decreased time to diagnosis, among other conclusions, when comparing RapSeq (a targeted gene panel) to a historical control. The authors of the second non-randomized study[3] found that the clinical utility of rapid-whole genome sequencing in acutely ill infants is significantly greater than for standard genetic tests. They also noted a reduction in likelihood of mortality.[3] The authors of the third non-randomized[4] study found significantly different diagnostic yields and effect on medical management when comparing infants who were tested with rapid versus non-rapid exome sequencing.

References Summarized

Health Technology Assessments

No literature identified.

Systematic Reviews and Meta-analyses

No literature identified.

Randomized Controlled Trials

1. Petrikin JE, Cakici JA, Clark MM, et al. The NSIGHT1-randomized controlled trial: rapid whole-genome sequencing for accelerated etiologic diagnosis in critically ill infants. *NPJ Genom Med*. 2018 Feb;3:6.
PubMed: PM29449963

Non-Randomized Studies

2. Brunelli L, Jenkins SM, Gudgeon JM, et al. Targeted gene panel sequencing for the rapid diagnosis of acutely ill infants. *Mol Genet Genomic Med*. 2019 Jul;7(7):e00796.
PubMed: PM31192527

3. Farnaes L, Hildreth A, Sweeney NM, et al. Rapid whole-genome sequencing decreases infant morbidity and cost of hospitalization. *NPJ Genom Med*. 2018 Apr;3:10.
PubMed: PM29644095

4. Meng L, Pammi M, Saronwala A, et al. Use of exome sequencing for infants in intensive care units: ascertainment of severe single-gene disorders and effect on medical management. *JAMA Pediatr*. 2017 Dec 4;171(12):e173438.
PubMed: PM28973083

Economic Evaluations

No literature identified.

Guidelines and Recommendations

No literature identified.

Appendix — Further Information

Previous CADTH Reports

5. Next generation DNA sequencing: a review of the cost effectiveness and guidelines. (*Rapid Response Report: Summary with Critical Appraisal*). Ottawa (ON): CADTH; 2014 Feb: https://www.cadth.ca/sites/default/files/pdf/htis/apr-2014/RC0519%20-%20Next%20Generation%20Sequencing%20Final.pdf
Accessed 2019 Aug 19.

Non-Randomized Studies

Alternative Intervention – Not Specific to Rapid Tests

6. van der Sluijs PJ, Aten E, Barge-Schaapveld D, et al. Putting genome-wide sequencing in neonates into perspective. *Genet Med*. 2019 May;21(5):1074-1082.
PubMed: PM30287924

No Comparator

7. Mestek-Boukhibar L, Clement E, Jones WD, et al. Rapid Paediatric Sequencing (RaPS): comprehensive real-life workflow for rapid diagnosis of critically ill children. *J Med Genet*. 2018 Nov;55(11):721-728.
PubMed: PM30049826

8. Stark Z, Lunke S, Brett GR, et al. Meeting the challenges of implementing rapid genomic testing in acute pediatric care. *Genet Med*. 2018 Dec;20(12):1554-1563.
PubMed:PM29543227

Guidelines and Recommendations – Methodology Not Specified

9. Cancer Research UK. Policy statement: patient access to molecular diagnostics and targeted medicines in England. London (UK): Cancer Research UK; 2018 Sep: https://www.cancerresearchuk.org/sites/default/files/access_to_molecular_diagnostic_tests_and_targeted_medicines_in_england_0.pdf
Accessed 2019 Aug 19.
See: Single Tests, Panel Tests or Whole Genome Sequencing?

10. Borghesi A, Mencarelli MA, Memo L, et al. Intersociety policy statement on the use of whole-exome sequencing in the critically ill newborn infant. *Ital J Pediatr*. 2017 Nov 3;43(1):100.
PubMed: PM29100554