# Paper Summary

<!--META_START-->

Title: Secondary findings from next-generation sequencing: what does actionable in childhood really mea

Authors: Julie Richer, Anne-Marie Laberge

DOI: https://doi.org/10.1038/s41436-018-0034-4

Year: 2019

Publication Type: Journal

Discipline/Domain: Medical Genetics

Subdomain/Topic: Genomic screening, secondary findings, pediatric actionability

Eligibility: Eligible

Overall Relevance Score: 92

Operationalization Score: 88

Contains Definition of Actionability: Yes

Contains Systematic Features/Dimensions: Yes

Contains Explainability: No

Contains Interpretability: No

Contains Framework/Model: Yes

Operationalization Present: Yes

Primary Methodology: Conceptual with applied framework review

Study Context: Evaluation of disorders on ACMG SF v2.0 list for pediatric actionability

Geographic/Institutional Context: Canada (Children’s Hospital of Eastern Ontario; Université de Montréal

Target Users/Stakeholders: Clinical geneticists, pediatricians, policy makers, genomic screening committ

Primary Contribution Type: Conceptual framework and applied disorder evaluation

CL: Yes

CR: Yes

FE: Yes

TI: No

EX: No

GA: Partial

Reason if Not Eligible: n/a

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Secondary findings from next-generation sequencing: what does actionable in childhood really mean?

**Authors:**

Julie Richer, Anne-Marie Laberge

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**Year:**

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**Publication Type:**

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**Discipline/Domain:**

Medical Genetics

**Subdomain/Topic:**

Genomic screening, secondary findings, pediatric actionability

**Contextual Background:**

The paper addresses the concept of “actionability” in reporting secondary genetic findings from next-gene

**Geographic/Institutional Context:**

Canada — Children’s Hospital of Eastern Ontario, Université de Montréal, CHU Sainte-Justine

**Target Users/Stakeholders:**

Clinical geneticists, pediatricians, healthcare policy makers, genomic testing guideline committees

**Primary Methodology:**

Conceptual analysis with applied framework-based review of disorders

**Primary Contribution Type:**

Conceptual framework plus systematic evaluation of conditions

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## General Summary of the Paper

This paper critically examines what “actionable in childhood” means in the context of secondary genomic

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## Eligibility

Eligible for inclusion: **Yes**

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## How Actionability is Understood

Actionability is defined as a disorder for which surveillance and/or preventive/treatment measures are ava

(i) Childhood onset with measures initiated in childhood, or

(ii) Adult onset but proven-effective measures when started in childhood.

> “An actionable finding can be defined as a disease-causing pathogenic variant for a disorder for which s

> “…we consider a disorder ‘actionable in childhood’ if… the disorder has either (i) childhood onset… or (

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## What Makes Something Actionable

- Proportion of cases presenting in childhood
- Availability of preventive/treatment measures in childhood
- Demonstrated effectiveness in childhood
- Quality of supporting evidence
- Acceptability and risk-benefit balance of interventions

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## How Actionability is Achieved / Operationalized

- **Framework/Approach Name(s):** WHO screening criteria applied to genomic secondary findings
- **Methods/Levers:** Disorder categorization by onset proportion; evidence grading for interventions; ass
- **Operational Steps / Workflow:**
  1. Apply WHO criteria related to actionability
  2. Gather natural history and management data
  3. Categorize disorders by childhood onset proportion
  4. Assess evidence quality for interventions
- **Data & Measures:** Published guidelines, GeneReviews, natural history studies
- **Implementation Context:** Pediatric genomic testing in Canadian/Western healthcare systems

> “…we categorized disorders based on the proportion of cases that presented in childhood…” (p. 124)

> “We propose… disclosure in childhood would be limited to disorders for which a majority of cases prese

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## Dimensions and Attributes of Actionability (Authors’ Perspective)

- **CL (Clarity):** Yes — clear definition of pediatric actionability and decision framework (p. 129)
- **CR (Contextual Relevance):** Yes — applies specifically to pediatric genomic disclosure context (p. 1
- **FE (Feasibility):** Yes — requires availability and acceptability of interventions (p. 126)
- **TI (Timeliness):** No — no explicit link of timeliness as necessary criterion
- **EX (Explainability):** No — explainability not discussed
- **GA (Goal Alignment):** Partial — alignment with child’s best medical interests emphasized (p. 126)

- **Other Dimensions Named by Authors:** Evidence quality threshold, proportion of cases affected, bala

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## Theoretical or Conceptual Foundations

- WHO Wilson & Jungner screening criteria
- Berg et al.’s semiquantitative metric for actionability
- Distinction between medical vs. patient-initiated actionability

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## Indicators or Metrics for Actionability

- Proportion of cases with childhood onset
- Quality of evidence grading (very low, low, moderate, high)
- Existence and professional consensus of guidelines

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## Barriers and Enablers to Actionability

- **Barriers:**
  - Low or very low quality of evidence for many conditions
  - Variable disease penetrance and expressivity
  - Potential psychological and social harms
  - Resource limitations for opportunistic screening
- **Enablers:**
  - Professional guidelines supporting early intervention
  - Evidence of effective prevention/treatment in childhood

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## Relation to Existing Literature

The paper builds on ACMG recommendations, critiques the lack of pediatric-specific thresholds, and inco

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## Summary

Richer and Laberge (2019) present a structured approach to defining and operationalizing “actionable in

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## Scores

- **Overall Relevance Score:** 92 — Provides explicit definition, clear pediatric criteria, and detailed dime
- **Operationalization Score:** 88 — Offers an applied framework and systematic evaluation; slightly limit

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## Supporting Quotes from the Paper

- “[An] actionable finding can be defined as a disease-causing pathogenic variant… to significantly improv
- “…the disorder has either (i) childhood onset… or (ii) adult onset, but such measures have been demon
- “…disclosure in childhood would be limited to disorders for which a majority of cases present in childhoo

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## Actionability References to Other Papers

- Berg JS et al. (2016) — Semiquantitative metric for evaluating clinical actionability
- Moret C et al. (2017) — Categorization of medical vs. patient-initiated actionability
- Wilson JMG, Jungner G (1968) — WHO screening principles