Paper Summary

<!--META_START-->

Title: Return of non-ACMG recommended incidental genetic findings to pediatric patients: considerations

Authors: Kevin M. Bowling, Michelle L. Thompson, Melissa A. Kelly, Sarah Scollon, Anne M. Slavotinek,

DOI: https://doi.org/10.1186/s13073-022-01139-2

Year: 2022

Publication Type: Journal

Discipline/Domain: Genomics / Medical Genetics

Subdomain/Topic: Incidental findings in pediatric genomic sequencing

Eligibility: Eligible

Overall Relevance Score: 88

Operationalization Score: 75

Contains Definition of Actionability: Yes (implicit, framed in return-of-results context)

Contains Systematic Features/Dimensions: Yes

Contains Explainability: Partial

Contains Interpretability: Partial

Contains Framework/Model: No formal named model, but structured criteria for return

Operationalization Present: Yes

Primary Methodology: Mixed Methods (case series across multiple genomic studies + conceptual analysi

Study Context: Four pediatric genomic sequencing studies (SouthSeq, KidsCanSeq, P3EGS, COAGS) re

Geographic/Institutional Context: USA (multiple academic medical centers, diverse patient populations)

Target Users/Stakeholders: Clinical geneticists, laboratory directors, policy-makers, pediatric healthcare p

Primary Contribution Type: Empirical cases + conceptual considerations for return of incidental genetic fi

CL: Yes

CR: Yes

FE: Yes

TI: Partial

EX: Partial

GA: Partial

Reason if Not Eligible: N/A

<!--META_END-->

Title:

Return of non-ACMG recommended incidental genetic findings to pediatric patients: considerations and c

Authors:

Kevin M. Bowling, Michelle L. Thompson, et al.

DOI:

https://doi.org/10.1186/s13073-022-01139-2

Year:

2022

Publication Type:

Journal

Discipline/Domain:

Genomics / Medical Genetics

Subdomain/Topic:

Incidental findings in pediatric genomic sequencing

Contextual Background:

The paper addresses the emerging challenge of incidental genetic findings (IFs) outside ACMG-recomme

Geographic/Institutional Context:

USA — University of Alabama at Birmingham, Baylor College of Medicine, UCSF, HudsonAlpha Institute

Target Users/Stakeholders:

Clinical geneticists, genetic counselors, policy-makers, laboratory directors, pediatricians.

Primary Methodology:

Mixed Methods — descriptive case series of 23 IFs in 21 pediatric patients across four genomic studies,

Primary Contribution Type:

Empirical case data + conceptual framework for decision-making in returning non-ACMG IFs in pediatric

General Summary of the Paper

This study examines the identification and return of incidental genetic findings (IFs) in pediatric patients fr

Eligibility

Eligible for inclusion: **Yes**

How Actionability is Understood

The paper implicitly defines actionability in the context of IF return as the potential for a genetic finding to

> “If the finding will alter patient care… then return of the result will be useful to the provider, patient, and

> “Actionability… exists on a continuum… Actionability may also encompass… awareness… to avoid a fu

What Makes Something Actionable

- Alters patient care (management, treatment, surveillance) in a beneficial way.
- Potential to prevent adverse outcomes or misdiagnosis.
- Enables timely screening or monitoring.
- Associated with conditions where preventive or mitigating actions exist.
- Can provide important awareness for at-risk family members.

How Actionability is Achieved / Operationalized

- **Framework/Approach Name(s):** No formal named model; uses structured considerations (Table 3).
- **Methods/Levers:** Case-by-case assessment using penetrance, severity, age of onset, family history,
- **Operational Steps / Workflow:** Phenotype-independent variant analysis → classification (ACMG-AMI
- **Data & Measures:** Variant pathogenicity, disease penetrance estimates, onset age, family history, tr
- **Implementation Context:** Pediatric genomic sequencing across diverse clinical sites.

> “Laboratories… [should] proactively plan for how they intend to characterize what constitutes an IF and

Dimensions and Attributes of Actionability (Authors’ Perspective)

- **CL (Clarity):** Yes — need to differentiate IFs from primary findings, especially in young patients.
  > “…differentiating incidental and primary findings can be difficult… especially when age of onset is high
- **CR (Contextual Relevance):** Yes — family history and patient context inform decision to return.
- **FE (Feasibility):** Yes — considers whether findings are clinically manageable or preventable.
- **TI (Timeliness):** Partial — early-onset conditions prioritized; timing influences utility.
- **EX (Explainability):** Partial — cases show explanation of variant-disease links, but not a formal emph
- **GA (Goal Alignment):** Partial — return aligned with patient/family health planning and prevention goa
- **Other Dimensions Named by Authors:** Severity of disease, penetrance, personal utility.

Theoretical or Conceptual Foundations

- ACMG guidelines for SFs.
- Ethical discourse on predictive testing in children.
- Concepts of clinical and personal utility from prior literature (e.g., Bunnik et al. 2015).

Indicators or Metrics for Actionability

- Age of onset distribution for the condition.
- Disease penetrance estimates.
- Availability of screening or preventive interventions.
- Severity of condition.

Barriers and Enablers to Actionability

- **Barriers:** Variable penetrance, uncertain onset, incomplete phenotype data, potential anxiety, lack of

- **Enablers:** Clear preventive/treatment pathways, strong family history, high penetrance, severe disea

Relation to Existing Literature

Builds on debates around returning genomic findings in children, extending from ACMG SF frameworks t

Summary

This paper provides one of the most detailed empirical and conceptual analyses of returning non-ACMG i

Scores

- **Overall Relevance Score:** 88 — Strong implicit definition of actionability, rich feature set, empirical g
- **Operationalization Score:** 75 — Detailed process descriptions and decision criteria; operationalized f

Supporting Quotes from the Paper

- “[Actionability]… if the finding will alter patient care… then return of the result will be useful…” (p. 11, Ta
- “Actionability… exists on a continuum… may also encompass… awareness… to avoid… misdiagnosis.”
- “Diferentiating incidental and primary findings can be difficult… especially when… age of onset… is high

Actionability References to Other Papers

- ACMG SF v2.0 and v3.0 recommendations (Kalia et al., 2017; Miller et al., 2021)
- Bunnik EM et al., 2015 (personal utility in genomic testing)
- NCCN guidelines for cancer screening
- ClinGen Actionability Working Group protocols