

BACKGROUND

In 2020, ACMG recommended offering secondary findings (SFs) for prenatal cases targeting **Childhood Onset Disorders (COD)**. Laboratories were advised to prioritize conditions with:

- **High penetrance**
- **Moderate-to-severe clinical presentation**
- **Pediatric onset**

This study evaluates the real-world uptake and yield at a large clinical laboratory.

METHODS & COHORT

Retrospective Review (2018–2026): Analyzed **226 prenatal exomes** to evaluate requests for ACMG and/or COD secondary findings.

Disease prevalence calculation: Primary diagnostic results were cross-referenced with genes on the COD list to determine prevalence.

Lifespan Comparison: Compared findings against all pediatric and adult exomes in patients processed in the same period.

RESULTS

60%
Prenatal SF Opt-in Rate
(135 / 226 Cases)

0%
COD SF Positive
(0 Cases Reported)

2.9%
ACMG SF Positive
(4 / 135 Cases)

7.9%
Diagnosis in COD genes
(18 / 226 Cases)

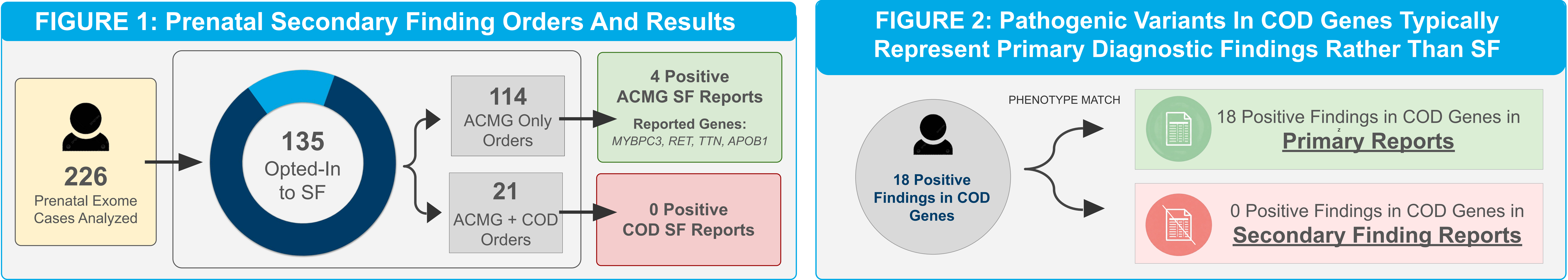


TABLE 1: Prenatal Diagnostic Results in COD SF Genes

Gene	Mode of Inheritance	Cases	Gene	Mode of Inheritance	Cases
COL2A1	Autosomal Dominant	3	CBL	Autosomal Dominant	1
COL1A2	Autosomal Dominant	2	CEP290	Autosomal Recessive	1
PTPN11	Autosomal Dominant	2	CHD7	Autosomal Dominant	1
CANT1	Autosomal Recessive	1	COL1A1	Autosomal Dominant	1
DHCR7	Autosomal Recessive	1	POMT1	Autosomal Dominant	1
GBA	Autosomal Dominant	1	RIT1	Autosomal Dominant	1

References: [1] Haverfield EV, et al. Physician-directed genetic screening for medically actionable disorders. *BMC Med.* 2021;19(1):199. [2] Monaghan KG, et al. The use of fetal exome sequencing in prenatal diagnosis: ACMG points to consider. *Genet Med.* 2020;22(4):675-680.

KEY TAKEAWAYS

High Interest in Secondary Findings: Most families (60%) chose to receive prenatal secondary findings, although only a small proportion ordered COD specifically (**Fig 1**).

Diagnostic Outcomes: No cases had positive COD secondary findings reports, but many had Positive Diagnostic results in genes on the COD SF list due to a phenotype match (**Fig 2**). This suggests that these phenotypes often present early as primary diagnostic indicators during pregnancy.

Evolving Landscape: Expect actionable SF yield to expand over time as genetic variant databases mature and refine classification metrics.