Request for secondary findings with exome sequencing in pre- and postnatal settings

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Background

- The American College of Medical Genetics and Genomics (ACMG) recommends reporting variants in 59 clinically actionable genes when clinical exome sequencing (ES) is performed.
- However, prenatal and pediatric testing for these largely adult disorders remains controversial.

Objective

- To compare the request for receiving secondary findings among a large, diverse cohort of families undergoing prenatal versus pediatric ES.

Study Design

- Inclusion criteria: non-diagnostic microarray and either a fetal sonographic anomaly or a pediatric structural anomaly or developmental disorder.
- Families counseled about secondary findings and given the choice of whether or not to receive them.
- Trio ES (samples from proband and biological parents) performed and results reported to families.

Results

- 97 prenatal and 247 pediatric families from 2017 to 2019.
- Maternal ethnicities: 46% Latina, 37% White, 10% Asian, 4% Black, and <1% each of other groups.
- Maternal age was younger and interpreter use was lower in the prenatal group.
- No difference in prenatal and pediatric request for secondary findings: 87% vs 80% (p=0.16).
- For each 5-year increase in maternal age, there was a trend towards a 10% decreased odds of request for secondary findings (OR 0.9, 95% CI 0.7-1.1).
- Secondary findings identified in 3% of cases that requested them (4 prenatal, 6 pediatric).

Conclusion

- Most families request secondary findings, and this does not differ in prenatal versus pediatric settings.
- Further research is indicated to elucidate reasons for requesting and declining secondary findings.

Most families undergoing exome sequencing request secondary findings in both prenatal and pediatric settings.

Questions?
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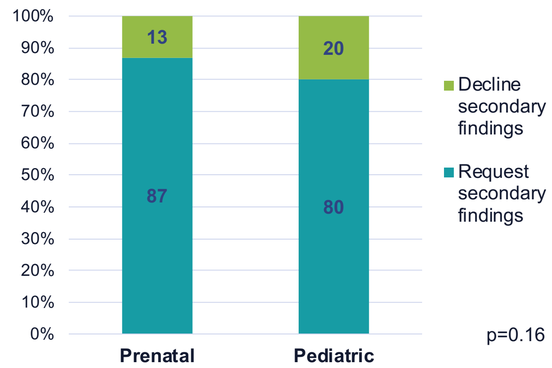
or email Dr. Sparks at teresa.sparks@ucsf.edu

Cohort characteristics, prenatal versus pediatric

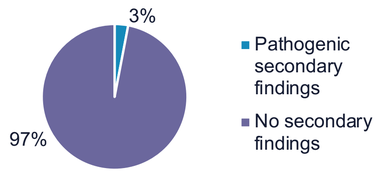
Characteristic	Prenatal	Pediatric	p-value
Maternal ethnicity (%)			
Latina	34.8	56.6	0.001
White	52.8	25.0	
Asian	9.0	10.9	
Black	3.4	4.7	
Am Indian/Native Am	0.0	1.4	
Hawaiian/ Samoan/PI	0.0	0.9	
Unknown	0.0	0.5	
Maternal age (years)	33	36	0.002
Private insurance (%)	78.4	10.5	<0.001
Interpreter use (%)	12.6	45.9	<0.001

Request for secondary findings, prenatal versus pediatric



* For each 5-year increase in maternal age, there was a trend towards 10% decreased odds of request for secondary findings (OR 0.9, 95% CI 0.7-1.1).

Proportion of cases with secondary findings



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