Title: Newborn sequencing using comprehensive genome analysis yields similar rates of findings across racial and ethnic groups: Results from the BabySeq Project

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Conflicts of interest:
RCG has received compensation for advising the following companies: Allelica, Atria, Fabric, Genome Web, and Genomic Life and is a cofounder of Genome Medical and Nurture Genomics. Nina Gold is an occasional consultant for RCG Consulting and has received an honorarium from Ambry Genetics.

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Abstract:

Newborn genomic sequencing (NBSeq) has the potential to identify apparently healthy children with treatable conditions that are not currently covered through public health newborn screening. The BabySeq Project ("BabySeq") is a randomized controlled trial of NBSeq that is partnering with communities to enroll a diverse cohort of infants across 5 US cities. Previous cohort studies have suggested that populations of European ancestries have a higher rate of pathogenic and likely pathogenic variants (PV/LPV) on genomic screening, likely due to biases in gene or variant reporting strategies. In the NBSeq context, it is unknown how rates of Mendelian disease risks (MDRs), defined as PV/LPV associated with monogenic disorders or carrier status, differ among racial and ethnic groups. We compared the frequency of PV/LPVs identified in BabySeq to evaluate differences in reporting rates between individuals who self-identify as White and those who identify as non-White. This provides initial data to understand and address potential genomic healthcare disparities as NBSeq gains traction globally.

Thus far, 224 infants in BabySeq have had genome sequencing. BabySeq currently queries 4314 genes with reported evidence of disease association. Filtered variants are analyzed for PV/LPV in genes with: strong/definitive disease association, high/moderate

penetrance, and childhood onset (plus ACMG v3.2 secondary findings). For initial analysis, we collapsed parent-reported infant race and ethnicity into 2 groups: (1) non-Hispanic White ("White") and (2) all other ethnicities, including infants of more than one race/ethnicity ("non-White") and compared the number of PV/LPV reported between groups using Fisher's exact test. We then analyzed the number of PV/LPV across all self-reported racial and ethnic identities (9 categories total).

A total of 118 (53%) of infants were non-Hispanic White, 103 (46%) were non-White, and 3 were unknown (1%). There have been 485 total PV/LPV reported for 224 infants: 32 MDRs (14%) and 453 carrier status (88%, avg 2/case). The total number of PV/LPV did not differ between White and non-White infants ($p=0.84$). There were also no differences in the number of PV/LPV across all self-reported racial categories ($p=0.89$) or ethnic categories ($p=0.83$).

In this project, rates of PV/LPV did not differ by parent-reported infant race or ethnicity. This suggests that NBSeq of >4000 genes yields similar rates of findings across infants from diverse racial and ethnic backgrounds, which is encouraging for population-wide utility and health equity.