Response to *Grosse et al.*

To the Editor: We thank Dr. Grosse and colleagues for two corrections to the introduction of our recent description of a genome-sequencing system for universal newborn screening (NBS), diagnosis, and precision medicine for severe childhood genetic diseases that currently have effective therapeutic interventions.[1] Firstly, that between 2006 and 2022, the number of core disorders recommended for NBS of dried blood spots (DBSs) in the United States—the Recommended Uniform Screening Panel (RUSP)—increased by six and not eight, as we had stated. Secondly, that between 2006 and 2018 the estimated number of infants with RUSP core conditions detected in the US by NBS of DBS increased by 207 per annum and not by 27, as we had stated.

Irrespective of the absolute increment, the expansion of NBS "one disease at a time" historically has failed to keep pace with the introduction of new, effective therapeutic interventions.[2,3] More than 700 childhood genetic diseases currently have effective therapeutic interventions.[4] The growing number of investigational new drug applications for novel gene-based therapeutics suggests that the gap between screened disorders and those that meet the principles for NBS will widen rapidly in the future.[5] Despite the expansion of conventional NBS and the growing availability of rapid diagnostic genomic sequencing, genetic diseases remain a leading cause of avoidable infant mortality in the US.[6] Population genome sequencing has the potential for transformative change in the way we screen, diagnose, and treat genetic diseases. Globally there are now at least 15 projects evaluating genomic NBS, and there is an aggregate planned enrollment of more than half a million infants (https://www.iconseq.org/the-consortium). We agree with Dr. Grosse and colleagues that it is now important to explore ways in which conventional and genomic NBS complement each other to close the gap in timely and equitable screening, diagnosis, and precision medicine for infants with hundreds of genetic diseases.

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