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Every baby deserves access to genetic screening

Genomics-based newborn screening has the potential to revolutionize healthcare, but new solutions are needed to ensure that the benefits are equitably available.

Early disease diagnosis has become ever more a priority in healthcare, and many argue that there is no better time than at the very start of life. In July 2024, Genomics England, which has been at the forefront of integrating genomics into a country's national healthcare system, announced the enrollment of the first baby in the Generation study, its flagship newborn genetic screening program that aims to sequence the genomes of 100,000 babies and return clinically actionable information to families. Similar initiatives, designed to generate evidence on the utility and challenges of implementing routine expanded newborn genetic screening, are ongoing in various other countries, including the Guardian Study, and the BabySeq 2 project in the USA.

These studies come at a time in which the scope of newborn screening, in countries where it is available, is highly fragmented. The number of disorders included in the screening panels varies across countries[1,2], including, for example, 6 diseases in Mexico, 9 in the UK, 30 in the USA and 40 in Italy. Criteria for including a disease in national guidelines for newborn screening tend to be conservative and typically include robust evidence linking mutations to phenotypes, disease severity, early onset and treatment availability. These new genomic screening programs aim to considerably expand the number of diseases screened, from 233 early-onset treatable diseases in the Generation study to returning a wider range of actionable genetic information to families in the BabySeq projects, including information on some genes associated with late-onset diseases[3].

The overarching goal of these initiatives is to prevent the lengthy diagnostic journey often encountered by families of children with genetic diseases, who typically face years-long waits and large numbers of tests before receiving a diagnosis. Early detection also opens the path to early intervention, which is typically associated with better outcomes. Recent advances in technologies such as molecular therapies and gene editing are also paving the way for personalized genetic therapies developed for individual patients in record time[4,5].

Nation-wide genetic screening, available to all newborns, could in principle also be a tool to narrow the disparities that exist in today's healthcare systems, providing to every family information about their baby's health, regardless of socioeconomic and geographical factors. Designing genomics-based newborn screening programs that bring benefit equitably to the population is, however, an extremely complex task, also given the costs, and there is an urgent need to generate robust evidence on the potential benefits and harms of the approach, at the population level, before it can be implemented more widely.

The psychological impact and uncertainty related to learning of a potentially life-changing diagnosis, at a critical time for a family, is one of the main concerns. The first iteration of the BabySeq project, which returned to families clinically relevant information revealed by the analysis of their baby's genome, including predisposition to some late-onset diseases[6], was run as a controlled trial, with some families randomly assigned to receive the genetic information and some not. The trial included questionnaires to assess the psychological impact of having this knowledge, and the study did not find negative psychosocial effects on families who received the genetic information, even when genetic disease risk was detected[7]. Although these results are encouraging, more data from ongoing and future initiatives will be crucial to ascertain the psychological impacts of expanded newborn screening.

A notable limitation acknowledged by the investigators is that the study enrolled participants mostly in clinics located in affluent areas, and people of European ancestry and high socioeconomic backgrounds were over-represented in the study. It is crucial that evidence is gathered in cohorts that are representative of the national demographic, and that the public is involved in the decision-making starting from the study design. The second iteration of the BabySeq project has moved in that direction, and the study was set up with the collaboration of a community advisory board of mothers from various community healthcare centers serving families from diverse ethnic and socioeconomic backgrounds. The Generation study in the UK was also designed following extensive consultations with various stakeholders, including bioethicists and patient advocates, once again highlighting the importance of public dialogue during the setting up of initiatives that will have wide impacts on healthcare.

A related issue is the availability of treatments, following diagnosis. In many countries, including the UK, pediatric clinics are already oversubscribed with long waiting lists, and new therapeutic modalities that hold the most promise for the treatment of genetic diseases are typically extremely expensive. If expanded newborn screening is set to be rolled out nationwide, now is the time to expand the capacity of healthcare services and ensure that treatments will be equitably allocated and available for the child's lifetime.

Although the availability of genomic data is likely to provide immediate lifesaving information for children, the impact that the existence of such data, and the way in which it will be stored and used, will have on the baby's lifetime, as well as for their family, remains to be seen. Consent provided by the family at birth might not reflect the wishes of the child in the long term — for example, wishes related to learning about late-onset disease risk. Secure infrastructure would also need to be built to accommodate the storage of extremely sensitive information. In healthcare systems based on medical insurance, an additional worry is how insurance providers would view information on genetic risk even before a disease manifests, if at all, and whether it may limit access to healthcare coverage, as it might be seen as a pre-existing condition by insurance companies, which risks widening inequalities.

Newborn genetic screening has the potential to revolutionize rare disease diagnostics, but to ensure that the benefits will reach everyone, various stakeholders need to start thinking now about how to accommodate the needs of people who receive genetic diagnoses in the long term, in terms of continued care, data protection and psychological ramifications.

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References

1. Giugliani, R. et al. *Front. Genet.* **13**, 1053559 (2022).
2. Loeber, J. G. et al. *Int. J. Neonatal Screen.* **7**, 15 (2021).
3. Holm, I. A. et al. *Pediatrics* **143**, S37–S43 (2019).
4. Kim, J. et al. *N. Engl. J. Med.* **381**, 1644–1652 (2019).
5. Dowling, J. J. et al. *Nat. Med.* **30**, 1882–1887 (2024).
6. Pereira, S. et al. *Genet. Med.* **25**, 100002 (2023).
7. Pereira, S. et al. *JAMA Pediatr.* **175**, 1132–1141 (2021).