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Should whole-genome sequencing become part of newborn screening?

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Should whole-genome sequencing be used in the public-health programs that screen newborns for rare conditions? That question is likely to stir debate in coming years in many of the more-than-60 countries that provide newborn screening, as whole-genome sequencing (WGS) becomes increasingly affordable and reliable. Newborn screening programs – which involve drawing a few drops of blood from a newborn's heel – have been in place since the late 1960s, and are credited with having saved thousands of lives by identifying certain genetic, endocrine or metabolic disorders that can be treated effectively when caught early enough. Advocates of routine WGS for newborns argue that the new technology could help detect and manage a wider array of disorders.

But the possibility of making whole-genome sequencing part of routine screening programs for newborns raises ethical, legal and social issues that should be weighed carefully, according to researchers at McGill University's Department of Human Genetics in Montreal.

In an article published March 26 in the journal *Science Translational Medicine*, Prof. Bartha M. Knoppers and colleagues lay out key questions and considerations to be addressed. "Any change in newborn screening programs should be guided by what's in the best interests of the child," says Prof. Knoppers, who is Director of the Centre of Genomics and Policy at McGill. "We must also tread carefully in interpreting the scientific validity and clinical usefulness of WGS results."

The researchers outline the following considerations:

- **What information to report?** Using WGS in newborn screening could generate vast amounts of information – including incidental findings such as paternity information or reproductive risks. What's more, health-related information can include non-validated or poorly predictive results, or may involve adult-onset conditions. One possible solution: perform WGS but have a list of pediatric conditions to be communicated to parents; other results could be retrieved for later disclosure, when they gain scientific validity and clinical usefulness, or when they can be reported to the "mature" child directly.
- **Impact on health care systems.** If WGS in newborn screening is implemented, public health care systems would have to be revamped to handle the massive amount of information generated. The added information could also lead to more false-positive results, imposing a big burden on families and on the resources of a health-care system.
- **Mandatory vs. voluntary.** Most newborn screening programs currently are mandated by law or use presumed parental consent. Should parental consent be required for screening that doesn't stand to directly benefit the infant during childhood?
- **Educating health professionals and parents.** Many doctors have little training in genetics, so health professionals and parents will need more education in genetics and genomics.
- **Communicating results over time.** The validity of tests and the communication and understanding of results over time pose numerous challenges for doctors and families.
- **Ensuring treatment and follow-up.** When treatment becomes available, a newborn screening report card would be invaluable on an individual basis, especially for single-gene disorders.
- **Validated variants.** An important challenge in WGS is the ability to offer a standardized and accurate interpretation of

genetic variants.

- **Storage of data.** Should raw data be stored in the patient's file? If so, under what conditions and for how long?
- **Insurability.** Data obtained through WGS newborn screening would be part of the medical record, potentially leading to issues regarding insurability.

"Without clear policy direction and public discussion on the possible future integration (or not) of WGS into newborn screening, more parents in years ahead may choose to pay for whole-genome sequencing through private testing services," says article co-author Karine Sénécal, an academic associate at the Centre of Genomics and Policy at McGill. "Medical and public education programs need to be put in place so that people understand the limits of whole-genome sequencing."

More information: "Whole-Genome Sequencing in Newborn Screening Programs," by B.M. Knoppers; et al. *Science Translational Medicine*, 2014.

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