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Extended Research Article

Evaluating whole genome sequencing for rare diseases in newborn screening: evidence synthesis from a series of systematic reviews

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Plain language summary

Evaluating whole genome sequencing for rare diseases in newborn screening: evidence synthesis from a series of systematic reviews

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Plain language summary

The government has funded a research project that tests newborns' entire DNA sequence (whole genome sequencing) for over 200 rare conditions, before babies appear to be ill. This could be a new screening programme. Policy-makers need a way to assess, for all 200 conditions, whether it improves lives and is a good value for the National Health Service.

Whole genome sequencing detects variations in our DNA. We all have many variations. They make us unique and only a few cause harm. It is difficult to predict true disease from a genetic finding. A baby may have a variant that looks harmful, but that does not mean they will develop the associated disease. Using whole genome sequencing to detect harmful variants could provide health benefits. Whole genome sequencing may also cause uncertainty and anxiety in parents and perhaps harm babies by giving them unnecessary treatment.

We assessed:

1. examining evidence from research studies to assess whole genome sequencing separately for 200 conditions by sampling 5
2. measuring uncertainty when predicting any condition from genetic findings
3. using an online resource with information on genetic conditions as evidence.

We also looked for, but could not find, studies that weighed up the cost and health implications of implementing whole genome sequencing in screening.

We met five times with parents, expectant parents and charity representatives to explore the challenges of whole genome sequencing. Challenges include communication, consent, data security, privacy and uncertainty.

We found, that:

- there is insufficient evidence for the five conditions to inform policy
- it would take 23 years to assess 200 conditions
- studies using whole genome sequencing only report the number of variants detected, not how well these predict disease
- the online resource does not have good quality evidence for screening policy.

None of the three approaches is currently useful for evaluating the benefits and harms of whole genome sequencing. We first need to collect more evidence.

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This article

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