# THIS WEEK

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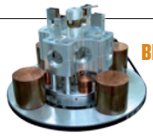

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# Sequenced from the start

*Four US studies are set to explore how genomic data can best help healthy and ill newborns. They must also settle some questions of ethics.*

Genetic sequencing has established itself as a powerful tool for diagnosis, but it is not yet clear how useful it will be for disease prevention or health management. A US$25-million project announced last week aims to explore that issue in perhaps the most high-stakes patient group: newborn babies.

In the Genomic Sequencing and Newborn Screening Disorders (GSNSD) programme, four teams will sequence the exomes — the protein-coding portions of the genome — or the whole genomes of more than 1,500 babies, including not only infants who are ill, whether or not the disease has been diagnosed, but also healthy babies. The programme is funded by the US National Human Genome Research Institute and the Eunice Shriver Kennedy National Institute of Child Health and Human Development (NICHD). The studies will examine how useful sequencing information is for families and doctors, and whether it is superior to data gathered through conventional newborn-screening methods, which check for about 60 genetic disorders.

The project joins a short but growing list of studies testing the utility of clinical sequencing in otherwise healthy individuals, but it is the first to focus on healthy and ill babies. As such, it will highlight five hot questions.

First, do we yet know enough about how genes code for health to make genomic data useful in preventing disease? Studies have found that sequencing can diagnose 15–50% of children with otherwise undiagnosable illnesses, but no one has yet asked what use it has for healthy children. Not all genetic traits will influence a person's health, and it is still not possible to say with any certainty what a given genetic variant will mean for a given individual.

Second, what kind of genetic findings should doctors return to patients, and does the answer differ between children and adults, or between ill and healthy people? The family that is unsure whether its ill baby will live or die is not in a good position to absorb information about a hypothetical future cancer risk. The family that has a baby's genome sequenced just to see what might be found may spend years worrying about that cancer risk in their perfectly healthy child. The key will be to find the children who will best benefit from this knowledge, because their individual disease risks are real enough that routine screening could save their lives. In the US health-care system, which is prone to over-diagnosis and over-treatment of cancer, for example, this is a tricky balance. Some of the GSNSD projects will check babies' genomes for genes not linked to any immediate illness, although each study is taking a different approach to how it will inform parents about risks.

Third, what is the quickest and cheapest way to conduct clinical sequencing so that it returns accurate information to patients in time to influence care decisions? Increasing the number of conditions being screened for will necessarily cause more false positives — as many as 20 for every true positive, according to one estimate. Those false positives will lead to increased medical costs and anxiety for families.

Fourth, who owns the genetic data? None of the GSNSD studies plans to give the raw genetic data to the children's families, even though that could allow the children to benefit from it throughout their lives.

Finally, should the data be shared with other researchers? This would be the best way for scientists to help tackle the tough question of how genes contribute to disease. But it is increasingly difficult to guarantee the privacy of genetic data (see *Nature* **493,** 451; 2013), and this is an important issue for babies, whose information will be known for their entire lives even though they themselves have not consented to the disclosure. One of the GSNSD projects will share data with the NICHD's Newborn Screening Translational Research Network, and another with the National Center for Biotechnology Information's Database of Genotypes and Phenotypes. The other two are still deciding.

***"The day when all children will be sequenced at birth — if not before — draws ever nearer."***

As researchers explore these questions, sequencing costs continue to drop and the day when all children will be sequenced at birth — if not before — draws ever nearer. Some people are wary of this, and are already warning of the dangers of what they consider to be a government-funded plan to store all citizens' data. If newborn sequencing is to fulfil its potential to save many children's lives, it is imperative that scientists get the ethics and the science right. ■

# Under threat

*The grey wolf is at risk of losing its endangered status under US law.*

In the mid-1990s in the United States, several courts were asked to decide whether wolves were illegal immigrants. Ranching groups that were against the proposed reintroduction of the wild animals to Idaho, Wyoming and Montana were trying to block their transport across the border from Canada. The appeal failed and the foreign wolves were delivered and released.

In recent decades, many more in the legal profession have become familiar with *Canis lupus*. The grey wolf, and its place in the US landscape, sharply divides opinion — both scientific and political. Broadly speaking, conservationists want the wolf population to expand into its historical range, whereas the ranching community is anxious about large numbers of a top predator roaming free. Both sides can point to scientific research and ecological opinion to support their stance.

The battle over the fate of the grey wolf is gearing up for a new conflict, perhaps the most significant yet. As we report on page 143, the US Fish and Wildlife Service (FWS) has extended the period for which