About the principles

Audio transcript

Slide 1

Hello, I'm Amanda Pichini. I'm the Clinical Lead for Genetic Counselling at Genomics England, working with the Newborn Genomes Programme.

And hi, I'm David Bick. I'm a doctor with several decades of experience in diagnosing and treating people who have a genetic condition. I currently work as a clinical advisor for the Newborn Genomes Programme.

With David, and others at Genomics England, we're working to establish how we can best use whole genome sequencing in newborns to test for a wide range of conditions that affect babies and young children.

But we can't do this by ourselves. We need your help in one key respect: helping us to establish how we choose which conditions to screen newborns for.

As you heard in the previous video, whole genome sequencing allows us to look for hundreds of conditions at once. But just because we can look for many, doesn't mean we should; we have to balance the potential benefits against possible harms.

To do this, we've worked with a group of experts to develop some draft principles to help guide us through making choices about which conditions to screen for. There are five draft principles in total. We'd like your views on whether these principles are the right ones, if they miss anything out, if they make sense, and if they're easy to understand.

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The first important thing to note is that screening isn't new. And, because it's not new, there are already principles and criteria which help screening programmes to decide which conditions should be screened for.

We have taken these existing screening criteria into consideration to develop the five principles we'd like your feedback on.

But, because the Newborn Genomes Programme is doing something quite different to previous and existing screening programmes it's right that we take a bespoke approach to our underpinning principles. At the heart of this is the need for the Programme to make sense to the UK families who will be part of it, especially because this is a research programme. Repurposing pre-existing screening principles is therefore not quite enough. Some fresh thought is needed.

[Amanda Pichini] As well as the need for the principles to make sense to UK families, the principles also have to help us provide a balance. This includes avoiding telling parents that we think that their child has a condition that they don't actually have – which is called a false positive. But, we also need to take care to avoid missing cases – that is, a false negative result.

The principles are also important in helping us to steer a course in understanding the overall benefits of helping babies with a treatable genetic condition, and how those benefits should be weighed against associated risks and costs. These include financial costs, impacts on health services, and emotional costs to families.

Our aim is that the principles that we will now explore and explain will help us in this balancing exercise.

Before going into detail on each of them, it's important to say that no one of these principles outranks the others. They come as a group, which means it's important that they all complement each other to cover the different ways that we need to make decisions about which genes to screen for.

Audio transcript

This is why it's so important you give us your feedback. We'll tell you a little more about how you can do this at the end, but for now – onto the principles.

Slide 3

[David Bick] Principle A requires that the genetic variant should only be included in the Newborn Genomes Programme if there's strong evidence that it causes the condition.

Each rare condition we could look for is caused by a gene with many different possible changes – the scientific term for such a change is a 'variant'. Some of these variants mean that the gene won't work properly. There are also gene variants which we know definitely don't cause disease.

However, there are some gene variants where there's less certainty about whether they do, or don't, cause a condition. This might be particularly challenging if a baby has no symptoms.

In this context of uncertainty, it's therefore really important that we look for gene variants that we know, to the best of our knowledge, will cause a condition. In other words, that we only screen for gene variants that would make a newborn or young child sick. This is the crux of what Principle A is focused on.

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[Amanda Pichini] For Principle B, you'll see that there are areas of text highlighted in red. These indicate that we would particularly welcome any views you might have on the red text here.

More generally, Principle B holds that a gene variant should only be included in our programme if individuals who have that variant would be expected to have symptoms that would significantly impact their quality of life – if it was left untreated.

So what's the rationale for including this principle?

First it's important that we only search for serious conditions that could significantly impact on the baby's quality of life.

Quality of life can be calculated according to a concept known as a quality-adjusted life year – which is also known as a QALY. For example, a QALY might measure the extent to which a person can carry out activities of daily life, free from pain.

Often QALYs are not well established for rare conditions or do not tell the whole story, and therefore we also need to take into account the testimony of the families who are affected by them.

It is important to note that while we can be really picky about the gene variants we look for (as described in principle A), there may be uncertainty as to how old the child will be when the condition starts to develop and the extent of their symptoms. For some conditions, the outcome will be pretty consistent in all children who have it, and in others the condition can look very different even in members of the same family.

The principle also demands consideration of a second factor. This focuses on the fact that, if left untreated, symptoms would typically start in childhood. Again, we would welcome feedback on the parameters we should set here – as shown by the red text.

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[David Bick] Principle C focuses on whether treating the condition early, or before symptoms develop, has been shown to lead to improved health outcomes for the child. It asks us to compare this with the situation for a child who receives treatment after the onset of symptoms.

Audio transcript

There are a few points that highlight why we've included this principle.

First, we need to know if it's better to identify and treat children before they become ill, rather than managing their condition after they've already presented with symptoms, and have been diagnosed. This is important because screening has to have a purpose – if it is used to identify conditions that could be treated optimally after symptoms appear, then its purpose is undermined.

The criteria set out for this principle focus on thinking a little more about what 'treatment' should encompass in this context. This is because we know that there are many ways to consider what a treatment or intervention means. We'd welcome your views on this, and the three criteria we've set out to establish this principle.

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[Amanda Pichini] Principle D determines that a minimally invasive confirmation test needs to be available to establish whether the child has the condition. This principle therefore focuses on what happens after a child has been screened.

There are several reasons that this principle is important.

For example, we can be really confident in the genetic results that are fed back to parents. But because we are offering a new screening test it's important that we follow up with a test to make absolutely sure that our results are right. To do this, the principle holds that the baby should have a test that a doctor might typically use to diagnose that condition. This already happens with other screening tests that are currently offered to babies.

Underpinning this principle is a need to provide parents with a clear 'yes' or 'no' answer – research on this tells us that parents want such a yes or no answer, and value not being left in a position of uncertainty.

The method through which this confirmatory test is offered is also important to consider. Carrying out a blood test or x-ray in a baby is a very different prospect to performing a biopsy – where you have to insert a needle into an organ. This is why this principle focuses on the need for there to be a minimally invasive test.

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[David Bick]: Principle E focuses on the need to screen only for conditions that have interventions or treatments available to everyone who uses the NHS – that is, where access is equitable. For example, this means that it should not matter where in the country the baby is diagnosed – the intervention has to be available to all.

The other aspect of this principle focuses on 'socially acceptable interventions'. Again, we would welcome your views on what this term might mean in practice – for example, should we only test for conditions where the treatment offered is standard care in the NHS? Would it be acceptable to test for a condition where the only intervention available is an experimental treatment or a clinical research study in the NHS?

Again, at the heart of these principles are parents and babies – and the recognition that parents should be able to access support and interventions if screening indicates that their baby has a treatable condition.

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[Amanda Pichini] Now we've taken you through the five draft principles we've developed, we need your help and views on them as they currently stand. And please remember that these principles come as a group, which means it's important they complement each other.
To give us your views, please respond to our survey which is linked to on our website. Once the survey closes, we'll analyse what you've told us and assess what your feedback means for these principles, and the conditions they will help us to choose to add to our programme at present.

In the future, as our knowledge of screening newborns using whole genome sequencing develops through the research programme, we might need to revisit these principles to test if they remain fit for purpose.

In addition to the survey, we've also developed a series of case studies if you'd like to know a little more about what newborn screening might mean for parents and babies.

If you have any questions about the survey, or the work of the Newborn Genomes Programme more generally, please contact us at: ge-newborns@genomicsengland.co.uk

Thank you.