Expert Q&A Sessions

Researchers' note: *This document contains materials generated during the Zoom session with the experts. The first part is the transcript of the live Q&A session. The transcript has been de-identified, and slightly edited for ease of reading. The second part contains the expert's response to additional questions that were not responded to during the Zoom session. After the Zoom session, these questions were collated and sent to the expert who was given a few days to provide a written response.*

Date of Zoom session: Sunday, 9 March 2025

Expert: A/Prof KaustuvBhattacharya, University of New South Wales, Sydney

Children's Hospitals Network

Title of presentation: Introduction to newborn blood screening (NBS)

PART 1: Q&A TRANSCRIPT

Juror: First off, I have two children, one's 16, one's four. And yes, we have done the blood spot screening programme. So, I have a little bit of an idea because the second one had jaundice and everything. So, we had a little bit more blood tests, and it's not quite the conditions that they all test for, but, you know, they do go, Oh, yeah, look, you got jaundice. So, I'm very grateful for that. That helped a lot. What I'm asking about is, have we done any genome testing with newborns already? I thought I saw a sentence in the book. And what has that brought to light and how was that received and that kind of thing?

Kaustuv: So, there's lots of genomic newborn screening research studies across the world. But as a research study, they're not rolled out for the population for general consumption. So, there are research studies that are looking at it and looking at the consent process, the results processes, which genes to look at. So, there's, there's quite a lot of complexity around this research, but nothing has really been rolled out anywhere in the world yet.

Juror: So I was just wondering like we've we've done something, I'm sure we've done something

Kaustuv. So we were doing, but we, they're research studies, so they're self limiting and people are trying to learn from them, but they're not done. They're being analysed.

Juror: So we've got no information yet.

Kaustuv: We've got some information, but it's an ongoing process for the next few years.

Juror: I've got two questions. First of which is how is a valid test determined? Like how do you define a valid test? And the second question is with regards to samples, what happens to them? Where do they go? Where are they stored? Are they stored, are they destroyed? Because there are obviously security concerns around the samples and what's done with them. Once the person has given the sample to to the doctor and or the clinic, they, they don't have any control after they've let go of that sample.

Kaustuv: So, the first, the first question is a valid test. And I'm going to broaden this out to another screening test, say breast cancer screening. OK. So for breast cancer, there's an x-ray that's performed and then that's a screening test. And there's a valid test to identify things that can then be biopsies to look for breast cancer. So, the diagnostic test in that case is a biopsy and the screening test is an, is an x-ray. So in order to validate a test, it has to reliably pick up what you're looking for. and the process of that is there's something called sensitivity, which means how reliably it picks up and specificity,

which is when you pick something up, does it pick up 15 different conditions And you really want a sensitive and specific test. And there's mathematical sort of equations that allow you to be as high, as high sensitivity and specificity as possible. That's the first thing.

And then in terms of storage of data, so these programmes are actually run by the states. So, each state essentially or jurisdiction sends the samples to centralised laboratory. There's only 5 in Australia and there are different consent processes and those are now being tightened in terms of how long, how long the samples are kept for. And they can be destroyed immediately or kept for two years or kept for 18 years. And there, there are different processes in the different jurisdictions and the data is held by the government or the state within the laboratory. In some instances, like if there's a baby that dies, you can go back and find out the cause of death from if you if you for the for the baby that dies early, say, for instance, through consent processes.

Juror: Yeah, I guess my, my question was twofold, because there's the, the issue of the actual sample and then there's the issue of the data collected from the sample. So they're closely related, but they're both sort of like security questions.

Kaustuv: So the data can be destroyed when you consent. I know most about NSW. If you want the card to be destroyed, the card and the data will be destroyed. I guess the data's de identified. So, the data will be kept, but the identification with the individual will be de-linked.

Juror: I'm sorry, that's the interesting thought thing I read going through this book a bit earlier was to that last comment where you said it's de-identified in the book where it says not all of the information can be fully de-identified. How much information can you still ascertain someone's personal identity with that information?

Kaustuv: So, for each card, each card has a, a code and is linked to an individual. And if the person wants their data to their cards data to be destroyed, then the link between the number and the individual is destroyed. OK, That's what's taken out. So, the data is still there and, and part of the reason for keeping the data is to look at the performance of the individual test. If you want to compare say all things are mechanical and if there's deviation over a period of time, we want to track that deviation. So, the data itself as a whole for 300,000 babies in terms of looking at any shifts in patterns, populations, things like that, that's actually important from a trend perspective, but it doesn't actually need to relate to an individual.

Juror: And the other thing as well is say for example, you have your data stored and it's still identifiable. What would stop a future government changing the policy like with the metadata heads that their policy are brought in with that they kept scope creeping like other additional governments having active information. Say, for example, if in the future they allow, say the police to access that information, would there be any way of safeguarding that data?

Kaustuv: Well, I can't, you know, I mean, it's a difficult question for me to answer, but at the moment there's several tier consent process or there's a consent process that's directly for the conditions that are target conditions. And each, each line consents for a different thing. And if you wanted, if, if you wanted the card destroyed or you wanted the data not to be identified, you have that right. If you didn't want de identified research. So de identified means that this is kind of what I was saying that you, you know, you've got the data, but you don't have the, you don't know who it, who's it from. You can consent for that as well. So what a future government does, I can't tell you, but this is this is I mean, Australia's quite a well regulated country. So I don't imagine that that's happened. It certainly hasn't happened in the last 40 years, 50 years actually of screening.

Juror: So as it seems like from the video that we watched earlier, it seems like the number of things you can test for went up from 50 to over 1000. Has that extended the sort of strain on the individual when they're being tested or what form does that testing take place?

Kaustuv: Sorry, I just to say that it's currently around 50 and the potential for more , they'll talk about this when with future talks, of the potential for dynamic testing is to really expand that well beyond 50. And what the number eventually could be or should be is yet to be determined. And that's something that you'll be considering over the next few weeks, but currently it's 50.

Juror: If there's this possibility of testing for all these different genetic conditions, how would they be prioritised? And would that be connected to how urgent they were to treat?

Kaustuv: Well, I think that , it's difficult to prioritise. That's the first thing. And, the prioritisation is, is an issue that I think is yet to be fully determined. But the factors that determine prioritisation is how treatable it is, how reversible the condition is, how expensive the treatment is, is there anyone available to do the treatment. So instead of talking abstract, say for instance a gene therapy might cost say $10 million for a condition which could actually divert funds from one area of health to another. And so there has to be a cost-effectiveness type of consideration for that kind of situation. So those are those are t the factors that come into this determination. And if you're just going to prolong life for a year, and even though that year is very important to that individual, is it worth the budget for the health system to spend say hundreds of millions of dollars for that year of life? And these are difficult questions, but have to be determined by ethically, cost-effectiveness data driven as well. So,there's is not just a straightforward answer.

Juror: My question is around the government run and government payment. So has the government indicated that they would be open to assisting with funding so if we did increase it up more? And then you know being that you know, you talked about state run and the labs etcetera by being informed you know by the government of the day per se and then obviously your child then needs assistance following that with connecting to specialists etcetera. Is there an expectation around government funding?

Kaustuv: So I think that that that is an open question. So part of this research is to determine that.. I mean, the government hasn't committed to anything at the moment in terms of these tests, treatments or health infrastructure. There's no commitment whatsoever to those things. But these are things that need to be determined as part of the what needs to be considered for an approval for the test to actually roll out. OK, so that's why you're here. And that's, that's possibly the crux of the issue really.

Juror: Just can I ask the following question? It's stated around the three-week age for treatment at the moment. Has that been maintained where it's been identified that a baby may have one of those conditions and that you have done it within the three weeks? Is there any cases of where it's taken currently longer than.

Kaustuv: Yes, it can take longer and the rarer the condition, the longer it is to ascertain what the actual condition is. It can take longer, but the results, results are currently reported quite quickly. So the objective is to do it by 20 days and such that intervention for those early onset conditions can start at that kind of time period. But you're right in considering that maybe there are other conditions that have an onset later on where you might have more time and you can take more time to think. And then what do you do then? Like the issue then is what do you do with the data? When do you notify? Who decides when you notify? So it becomes a more complex issue if you delay disclosure of the result.

Juror: So at the moment for testing for sort of 50 different conditions or diseases and you get about a one and 1000 come back as a positive. If you're then testing for potentially 1000 different things, do

you have any idea what the expectations of the positives are going to be in that number? And will we be overwhelmed?

Kaustuv: I think the potential to be overwhelmed is real and again, that's part of the reason why you're considering these things within the broader context of the healthcare system and the priorities of that healthcare system are part of this consideration.

[end of transcript]

PART 2: RESPONSE TO ADDITIONAL QUESTIONS

***Q**: So I have some existing questions from the booklet. What do we currently tell parents and who tells them? Do these tests take the same time to do and in the same way? How long does the test results take in both test the biochemical and genome? Are they done at the hospitals? Why do we only test 99%of babies currently not 100% is it a opt out system?*
Answer:

There are resources available online, booklets issued and information on both state and federal websites. It's not clear how many people access these resources:

https://www.health.nsw.gov.au/kidsfamilies/MCFhealth/Publications/new-born-bloodspot.pdf

https://www.health.gov.au/our-work/newborn-bloodspot-screening/what-is-screened

Generally most tests are completed by day 20 of the baby's life.

Genome is not done anywhere in the world as a routine but lots of groups are doing research to see if they could do newborn genome screening. Research means that it is only done for a period of time in people that consent to do it. The testing stops at the end of the research period – for example one year, the results are analysed and people the decide whether they implement the test. The whole process may take 5 – 10 years from a research study to implementation even if the research test was only performed in the first year.

We have an opt in system – you have to tick a box on a card and sign to say you want the test.

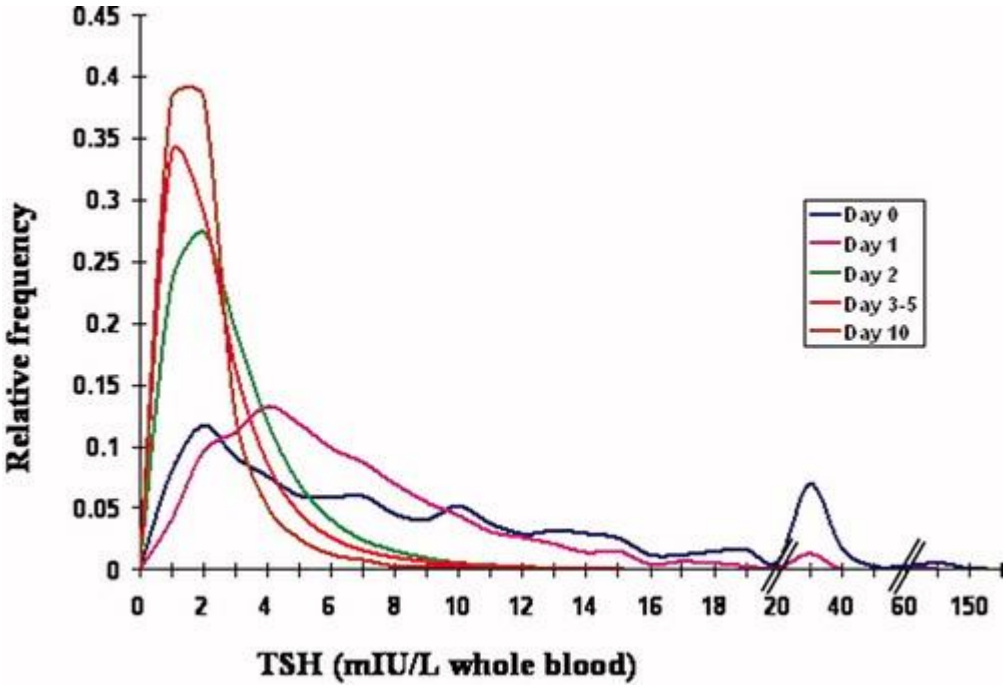
Currently about 99.5% of parents opt in and 0.5% opt out across a screening population of 300,0000 babies per year.

***Q**: Will we still do the biochemistry test if the genome test is done?*
Answer: Yes

[Note from research team: This question will be discussed by Dr Kristen Nowak during Zoom session 2 on the 16th March.]

***Q**: You mentioned we must reduce false positive results, what are we doing to reduce these?*
Answer: For biochemical tests eg TSH for hypothyroidism we can have a graph like the one overleaf:

Current Opinions Newborn screening
Bridget Wilcken &Veronica Wiley
Pages 104-115 | Received 16 Aug 2007



High levels of TSH are more likely to have low levels of thyroxine (hypothyroidism) so from the graph above you have to select a level above which you call the baby back. Let's say above 20 the test can be considered 100% specific to identify hypothyroidism – that is everyone we call back has the condition.

Where you draw that line (the cut-off) determines how sensitive the screening test is. (That means are we picking up all the cases we want to). Let's say we draw the line at 10– we will have 100% sensitivity but maybe half of the people screened called back don't have hypothyroidism. If we want 100 % sensitivity in picking up cases we will also decrease specificity (meaning we will pick up false positive cases.). Labs determine the cut-off by looking at a compromise position between 100% sensitivity and 100% specificity.

***Q**: I have a few questions. Does heritage change what disease are run or how the tests are run? How much strain will be put on the health system to treat all the new conditions being tested and found?*

Answer: Your ancestry determines your genetic traits. We can't take all that information for a test that runs on 300,000 babies per year. This is more of a public health determination – what tests do we run that benefit the whole community based on current healthcare structures. Every new condition will put a strain on the public health service – but how much strain depends on the condition, treatment and follow up.

***Q**: He mentioned about prolonging life for a year and is it worth it. There are many cases of someone is giving say 6 months to live and they wind up living another 5 years. Is saying they will only have their life prolonged by a year a form of bias stopping someone getting the treatment they need?*

Answer: That's a different to scenario to what we are discussing. We are discussing testing healthy newborns – we do not know what conditions they do or don't have. The question is more when you

have a healthy newborn, should we identify a condition that we cannot treat – if we identify a fatal untreatable condition in a baby – the baby may survive 6 months of 5 years as you say, but should we be identifying that and discussing that in the first 3 weeks of life? That's really something for the jury to decide on.