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, 16 March 2025

Expert: Dr Kristen Nowak, WA Department of Health

Title of presentation: How genomics could be used in Australian Newborn Bloodspot Screening

PART 1: Q&A TRANSCRIPT

Juror: Hi, Kristen. Now you've raised some awesome points along the video. So I'm really, really grateful that you did stuff like that. What I'm concerned about, my husband is a computer programmer and he has worked in security even up to AI security kind of thing like bit out there, which is fun stuff. Now, have we thought of a timeline of how long this is going to go because like as in to set it up infrastructure wise? Because this seems like a lot like not just a tiny little programme, it's going to be huge. Have there thoughts of, you know, that kind of stuff going on at all?

Kirsten: So at the state and territory and Commonwealth Health Department levels, genomic screening has not been purposely deliberated as yet. Although, each of the individual labs may have this possibility on their horizons. And obviously data security and storage are something that's really important within all health systems and within pathology labs. Obviously storing genomic data at scale for a whole subpopulation (like I mentioned, 300,000 babies per year), that to my knowledge hasn't been considered as yet. Then also how long you would store the data for? There's accreditation requirements and quality assurance for laboratories and they will have to keep their data for a certain amount of time. But I guess these data may become more important as time goes on as well. Those types of conversations have not yet occurred as far as I'm aware, but they're really important considerations. So that would be something that would be needed to be prepared and set up and decided upon before any programme or newborn screening using genomics would start in the country.

I'm not sure if I've answered that sufficiently. Basically, we really haven't started discussing how this is going to go. So yes, I think if we're going forward with genomic newborn screening, we will need to have more information about all these aspects. Thank you for your question.

Juror: You brought up some wonderful points, I must admit. But I do tend to query because sometimes when you go back to the beginning, you find the answers of where to go now forward. So what? What initially did the spot baby spotting start? Why did it start and then that, yeah, so sometimes you got to go back to the beginning.

Kristen: In Australia, the newborn blood spot screening programmes started almost 60 years ago. So, they're very tried and tested and the principles are the same as what I mentioned in those two frameworks that we have in Australia for population screening more broadly and then for newborn screening. So, it's about detecting babies hopefully before any symptoms arise, or symptoms that aren't overt, and being able to intervene in various ways. It might be to avoid certain aspects of food or it might be that there is a gene therapy, those types of things. It's to try to alleviate the disease as much as possible. And that's been the conscious purpose - that there is a benefit to the child in identifying that disease before the symptoms become overt.

Juror: Hey, thanks for the video. The question that I wanted to ask, does most of the cost from like the new programme like genomic sequencing, is it manual work or is it like automated, like compute?

Kristen: Yeah, that's a great question as well. So, traditionally genetics and genomics have been more manual because it is usually a very small number of patients being tested or even one patient at a time. But over the last few years, as genomic technology has advanced rapidly, genetic and genomic tests are looking at many more genes at once, and for more and more patients and people (hey might not necessarily be a patient yet - they might not necessarily have a disease. The tests might be predicting a disease). Many more people are becoming eligible for genomic testing. Robotics at scale, laboratory processes are becoming used more than ever in laboratories. I did just touch on it very briefly in the presentation is that we will likely to need, if we're looking at 300,000 babies and potentially multiple genes, we probably will need quite a deal of automation in the laboratories doing those tests. And then there's the analysis as well. The genomic information that can be created can be quite complex. To have one laboratory scientists looking at the data would be very cumbersome. So, they would have some bioinformatic processes to speed that up. You're very much on the money there with your question. There will however still needs to be humans to be able to do certain aspects of data interpretation. But I think with the automation, it will obviously speed things up. It will make things more efficient, but it also can reduce any differences that different humans may potentially introduce. So that would have to be, I think, something that would need to be put in place just to make sure that analysis can happen in the time period that would be needed for newborn screening.

Juror (via chat, read by facilitator): So the first text question, Kristen, is during the jury process, would it be possible to access a list of the diseases that would potentially be looked for if we used a genomic approach? And do we know there's particular diseases that might be identified as kind of having more value for money or being a better test to choose?

Kristen: I'm not sure if I could answer that in terms of the list of diseases for this jury process. I think one of the staff looking after the jury would need to answer that. There are lists that are currently being looked at a research level. But as I said before that the States and territory health departments and the Commonwealth Health Department are not actively discussing this topic just at the moment. So, there is not a list that we would have available, but there may be one from research that might be able to be shared to show the tests that are being considered. I think mostly the diseases being researched are those that fit the framework principles that I've just touched on before. So those that are usually screened are normally early onset conditions, and normally ones that would have some type of intervention that could be provided to that child in the family. But I guess the genomic testing, because it can look at many hundreds of genes at once, potentially those principles could be loosened a little. And I think that is something that we are looking at nationally at the moment.

With the biochemical testing or just doing 1 gene test at a time, would a disease that maybe might not present until 8 or 10 years of age, would that still be eligible? What if the intervention worked for some babies with that disease but maybe not all of them - would that still be a disease that we would consider? Sometimes diseases are not what they call fully penetrant. What it might mean is some people with that gene defect or gene error might get that disease, but some people don't, and it might be due to a reason we don't understand yet or maybe they get the disease in their 30s or 40s or they get a much milder disease. So, these are all considerations that we are having with the traditional current newborn screening. I'm imagining these would be very, very important aspects to consider for genomic testing as well. With biochemical testing you can look at many biochemicals at once, it's quite cheap and effective. Compared to biochemical tests, genomics testing is at the moment still a bit more expensive, but it is coming down in price almost year upon year because the technology is getting better. But you may have heard already, some diseases can't be picked up by the biochemical methodology, whereas they could potentially be picked up by genetic testing. So genetic and genomic testing would offer additional ability to pick up extra conditions that can't be done by the other methodologies that we use now.

Juror (via chat, read by facilitator): [Juror's name] had had asked a similar question actually that is the testing going to be appropriate for people from from First Nations in the programme, do you think, Kristen?

Kristen: Yeah, it's a really, really important consideration because we want any new programmes, especially when they're looking at population levels, to be as equitable as possible across all ancestral backgrounds. At the moment there are not genomes for Indigenous peoples in Australia that are readily available for us to compare. So, when we do a test in genetics or genomics, there are lots and lots of different variations and we will compare those to a reference, a so called reference genome. And if we see those variations at 5 or 10% of the population, we know that they're likely not to cause a disease. Too many people are walking around with these variations and they don't have those diseases. We would instead be looking for very rare variations. But some of the sequencing projects that have looked at First Nations peoples have found that their variations have never been reported before in European or Asian populations. So, we just don't know how to interpret these variations at this stage and we don't have a good understanding whether certain variations are fairly common in that particular Aboriginal community or a certain variation is a very unique one and it is linked to disease. We anticipate that we'll be able to see some variations in Indigenous peoples and others with culturally, linguistically and diverse backgrounds that will be obvious that they ares such a big variation in that gene that they're likely to cause disease or we have seen them in other genomes before. But we are imagining that there will be other variations that we just don't know how to interpret yet. But as I previously mentioned, the more and more we get more information about First Nations people, the better understanding we all will have on how to interpret those variations. I'm sorry, I hope I didn't get too technical there, but it's quite complex. But we're still at a tipping point, I think to be able to provide the best interpretation of those variants for these populations at the moment.

/end of transcript

PART 2: RESPONSE TO ADDITIONAL QUESTIONS

Q: Would the costs go down over time? do the current biochemical test get done by private companies? I'm kinda fine with a rollout across the country in stages based on population at hospitals where babies are born? I think it should be for the child as what would happen if the baby is not from the father

Answer: It is quite likely the costs may go down over time as DNA technology has had a trend of doing this as the technology has improved. However, how much costs go down or when this may be is not known.

No, the current biochemical tests are performed by state (publicly funded) laboratories.

Currently, babies born in all hospitals in a state or territory (both public and private hospitals, plus those born out of a hospital) are offered newborn bloodspot screening in Australia and all their bloodspot cards are sent to the same laboratory for that state or territory for processing and analysis.

In theory, a gradual roll out of a new genomic newborn screening program focussing on babies born at certain hospitals (e.g. those that had higher number of births) might be possible. However, serious consideration as to the pros and cons of doing a staged roll out would be needed (e.g. the benefit of the laboratories having some time to build their capacity vs the harm of some children with certain conditions perhaps being missed as they weren't yet offered the screening), to ensure the benefits outweighed the harms.

It is very unlikely that genomic newborn screening programs will directly reveal information about the paternity or parentage of a child.

Q: What is an acceptable time to get the analysis to the family?

Answer: An acceptable time to produce results from newborn screening would depend on the urgency of identifying the condition/s being screened for and then the ability to provide the life-saving or disease-modifying intervention to the baby. If results were not available until after the baby was already needing medical attention for their condition, or after a time that an intervention would be (optimally) effective, then this would be an unacceptable time frame.

Current Australian Newborn Bloodspot Screening Programs aim to have all the initial results by 7 – 10 days after the child's birth (however it may take several weeks for some results to be finalised for conditions with less urgency). The results for some conditions are known before this, and if a baby screens positive for any disease they will be recalled straight away.

It is not presently feasible for genomic technology to produce results at scale in a similar short timeframe as the existing methods used for Australian Newborn Bloodspot Screening Programs. This is another reason why it is currently assumed that genomic testing will not be able to substitute (completely) for the methods presently used for newborn bloodspot screening, as it wouldn't be able to produce results in a timely manner for these particular conditions.

Q: Who will have access to the results? How will this information be stored?

Answer: It is envisaged that any genomic results generated through newborn screening would be available to the Program in which they are collected (e.g. a Newborn Bloodspot Screening Program). Any generated results indicating the baby had a disease that was being screened for would then be shared with a relevant clinician who would assist with recalling and reviewing the baby and their family to confirm the presence of that disease.

Genomic results generated in newborn screening would presumably be treated like other pathology results and would be stored securely within health departments as per their local privacy and data legislation and processes, and for the required amount of time as outlined for Australian pathology laboratories. Depending on the local systems and legislation in each state or territory, some genomic results from newborn screening may be included in the baby's electronic medical record if this is available. This would need to be agreed to by parents at the time of them consenting to the screening.

It would need to be determined if genomic data from newborn screening could be stored and then accessed for future reanalysis in case a child later in life started having certain symptoms, e.g. could a genomic cause of this other disease be determined by analysis of the genomic data generated at birth? If this situation is made a possibility, it would need to be clearly outlined in any consenting process the parents would initially undertake to participate in newborn screening.

Q: When deciding on tests on diseases that are currently no cure for, are you considering the chances of lifestyle changes could allow for a better quality of life?

Answer: In relation to the "intervention" that might be available for a possible condition to be screened, the Australian Newborn Bloodspot Screening Policy Framework states that the aspects below should be considered. You'll note that there is no specific wording to indicate whether the intervention should be a medical or lifestyle one, however it does consider the impact of the intervention on the quality and length of life:

"There should be an accepted intervention for those diagnosed with the condition.

7.1 What accepted intervention(s) is (are) available for newborns that receive an early diagnosis through screening?

7.2 How well is the intervention and treatment pathway understood? Is there agreement on when intervention is required?

7.3 How effective is the intervention? Does it alleviate the symptoms of the condition or slow or halt its progression? What influence does the intervention have on quality and length of life?

7.4 How urgent is the intervention? Does the intervention need to be initiated before symptoms of the condition present?

7.5 Is the intervention readily available and accessible?

7.6 What are the potential harms associated with the intervention, and to what extent can these harms be mitigated or managed?

7.7 What is the cost of the intervention? What costs will be incurred for the diagnosis, management and treatment of conditions, including the costs for false positives?

7.8 Is there equitable access to the intervention for families, including those from rural and remote areas?"

Q: When newborn screening was first introduced, how was it rolled out? Nationally or state by state?

Answer: Australian Newborn Bloodspot Screening Programs have been delivered in Australia for around 60 years. Although there is a high degree of national harmonisation, each state and territory operates their own programs. As such, our understanding is that initially each state and territory initiated their programs at different times, although this was generally around the same time (and was just for a single condition to begin with in the 1960s, phenylketonuria; PKU). Later conditions were added at different times by each state and territory. For example, screening for congenital hypothyroidism began in two states in 1977, with other states and territories starting screening in the following years. Similarly NSW started screening for cystic fibrosis first, in 1981, with other states and territories screening for this condition by 1999.

Q: There was a point raised that the genomic tests may be less reliable than the blood spot tests, if this is the case and it may result in more false positives why would you move to genome testing, particularly given the additional cost and complexity?

Answer: The traditional methods used for Australian Newborn Bloodspot Screening Programs detect a consequence of a gene variation, for example a change in the amount of an enzyme/metabolite/protein outside the normal range of variation expected in the general newborn community. This approach is called biochemical testing and it is ideal for screening as it indicates that the underlying gene variation does have an effect that is significant and indicative of a disease.

However, when directly testing the gene itself, it may be difficult to always predict the consequence of all variations found in that gene. Some variations will be obvious as to their consequence, as they have previously been identified in patients with a disease. However, some variations might not have ever been described before. In this case, if there is not a subsequent test that the screening team can do in the laboratory to test the likely or actual consequence of this variation, or a test that a clinician can do with the baby itself (e.g. imaging) then it may be difficult to accurately predict what might happen as a result of this gene variation (e.g. will the variant cause a condition or not, and, if it will cause a condition, how severe might that be?).

A benefit of genomic testing is that it can detect conditions that are not able to be detected by biochemical testing. This means that genomic testing could be used to detect a condition that could not otherwise be included in newborn screening if using other methods, and a greater opportunity to screen for more conditions.

As such, given these aspects outlined in this answer, currently experts in the field believe that it is unlikely genomic testing will (completely) substitute for the existing biochemical testing used in newborn bloodspot screening. Instead, there exists the belief that genomic testing would augment/supplement existing methods to potentially allow a greater number and breadth of conditions to be screened.

Q: Considering that it can take a year or more for new conditions to be added to newborn screening programs, I'm curious about what happens to conditions that are extensively researched but ultimately not included. Who makes the decision on their eligibility, and what process is followed? Is this decision-making process transparent and available to the public, or is it handled internally?

Answer: Yes, the current decision-making process is transparent and available to the public. The process is published on the Commonwealth Department of Health and Aged Care's website:

https://www.health.gov.au/resources/publications/newborn-bloodspot-screening-nbs-our-national-decision-making-pathway-fact-sheet?language=en.

Newborn bloodspot screening (NBS) – Our national decision-making pathway fact sheet | Australian Government Department of Health and Aged Care

As shown in this process, the national Newborn Bloodspot Screening Program Management Committee provides initial advice about the condition and its alignment to the National Newborn Bloodspot Screening Policy Framework to the Cancer and Population Screening Committee (comprised of one senior representative from each state or territory health department and the Commonwealth Department of Health and Aged Care). This Committee then provides advice to the Health Chief Executives Committee (comprised of all Australian Secretaries or Directors General of health departments), who in turn advise the Health Ministers' Meeting (comprised of all Australian Health Ministers). If the Health Ministers agree there appears to be sufficient evidence to warrant a detailed review of the condition for addition to Australian NBS Programs, they will refer the condition to the Medical Services Advisory Committee (MSAC).

If after MSAC review a condition is deemed currently not suitable for addition to Australian Newborn Bloodspot Screening Programs, it is put on a list for future consideration as evidence changes. If MSAC recommends a condition should be added, this advice (and potentially addition information now covered in the MSAC review) is considered by all Australian Health Ministers, before the ultimate decision as to whether or not to add a condition is made.