National Australian Citizens' Jury on using genomics in newborn bloodspot screening
Comments and response from Human Genetics Society of Australasia

The Human Genetics Society of Australasia (HGSA) is grateful to have observed the *National Australian Citizens' Jury on using genomics in newborn bloodspot screening,* and thanks for the Jurors for their time and commitment to participating in the Jury process. The HGSA offers the following response to the Jury recommendations.

This response has been prepared by the HGSA Newborn screening committee, noting that the jury discussed whole of genome newborn screening without reference to whether this technology would be used as a first tier screening method or as an adjunct to the current newborn bloodspot screening program.

HGSA also notes that issues of phenotypic variability, the uncertainty of effect of some genetic variants and how to address the many challenges of implementation including the ethical, legal and social aspects could not be discussed in detail, during the Jury process.

Response to the 11 jury recommendations

1. **Equity**: Genomics must be used in the same way in newborn bloodspot screening programs (NBS) across Australia.

HGSA Newborn Screening Committee Response: Agree.

2. **Benefit to the newborn**: Use of genomics in NBS must benefit the newborn at the time of screening or in the first few years of life.

HGSA Newborn Screening Committee Response: Agree, with reservation #2 noted below.

3. **Regulation**: An independent government mandated Commonwealth regulatory body should develop frameworks and make decisions to address key policy challenges, on an ongoing basis.

HGSA Newborn Screening Committee Response: Agree, with the regulatory body including current newborn screening expertise and aligned with other newborn screening programs eg hearing.

4. **Financing arrangements**: NBS programs should remain publicly funded.

HGSA Newborn Screening Committee Response: Agree.

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5. **Consent**: Parents must be given specific options (detailed by the jury) regarding the storage and use of genomic data to support informed consent. These options should be given before the birth. Screened children to have the right to give or withdraw consent to ongoing data storage.

HGSA Newborn Screening Committee Response: Agree, with reservation #5 noted below

6. **Information reported to parents**: Information reported to parents must be in the best interest of the health and wellbeing of the child and their family, including details of further testing or follow up. Adult-onset conditions should not be reported. Information should be in simple terms, multiple languages, and with available cultural services and support.

HGSA Newborn Screening Committee Response: Agree, with reservation #6 noted below

7. **Data protection**: All data collected or generated in NBS must be protected to the same standard as other sensitive medical data in Australia.

HGSA Newborn Screening Committee Response: Agree, with comment #7 noted below

8. **Comprehensive, coordinated support for parents of affected children**: Parents and children must have access to appropriate support services that are culturally and socially appropriate, comprehensive and adequately funded, with a focus on coordination and continuity of multidisciplinary care. This includes addressing positive results, false positives and the needs of 'patients in waiting'.

HGSA Newborn Screening Committee Response: Agree, with comment #8 noted below

9. **Training for healthcare professionals**: Up-to-date training for all relevant health disciplines.

HGSA Newborn Screening Committee Response: Agree, with comment #9 noted below

10. **Parent and carer education**: Need for clear, concise, current information about the risks, benefits and outcomes of genomics in NBS program, provided before and after birth, via multiple formats and channels.

HGSA Newborn Screening Committee Response: Agree.

11. **Retention and use of genomic data from NBS**. This was the only area in which the jury were not able to reach an 80% majority vote. The jury developed two broad testing and data extraction options:

    i. Whole genome sequencing where the WGS data is extracted and could be retained with appropriate consent. [21 jurors (70%) supported this option]

    ii. While the whole genome may be sequenced, only data that we already understand and can act on would be extracted or collected. [9 jurors (30%) supported this option]

HGSA Newborn Screening Committee Response: It is clear more work is needed in this space noting that retention of data must meet local legislation and pathology requirements.

Reservations and Comments

#2 Although the goal is to benefit the newborn, the Committee notes that it is only possible to judge whether use of genomics in NBS is likely to benefit the newborn at the time of screening or in the first few years of life. In a newborn with no symptoms, it is not always possible to predict whether a positive screen result will benefit the baby. This is for a few reasons, including phenotypic variability (genes and environment interact to produce a wide range of human traits, so these traits can't always be precisely predicted), and difficulties in laboratory testing (because of variants of unknown significance, and because even 'certainly pathologic variants' have variable penetrance – they might produce more or less severe outcomes). The Committee notes that the benefits described in Recommendation 6 are broader than in Recommendation 2. The National Policy Framework (Australian Health Ministers' Advisory Council, 2018) focuses on 'benefit to the baby or family', which is consistent with Recommendation 6.

#5 Building on this recommendation, there are questions and issues that could be explored in future research:

- Screening consent conversations usually happen during regular appointments in maternity clinics (that is, during pregnancy care). The recommendation shows how nuanced these conversations need to be. How can these nuances be communicated during pregnancy care appointments in a meaningful way?
- Creating a new approach to consent may first need consultation with state health ministry legal departments.
- The UK model of consent to each step of the pathway might be considered.
- There are further complexities around data storage/deletion that could be explore e.g. Storing/deleting data for all or only target genes? Keeping the result but not the sequence data?

#6 The research team has communicated to the Committee that the jury were broadly in favour of reporting 'normal' results to parents, but were advised by policy observers that this would be too costly for the program. The HGSA Committee considers it important that 'normal' results should be reported to families. This suggests that there is disagreement among experts about this issue. Further research on the likely costs, and on public views, may be useful. It would be helpful to do more research to clarify how 'the best interest of the ... child and their family' should be understood. For example, does this include notification of carrier status (e.g. of xALD in females)? The Committee notes there are currently differences in reporting practices between states (what is reported, how and to whom). There will be an assumption that whoever receives the report shares this with the family.

#7 There should also be a framework for allowable access to data and what data must be kept, in line with legislation around public records and medical information.

#8 Delivering appropriate and timely support for parents of affected children is an essential component of any healthcare implementation strategy and requires a coordinated and federally funded approach. It should be noted support services as detailed are not available for most currently screened disorders. Reliance on overburdened Hospital based specialist services to provide these services or provide expert support to non-expert clinicians will result in clinical variation and inequity. Identifying the components of a successful implementation system that addresses the needs of the patient, laboratory and clinical providers (eg Paediatricians and GPs) is essential to define the workforce requirements. Genetic counsellors embedded in the laboratory, supported by clinical specialists is one effective strategy that has been used in other settings (eg reproductive carrier screening).

#9 Note the current limitations in genetic literacy amongst healthcare professionals generally.