Mainstreaming genomic testing: pre-test counselling and informed consent

There is unprecedented, increasing demand for genomic testing in Australia.[1,2] Recent developments in paediatric neurology alone include Medical Benefits Schedule, industry and research sponsored testing for monogenic causes of epilepsy, neuromuscular disorders, and syndromic intellectual disability, among others. To be ethically and legally valid, patients must undergo pre-test counselling before they consent to genomic testing.

Professional genetic counselling is a specialty developed to meet this need. Professional genetic counsellors have a Master of Science degree which includes clinical genetics and genomics, counselling, research, and health communication. They adhere to standards set by the National Alliance of Self-Regulating Health Professions through the Human Genetics Society of Australasia. The profession employs a psychotherapeutic approach to helping patients and families make decisions regarding genetic testing and follow-up of results. Genetic counsellors address several issues (Box 1), conversations are patient-centred and establishing good rapport, and improving genetic literacy is paramount.

There is insufficient genetic counsellor capacity in Australia to meet increasing demand. To optimise efficiency and minimise burden on existing genetics services, increased access to genomic testing requires some delegation to clinicians not primarily trained in genetics (referred to as mainstreaming).[7] Previous studies have identified varying levels of interest and competence among non-genetics clinicians performing genetic counselling in Australia.[7]

Although clinicians are experienced in consenting patients for many types of investigations, genomic tests present unique challenges.[2,8] These tests can provide data that are relevant in the present and in the future. Results can have significant implications for the patient and their wider family. This increases the potential for psychosocial harm, presenting ethical, legal and financial challenges.[2,8]

This article is a collaborative reflection (genetic counsellors, a clinical geneticist, and a specialist physician) following an adverse outcome with mainstreamed genomic testing (Box 2). An infant was diagnosed with an *SCN1A*-related disorder; here, we describe parental perspectives, to highlight the importance of pre-test counselling and fully informed consent.

Patient burdens of responsibility with genomic testing

Despite the expertise of the specialist physicians performing the consent, this family had a negative experience with genomic testing, feeling that they had been insufficiently informed. Their distress was identified after professional genetic counselling.

Although barriers to mainstreaming can include low clinician engagement or unfamiliarity with testing, this was not the primary issue in our case.[11] The hospital setting, the parents' sense of overwhelm, and their lack of genetic literacy may have contributed to the adverse outcome.

It is usual for clinicians to emphasise individual clinical implications when consenting for medical investigations. They may inadvertently minimise or overlook broader family and financial implications that genetic counsellors routinely discuss. Additionally, the setting of acute illness, stress and hospitalisation may decrease comprehension even for highly educated families.

In our case, the parents were not prepared for the wider implications of the genomic testing outcome, resulting in sudden awareness of personal and familial impacts, loss of autonomy, and distress. Subsequent reluctance for future testing, result disclosure and follow-up occurred. The couple's request to undergo their own testing to facilitate pre-implantation genetic testing, without result disclosure, presented the genetic counsellor with a range of clinical and ethical issues that were difficult to reconcile.

The disclosure or non-disclosure of genetic results is a well known ethical dilemma.[12] Contextual factors for this couple included a devastating new diagnosis and the everyday reality of navigating the health care system with a sick child. Successful psychological adaptation to genetic test results starts with comprehensive pre-test counselling including education. This promotes autonomy and trust between patients and care providers to successfully navigate post-test implications.

The ethics of pre-test counselling

Overarching ethical principles which guide all health care practitioners include veracity, dignity, and accountability. Genetic counsellors relay risk information and options to patients and their families, so these principles are integral to the way information is framed, understood, and utilised by patients.

1 Essential components of pre-test counselling

- Optional; include other options[3]
- Decisions based on personal values and needs[3-6]
- Information: specific genes, inheritance patterns, penetrance, possible phenotypes[4,5]
- Testing process/timeframes including how results will be returned[5,6]
- Clinical implications for patient and family members of potential test outcomes (pathogenic, negative, variants of uncertain significance, additional findings)[3,5,6]
- Recurrence risks and future pregnancy options[6]
- Costs[6]
- Insurance[5]
- Privacy and confidentiality[4-6]

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2 Case study: Why weren't we warned?

A 7-month-old girl had recurrent admissions to a tertiary paediatric centre in the setting of presumed epileptic seizures. The events commenced around 3 months of age, initially infrequently but increasing to weekly. Although most childhood epilepsies are not monogenic, clinicians are increasingly considering genomic testing for children with epilepsy, because genetic diagnosis may confirm the clinical diagnosis, guide medication choices, inform prognosis, and optimise access to supports.[9]

Limited clinical genetics services mean consent for genomic testing may be performed by the treating specialist clinician. In this case, a member of the neurology team consented the child's parents for an epilepsy gene panel.

The neurologist subsequently disclosed to the parents that testing identified an *SCN1A* pathogenic variant in their daughter. *SCN1A*-related disorders represent a broad clinical spectrum, from simple febrile seizures to intractable epilepsy with associated developmental disability, including Dravet syndrome.[10] They are inherited in an autosomal dominant pattern with incomplete penetrance, but commonly occur de novo in probands.[9] If a parent has the variant, they are at risk of *SCN1A*-related disorders themselves, and there is a 50% recurrence risk for siblings. Moreover, genetic relatives of an affected parent are also at risk of having the variant, with the associated health and reproductive risks.

The parents were referred to the genetics service for post-test counselling. They were both tertiary-educated professionals in their early 30s who also had a healthy 3-year-old daughter. Both children were born following in vitro fertilisation (IVF) pregnancies; the couple had embryos in storage and were planning another pregnancy.

The parents and genetic counsellor discussed the impact of the child's diagnosis. Both parents reported significant anxiety since receiving the diagnosis: the mother said the worry about seizures kept her awake at night and she was taking medication for anxiety; the father said he worried as soon as he woke up each morning. He was "upskilling in many areas" to allow him to advocate for his daughter in hospital as they found previous admissions very stressful. They were concerned about potential developmental impacts of the *SCN1A*-related epilepsy and hoped to mitigate this by providing a stimulating environment for their daughter.

After a child has received a genetic diagnosis, parents will typically be offered segregation testing to determine if they carry the pathogenic variant and to inform the risk to genetic relatives. During the consultation, it became clear that they had not fully understood the wider implications of their youngest daughter's genomic testing for other family members, including themselves, their other child(ren), and their extended family; this was information for which they were not emotionally prepared.

They agreed to testing provided results were not disclosed to themselves, only to their IVF clinicians. The counsellor explained that this would limit the utility of results to manage health risks for others in their family, including themselves and their older child. It was suggested that the counsellor and parents should work together so the couple could feel comfortable with personal disclosure of their results, and the genetic counsellor could manage any risks to family members.

The next day the mother called the counsellor. She feared receiving more information would derail her mental health further. The couple were coming to terms with finding out their own risks. The counsellor discussed strategies that could be used to manage risks from results, including a letter that could be shared with extended family and delayed discussions for recommended sibling follow-up. Segregation testing proceeded and showed that neither parent had the *SCN1A* pathogenic variant.

Modern genetic practice presents ethical matters of "unprecedented intensity".[8]

Genetic counsellors must balance non-maleficence and beneficence, assessing multidimensional risks including physical, emotional, social and financial health for the patient and their family. Moreover, families, communities and societies may hold dissonant perspectives.[11] In Australia, genetic counsellors are guided by Human Genetics Society of Australasia best practice standards.[13] These require that patients are informed about all aspects of the testing process and potential implications as part of the consent process.

Components of pre-test counselling

Pre-test counselling must not overstate the utility of genetic testing without contextualising the risk of uninformative, uncertain or unexpected results. Unintended findings can raise personal, medical, health economic and ethical issues.[3] In Australia, lobbying is underway to introduce consumer protection against genetic discrimination related to life insurance.[14] Increasingly expansive electronic medical records mean privacy must be discussed. Patients must be informed of circumstances when other family members would need to be notified of a result.[8] Fully informed consent is then obtained, with potential ethical issues identified and managed early, in partnership with the patient.

Pre-test counselling (Box 1) facilitates fully informed consent, thus preparing the patient or family for possible outcomes. Outcomes of poor genetic counselling processes include increased patient anxiety and distress, coping difficulties, and non-compliance with treatment.[4] In our case study, insufficient pre-test counselling led to the risk of harm after loss of trust in the health care system, and further harm could result from non-engagement with services.

Recommendations

Our case provides a concrete example of downstream effects from inadequate pre-test consent. Recommendations from the case apply at several system levels. Aspects of hospitalisation increase the risk of an inadequate consent, including patient and family distress due to illness, language and cultural barriers, limited supervision of junior medical officers, and environmental factors. Clinicians should consider arranging a separate time and space to hold the discussion with a second appointment if necessary. Junior medical officers need supervision while upskilling in offering genomic testing and formal competency assessment. Health organisations should establish care pathways to determine which patients will be referred to clinical genetics services, to optimise patient experience of genomic testing and to minimise inconsistencies of care across departments. Such pathways require adequate resourcing, including genomic expertise and administrative support.[15]

Further research is needed to better characterise factors associated with negative outcomes. A study assessed the need for pre-test counselling, finding most participants had little to no decisional conflict about proceeding with testing and reached a decision quickly.[5] However, 30% of participants experienced decisional regret. Most patients and families benefit

from additional time and resources to improve their genomic literacy. Pre-test decision aids and technologies such as telehealth could be used to improve genomic literacy and optimise access to genetic counsellors.[6,16] The model of care should define higher risk patients to refer for professional genetic counselling at defined service points in the care pathway.[2,6,12]

Clinical groups should consider embedding professional genetic counsellors into their clinics. Examples in Melbourne include neurogenetics and cardiac inherited diseases clinics at the Royal Melbourne Hospital, the neuromuscular clinic at the Royal Children's Hospital, and in paediatric oncology at Monash Children's Hospital. This allows upskilling of mainstream clinicians and builds inter-departmental relationships. Barriers to integrating genetic counsellors across the health care system include a lack of resource allocation for this role and low organisation confidence in employing genetic counsellors outside of genetics departments. Administrative burdens associated with genomic tests may divert genetic counsellors away from using their core skills in counselling and patient support.

There are published models of care for genomic medicine; however, this case highlights a gap in the theory and implementation.[15] Organisations should adopt a model of care that is clearly communicated to staff and consumers. Professional roles and responsibilities within the model should be defined to help frontline staff navigate care pathways in a new specialty. Measurement of goals and outcomes should reflect unique genomic medicine issues. Contemporaneous feedback of frontline consumer and clinician experience to leaders would promptly identify unintended consequences and enable modifications at each system level.

Finally, in Australia, genomic education is not adequately addressed in medical or nursing undergraduate training. Research shows limited uptake at the postgraduate level.[17] Nurses may be well placed to support mainstreaming of genomics as the first point of contact for many patients; like genetic counsellors, they are trained in patient advocacy, education, and health care navigation. Internationally and domestically, work is needed to improve nurses' genomic educaton.[17] Improved genomic literacy in clinicians (including doctors and nurses, who together represent the largest group of health care professionals) would allow them to better identify at-risk patients for referral to a genetic counsellor, to improve genetic counsellor integration at an organisational level, and to join genetic counsellors in advocating for expanded training places and career development opportunities at a national level.

Conclusion

This family's experience demonstrates safety concerns in current mainstreaming of genomic medicine and suggests rigorous examination of consumer experiences is required before practices are scaled up further. Of concern, this case is not isolated in the experience of the authors. Genetic counselling involves expanding the patient's awareness beyond immediate medical management concerns. Informed consent is facilitated by exploring different potential results, their utility and potential wider impacts. The loss of the psychotherapeutic pre-test component when mainstreaming genomic testing risks increasing decisional regret and the related psychosocial burdens for the patient, as well as the chance of ethical and legal complications. Truly informed consent is a highly complex process which requires special consideration in genomic practice.

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