Perceptions of severity and their influence on reproductive decision-making following reproductive genetic carrier screening

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ABSTRACT

The concept of severity in healthcare is multidimensional and subjective. It is a primary consideration in reproductive genetic carrier screening design where the focus is providing reproductive couples with information about the chance of severe genetic conditions in their offspring. When offering this screening, it is important to understand how condition severity is perceived and incorporated into reproductive decision-making. We analysed data from forty-one semi-structured interviews with people who received a screening result indicating an increased chance for having children with a genetic condition. Thematic analysis revealed a desire for comprehensive information about the condition including clinical features, prognosis, impact on quality of life, and treatment/management options. Participants integrated this information with their personal circumstances, beliefs/values, and lived experience to form a perception of the severity of the condition. For rare and reduced-penetrance conditions where clinical information was limited or ambiguous, decision-making was more complex and greater anxiety was experienced. For conditions with a severity spectrum, reproductive decisions were based on the 'worst-case' clinical presentation. Where the impact of the condition was perceived as significant, the imperative to avoid that condition in future children appeared to be greatest. Participants reported feeling that knowing their increased reproductive chance of the condition conferred a responsibility to avoid the condition, to prevent suffering and/or reduced quality of life for their children and future generations. These findings offer critical insight into how severity is perceived and the role it plays in reproductive decision-making and justifies a carefully considered approach to screening panel design.

Keywords: genetic carrier screening, population screening, severity

INTRODUCTION

Reproductive genetic carrier screening (RGCS) offers information to prospective parents about the chance of having children with an autosomal recessive or X-linked genetic condition (1). Due to the nature of recessive inheritance, carrier couples often have no family history or knowledge of the condition until the birth of an affected child. Following this diagnosis, parents can experience significant grief and loss facing their child's severe disability, suffering or, in some cases, premature death. Awareness and availability of RGCS is increasing and many professional societies now recommend it is offered to people planning a pregnancy or early in pregnancy (1,2). There is general consensus that screening should focus on severe conditions. However, the concept of severity is difficult to define due to its subjective and context-dependent nature (3). An understanding of genetic risk enables reproductive couples to make informed decisions which may include using reproductive interventions to avoid having children with the condition. For example, opting for *in vitro* fertilisation (IVF) with preimplantation genetic diagnosis (PGT-M) or prenatal diagnostic testing (PND) with selective termination.

Severity has been defined as the degree of suffering caused by the condition or the effect on quality of life (4). Severity, therefore, carries with it an element of how the condition is experienced, both by the affected individual, and their family. Perceptions of severity are inherently complex with various dimensions and not all who have a particular genetic condition experience or conceptualise their condition in the same way (5). Many interconnecting medical, temporal and socioeconomic factors

contribute to one's view - for example, family situation, access to quality healthcare services and availability of effective treatment options (6). Quantifying or standardising the concept of severity has proven to be challenging, particularly for conditions with variable presentation or penetrance (3). Several attempts have been made to develop algorithms stratifying conditions based on their severity (7,8). These algorithmic approaches typically prioritise clinician opinion and biomedical data. Research or engagement with people and families living with genetic conditions has been limited. However, there appear to be differences in how conditions are defined and categorised under these algorithms compared to the reality of those experiencing them (5).

The Australian Reproductive Genetic Carrier Screening study (known as "Mackenzie's Mission") investigated how best to provide an accessible, nationwide government-funded RGCS (9). A panel of ~1300 genes associated with over 700 genetic conditions was developed, the 'severity' or 'seriousness' of the condition being one of the primary considerations for gene inclusion (10). Gene inclusion was based on conditions that a multidisciplinary committee assessed as being severe enough that people may choose to access reproductive intervention to avoid having children with the condition (9,10). Recognising that any assessment of severity is subjective, the study incorporated methods to explore the reproductive choices made by people who received "increased chance" results to inform future program design. The decisions around condition inclusion/exclusion ultimately shapes what results are returned to couples. Offers of RGCS need to integrate the clinical understanding of condition severity with the perspectives of those who are undertaking screening in order to provide information that is relevant to prospective parents for their

reproductive decision-making. Therefore, we conducted a sub-study within Mackenzie's Mission which aimed to explore how participants who received increased chance RGCS results perceived the severity of the identified genetic condition and how these perceptions influenced their subsequent reproductive decisions.

METHODS

Study setting

This study used a qualitative approach to explore experiences and perceptions, with respect to condition severity, of people who received increased chance results through RGCS offered in Mackenzie's Mission. The Mackenzie's Mission research protocol is published elsewhere (9). In brief, participants were reproductive couples over 18 years old, either planning a pregnancy or in early pregnancy (<10 weeks' gestation). Couples were recruited by their healthcare provider. Couples accessed pre-test information and provided consent, via an online portal. Consenting couples then provided saliva samples for testing. Increased chance couples received genetic counselling and had access to funded PND or one funded cycle of IVF with PGT-M.

Post-result interviews

Each individual who received an increased chance result was invited to take part in a one-on-one interview three months post-result. The invitation email was sent separately to both members of the reproductive couple followed by a reminder email if no response was received. We purposively sampled to include perspectives from participants carrying a diverse range of genetic conditions as well as those pregnant at time of enrolment. Interviews were conducted via telephone (by ET, ADA, and BM) between June 2021 and November 2022. Verbal consent was obtained at the start of

each interview. The semi-structured interview guide was developed by the Mackenzie's Mission psychosocial and epidemiology sub-committee, including a broad scope of suggested topics, open exploratory questions, and conversation prompts. All interviews were audio-recorded and transcribed verbatim. Transcription was completed by a professional transcription service or a student researcher and checked against recording for accuracy. Names/identifiers were removed and replaced with pseudonyms and a unique study code.

Severity sub-study

To explore perceptions of severity and their role in reproductive decision-making, transcripts from all three-month post-result interviews were analysed (by ES) with a specific focus on severity. Discourse relevant to severity was identified through close reading of the transcripts looking for specific instances where severity was discussed, referred to, or where it appeared to have influenced decision-making. This was followed by reflexive thematic analysis of the relevant content using a six-stage analytical framework (11,12). This involved familiarisation with the raw interview data with first impressions documented, then systematically free-coding each anonymised transcript, inductively developing a coding system. Related codes were then grouped, identifying candidate themes which were then refined, categorised, and named. To establish consensus and enhance reliability, 10 of the interview transcripts were co-coded (by ET). Coding and establishment of themes was an iterative and collaborative processes. ES maintained a reflexive journal throughout the study regularly documenting thoughts, emotional responses, biases and assumptions held that may influence the interpretation of data. These reflections were used to critically evaluate positionality in the research, enhancing the transparency and rigor of analysis.

RESULTS

Participant characteristics

In the Mackenzie's Mission three-month post-result interviews, a total of 41 participants (26 female, 15 male) representing 33 reproductive couples took part (Table 1). Interviews ranged from 20 to 93 minutes. In two couples, one member of the couple had a dominantly inherited genetic condition not screened in Mackenzie's Mission. Four participants from independent couples already had a child with a genetic condition before taking part in Mackenzie's Mission.

When the 41 interview transcripts were assessed for this sub-study to identify discourse around condition severity, 35 participants had considered condition severity a significant factor in their decision-making. Observation of the 6 transcripts in which severity was not described as contributing to decision-making showed characteristics including: already going through IVF, having made a decision (after receiving their results) to not have more children, a decisive (less contemplative) approach to decision-making or lack of engagement/misunderstanding of interview question.

THEMES

1) Defining severity: understanding the impact of the condition

Upon receiving the result, all participants recalled seeking as much information about the condition as possible, particularly with respect to clinical presentation, prognosis/life expectancy, impact on quality of life, impact on daily life of future children and treatment/management options (Table 2, Quote 1). These aspects

framed how severity was defined by participants. The information was desired at the point of result disclosure and acquired through the study genetic counsellor/specialist as well as via subsequent web-based searches. Some participants recalled feeling that the inclusion of the condition on the screening panel implied that it was deemed severe enough to justify screening for it (Table 2, Quote 2).

Participants who perceived that they had received comprehensive information about the condition appeared to find it easier to assess condition severity and to make reproductive decisions. For very rare conditions, the lack of available research and information appeared to limit these participants' ability to develop a perception of severity (Table 2, Quote 3). Such unknowns and gaps in information appeared to cause anxiety and stress among participants (Table 2, Quote 4).

Conditions with variable clinical presentation or penetrance meant that information provided about these conditions was perceived as ambiguous, contributing to difficulty in decision- and meaning-making (Table 2, Quote 5). Participants appeared to find using this information for decision-making challenging and ultimately tended to focus on most the severe manifestation of the variable condition in developing a perception of severity (Table 2, Quote 6). Considering these 'worst' scenarios elicited emotional responses that drove decision-making.

2) Perceiving Severity: contextualising clinical information

While there were a range of external factors influencing how the severity of the condition was defined by participants, there also seemed to be a process by which people acquired that information, processed it, and integrated it with their own

personal values, beliefs, perceptions, and lived experience. This pathway of meaning-making contextualised the objective clinical information. Participants applied this information to their own personal situation and circumstances and ultimately developed their own perception of the severity of the condition.

Previous knowledge or awareness of genetic conditions seemed to influence this meaning-making process. Participants with no family history or lived experience of genetic conditions expected a healthy child and any deviation from this outcome appeared difficult to reconcile (Table 2, Quote 7). The increased chance result was described as a shock and the unfamiliarity of the condition often led to the participant perceiving it as severe and to be avoided through reproductive choices (Table 2, Quote 8).

Participants with previous knowledge or awareness of genetic conditions showed characteristics that demonstrated greater preparedness for the possibility of an increased chance result. The effect of these previous experiences was influenced by whether their experience had been viewed positively or negatively and if they had a role in caregiving or supporting the person with the condition. Positive interactions involved people affected by a genetic condition that the participant perceived to have good quality of life whereas negative interactions involved a low perceived quality of life.

Positive previous experiences provided context for the condition identified through RGCS. In this circumstance, participants tended to have a more holistic view of the condition and disability more generally. They seemed to also consider the person

behind the condition. For these participants, there was a perception that genetic conditions can be managed and people with genetic conditions have positive aspects to their lives and thus the condition may not necessarily need to be avoided through reproductive decisions (Table 2, Quote 9).

Negative previous experiences of a genetic condition highlighted the possible challenges faced by people with genetic conditions, their families and the wider community. Such experiences included more severe presentations of the condition, or instances where a condition was poorly managed, so it significantly impacted quality of life. Witnessing hardships or daily struggles first-hand gave insight into the reality of living with a genetic condition. For example, Amina's first child passed away from a genetic condition and, through Mackenzie's Mission, she learnt that she and her partner also had an increased chance for another condition. The experiences of Amina and other participants seemed to facilitate a more comprehensive understanding of genetic conditions and disability and elicit a stronger desire to avoid having children with the condition for which they received an increased chance result (Table 2, Quote 10). Previous experiences of a serious genetic condition also seemed to increase awareness and anxiety about the possibility of genetic conditions (Table 2, Quote 11).

The two participants with a genetic condition themselves expressed reluctance to have a child with their condition. They compared their condition with the condition identified through RGCS, using their own condition as scaffolding for assessing the severity of the condition for which they received an increased chance result (Table 2, Quotes 12 & 13).

Often participants reflected on their own childhood and identified aspects of their life they valued or felt were fundamental in their development. If the condition impacted these aspects of life, then the condition or those particular features were perceived as more severe. Some participants described a greater sense of loss in opportunity and quality of life when considering having children who might not experience life the way the participant had (Table 2, Quote 14).

3) Applying Severity: influence of perceptions on reproductive decisions

How participants viewed the condition and perceived its severity appeared to strongly influence whether they wanted to actively avoid it through their reproductive decisions. For conditions that were perceived by the participant as mild, there tended to be less need or urgency to take steps to avoid having children with the condition (Table 2, Quote 15). Unmistakably, across all participants, as the perceived severity increased, so did the desire to avoid that condition in pregnancy (Table 2, Quotes 16 & 17). Among all participants, both IVF with PGT-M and PND with pregnancy termination were ubiquitously viewed as challenging pathways. In some instances, participants described considering the condition severity with respect to the hardship of reproductive interventions (Table 2, Quotes 18 & 19). Female participants facing the physical experience of pregnancy and potential termination appeared more risk averse, while male participants tended to view the statistics optimistically and were more pragmatic in their approach to termination.

Many participants described a parental instinct to protect their unborn child. They wanted to prevent the child from suffering or experiencing the social/medical

challenges associated with severe genetic conditions. Multiple participants articulated that they would prefer to go through the challenges of reproductive intervention now to avoid future challenges associated with having children affected by a severe genetic condition (Table 2, Quote 20). Participants shared concerns about the impact on them as parents of a child with a severe genetic condition. Some doubted their ability to provide the necessary care and support to a child with significant health issues/disability. (Table 2, Quote 21). *Female participants often reflected on the emotional and caregiving challenges while male participants tended towards logistical and financial implications.* Participants also considered the impact of the genetic condition on their family unit and reported feeling it was ethically problematic to bring a child into the world with a severe condition considering the medical and/or social challenges they would face (Table 2, Quote 22). This perceived ethical obligation to avoid having children born with a severe condition also included consideration of future generations. For some participants, a decision made now could prevent transmission to offspring and they expressed an interest in minimising the impact of the condition in the population.

4) Needing support in conceptualising severity: desiring clear and direct communication from healthcare providers

When reflecting on their experience of receiving their increased chance result, some participants emphasised that their expectations of healthcare providers were to provide information about the condition and its impacts (Table 2, Quotes 23 & 24). There was a recognition that this information was crucial to inform reproductive decisions (Table 2, Quote 25). Participants described how the information shared by healthcare providers was central in forming understanding of the condition and its

severity. Furthermore, how the condition was presented appeared to shape initial perceptions of the condition (Table 2, Quotes 26 & 27).

Many participants looked to their healthcare providers for guidance as to what reproductive decisions they should make. Some appeared to lack the confidence and framework to make the decisions themselves and thus desired more involvement from their healthcare provider during reproductive decision-making (Table 2, Quote 28).

DISCUSSION:

Our study provides important insight into how perceptions of condition severity are formed and influence reproductive decision-making following an increased chance RGCS result. Conditions were understood through information seeking, drawing on healthcare provider descriptions of the condition and web-based information. This information was then scaffolded on personal experiential knowledge of genetic conditions, health concerns and disability to create a perception of the severity of that condition. The belief that a condition is severe served as justification for choices regarding use of reproductive interventions to avoid the individual, familial and societal impacts of having children with the condition. When facing reproductive decisions, perceived severity of the condition played a central role in decision-making. Where there was limited or ambiguous information about the condition (or variant/s), reproductive decision-making became more complex. Couples receiving increased chance results looked to their healthcare providers for clear and comprehensive information about the condition, and guidance and support around reproductive decision-making. This novel study illuminates the process of making

meaning of condition severity in the context of increased chance results following RGCS and highlights the need for comprehensive decision-making support as RGCS becomes more widespread.

The vast majority of genetic conditions are rare and lack public awareness (6). When offering RGCS at population scale, most couples who receive an increased chance result will have no prior knowledge or lived experience of the condition, or disability more generally (13). Couples undertaking RGCS will need to make reproductive decisions without experiential knowledge of the condition. Understanding the increasingly complex clinical information required to make informed decisions about pregnancy is challenging for patients (14). Adequate health literacy is required to accurately assess the nature and severity of the condition (15). The need for clear and comprehensive information about the relevant condition highlights our participants' desire to make well informed decisions.

As prognostic information was reconciled, it appeared to be integrated with personal experience which framed the interpretation of condition severity. Experiential knowledge, that which is gained through lived experience, contributes significantly to one's beliefs, perceptions and decision-making (16,17). Among our participants, positive experiences or contact with people with genetic conditions created an optimistic view of managing life with health issues, whereas the more negative experiences reinforced the challenges faced by individuals and their families. Experiential knowledge can be valuable in helping a person understand what it might be like to have children with a genetic condition, but as experiences and perception of severity can vary, one person's experience may not represent all experiences,

potentially leading to misconceptions about the condition. For participants in our study without any relevant experiential knowledge, facing reproductive choices was overwhelming with fear-based responses appearing to drive decision-making. For some, contact with patient/online support groups facilitated deeper conversations about the reality of life with an affected child. Exploring a person's perception of the severity of a condition can provide a deeper understanding of how they are defining and understanding condition severity in the context of their lived experience, personal values and situation. An improved understanding of how perception of severity is developed and its influence on reproductive decisions may enable more effective genetic counselling.

For some, the inclusion of the gene (and its associated condition) on the RGCS panel was seen as a confirmation that the condition was severe and an endorsement of screening for the condition. Thus, the clinical categorising of a condition as 'severe' has potential implications for how it is perceived (18). A condition included in the screen was presumed by participants in our study to be severe enough to justify screening for and, therefore, severe enough to justify taking steps to avoid in offspring. This finding has important implications for the aims and design of population-wide RGCS and supports a cautious approach to gene inclusion.

The decision to actively avoid the condition through reproductive options appeared more straightforward for couples who had adequate information to assess the severity and perceived the condition as very severe. However, reproductive decisions were more convoluted when the information was ambiguous or limited. Less information is available describing the nature of very rare conditions and

protocols for treatment and management may not be clearly defined. As principles of screening (19,20) require the condition to be well understood, very rare conditions do not align with this population screening criterion. However, the infrequency with which they occur could continue to preclude inclusion in RGCS panels despite their potential severity and utility in reproductive decision-making. Advances in screening technology now mean these conditions can be included despite their rarity but the lack of information does make reproductive decision-making more complex. While acknowledging the challenges in making reproductive decisions based on limited clinical information about very rare conditions, participants in this study valued the results and expressed gratitude for the awareness of their risk.

Greater decision-making complexity was also observed where the condition was highly variable and for conditions with reduced penetrance. In these situations, the "worst-case" presentation of the condition appeared to serve as a decision-making reference point. This is understandable but challenging for conditions where the most severe presentation is rare (e.g. alpha-1-antitrypsin deficiency). There is no consensus on how likely the most severe presentation should be for a gene to be included in an RGCS panel. Including highly variable and reduced penetrance conditions may lead to unnecessary reproductive interventions. Further consideration is needed to weigh this outcome against the potential to avoid severe cases. If such conditions are included in RGCS panels, it is imperative that reproductive couples have access to genetic counselling to support their decision-making.

Participants in our study expressed a strong desire for a healthy child. Reproductive decision-making also appeared to be driven by a perceived moral or societal obligation to avoid having children with the condition, even, in cases of mild/moderate perceived severity for some. The pressure of this perceived parental responsibility could have the potential to impede reproductive autonomy (21). The "good-parent belief" is applied in medical decision-making of parents of seriously ill children (22). In sum, "*The good parent makes informed, unselfish decisions in the child's best interest"* and *"tries to prevent suffering and protect health"* (23). This model can be translated to the RGCS setting, where the described child is a potential future child. Thus, prospective parents may perceive a strong imperative to make "good" decisions on behalf of future children, to protect them and, where possible, mitigate the challenges they may face.

To optimise reproductive utility, it is important that reproductive decisions are sufficiently informed and align with participants' values. Genetic counsellors promote reproductive autonomy by using a predominantly non-directive approach providing balanced information and supporting the patient reproductive decisions (24). However, our participants articulated desire for guidance and reassurance when choosing their reproductive path, challenging this non-directive model. An alternative approach to genetic counselling is a shared decision-making model where some guidance on the behalf of the healthcare professional is acceptable in the context of facilitating the decision-making *process* but not the *outcome* (24,25). Participants lacked the experiential knowledge of the condition and appeared to feel unqualified or ill-prepared to navigate reproductive decision-making. Thus, genetic counsellors could take an active role by engaging the patient in discussion about perceived

severity of the condition and how they are contextualising information within their own life experiences whilst gently challenging any assumptions and misinformation. In making informed reproductive choices, genetic counsellors can facilitate the process by providing a structured approach to working through the considerations. Other tools such as decision aids and interactive web-based information resources may also be useful and have been developed to support decision-making (26). Such tools could facilitate shared reproductive decision-making in line with the couple's values and beliefs, presenting the information in a clear, accessible, and methodical way.

LIMITATIONS

This study, the first of its kind in which participants had been offered population level RGCS for a very large number of genes, included a wide range of perspectives in this qualitative dataset. Nonetheless, the sample, and the larger Mackenzie's Mission study, has limited participation by people who are not actively engaged with the healthcare system as the program required enrolment following an appointment with a primary healthcare professional. Therefore, our participants may be more proactive or information-seeking when compared to the general public which could influence how they develop a perception of condition severity and make reproductive decisions. Generalizing these findings to population groups not included in this study may be problematic. This qualitative study did not aim to quantify or compare the different patient groups and their experiences and further research is required to comment on the frequency or correlation between differing views.

CONCLUSION

Population-wide accessible RGCS has the capacity to shift the norms that influence what a society perceives as a severe condition, what is considered routine care, and what are acceptable interventions (27, 28). Thus, careful consideration is needed when deciding which genes are included in such screening panels. Our findings highlight the complex subjectivity behind perceptions of severity and the need for RGCS programs to be judicious when deciding what conditions to include, and how to provide information to those making decisions to undertake screening. Implementation of population-wide RGCS necessitates strong context-bound inquiry into the perception and experiences of the population for which RGCS is being designed and intended. While acknowledging the challenges in making reproductive decisions based on limited clinical information, participants in this study valued the results and expressed gratitude for the awareness of their genetic risk. Genetic counsellors have the requisite expertise to synthesise complex and potentially uncertain clinical information in a way that promotes understanding. Recognising a patient's desire for more direct communication and guidance around decision-making can help the healthcare professional support the couple through a shared decision-making model. Given the potential complex decision-making that can arise through RGCS, access to comprehensive support should be an essential part of any RGCS program.

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Author contributions

BM and ADA designed the post-result interviews with increased chance couples; ET, ADA and BM conducted the interviews; LF, LD, ES, ET and ADA designed the severity sub-study; ES conducted data analysis with co-coding by ET; ES drafted and ADA, ET, LF, LD and BM revised the manuscript. All authors approved the final version.

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Competing interests

The authors declare there are no competing financial interests in relation to the work described.

Informed consent statement

Participants provided informed verbal consent after reviewing the participant information content.

Ethics approval

Ethics approval was granted by Royal Children's Hospital Human Research Ethics Committee (2019.097) and ratified by University of Technology Sydney Human Research Ethics Committee (ETH22-7554) for this sub-study.

Data Availability

The datasets generated and/or analysed during the current study are available from the corresponding author on reasonable request.

References

1) Gregg, A. R., Aarabi, M., Klugman, S., Leach, N. T., Bashford, M. T., Goldwaser, T., et al. Screening for autosomal recessive and X-linked conditions during pregnancy and preconception: A practice resource of the American College of Medical Genetics and Genomics (ACMG). *Genetics in Medicine : Official Journal of the American College of Medical Genetics*, *23*(10), 1793 9 (2021)
2) Henneman, L., Borry, P., Chokoshvili, D., Cornel, M. C., Forzano, F., Hall, A., et al. Responsible implementation of expanded carrier screening. *European Journal of Human Genetics*, *24*(6), e1 (2016).
3) Dive, L., Archibald, A. D., Freeman, L., & Newson, A. J. How should severity be understood in the context of reproductive genetic carrier screening? *Bioethics*, *37*(4), 359-366 (2023)
4) Savell, K. & Karpin, I. 'The meaning of" serious disability" in the legal regulation of prenatal and neonatal decision-making', *Journal of Law and Medicine*, 16(2), pp. 233–245 (2008).
5) Boardman, F. K., & C. C. Clark. What is a ‘serious’ genetic condition? The perceptions of people living with genetic conditions. *European Journal of Human Genetics* 1–10 (2021).
6) Kauffman, T. L., Davis, J. V., Jarvik, G. P., Berg, J. S., Harding, C., Kennedy, K. A., et al. Patients' ratings of genetic conditions validate a taxonomy to simplify decisions about preconception carrier screening via genome

sequencing. *American journal of medical genetics. Part A*, *170*(3), 574–582 (2016).

7) Lazarin, G. A., Hawthorne, F., Collins, N. S., Platt, E. A., Evans, E. A., & Haque, I. S. Systematic Classification of Disease Severity for Evaluation of Expanded Carrier Screening Panels. *PloS one*, *9*(12), e114391 (2014).
8) Korngiebel, D. M., McMullen, C. K., Amendola, L. M., Berg, J. S., Davis, J. V., Gilmore, M. J. Generating a taxonomy for genetic conditions relevant to reproductive planning. *American journal of medical genetics. Part A*, *170*(3), 565–573 (2016).
9) Archibald, A. D., McClaren, B. J., Caruana, J., Tutty, E., King, E. A., Halliday, J. L., et al. The Australian Reproductive Genetic Carrier Screening Project (Mackenzie's Mission): Design and Implementation. *Journal of personalized medicine*, *12*(11), 1781 (2022).
10) Kirk, E. P., Ong, R., Boggs, K., Hardy, T., Righetti, S., Kamien, B. et al. Gene selection for the Australian Reproductive Genetic Carrier Screening Project ("Mackenzie's Mission"). *European journal of human genetics: EJHG*, *29*(1), 79–87 (2021).
11) Braun, V. & Clarke, V. 'Using thematic analysis in psychology'. *Qualitative Research in Psychology* 3(2), 77–101 (2006).
12) Braun, V. & Clarke, V. 'Reflecting on reflexive thematic analysis'. *Qualitative Research in Sport, Exercise and Health* 11(4), 589–597 (2019).
13) Rowe, C.A., Wright, C.F. Expanded universal carrier screening and its implementation within a publicly funded healthcare service. *J Community Genet* **11**, 21–38 (2020)

14) van der Steen, S. L., Houtman, D., Bakkeren, I. M., Galjaard, R. H., Polak, M. G., Busschbach, J. J. et al. Offering a choice between NIPT and invasive PND in prenatal genetic counseling: the impact of clinician characteristics on patients' test uptake. *European journal of human genetics: EJHG*, *27*(2), 235–243 (2019).

15) Jordan, J. E., Buchbinder, R., & Osborne, R. H. Conceptualising health literacy from the patient perspective. *Patient education and counseling*, *79*(1), 36–42 (2010).

16) Archibald, A. D., & McClaren, B. J. Perceived relevance of genetic carrier screening: Observations of the role of health-related life experiences and stage of life in decision making. *Journal of Community Genetics*, *3*(1), 47-54 (2011)

17) Boardman, F. K., Young, P. J., Warren, O., & Griffiths, F. E. The role of experiential knowledge within attitudes towards genetic carrier screening: A comparison of people with and without experience of spinal muscular atrophy. *Health expectations: an international journal of public participation in health care and health policy*, *21*(1), 201–211 (2018).

18) Wertz, D. C., & B. M. Knoppers. 'Serious genetic disorders: Can or should they be defined?' *American Journal of Medical Genetics* 108 (1):29–35 (2002)

19) Andermann, A., Blancquaert, I., & Déry, V. Genetic screening: A conceptual framework for programmes and policy-making. *Journal of Health Services Research & Policy*, *15*(2), 90-97 (2010).

20) Wilson JMG, Jungner G. Principles and practice of screening for disease. Geneva: World Health Organization (1968).

21) Matar, A., Kihlbom, U., & Höglund, A. T. Swedish healthcare providers' perceptions of preconception expanded carrier screening (ECS) -a qualitative study. *Journal of Community Genetics*, 7(3), 203–214 (2016)

22) Weaver, M. S., October, T., Feudtner, C., & Hinds, P. S. “Good-Parent Beliefs”: Research, Concept, and Clinical Practice. *Pediatrics*, *145*(6) (2020).

23) Hinds, P. S., Oakes, L. L., Hicks, J., Powell, B., Srivastava, D. K., Spunt, S. L. et al. “Trying to Be a Good Parent” As Defined By Interviews With Parents Who Made Phase I, Terminal Care, and Resuscitation Decisions for Their Children. *Journal of Clinical Oncology*, *27*(35), 5979-5985 (2009).

24) Biesecker, B. Reproduction, ethics, the ethics of reproductive genetic counseling: Nondirectiveness. In T. H. Murray & M. J. Mehlman (Eds.), *Encyclopedia of ethical, legal, and policy issues in biotechnology* (pp. 977– 983). Wiley (2000).

25) van den Berg M, Timmermans DR, Kleinveld JH, van Eijk JT, Knol DL, van der Wal G. Are counsellors’ attitudes influencing pregnant women’s attitudes and decisions on prenatal screening? Prenat Diagn.;27:518–24 (2007).

26) King, E., Halliday, J., Archibald, A. D., Delatycki, M., Newson, A. J., & McClaren, B. J. Development and use of the Australian reproductive genetic carrier screening decision aid. *European Journal of Human Genetics*, *30*(2), 194-202 (2022).

27) Kater-Kuipers, A., de Beaufort, I. D., Galjaard, R. H., & Bunnik, E. M. Ethics of routine: a critical analysis of the concept of 'routinisation' in prenatal screening. *Journal of medical ethics*, *44*(9), 626–631 (2018).

28) Kleiderman, E., Boardman, F., Newson, A.J., Laberge, A.M., Knoppers, B.M & Rvaitsky, V. Unpacking the notion of “serious” genetic conditions: towards

implementation in reproductive decision-making?. *European Journal of Human Genetics* (2024).