

# Ethical issues in reproductive genetic carrier screening

Publicly funded reproductive carrier screening programs must weigh up a number of ethical considerations

**R**eproductive genetic carrier screening (RCS) is undertaken by individuals or couples to determine their likelihood of having a child with particular autosomal recessive or X-linked genetic conditions. It can be undertaken by anyone of reproductive age who wishes to have it, regardless of their family history or ancestry, and either before or during pregnancy.<sup>1</sup> Some forms of RCS are currently available in Australia on a user-pays basis, costing around \$400–\$500 per person. It is usually accessed via general practitioners but can also be accessed directly from testing companies.<sup>2</sup> People who receive an increased chance result are offered genetic counselling to explore their reproductive options, which might include steps to avoid having a child with a genetic condition. Taking the test before pregnancy gives those with an increased chance result a wider range of reproductive options compared with prenatal testing.<sup>3</sup>

The Australian Reproductive Genetic Carrier Screening Project (Mackenzie's Mission), announced by federal Health Minister Greg Hunt in 2018, is a research project offering RCS to 10 000 Australian couples. Recruitment via participating health professionals commenced in late 2019. Mackenzie's Mission is gathering evidence — including clinical, laboratory, psychosocial, health economic and ethical aspects — to inform how publicly funded screening could be operationalised in Australia within ten years.<sup>4</sup>

Here, we reflect on the ethical implications of RCS in Australian health care.<sup>5</sup> While the issues raised apply to all types of RCS, we focus on aspects relating to large scale, publicly funded initiatives like Mackenzie's Mission.

## Ethics and the goals of RCS

A central ethical issue for large scale RCS initiatives is how their goals are described. Two main foci for articulating the goals of such programs are (i) outcomes for individuals and their families, such as reproductive autonomy; and (ii) outcomes for populations, such as reduced incidence of certain genetic conditions.

It has been argued that a goal of seeking to reduce the population incidence of babies who will develop severe genetic conditions is inappropriate for RCS.<sup>6</sup> This line of reasoning draws partly on concerns about perceived coercion; when RCS is offered routinely, couples may perceive that participating is the right thing to do, even if testing is optional.<sup>7</sup>

Additionally, such a goal might be interpreted as implying that couples who receive an increased chance result are then obliged to take action to avoid the birth

of an affected child. Any future national program must be delivered as a genuinely optional intervention, respecting couples' values and preferences.

It has also been argued that the goal of reducing the incidence of certain genetic conditions in the population expresses an unfavourable judgement about the value of the lives of people who currently live with such a condition.<sup>8</sup> Therefore, in the case of RCS it is considered more ethically acceptable for a program's stated aim to be aligned with the first set of outcomes mentioned above; namely, to support couples' reproductive autonomy through provision of relevant information to enable choices that are consistent with their values.<sup>1</sup>

RCS programs are also motivated, at least in part, by the desire to mitigate harms that couples who have parented a baby or child with a severe or fatal genetic condition experience. These harms include the grief of losing a child or witnessing one's child suffering. RCS might enable some parents to avoid such distressing experiences. Emphasising the severity of a condition included in a screening program arguably lessens any implied negative judgement about people living with genetic conditions screened for. However, ethical debate on what constitutes a severe or serious condition remains ongoing.<sup>9</sup>

## Ethical aspects of gene selection

A significant component of designing a publicly funded RCS program is determining which genes warrant inclusion for testing.<sup>10</sup> Since screening can be stigmatising for people living with the genetic conditions screened for, it is considered most ethically defensible to screen only for genes associated with severe childhood-onset conditions.<sup>1,3</sup> However, because perceptions surrounding seriousness and severity are not purely objective,<sup>9</sup> any RCS program must carefully weigh the diverse ways in which a condition can present, as well as the implications of that condition for the person and their family.

There are also ethical aspects regarding the classification of gene variants identified during the testing process.<sup>11</sup> There can be a degree of uncertainty as to how strongly a particular variant is associated with a genetic condition, an issue compounded in population screening because there is no index case (proband) to facilitate interpretation. This has ethical implications because reporting a variant as disease-causing when it is not may mean a couple will experience additional uncertainty and perhaps go through unnecessary tests or interventions. On the other hand, not reporting a variant that does turn

Lisa Dive 

Ainsley J  
Newson 

University of Sydney,  
Sydney, NSW.

ainsley.newson@  
sydney.edu.au

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out to be disease-causing means a couple may go on to have a child with a serious condition despite receiving a low chance result from RCS. This issue will remain important for some time, especially as variant databases are still developing.

### Consent for RCS: enabling meaningful choices

Whether and how to gain consent can be contentious in many public health screening programs.<sup>12</sup> While both consent and pre-test education are important for RCS,<sup>1</sup> determining how best to do this can be complex. It has been argued that when screening is perceived as routine, people will be less likely to reflect critically on whether it is appropriate for them, or to consider whether the results will be relevant to their decision making.<sup>7</sup> Support for pre-test decision making such as educational videos and decision aids can help couples consider the implications of an increased chance result and their options for reproduction.

Mackenzie's Mission is one of several large scale population-based RCS initiatives globally that have curated large panels of genes to test using a couple-based model.<sup>5,10,13</sup> It is important for participants to understand that RCS is designed to provide the couple with information that might help with decisions about reproduction, rather than to convey genetic risk information for their own health. Participants will also be encouraged and supported to reflect on their values and their goals for testing, to help them decide whether this screening will be useful or important for them.<sup>14</sup>

### Reporting results: ethical implications

Results of any genetic test can be complex and might be uncertain.<sup>15</sup> As such, results from RCS need to be provided in a way that is meaningful and useful. To optimise the utility of their results, participants will require a basic understanding of key concepts such as what it means to carry a recessive genetic condition, and the implications of an increased chance finding. It is also important to ensure that participating in screening is not interpreted as guaranteeing that someone will have a healthy child.

Publicly funded population RCS globally is tending towards reporting couple-based findings. Evidence suggests that participants understand and accept this approach and that it is feasible as a population screening model.<sup>5,13,16</sup> Mackenzie's Mission participants will be informed when they both carry the same disease-causing variant for an autosomal recessive condition, or when the genetic mother is found to carry one of the X-linked conditions screened for.

Reporting only couple-based findings is justifiable from an implementation perspective, for both programmatic and pragmatic reasons. Programmatically, RCS aims to inform reproductive choices, so it provides couples with information relevant to those choices. Any potential for false reassurance can be carefully addressed during the pre- and post-test education processes. Pragmatically,

publicly funded RCS would be prohibitively expensive to offer if it reported individual carrier results, as the majority of individuals screened are likely to be a carrier for something.<sup>16</sup> Each of these people would then need individual follow-up, despite their future offspring having a very low chance of actually having that autosomal recessive condition, even if they were to re-partner.<sup>17</sup>

Moreover, this information has no clinical utility for the individual's own health. It also has the potential to provoke anxiety. As such, it is premature and potentially inequitable to provide individuals with information relating to their individual carrier status without providing further support. Further research will inform considerations of the ethical and psychosocial aspects of using an RCS framework to report individual results, including the possibility of offering individual results for a limited number of the more prevalent conditions on the panel.

### Public funding

How RCS is funded is also ethically relevant, not least due to the perceived endorsement of screening by the state when a program is publicly funded. A formal, publicly funded, screening program may have advantages,<sup>18</sup> but public funding might also carry tacit value implications. Experience with antenatal screening suggests that blame and guilt can be associated with declining an offer of screening.<sup>19</sup> Funding models can also reinforce routinisation, where a screening offer might be perceived as encouraging or even coercing couples to terminate a pregnancy if a genetic condition is identified in the fetus.<sup>7</sup>

Within public funding structures, ethical issues also arise from the mode of offer of RCS, either in the context of a formal population screening program (likely to be delivered by centralised, publicly funded entities) or via a Medicare item number. Provision via Medicare will allow any provider who can meet the item number requirements to offer the test, and as such is likely to attract a greater commercial presence in RCS. The resulting fragmentation might constitute a lost opportunity for uniform evaluation of program effectiveness and might also give rise to inconsistencies in aspects of test provision, such as counselling. On the other hand, provision through Medicare may also enable RCS to be rolled out more quickly than establishing a formal population screening program.

Cost-effectiveness of population-wide RCS has not yet been established conclusively by the existing evidence,<sup>11</sup> however, one of the aims of Mackenzie's Mission is to generate such evidence for the Australian health care system.

### RCS and community values

Underlying these ethical considerations is the question of how RCS reflects societal values. While most people are likely to agree on core principles such as respecting couples' choices about whether to participate in

screening, there will also be variations in preferences between communities, families and individuals.<sup>20</sup> Future delivery of a national RCS program in Australia will need to recognise and respond to this diversity, while also upholding the values that motivate the program. The central values for RCS in Australia are good health outcomes for families and communities, alongside respect for all Australians, equity in program design and delivery, and reproductive autonomy.

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