

Ethics of Reproductive Genetic Carrier Screening: From the Clinic to the Population

Lisa Dive^{ID}* and Ainsley J. Newson, Sydney Health Ethics, The University of Sydney

*Corresponding author: Lisa Dive, Sydney Health Ethics, The University of Sydney, Level 1, Medical Foundation Building K25, Camperdown NSW 2006, Australia. Tel: +61 2 9036 3172; Fax: +61 2 9036 3436; Email: lisa.dive@sydney.edu.au

Reproductive genetic carrier screening (RCS) is increasingly being offered more widely, including to people with no family history or otherwise elevated chance of having a baby with a genetic condition. There are valid reasons to reject a prevention-focused public health ethics approach to such screening programs. Rejecting the prevention paradigm in this context has led to an emphasis on more individually-focused values of freedom of choice and fostering reproductive autonomy in RCS. We argue, however, that population-wide RCS has sufficient features in common with other public health screening programs that it becomes important also to attend to its public health implications. Not doing so constitutes a failure to address the social conditions that significantly affect people's capacity to exercise their reproductive autonomy. We discuss how a public health ethics approach to RCS is broader in focus than prevention. We also show that additional values inherent to ethical public health—such as equity and solidarity—are essential to underpin and inform the aims and implementation of reproductive carrier screening programs.

Introduction

Reproductive genetic carrier screening (RCS) involves testing people for their genetic carrier status in order to determine the likelihood that they could go on to have a baby with a serious recessive or X-linked genetic condition.¹ It can be undertaken at various life stages, but we will focus on couples² who undergo testing when they are in early pregnancy or are intending to have a baby.

Historically, detection of carrier status has occurred in two contexts: clinical carrier testing for those who have a relevant family history, or population-level carrier screening programs in groups with a higher prevalence of a particular condition or conditions (ancestry-based screening).³ In both situations, detection of carrier status can inform subsequent reproductive decision making. If two people who intend to have a child are found to carry a disease-causing gene change (mutation) in the same autosomal recessive gene or the woman is a carrier of a mutation on the X-chromosome, then they may consider various reproductive options. These include interventions to avoid having a baby with the identified genetic disposition, or to make plans for the birth of a child with that condition. In comparison with clinical carrier testing, ancestry-based screening tests tend to have a greater emphasis on reducing the prevalence of

certain conditions with comparably high occurrence in the relevant community (Raz, 2007).

RCS is now starting to be implemented in various countries as an opt-in population screening initiative,⁴ offered to those of reproductive age regardless of family history or ancestry. In Australia, a research program in which up to 10,000 couples will undergo RCS commenced in 2019 (Dive and Newson, 2021). This program was funded following long-term professional and public advocacy, most recently a direct approach to Australia's federal health minister by the parents of a baby who had died from Spinal Muscular Atrophy Type 1 (Casella, 2020). Being (at least partly) the result of decades of advocacy from the clinical genetics sector, this pilot is building on existing clinical carrier testing practices and infrastructures (such as laboratory services, clinical interpretation of results and genetic counselling) to offer carrier screening more widely. As such, it is strongly influenced by the clinical *testing* paradigm, with issues such as concerns about missed cases being raised, despite the project being undertaken with the view to inform a future population *screening* program. Several other countries are trialling or have implemented similar programs (for example, the Netherlands (Schuurmans *et al.*, 2019), Belgium (Badoer *et al.*, 2020) and Israel (Singer and Sagi-Dain, 2020)). Early evidence suggests that RCS programs like these are being met with support from

doi:10.1093/phe/phab017

Advance Access publication on 14 June 2021

© The Author(s) 2021. Published by Oxford University Press.

This is an Open Access article distributed under the terms of the Creative Commons Attribution Non-Commercial License (<http://creativecommons.org/licenses/by-nc/4.0/>), which permits non-commercial re-use, distribution, and reproduction in any medium, provided the original work is properly cited. For commercial re-use, please contact journals.permissions@oup.com

target populations (Ong *et al.*, 2018; Plantinga *et al.*, 2019; Schuurmans *et al.*, 2020).

These developments point to a convergence of existing public health approaches to ancestry-based screening and clinical approaches to carrier testing. While early ancestry-based carrier screening programs sought to reduce the incidence of a limited number of high-prevalence conditions, advances in genomic sequencing technology have allowed an expansion of screening targets. At the same time, clinical carrier testing is being scaled up and offered to the broader population (regardless of family history) as a form of screening. Consequently, population RCS programs can now screen more individuals for a much wider range of genetic conditions—known as ‘expanded carrier screening’ (Henneman *et al.*, 2016). This convergence between public health and clinical care also points to an emerging incongruence between RCS screening programs and the ethical values used to justify them.

It is also important to observe that RCS is now commercially available in many countries for those with the means to pay for it. Such commercial tests often use large gene panels more akin to screening than targeted clinical testing, yet are marketed to individuals. In Australia, commercial test products are forming an additional significant comparator for the design and implementation of publicly funded RCS. Of course, commercial test offers can only be accessed by those who can pay for them. Such inequitable access has been part of the motivation for public funding of RCS, along with wider awareness of the benefits of RCS for people without relevant family history or ancestry.

A public health paradigm usually brings with it an emphasis on prevention, however to date the ethical justification for RCS has remained predominantly framed in terms of reproductive autonomy and choice (Clarke, 1997; de Jong and de Wert, 2015; van der Hout *et al.*, 2019). Broadly, reproductive autonomy can be understood as the capacity to reflect critically on one’s values and preferences to inform decision making about reproduction. This notion typically builds on the more individualistic concept of autonomy that dominates clinical ethics (Dive and Newson, 2018), although it increasingly recognizes the relational aspects of autonomy too. However, even a relational understanding of autonomy emphasizes the relational context of the *individual* and the impact it has on their goals, values and choices. As such, RCS that primarily aims to foster reproductive autonomy by providing information relevant to reproductive decision making is informed by a clinical paradigm: clinical ethics approaches tend to emphasize best outcomes for individuals, while public health is

concerned with improving the health of populations (although individuals may, of course, benefit too).

There are valid reasons for emphasizing that reproductive autonomy (as a concept drawn largely from clinical ethics) is an important goal of RCS and that a prevention paradigm (from public health ethics) is problematic. This may lead some to characterize RCS as a clinical intervention. However RCS, as a screening offer made available across the population and funded publicly, has sufficient features in common with other screening programs that it may be characterized as a public health intervention too. We therefore argue in this paper that determining the goals of RCS and their implementation requires an explicit commitment to plural values, drawn from both clinical ethics and public health ethics. This includes supporting the reproductive autonomy of all who undergo RCS, as well as paying heed to the social factors that can undermine or limit reproductive choices.

We begin by describing some key features that tend to be prominent within clinical ethics paradigms and explain why and how such approaches have until now been dominant in the ethical justifications for RCS programs, particularly when framed in terms of reproductive autonomy. We then discuss how RCS can be considered a public health intervention with similarities to clinical testing, rather than a purely clinical intervention, and explore the ethical implications of this conceptual shift. We therefore conclude that only a pluralistic approach that incorporates elements from both clinical and public health ethics can respond adequately to the ethical challenges posed by population-level genetic carrier screening initiatives. In making our argument, we draw primarily on the example of the Australian Reproductive Genetic Carrier Screening Program (ARGCSP, or Mackenzie’s Mission). While our discussion will be relevant to all population genetic screening initiatives, we focus our analysis on programs like the ARGCSP: namely couples-based⁵ genetic carrier screening that is available to anyone and is publicly funded (Kirk *et al.*, 2021).

Clinical Ethics Approaches

Clinical ethics⁶ refers to a range of approaches within bioethics that are oriented toward the context of the delivery of health care services. The main focus of clinical ethics is the patient–clinician dyad, with particular emphasis on the clinician’s obligations towards their patient and the autonomy of the patient (Gillon, 2003; Entwistle *et al.*, 2010; Beauchamp and Childress, 2019).

In the following section, we interrogate the concept of reproductive autonomy as it relates to RCS, but first we will situate that concept within the broader clinical ethics paradigm. Acknowledging that there is much diversity within this field, here we set out one of the more influential approaches, particularly with regards to how autonomy is understood in the health care context.

The application of bioethics in the clinical domain is significantly (though not uncontroversially) influenced by the four principles, as explicated in Beauchamp and Childress' seminal text *Principles of Biomedical Ethics*: autonomy, beneficence, non-maleficence and justice (Beauchamp and Childress, 2019). The first three principles reflect the focus on the individual, acting in their best interests and avoiding harm. In recent decades, there has been a marked move away from medical paternalism, with respect for patient autonomy considered to be an obligation that counters concern over paternalistic interference with patients' wishes. It has been argued, again not uncontroversially (Dawson, 2010), that respecting patients' autonomy should be considered 'first among equals', since to some extent this principle encompasses the other three. Such an approach reflects the priority often afforded within clinical ethics to the individual patient and their interests (Gillon, 2003).

While clinical ethics focuses primarily on the individual, more recently there is increasing acknowledgement of their social and relational contexts (Donchin, 2000; Mackenzie and Stoljar, 2000; Christman, 2014; Walter and Ross, 2014). Yet even with this more sophisticated understanding of the relational aspects of autonomy, the emphasis remains largely on a specific patient in the context of the clinical interaction. The obligations of health care practitioners are to foster patients' capacities to make decisions consistent with their own considered values. The end goal focuses on the individual good: achieving the best outcome for an individual patient.

In practice, clinical ethics tends to manifest in a focus on patients' preferences and choices. The implications for decisions about genetic carrier *testing* (i.e. in a clinical context), informed by clinical ethics approaches, are that the process is designed to support the needs of a specific individual or couple. Genetic carrier testing would be offered if it were considered to have clinical utility for the particular person, who would participate in an informed consent process incorporating genetic counselling to help them understand the test and its implications for them and their family (The American College of Obstetricians and Gynecologists, 2017). This approach ceases to become feasible in the context of offering carrier screening to whole populations, as clinical models of in-depth individual genetic counselling are difficult to

offer at scale. However (and as we outline in the following section), in discussions of population RCS to date the emphasis has focused on individual autonomy, specifically reproductive autonomy.

In the context of reproductive medicine, the concept of reproductive autonomy is a prominent one (Hildt, 2002; McLeod, 2002). An emphasis on reproductive autonomy requires health care professionals to provide information and support to enable prospective parents to make the right choices for them about their reproductive options. As mentioned earlier, reproductive autonomy is best understood as a persons' capacity to reflect critically on their values and goals as relevant to reproductive decision making, and to make reproductive choices that align with their longer-term goals, values, and preferences for the kind of life they wish to live. As such, in order to respect and foster patients' reproductive autonomy, health care professionals have an obligation to provide information and support that is valuable to patients in the context of reproductive decisions they wish to make. Some have argued, however, that the individualistic focus of reproductive autonomy neglects the wider family and social contexts in which reproductive decisions are made (Johnston and Zacharias, 2017). There are also concerns that choice and autonomy in reproduction are not as free as they may first appear (Seavilleklein, 2009). As such, societal factors that are more typically the domain of public health ethics—including socio-economic conditions, family context, and cultural or religious values—are likely to be relevant to a richer understanding of reproductive autonomy and the conditions that make it possible. However, before showing how tenets of public health ethics can inform RCS, we will first explain why there seems to be a deeply entrenched resistance to such an approach. The reticence to conceptualize RCS as, at least in part, a public health initiative is part of why such programs are typically described in terms of reproductive autonomy.

Reproductive Autonomy and Screening Ethics

RCS programs have typically been justified with reference to the concept of reproductive autonomy (De Wert *et al.*, 2012). This way of ethically framing RCS maintains that the desired goal is to provide couples with relevant information to help them to make reproductive choices that align with and reflect their values and preferences. This approach to RCS is consistent with the clinical ethics paradigm described above. It focuses on outcomes for individuals, couples and/or families as well as their

capacity for autonomy in relation to reproductive decision making. It is considered that facilitating individuals to obtain information about their genetic carrier status will be valuable to them because it will enhance their capacity to make reproductive decisions consistent with their own values and preferences.

The emphasis on reproductive autonomy—and thus a clinical ethics framing—as the primary driver of RCS is based on a previous rejection of (a form of) public health ethics as an ethically appropriate paradigm for such programs (De Wert *et al.*, 2012; Henneman *et al.*, 2016; Ravitsky, 2017). The main reason driving this rejection is that there are concerns about the normative implications of a so-called prevention-oriented approach (as is typically associated with population screening) in relation to reproductive decision making. While we will argue below that a false dichotomy is often drawn between an autonomy-focused approach to RCS and a public health or prevention-oriented framing, we will outline here why the latter is usually deemed unacceptable.

There are three main aspects of the argument against treating RCS as a public health program: a comparison with eugenics; concerns that such an approach expresses negative attitudes towards disability and difference; and the potential for routinization. We outline each of these aspects before going on (in the following section) to argue for the importance of addressing the societal impacts of a population-wide screening program, even if it is intended primarily to support the reproductive autonomy of participants.

Eugenics

Public health programs such as screening usually aim to prevent or reduce the prevalence or impact of certain health conditions within a population. A central objection to this framing for RCS stems from the premise that population-level goals, such as prevention (and its attendant effects, such as cost saving), are ethically inappropriate in this context. This argument is strongly grounded in the justifiably robust moral objections to eugenics as practiced in the twentieth century, notably in Nazi Germany but also in the United States and the United Kingdom, among other countries (Wikler, 1999).

Eugenics was defined by Francis Galton as ‘the science of improving stock’ (Galton 1883, p. 17); it can be understood as applying the science of heredity for the benefit of a human population. While this definition might sound benign, eugenics programs in the early twentieth century made erroneous presumptions that genetics was

responsible for a range of undesirable social characteristics like poverty, unemployment and drunkenness, among others (Wikler, 1999). As a result, eugenics was used as the justification for a wide range of strategies ranging from financial incentives to encourage procreation between couples possessing characteristics perceived as desirable, through to abhorrent practices including segregation, incarceration, involuntary sterilization, and even, in Nazi Germany, murder. The horrific and coercive nature of eugenic programs became more widely understood later in the twentieth century, a time of emerging emphasis on individual rights and choices in the context of biomedicine. As such, there was a rejection of any program or intervention that claimed any connection with eugenics.

RCS—as a reproduction-based intervention that will have some influence on which babies are born—does, *prima facie*, appear to have some similarities to eugenic programs of the past. As a comparative example, studies of prenatal screening to detect Down Syndrome show that a substantial majority of pregnancies diagnosed with the condition prenatally are terminated (Collins *et al.*, 2008; Morris and Alberman, 2009; Maxwell *et al.*, 2015). Such findings suggest that RCS to detect carrier status for serious genetic conditions might aim to reduce the prevalence of certain genetic conditions across a population. Accordingly, there is a strong aversion to describing population RCS programs in terms of prevention-based public health screening goals. Implementing RCS with a specific aim to reduce the prevalence of (or to prevent) certain genetic conditions carries the implication that the program seeks to influence what kind of people will be born (De Wert *et al.*, 2012). A similar reticence to acknowledge a public health rationale has been characteristic of prenatal diagnosis, which has also sought to distance itself from the practice of eugenics (John, 2015; Ravitsky, 2017). RCS initiatives therefore typically emphasize the reproductive autonomy of participating individuals and families. Framing RCS in these terms reflects and is primarily informed by a clinical ethics paradigm with its associated emphasis on outcomes for individuals, freedom of choice and autonomy. With reproductive autonomy as the primary goal of the program, the key outcome is providing information to individuals or couples ‘to facilitate informed reproductive decision making’ (Henneman *et al.*, 2016, p. e3).

Disability Critique

Related to the eugenics objection to conceptualizing RCS with reference to public health goals is the argument

that such an approach expresses a negative judgement of or a discriminatory attitude towards people living with the genetic condition that is being screened for (Asch, 1999; Scully, 2008, 2018a). On this view, a publicly funded program that explicitly aims to reduce the prevalence of a disability carries a tacit implication that the life of someone affected by that condition is less valuable or desirable than other lives. Disability scholars have observed that impairment is determined both by biological characteristics of the phenotype, and also the socio-environmental factors that arise from social expectations of how a human body should look and function (Scully, 2008). Furthermore, they have observed that narratives of disability and difference are often not shaped by those who actually live with the condition in question (Scully, 2018b). There is a valid concern that if RCS becomes widespread and the number of people living with genetic conditions decreases, there is a risk that communities will become less accepting and inclusive.

Routinization

If a screening test is offered on a large scale as a matter of routine, then there is a concern that it will diminish the ability of women, couples and families to make their own (informed) choices about whether to participate (Bennett, 2001; Kater-Kuipers *et al.*, 2018). A routine offer of screening might be perceived as coercive, generating pressure to screen, and there may also be (actual or perceived) pressure to terminate an affected pregnancy. One significant contributor to routinization is the way a screening test is described and offered by healthcare professionals. Other factors that can also increase perceptions of routinization are if the screening test is easy and relatively non-invasive (such as a blood or saliva sample), and the institutional context of the program, particularly whether it is publicly funded.

Concerns about the impact of routinization on freedom of choice have further reinforced the emphasis on reproductive autonomy, and thus a clinical ethics framing, as the appropriate focus for RCS programs. On this view, the importance of participation being optional and adequately informed are emphasized, as is the avoidance of coercion (De Wert *et al.*, 2012; van der Hout *et al.*, 2019). The tendency for ethical analysis of RCS programs to shift away from a public health paradigm (which would typically be invoked for screening programs) back to focusing on the decision making processes for participants means that the emphasis moves away from health outcomes for populations, instead prioritizing decision making for individuals and families. It

is often argued that the goals of RCS—even when delivered as a large scale population screening program—should be limited to generating reproductive options and fostering the autonomy of participating women and couples (De Wert *et al.*, 2012; de Jong and de Wert, 2015; Holtkamp *et al.*, 2017). Thus with the primacy of individual decision making and autonomy, clinical ethics paradigms remain central to the ethical acceptability of RCS.

While we agree that reproductive autonomy is important to emphasize in RCS, we will argue that RCS also has sufficient features in common with other screening programs that ethical considerations relevant to public health become important to take into account as well. Crucially, this does not entail abandoning central concepts such as reproductive autonomy. Indeed, in tracing the development of reproductive autonomy, Johnston and Zacharias emphasize that reproductive decisions occur within a social context that can include barriers to accessing services, lack of adequate information, and various other forms of deeply entrenched social and health inequalities (Johnston and Zacharias, 2017). Nor does engaging with public health ethics necessitate endorsing the prevention paradigm as the priority over outcomes for individual participants. A public health ethics approach to RCS is essential to bring focus to the societal and contextual factors that affect people's capacity to make reproductive choices that align with their values and preferences. We will argue that this approach also allows for recognition of wider social considerations such as entrenched disparities in access to reproductive interventions between different sub-populations; for example in Australia, between majority (typically European) populations and minority populations including Aboriginal and Torres Strait Islander peoples. These contextual factors form a crucial requirement for the development of an ethical RCS program at population scale. In the following section, we will explore how RCS meets various justificatory criteria that have been proposed for public health programs, to show that it is essential to incorporate ethical considerations from public health into RCS program design.

Is RCS a Public Health Intervention?

With technological advances making it increasingly feasible to offer RCS to any couple who wants to use it, it is unclear that a clinical ethics paradigm alone is sufficient to address all the ethical issues that such a population-level screening initiative raises. Here we argue that RCS can be understood as a screening initiative; therefore,

some aspects of public health ethics will be beneficial—if not essential—in analysing and responding to the ethical issues that RCS raises.

Screening can generally be understood as a program that tests people with no known elevated background risk to determine if they are at increased risk of a health condition, or otherwise warrant further testing or treatment (Juth and Munthe, 2011). Screening programs typically offer testing to everyone in the population (or relevant sub-groups of the population) irrespective of their *a priori* risk profile, with a goal of reducing the prevalence or impact of disease⁷ in that population (Newson, 2011). RCS, we contend, should be understood as a screening program because of the ways in which it differs from (clinical) genetic carrier testing, as well as the features it has in common with other screening programs. As previously mentioned, traditionally detection of carrier status has been offered to people who have a particular genetic condition in their family, or who are a member of a group that has an elevated risk of a particular genetic condition. Now, RCS programs can test for carrier status of a wider range of conditions, and are available universally, i.e., to anyone who wishes to have it. RCS also differs from clinical testing and ancestry-based screening in that the same test panel is typically used for everyone who participates in the program, rather than detecting a variant already known in a particular family or ethnic group.⁸ Further, as we discuss below individual family history may not be available and so laboratory interpretation of test results may need to be more conservative than in a clinical paradigm.

RCS and the Justificatory Criteria for Screening

While RCS is distinct from genetic carrier testing in the clinical context, it also differs in some significant ways from traditional screening programs. In the 1960s, Wilson and Jungner set out the now well-established justificatory criteria to determine the acceptability of public health screening programs (Wilson and Jungner, 1968). These criteria emphasize the requirement for screening to enable early identification of a condition, and the availability of an effective treatment. Other criteria relate to determining accurately whether a condition is present, the safety of the screening test, and the severity of the condition.

Population level RCS challenges the existing criteria that justify public health screening programs. While Wilson and Jungner's criteria address the complexity involved in detecting disease early in order to treat it, genetic screening to inform reproductive choice constitutes a departure from the traditional goals of

population screening programs (Andermann *et al.*, 2008). The criteria were developed with a view to being applied to particular diseases or health conditions (such as various cancers), not as the basis for more open-ended screening initiatives like RCS. Requirements such as the detectability of the health condition and the existence of a treatment for it cannot be applied to RCS, which might test for variants in hundreds of different genes at a time. This raises the question of whether screening criteria can be used in RCS at all. We contend that it is both possible to apply criteria to RCS, and to do so while upholding a commitment to plural values.

The limitations in applying Wilson and Jungner's framework to determine the appropriate scope of a genetic screening panel have led many countries to assess genetic screening programs using criteria that, while drawing on Wilson and Jungner's original criteria, capture extra elements relevant to initiatives like RCS. For example, additional criteria may reflect subsequent technological developments specific to genetic screening (Cameron and Burton, 2014). Others have observed that genetic screening might also have benefits for the wider family rather than only for the individuals screened (Molster *et al.*, 2017).

Nevertheless, some important elements of the core justifiability for screening programs remain highly relevant to genetic screening. One of these is the validity and reliability of the test (Wilson and Jungner, 1968, p. 21–22). This and other aspects are picked up in a prominent framework for evaluating genetic tests, known as ACCE, which assesses four aspects of the test: analytic validity, clinical validity, clinical utility and ethical, legal and social issues (Haddow and Palomaki, 2004). Additionally, Andermann *et al.*'s (2008) guidance for genetic screening programs broadens Wilson and Jungner's criteria related to accurately identifying and treating a specific disease (which may not always be suitable for genetic screening, due to a lack of treatments) into a requirement for clinical utility or actionability, which genetic screening can satisfy (Andermann *et al.*, 2008; Inthorn, 2014).

As genetic screening criteria have been further developed and refined, there has been increased emphasis on the service delivery context of genetic testing—such as organizational aspects, economic considerations and patient perspectives—as being crucial to inform public health considerations (Molster *et al.*, 2017; Pitini *et al.*, 2018, 2019). These developments reflect some of the emerging or expanded criteria that take into account factors like equity and access (Andermann *et al.*, 2008). Inthorn (2014) describes this broader requirement in terms of the screening test providing information that opens up options for couples or families—a view

supported by Andermann and colleagues, who also recommend that policy makers be guided by a decision support guide rather than a list of criteria to determine the acceptability of a proposed genetic screening program (Andermann *et al.*, 2011).

Thus, Wilson and Jungner's criteria—and others that have extended them for genetic screening—can be used to assess the ethical defensibility of a targeted screening program. However, the complexity of genetic screening (whether for reproductive or other purposes) and the rapidly evolving nature of the science of genetics, means that decisions about population screening such as RCS must be considered in an iterative way. To do so requires a demonstrably robust and transparent process that shows how the evidence has been used, and the trade-offs that have been considered. One possible approach would be to adapt a structured framework from Andermann *et al.* (2010). While a full description is beyond the scope of this article, this framework offers a flexible and revisable approach to documenting, weighing and reasoning about the different factors relevant to a decision about whether and how to implement genetic screening in a population.

RCS as Screening

While various characteristics of genetic screening generally, and RCS in particular, distinguish these programs from other forms of screening, population-wide offers of RCS nevertheless share certain features with them. There are also further reasons that support approaching RCS as a population screening program. One is that RCS programs are typically publicly funded. When a government pays for a test and offers it to everyone, it lends legitimacy to the program and can make people more inclined to think that participating is the right thing to do.

Another reason to treat RCS as a screening program is that there are features of a clinical genetic carrier test that may not be feasible to offer at scale. Such features typically revolve around decision making within the clinician-patient dyad and responding to the values emphasized in clinical ethics. An example is how variant classification is approached: in a clinical setting, the test results would usually be interpreted with reference to the patients' family history. Yet when all participants receive the same test, as is the case in population RCS, variant calling and reporting would likely be more cautious, so as to mitigate harm from overdiagnosis or overtreatment.

A further similarity between RCS and population screening is the way pre-test information is offered to inform the decision making process about whether to undertake screening. In the ARGCSP, participants have access to standardized education materials and a

decision aid. These are important tools to enable adequately informed choices and foster reproductive autonomy. The standardization, however, represents to some extent a departure from the typical clinical interaction between a health care professional and a patient. Only those couples who receive an increased chance result will have access to a more in-depth consultation with a health professional. These features collectively make the program look more like a public health program—where an intervention is offered across the population—rather than a clinical intervention. As such, the clinical ethics paradigm has only a limited capacity to address *all* the ethical issues relevant to population-wide RCS.

Inthorn (2014) suggests that RCS policy could benefit from application of fuzzy logic⁹ techniques as a way of capturing and quantifying the different factors and levels of uncertainty that come into decisions about such programs. Such a strategy reflects the complex and multifactorial nature of the decisions that must be made about designing, implementing and participating in RCS programs. Fuzzy logic may have a role to play, for example, in the algorithms of decision aids to support couples in their deliberations about whether to participate in screening, or how to assess options arising from the results. Both Inthorn's and Andermann *et al.*'s analyses of factors relevant to population RCS show that decisions about RCS—whether about program design and implementation, or decisions about participation—are highly complex and subject to shift over time. While this complexity presents practical challenges, there are ways of engaging with it that ensure the different ethical considerations are addressed at various stages of RCS design and implementation.

In summary, even though RCS programs challenge the established ethical considerations (including justificatory criteria) for public health screening, our position is that RCS is sufficiently similar to other population screening programs—and sufficiently distinct from clinical genetic testing—that public health ethics is relevant to RCS program design. That is, RCS can and should be seen as a (certain kind of) public health intervention. Therefore, public health ethics considerations become important for the design and implementation of such programs. In the following section, we explore what the ethics of public health can offer to inform RCS programs.

RCS and Public Health Ethics

While RCS can be distinguished from public health screening programs—for instance, since it does not test for a particular condition—it has many synergies

with others, such as being available to anyone in the target population, testing people who are not symptomatic or at elevated risk for a condition, and often being publicly funded. It also differs sufficiently from a clinical genetic testing paradigm that consideration of public health ethics becomes important in program design. In this section we outline some prominent features of (various approaches to) public health ethics and consider how they might be useful or important in analysing the ethical considerations relevant to population level RCS programs.

One of the more influential attempts to characterize public health ethics occurred when Childress *et al.* set out to ‘map the terrain’ in 2002, when public health ethics was a nascent area of inquiry (Childress *et al.*, 2002). In so doing, they consider how to justify a public health intervention when it conflicts with what they term ‘general moral considerations’ (p. 171). However, the moral considerations they outline are broadly utilitarian with an individualistic focus and, as such, they draw significantly on the clinical ethics paradigm. They consider factors such as producing benefit and avoiding harm, and emphasize interests of individuals such as privacy, transparency, and so on. They propose various conditions under which a public health program may be justified in infringing on those general moral considerations; the conditions include factors such as the effectiveness of the intervention, the proportionality of the response, and necessity of addressing the issue.

Dawson (2011) argues that this approach to public health places individuals and what is termed ‘the public’ in opposition to each other. He is concerned that such an individualistic emphasis within public health will always prefer non-interference in individual rights. We share these concerns, particularly because in many cases public health and individual interests align, rather than standing in opposition to each other. Furthermore, we also endorse Dawson’s position that an account of public health ethics that emphasizes individual rights like privacy and liberty ignores the fact that individuals exist within a social context and there is no neat delineation between the private and public spheres, or a separation of an individual from their position within various social structures. Public health often consists of interventions that might not benefit individuals directly but contribute to a collective or common good. Jennings points out that the liberal approach is ill-equipped to address community norms and institutions that ‘are themselves an important determinant of health for individuals and communities’ (Jennings, 2007, p. 34). Social determinants such as education, income, housing, employment,

socio-economic status and so on are known to exert substantial influence on health (Marmot and Wilkinson, 2005), but they are subject to influences far beyond the individual’s sphere of control. Health is an area where the interdependencies between public and private aspects of people’s lives are particularly evident, due to the government’s role in both providing health services and in safeguarding the health of the population. Therefore, in considering the ethics of public health interventions, a presumption towards non-interference in individual liberty can actually undermine collective efforts based on shared dependencies and interests. An approach that favours solidarity—which can be understood as a ‘positive identification with another and their position...driven by sympathy and understanding’ (Dawson and Jennings, 2012, p. 74)—and which values community, recognizes the interdependency that is fundamental to our humanity and gives a richer normative basis for understanding public health (Dawson and Jennings, 2012).

How then is this characterization of the ethics of public health, with its recognition of community and interdependency, relevant to RCS programs? When an intervention like carrier screening to inform reproductive choices is expanded into a universally offered publicly funded screening program, collective values such as solidarity and equity become important to embed in the program. While a primary emphasis on reproductive autonomy is justified, particularly to ensure the non-coercive nature of screening, values like equity and solidarity also have significant implications for program design.

In the following section, we explore some of these implications and advocate for a form of public health pluralism for RCS. Before we do this, we will also note that a public health ethics paradigm can help address some of the concerns over eugenics,¹⁰ disability critiques and routinization as described above. Tolerance for diversity and difference (based in the values of solidarity and trust) with a recognition of our human interdependency also requires that RCS programs explicitly seek to shift social norms so that they are more accepting of diversity, including disability. As we have discussed, it is a possible consequence of screening for genetic conditions that disability could become less prevalent in the population, so societal acceptance of people living with disabilities might be eroded over time and generations. Such shifts would be detrimental to all members of society, so RCS programs must be implemented concurrently with parallel efforts to mitigate the possibility of a normative drift towards less accepting attitudes to disability, difference and diversity.

RCS programs that fail to incorporate values from public health ethics therefore run the risk of exacerbating entrenched inequities and eroding fundamental communal values that enrich our societies. An explicit commitment to foster communal values, as well as reproductive autonomy, is essential when designing and implementing population wide RCS. In the following section, we start to sketch out how a value pluralistic approach to RCS might look.

A Value Pluralistic Approach to RCS

So far, we have argued that while there are important reasons for public RCS programs to emphasize reproductive autonomy as a primary goal, such programs are sufficiently similar to other public health screening programs, and different from clinical genetic testing, that it is also important for them to commit explicitly to values from public health ethics. Furthermore, reproductive autonomy cannot be fostered effectively without addressing the social context that constrains reproductive decisions, and doing so requires efforts to address the social determinants that are the focus of public health. Such a commitment has implications for program design, implementation and evaluation.

Wilkinson introduces ‘public health pluralism’ as an alternative to what he terms the ‘pure choice’ perspective on prenatal screening (Wilkinson, 2015). The pure choice view, Wilkinson contends, is the understanding that the sole (or main) aim of prenatal screening is (or should be) to enable reproductive choice. This characterization of the pure choice view is a similar approach to the emphasis on (a narrow conception of) reproductive autonomy as outlined above. While it is debatable whether the typical clinical ethics framing of prenatal screening is purely or solely to promote choice, for the purposes of this article, we will accept that a pure choice view offers a valid encapsulation of the prevailing approach to prenatal screening on a clinical ethics account.¹¹

Wilkinson contrasts a pure choice approach with public health pluralism: the view that a public health program funded by the state needs to commit explicitly to *multiple* goals (not a single aim), and that public health goals—broadly, seeking to improve the health of the population via collective interventions—should be a high priority. Importantly, Wilkinson argues that public health pluralism is a tenable position that can avoid accusations of eugenics and the expressivist or disability critiques that have been used as a basis for justifying the pure choice approach. Public health pluralism

can do this because it can itself include an explicit commitment to fostering participants’ reproductive autonomy as one of its goals.

As discussed above, reproductive autonomy is frequently presented as an alternative to prioritizing prevention-oriented—and thus arguably eugenic and discriminatory—goals for prenatal or preconception genetic screening (De Wert *et al.*, 2012; Ravitsky, 2017). Yet juxtaposing outcomes for individuals (or families) against outcomes for the population is somewhat of a false dichotomy. Logically, there is no reason why RCS cannot have plural goals: to inform couples’ reproductive decisions, but also to improve health at the population level. In other words, the two aims for RCS are not mutually exclusive. Nor are they jointly exhaustive, as there could be other ways of justifying such a program. We have argued that RCS should be considered a screening program, but also that there are important critiques of a preventive (or public health) framing for RCS. As such, we consider that an explicit commitment to plural values, including those of public health, is the best approach for RCS. Accordingly, any robustly ethical RCS program should be developed and implemented with an explicit commitment to a form of public health pluralism.

The form of public health pluralism that we endorse comprises aims of public health that are broader than those Wilkinson posits. Wilkinson’s public health pluralism for prenatal screening comprises four goals: (i) reducing ‘disability and disease’ prevalence in newborns, (ii) improving the health of mothers and babies, (iii) reducing costs to health and welfare systems; and (iv) respecting autonomy (Wilkinson, 2015). Notably, Wilkinson emphasizes consent and choice in the context of autonomy, to which we would add that it is essential to respond to the broader factors that affect a person’s (or couple’s) capacity to exercise their autonomy in practice. To this end, we contend that Wilkinson’s list of goals requires revision. We would augment his goal (ii) to be oriented to improving the health of mothers, babies *and their families*. Including the health of families recognizes the social and relational context in which reproductive decisions are made. We would also clarify that goal (iv) respecting autonomy must incorporate promoting social conditions to enable the exercise of autonomy. Goal (i) reducing disability and disease prevalence in newborns is not an appropriate population goal for RCS. It could, however, be a driver for individual program participants if it aligns with their reproductive goals and values; for example avoiding suffering associated with the unexpected birth of a child with a serious genetic condition.

By offering screening to inform reproductive decision making in a way that is cognisant of the social factors that can constrain such decisions, RCS can coherently hold concurrent plural goals oriented towards both the health of individuals and the health of the population. In this way, screening programs can aim to improve the health of the population without having a stated goal of reducing the prevalence of specific genetic conditions. Wilkinson's third goal, reducing health and welfare costs, may be a measurable impact of RCS, but is ethically unsuitable as a goal because it will undermine other goals such as reproductive autonomy. In place of Wilkinson's goals (i) and (iii), we suggest two further goals. These are to emphasize additional aspects of non-liberal approaches to public health. On this view, public health is also aimed at: (v) reducing inequity in access to health interventions such as RCS; and (vi) recognizing and responding to social constructions and determinants of health and illness. Addressing these additional population health goals is essential in order to foster all families' capacity for reproductive autonomy.

An explicit commitment to value pluralism—that is, both to reproductive autonomy and to the communal values entailed in an approach that seeks to improve the health of the population—is particularly important when articulating the goals of a screening program. This commitment will in turn determine the measures of success by which the program is evaluated. At the heart of some criticisms of approaching RCS as a public health program is the aversion to program goals that measure success as the reduced prevalence of particular genetic conditions in the population. Similar criticisms have been made of attempts to justify prenatal genetic diagnosis based on cost savings that will result from decreased demand on health care resources if fewer people are born with genetic conditions. It has been argued that factors such as efficiency can only come into consideration once other moral considerations (such as safeguarding the autonomy of participants) have been sufficiently addressed (John, 2015). While reduced prevalence of certain conditions might be a consequence of offering population-wide RCS, as a primary program goal it is ethically problematic because it implies an obligation to participate in screening, and may be perceived as exerting pressure on couples to avoid conceiving a child with a genetic condition, or to terminate an affected pregnancy. Such a program goal also explicitly devalues the lives of people who live with genetic conditions. Therefore, public health values must be reflected in other ways.

How does public health pluralism (on our broader account), or an explicit commitment both to foster

participants' reproductive autonomy while also upholding communal values from public health, translate into practice? It can affect all aspects of RCS provision. At the level of program design and implementation, a commitment to communal values generates several demands. Deciding what genes to include on the testing panel should draw on a wide range of perspectives (Kirk *et al.*, 2021). Equity of access requires that screening be available to all people who want it, so it is important to consider options such as sample collection via post and consultation via telehealth to ensure accessibility in regional, rural or remote areas. An important component of ensuring equity of access is that a national RCS program needs to engage collaboratively with community groups such as culturally and linguistically diverse communities and Indigenous peoples to ensure that RCS is implemented in culturally appropriate ways. It is already known that systemic factors can affect both access to health care and the quality of care offered to minority groups (Geneviève *et al.*, 2020). Partnering with different community groups to co-design how RCS is implemented will increase the likelihood that already marginalized populations will be able to benefit from a population-wide RCS offering.

Furthermore, responding to variations in health literacy and ensuring widespread education of primary health care professionals are important considerations that can improve equity of access. Part of the motivation for projects like the ARGCSPP is to reduce inequality in access to RCS. At present such testing is only available in Australia to those who can afford to pay for it, and who are informed about it by their health professional (Robson *et al.*, 2020).¹²

Another requirement of a commitment to public health values such as equity and solidarity in RCS in Australia involves improving and integrating knowledge about genetic variants from Australian populations that are not well represented in publicly available genetic databases. At present, the evidence base for such knowledge is comparably less established than it is for European populations, reflecting wider global underrepresentation of minority ethnic groups in genomic research (Easteal *et al.*, 2020). This means that RCS may provide a different standard of test in some groups compared to others. Any future RCS program in Australia needs to take place alongside initiatives that seek to address the lack of ancestral diversity in genomic reference datasets, insofar as this is possible (Delatycki, Kirk, *et al.* 2021, personal communication). It must also take place in a context that recognizes and responds appropriately to historical and persisting health disparities between different ethnic groups, and to the systemic injustices

experienced by Aboriginals and Torres Strait Islander peoples in Australia. Doing so will involve not only addressing the wider determinants of health, but also a commitment to engaging with diverse communities to co-design RCS programs that are inclusive, accessible and culturally safe.

A commitment to value pluralism can also be demonstrated from the couples' perspective in RCS. When an increased chance result is returned, collective values impose a requirement to ensure that follow-up testing and assisted reproduction (if desired) are also available and appropriately resourced. Ensuring that everyone receives appropriate support, particularly those who have an increased chance finding following screening, is underpinned by the value of solidarity. While solidarity remains a contested concept (Dawson and Verweij, 2012; Kolars, 2020), it offers unique and important insights for how RCS can enact public health pluralism. While not a straightforward concept to define, solidarity is at the heart of public health: a relational concept that is reflected in various ways that we 'stand up beside' each other (Dawson and Jennings, 2012). In the context of RCS, this involves an explicit commitment to valuing difference and diversity and ensuring that any public screening program does not undermine the social conditions that allow people who live with genetic conditions to flourish. While this is a substantial and complex challenge for policy makers and health care professionals, it reflects an ongoing tension between disability rights and developments in genetics (Scully, 2008). Attending to the way that RCS programs conceptualize health and disability, with attention to the socio-environmental factors that contribute to impairment, is essential groundwork for any RCS program.

Other public health values such as reciprocity, the societal obligation to support individuals in the pursuit of public health goals (Upshur, 2002), are also relevant. RCS, when implemented with a commitment to communal values such as solidarity and reciprocity, will ensure that the needs of people who receive an increased chance finding will be met, even without knowing in advance who they are or what their preferences for support will be (they might include options such as further prenatal testing, access to assisted reproduction, or social supports for raising a child with a genetic condition).

It has been argued that RCS or prenatal screening programs must be explicit that their primary goal is *not* seeking to reduce the prevalence of certain conditions, nor to reduce health care costs (de Jong and de Wert, 2015). We contend, however, that it is possible—and indeed preferable—for RCS to hold plural goals, and that these must be oriented to population-level health

outcomes (such as reducing inequity and addressing the social determinants of health and illness, but not—or at least not as program goals—reducing prevalence nor health care costs) in addition to a commitment to promoting reproductive autonomy, construed broadly to encompass the conditions that shape reproductive options. To enact this commitment, it is important for RCS to be perceived by potential participants as genuinely optional (the absence of coercion). This is an essential component of RCS program design, to ensure that population-level benefits will not take precedence over the well-being of program participants. A way of reinforcing the commitment to avoid coercion is to ensure that programs are evaluated by the increased *offer* of screening, rather than increased *uptake* (Ravitsky, 2017).¹³ Meeting such a goal requires efforts to reach all people who might want screening, as well as supporting them to make a good choice for them about whether to participate. The measure is how successful the program is in making this offer. As such, this outcome measure reflects values of equity and removes the incentive to encourage people to participate.

Conclusion

With publicly funded RCS increasingly being offered in various countries, attention to the ethical framing of such programs is essential. Typically, they are justified with reference to reproductive autonomy, a concept predominantly drawn from a clinical ethics paradigm, which has some limitations for population offers of RCS. However, there are also valid reasons why paradigms focusing on public health principles, particularly prevention, have been rejected—including because this approach has a troubled history and expresses unfavourable judgements about the value of the lives of people living with genetic conditions. Nevertheless, we have argued that it remains important to incorporate public health ethics into RCS programs, because such programs have many features in common with public screening programs and differ in ethically relevant ways from clinical genetic testing. As such, RCS is fundamentally *both* a clinical offering and a public health program, so it needs to integrate certain ethical approaches from both these paradigms. Furthermore, failure to consider the population-level impact of RCS has the potential to undermine reproductive autonomy by failing to address the social determinants that constrain many people's reproductive decisions. We have considered how various approaches to public health ethics can enrich RCS programs and have started to explore what an explicit commitment to plural values would entail.

Funding

This article was produced under the Australian Reproductive Genetic Carrier Screening Project (Mackenzie's Mission), which is funded by the Australian Government's Medical Research Future Fund as part of the Australian Genomics Health Futures Mission [GHFM73390 (MRFF-G-MM)].

Conflict of Interest

None declared.

Notes

1. Note that RCS, in this article, describes a program that screens people without a known increased risk of having a child with a genetic condition, to determine whether they carry certain recessive genetic conditions. Typically the programs we refer to use a large screening panel, so are very similar to programs described as Expanded Universal Carrier Screening (EUCS).
2. In this article, we refer to the reproductive decisions undertaken by women, couples or families. In so doing, we take 'women' to mean anyone who is able to become pregnant, whether or not they identify as a woman; we also take 'couples', '(intended) parents' and 'families' to include a broad range of non-heterosexual couples and other family structures who might seek to have a child, including those who will use donor gametes.
3. Examples of the latter include screening for β -thalassaemia in Cyprus and for Tay-Sachs disease among Ashkenazi Jewish populations (Hoedemaekers and Have, 1998; Holtkamp *et al.*, 2017; Rowe and Wright 2020).
4. In this article, we will use the terms 'initiative' or 'program' to describe an RCS test offer that could be either a formally established RCS screening program, or a publicly funded test that is available to anyone regardless of ability to pay, and is delivered by range of providers.
5. ARGCSF participants will receive an 'increased chance' result if together they have an increased chance of having a child with one of the genetic conditions screened. This will occur if both intended genetic parents are carriers for the same recessive condition, or when the intended genetic mother is found to be a carrier for an X-linked condition. This approach, namely reporting couples-based findings (rather than individual results), is increasingly becoming the accepted approach worldwide, with evidence suggesting that it is acceptable for participants, and that it makes population screening more feasible (Delatycki *et al.*, 2019; Schuurmans *et al.*, 2019; Plantinga *et al.*, 2019).
6. For the purposes of this article, we take 'clinical ethics' to be synonymous with 'medical ethics'. Both address the ethical considerations that arise in the clinical health care context and are a subset of bioethics.
7. A critique of the concept of disease is beyond the scope of this paper, but we recognise that it is a contentious term. In particular, understandings of health and disease play an important role in how we respond to variant bodies. Some of the conditions that RCS could detect might not be considered diseases by everyone.
8. Here it is important to acknowledge that the body of scientific knowledge that informs the development of gene panels in initiatives like RCS may not always be appropriately representative of population diversity, and that variant data to support delivery of RCS in historically underserved groups may not yet be of the same standard as that in other (mostly European) populations. While gene lists in population screening programs are curated with the aim of serving the whole population of the jurisdiction in which the particular program is to be implemented, it is important to ensure that these initiatives take place alongside efforts to ensure the data on which they are based reflects appropriate genetic diversity of the population. Furthermore, test panels are chosen so as to be as appropriate as possible for all members of the population.
9. Fuzzy logic is an approach to logical reasoning that allows for imprecise or 'fuzzy' truth values, as opposed to binary truth values. Fuzzy logic is used mostly in computing to allow algorithms to work with propositions that have degrees of truth rather than being entirely true or false.
10. We recognise that a comprehensive response to the eugenics critique of RCS requires a more in-depth treatment than is feasible here. We are addressing this issue in a separate paper.
11. Further issues with a clinical ethics focused approach include that it does not account for costs that can arise from choices, can fail to consider the social and relational aspects of autonomy, and may not acknowledge the broader social construction of choices. That is to say, a pure choice view of prenatal screening is too narrow and fails to represent the more nuanced and complex aims of prenatal screening.

12. The latter, being informed, should now be standard care. In 2019, practice guidelines from the Royal Australian and New Zealand College of Obstetricians and Gynaecologists were updated to require that all women (whether pregnant or planning a pregnancy) be offered information about carrier screening.
13. We thank the anonymous reviewer who noted that informed decisions are a worthwhile aim, but we also recognise that informed decisions are both complex to define conceptually, and more resource intensive to measure. Nonetheless, attempting to evaluate RCS by measuring informed choice would be a useful avenue to pursue, perhaps with a subset of those screened as part of the program evaluation.

Acknowledgements

The authors thank Edwin Kirk, Nigel Laing, Martin Delatycki, and Angus Dawson for their insights that have informed aspects of this article.

References

- Andermann, A., Blancquaert, I., Beauchamp, S., and Costea, I. (2011). Guiding Policy Decisions for Genetic Screening: Developing a Systematic and Transparent Approach. *Public Health Genomics*, **14**, 9–16.
- Andermann, A., Blancquaert, I., Beauchamp, S., and Déry, V. (2008). Revisiting Wilson and Jungner in the Genomic Age: A Review of Screening Criteria over the past 40 Years. *Bulletin of the World Health Organization*, **86**, 317–320.
- Andermann, A., Blancquaert, I., and Déry, V. (2010). Genetic Screening: A Conceptual Framework for Programmes and Policy-Making. *Journal of Health Services Research & Policy*, **15**, 90–97.
- Asch, A. (1999). Prenatal Diagnosis and Selective Abortion: A Challenge to Practice and Policy. *American Journal of Public Health*, **89**, 1649–1657.
- Badoer, C., Marangoni, M., Grenet, M.-L., and Smits, G. (2020). Development of an Expanded Carrier Screening Program in Belgium. Poster presented at the annual meeting of the Belgian Society for Human Genetics, March 2020.
- Beauchamp, T. L. and Childress, J. F. (2019). *Principles of Biomedical Ethics*, Eighth Edition. New York: Oxford University Press.
- Bennett, R. (2001). Antenatal Genetic Testing and the Right to Remain in Ignorance. *Theoretical Medicine and Bioethics*, **22**, 461–471.
- Cameron, L. and Burton, H. (2014). *Genetic Screening Programmes: An International Review of Assessment Criteria*. Cambridge, UK: PHG Foundation.
- Casella, R. (2020). *Mackenzie's Mission*. Sydney, Australia: Allen & Unwin.
- Childress, J. F., Faden, R. R., Gaare, R. D., Gostin, L. O., Kahn, J., Bonnie, R. J., Kass, N. E., Mastroianni, A. C., Moreno, J. D., and Nieburg, P. (2002). Public Health Ethics: Mapping the Terrain. *The Journal of Law, Medicine & Ethics*, **30**, 170–178.
- Christman, J. (2014). Relational Autonomy and the Social Dynamics of Paternalism. *Ethical Theory and Moral Practice*, **17**, 369–382.
- Clarke, A. (1997). Prenatal Genetic Screening: Paradigms and Perspectives. in P.S. Harper and A.J. Clarke (eds.) *Genetics, Society and Clinical Practice*. Oxford, UK: Bios Scientific Publishers. pp. 119–140.
- Collins, V. R., Muggli, E. E., Riley, M., Palma, S., and Halliday, J. L. (2008). Is down Syndrome a Disappearing Birth Defect? *The Journal of Pediatrics*, **152**, 20–24.
- Dawson, A. (2010). The Future of Bioethics: Three Dogmas and a Cup of Hemlock. *Bioethics*, **24**, 218–225.
- Dawson, A. (2011). Resetting the Parameters: Public Health as the Foundation for Public Health Ethics. in A., Dawson (ed.), *Public Health Ethics: Key Concepts and Issues in Policy and Practice*. Cambridge, UK: Cambridge University Press. pp. 1–19.
- Dawson, A. and Jennings, B. (2012). The Place of Solidarity in Public Health Ethics. *Public Health Reviews*, **34**, 65–79.
- Dawson, A. and Verweij, M. (2012). Solidarity: A Moral Concept in Need of Clarification. *Public Health Ethics*, **5**, 1–5.
- de Jong, A. and de Wert, G. M. (2015). Prenatal Screening: An Ethical Agenda for the near Future. *Bioethics*, **29**, 46–55.
- De Wert, G. M., Dondorp, W. J., and Knoppers, B. M. (2012). Preconception Care and Genetic Risk: Ethical Issues. *Journal of Community Genetics*, **3**, 221–228.
- Delatycki, M. B., Laing, N., and Kirk, E. (2019). Expanded Reproductive Carrier Screening-How Can We Do the Most Good and Cause the Least Harm? *European Journal of Human Genetics : EJHG*, **27**, 669–670.
- Dive, L. and Newson, A. J. (2018). Reconceptualizing Autonomy for Bioethics. *Kennedy Institute of Ethics Journal*, **28**, 171–203.

- Dive, L. and Newson, A. J. (2021). Ethical Issues in Reproductive Carrier Screening. *Medical Journal of Australia*, **214**, 165–167.
- Donchin, A. (2000). Autonomy and Interdependence: Quandaries in Genetic Decision Making, in C. Mackenzie, and N. Stoljar (eds.) *Relational Autonomy: Feminist Perspectives on Autonomy, Agency, and the Social Self*. New York: Oxford University Press. pp. 236–258.
- Easteal, S., Arkell, R. M., Balboa, R. F., Bellingham, S. A., Brown, A. D., Calma, T., Cook, M. C., Davis, M., Dawkins, H. J. S., Dinger, M. E., Dobbie, M. S., Farlow, A., Gwynne, K. G., Hermes, A., Hoy, W. E., Jenkins, M. R., Jiang, S. H., Kaplan, W., Leslie, S., Llamas, B., Mann, G. J., McMorran, B. J., McWhirter, R. E., Meldrum, C. J., Nagaraj, S. H., Newman, S. J., Nunn, J. S., Ormond-Parker, L., Orr, N. J., Paliwal, D., Patel, H. R., Pearson, G., Pratt, G. R., Rambaldini, B., Russell, L. W., Savarirayan, R., Silcocks, M., Skinner, J. C., Souilmi, Y., Vinuesa, C. G., and Baynam, G. (2020). Equitable Expanded Carrier Screening Needs Indigenous Clinical and Population Genomic Data. *The American Journal of Human Genetics*, **107**, 175–182.
- Entwistle, V. A., Carter, S. M., Cribb, A., and McCaffery, K. (2010). Supporting Patient Autonomy: The Importance of Clinician-Patient Relationships. *Journal of General Internal Medicine*, **25**, 741–745.
- Geneviève, L. D., Martani, A., Shaw, D., Elger, B. S., and Wangmo, T. (2020). Structural Racism in Precision Medicine: Leaving No One Behind. *BMC Medical Ethics*, **21**, 1–13.
- Gillon, R. (2003). Ethics Needs Principles—Four Can Encompass the Rest—and Respect for Autonomy Should Be “First among Equals”. *Journal of Medical Ethics*, **29**, 307–312.
- Haddow, J. E. and Palomaki, G. E. (2004). ACCE: A Model Process for Evaluating Data on Emerging Genetic Tests. in M.J. Khoury, J. Little, and W. Burke (eds.), *Human Genome Epidemiology: A Scientific Foundation for Using Genetic Information to Improve Health and Prevent Disease*. Oxford, UK: Oxford University Press. pp. 217–233.
- Henneman, L., Borry, P., Chokoshvili, D., Cornel, M. C., van El, C. G., Forzano, F., Hall, A., Howard, H. C., Janssens, S., Kayserili, H., Lakeman, P., Lucassen, A., Metcalfe, S. A., Vidmar, L., de Wert, G., Dondorp, W. J., and Peterlin, B., on behalf of the European Society of Human Genetics (ESHG) (2016). Responsible Implementation of Expanded Carrier Screening. *European Journal of Human Genetics*, **24**, e1–e12.
- Hildt, E. (2002). Autonomy and Freedom of Choice in Prenatal Genetic Diagnosis. *Medicine, Health Care and Philosophy*, **5**, 65–72.
- Hoedemaekers, R. and Have, Ht. (1998). Geneticization: The Cyprus Paradigm. *The Journal of Medicine and Philosophy*, **23**, 274–287.
- Holtkamp, K. C., Mathijssen, I. B., Lakeman, P., van Maarle, M. C., Dondorp, W. J., Henneman, L., and Cornel, M. C. (2017). Factors for Successful Implementation of Population-Based Expanded Carrier Screening: Learning from Existing Initiatives. *European Journal of Public Health*, **27**, 372–377.
- Inthorn, J. (2014). Fuzzy Logic and Preconceptional Genetic Carrier Screening. *Archives for the Philosophy and History of Soft Computing*, **1**, 1–10.
- Jennings, B. (2007). Public Health and Civic Republicanism: Toward an Alternative Framework for Public Health Ethics, in A. Dawson and M. Verweij (eds.) *Ethics, Prevention and Public Health*. Oxford: Clarendon Press. pp. 30–58.
- John, S. (2015). Efficiency, Responsibility and Disability: Philosophical Lessons from the Savings Argument for Pre-Natal Diagnosis. *Politics, Philosophy & Economics*, **14**, 3–22.
- Johnston, J. and Zacharias, R. L. (2017). The Future of Reproductive Autonomy. *Hastings Center Report*, **47**, S6–S11.
- Juth, N. and Munthe, C. (2011). *The Ethics of Screening in Health Care and Medicine: Serving Society or Serving the Patient?*, vol. **51**. Springer Science & Business Media: Springer.
- Kater-Kuipers, A., De Beaufort, I. D., Galjaard, R.-J. H., and Bunnik, E. M. (2018). Ethics of Routine: A Critical Analysis of the Concept of ‘Routinisation’ in Prenatal Screening. *Journal of Medical Ethics*, **44**, 626–631.
- Kirk, E. P., Ong, R., Boggs, K., Hardy, T., Righetti, S., Kamien, B., Roscioli, T., Amor, D. J., Bakshi, M., Chung, C. W. T., Colley, A., Jamieson, R. V., Liebelt, J., Ma, A., Pachter, N., Rajagopalan, S., Ravine, A., Wilson, M., Caruana, J., Casella, R., Davis, M., Edwards, S., Archibald, A., McGaughran, J., Newson, A. J., Laing, N. G., and Delatycki, M. B. (2021). Gene Selection for the Australian Reproductive Genetic Carrier Screening Project (“Mackenzie’s Mission”). *European Journal of Human Genetics*, **29**, 79–79. Published online 16 July, doi: 10.1038/s41431-020-0685-x.
- Kolers, A. (2020). What Does Solidarity Do for Bioethics? *Journal of Medical Ethics*. doi: 10.1136/medethics-2020-106522.

- Mackenzie, C. and Stoljar, N. (2000). Introduction: Autonomy Reconfigured. in C. Mackenzie and N. Stoljar (eds.), *Relational Autonomy: Feminist Perspectives on Autonomy, Agency, and the Social Self*. New York: Oxford University Press.
- Marmot, M. and Wilkinson, R. (2005). *Social Determinants of Health*. Oxford: Oxford University Press.
- Maxwell, S., Bower, C., and O’Leary, P. (2015). Impact of Prenatal Screening and Diagnostic Testing on Trends in down Syndrome Births and Terminations in Western Australia 1980 to 2013. *Prenatal Diagnosis*, **35**, 1324–1330.
- McLeod, C. (2002). *Self-Trust and Reproductive Autonomy*. Cambridge, MA: MIT Press.
- Molster, C. M., Lister, K., Metternick-Jones, S., Baynam, G., Clarke, A. J., Straub, V., Dawkins, H. J., and Laing, N. (2017). Outcomes of an International Workshop on Preconception Expanded Carrier Screening: Some Considerations for Governments. *Frontiers in Public Health*, **5**, 25.
- Morris, J. K. and Alberman, E. (2009). Trends in Down’s Syndrome Live Births and Antenatal Diagnoses in England and Wales from 1989 to 2008: Analysis of Data from the National down Syndrome Cytogenetic Register. *British Medical Journal*, **339**, b3794.
- Newson, A. J. (2011). Population Screening. in A., Dawson (ed.), *Public Health Ethics: Key Concepts and Issues in Policy and Practice*, Cambridge, MA: Cambridge University Press. pp. 118–142.
- Ong, R., Howting, D., Rea, A., Christian, H., Charman, P., Molster, C., Ravenscroft, G., and Laing, N. G. (2018). Measuring the Impact of Genetic Knowledge on Intentions and Attitudes of the Community toward Expanded Preconception Carrier Screening. *Journal of Medical Genetics*, **55**, 744–752.
- Pitini, E., D’Andrea, E., De Vito, C., Rosso, A., Unim, B., Marzuillo, C., Federici, A., Di Maria, E., and Villari, P. (2019). A Proposal of a New Evaluation Framework toward Implementation of Genetic Tests. *PLoS One*, **14**, e0219755.
- Pitini, E., De Vito, C., Marzuillo, C., D’Andrea, E., Rosso, A., Federici, A., Di Maria, E., and Villari, P. (2018). How is Genetic Testing Evaluated? A Systematic Review of the Literature. *European Journal of Human Genetics*, **26**, 605–615.
- Plantinga, M., Birnie, E., Schuurmans, J., Buitenhuis, A. H., Boersma, E., Lucassen, A. M., Verkerk, M. A., Langen, I. M., and Ranchor, A. V. (2019). Expanded Carrier Screening for Autosomal Recessive Conditions in Health Care: Arguments for a Couple-Based Approach and Examination of Couples’ Views. *Prenatal Diagnosis*, **39**, 369–378.
- Ravitsky, V. (2017). The Shifting Landscape of Prenatal Testing: Between Reproductive Autonomy and Public Health. *Hastings Center Report*, **47**, S34–S40.
- Raz, A. E. (2007). *Community Genetics and Genetic Alliances: Eugenics, Carrier Testing, and Networks of Risk*, London, UK: Routledge.
- Robson, S. J., Caramins, M., Saad, M., and Suthers, G. (2020). Socioeconomic Status and Uptake of Reproductive Carrier Screening in Australia. *Australian and New Zealand Journal of Obstetrics and Gynecology*, **60**, 976–979. doi: doi.org/10.1111/ajo.13206.
- Rowe, C. A. and Wright, C. F. (2020). Expanded Universal Carrier Screening and Its Implementation within a Publicly Funded Healthcare Service. *Journal of Community Genetics*, **11**, 21–38.
- Schuurmans, J., Birnie, E., Ranchor, A. V., Abbott, K. M., Fenwick, A., Lucassen, A., Berger, M. Y., Verkerk, M., Van Langen, I. M., and Plantinga, M. (2020). GP-Provided Couple-Based Expanded Preconception Carrier Screening in the Dutch General Population: Who Accepts the Test-Offer and Why? *European Journal of Human Genetics*, **28**, 182–192.
- Schuurmans, J., Birnie, E., van den Heuvel, L. M., Plantinga, M., Lucassen, A., van der Kolk, D. M., Abbott, K. M., Ranchor, A. V., Diemers, A. D., and van Langen, I. M. (2019). Feasibility of Couple-Based Expanded Carrier Screening Offered by General Practitioners. *European Journal of Human Genetics*, **27**, 691–700.
- Scully, J. L. (2008). Disability and Genetics in the Era of Genomic Medicine. *Nature Reviews Genetics*, **9**, 797–802.
- Scully, J. L. (2018a). Disability and the Challenge of Genomics. in S. Gibson, B. Prainsack, S. Hilgartner, and J. Lamoreaux (eds.), *Routledge Handbook of Genomics, Health and Society*. London: Routledge. pp. 186–194.
- Scully, J. L. (2018b). From “She Would Say That, Wouldn’t She?” to “Does She Take Sugar?” Epistemic Injustice and Disability. *International Journal of Feminist Approaches to Bioethics*, **11**, 106–124.
- Seavilleklein, V. (2009). Challenging the Rhetoric of Choice in Prenatal Screening. *Bioethics*, **23**, 68–77.
- Singer, A. and Sagi-Dain, L. (2020). Impact of a National Genetic Carrier-Screening Program for Reproductive Purposes. *Acta Obstetrica et Gynecologica Scandinavica*, **99**, 802–808.

- The American College of Obstetricians and Gynecologists. (2017). Carrier Screening in the Age of Genomic Medicine. Committee Opinion No. 690. *Obstetrics and Gynecology*, **129**, 35–40.
- Upshur, R. E. (2002). Principles for the Justification of Public Health Intervention. *Canadian Journal of Public Health*, **93**, 101–103.
- Hout, S., Dondorp, W., and de Wert, G. (2019). The Aims of Expanded Universal Carrier Screening: Autonomy, Prevention, and Responsible Parenthood. *Bioethics*, **33**, 568–576.
- Walter, J. K. and Ross, L. F. (2014). Relational Autonomy: Moving beyond the Limits of Isolated Individualism. *Pediatrics*, **133**, S16–S23.
- Wikler, D. (1999). Can we Learn from Eugenics? *Journal of Medical Ethics*, **25**, 183–194.
- Wilkinson, S. (2015). Prenatal Screening, Reproductive Choice, and Public Health. *Bioethics*, **29**, 26–35.
- Wilson, J. M. G. and Jungner, G. (1968). *Principles and Practice of Screening for Disease*. Geneva: World Health Organization, available from: https://apps.who.int/iris/bitstream/handle/10665/37650/WHO_PHP_34.pdf [accessed May 2021].