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Consistency of what? Appropriately contextualizing ethical analysis of non-invasive prenatal testing.

Ainsley J. Newson, Zuzana Deans, Lisa Dive & Isabella Catherine Holmes

It is unarguable that the implementation and use of non-invasive prenatal testing (NIPT) should be critical and appropriate. After all, decisions that influence when and how to have children have utmost ethical significance. Bowman-Smart et al (2021) argue that the implementation of NIPT should be consistent. They also suggest that, at present, consistency is not being achieved when it comes to decisions about seeking information via NIPT. Their position seems to be that the distinction between medical and non-medical traits is less relevant than the importance of the phenotype itself. The right approach, on their view, is one in which information provision "focuses on the morally relevant features of a trait". They also imply that, because a wide range of information may inform "what lives [prospective parents] want their children to have", NIPT should not be confined to reporting information about 'medical' considerations.

We agree that it is important to "think critically about what kind of information should be available to prospective parents" (Bowman-Smart et al. 2021). Nevertheless, we offer three critiques: (1) that the authors' argument overlooks information-related limitations; (2) that their analysis conflates population health and clinical paradigms; and (3) that the justification for what information prospective parents should be able to access requires broader

considerations than medical relevance. These critiques together underscore the importance of agreeing and clarifying comparators when making consistency claims.

Information, and its limits

Information plays a big part in reproductive genetics. Bowman-Smart et al discuss various kinds of information that parents may wish to access about their fetus. Yet in so doing, they overlook problems that an 'information' approach may give rise to. First, their approach reflects an unrealistic epistemic optimism, namely a presumption that information is inherently valuable and always generates knowledge. This is not just a technological limit, but a conflation between the kind of non-communicable 'information' contained within DNA and the kind of communicable information we gather from its analysis (Manson 2006).

Second, in claiming that consistency of decision-making about NIPT should focus on phenotype, the authors prematurely dismiss the importance of genotype. This emphasis overlooks phenomena such as variable penetrance and expressivity (Dive, Archibald, and Newson 2022), and the general lack of predictive certainty between genotype (which is what NIPT will assess) and phenotype. While the authors stress the importance of phenotype, access to expanded results from NIPT may not provide the kind of information needed to understand what the phenotype of their fetus will be. This is true even of well-defined conditions such as Trisomy 21.

Third, if we were to take the approach to consistency to its logical conclusion, it would invite the provision of information that parents claim they want, but that has potential to cause harm – such as has occurred with variants of uncertain significance (Watts and Newson 2021). Concerns such as epistemic fatigue may arise when a phenotype has "morally relevant features," but the genotype linked to that phenotype is uncertain.

Conflating population health and clinical care

While it is necessary to "distinguish between ethical issues related to… NIPT in general [i.e., a clinical intervention], and … NIPT in a population screening program", the authors conflate these contexts. Specific ethical considerations apply when information is offered in a population screening context compared to clinical practice. A screening test is offered as a uniform intervention, to a defined population (in this case, pregnant people). Most aspects of the offer are standardized, including the scope of the testing – individual tailoring is rare (Dive and Newson 2021).

Ethical issues in screening incorporate tenets from public health ethics. However, in the context of population screening with implications for reproductive decisions, prevention should not be the primary aim. Instead, the goal is to facilitate reproductive choice. Nevertheless, a set of values informed by public health pluralism remain important (Dive and Newson 2021). There is a small literature exploring public health ethics analyses in the context of reproductive genetic screening (Dive and Newson 2021; Wilkinson 2015; Potter et al. 2008), as well as an emerging literature highlighting the care that should be taken when determining what variants to look for, and report (Watts and Newson 2021; Kirk et al. 2021; Dive, Archibald, and Newson 2022). Additionally, frameworks exist that critically apply Wilson and Jungner's 1968 criteria to genetic and genomic information (see, e.g. Andermann, Blancquaert, and Déry 2010). These suggest that concept of 'treatable' may need to be construed more broadly than in 'typical' population screening.

A clinical intervention, in contrast, is offered in the context of a doctor-patient relationship. Decisions about whether and how to use NIPT are informed by mutual engagement and with appropriate time for reflection. It may be possible to tailor NIPT to suit the values and interests of the patient. A central tension in Bowman-Smart et al's analysis is that they conflate screening offer and clinical offer. While an augmented form of public health ethics might apply for prenatal screening, the provision of NIPT in a clinical context demands a different analysis. The authors go on to raise concern that the use of NIPT beyond a narrow range of conditions leads to inconsistencies with "traditional screening criteria." There are two issues here: first that genetics and genomics have moved past these criteria, as noted above. Second, an approach informed by public health pluralism would not condone the non-medical use of NIPT to identify biological sex, as this would not reduce inequity, promote health or reduce health disparities (applying Dive and Newson 2021). As such, it is not that there is an inconsistency with these approaches but that provision of non-medical information in NIPT does not align with public health pluralistic goals. [1] Population screening is a form of triage – it is designed to identify those who may be offered further information. It is not intended to be used to identify and convey information that would not meet screening criteria.

[1] Information from NIPT may, as the authors recognize, also arise incidentally. But there is a distinction between something arising incidentally and something being deliberately sought. While information may be deemed relevant by parents, the perception of relevance and it being justified to provide are distinct questions.

Further comparators regarding what information prospective parents should have access to

In a paper cited by the authors, we considered whether parents should be able to obtain results from NIPT for information only, with no intention to terminate (Deans, Clarke, and Newson 2015). Bowman-Smart et al's line of reasoning might generate the conclusion that if a trait is relevant to parents, and the phenotype is on a par with information already routinely provided, then information about this new trait can be provided too.

However, there are other ways that consistency in ethical decision-making can be found. We contend that a reasonable comparator to NIPT for information only would be with genetic testing in childhood. When testing for information only, the fetus is on course (in a wanted pregnancy) to become a child.(Deans, Clarke, and Newson 2015) This consideration should be the starting point when determining the ethical justification for using NIPT for non-medical traits.

The current clinical consensus on childhood genetic testing is to test only as needed, making judgements on, for example, whether the test would be helpful for identifying and managing a condition that will present in childhood (see, e.g. Vears et al. 2020). This is because testing a child for an adult-onset condition would, *prima facie*, be inappropriate for several reasons, not just the right to an open future. Given this established position on childhood testing, an additional argument would be needed to justify why an individual on the same trajectory towards adulthood as the child should be treated differently.

We also argued that obtaining genetic information about the unborn individual could be wrong for multiple reasons: for example, harm may result from stigmatization or unrealistic expectations, and the information could undermine the individual's future autonomy (Deans,

Clarke, and Newson 2015). Bowman-Smart et al. challenge this stance by questioning the concept of the right to an open future and whether information itself can impede capabilities. However, it is inescapable that genetic knowledge about an unborn child who will later be born may be future-affecting in the same way as genetic information about the child after birth may be future-affecting. An individual whose parents sought a raft of genetic information about them prenatally can exercise less autonomy than an individual who is in a position to choose who has knowledge of their personal information (including whether they themselves access this information).

Of course, it may be that the authors' intention is not to rebut our position on the use of information only. Indeed, we seem aligned at a later point in their paper, where the discussion turns to decisions about terminating a pregnancy based on non-medical information. While we do not have space in this commentary to engage with this prosect, we do feel the ethical gravity of such a decision is underplayed given the moral significance of decisions made in relation to pregnancy.

We suggest a complete picture of the ethical provision of NIPT includes an understanding of the limitations of prenatal genetic information, and that there are distinctions between population screening and clinical testing that impact Bowman-Smart et al's argument. While we agree that consistency is important, we suggest different lines of consistency when it comes to NIPT for non-medical information.

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