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SCREENING HUMAN LIFE – THE LEGAL AND ETHICAL IMPLICATIONS OF NON-INVASIVE PRENATAL TESTING

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INTRODUCTION

We now have easy and low risk tests that can be undertaken at an early stage of pregnancy that can yield a range of information about the future child. This technology is known as non-invasive prenatal testing (NIPT) and can provide parents with accurate information about the health or disability of the developing child. It also has the potential to yield uncertain and trivial data, or information that has no immediate clinical purpose. This paper examines the aims and public narratives associated with this technology, and the disruptive potential of these tests in ethical and regulatory terms as they are released into a global village. It also explicitly considers how and where we live (and access services) impacts on parental decision making and the evolution of these tests. This paper is developed in eight parts. In part one, we address conventional reproductive screening and diagnostic testing and the introduction of NIPT. In part two, we examine the aims and public narratives associated with this technology. In part three, we consider the implementation of these tests on the domestic and global stage. In part four, we examine the disruptive quality of this technology, before moving on to examine (in part five) how socio-economic and global factors may influence parental decision making and the future implementation of these tests. In part six, we look forward and consider possible pressure points and challenges arising from environmental, political and societal changes. In part seven, we evaluate possible regulatory responses, before making some closing remarks about the type of future society that we want to create.

PREGNANCY SCREENING AND NIPT

In many countries, conventional combined screening - the process of identifying whether a fetus has an increased chance of having a condition – involves the use of maternal serum tests and ultrasound imaging and is a routine part of prenatal care during the early/ mid-stages of a pregnancy. These tests have relatively high false positive rates, and further invasive tests (amniocentesis or chorionic villus sampling) are required for a diagnostic result. The invasive tests carry an increased risk of

miscarriage (about 1%[1]) and require a certain skillset that may not be freely available in low resource States. Researchers have therefore looked for safer and reliable alternatives for establishing the likelihood of specific birth outcomes.

NIPT technology was first introduced for aneuploidy detection in about 2011 – utilising the discovery of circulating cell free fetal DNA in the maternal blood stream - and has been swiftly developed and exploited by the commercial sector as a clinical offering across the globe.[2] NIPT is now available through private sector providers in over 60 countries.[3]

These tests involve the taking of a maternal blood sample during the early stages of pregnancy. There is no physical risk to the pregnancy or the fetus. The sample is then subject to laboratory analysis using the cell-free fetal DNA in the maternal blood. The analysis can provide a range of information about the developing fetus including the likelihood of aneuploidy or other anomalous genetic condition. It can also provide secondary findings about the pregnant woman. In some cases, the laboratory analysis can be undertaken at an earlier stage than conventional screening and invasive testing. Early and safer testing is prima facie advance but, as with any technology, we should be cautious about implementation. The accuracy and quality of the information produced varies from the diagnostic (eg some inherited genetic conditions, fetal sex and rhesus D status (called NIPD)), to near diagnostic (eg Down Syndrome where the sensitivity and specificity rates have been demonstrated to be greater than 95%[4]), to variable and uncertain in terms of future outcome (eg chromosomal micro deletions and micro duplications[5]). NIPT also has the potential to provide a range of non-health related information, and whole human genome testing/ exome sequencing has been demonstrated in a research setting.[6] This mixed pattern of accuracy, the potential to generate large datasets and risk-based/ equivocal information is potentially problematic for stakeholders (including parents, clinicians and regulators). Against this background, it is generally agreed that non-directive counselling is required to inform the testing process.[7]

PUBLIC NARRATIVES

'Reproductive autonomy' and 'public health' have become the predominant narratives associated with the aims and purposes of NIPT,[8] and some commentators see them as "competing and largely irreconcilable rationales".[9] However, these approaches tend to conceptualise the narratives narrowly and obscure the practical reality of implementation and use. 'Reproductive autonomy' frames NIPT as a facilitator and enhancer of parental (and specifically maternal) autonomy by providing information and informing choices about the pregnancy. Information about the unborn child may help parents decide whether to continue with or terminate the pregnancy. In this narrative, testing ought to relate to the exercise of autonomous decision-making – in other words, the information sought should facilitate possible decisions about the pregnancy.[10] However, it can be argued that the physical and psychological well-being of the mother is so inextricably connected to her unborn child, that there is a plausible basis for asserting a qualified right to know even trivial and non-health information that the pregnant woman attaches significance too.[11]

The autonomy narrative rests on the foundation that maternal and parental choices are free and informed, and is about emphasising and prioritising individual preferences and values. [12] This may be significant in cultural contexts that do not prioritise individual autonomy. Further being 'free' necessitates an absence of undue influence/ pressure on the decision-maker and on the choices made using the results. Being 'informed' requires that the parents have adequate information about the tests, the test conditions/traits and what the results mean. These requirements are challenging given the complexity of genetic risk and the range of information that could be available to us in near future.

The presentation of pregnant women as "choice makers" is also problematic because it makes certain assumptions about the decision-making process that are not necessarily borne out in practice and in cultural contexts.[13]

The 'public health' narrative focuses on broader societal considerations, either promotion of a consequential public health benefit or the avoidance of some consequential public harm. In its narrowest form, testing is the means to prevent something – a trait, condition or characteristic - that is unwanted. This is relatively unproblematic in the case of treatable conditions – where testing could inform, enable or facilitate measures aimed at improving the health or outcomes for the fetus. Currently, there are few examples of these types of condition (eg rhesus status and female congenital adrenal hyperplasia) but the opportunities for effective in-utero treatment are likely to expand in the future. However, the explicit improvement of public health through the removal of unwanted life is rarely articulated, and is frequently resisted ethically for anomaly and non-health testing.[14] Such arguments raise discriminatory and eugenic concerns[15] and therefore policymakers tend to emphasise the autonomy narrative instead.

In relation to anomaly testing, Ravitsky argues that "the only options available to most women following prenatal diagnosis of a serious disability or health condition are termination of the pregnancy or preparation for the arrival of a child with special needs or health challenges."[16] This argument rests on a stark presentation of choice. Some parents may have no desire to act - knowing something, even unplanned news, may still be wanted[17] - and testing can produce reassurance or some degree of certainty. The statement also presupposes that testing is limited to serious disabilities or conditions where lawful options to terminate are available.[18] In relation to non-health traits or minor disability, there may be no lawful choice for the parents to make. Even if there are lawful options, they may not be actionable because of parental values and beliefs.[19]

There are reasons why public health considerations might feature in relation to fetal anomaly testing and justify state intervention and the qualification of 'autonomy'. NIPT "can reduce adverse pregnancy outcomes by limiting the number of unnecessary invasive tests and the accompanying risks and parental anxiety associated with these tests. Advance knowledge may help prepare families psychologically and physically for the birth of a child with disability. The ability to identify disability or conditions accurately could have a role to play in public health planning and the distribution of future State resources. The potential benefits of a publicly funded scheme might include central coordination and greater quality control over testing. Specific public funding of NIPT would also remove the current inequity for those who cannot afford the expense of private testing."[20] Other considerations might include the avoidance of discrimination/ stigmatisation of disability,[21] the spectre of the designer baby and the regulation of patient care.[22] NIPT shines a spotlight on the liminal status of the developing child and is clearly associated with the abortion debate.[23] Global commercial context and precautionary reasoning may also legitimize some limited State intervention.[24]/[25]

IMPLEMENTATION

The UK NHS operates NIPD in relation to certain genetic conditions and fetal sex determination is only available when linked to a specific condition.[26] The UK National Screening Committee recommended an evaluative rollout of NIPT as a contingent test for Down, Edwards' and Patau syndromes in early 2016 – as an intermediate step between conventional screening and the diagnostic tests. NIPT will only be offered within the fetal anomaly screening programme where conventional screening has highlighted a risk greater than one: one-hundred and fifty, and full implementation is

scheduled for 2018. There are a wider range of test options, including fetal sex determination, available in the private sector,[27] and some NHS hospitals are already facilitating private testing using NHS Cytogenetic labs.[28]
There has been inconsistent global implementation of NIPT, but the commercial application/ promotion and simplicity of sampling makes health tourism feasible. The internet provides a platform for information about and promotion of the tests/ conditions – some of it reliable and some less so – making it difficult to identify trustworthy sources.[29] Although the manufacture and sale of tests kits in the UK are regulated,[30] control may not extend to testing outside the EU where many commercial providers operate. Therefore, the environment in which NIPT has been launched makes effective regulatory intervention challenging.[31]

DISRUPTIVE QUALITY

Like any new technology, there is the potential to disrupt existing societal, ethical and regulatory frameworks in positive and negative ways. NIPT presents a prima facie advance for reproductive management and choice, but the simplicity and safety of the sampling process may well prove to be an 'achilles' heel'. Protecting autonomy requires careful handling of the consent process and this requires time and resources to accommodate variations in education, intelligence and language. There is already evidence that informed consent is being neglected in conventional screening tests.[32] If the range of tests is expanded, and NIPT becomes just another blood test, this will only exacerbate the situation. There is the risk of premature adoption by parents – where test results are treated as diagnostic when they are not.[33] Normalisation within screening programmes may make it harder for women to make informed choices about testing; and pressure from researchers to implement these tests as a technical gain (irrespective of patient autonomy) should not be underestimated.[34]
Publicly funded environments also promote the tests,[35] and this puts pressure on decision-making generally. It has been argued that NIPT has the potential to lower acceptable thresholds around certain kinds of life, as well as expressing "hurtful" attitudes/ messages to people living with those traits.[36] More information does not necessarily equate with better choices, especially if outcomes are uncertain and results unreliable and hard to interpret.[37] There is also an unmistakeable shift from ex post responses (to remedy, accommodate, prepare etc) to ex ante prevention of certain forms of life, and this adds to the pressure on parents when making decisions. Apart from the obvious risks associated with a 'genomic future', the dramatic evolution of technology creates practical problems during implementation - increasing levels of information (particularly in relation to conditions with variable outcomes) are likely to require extra support and sophistication from genetic counsellors. Keeping those services sufficiently in touch with the evolving technology may be challenging and expensive for providers.[38]
These tests also provoke a tension between the informational interests of pregnant women in making informed choices (including having information about their baby) and the interest of future persons (the subject of testing if born) in deciding what genetic information should be available to others. Increased genetic data is likely to put pressure on conventional notions of privacy and generate practical problems for resourcing and managing any right to know or not know.[39]

SOCIO-ECONOMIC FACTORS

There is tendency for the autonomy narrative to ignore "the unequal way these choices affect women with different socioeconomic resources in different political contexts, especially in societies without a strong social welfare safety net."[40] To examine how these factors may influence parental decision-making and implementation, we shall concentrate on three specific areas: a) test access, b) information/ results and c) post-test choices. In relation to a), parental access may be dependent on location – not just which State but also where they live within a State. There is certainly evidence of urban and rural variation in terms of NIPT access in low resource countries.[41] The affordability of tests will impact uptake and discrepant availability and cost variation[42] may have a ripple effect on equality of access and health tourism. In relation to b, concern has already been expressed about the reliability of online sources,[43] the reading age required for some promotional material,[44] and language/ education barriers to access.[45] In relation to c, choices may be influenced by family resources (ie the affordability of raising a child with disability) and are likely to be shaped by available State support. Current and foreseeable living environments and family size may also influence parental decision making in this context. The acceptability and stigma attached to raising a child with disability may be influenced by local conditions as well as religious factors. Mozersky et al. have highlighted the danger of unitary global policies[46] and the limits of individual autonomy, especially where lawful abortion is severely restricted.[47] Not all societies place the same weight and values on individual autonomy – for example, there are different cultural perspectives about sex selection that extend from unacceptable discrimination to legitimate 'family balancing'.[48] There are also different societal thresholds for disability and prevalence of genetic variation,[49] producing different State priorities and inevitable global variations around NIPT. National and professional resources (eg availability of public funding, insurance and genetic counsellors) may also be important.[50]

PRESSURE AND CHALLENGES

Whilst, we cannot exclude public health considerations from anomaly and non-health related testing, they may be hidden under the guise of 'autonomy' and impede the realisation of reproductive choice.[51] As the range of testable conditions/ traits increase, availability is likely to put consent processes under pressure in public health regimes operating with finite resources. Population growth[52] will add to the pressure on scarce resources potentially impacting on services supporting individuals with disability. Significant growth in the global commercial market is predicted,[53] cross border access may be difficult to stop and commercial exploitation all have the potential to undermine patient autonomy. If more test options are made available, parents may find it hard to resist the urge to test, even for traits unactionable by lawful means. Western law increasingly places emphasis on patient rights[54] and we have argued elsewhere that there is a plausible argument for a mother to claim a qualified right to know information about her developing child.[55] This backdrop appears bleak but if a eugenic future is to be resisted, we need to think very carefully about how we implement and regulate expansion of this technology. If a State cannot guarantee parental autonomy, it should not promote policies using this narrative. Whilst Ravitsky has suggested that a range of social policies could be used to underpin autonomy,[56] we are more sceptical about the effectiveness of such measures where pressure due to limited space, resources and commercial greed persist.[57] Equally, if public health considerations underpin the offer of testing, they need to be put front and centre in the narrative.

POSSIBLE REGULATORY RESPONSES[58]

Faced with these predictions, domestic regulators might adopt mandatory (negative) legal rules and guidelines against all NIPT services into a jurisdiction. These rules might provide for the licensing of NIPT with specific requirements relating to advertising, access, counselling, scope etc.[59] However, positive forms of regulation may be more effective, and States should consider informational mechanisms including renewable certification of NIPT websites, online forums and related services[60] and 'internet prescriptions' (where doctors highlight 'approved' online sources of information/ support about these tests). National guidance could be circulated to NIPT suppliers within a jurisdiction.[61] Organisational and incentive policy instruments may also assist - public funding could squeeze the private sector although this would depend on the degree of service equivalence and have significant resource implications for States. If post-birth concerns about information are to be addressed, we need a regulatory framework that makes provision for the storage, security and future destruction of important personal data (including genetic data) and that takes an acceptable position on any right to know and not to know. We are less optimistic about the effectiveness of international regulatory efforts, but the use of chokepoints, local asset enforcement and reciprocal cross border enforcement/co-operation might be warranted.[62]

CONCLUSIONS

Whilst eugenic and discriminatory outcomes need to be resisted, we must lower our expectations about the effectiveness of policies that seek to regulate reproductive choices in the global village. Although the march towards greater reproductive rights and access to genetic information may be hard to roll back, we do need to be honest and transparent about the limits of autonomy as a rationale for genetic testing. There is plainly a risk that the pursuit of greater reproductive choice may end up impeding the very rights we seek to enhance. Whilst the desire to embrace greater reproductive choice is understandable, we need to acknowledge and act upon the issues we are creating for future generations.

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