

Online Research @ Cardiff

This is an Open Access document downloaded from ORCA, Cardiff University's institutional repository: <https://orca.cardiff.ac.uk/123798/>

This is the author's version of a work that was submitted to / accepted for publication.

Citation for final published version:

Thomas, Gareth M., Rothman, Barbara Katz, Strange, Heather and Latimer, Joanna 2021. Testing times: the social life of non-invasive prenatal testing. *Science Technology and Society* 26 (1) , pp. 81-97.
10.1177/0971721820960262 file

Publishers page: <https://doi.org/10.1177/0971721820960262>
<<https://doi.org/10.1177/0971721820960262>>

Please note:

Changes made as a result of publishing processes such as copy-editing, formatting and page numbers may not be reflected in this version. For the definitive version of this publication, please refer to the published source. You are advised to consult the publisher's version if you wish to cite this paper.

This version is being made available in accordance with publisher policies.

See

<http://orca.cf.ac.uk/policies.html> for usage policies. Copyright and moral rights for publications made available in ORCA are retained by the copyright holders.



Post-print version (final draft post-refereeing)

To be published in: *Science, Technology and Society*

Testing times: the social life of non-invasive prenatal testing (NIPT)

Gareth M. Thomas¹, Barbara Katz Rothman^{2,3}, Heather Strange⁴, and Joanna E. Latimer⁵

¹ School of Social Sciences, Cardiff University, UK

² City University of New York, USA

³ Faculty of Health Sciences at the University of Eastern Finland, Finland

⁴ School of Medicine, Cardiff University, UK

⁵ Department of Sociology, University of York, UK

Abstract

Non-invasive prenatal testing (NIPT) is a genomic technology used to predict the chance of a foetus having a genetic condition. Despite the immediacy of this technology's integration into clinical practice, there is a dearth of evidence outlining how both patients and professionals experience NIPT *on the ground*. In this article, we draw upon our collective empirical research – specifically on earlier screening technologies (BKR), Down syndrome screening (GT), genetic screening/testing (JL), and NIPT (HS) – to outline the most pressing, and often controversial, issues which, we argue, remain unresolved and vital to consider regarding NIPT. We begin with a brief introduction to NIPT as a prenatal technology and the bodies of literature which unpack its 'social life'. In what follows, BKR discusses NIPT within the context of her research on 'the tentative pregnancy' and diagnostic testing in the USA. In the following sections, GT, HS, and JL identify different, but related, concerns with respect to NIPT, particularly around routinisation, commercialisation, choice, abortion, and configurations of disability and 'normalcy'.

Keywords

Choice; disability; ethics; non-invasive prenatal testing (NIPT); pregnancy; technology

Introduction

Non-invasive prenatal testing (NIPT) is a genomic technology used to screen for certain genetic conditions (typically aneuploidies, such as Down syndrome) during pregnancy. By analysing cell-free foetal DNA in a pregnant woman's blood at 8-10 weeks' gestation, NIPT is used to predict the chance of a foetus having a genetic condition, but cannot provide any indication of 'severity'. Although most pregnant women will receive a lower-chance (or 'screen-negative') result, some will receive a higher-chance (or 'screen-positive') result, which is said to indicate that it is likely a foetus has a genetic condition. In such instances, diagnostic testing (chorionic villus sampling or amniocentesis) can be used to validate an NIPT result since NIPT is classified in public prenatal screening programmes as a screening, not a diagnostic, test.

As NIPT is 'non-invasive', meaning that only a maternal blood test is required, it presents no risk of miscarriage or other 'adverse' outcomes typically associated with diagnostic testing. NIPT is set apart from previous technologies as it can be used earlier in pregnancy than previous screening techniques, and it is heralded as posing no physical risk to the health of the mother or foetus. NIPT is, thus, presented as helping to differentiate those pregnancies 'at risk' from those that are not, and as subsequently more efficient and value-for-money since, in theory, NIPT should reduce the need for (invasive) diagnostic testing.

Furthermore, the high specificity and sensitivity of NIPT are reported in multiple publications and commercial advertisements (Bryant, 2017), including the highest sensitivity (>99%) and lowest false-positive rate (1%) for Down syndrome. However, research on the performance of NIPT in clinical practice suggests varying – in fact, significantly lower – positive predictive values for different genetic conditions (Neufeld-Kaiser, Cheng & Liu, 2015; Valderramos, Rao, Scibetta et al., 2016). Nonetheless, suggestions are that there has been an extraordinary uptake of NIPT, with estimations that more than half a million NIPT procedures have been performed in over 61 countries (Warsof, Larion & Abuhamad, 2015). Moreover, the value of the global market for NIPT is estimated to reach \$5.67 billion by 2028 (BIS Research, 2019).

Given NIPT is an innovative technology in transition, with little sense of how it will be assimilated and interpreted by patients and professionals in practice, its social implications remain at the margins of debate. We may, for instance, ask questions about how NIPT is being enrolled and translated in practice, what its un/intended consequences might be, and what social, cultural, and ethical issues it raises. Whilst there is an increasing amount of international research on NIPT, albeit mostly from the fields of medicine and bioethics, much of this work is limited to two topics. First, it

examines the decision-making processes of parents, using either quantitative data (Gil, Guinta, Macalli et al., 2015; Vahanian, Baraa Allaf, Yeh et al., 2014) or qualitative data (Lau, Chan, Salome Lo et al., 2012; Lewis, Hill, Silcock et al., 2016; Vanstone, Cernat, Nisker et al., 2018). Positive experiences are often reported in relation to NIPT's *perceived* accuracy, safety, and capacity to provide an earlier test result. However, women also identify concerns including: the ethical issues of NIPT; anxiety about prenatal screening; issues with the commercial advertisements of this technology; difficulty in interpreting risk-ratios; a lack of knowledge about the conditions tested for (due to an expansion of funding and conditions); a lack of follow-up care after a result; judgments about disability; implications of early availability of information about foetal sex or 'non-medical' traits; 'too much screening' (Bowman-Smart, Savulescu, Mand et al., 2019, p. 237); financial barriers relating to access, and; the stigmatisation of abortion. Cernat et al. (2019: 27) synthesise qualitative studies on women's experiences with, and preferences for, 'informed decision-making around NIPT'. Such research documents how pregnant women preferred to learn about NIPT from clinicians but were unsatisfied with the quality and quantity of information offered during counselling (so attempted to locate information from elsewhere). Moreover, women mostly have a strong understanding of the test and its implications, but described NIPT as 'easy or just another blood test' (2019: 27).

Second, research has identified the attitudes towards NIPT held by pregnant women (Farrell, Agatista & Nutter, 2014; Hill, Fisher, Chitty et al., 2012; Lau et al., 2012; Lewis, Silcock & Chitty, 2013; Silcock, Chitty & Liao, 2014), pregnant women *and* male partners (van Schendel, Kleinveld, Dondorp et al., 2014), mothers of children with Down syndrome (Kellogg, Slattery, Hudgins et al., 2014), and members of the public (Allyse, Sayres, Goodspeed et al., 2015). A small body of research examines the views (and apprehensions) of medical professionals – such as genetic counsellors, consultants, nurses, midwives, and obstetricians – with respect to NIPT (Buchanan, Sachs, Toler et al., 2014; Musci, Fairbrother, Batey et al., 2013; Sayres, Allyse, Norton et al., 2011). In their interviews with professionals, for example, Gammon, Kraft, and Michie et al. (2016) found that there was not enough time for them to adequately counsel and educate patients on their options. In addition, professionals wanted more information from professional societies, labs, and publications about NIPT, whilst some questioned whether the expansion of NIPT to include microdeletions could be done in an ethical manner. Related to this, there is a relatively large literature on the ethical issues of NIPT from scientists, bioethicists, medical professionals, and academics (de Jong & de Wert, 2015; Deans, Clarke & Newson, 2015; Kater-Kuipers, Bunnik, de Beaufort et al., 2018; Minear, Alessi, Allyse et al., 2015; Mozersky, Ravitsky, & Rapp et al., 2017).

Many accounts report that women and members of the public viewed NIPT as a positive development in prenatal care due to its perceived safety, accuracy, timing, and capacity to detect genetic conditions beyond Down syndrome. Yet concerns have equally been raised about financial costs and unequal access, how parents manage risk information, a lack of NIPT knowledge among parents, a misalignment with 'informed choice', the potential routinisation of NIPT, a possibility of inaccurate results, a felt pressure to *have* NIPT, and the difficulty of determining 'quality of life' and 'severity' of a genetic condition. Other anxieties include ethical worries about 'eugenics', screening for late onset disorders, using NIPT for enabling non-medical sex selection, a continued stigmatisation/discrimination of people with disabilities, and how women may not be able to fully prepare for the choices they will (perhaps unexpectedly) be confronted with. Research shows, then, how expectant parents and members of the public both support and question the use, and underlying value, of NIPT. Others explore the discrepancies between medical professionals and expectant parents. For example, in contrast to their providers, women in studies by Hill et al. (2016) and Silcock et al. (2014) were willing to wait longer for test results with lower accuracy if a test had no miscarriage risk whereas for medical professionals, accuracy and early testing were more important.

What is clear is that despite the immediacy of this technology's integration into (routine) clinical practice, and there being a growing body of literature on NIPT, there is still a dearth of evidence which outlines how both patients and professionals experience this *on the ground*. In this article, we draw upon our own empirical research on prenatal screening and testing (BKR; GT), genetic screening and testing (JL), and NIPT (HS) to outline the most pressing, and often controversial, issues which, we argue, remain unresolved yet vital to consider with respect to NIPT. We begin with the work of BKR, who discusses NIPT within the context of her work on 'the tentative pregnancy' and diagnostic testing in the US. In what follows, GT, HS, and JL identify different, but related, concerns regarding NIPT, particularly around notions of routinisation, choice, abortion, and configurations of disability and 'normalcy'. By identifying the concerns that we have regarding the development and diffusion of NIPT, we concurrently sketch out key points of consideration which future research might focus upon.

Earlier and Risk Free (BKR)

This is not the first time the solution to a problem created its own problems. I studied women's experiences with amniocentesis, the earliest version of prenatal screening using genetic technologies, back when it was new and first being 'rolled out', as they now say about newer testing regimens (Rothman, 1986). The technologies involved were,

comparatively speaking, quite primitive. The test was framed around the issue of Down syndrome, and the diagnosis consisted of cutting and pasting, and counting the number of chromosomes in, foetal cells found in the amniotic fluid. On a tour of the laboratory where the results were determined, I was shown a table with photos of chromosomes, scissors at hand. The extra chromosome that marked Down syndrome offered a clear diagnosis. Prognosis – what this will mean for the potential person who would carry that extra chromosome if the pregnancy is continued – was then, as it is now, considerably less clear. Some of those with Down syndrome do not survive the pregnancy long enough to become people; some go on to graduate college and become spokespeople as part of disability advocacy.

Amniocentesis was done relatively late in pregnancy. Results came in well after 20 weeks, more than halfway through the pregnancy, often at the very end of the time an abortion could be legally performed. The test had to be done late because the foetus had to have developed far enough so that a needle, inserted through the abdomen into the uterus, could remove amniotic fluid without damaging the foetus. At its inception, ultrasound was not yet available and risks of foetal damage were quite high. As ultrasound entered routine practice, the risk of the needle hitting the foetus or doing other damage was considerably lower. But the risk remained; amniocentesis did, sometimes, cause miscarriage.

The way that maternal age over 35 got to be defined as a 'high risk' was a remarkably random apples and oranges equation of two risks. At the age of 35, the risk of amniocentesis causing a miscarriage equalled the 'risk' of a foetus having Down syndrome. That a miscarriage – just as Down Syndrome – could have wildly different meanings in different women's lives was essentially ignored. The two numbers matched and the two experiences, Down syndrome births and iatrogenic miscarriages, were equated.

Even then, the pressure to know, to learn the condition of the foetus, was powerful. For women who said that they were sure they would not terminate, the language switched to preparation; they were told to have the test, by the genetic counsellors I observed, by the reports of the women I interviewed, so that they could be prepared. It was unclear what preparation one could, or should, do for a coming baby when the prognosis was that unclear. All the women I observed and interviewed, as was true for 99% of American women then (and now), were planning to give birth in hospitals, where high-risk births were routinely handled. There was absolutely no research on whether women (or their families) did better emotionally or as measured on any other outcomes, knowing the diagnosis earlier in the pregnancy or learning at or after the birth.

When I questioned the genetic counsellors on why they were pushing so hard for women who were determined not to terminate the pregnancy to go ahead and have the amniocentesis, some told me that 'well, she says she won't terminate but once they know, they do'; 'They can't go through with the pregnancy once they know this'. And the genetic counsellors had the same negative understandings and feelings about Down syndrome that were culturally dominant. As one said to me: 'Sure they can be sweet children. And they grow up to be ugly adults' (Rothman, 1986, p. 47). Others were more accepting of women's choices to keep the pregnancy, but the value of preparation was always assumed. Genetic counselling was being done by people who had to believe that information was good – providing information was their job.

It was not until I was researching the early introduction of prenatal testing, and specifically amniocentesis, in the Netherlands that I heard that idea of preparation questioned. Midwives there provided continuity of care, seeing women through from early pregnancy to post-birth, and as community midwives, often working with those women throughout their childbearing years. When prenatal screening was offered, it was the midwives who were the frontline of presentation to the women. And in focus groups I ran asking about how that was being experienced, the value of preparation was questioned. If there is nothing that can be done, if the foetus cannot be treated or saved, then 'why spoil the pregnancy?' (Rothman, 2000). It was a new thought; the medical model does not think of a pregnancy as itself something which can be good or bad, enjoyed or ruined. Pregnancy is a production process, and outcome measures – foetal and maternal outcomes – are all that count. Even now, there is no space for a 'healthy' or 'good' pregnancy in medical language: pregnancies come in risk levels, and the best you can hope for is a 'low-risk' one.

As much as preparation was valued, the lateness of the testing and the risks of the procedure permitted women who did not want to learn foetal conditions an acceptable 'out'. Women could say, as many of those I interviewed did, that the testing came too late; the foetus was no longer just a foetus, but their baby, and they had engaged into the mothering role. This baby was theirs to love, no matter what. Terminations for unwanted pregnancies happen relatively early when they are made available. Women can opt to basically become 'unpregnant', to return to their pre-conception state. For a planned or accepted pregnancy, by late pregnancy, when foetal movement can be felt, when job changes have been made, rooms are being furnished and decorated, layettes are being gathered, a termination is a very different thing.

The shadow of potential knowledge from the testing spread through the early pregnancy. Women who were anticipating the possibility of 'bad news' (ironically called a 'positive result' in medical terminology) were hesitant to enter into the maternal role. I found that those who were actively awaiting the results of prenatal diagnosis were more likely to claim not to have felt foetal movement until the results came in. These results were sometimes late enough so that an observer could see foetal movement through the abdomen and clothing of the women who did not feel it. The other women I interviewed who had delayed feeling movement that late were those who had previously miscarried, and did not feel the movement until the point of earlier loss was passed. It was this emotional pain and suffering that the Dutch midwives were also calling upon when they asked 'why spoil the pregnancy?'

This lateness served itself as a reason why a woman might refuse the testing. The risks of miscarrying a wanted healthy pregnancy, while testing to be reassured of its healthy status, was of course a further legitimate reason. From the time that I did research in the early 1980s, I followed reports that newer, earlier, less invasive testing was on its way. Foetal cells are known to be found in maternal blood and it was just a matter of time, we were repeatedly assured, before early, non-invasive prenatal testing will be available. I leave it to the historians of medicine to explain why that promise was put forth regularly and often for over thirty years before it became reality, but it does appear that the time has come; non-invasive prenatal screening has arrived.

I am not, for one moment, making the claim that this is not progress. In pregnancy terminations, I am absolutely sure that earlier is better for the women involved, and it would be a good thing if NIPT does indeed result in earlier terminations for women who are seeking it, and not just a longer and more complex screening experience before a diagnosis is reached. Avoiding iatrogenic miscarriages is clearly a fine thing. What I am claiming is that – as is often the case – the solution to a problem may bring problems of its own. The problems that I see lie in the intersection between 'earlier' and 'safer'. Because it is both early and safe, the opportunities for legitimately rejecting the testing are closed down. With safe and early testing, if a woman is quite clear in her mind that she is not planning on terminating the pregnancy, the refusal of information still remains difficult. We are living in the information age. When this questioning of valuing preparation comes up at academic discussions of prenatal screening, a clear valuing of information is displayed. Of course, someone is sure to say that some people may not want to plan or be prepared. 'Those people' are, arguably, seen as one would see reckless, foolish teenagers, those Others who do not prepare themselves for life. Academics value caution, study, learning, preparation. We could not do our work if we had not held those values. Our childhood friends who did not plan, they dropped out of school, got pregnant too soon, and

went down wrong paths. We – the planners and prepared – we get ahead. It is a difficult, devalued choice one makes to refuse information.

But with early screening, the potential bad news arrives pretty much along with the determination of pregnancy. The woman does not adjust to the physical experience of the pregnancy, begin planning for her life of what a baby will mean over a period of months, and then she confronts the testing. Determination and testing now come close together. Given the powerful medicalisation of pregnancy, the ‘determination’ of pregnancy is itself a medical event. With medicalisation, a missed period and uncomfortable breasts, just as one was trying for the first time to get pregnant, are redefined as ‘symptoms’ and medical testing provides the diagnosis of the condition of pregnancy. And with that testing is offered prenatal screening. Before the woman has had the opportunity to make decisions about the pregnancy and its place in her life, its wantedness, what this means for her and her family based on the lived experience of pregnancy, she is offered testing on the condition of the foetus. The future child, as such, enters the woman’s life via its diagnostic categorisation.

Think of it this way. The old scenario was that this baby, who is coming in a few months, for which we just moved to a bigger apartment, who is making me sleep on my side with its kicking, who has pushed me out of every pair of pants (trousers) I owned into special maternity clothes, this baby who will sleep in this cradle my cousin used for her children and promised to send, who will be wearing this beautiful sweater my mother is knitting, this baby has just been diagnosed with Down Syndrome. Or whatever else is diagnosable. Should we continue the pregnancy? The new scenario is that you are pregnant, have not done anything about it yet, it is not even Spring and the due date is in October, and the baby will have Down syndrome. Care to continue the pregnancy or start again? And, if you are a woman deemed at risk of reproducing a child with aneuploidy, *can* you simply start again – is your body capable of producing a ‘healthier’, less at-risk foetus?

I hear the voices of those genetic counsellors from older times: once she knows, she will not be able to continue. They change their minds when they have the diagnosis. Making that diagnosis earlier will, in all likelihood, make that all the truer. At an early point in pregnancy, the experience is less about continuing than starting. Should one look for a larger apartment, a job break, talk to family about lending the family cradle, decide what kind of look you want in maternity clothes, all when you know the diagnosis at the start? It comes to feel more like what people have called ‘starting over,’ rather than ending a pregnancy. This, again, might be just fine, if ending the pregnancy is the best

solution. And for some conditions, and some familial situations, it may indeed be the best solution. But what about for conditions such as Down syndrome, where the diagnosis tells us so little about the prognosis?

These issues are often framed as a battle between women's rights to choose and the disability movement. It is far more complex than this. Women are making these choices not in the world the activists are trying to create, but living in a world which makes the disability movement necessary. Pregnancy is inherently a condition of change, a process occurring both in a moment of time and across time. Earlier and safer screening is changing the experience of pregnancy in ways which are not entirely predictable. Just as I needed to study what the testing meant for the women who were experiencing amniocentesis then, we need the ongoing research now. The answers are not to be found in what the testing/testers offer and promise – safe and early diagnosis – but in what the women undergoing it are experiencing.

What Next? (GT; HS; JL)

Following BKR's introduction to various concerns stemming from her research on prenatal screening/testing, we outline what we believe are the most pressing concerns, and points of contention, regarding the development and diffusion of NIPT. Our claims build upon our empirical research on dysmorphology (Latimer, 2007, 2013; Latimer and Thomas, 2015), Down syndrome screening (Thomas, 2016, 2017), and NIPT (Strange, 2015, 2018). Taken together, this body of work explores patients and professionals' experiences with, and the cultural meanings of, medical technologies, specifically: the interface between new genetic technologies and the clinical translation in, and by, the diagnostic practices of paediatric genetics (JL); routine practices of prenatal screening and diagnosis (GT), and; the development and clinical introduction of new genomic prenatal screening technologies (HS). By exploring how biomedical technologies are situated by, and translated in, everyday practices, our studies bridge conceptual gaps between the sociology of procreation, risk, disability, choice, genetics, and family. In what follows, and informed by this work, we identify key concerns and points of consideration regarding the development and diffusion of NIPT which, we suggest, future research might focus upon.

Termination of Pregnancy

Strange's (2015, 2018) research show us that the dilemma of whether to 'continue the pregnancy or start again' – by choosing to end a pregnancy after a 'positive' diagnosis is provided – was fundamental to user experiences, and

interpretations, of NIPT. Genetic counsellors, midwives, patients, and medical professionals each raised termination as a point of central concern when discussing experiences with NIPT. Midwives working in private clinics explained how even ‘low-risk’ women seeking out NIPT – in contrast to the way in which such women approached screening before NIPT was introduced – actively raised questions around termination of pregnancy and what a ‘screen positive’ result may mean during pre-test consultations. Though frequent, discussions of abortion/termination were typically difficult and emotive. The ongoing, and very public, politicisation of the abortion debate, coupled with the silencing and stigmatisation of women’s lived experiences of abortion, meant that for women facing the question of whether to ‘continue the pregnancy or start again’ (although this dilemma, as a result of NIPT’s much-valued ‘earliness’, would arrive at an earlier and potentially ‘easier’ stage in pregnancy than previously possible), the process of going through testing, receiving, and making sense of results, and the work of coming to a decision on what action to take, remained difficult and disruptive.

Despite its close alignment with experiences of prenatal testing, the subject of abortion/termination is often, arguably, divorced from debates about reproductive techniques. There is an explicit lack of public discussion on the (unspoken) practice of the ‘selective’ or ‘therapeutic’ abortion of pregnancy in a context of prenatal technology, yet it is intimately tied up with technologies such as NIPT. Already located within a context of secrecy and shame, termination/abortion and its relationship with disability and medicine, whilst a difficult and problematic topic, needs to be at the forefront of debates around NIPT. There remains a strong need to move debate and discussion beyond the dominant framings of ‘informed consent’ and ‘reproductive autonomy’ alone. The expansion of these discussions demands revisiting regulatory frameworks, too, such as existing (ambiguous) abortion laws.

Commercialisation

Although NIPT offers clear clinical advantages, the ways in which tests are being introduced and made routine within numerous clinical and social spaces is being shaped to a great extent by commercial drivers and concerns. This makes NIPT’s diffusion into the clinic clearly distinct from the ways in which previous forms of screening came to be used and made routine (especially in the UK), thus disrupting the argument that the introduction of NIPT into population-wide screening is simply an extension of, and improvement to, an existing programme. The ongoing development and rapid expansion of NIPT has been driven, to a large extent, by commercial sector research, development, and marketing. A large number and wide range of companies, from small-scale start-ups to established ‘pharmaceutical

giants', are actively involved in the now-global, and highly profitable, NIPT market. First generation NIPT tests – paralleling the way in which already-routine and established technologies are typically used – provided results only for foetal sex, Down syndrome, and other common trisomies (Edwards' syndrome and Patau syndrome). In more recent years, companies have expanded the range of tests they offer through sequencing methods. Most of the larger NIPT brands now offer to provide (at an additional cost) results on sex chromosome abnormalities, sex-linked conditions, and microdeletions, and a more limited number of companies offer whole genome sequencing (WGS)-based NIPT tests promising to analyse every chromosome of a baby. Genomic data of the type that may be gathered via such advanced NIPT testing is of significant commercial value in itself, being a valuable resource for commercial research and development activities. Questions remain as to whether biobanks of foetal (and maternal) genomic material may be, or already are, generated as a result of widespread, and if so globally dispersed, NIPT testing and who would be responsible for ensuring regulatory oversight here.

The power and intensity of commercial NIPT research and development, coupled with the rapid expansion and clinical translation of new tests, raises several concerns. The way in which these new, commercially-driven tests are reaching out into, and affecting the lives and pregnancies of, women (and also their partners) is, in many cases, yet to be understood. Crucial questions around the quality and influence of in-clinic pre- and post-test counselling and online (direct-to-consumer) information provision remain largely unanswered. In locations where prenatal care is typically state-funded, the influence of commercial drivers on state-provided services is unknown. Are such services under pressure to enrol NIPT in population-wide antenatal screening programs – and make the tests available to all, regardless of economic status – as a result of NIPT being made 'normal' and 'routine' through its growing prevalence within private prenatal care? Will access to NIPT, which is mostly available only to those with the economic means to pay for it, become a way of enacting maternal responsibility which creates an added pressure to undertake further interventions? Will testing for rare genetic 'abnormalities' and 'conditions' (testing options which would previously only be made available to those at known 'risk' and who have a pre-existing/experiential understanding of a condition being tested for), become 'routine' as well? How does opening up private sector provision affect care practices? Will public health services, such as the NHS, feel the pressure to 'match' private testing services to help ensure equitable access and a high quality of service provision? These concerns and questions remain unaddressed, yet they must be attended to as a matter of urgency, given that many of the ethical and social concerns about NIPT stem from the commercialisation of this technology.

Choice

NIPT intensifies long-debated issues in prenatal medicine, such as assessing if 'non-directive care' and 'informed choice' are achieved in practice and whether screening heightens anxieties. In interviews with medical professionals in the Netherlands, Kater-Kuipers et al. (2018) found that they were concerned pregnant women do not always make informed choices about NIPT, and that pre-test counselling is in need of improvement. However, NIPT also raises new ethical issues specific to the technology, such as the expansion of funding and conditions together with the implications of early availability of information about foetal sex (Vanstone et al., 2018). One concern is that rolling out NIPT for 'low-risk women' (given research has mostly been carried out among 'high-risk' populations), involving screening at an earlier gestation and reducing the number of diagnostic tests (associated with iatrogenic miscarriages), may create added pressure to accept an offer of NIPT. What happens to 'choice' when screening is at an earlier gestation and 'risks' associated with diagnostic testing are diminished? Does this affect a woman's ability to 'choose not to choose' (Kelly, 2009)? Will women think less deeply about screening, thereby creating problems if they receive a result that they are not prepared for? This relates to recent work about how the notion of 'reassurance' is powerful, but ill-defined and vague (Thomas, Roberts & Griffiths, 2017). In a rare observational study of genetic counselling sessions and qualitative interviews with women offered NIPT at a US hospital, Mozersky (2015, p. 31) suggests NIPT provides a 'much desired reassurance', yet without women 'having contemplated the potential negative outcomes and limitations of testing'. In situations where women do not receive reassuring results, they can appear 'unprepared and shocked by what NIPT can and cannot reveal' (2015, p. 31). Mozersky's further identifies how central ethical questions about prenatal screening, such as abortion or the value of disabled children, regularly do not emerge during clinical encounters. Considerations of the future are deferred; this has practical value but could have consequences if/when a 'positive' result is established.

The production of uncertain, or unexpected, data is a crucial consideration for the widespread rollout of NIPT. How do pregnant women understand, and make sense of, 'inconclusive results' (usually occurring when the proportion of foetal DNA in the sample is not high enough for an accurate analysis), 'variants of uncertain significance' (variation in the normal sequence of genes, the significance of which is unknown), and 'incidental findings' (undiagnosed medical conditions found unintentionally, such as incidental maternal cancer diagnoses)? This consideration of choice is complicated further by the offer of screening for multiple conditions. NIPT is being offered

as alternative screening method, yet as well as being available now for 'high-risk' and 'low-risk' populations, new methods of analysis (such as WGS) means that women are potentially screened in more genetic/genomic detail than before, and with a more limited knowledge of the conditions being tested for. Whilst informed, non-directive choice may be the ultimate goal of prenatal screening programmes, in the context of genetic technology, procreative choices are, as Latimer (2013) has shown, often uncertain, mediated, situated, and relational.

We may ask, as NIPT expands in scope, who decides what will be routinely screened for? Will information on all identified genetic variants be shared with women and their partners/families? Does the pregnant population at large have a right to access this information? How will they, with professionals, contend with the production of uncertain knowledge – that is, genetic variations which are not well understood and widely known? Will pregnant women receive support in the form of expert counselling to digest results for a large range of genetic conditions and disorders? Who would provide and fund such a service? The above concerns connect to considerations of disability and the morphing definition of normality in a context of expanding genetic testing.

Disability and 'Normalcy'

Disability has historically had a problematic relationship with prenatal medicine, the suggestion being that screening for genetic conditions (e.g. Down syndrome) sends a negative message to disabled people about their value and worth. Nonetheless, NIPT brings both old and new ethical issues to the table (Bryant, 2017). Within the context of NIPT, there has been little consideration of how the medical and scientific community respond to concerns raised by disability rights groups. In the UK, the 'Don't Screen Us Out' campaign spell out their anxieties about an increased number of foetuses with Down syndrome being aborted and what they consider to be the backdoor eradication of people with the condition from society. The campaign calls for a delay in the implementation of NIPT and for the provision of appropriate support and balanced information for parents who receive a diagnosis of Down syndrome. The latter includes undertaking a full ethical review, offering improved training and guidance requirements for medical professionals, producing accessible provisions for parents who continue the pregnancy post-diagnosis, and giving information about palliative care and adoption/foster services from birth.

Here, there appears to be a recognition that NIPT emerges within a society that, in many ways, is hostile to bodily difference. We may ask how much choice is promised when offering screening in societies which significantly devalue life with disability by marking it out as a devalued bodily state. Since NIPT has the potential to detect an

expanding range of different conditions and genetic variations, concerns about its eugenic potential – and the enduring negative valuation of disabled people and/or those diagnosed with genetic ‘anomalies’ – are particularly acute. Korngiebel, McMullen, and Amendola et al. (2016) discuss the development of taxonomies to categorise ‘types’ of genetic conditions in order to simplify reproductive decisions (which may be based on severity, time of onset and/or predictability), although it is unclear how much input has been provided by other affected families. The introduction of NIPT, collapsing the boundary between screening and diagnosis (Strange, 2015), makes the process of getting a diagnosis ‘earlier and safer’, yet it also reignites longstanding debates on the ethics of prenatal testing – particularly around disability (Thomas, 2017), routinisation (Cernat, De Freitas, Majid et al., 2019), and an ‘informal eugenics’ (Thomas and Rothman, 2016) – which have yet to be resolved.

Indeed, the routinisation of NIPT is likely to extend the dichotomy of normal/abnormal. In an era when human lives are increasingly measured and weighed in accordance with medical and scientific framings, notions of what is ‘normal’ have changed drastically – and the concept continues to haunt reproductive practices (Davis, 2014). There is a fear that ‘the normal is shrinking’ at the same time as our consciousness of the riskiness of procreation is intensified (Latimer, 2013, p. 192). As biomedicine extends its gaze, medical professionals must carefully extract certainty from the mass of uncertainty produced by prenatal techniques. With screening supposedly becoming more ‘accurate’, less ‘invasive’, and more ‘accessible’, the fragility of ‘the normal’ is exposed by the increasing possibility that genetic duplications, deletions, translocations, inversions, and insertions will be detected. As the body itself is more fully probed and finely computed, the category of the normal shrivels and the parallel category of the abnormal swells. In her study of paediatric genetic diagnosis, Latimer (2013) documents how there are over 4,000 syndromes identified and described in clinical databases, with new additions coming on stream on a consistent basis. This swelling of ‘the abnormal’ may have the effect of normalising otherwise stigmatised identities as difference and diversity becomes more pronounced and, one may assume, widely accepted. However, this is speculative and the historical, and recent, treatment of disability and difference suggests NIPT presses greater consideration of what constitutes an ‘acceptable’ life.

Public Debate

Along with concerns of choice and routinisation, the controversies and complications of NIPT have also, mostly, been muffled. This is a familiar story; earlier forms of Down syndrome screening were introduced without serious

public, scientific, and ethical debate (although the British Medical Association has recently called for this to happen in relation to NIPT). Whilst ethical points of consideration have been raised in a series of reports (Nuffield Council on Bioethics, 2016, 2017), there has arguably been a containment and defusing of debate. As we show at multiple points in our research, recourse to the rhetoric of informed choice is insufficient and has already been shown to be inadequate and ineffective in practice. The speed with which a technique spreads does not necessarily reveal its social acceptability, thus masking possible controversial social values embedded within them. The worldwide routinisation of Down syndrome screening has ensured that NIPT, like its predecessor, has not been subjected to extensive public scrutiny, other than within the campaigns of several disability rights groups. Despite these bold attempts, the debate has yet to fully begin, despite the technology having entered some clinical practice.

It is clear that NIPT is viewed as an extension of an existing program or, at least, an update of an established program without the risks of physical and psychological traumas of iatrogenic miscarriage and late termination. It is perceived as an example of medical progress, that is, a mostly incremental and uncontroversial transformation of a new technique into a routine medical technology (Löwy, 2014). Since Down syndrome screening is routinised, the diffusion of NIPT into clinical practice has been mostly untroubled and unchallenged; 'where new tests fit old paradigms, uptake is higher and concerns are more mute' (Kerr & Cunningham-Burley, 2000, p. 289). The risk is that NIPT is seen similarly as a routine, and typically unproblematic, procedure, without a critical dissection of key social and ethical concerns raised by the introduction of this new, genomic technology.

Conclusion

In this article, we have sought to outline what we believe are some crucial and challenging reflections on a morally complex technology and the future bio-politics of procreation. A policy drive toward early detection, and the rapid growth of 'low-risk' prenatal diagnostics, raises new questions not just about its ethical properties, but also bio-political justifications for routine prenatal testing in both a complex and controversial context. More work needs to be done, although we understand that the current shortage of studies around parents' experiences of the procedure is understandable since the introduction of NIPT into clinical practice is in its infancy. Nonetheless, NIPT represents uncharted territory and triggers new and unsettling questions which require urgent attention. More research is needed to ensure that the opinions, concerns, and experiences of parents, medical professionals, and others (policymakers, disability rights groups) are identified and considered. Furthermore, we would recommend that future

research considers the significant role of policy – from key performance indicators (such as uptake rates), to clinical documentation, to cost-benefit analyses – in shaping the goals of screening and the ways in which it is administered. Ensuring that accurate and balanced information, informed by empirical evidence including both beneficiaries' (parents) and stakeholders' (medical professionals; policymakers, disability advocates) perspectives and experiences, will require policy guidance from regulators and professional societies (Minear et al., 2015).

Testing techniques, such as NIPT, raise important questions around how technologies are used, regulated, and marketed, along with how they impact upon our conceptions of choice and responsibility, and how both ethical and public concerns shape their development and diffusion. NIPT is not simply an improvement on a current technology, we argue, but a paradigm-shifting global technology – a mainstreaming of genomics, the likes of which are yet to be seen in the prenatal landscape. It must, we argue, be treated as such.

References

- Allyse, M, Sayres, L.C., Goodspeed, T., Michie, M. and Cho, M.K. (2015). "Don't want no risk and don't want no problems": public understandings of the risks and benefits of non-invasive prenatal testing in the United States." *AJOB Empirical Bioethics*, 6(1),5-20.
- BIS Research. (2019). *Global Non-Invasive Prenatal Testing (NIPT) Market: Focus on Tests, Methods, Platforms, Applications, 26 Countries' Analysis, Patent Landscape, and Competitive Landscape - Analysis and Forecast, 2018-2028*. California: BIS Research.
- Bowman-Smart, H., Savulescu, J., Mand, C., Gyngell, C., Pertile, M.D., Lewis, S. and Delatycki, M.B. (2019). 'Is it better not to know certain things?': views of women who have undergone non-invasive prenatal testing on its possible future applications. *Journal of Medical Ethics*, 45(4),231-238.
- Bryant, L. (2017). Ethical issues of non-invasive prenatal testing for Down syndrome. *eLS*,1-6.
- Buchanan, A., Sachs, A., Toler, T. and Tsipis, J. (2014). NIPT: current utilization and implications for the future of prenatal genetic counseling. *Prenatal Diagnosis*, 34(9),850-857.
- Cernat, A., De Freitas, C., Majid, U., Higgins, C. and Vanstone, M. (2019). Facilitating informed choice about non-invasive prenatal testing (NIPT): a systematic review and qualitative meta-synthesis of women's experiences. *BMC Pregnancy and Childbirth*, 19(1),27.

- Davis, L.J. (2014). *The End of Normal: Identity in a Biocultural Era*. Michigan: University of Michigan Press.
- de Jong, A. and Wert, G.M. (2015). Prenatal screening: an ethical agenda for the near future. *Bioethics*, 29(1),46-55.
- Deans, Z., Clarke, A.J. and Newson, A.J. (2015). For your interest? The ethical acceptability of using non-invasive prenatal testing to test 'purely for information'. *Bioethics*, 29(1),19-25.
- Farrell, R.M., Agatista, P.K. and Nutter, B. (2014). What women want: lead considerations for current and future applications of noninvasive prenatal testing in prenatal care. *Birth*, 41(3),276-282.
- Gammon, B.L., Kraft S.A., Michie, M. and Allyse, M. (2016). 'I think we've got too many tests!': Prenatal providers' reflections on ethical and clinical challenges in the practice integration of cell-free DNA screening. *Ethics, Medicine and Public Health*, 2(3),334-342.
- Gil, M.M., Giunta, G., Macalli, E.A., Poon, L.C. and Nicolaides, K.H. (2015). UK NHS pilot study on cell-free DNA testing in screening for foetal trisomies: factors affecting uptake. *Ultrasound in Obstetrics and Gynaecology*, 45(1),67-73.
- Hill, M., Fisher, J., Chitty, L.S. and Morris, S. (2012). Women's and health professionals' preferences for prenatal tests for Down syndrome: a discrete choice experiment to contrast noninvasive prenatal diagnosis with current invasive tests. *Genetics in Medicine*, 14(11),905-913.
- Kater-Kuipers, A.B.E.M., Bunnik, E.M., de Beaufort, I.D. and Galjaard, R.J.H. (2018). Limits to the scope of non-invasive prenatal testing (NIPT): an analysis of the international ethical framework for prenatal screening and an interview study with Dutch professionals. *BMC Pregnancy and Childbirth*, 18(1),409.
- Kellogg, G., Slattery, L., Hudgins, L. and Ormond, K. (2014). Attitudes of mothers of children with Down syndrome towards non-invasive prenatal testing. *Journal of Genetic Counselling*, 23(5),805-813.
- Kelly, S.E. (2009). Choosing not to choose: reproductive responses of parents of children with genetic conditions or impairments. *Sociology of Health and Illness*, 31(1),81-97.
- Kerr, A. and Cunningham-Burley, S. (2000). On ambivalence and risk: reflexive modernity and the new human genetics. *Sociology*, 43(2),283-304.
- Korngiebel, D.M., McMullen, C., Amendola, L., Berg, J.S., Davis, J.V., Gilmore, M.J. et al. (2016). Generating a taxonomy for genetic conditions relevant to reproductive planning. *American Journal of Medical Genetics Part A*, 170A(3),565-573.

- Latimer, J. (2007). Diagnosis, dysmorphology, and the family: knowledge, motility, choice. *Medical Anthropology*, 26(2),97-138.
- Latimer, J.E. (2013). *The Gene, the Clinic and the Family: Diagnosing Dysmorphology, Reviving Medical Dominance*. London: Routledge.
- Latimer, J.E. and Thomas, G.M. (2015). In/exclusion in the clinic: Down's syndrome, dysmorphology, and the ethics of everyday medical work. *Sociology* 49(5),937-954.
- Lau, T.K., Chan, M.K., Salome Lo, P.S., Chan, H.Y.C., Chan, W.K., Koo, T.Y. et al. 2012. Non-invasive prenatal screening of foetal sex chromosomal abnormalities: perspective of pregnant women. *The Journal of Maternal-Foetal & Neonatal Medicine*, 25(12),2616-2619.
- Lewis, C., Silcock, C. and Chitty, L.S. (2013). Non-invasive prenatal testing for Down's syndrome: pregnant women's views and likely uptake. *Public Health Genomics*, 16(5),223-232.
- Lewis, C., Hill, M., Skirton, H. and Chitty, L.S. (2016). Development and validation of a measure of informed choice for women undergoing non-invasive prenatal testing for aneuploidy. *European Journal of Human Genetics*, 24(6),809-816.
- Löwy, I. 2014. Prenatal diagnosis: the irresistible rise of the 'visible foetus'. *Studies in History of Philosophy of Biological and Biomedical Sciences*, 47(Part B),290–299.
- Minear, M.A., Alessi, S., Allyse, M., Michie, M. and Chandrasekharan, S. (2015). Noninvasive prenatal genetic testing: current and emerging ethical, legal, and social issues. *Annual Review of Genomics and Human Genetics*, 16,369-398.
- Mozersky, J. (2015). Hoping someday never comes: deferring ethical thinking about noninvasive prenatal testing. *AJOB Empirical Bioethics*, 6(1),31-41.
- Mozersky, J., Ravitsky, V., Rapp, R., Michie, M., Chandrasekharan, S. and Allyse, M. (2017). Toward an ethically sensitive implementation of noninvasive prenatal screening in the global context. *Hastings Center Report*, 47(2),41-49.
- Musci, T.J., Fairbrother, G., Batey, A., Bruursema, J., Struble, C. and Song, K. (2013). Non-invasive prenatal testing with cell-free DNA: US physician attitudes toward implementation in clinical practice. *Prenatal Diagnosis*, 33(5),424-428.

- Neufeld-Kaiser, W.A., Cheng, E.Y. and Liu, Y.J. (2015). Positive predictive value of non-invasive prenatal screening for foetal chromosome disorders using cell-free DNA in maternal serum: independent clinical experience of a tertiary referral center. *BMC Medicine*, 13,129.
- Nuffield Council on Bioethics. (2016). *Evidence Review: Decision-Making by Expectant Parents – NIPT, NIPD, and Current Methods of Prenatal Screening for Down’s Syndrome*. London: Nuffield Council on Bioethics.
- Nuffield Council on Bioethics. (2017). *Non-Invasive Prenatal Testing: Ethical Issues*. London: Nuffield Council on Bioethics.
- Rothman, B.K. (1986). *The Tentative Pregnancy: Prenatal Diagnosis and the Future of Motherhood*. New York: Viking Press.
- Rothman, B.K. (2000). *Spoiling the Pregnancy: The Introduction of Prenatal Diagnosis to the Netherlands*. Catharina Schrader Stichting of the Dutch Organization of Midwives. Bilthoven, Netherlands.
- Sayres, L.C., Allyse, M., Norton, M.E. and Cho, M.K. (2011). Cell-free foetal DNA testing: a pilot study of obstetric healthcare provider attitudes toward clinical implementation. *Prenatal Diagnosis*, 31(11),1070-1076.
- Silcock, C., Chitty, L.S. and Liao, L.M. (2014). Will the introduction of non-invasive prenatal diagnosis for Down's syndrome undermine informed choice? *Health Expectations*, 18,1658-1671.
- Strange, H. (2015). *Non-Invasive Prenatal Diagnosis: The Emergence and Translation of a New Prenatal Testing Technology*. Unpublished PhD Thesis, Cardiff University.
- Strange, H. (2018). Professional and patient discourses in the fetus as a patient. In D. Schmitz, A. Clarke and W. Dondorp (Eds), *The Fetus as a Patient: A Contested Concept and its Normative Implications* (pp. 78–93). London: Routledge.
- Thomas, G.M. (2016). An elephant in the consultation room? Configuring Down’s syndrome in UK antenatal care. *Medical Anthropology Quarterly*, 30(2),238-258
- Thomas, G.M. (2017). *Down’s Syndrome Screening and Reproductive Politics: Care, Choice, and Disability in the Prenatal Clinic*. London: Routledge.
- Thomas, G.M. and Rothman, B.K. (2016). Keeping the backdoor to eugenics ajar?: Disability and the future of prenatal screening. *American Medical Association Journal of Ethics*, 18(4),406-415.

- Thomas, G.M., Roberts, J., and Griffiths, F. (2017). Ultrasound as a technology of reassurance?: How pregnant women and health care professionals articulate ultrasound reassurance and its limitations. *Sociology of Health and Illness*, 39(6),893-907.
- Vahanian, S.A., Baraa Allaf, M., Yeh, C., Chavez, M.R., Kinzler, W.L. and Vintzileos, A.M. (2014). Patient acceptance of non-invasive testing for foetal aneuploidy via cell-free foetal DNA. *The Journal of Maternal-Foetal & Neonatal Medicine*, 27(1),106-109.
- Valderramos, S.G., Rao, R.R., Scibetta, E.W., Silverman, N.S., Han, C.S. and Platt, L.D. (2016). Cell-free DNA screening in clinical practice: abnormal autosomal aneuploidy and microdeletion results. *American Journal of Obstetrics and Gynecology*, 215(5),626.e1-626.e10.
- van Schendel, R.V., Kleinveld, J.H., Dondorp, W.J., Pajkrt, E., Timmermans, D.R., Holtkamp, K.C. et al. (2014). Attitudes of pregnant women and male partners towards non-invasive prenatal testing and widening the scope of prenatal screening. *European Journal of Human Genetics*, 22(12),1345-1350.
- Vanstone, M., Cernat, A., Nisker, J. and Schwartz, L. (2018). Women's perspectives on the ethical implications of non-invasive prenatal testing: a qualitative analysis to inform health policy decisions. *BMC Medical Ethics*, 19(1),27.
- Warsof, S.L., Larion, S. and Abuhamad, A.Z. (2015). Overview of the impact of noninvasive prenatal testing on diagnostic procedures. *Prenatal Diagnosis*, 35(10),972-979.

Biographies

Gareth M. Thomas

Gareth M. Thomas is a Lecturer in Sociology at the Cardiff University School of Social Sciences, UK. He is primarily interested in medicine, disability, stigma, reproduction, and place. His PhD was an ethnography of Down's syndrome screening in two UK hospitals, which formed the basis of his monograph *Down's Syndrome Screening and Reproductive Politics: Care, Choice, and Disability in the Prenatal Clinic* (Thomas 2017) and was nominated for the *Foundation for the Sociology of Health and Illness Book Prize 2018*. He has also co-authored the edited collection *Disability, Normalcy, and the Everyday* (Thomas and Sakellariou 2018).

Barbara Katz Rothman

Barbara Katz Rothman, PhD, is Professor of Sociology at the City University of New York (CUNY), and Fulbright-Saastamoinen Distinguished Chair in Health Sciences at the University of Eastern Finland. Her books include most recently, *A BUN IN THE OVEN: HOW THE FOOD AND BIRTH MOVEMENTS RESIST INDUSTRIALIZATION*; and *IN LABOR; THE TENTATIVE PREGNANCY; RECREATING MOTHERHOOD; THE BOOK OF LIFE; WEAVING A FAMILY: UNTANGLING RACE AND ADOPTION, AND LABORING ON*. She is Past President of Sociologists for Women in Society; Society for the Study of Social Problems, and Eastern Sociological Society and recipient “Midwifing the Movement” award from the Midwives Alliance of North America.

Heather Strange

Heather Strange is a Research Associate at Cardiff University’s Centre for Trials Research/School of Medicine, UK. Her PhD was a study of the development and early clinical introduction of non-invasive prenatal testing (NIPT) technologies into the UK. She has a background in medical sociology, science and technology studies and bio/medical ethics and her primary research interests are prenatal testing practices and their associated technologies, the mainstreaming of genomics, and the sociology of reproduction. Within her current role she uses a range of ethnographic and qualitative methodologies to help guide the conceptualisation, co-production, implementation and evaluation of healthcare improvement research.

Joanna E. Latimer

Joanna Latimer is Professor of Sociology, Science & Technology & Director of the Science & Technology Studies Unit (SATSU), University of York, UK. My research focuses on the cultural, social and existential effects and affects for how science, medicine and healthcare are done. I work ethnographically, examining everyday processes of inclusion and exclusion. I am especially interested in the worlds people make together and the biopolitics they are entangled in and circulate. Making contributions at the leading edge of social theory I have published many articles and books, including *The Conduct of Care* (2000), *(Un)knowing Bodies* (2009) and *The Gene, The Clinic and The Family* (2013), awarded the 2014 FSHI annual book prize. Currently I am writing up my study of ageing and biology as a new book for Routledge, *Naturecultures at the Limits to Life: Ageing, Biology and Society in the 21st Century*.

Notes

ⁱ An NIPT information leaflet was recently scrapped in the UK after complaints from disability rights groups that its focus on disability, and specifically Down syndrome, was 'overly medical' and 'negative'.