'Regulating in the Global Village: The Case of Non-Invasive Pre-Natal Tests'

***Authors: Professor Roger Brownsword*[*] *& Mr Jeffrey Wale*[**]**

Abstract

In the context of the global village, this paper focuses on the development of Non-Invasive Prenatal Testing (NIPT)—a test that provides clinicians and prospective parents with an easy, early and safe opportunity to obtain potentially reliable genetic and health information about the future child.

In the first part of the article, we identify various concerns relating to NIPT, now released into an environment that is remarkably difficult to regulate. For example, we question whether the online information about NIPT upon which women might rely will be reliable and up-to-date, whether women might use Internet suppliers to work round local legal restrictions, and whether the stored test results might impact on future children.

In the second part of the article, whilst recognising the limited opportunities for making effective regulatory interventions in the global village, we suggest some possible responses to the particular concerns about NIPT identified in the paper.

[*] King's College London and Bournemouth University
[**] Bournemouth University

*1. **Introduction***

The development of Non-Invasive Prenatal Testing (NIPT)—a simple blood test administered about ten weeks into a pregnancy—has provided clinicians and parents with an easy, early, and safe opportunity to obtain largely reliable information about the baby.[1] Although subsequent diagnostic tests may be required,[2] for many women NIPT promises to reduce the need for, and occurrence of, invasive testing and the consequential risk of miscarriage.[3]

While parents can already commission NIPT through the private sector—for example, Sequenom's MaterniT 21 PLUS test provides information on gender and for certain common and rare chromosomal abnormalities—the public health sector tends to lag behind, sometimes operating a contingent model where publicly funded testing is only offered as an option for certain risk groups.[4]

If NIPT were being introduced in a highly regulated environment, rather than in the 'global village', it might be possible to assuage whatever concerns are prompted by the test. However, once NIPT, together with information about the test, is in circulation in the global village, we can make two assumptions (both of which are echoed by the Nuffield Council on Bioethics in a recent report on the ethics of NIPT).[5] First, the Internet will play an important role in relation to pre-test decisions about the use of NIPT as well as post-test and post-birth decisions and outcomes.[6] Secondly, making *effective* regulatory interventions in relation to NIPT services that are available online will be challenging.[7]

In this paper, we start by assessing the opportunities, concerns and challenges that arise from the availability and use of NIPT—particularly concerning the reliability of online information about NIPT, the use of Internet suppliers to work round legal restrictions, and the impact on future children—and, then, we consider some possible domestic and global responses.

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[1] For discussion, see *Vardit Ravitsky*, 'Non-Invasive Prenatal Testing (NIPT): Identifying key clinical, ethical, social, legal and policy issues' (commissioned by the Nuffield Council on Bioethics) 2015, available from http://nuffieldbioethics.org/wp-content/uploads/NIPT-background-paper-8-Nov-2015-FINAL.pdf (accessed 22/02/17) at para 19.

[2] This is the current position with chromosomal disorders: trisomy 21(Down's syndrome), trisomy 18 (Edwards syndrome) and trisomy 12 (Patau syndrome).

[3] *R Akolekar et al.,* 'Procedure-related Risk of Miscarriage following Amniocentesis and Chorionic Villus Sampling: A Systematic Review and Meta-analysis', (2014) 45(1) Ultrasound in Obstetrics and Gynecology 16-26.

[4] For example, the current (UK) NHS pilot offers NIPT following conventional screening tests (including serum screening and ultrasound) to high risk groups for trisomies 13, 18 and 21 (>1:150).

[5] Nuffield Council on Bioethics, *Non-invasive prenatal testing: ethical issues* (London: Nuffield Council on Bioethics, 2017) (NCOB).

[6] NCOB (n 5), at paras 2.31 (information about the test), 4.48 (NIPT and sex selection), and 4.54 (direct-to-consumer services).

[7] NCOB (n 5) para 4.48.

2. NIPT in the Global Village: Opportunities, Concerns and Challenges

In this part of the paper we present some general remarks about the opportunities and challenges to which NIPT, in the context of the global village, gives rise, before considering questions and concerns that relate specifically to the pre-test, post-test, and post-birth phases.

2.1 Opportunities and challenges

On the face of it, the availability of NIPT (informing women about the status of their baby) in conjunction with the Internet (informing women about NIPT) is a significant advance. For those who advocate the facilitation of reproductive choice or who argue for a parental right to know specific genetic and developmental information about the unborn child, these new opportunities seem to be entirely for the good.

Nevertheless, NIPT gives rise to various reservations and challenges—such as objections to the 'medicalisation' of pregnancy, the 'commodification' of life, the 'trivialisation' of abortion, and the like, Moreover, there are issues around the range and quality of the information that can and should be obtained, particularly if it involves analysis of the whole human genome;[8] there is a concern that NIPT can generate uncertain and equivocal data as well as about the eugenic and normative implications of public health screening of particular disorders or conditions;[9] and, of course, NIPT enhances parental choices only if the information presents lawful and transparent options.[10]

Once NIPT is placed in the context of the Internet, further concerns and challenges emerge. For, while the Internet supports a range of services that might inform and educate parents about their reproductive options, as well as enabling the sharing of experiences with NIPT, it also provides a framework for laboratories and health service providers, whether for profit or not for profit, to promote the test. Moreover, patient access to online services can lead to problems for health professionals—for instance, where there is parental confusion, or unfounded expectations about the outcomes of prenatal testing; or where data is equivocal and creates difficult moral decisions for parents.[11]

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[8] *J O Kitzman et al*., 'Noninvasive Whole-genome Sequencing of a Human Foetus', (2012) 4(137) Science Translational Medicine 137.

[9] See for example, http://dontscreenusout.org/ (accessed 16/02/2017). See also NCOB (n5) at paras 5.18-5.19.

[10] For discussion, see *Jeffrey Wale*, 'Don't forget the legal framework: the public provision of non-invasive prenatal testing in England & Wales', (2015) 4 Medical Law International 203-215.

[11] See *PK Agatisa et al*., 'A First Look at Women's Perspectives on Non-invasive Prenatal Testing to Detect Sex Chromosome Aneuploidies and Microdeletion Syndromes'.(2015) 35(7) Prenatal Diagnosis 692-8(available at http://www.ncbi.nlm.nih.gov/pubmed/25800864).

2.2 Pre-test considerations

If NIPT is to meaningfully inform reproductive choice, women need to have intelligible, reliable, balanced and accurate information about the test. However, there is no guarantee that information derived from a multiplicity of sources (both offline and online) will meet these standards; and, when women derive their information from Internet sources, the risks are all the greater.[12] In the global village, how are trustworthy sources to be differentiated from the non-trustworthy?[13]

Already, there is evidence—confirmed by the Nuffield Council on Bioethics' own review[14]—that online information about NIPT falls short. For instance, there is evidence that commercial test providers are pitching their online communications above the recommended reading age for public health information',[15] and that some commercial web advertising may contain inadequate or outdated information[16] (the latter being a particular risk when technology advances so quickly). Whilst the threat of deliberate miss-selling or fraud might be unlikely, it is no surprise that commercial test providers tend to emphasise the benefits rather than limitations of the technology in their marketing material.[17] Links to peer reviewed citations are not always present and this can make it difficult to evaluate the nature and currency of the claims made.[18] Further, private test providers do not always mention the specific abnormalities that can reliably be detected through conventional trimester screening,[19] or the differentials in failure rates between different testing technologies.[20]

[12] See NCOB (n 5) at para 4.22 (for the Council's own review of the adequacy of 'information made available on the websites and in patient leaflets of manufacturers, hospitals and clinics').

[13] See NCOB (n 5) at paras 4.21-4.34 and 6.5-6.10.

[14] See n 12.

[15] *MB Mercer, PK Agatisa and RM Farrell,* 'What patients are reading about non-invasive prenatal testing: an evaluation of Internet content and implications for patient-centered care' (2014) 34(10) Prenat Diagn 986-93; *JW Aarts et al.,* 'Patient-focused internet interventions in reproductive medicine: a scoping review' (2012) 18(2) Hum Reprod Update 211-27 at 212; and *Heather Skirton et al.*; 'Non-invasive prenatal testing for aneuploidy: a systematic review of Internet advertising to potential users by commercial companies and private health providers' (2015) 35(12) Prenat Diagn 1167-75.

[16] *Skirton* (n 15); *Mercer* (n 15).

[17] *Skirton* (n15) at 1174; Mercer (n 15).

[18] The ARC website suggests that 'to be of the highest quality, test performance data should be published in a peer reviewed scientific journal and should report pregnancy outcomes from studies involving 1000s of women.' Available from: http://www.arc-uk.org/tests-explained/non-invasive-prenatal-testing-nipt (accessed 16/02/17).

[19] *Mercer* (n 15).

[20] *Yuval Yaron*, 'The implications of non-invasive prenatal testing failures: a review of an under-discussed phenomenon' (2016) 36(5) Prenatal Diagnosis 391-396.

2.3 Post-test considerations

Once parents have the test results they will need to interpret them. They may need help to do this, both in terms of what the test results demonstrate and the potential implications for their future child. There is strong support for post-test counselling,[21] and in theory, there is nothing to prevent counselling being made available through online or telemedicine models. Indeed, there is some evidence that online decision making aids might be helpful for parents in the context of NIPT.[22]

Once parents have interpreted the results, they might be faced with a difficult choice—whether to continue with or terminate the pregnancy. If they decide to continue, they may still want additional information and support. If they decide to terminate the pregnancy, they have to consider what lawful options are available within their home country—not all States allow open-ended terminations and many impose time conditions and grounds. This highlights another issue: testing for choices that are unlawful is confusing to parents and there is no guarantee of a coherent global narrative around testing and lawful choice.[23] Of course, parents with sufficient means might consider travelling abroad to access treatment options not otherwise available at home. This might create concerns and issues for both the home and foreign State—for the former because of the circumvention of domestic laws, and for the latter because of increased demand for (public) health services.[24] We only need to look at Northern Ireland (which operates a stricter abortion regime compared to the rest of the UK) and the evidence of overseas travel to access abortion services not available at home.[25]

Some parents might also look to e-commerce services and products (including abortifacients) not available at home following a positive test result. This is turn may create issues around internet dispensing and concerns over the quality and safety of online medicines.[26] Such services may also run counter to the local regulatory models—for example, in England a medical assessment is required in every case before it is lawful to supply drugs that are intended to procure an abortion.[27]

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[21] *Mercer* (n 15) 989.

[22] *Lean Beulen et al.,* 'The effect of a decision aid on informed decision-making in the era of non-invasive prenatal testing: a randomised controlled trial' (2016) 24 Eur J of Human Genetics 1409.

[23] For a domestic discussion, see *Wale* (n 10).

[24] For discussion in the context of sex selection, see NCOB (n 5) at paras 4.47-4.48.

[25] See for example the difficulties created around State funding in *R (on the application of A) (A Child) (by her litigation friend B) v Secretary of State for Health UKSC 2015/0220.*

[26] *LBS Clifton*, 'Internet Drug Sales: Is It Time to Welcome Big Brother into Your Medicine Cabinet' (2004) 20(2) Journal of Contemporary Health Law and Policy 541-570, at 554.

[27] *S59 Offences Against the Person Act 1861* and *S1 Abortion Act 1967*; Department of Health, *Guidance in Relation to the Requirements of the Abortion Act 1967* (London: HMSO, 2014) at para 11.

2.4 Post-birth considerations

Post-birth concerns extend to the continued security and management of personal data. NIPT tests have the potential to capture a wide range of information including incidental findings about the mother and child. The potential involvement of private and cross-border laboratories creates the opportunity for this information to be held in uncontrolled or semi-controlled regulatory environments. This in turn creates the risk of deliberate and accidental misuse and spread of data, which by its very nature is usually sensitive and deeply private.[28]

We have outlined elsewhere[29] a plausible basis for asserting a qualified right to know by the pregnant woman in relation to personal health information encompassing information about the developing fetus. However, post-birth, should the child (X) have a right to know and access information held about his or her genetic profile, health or other personal characteristics? What about X's right to access incidental findings about his or her mother? And, what if X claims a right not to know? The questions for future generations, like the concerns, are extensive.

3. ***Possible Responses***

How might regulators respond to the kinds of concerns that we have flagged up—not so much concerns about NIPT itself but about the availability and use of NIPT in the context of the global village? In this part of the paper, we start with some general remarks about the regulatory challenges before looking at responses to the concerns raised, specifically pre-test, post-test, and post-birth.

3.1 Regulatory challenges in the global village

Famously, in the early days of the Internet, the self-styled 'cyberlibertarians' maintained not only that online content should not be regulated but also that regulating it would prove impossible. Even if 'impossible' over-stated the degree of difficulty, early cases, such as *LICRA v Yahoo!* (2000),[30] underlined the challenges facing regulators in one jurisdiction who seek to restrain the supply of online services that are hosted in another. Nevertheless, some responses might be feasible.[31]

First, internet service providers, or other online intermediaries, might be prepared to act as 'chokepoints', restricting supply of goods, services, or information from target sites.[32]

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[28] Of course, there are already international instruments, such as the EU General Data Protection Regulation 2016, that seek to address and co-ordinate State responses to the problem of personal data and privacy.

[29] *Roger Brownsword and Jeff Wale*, 'The Development of Non-Invasive Prenatal Testing: Some Legal and Ethical Questions' (2016) Band 24 Annual Review of Law and Ethics 31.

[30] https://en.wikipedia.org/wiki/LICRA_v._Yahoo! (accessed 26/02/17).

[31] Generally, see Roger Brownsword and Morag Goodwin, *Law and the Technologies of the Twenty-First Century* (Cambridge: Cambridge University Press, 2012) Ch 14.

[32] Natasha Tusikov, *Chokepoints: Global Private Regulation on the Internet* (University of California Press, 2016).

Secondly, it might be possible, as in the Yahoo case, for local regulators to target assets or personnel in the home jurisdiction. Thirdly, there might be opportunities for various kinds of reciprocal cross-border enforcement or other forms of cooperation between national regulators.[33] That said, once local regulators seek to control Internet-based services that are hosted outside their jurisdiction, we have to lower our expectations about the effectiveness of interventions.

3.2 Responding to pre-test concerns

Responding to the principal pre-test concern—that the information given about, and around, NIPT will not be reliable and up-to-date—domestic regulators might adopt mandatory legal rules and guidelines that are applicable to all suppliers of NIPT services.[34] These rules might provide for the licensing of NIPT with specific requirements relating to advertising, access and so on.[35] There is a case for the renewable certification of websites and online forums supplying information about NIPT and related services. This might include the use of certification logos (a symbol of a trustworthy source), perhaps indicating the date of last approval.[36] The position might also be reinforced through 'internet prescriptions'—where licensed medical practitioners are required to highlight 'approved' online sources of information and support about these tests.[37]

Perhaps more controversially, if private provision creates an unacceptable regulatory risk, a State might respond by offering publicly funded tests. Free access to NIPT testing would potentially squeeze the private sector (even without formal abolition) although this would depend on the degree of service equivalence. Of course, as with the responses already indicated, this has significant resource implications that may prove unrealistic.[38] Perhaps a more workable solution is some form of public/private partnership that utilises the proposed system of licensing, certification and professional body regulation/guidance.[39] Ultimately, States must decide what is a 'reasonable informational expectation' in the context of

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[33] See, e.g. Lawrence Lessig, *Code Version 2.0* (New York: Basic Books, 2006) Ch 15.

[34] See for example, the recent recommendations of the NCOB (n 5), chapter 6.

[35] Although any rules would need to overcome existing international guidelines that licensing practices should not be used to restrict parental or healthcare providers' choice (NCOB (n 5) at para 2.85).

[36] Compare the mandatory EU internet logo and rules for online supply of medicines (see https://www.gov.uk/government/news/new-mandatory-logo-for-selling-medicines-online (accessed 23/02/17).

[37] The importance of accurate, balanced and non-directive public sector sources of information about NIPT is recognised in the recent report by the NCOB (n 5) at para 6.27.

[38] For discussion of the practical and financial difficulties of a publicly funded testing regime, see *C Munthe*, 'A New Ethical Landscape of Prenatal Testing: Individualizing Choice to Serve Autonomy and Promote Public Health: A Radical Proposal', (2015) 29(1) Bioethics 43.

[39] The NCOB (n 5), Ch 6, envisages a combination of healthcare and disciplinary regulation and agreement with NIPT providers and manufacturers.

pregnancy,[40] and then decide on the allocation of costs between the public and private sectors. The public narrative is important and there should be some convergence between the aims of testing and any regulatory environment in which this information is processed and decisions made.[41]

The blogosphere including parent based websites are harder to regulate. Although freedom of expression might be legitimately restricted for the protection of health and morals,[42] any State should be cautious about imposing restrictions where there is no evidence of fraud or malice on the part of users and operators. To be sure, laws might be made to restrict or mandate online claims about the technology or that require support from peer reviewed sources where claims are made;[43] but, it might be more productive to focus on addressing outdated or inaccurate claims by supporting those that engage productively through some form of approved certification process.[44]

3.3 Responding to post-test concerns

The principal post-test concerns relate to: (i) the range of results returned to pregnant women; (ii) the need for information and support to assist decision-making; and (iii) the purposes for which the test results might be applied. So, for example, the Nuffield Council on Bioethics has recently proposed: (i) that there should be strict domestic limits on the sweep of information to be returned;[45] (ii) that mandatory parental support should be available from all providers;[46] and (iii) that test providers should be prohibited from generating or reporting information about the sex of the fetus unless 'there is concern that the fetus may be showing signs of a significant sex chromosome aneuploidy or is at risk of a sex-linked disorder.'[47]

Beyond domestic regulation, co-operative global state engagement around the implementation of NIPT would be beneficial. There is the scope to develop guidelines around many of the issues discussed.[48] Evidence of 'healthcare tourism' might be addressed through reciprocal international agreements that at least address the resource implications of this

[40] *Z Deans, AJ Clarke and AJ Newson*, 'For Your Interest? The Ethical Acceptability of Using Non-invasive Prenatal Testing to Test "Purely for Information"', (2015) 29 Bioethics 19-25 at 25.

[41] For discussion, see Wale (n 10).

[42] See for example, *Art 10(2) of the European Convention on Human Rights*.

[43] *Skirton* (n 15); *Mercer* (n 15) 987; and ARC (n 18).

[44] NCOB (n 5) para 6.39.

[45] NCOB (n 5) paras. 6.4-6.18.

[46] Ibid., para 6.40.

[47] Ibid., para 6.16.

[48] See, for e.g., *Heather Skirton et al.*, 'Offering prenatal diagnostic tests: European guidelines for clinical practice guidelines', Eur J Hum Genet, (2014) 22(5) 580-6.
(available at http://www.ncbi.nlm.nih.gov/pubmed/?term=24022298); and the proposed EU IVD Regulation (NCOB (n 5) at para 1.39).

behaviour. However, recalling the caveats in 3.1, we cannot assume that all states will be willing reciprocators or co-operators.

3.4 Responding to post-birth concerns

If the post-birth concerns are to be addressed, there has to be a regulatory framework that (i) makes provision for the storage, security and future destruction of important personal data (including genetic data) and (ii) takes an acceptable position on the right to know and not to know.

With regard to the former, there are obvious advantages in a coordinated global approach that encourages (if not requires through licence or other means) providers to be transparent about their processes for handling/storing data and the mechanisms for addressing any future areas of dispute. Again, there might be some regulatory advantage in restricting or encouraging the use of services to jurisdictions that operate similar rules around data protection and privacy. A default restriction on the use of NIPT data for any other purpose and a personal right to anonymity about the fact of testing might be appropriate (where not already available).

With regard to the latter, while domestic regulators can consult with and then be guided by their community's view of reasonable informational expectations, the positions taken are likely to differ from one state to another, this militating against global agreement.

4. Conclusions

In this short paper, we have focused on the development of a new form of genetic test, NIPT, in the context of the global Internet economy. Unlike some novel technologies, NIPT is not necessarily being piloted under carefully controlled conditions; rather it is being released at once into an environment that is particularly difficult to regulate.

We have suggested that, over and above the reservations that some might have about NIPT, this raises several further concerns—particularly with regard to the reliability of the online information about NIPT, the possibility that women might use Internet suppliers to work round local legal restrictions, and the impact of stored genetic information on future children.

While the global village is not easily regulated, we have suggested some responses that regulators might make to the aforementioned concerns. However, whatever we might make of these concerns, the reality is that, like other technologies relating to reproduction, NIPT will be exploited if women see a benefit and if commercial providers find a market for their services.