NUFFIELD COUNCIL ON BIOETHICS

Call for views and evidence on non-invasive prenatal testing

Consultation document

Introduction

The Nuffield Council on Bioethics is considering the ethical issues raised by the increasing availability of non-invasive prenatal testing (NIPT) in the UK. We use the term NIPT to mean all kinds of prenatal genetic testing using fetal DNA from the placenta extracted from a sample of the mother's blood. More information about NIPT can be found at: www.nuffieldbioethics.org/NIPT/background

To inform our deliberations, we would like to hear from as many people and organisations who have an interest in NIPT as possible. The questions in this consultation document may be particularly suitable for people responding on behalf of an organisation and people whose work focuses on the ethical issues raised by NIPT, such as academics working in the field.

When responding, feel free to answer as many or as few questions as you wish, and please use the 'any other comments' section to contribute any views or evidence that do not fit elsewhere. Where possible, please explain the reasons behind your responses and the evidence or experience on which you are basing them.

A shorter online survey that can be completed anonymously by anyone with a personal or professional interest in NIPT is available at: www.surveymonkey.co.uk/r/NuffieldNIPT. If you know someone with learning difficulties who would like to contribute to the Council's project on NIPT, please contact Anna Wilkinson on awilkinson@nuffieldbioethics.org

The Nuffield Council on Bioethics is an independent body based in the UK. The findings and recommendations of our project on NIPT will be published around the end of 2016. Find out more about the Council and the project at: www.nuffieldbioethics.org/NIPT

How to respond

Please complete this form and email it to Anna Wilkinson at: awilkinson@nuffieldbioethics.org.

If you would prefer to respond by post, please send your submission to:

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Closing date for responses: 1st August 2016

If you have any questions, please contact Anna Wilkinson at the above address. Thank you for taking the time to respond.

Your details

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Questions

NIPT as part of NHS antenatal care

The UK National Screening Committee (UKNSC) has recommended that NIPT for Down Syndrome, Patau Syndrome and Edwards Syndrome be offered on the NHS to pregnant women whose babies are found to have a high risk of having one of these conditions following the 11-14 week screening tests. The UKNSC has proposed that this should be implemented as part of an evaluation process to understand better how offering NIPT in this way will affect the screening pathway and the choices that women make. The exact specifications of the evaluation are currently being developed. Find out more.

1 If this recommendation was implemented fully into NHS antenatal care, what benefits or concerns might this raise for pregnant women and their partners?

General concerns:

- CMF is supportive of reducing the unintended adverse consequences of screening procedures but we do not welcome the proposal to add NIPT/cfDNA analysis as a contingent test for those in whom initial screening has indicated a high risk. This development purports to reduce the overall number of referrals for invasive diagnostic procedures (amniocentesis or chorionic villous sampling) and thereby reduce the number of inadvertent miscarriages that arise as the result of those procedures, of babies who are almost always healthy. However a concomitant effect would be an increase in the number of babies with Down Syndrome who would be lost because of the increased detection rate. Findings from a pilot study by the National Institute for Health and Research (RAPID evaluation study) suggest that an additional 102 babies with Down Syndrome would be detected every year. On the basis that 90% of women will choose to abort,[1] this would mean that an additional 92 babies with Down Syndrome could be aborted each year.

- The same technology that allows NIPT to detect trisomy also detects other genetic features including gender and will in time permit the detection of a wide range of genetic 'conditions' and predispositions. Increasingly widespread use of

[1] Morris JK, Springett A. (December 2014) The National Down Syndrome Cytogenetic Register for England and Wales: 2013 Annual Report. http://www.binocar.org/content/annrep2013_FINAL.pdf

NIPT to analyse more and more genetic features up to the entire genome would mean the complexity of data would lead to a significant increase of false-positives, requiring confirmation by invasive tests of abnormalities whose relevance or significance is little known or not known at all. This uncertainty would lead many parents to not take any risk, with the resulting paradox: the number of invasive diagnostics would rise because of the use of the new test that should precisely be diminishing the use of invasive diagnostics. That increase in the number of invasive tests would also lead to an increase in the number of unintended miscarriages, often of normal fetuses.

- The pressure incrementally to extend the availability of the test for a broader range of conditions, towards the point where it becomes part of routine screening, would be hard to resist and certainly not cost-neutral.

Potential benefits:

- The first benefit for a pregnant woman and her partner would be the availability of a simple blood screening test that would reduce the likelihood of her having to have an unnecessary diagnostic invasive test, with the attendant risk of provoking the inadvertent miscarriage of a baby without any abnormality..
- A positive NIPT screening result, followed by a diagnostic invasive test that confirms trisomy, would enable parents to prepare for the arrival of a child with special needs. The availability of time for reflection, qualified counselling and support, written and online resources and the opportunity to meet with parents of children with trisomy-related disabilities, and the children themselves, would all be helpful in this.[2]

Concerns include:

- Increased anxiety for those whose risk levels, following existing initial screening tests, are considered just below the threshold level and would not therefore 'qualify' for the new, more sensitive test.
- The public misconception that NIPT is a 'diagnostic' test, on a par with invasive testing, not a screening test that would need to be followed by a diagnostic invasive procedure. Research has found that in over half of discussions, health care providers did not clarify the fact that screening is not diagnostic.[3]
- Increased sense of 'tentativeness' in pregnancy – the mother is wary of committing emotionally or relationally to her unborn child lest the baby be shown by tests to carry an abnormality.
- Increased anxiety and uncertainty for women confronted by ambiguous results. Since the outcome of Down Syndrome represents a spectrum of disability, it is almost impossible to predict the implications for a particular child.[4]

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[2] Parens E and Asch A. The Disability Rights Critique of Prenatal Genetic Testing: Reflections and Recommendations. Hastings Center Report 1999; 29(5): S1-S22

[3]http://journals.lww.com/greenjournal/Abstract/2016/06000/Patient_Health_Care_Provider_Conversations_About.23.aspx

[4]http://dontscreenusout.org/wp-content/uploads/2016/02/Abortion-and-Disability-Report-17-7-13.pdf Professor John Wyatt, Oral Evidence Session 4, page 60

- The difficulty in explaining and understanding risk. As stated below, counselling about false-positive rates is troubling and should be distinguished from the positive predictive value.[5]
- Reinforcement of the notion that children with chromosomal abnormalities (and thereby special needs) should be 'screened out' and destroyed.
- Abortions for congenital abnormality often occur late in pregnancies. Psychological morbidity attends most abortions but is likely to be considerable when the pregnancy is advanced and the baby very much wanted. (See below, under 3).
- Increased likelihood of some women making choices they later regret. A British Parliamentary Inquiry into abortion on the grounds of disability concluded that: '….*the studies have all found that around 20% of women, between one and two years after an abortion for fetal abnormality, have a psychiatric condition, usually a complicated grief reaction, a depressive disorder or post-traumatic stress disorder.'*[6] The availability of perinatal palliative care would encourage a higher proportion of pregnant women carrying a baby with a trisomy disorder to continue their pregnancies and avoid many of the mental disorders associated with regret. In one British study, when parents were offered perinatal hospice as an option, 40% chose to continue with their pregnancies.[7] The comparative figure is US studies was between 75% and 85%.[8]
- As awareness of the test increases, and its cost comes down, then many pregnant women will seek to access the test privately. They may not receive pre-test information and counselling. They will receive results outlining all manner of variable predictive risks faced by their babies, but will not have the context in which to discuss, assess and weigh the relevance of those results. This will increase anxiety further and make abortion a more likely outcome, sometimes without evidence of trisomy.
- The routinisation and ease of accessing the tests are likely to lead to societal attitudes that it is a 'duty' to test rather than an option. Evidence from the Parliamentary Inquiry reflected this concern.[9]
- The test can also be used to determine the sex of the baby. The International Bioethics Committee of UNESCO (IBC), sounding their concerns over the test, has said that: *'Another risk lies in the cultural prejudices of preferring a child of the male sex, the sex of the baby being one of the characteristics that can obviously be discovered by NIPT. As this test can be carried out at a very early stage of the pregnancy it would be difficult, even impossible for doctors to forbid the communicating of sex to the parents, and especially at a time when many*

[5]http://journals.lww.com/greenjournal/Abstract/2016/06000/Patient_Health_Care_Provider_Conversations_About.23.aspx
[6] http://www.abortionanddisability.org/resources/Abortion-and-Disability-Report-17-7-13.pdf
[7] Breeze AC et al. Palliative care for prenatally diagnosed lethal fetal abnormality. Arch Dis Child Fetal Neonatal Ed. 2007 Jan;92(1):F56-8
[8] http://www.aaplog.org/wp-content/uploads/2015/07/AAPLOG-Practice-Bulletin-1.compressed.pdf
[9]http://orca.cf.ac.uk/50207/1/Oral%20Evidence_Parliamentary%20Inquiry%20February%202013_DisCopy.pdf

countries have liberalised abortion. This could lead to a selection based on sex, which is against ethical values of equality and non-discrimination.'[10]

2 If this recommendation was implemented fully into NHS antenatal care, what might be the implications for the healthcare professionals involved in offering and providing prenatal screening and testing?

- Initially (see 1, above), a reduced number of invasive tests and associated inadvertent miscarriages.
- Increased rate of discovery of babies affected by Down Syndrome and other trisomies and, if current trends continue, overall increase in abortion numbers leading to a projected decline of 13% reported live births of babies with Down, Patau and Edwards Syndromes.[11] Healthcare professionals would be enabling a kind of informal eugenics, which would raise issues of conscience for many.
- Ground E of the Abortion Act does not specify what amounts to 'serious handicap'. In practice it is left to individual clinicians to 'interpret' the results of screening tests to parents and to inform them of likely implications. There is potential for significant differences (and even conflict) between doctors as to which disabilities fall within the scope of the law and which do not. This is concerning for parents, practitioners, lawmakers and those with disabilities. If NIPT is introduced, clinicians will find themselves in this situation more commonly, sometimes at a stage of pregnancy when the fetus is potentially viable.
- A culture shift among healthcare professionals would be required. At present, subtle or direct pressure may be placed on parents who decide not to abort their child.[12] Some parents have already been made to feel that to bring into the world a child with known disability is somehow irresponsible and blameworthy,[13] a precedent that suggests that this trend will worsen.
- CMF supports the recommendations of the Parliamentary Inquiry into Abortion on the Grounds of Disability (2013)[14] that include: 'Guidelines for the medical profession should include training for obstetricians, fetal medicine specialists and midwives on the practical realities of the lives of children living with the different conditions which are screened for through ante-natal tests.'

3 If this recommendation was implemented fully into NHS antenatal care, it might lead to an increase in the number of terminations of pregnancies with a diagnosis of Down Syndrome, Patau Syndrome or Edwards Syndrome. What benefits or concerns might this raise?

[10] 'Report of the IBC on Updating Its Reflection on the Human Genome and Human Rights', October 02nd 2015,: http://unesdoc.unesco.org/images/0023/002332/233258e.pdf
[11] http://www.binocar.org/content/annrep2013_FINAL_nologo.pdf
[12] http://www.cmfblog.org.uk/2013/02/19/women-who-keep-their-disabled-babies-face-coercion-discrimination-and-disdain/
[13] Nuffield Council on Bioethics, Genetic Screening: Ethical Issues, London 1993, para 8.11.
[14] http://dontscreenusout.org/wp-content/uploads/2016/02/Abortion-and-Disability-Report-17-7-13.pdf

We see no benefits arising. Concerns centre around the violation of the rights of disabled people, the denial of the joyous experience of life that people with Down Syndrome describe and also inspire in others, and the fostering of a culture in society of 'zero defect' with its eugenic undertones.

- As mentioned above, implementing NIPT as proposed would lead to an additional 92 babies with Down Syndrome being aborted each year. Down Syndrome is fully compatible with life outside the womb. People with Down Syndrome typically live for 50 or 60 years, depending on co-morbidities, finding fulfilment and contributing greatly to family and community life. Research published in the American Journal of Medical Genetics found that nearly 99% of people with Down Syndrome are happy with their lives, more than three-quarters of parents of a child with the condition had a more positive outlook on life and almost 90% of siblings said they considered themselves better people because of their family member with Down Syndrome. Those with Edwards and Patau Syndromes may also live for days, weeks, months or even years; even the briefest lives afford opportunities for parental bonding, and support from palliative care and perinatal hospice teams can transform the experience for families.
- Abortions for congenital abnormality often take place later in pregnancies. It is not surprising therefore that psychological morbidity is considerable. Morbidity following termination of pregnancy for fetal disability has been shown to be both prevalent and persistent,[15] and associated with long-lasting consequences for a substantial number of women.[16] Rather than leading to psychological well-being, termination of pregnancy for fetal disability can be an emotionally traumatic major life event which leads to severe post-traumatic stress response and intense grief reactions that are still detectable some years later.[17] In fact women who terminate pregnancies for fetal anomalies experience grief as intense as those who experience spontaneous perinatal loss with approximately a fifth developing major depression and/or requiring psychiatric intervention.[18]
- Their families are also not immune with even very young children and those sheltered from knowledge of the event showing reactions to their parents' distress and maternal absence.[19]
- To introduce a screening test that would result in the increased selective elimination of children with Down Syndrome due to a lack of proper inclusion, accommodation, and support, would violate the rights of disabled persons

[15] Davies V et al. Psychological outcome in women undergoing termination of pregnancy for ultrasound-detected fetal anomaly in the first and second trimesters: a pilot study. Ultrasound Obstet Gynecol 2005;25(4):389-92(April)

[16] Kersting A et al. Grief after termination of pregnancy due to fetal malformation. J Psychosom Obstet Gynaecol 2004;25(2):163-9(June)

[17] Kersting A et al. Trauma and grief 2-7 years after termination of pregnancy because of fetal anomalies--a pilot study. J Psychosom Obstet Gynaecol 2005;26(1):9-14 (March)

[18] Zeanah CH et al. Do women grieve after terminating pregnancies because of fetal anomalies? A controlled investigation. ObstetGynecol 1993;82(2):270-5 (August)

[19] Furlong RM, Black RB. Pregnancy termination for genetic indications: the impact on families. Soc Work Health Care 1984;10(1):17-34(Autumn)

(under the Convention on the Rights of Persons with Disabilities)[20] and our ethical obligations to disabled people and communities. The Convention has as a principle the 'respect for difference and acceptance of persons with disabilities as part of human diversity and humanity'.[21] In Concluding Comments on the country reports from Spain and Hungary, the Committee on the Convention called for action to prevent discrimination within abortion law on the grounds of disability.[22]

- We would argue that unborn persons are persons still, and that they should be protected from discrimination by Article 14 of the European Convention on Human Rights,[23] recognised by the UK Human Rights Act, 1998.
- To assume that Ground E provision should automatically apply to Down Syndrome is to stretch the application of the Abortion Act (1967) to the point of completely misshaping it. **Down Syndrome should not be classed as a 'serious handicap' and screening for it should only be offered to mothers in order better to prepare them and their families to be joined by a child with special needs.**
- Justifying terminations on the grounds of disability devalues the lives of those already living with a disability. Giving Down Syndrome Ground E status implies that the life of a person with the syndrome would have been better terminated before birth – that theirs is a life 'not worth living'. Ultimately, it fosters in society the notion that only the (genetically) perfect, or those who reach a certain arbitrary minimal standard, are acceptable and that it is socially desirable to prevent people with some or all disabilities from being born. The Disability Rights Commission has said: '*Ground E is offensive to many people; it reinforces negative stereotypes of disability; and there is substantial support for the view that to permit terminations at any point during a pregnancy on the ground of risk of disability, while time limits apply to other grounds set out in the Abortion Act, is incompatible with valuing disability and non-disability equally.'*[24]
- These concerns are echoed by the International Bioethics Committee that comments: '*The widespread use of genetic screening and in particular of NIPT may foster a culture of "perfectionism" or "zero defect" and even renew some "eugenic trends", with the consequence that it could become more and more difficult to accept imperfection and disability as a part of normal human life and a component of the diversity we are all called on to acknowledge and respect. The anxiogenic effect is also to be considered. The right of an individual to make autonomous choices is to be made consistent with the right not to be subjected to discrimination or stigmatization based on genetic*

[20] https://www.un.org/disabilities/convention/conventionfull.shtml
[21] UN Convention on the Rights of Persons with Disabilities 2006, Article 3 http://www.un.org/disabilities/convention/conventionfull.shtml
[22] Committee on the Rights of Persons with Disabilities, 'Consideration of Reports submitted by States under Article 35, Concluding Observations – Spain' (19 May 2011), para 18. Similarly, for Hungary (22 October 2012), para 18.
[23] https://www.equalityhumanrights.com/en/human-rights-act/article-14-protection-discrimination
[24] http://news.bbc.co.uk/1/hi/health/1502827.stm

characteristics and the duty to respect every human being in her or his uniqueness.'[25]

4 Do you think the UK National Screening Committee's criteria for appraising the viability, effectiveness and appropriateness of a screening programme are appropriate for appraising prenatal screening programmes?

No. Criterion 3 states that 'where there is no prospect of benefit for the individual screened then the screening programme shouldn't be further considered'. The individual being screened with NIPT is the fetus. The screening conveys no benefit to the fetus – indeed, it could be said to put the continuation of his/her life in danger – and, as such, is inappropriate.

WHO criteria governing screening protocols include the requirement that: '*there should be treatment for the condition being screened'.*[26] In cases of trisomies, prenatal screening tests are carried out not to identify individuals with special needs, in order that they may be more effectively treated, but with the expectation of eliminating them from the population. This type of screening offers no benefit to the fetus being screened and also results in collateral damage in that unaffected fetuses may also die as a result of inadvertent miscarriage. We submit that this is contrary to the Hippocratic Oath,[27] the Declaration of Geneva[28] and to the general strategy of medicine. There is no treatment on offer for Down Syndrome and in over 90% of cases the outcome is to terminate the life of the one screened.[29]

Information and counselling

5 **How would you rate the information and counselling currently provided by the NHS to pregnant women and their partners to help them make decisions about currently available prenatal screening (eg. using ultrasound) for genetic conditions during pregnancy, if you have experience or evidence relating to this?**

- Evidence from the Parliamentary Inquiry, already mentioned, suggests that healthcare professionals tend to assume women will participate in screening and that little attention is given to explaining the purpose or possible outcomes and options. In one study in a London teaching hospital, 27% of women did not know that they had received blood tests during pregnancy to detect spina bifida.[30]
- As the number of available genetic tests increases, so does the problem of providing suitable and sufficient pre-test information and counselling. Yet this is surely essential if consent is to be fully informed. Screening tests come with

[25] http://unesdoc.unesco.org/images/0023/002332/233258e.pdf, section IV, para 125
[26] Wilson JMG, Jungner G. (1968) Principles and practice of screening for disease (large pdf). WHO Chronicle Geneva:World Health Organization. 22(11):473. Public Health Papers, #34.
[27] http://www.pbs.org/wgbh/nova/body/hippocratic-oath-today.html
[28] http://www.wma.net/en/30publications/10policies/g1/
[29] Morris JK, Springett A. (December 2014) The National Down Syndrome Cytogenetic Register for England and Wales: 2013 Annual Report. http://www.binocar.org/content/annrep2013_FINAL.pdf
[30] Marteau, T et al. Journal of Psychosomatic Research (1988), 32:403-408.

the aura of medical authority and respectability; to decline them may seem to be 'going against medical advice'.

- US Obstetrics and Gynaecology research found that the average time provided by healthcare providers to prenatal genetic screening counselling amounts to just 1.5 minutes, and does not adhere to College recommendations.[31] False-positive rates were seldom discussed and in half of the conversations between providers and parents, it was not made clear that prenatal genetic screening is not a diagnostic test. Cursory explanations and inadequate information undermine the integrity of consent in any healthcare setting. Following Montgomery v Lanarkshire Health Board, doctors must now ensure that patients are aware of any "material risks" involved in a proposed treatment, and of reasonable alternatives. The Supreme Court's ruling outlined the new test: '*The test of materiality is whether, in the circumstances of the particular case, a reasonable person in the patient's position would be likely to attach significance to the risk, or the doctor is or should reasonably be aware that the particular patient would be likely to attach significance to it.*'[32]
- In the UK Parliamentary Inquiry into Abortion on the Grounds of Disability, a '*considerable number of witnesses reported from their experience that after the discovery of a fetal disability, the presumption of the medical profession was that parents would opt for abortion'.*[33] *'Parents can find themselves given only a leaflet on abortion and plenty of support or advice on having an abortion rather than a support package and/or information specific to the condition diagnosed.'*[34]
- We support the recommendations of the Parliamentary Inquiry that '*It should be best practice that parents are provided with practical and balanced information as soon as possible after discovery of a fetal disability and before leaving hospital so that they can make an informed choice. This should include leaflets or other information written by relevant disability groups. Parents should be offered contact with families with a child with a similar diagnosis without delay'* and that '*following a prenatal discovery of a fetal disability, parents should be encouraged and supported to consider adoption for their child as one of the options available to them. Literature distributed by patient interest groups to couples should promote adoption as a positive option'.*[35]

6 How would you rate information and/or counselling provided by the NHS about NIPT available as part of research studies or through the private sector, if you have experience or evidence relating to this?

[31] http://journals.lww.com/greenjournal/Abstract/2016/06000/Patient_Health_Care_Provider_Conversations_About.23.aspx
[32] https://www.supremecourt.uk/decided-cases/docs/UKSC_2013_0136_Judgment.pdf
[33] http://dontscreenusout.org/wp-content/uploads/2016/02/Abortion-and-Disability-Report-17-7-13.pdf For instance, Written evidence, Q8, Respondent 8, parent; Written Evidence, Q11, Respondent 21; Written Evidence, Q5, Respondent 30
[34] *Ibid:* Section 3; para 51.
[35] *Ibid: p5: 8,6.*

No experience

7 How would you rate the information and/or counselling currently provided by private healthcare clinics to pregnant women and their partners to help them make decisions about NIPT, if you have experience or evidence relating to this?

No experience

8 What information about NIPT and the conditions being tested for do you think should be conveyed to pregnant women and their partners? How do you think that information could best be conveyed and by whom?

- When pregnancy is confirmed, non-directive information about all screening tests should be made available. The distinction should be drawn between those tests that carry treatment options and those where the only available 'treatment' would be the termination of the pregnancy. It should not be assumed that a woman wishes to undergo every test. Time and trained pre-natal counsellors must be available so that women and their partners can understand their options and related risks, and make fully informed decisions. The culture in obstetric departments must change to one where the woman and her partner can comfortably refuse screening without experiencing a negative attitude in response.
- As we have stated above, we do not support the introduction of NIPT tests as standard in the NHS.
- If they were to be introduced then it must be made clear that NIPT is not a diagnostic test, but a screening test and confirmatory invasive procedures may be necessary.
- If the result of any screening test, including NIPT (and any subsequent invasive test), suggests that the baby may have Down Syndrome or another trisomy, then parents should be offered the option to meet others who have first-hand experience of the condition or disability in question. This includes affected patients and their families, disability-specific support groups, healthcare professionals caring for babies, children and adults with the relevant condition. There should be counselling and support offered and available for those who choose an abortion on the grounds of disability both before and after abortion. For parents who choose to continue with their pregnancy, there needs to be improved, positive and consistent care and support from across the medical profession.

9 What might be the implications for the NHS of increasing numbers of pregnant women purchasing NIPT through the private sector?

- Non-invasive testing, currently available through private healthcare, has already increased the number of children with Down Syndrome being aborted.[36]
- As stated above, over time it is likely that those purchasing NIPT privately will be given a mass of information outlining all manner of variable predictive risks faced by their babies. Anxiety levels are likely to rise and the experience of pregnancy become yet more tentative. Pregnant women and their partners will need help to understand, weigh and respond to the information they have been given and the burden of this is likely to be felt by NHS workers.
- The breadth and complexity of risk-related data that would result from widespread use of NIPT will inevitably increase both the demand for invasive testing as parents seek confirmation of positive screening tests, and the demand for abortion by parents unwilling to take any risk. Ironically, a test intended to reduce the number of invasive tests would likely increase them, and the promise of fewer inadvertent miscarriages would also founder. The NHS would inevitably 'pick up the tab' for 'treatment' following NIPT tests purchased privately.
- Ultimately, public demand for the test to be integrated into routine primary antenatal screening, not simply offered to those found to be at risk by other measures, will be difficult to resist. The National Screening Committee estimates that using the new test as part of primary screening would detect 289 more trisomy babies annually. Assuming a 90% abortion rate, 260 more abortions would be requested and fetal lives lost.

10 What benefits and concerns might be raised if pregnant women were able to purchase NIPT directly from providers (e.g. where a kit is sent to the pregnant woman in the post), rather than through a healthcare clinic following a face-to-face consultation?

We see no benefit. Concerns include:

- Absent or cursory pre-test and post-test counsel and information by trained staff
- A mass of complex and confusing data without a context in which to discuss meaning and relevance.
- Raised levels of anxiety and tentativeness about the pregnancy.
- The danger of knee-jerk requests for abortion.

11 A small proportion of NIPT tests will return an inconclusive result, even if repeated. How should healthcare professionals, both in the NHS and in private clinics, deal with inconclusive results?

- The question assumes the test will be offered by the NHS, a policy which we do not support

[36] New blood test blamed as women choosing to abort babies with Down syndrome and other serious disabilities soar in three years, The Daily Mail, 13 June 2015 http://dailym.ai/1efQRPw

- If it is offered, healthcare professionals must make clear *before* screening that the new test is not conclusive – it is an advanced screening test but not a diagnostic test. There is already a general perception that the NIPT test at ten weeks will replace other testing because of its reliability. False-positive rates for NIPT are in the order of 0.1%–0.2%.[37] The Positive Predictive Value (PPV) gives the best measure of reliability, and its significance should be explained to the parents. In the largest studies the PPV is 95% for Down Syndrome, lower for other trisomies.[38]
- Test failure rates vary in studies from <1% - >12%,[39] with between a half and a third failing again on retesting. Consent to the NIPT should be fully informed. Delays between first and subsequent tests will clearly be anxious times for patients and their families. Pre-test and post-test information provision and counselling for positive and negative NIPT results should be available.
- Following Montgomery v Lanarkshire Health Board[40] the requirement upon doctors, as part of the consent process, to inform patients about risk associated with any procedure, or its alternatives, has been enhanced. The risks of false positive and inconclusive outcomes must be explained. The information provided should, for example, include: 'an explanation of the investigation, diagnosis or treatment; an explanation of the probabilities of success, or the risk of failure; or harm associated with options for treatment. The patient should be given time to ask questions. The GMC and the courts expect patients to be given all information material to their decision, with the proviso that it would not cause the patient serious harm'.[41] This sets the bar higher than the previous Bolam test and failure to comply risks legal action.

12 What issues are raised by incidental findings that can arise following NIPT (such as genetic abnormalities or cancerous cells in the pregnant woman), both in the NHS and in private clinics?

- In a very small number of cases, discordant NIPT results, where the fetus is chromosomally normal but the NIPT test is abnormal, may indicate the incidental presence of maternal malignancy.[42] Other reasons for discordance include maternal obesity and multiple pregnancies. Once again, pre-test and post-test information and counselling are important provisions.
- Test results should not be withheld from the patient, even if some studies have shown that such early detection does not always improve patient outcomes.[43]

[37] http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4827766/
[38] http://nsgc.org/page/abnormal-non-invasive-prenatal-testing-results
[39] http://bmjopen.bmj.com/content/6/1/e010002.full
[40] https://www.supremecourt.uk/decided-cases/docs/UKSC_2013_0136_Judgment.pdf
[41] http://www.medicalprotection.org/uk/resources/factsheets/england/england-factsheets/uk-eng-consent-the-basics
[42] https://jama.jamanetwork.com/article.aspx?articleid=2389341
[43] http://www.ncbi.nlm.nih.gov/pubmed/26278647

- Onward referral to appropriate specialists at the first opportunity, to minimise the length of anxious waiting times.

What should NIPT be testing for?

In the future, NIPT may allow pregnant women and their partners to test their unborn babies for a wider range of genetic conditions, including those that develop in adulthood. It may also be possible to find out about non-medical information relating to the behaviour and physical appearance of the future child. It is possible to use NIPT for 'whole genome sequencing', which reveals the complete DNA make-up of the unborn baby. At the moment this is very difficult and expensive, but will very likely become cheaper and easier in future.

13 Should potential parents be able to find out the sex of their unborn baby for non-medical reasons from 10 weeks of pregnancy using NIPT? Please give reasons for your answer.

- Presently, many parents ask to know the likely sex of their baby at the 20 week scan, to limit the scope of name choice, for general preparation in advance of the birth, or simply out of curiosity. That NIPT should provide this information with greater certainty and earlier in pregnancy is not a problem in principle. However, in cultures where there is a bias towards male babies, NIPT may contribute to the pursuit of illegal abortion on the grounds of gendercide.
- The International Bioethics Committee of UNESCO (IBC), sounding their concerns over the test, has said that: '*Another risk lies in the cultural prejudices of preferring a child of the male sex, the sex of the baby being one of the characteristics that can obviously be discovered by NIPT. As this test can be carried out at a very early stage of the pregnancy it would be difficult, even impossible for doctors to forbid the communicating of sex to the parents, and especially at a time when many countries have liberalised abortion. This could lead to a selection based on sex, which is against ethical values of equality and non-discrimination*'.[44]
- In 2015, the Crown Prosecution Service ruled that it would not be in the 'public interest' to prosecute two doctors, who agreed to arrange terminations for women who requested them on the basis of gender preference, despite acknowledging that there was sufficient evidence to warrant a prosecution with a realistic prospect of conviction.[45]
- 'Abortion on demand' is perceived to be the culture in UK, and the wording of the Abortion Act 1967 is sufficiently limp that a woman could argue that her mental health, or that of her existing family, would be put at risk by having a female baby. In this climate, using NIPT to identify the gender of the baby, for non-medical reasons, we believe would prove to be an incremental step

[44] 'Report of the IBC on Updating Its Reflection on the Human Genome and Human Rights', October 02nd 2015,: http://unesdoc.unesco.org/images/0023/002332/233258e.pdf

[45] http://www.telegraph.co.uk/news/uknews/law-and-order/11470814/Door-wide-open-to-gender-abortion-as-CPS-blocks-prosecution-of-doctors-campaigners-claim.html

towards legalising abortion on the grounds of gender, and we therefore oppose it.

14 What genetic information, if any, do you think parents <u>should</u> be allowed to find out about their unborn baby using NIPT? Please give reasons for your answer.

- Whatever information, genetic or otherwise, that NIPT brings to light, should be used only to enable medical staff, parents and other family members to be better prepared for the arrival of the new baby or to enable therapeutic interventions (medical or surgical) to improve the baby's health before birth or in the perinatal period.
- Waiting for a child, that is known to be impaired to be born can be a distressing and anxiety-ridden experience. There is much to be said for not knowing in advance, so that parents can give themselves to loving the mysterious gift that is not yet 'unwrapped'.

15 What genetic information, if any, do you think parents <u>should not</u> be allowed to find out about their unborn baby using NIPT? Please give reasons for your answer.

See above, under 14.

16 Do you think whole genome sequencing of unborn babies using NIPT should be allowed? Please give reasons for your answer.

- No.
- Using the test in this way can only lend weight to the view that there is no room in modern society for those with certain genetic abnormalities. This is a form of eugenics. It also says to those living with such disorders that their lives would have been better not lived, that their lives are not worth living and certainly not worth as much as those deemed to have a full and normal complement of chromosomes and/or genes.
- These concerns are echoed by the International Bioethics Committee that comments: *'The widespread use of genetic screening and in particular of NIPT may foster a culture of "perfectionism" or "zero defect" and even renew some "eugenic trends", with the consequence that it could become more and more difficult to accept imperfection and disability as a part of normal human life and a component of the diversity we are all called on to acknowledge and respect. The anxiogenic effect is also to be considered. The right of an individual to make autonomous choices is to be made consistent with the right not to be subjected to discrimination or stigmatization based on genetic*

characteristics and the duty to respect every human being in her or his uniqueness'.[46]

- A widespread use of NIPT screening to analyse more and more genetic features up to the entire genome would mean the complexity of data would lead to a significant increase of false-positives, requiring a confirmation by invasive tests of abnormalities whose relevance is not known at all. This unknown might lead the parents not to take any risk, with the resulting paradox: the number of invasive diagnostics would rise because of the use of the new test that should precisely be diminishing the use of invasive diagnostics. With that increase in the number of invasive tests would also come an increase in the number of unintended miscarriages of often normal fetuses.

Implications for wider society

17 What, if anything, might the increasing availability and use of NIPT mean for people living with genetic conditions? Please provide evidence or examples if possible.

- To quote from the Don't Screen Us Out campaign: *'To introduce a screening test that would enable the increased selective elimination of children with Down Syndrome due to a lack of proper inclusion, accommodation, and support, would violate disabled rights and our ethical obligations to disabled people and communities.'*[47]
- Prof John Wyatt, emeritus neonatal paediatrician, comments: '*The very existence of screening programmes expresses discriminatory social and professional attitudes, implying that the lives of disabled people are of less value than those of the healthy, and that they constitute a burden to themselves, to their parents and to the community as a whole'.*[48]
- What data protection policies will be in place to prevent 'genetic disadvantage' leading to discrimination in the job market, insurance provision and the like?

Regulation

18 Is current regulation covering the provision and marketing of NIPT in the UK sufficient and appropriate?

- The potential simplicity of NIPT raises the prospect of such tests being offered on a direct-to consumer basis, perhaps via the internet or mail order as has already happened in the USA for fetal sexing.[49]

[46] http://unesdoc.unesco.org/images/0023/002332/233258e.pdf, section IV, para 125
[47] http://dontscreenusout.org/
[48] Wyatt J. Matters of Life and Death. Nottingham: IVP, 2009:118
[49] Bianchi DW. At-home fetal DNA gender testing: caveat emptor. Obstet Gynecol 2006;107:216–8.

- Private companies should not be able to sell NIPT direct to the public without ensuring the availability of trained genetic counselling services to recipients. The lack of such supporting services may diminish informed decision-making and render families vulnerable to targeting by unethical or fraudulent 'providers' and financial exploitation.
- Removal of miscarriage risk may result in women seeking prenatal diagnosis for an increasing number of conditions or for paternity testing.[50]
- Data protection – the technology has the potential to reveal genetic predisposition to later-onset conditions that, if made available, could expose an individual to discrimination and prejudice his or her access to employment, insurance etc

Ethical values

We would like to identify the ethical values that are relevant or important in the context of NIPT. These might include: enabling informed decision making about reproduction, reducing harm, protecting the interests of future children, fair use of public resources, and the promotion of equality among members of society.

19 What ethical values do you think are important or relevant in the context of NIPT?

- The value of a human life is not to be measured in terms of conformity to a genetic norm or by economic 'productivity', any more than by age (before or after birth), colour, race, gender or creed.
- Discrimination on the grounds of genetic 'competence', or of cost to the Exchequer, is a form of eugenics and is contrary to commonly-held ethical instincts.
- Permitting the use of NIPT will result in increased pressure on regulators to expand the categories of defects eligible for screening, as public demand grows. This would inevitably lead to more abortions on the basis of disability. The International Bioethics Committee's report warned that *'[t]he potential ethical disadvantages of NIPT can be summarised as routinisation and institutionalisation of the choice of not giving birth to an ill or disabled child.*'
- Consent must be fully informed and all the more so following Montgomery v Lanarkshire Health Board. This requires pre-test and post-test information and counsel by trained staff, able to give neutral advice. Health professionals should signpost families receiving a diagnosis of disability to information leaflets covering all their options, to telephone and online helplines manned by trained professional counsellors, and to local and national support groups for those with specific conditions. Following her decision, and regardless of what choice the woman and her family may make, ongoing support must be part of that provision.

[50] Guo X, Bayliss P, Damewood M, Varney J, Ma E, Vallecillo B, et al. A noninvasive test to determine paternity in pregnancy [letter]. N Engl J Med 2012;366:1743–5.

- Consent must be free of coercion. To quote from the Bruce Inquiry: '*We should not underestimate the coercive power present in a system where a conveyor belt of expectation moves in the direction of choosing not to give birth to children with special needs who are regarded either as a burden or as, in some sense, not fully human*'.[51] We recommend that there be the opportunity for reflection and, if possible, for contact with individuals and/or families with the same condition, before a decision is reached.
- The high degree of accuracy of NIPT as early as seven weeks of pregnancy carries a number of socio-ethical implications, such as the selective termination of fetuses according to sex, in communities where it is culturally desirable to have male offspring.[52]
- The number of laboratories offering this service will need to keep pace with anticipated growing number of requests, if a postcode lottery in access is to be avoided.

Any other comments

20 Please tell us anything else you would like to raise in relation to NIPT.

- Bringing up a child with special needs often involves substantial emotional and financial cost for families. Practical support for the longer term must be in place for families, and access routes to financial, emotional and practical support as well as treatment need to be clearly signposted. These should include routes for exploring adoption for those families who feel personally ill-equipped but who wish to offer their child 'the gift of life'.
- More statutory funding should be provided for information, care and support groups and organisations for those with disabilities.

Your response

21 May we include your name/your organisation's name in the list of respondents that will be published in the final report?

x Yes
 No, I/we would prefer to be anonymous

If you have answered 'yes', please give your name or your organisation's name as it should appear in print (this is the name that we will use in the list of respondents in the report): Dr Rick Thomas
Christian Medical Fellowship

[51] http://admin.cmf.org.uk/pdf/publicpolicy/Bruce_Inquiry_submission_0313.pdf
[52] Marteau TM, Chitty LS, editors. Special Issue: Fetal sexing: Global Perspectives on Practices, Ethics and Policy. Prenat Diagn 2006,26:597–653.

22 May we quote your response in the report and make it available on the Council's website when the report is published?

x Yes, attributed to my organisation
 Yes, anonymously*
 No

Obtaining consent to publish a response does not commit the Council to publishing it. We will also not publish any response where it appears to us that to do so might result in detriment to the Council's reputation or render it liable to legal proceedings.

*If you select this option, please note that your response will be published in full (but excluding answers to questions 21 onwards in this form), and if you wish to be anonymous you should ensure that your name, and any other identifying information, does not appear in the main text of your response. The Nuffield Council on Bioethics cannot take responsibility for anonymising responses in which the individual or organisation is identifiable from the content of their response.

Using your information

We ask for your email address in order that we can send you a link to the report when it is published and notify you about activities related to this project. Please note that we do not make your email address available to anyone else, and we will not include it with the list of respondents in the report.

23 May we keep your email address for these purposes?

 X Yes
 No

24 Would you like to receive our monthly newsletter by email which provides you with information about all of the Council's activities?

 Yes
 x No