Nuffield Council on Bioethics
by email

25 July 2016

Call for views and evidence on non-invasive prenatal testing

Dear Sir/Madam

The British Medical Association (BMA) is an apolitical professional association and independent trade union, representing doctors and medical students from all branches of medicine across the UK and supporting them to deliver the highest standards of patient care. We have a membership of 170,000.

The Association welcomes the opportunity to respond to the Nuffield Council on Bioethics’ Call for views and evidence on non-invasive prenatal testing (NIPT). Our submission is attached and the key points are outlined below:

- NIPT has the potential to deliver significant clinical benefits, enhance reproductive autonomy and inform decision making about pregnancy management.
- Parents should be given as much information as necessary to enable them to make an informed decision about whether to opt for testing and, if so, how to respond to an unfavourable result.
- Genetic testing via a health professional should continue to be the norm, and is preferable, however we recognise that this cannot be enforced.
- Non-invasive fetal whole genome sequencing has the potential to raise a range of ethical issues, including difficulties in obtaining informed consent, the acceptability of retaining the data it generates, and the impact on public health services if the test is accessed in the private sector.

We hope that our submission is useful – please do not hesitate to contact us for more information if required.

Yours sincerely

Raj Jethwa
Acting policy director
Nuffield Council on Bioethics – Call for views and evidence on non-invasive prenatal testing

British Medical Association response – July 2016

Introduction

Non-invasive prenatal testing (NIPT) has the potential to deliver significant clinical and individual benefits and help to enhance autonomy and inform decision making about pregnancy management. It will lead to more women who are classed as “high risk” being reassured about the genetic status of their pregnancy without having to go through invasive testing and reduce the number of iatrogenic miscarriages.

While technological advances in prenatal testing bring many welcome advantages they will also engage a number of ethical issues. Many of these are not new and have arisen previously in relation to other forms of prenatal or genetic testing or screening, for example: the potential for “routinisation” and its impact on informed consent, questions about the divulgence of incidental findings, and concerns related to the commercial availability of tests direct to consumers, potentially without the direct involvement of a healthcare professional. The ease with which NIPT can be carried out, its risk-free nature and the anticipated increase in demand for testing mean that these issues remain relevant and merit further examination in this specific context. Moreover, as the technology improves and the ability to test for a wide spectrum of genetic disease, genetic predispositions and non-medical traits becomes more efficient and cost-effective, there is the potential for further, significant ethical tensions to arise, particularly regarding the impact on the privacy interests of the future child if genetic data is retained and the pregnancy is carried to term.

This is area of great complexity and we have only begun to have initial discussions about NIPT, its potential impact on the NHS, and the ethical issues testing may raise. Rather than a detailed response to all the questions therefore, our response highlights a few key issues drawing on recent discussions within our medical ethics committee - which comprises doctors and experts in medical law, philosophy and theology - and on our existing guidance on genetic and prenatal testing. BMA policy is principally decided at our annual representatives meeting but also at other times through consultation with and expert input from our branch of practice and professional committees.

Information and counselling

The purpose of antenatal screening and testing is to provide women and their partners with information which allows them to make informed decisions regarding their pregnancy and/or prepare for their future child. They need timely, good quality information about the test (including the possibility of false positives or negatives), the conditions tested for, the implications of the result and the options open to them.

Currently, women who know their pregnancy is at risk of a serious disorder, must balance the risk of miscarriage triggered by invasive testing (around 1 in 100) with the advantage of knowing whether their fetus has a genetic condition. A significant advantage of NIPT therefore is that it broadens the available testing options in such cases and can help by removing the anxiety of not knowing whether a pregnancy is affected by a genetic condition.
Earlier identification of Down Syndrome, Patau Syndrome or Edwards Syndrome allows more time for women to make the right decision for them and their family about whether to continue with the pregnancy. It also allows more time to:

- undergo further testing if necessary
- prepare for the birth of an affected child who may have special needs
- find out more information about the condition
- access support networks
- plan for the child’s future.

Where women choose to end their pregnancy due to the results of testing and they meet the criteria for a lawful abortion, NIPT may allow a decision to be made earlier. From a clinical perspective, abortion is safer carried out earlier in pregnancy, and for those who adopt a gradualist approach to the status of the fetus, morally preferable.

There have been concerns raised that as NIPT only requires a blood test, as opposed to a more risky invasive procedure, it could come to be seen as “routine” by patients such that the potential implications and consequences of a positive result may not be fully understood or anticipated. The practical ease with which the test can be undertaken, and the lack of risk, may also reduce the emphasis on information giving and counselling from health professionals, thus undermining informed consent. Avoiding routinisation has been described as potentially the “greatest ethical challenge” of NIPT. Concerns have also been raised that women, who with invasive testing may otherwise have had a reason to refuse testing, could feel pressured into having the test, thereby undermining rather than enhancing reproductive autonomy.

We recognise that concerns about routinisation have been raised previously in relation to prenatal testing more generally, our guidance is that health professionals have a general ethical and legal duty to ensure that patients are given sufficient information to understand what is proposed and are given the opportunity to give or withhold consent. In Medical Ethics Today we advise that “parents should be given as much information as necessary to enable them to make an informed decision about whether to opt for testing and, if so, how to respond to an unfavourable result” and that “when giving information to patients, health professionals should also present the possibility of refusing all prenatal screening as a reasonable and acceptable option.”

Objectives of prenatal testing

The BMA would have concerns if access to testing was contingent on an anticipated change in pregnancy management. As discussed above there are a range of benefits associated with providing women with information about their pregnancy. Restricting access to women who

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would consider terminating a pregnancy would be, in our view, inappropriate. As stated above, as much information as possible should be given to women and their partners to make an informed decision and whether to opt for testing and if so how to respond to an unfavourable result. Although it is important to use limited resources carefully in a publically-funded health system, “clinical benefit” is much broader than pregnancy management and it is unreasonable to expect a women to decide in advance how she would respond to an unfavourable result.

NIPT available direct to the consumer

As NIPT only requires a blood sample, in theory this can be taken, shipped and analysed overseas. NIPT may therefore be offered to consumers from anywhere in the world, making restrictions on what tests can be offered and regulations governing their use difficult, even if they were considered to be desirable. The BMA has taken the view that genetic testing via a health professional should continue to be the norm, and is preferable as accessing testing directly, without the input of a health professional, may not allow a discussion to take place as it would if part of an informed consent process. However we recognise that this cannot be enforced. Although it would be feasible to restrict the advertising or sale of testing kits in the UK, it is not possible to prevent people from using services in other countries, such as those accessed via the internet.

We have raised concerns previously about the accuracy and quality of information provided to those seeking testing through commercial companies, particularly given that they have a financial interest in people taking the test. As stated above women and their partners need accurate information so as to weigh up whether they want to take a test. The acceptability of testing direct to the consumer will, in part, depend on the information it aims to provide. Of particular concern are tests where the results can have significant implications, there is a high likelihood for misinterpretation, or there is a risk of harm, severe distress or anxiety to those seeking testing or others.

The availability of NIPT directly to consumers may also represent a challenge to NHS staff. Where the tests are for conditions or predispositions which would not normally be tested for within the normal screening or testing pathway or if they produce findings which are of unknown clinical utility or which only offer a risk of susceptibility to disease, patients may look to NHS clinicians or other staff to help with the interpretation of results and provide guidance. This can create a pressure on limited resources which would not otherwise have existed. Given the broad spectrum of information it can yield, this will be a particular problem if the technology for sequencing the fetal genome becomes commercially viable.

To help address concerns that patients may be accessing testing based on imperfect knowledge and understanding of its implications the BMA has in the past called for official government websites which would provide accurate information about testing to consumers. This could include the benefits of prior discussion with a health professional and the standards they should expect to receive from companies. We are aware that the National Screening Committee has recently produced general guidance for individuals who are considering having a private screening test. International rules governing the quality of information could also be explored, similar to the agreement within the pharmaceutical industry about the type of product information that should be provided with medication.

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Incidental findings

Finding additional, unsought or unexpected information through genetic testing is a longstanding issue which is likely to become more problematic if sequencing develops, more genetic information is yielded and genome sequencing becomes clinically and commercially viable. We are aware that NIPT has led to the detection of potential cancer in some pregnant women. This is not an issue which we have discussed to date specifically in relation to the detection of cancer and NIPT, but such findings have the potential to raise significant ethical issues and challenges for health professionals. In particular it raises questions about whether the information should be disclosed when it may or may not be clinically significant and when it could lead, in some cases to overdiagnosis and unnecessary investigations and treatment. In our view, more research is needed to inform discussions and stakeholder guidance to health professionals on this issue.

In Medical Ethics Today we provide the following advice in relation to incidental findings and genetic testing in more generally, including how doctors should approach the potential for incidental findings to occur as part of the consent process and on the disclosure of such results, both where this has and has not been discussed prior to testing:

“If there is a reasonable chance of other information being inadvertently discovered from a particular test, this should be discussed with the patient...during the consent process in order to ascertain the individual’s wishes about disclosure. The discussion should give examples of the type of information that could be discovered and the procedures that will be followed in that event.

When information is discovered unexpectedly, and this discussion has not taken place, the BMA believes there should be a general presumption that significant information will be shared because it would be wrong deliberately to withhold it on the assumption that it would not be in the individual’s interests to know. However, there may be exceptions to this rule, such as where it is judged that revealing the information could cause severe psychological harm to the patient ...When such information is to be given, this must be done sensitively and taking a cue from the individual about how much information he or she is ready and willing to accept at that particular time.”

Non-invasive fetal whole genome sequencing (NIFWGS)

Our medical ethics committee has had initial discussions about the ethical dilemmas that may arise from the sequencing the fetal genome non-invasively and these inform our response here.

The consultation document asks whether prenatal whole genome sequencing should be allowed. In discussing this, it is important to distinguish the motivations behind seeking a test of this kind, the different types of information it can produce and the information which is to be disclosed, and to whom, following testing.

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The current applications of NIPT are restricted to fetal sex determination, some single gene disorders which are inherited in a dominant fashion from the father or which arise *de novo*, and for aneuploides. By contrast, sequencing the full fetal genome has the potential to detect any of the single gene disorders known to exist, genetic mutations associated with other conditions and, in principle, *de novo* mutations. NIFWGS therefore might act as a universal, non-invasive prenatal test for all diseases or conditions which have a genetic cause or component. It could provide a significant benefit to pregnant women at risk for genetic conditions but who are only currently offered invasive prenatal testing and it may also help to determine previously unexplainable fetal abnormalities or losses. If no other, more directed, tests exist, there is a clinical benefit to testing via NIFWGS and if the disclosure of information were to be limited to that which is relevant to pregnancy management, the immediate health interests of their fetus or welfare of their future child, its use does not generate any obvious ethical dilemmas over and above any other form of prenatal testing.

Where NIFWGS is sought just for information purposes, or where the information that is disclosed to women and their partners will not result in direct clinical benefit, this does have the potential to cause ethical tensions. Whole genome sequencing could potentially provide parents with information about their fetus in relation to all diseases or conditions with a known genetic cause or component. This is irrespective of the seriousness of the disease, the onset of the condition, the level of risk, or whether the provision of information would result in some benefit. NIFWGS could also provide prospective parents with findings of unknown clinical utility and about non-medical inherited traits.

If the decision is taken to carry the pregnancy to term, a key issue is the impact that NIFWGS may have on the autonomy and privacy interests of the future child. Currently, in relation to the genetic testing of children, parental access to information which would not provide some tangible benefit to the child is either restricted or at least discouraged, on the basis that a child’s genetic status is his or her own private information and intervening into this private sphere without justification would be inappropriate. NIFWGS could mean that this information is generated and potentially disclosed prenatally. It may include information which is relevant to adult onset conditions, for which testing would usually only be undertaken once the person could consent to testing, or in relation to a susceptibility to disease, for which testing would also not typically be conducted on a child.

Although legally the disclosure of this type of information to a woman about her fetus may not be problematic, it does have the potential to raise significant ethical issues. As individuals cannot “unknow” what may have been revealed through NIFWGS, its disclosure and retention may restrict their ability to make choices about their health – including the choice of whether or not to find out information about their genetic make-up. It could also have other negative practical implications, for example when applying for insurance in the future. This is particularly important given that it is uncertain how genetic information may be used in the future.

It is likely that the use of NIFWGS, should it reach mainstream clinical practice, would be restricted in the NHS. However, if there is a commercial demand for the test, it may be available via the private sector. Restricting parental access to NIFWGS would be highly problematic and

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health professionals would need to be confident to respond to subsequent enquiries and concerns; this is likely to be complex and time-consuming. As with all genetic testing, informed consent would be important and at the outset any consent process should include information on the range of information that would be produced and the difficulties this could raise. However, given the range of information which NIFWGS could yield and the potential for there to be detrimental, but as yet unknown, consequences for the interests of the future child, obtaining and being assured that a patient has provided informed consent would be difficult. There are also further questions relating to whether, and if so under what circumstances, retention of the information generated from NIFWGS would be permitted under current legislation. We have had some initial discussions with the Information Commissioner’s Office about this and have also begun to consider how, and to what extent, information derived from such testing would be stored and communicated as the child gains competence to make decisions. This is an issue that requires further discussion.