Non-invasive prenatal testing (NIPT) – Eugenics or progress?
Current screening programme

- Started screening for Down syndrome based on amniocentesis in 1960.
- Since 1989, have used maternal age and serum markers.
- Originally to reduce numbers of DS births and economic reasons. (No longer considered ethical, Warwick Systematic Review, 2015)
- Can be done from 10 weeks.
- Fairly accurate between 71-95% detection rate with 5.4% false positive. (Wolfson Institute of Preventative Medicine)
- Higher than 1:150 are deemed high risk and offered amniocentesis.
- NIPT now offered by private clinics and some NHS hospitals.
What is NIPT?

- A blood test also known as Serenity, Harmony, Panorama, MaterniT, Nifty, Safe, Verifi etc
- Examines the chromosomes in the cell free fetal DNA
- Can be done from approx 9 weeks
- Results can be available within three days
- Higher accuracy than current combined test, 97% detection rate, 0.9% false positive (Taylor-Phillips, 2016)
- Can be used to test for many things, currently mainly fetal sex, Down’s, Edward’s and Patau’s syndromes
- Also a number of other sex chromosome associated conditions and microdeletions
NIPT and the NHS

- 2015 a study was completed on NIPT, RAPID study (Chitty et al, 2015)
- Consultation was completed by National Screening Committee October 2015 (NSC)
- Jan 15 2016 recommendation was given by the NSC to “evaluatively roll-out” the test in the NHS (has to be ratified by the government, although it is in the NHS constitution that any screening programmes recommended by the NSC will be rolled out (https://www.gov.uk/government/publications/the-nhs-constitution-for-england/the-nhs-constitution-for-england) This is a problem in itself as there are several members of the NSC who already offer NIPT in their clinics and with the prediction from one of the manufacturers (Premaitha) that there will be an increase in the private payer market once the test is provided by the NHS)
- Jan 18 2016 Ethics meeting by the Nuffield Council on Bioethics (NCB) on NIPT
- March 2016 decision to create a working party on NIPT by NCB
- August 2016 was the close of the consultation by NCB
- Report due end of 2016/early 2017
Would the world be a better place without people like my daughter? DOMINIC LAWSON likens the new test for Down’s syndrome to State-sponsored eugenics
Blood test for Down's set to be offered on the NHS: Super-safe and 99% accurate exam would replace invasive procedure which can trigger a miscarriage for Down's syndrome.

Would the worl...
The good, the bad and the ugly

Hundreds of babies could be saved after Down’s Syndrome blood test is approved for NHS

Women will no longer face miscarriage through invasive Down’s Syndrome tests
Why all the fuss?

- Ethical dilemmas
- There is a long established Fetal Anomaly Screening Programme that prospective parents can choose whether to participate in. The United Kingdom National Screening Committee recommendation on non-invasive prenatal testing does not change the choices available to prospective parents within the programme. We are satisfied that the UK is compliant with its obligations under the United Nations Convention on the Rights of Persons with Disabilities and that the Programme is compliant with all obligations under the Equality Act 2010. We would also note that English law does not recognise a foetus as a separate legal person.
The introduction of a new test for Down syndrome

- What does this say to people with Down syndrome?
- Is it benign to introduce new tests?
- What does it say about valued characteristics in our society?
- If we were to test for another characteristic that is perceived by some societies as a negative, to allow women to make a choice, what would we think. For example, take another genetic characteristic of being female, or perhaps having dark skin, both of which in some societies are perceived as negative. What if we were continuously striving to test for those things to enable women to make a choice, what would that say to the female or black people among us? How would that make them feel? Would we then think it a benign thing to do to introduce another new test for those things? Or would it serve to once again reinforce that those characteristics were valued less by society than being male or white or having 46 chromosomes?
Is the fact that something that is long established a good reason for continuing down the same path?

Right that we look at the original reasons for starting screening – cost effectiveness and avoiding handicap. Those reasons are said by the systematic reviewers from the University of Warwick to be no longer ethical, even though representatives of the Royal College of Obstetricians and Gynaecologists and the British Maternal and Fetal Medicine Society thought that in considering the cost of NIPT, the cost of raising that child should be brought into account (NSC Consultation, 2015). If this is the attitude of some of the medical professionals, we can see that perhaps the third point about it being women’s choice to test may be compromised.
A woman’s choice to participate in testing?

- Awareness of option not to test
- Doctors find it easier to accept decision to test
- Irresponsible not to test
- Level of information, is it really diagnostic? And lack of accurate information about Down’s syndrome
### Panorama’s claim

<table>
<thead>
<tr>
<th>Sensitivity false-positive rates</th>
<th>Natera Panorama <em>1,2,3,4</em></th>
<th>Ariosa Harmony™ 5,6,7,8</th>
<th>Sequenom MaterniT21™ 9,10,11,12</th>
<th>Illumina VeriFii® 13,14,15</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Trisomy 21</strong></td>
<td></td>
<td></td>
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<tr>
<td>Down syndrome</td>
<td>&gt;99% (83/83) 0%</td>
<td>99% &lt;0.1%</td>
<td>99.1% 0.1%</td>
<td>99.9% 0.2%</td>
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<tr>
<td><strong>Trisomy 18</strong></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Edwards syndrome</td>
<td>96.4% (27/28) &lt;0.1%</td>
<td>98% &lt;0.1%</td>
<td>&gt;99.9% 0.4%</td>
<td>97.4% 0.4%</td>
</tr>
<tr>
<td><strong>Trisomy 13</strong></td>
<td></td>
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<td></td>
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<tr>
<td>Patau syndrome</td>
<td>&gt;99% (13/13) 0%</td>
<td>80% &lt;0.1%</td>
<td>91.7% 0.3%</td>
<td>87.5% 0.1%</td>
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<tr>
<td><strong>Monosomy X</strong></td>
<td></td>
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<tr>
<td>Turner syndrome</td>
<td>92.9% (13/14) &lt;0.1%</td>
<td>91.5% 0%</td>
<td>94.4% 0.6%</td>
<td>95.0% 1.0%</td>
</tr>
<tr>
<td><strong>Sex-chromosome trisomies</strong></td>
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<tr>
<td></td>
<td>&gt;99% (5/5)</td>
<td>99%</td>
<td>96.2%</td>
<td>67%–100%</td>
</tr>
<tr>
<td><strong>Female</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td></td>
<td>&gt;99.9% (469/469) 0%</td>
<td>99% 0%</td>
<td>99.1% 0.5%</td>
<td>97.6% 0.8%</td>
</tr>
<tr>
<td><strong>Male</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>&gt;99.9% (533/533) 0%</td>
<td>100% 1%</td>
<td>99.4% 0.9%</td>
<td>99.1% 1.1%</td>
</tr>
<tr>
<td><strong>Triploidy</strong></td>
<td></td>
<td>Unable to detect</td>
<td>Unable to detect</td>
<td>Unable to detect</td>
</tr>
</tbody>
</table>

Four known mosaic cases were included: two monosomy X, one T18, and one T18. Both cases of monosomy X were called high-risk, the T18 was called low-risk, and the T13 was no-called. False-positive and false-negatives can occur on all chromosomes due to maternal, fetal, and/or placental mosaicism or as a result of other causes.
Positive Predictive Value of NIPT vs. Combined Screening

Trisomy 21 PPVs: NIPT vs. First Trimester Combined Screening

A woman’s choice to participate in testing?

- Responsibility of government? Placing responsibility at woman’s door, allow government to wash their hands of it
- Societal pressure to test, irresponsible not to as no risk to baby
- Risk less counselling and informed decision making than currently as non-invasive, doctors don’t see counselling as as important (Ravitsky, 2015)
- Could be more information if recommendation by the National Society of Genetic Counsellors that all women see a genetic counsellor before undergoing NIPT is followed.
The amount of money spent on testing versus the amount of money spent on research to help those with Down syndrome

There are some claims that introducing this test will actually save money. However I am not sure that if I was a woman with a 1:150 chance of having a baby with Down syndrome, I really wanted to know for sure and I was properly informed about the possibilities of false positives and false negatives, that I wouldn’t actually want the amniocentesis to be sure as well as NIPT

£232 (or between £100-£500 depending on uptake of test) per woman, is a substantial outlay for 10% more accurate information
Number of lives saved?

- 25 lives saved if figure of 0.5% procedural related miscarriage figure used (5 if 0.1% used, Akelokar, 2015)
- 102 more cases of Down’s syndrome detected
- @90% termination rate
- Loss of life approx. 65
- May not be as high, Nicolaides says no increase in terminations, BUT anecdotal, and 90 terminations in a population of 698,500 pregnant women per year, is not going to be noticeable anecdotally.
- Current studies show, 6.2% of women are making decision to terminate based on non-diagnostic NIPT (Shrinking community – reduces options re friendship, marriage, reduces services and expertise, reduces funding for research)
The Future

- NIPT – where do we draw the line?
Organisations

- Nuffield Council on Bioethics
  [http://nuffieldbioethics.org/project/non-invasive-prenatal-testing/](http://nuffieldbioethics.org/project/non-invasive-prenatal-testing/)

- Abortion (Disability Equality) Bill
  [http://services.parliament.uk/bills/2016-17/abortionanddisabilityequality.html](http://services.parliament.uk/bills/2016-17/abortionanddisabilityequality.html)
Questions?

Discussion points

• Are women able to give truly informed consent to testing?

• Should this test be funded by the NHS?

• Does screening for Down syndrome fall foul of the Equality Act and therefore should this moment be used to have a nationwide discussion about testing for Down syndrome?
References


Wolfson Institute of Preventive Medicine (n.d.) The Combined Test. Available at: http://www.wolfson.qmul.ac.uk/service-1/antenatal-screening/screening-tests/the-combined-test#performance