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Non-invasive prenatal testing in England

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(No conflicts of interest)

Regulatory position and current NIPT practice in England

UK NHS only supports NIPT for specific named conditions in high risk families.

UK NHS and National Screening Committee do not at present support NIPT for population screening programmes.

For Down's syndrome screening programme, current UK NSC plans are for non-invasive prenatal *testing* (NIP*T)* to be an *add-on* to the existing *screening test*, i.e. a second line *screen*, offered only to women with a high risk result from the initial screening test, and with invasive diagnostic testing still being offered to those women who get a second high risk result. These plans are conditional on supportive findings from ongoing research.

In the private sector, NIPT is widely available for a wide range of purposes.

Public debate?

Versions of existing debates about designer babies etc. continue, especially in *screening* context.

Proponents of NIPT in screening context emphasise removal of miscarriage risk.

Much debate – both public and professional - is based on promises *that have yet to be delivered* about the production of diagnostic quality information using non-invasive technologies.

Current testing dilemmas?

- *Attitudes* to current pathway *and its limitations (e.g miscarriage risk)* have to be "traded off" against attitudes to avoiding the birth of a child with a disability.
- *Test uptake* is influenced by result of trading off the (available) means against the (desired) ends

We know less about this than we should, because:

- Most of the literature treats means and ends as inseparable – *which they essentially are until something - e.g. testing technology - changes*
- Preoccupation with helping people understand risk may be missing the point

NIP*D* changes *the means* of acquiring information

Whose test uptake decisions might be changed by reducing the “cost” (risk to the pregnancy) of acquiring information about the baby?

Most likely to be changed

- People put off by some aspect of *current* technology.

And most likely to stay the same

- People not wishing to avoid the birth of a child with Down’s syndrome.
- People who would not consider a termination for DS.
- People who accept the current testing technology.

Issues regarding promotion of NIPT: 1 Accuracy

The best non-invasive test *still picks out a lot of babies who turn out not to have Down's syndrome* ("false positives", in test parlance) as well as ones that do.

Those who are surprised at this fact tend to have mixed up the *specificity* of a test with its *positive predictive value*.

If a test is highly specific - as NIPT undoubtedly is - that means that only a small proportion of babies without Down's syndrome will "test positive".

But a general population sample will consist almost entirely of unaffected babies, so even a small proportion of this large fraction will generate a lot of "test positive" results.

Accuracy (contd.)

Nearly all the babies *with* Down's syndrome will also "test positive" using NIPT technology, but in a general population sample, there will not be many of them.

The proportion of the "test positive" babies who have Down's syndrome – the test's "positive predictive value" (the PPV) - may actually be quite low.

The PPV will be better in a high risk sample, because the proportion of babies with the condition will be higher, but an *a priori* risk of 1 in 200 still translates into a PPV of only around 60%, i.e. 4 in 10 of the test positives *will not have* Down's syndrome.

Accuracy (contd.)
NIPT for Down's syndrome as an add-on test

Will lead to fewer "false alarms" and fewer people worrying about miscarriage – or facing one.

BUT: some women will need three tests not two.

AND: NIPT likely to be offered to wider pool of women than invasive testing (by altering risk cut-off), increasing detection rates but labelling more women "high risk" and delaying reassurance .

Issues regarding promotion of NIPT: 2 Information about more conditions

Which conditions?

Who decides?

“Set menu” or “A la carte”?

The challenge of providing enough information to enable all pregnant women to make informed, individualised test choices for all conditions is clearly formidable.

BUT we could have done a lot of this before…

Issues regarding promotion of NIPT: 3 Psychological factors

Anxieties – some of them enduring - associated with a two (or three) stage process (probabilities not diagnoses, miscarriage risk, being a "false positive") would remain when using non-invasive tests that were *non-diagnostic*.

If available for a specified condition, non-invasive *diagnosis* could reduce all of these anxieties in people who would have had a test for that condition anyway.

Non-invasive *diagnosis* could also reduce the *cognitive demands* (e.g. understanding probabilities) made by two-stage testing but could *increase the decision-making burden overall if more than one condition was involved*.

New recruits to prenatal testing?

As and when non-invasive diagnosis becomes a reality for some conditions, what of the "new recruits" to prenatal testing, *previously deterred by miscarriage risk*?

Although for any one condition, test uptake decisions should become easier in terms of their cognitive demands, they would *not necessarily be less stressful in emotional terms*.

The avoidance of miscarriage risk may have provided a kind of *"psychological shelter*", protecting a lot of people from having to make other decisions.

For some women, accepting an offered test will require them to confront long held attitudes to disability and to ending a pregnancy, and that could be quite disturbing.

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