Pre-implantation Genetic Diagnosis: Are UK Funding Decisions Fair?

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ABSTRACT: Pre-implantation genetic diagnosis (PGD) is a method of allowing couples with a history of a serious genetic condition to have an unaffected child. Embryos created by in vitro fertilisation can be tested for a specific genetic abnormality and only those without the abnormality are transferred to the womb. Alternatives for these couples include achieving pregnancy naturally and either risking having an affected child, or undergoing prenatal diagnosis and choosing to terminate an affected pregnancy. There is no recent national guidance on funding PGD in the United Kingdom, though many cycles have been funded on the National Health Service. Some Primary Care Trusts have specific funding policies for PGD and others assess applications individually. This means that the NHS funds requests more readily in some areas than others, making the provision of PGD inequitable. National commissioning guidance might help the UK to adopt a more uniform and consistent approach to funding PGD.

Pre-implantation genetic diagnosis (PGD) is a treatment which can allow families with a history of a serious genetic condition to have a child who is unaffected by that condition. This is done using in vitro fertilisation. Eggs and sperm are taken from the couple and cultured together to produce embryos. These are each screened for the known mutation using fluorescent in situ hybridization for cytogenetic diagnosis or the polymerase chain reaction for molecular diagnosis. Only embryos without the mutation are implanted in the mother. The treatment was first developed in England in the 1990s and has been used increasingly since then (1).

There are a range of genetically transmissible conditions for which PGD is possible. These include autosomal recessive disorders such as cystic fibrosis, autosomal dominant disorders including Huntington's disease and X-linked disorders such as haemophilia and Duchenne muscular dystrophy (4).

In addition to the specific genetic or chromosomal disorders discussed above, PGD techniques can also be used for other indications (4,5). These include:

- Detection of ‘susceptibility genes’ for a hereditary pre-disposition to diseases such as hereditary forms of breast and colorectal cancer (4,5). Susceptibility genes increase the risk of developing a disease, but do not solely determine whether or not a disease develops (4).

- Preimplantation genetic screening for aneuploidy (an abnormal number of chromosomes), intended to improve poor pregnancy outcomes (4,6).

- The creation of so called ‘saviour siblings’ where tissue type can be matched to an existing sibling affected with a disease, so that the new baby’s umbilical cord stem cells or bone marrow could be used to treat the affected sibling (4,5).

PGD can also be used for couples who are suffering from recurrent miscarriage or infertility. Chromosome translocations may be detected as the cause and PGD could be used to achieve pregnancy. The issues for these couples are different than for couples with a history of a serious genetic condition as they do not face the possibility of conceiving an affected child, they risk not conceiving at all without the use of PGD.

There are alternatives for families with a history of a serious genetic condition who wish to conceive an unaffected
child. These include achieving pregnancy naturally and risk-
ing having a child with a serious genetic condition, or con-
ceiving naturally, and then undergoing prenatal diagnosis
(PND) via amniocentesis or chorionic villus sampling. If the
fetus is found to have the condition, the parents may then
choose to terminate the pregnancy (2). Other options avail-
able include adoption, choosing not to have a child and con-
sidering assisted conception techniques in which one or both
partners would not be the biological parent of the child. Many
of these may not be acceptable to couples (7).

PGD is a controversial treatment with many conflicting
ethical and moral arguments. Its use has been heavily de-
bated internationally. In Germany, three parliamentary bills
were introduced for discussion in April 2011. One called for a
complete ban of PGD and is backed by the German Chancel-
or Angela Merkell, the others would allow PGD in certain
circumstances. At present, the law on PGD in Germany is
unclear (8).

Licensing

The Human Fertilisation and Embryology Authority
(HFEA) is the UK’s independent regulator of treatments and
research involving eggs, sperm and embryos. It is responsi-
ble for licensing PGD centres themselves and licensing the
conditions for which PGD is allowed. If a clinic wishes to per-
form PGD for a condition, it must apply for a licence. The
HFEA considers several issues when deciding if a licence
should be granted for a certain condition. These include the
severity of the condition, its impact, ethical issues associated
with the procedure for each condition, technical laboratory
standards, staff training and the provision of genetic counsel-
ing (9).

There are currently 182 conditions licensed by the HFEA
for PGD, several more are under consideration (10). Cases
involving HLA tissue typing must be approved on a case by
case basis (9). The HFEA’s role in licensing eliminates the
need for Primary Care Trusts to make difficult ethical deci-
sions regarding which conditions PGD should be allowed for
as they can defer to the HFEA’s list.

Demand

Although there are many indications for PGD, it does not
seem to have been a widely used intervention to date. The
HFEA reports that in the UK in 2008, 182 patients underwent
214 cycles of PGD. There were 54 live births resulting in 66
babies (11).

Statistics from the 10th report of the European Society of
Human Reproduction and Embryology PGD Consortium for
the year 2007-2008 showed that since data collection began
in 1999, there has been a steady increase in the use of PGD
annually.

In 2007, it was found that 57 centres across Europe were
participating in PGD and reported 5887 cycles. 1516 preg-
nancies were achieved and 1206 babies were born (12).

A survey in 2010, of 210 couples at risk of passing a seri-
ous genetic condition to their children found that 42% of cou-
uples had not heard of PGD. When told about it and the alter-
atives available, 80% of couples said that PGD would be
their preferred reproductive choice if there were no waiting
list. If the waiting list was to be 2 years, this fell to 46% (13).
This study suggests that if PGD became more widely avail-
able, demand would increase significantly.

Success Rates and Risks

Data from the HFEA in 2008 showed that success rates,
measured as cycles resulting in a live birth per number of
cycles started, was 25.2% for PGD. This compares to 24.1%
for IVF treatment. Figures from preceding years revealed that
success rates were closely linked to maternal age, with suc-
cess rates for women under 35 at 33.3% and no successful
pregnancies in women over 40 (9).

A study of 129 children aged 2 found that there was no
difference in temperament, language development, health
status or parental stress between children conceived natu-
 rally, those conceived using IVF/ICSI and those conceived
using PGD (14).

Risks of PGD are similar to the risks associated with IVF
including multiple pregnancy, ectopic pregnancy, hyperstimu-
lation syndrome and stress (15). Other specific risks associ-
ated with PGD are risk of the embryo being damaged during
cell removal for testing. Testing may not be 100% accurate
and misdiagnosis rates are quoted at approximately 1% (5).

Cost effectiveness

Cost of PGD varies between different PGD centres.
These range from £7000 quoted in the EMSCG policy (2), to
£1500 for PGD with the additional costs of IVF at £3000 and
drugs at £800 as quoted in the HGC survey 2009 (3).

It is not possible to directly compare the cost of PGD with
PND with termination as these will vary depending on the
type of termination performed and the stage of pregnancy.
These costs, however, would presumably be considerably
lower than those of PGD.

Table 1 is taken from the EMSCG policy to demonstrate
relative costs of PGD versus lifetime care of a child affected
with a genetic condition (2). The cost of an affected child will vary according to condition, but is likely to be considerable.

**National Guidance & Regional Policies**

There is currently no NICE guidance on PGD. The Department of Health (DoH) last issued direct guidance on PGD in 2002 (7). In conjunction with Genetics Commissioning Advisory Group, the DoH recommended that PGD may be a legitimate approach to reproduction for certain individuals. It advised that funding for PGD should be considered on an individual basis. It suggested that commissioners look to the HFEA to advise on which conditions are licensed for PGD and that priority should be given to couples with no healthy living children where their risk of an affected child was greater than 10%. It stated that criteria for IVF treatment are not appropriate as criteria for PGD as the issue for the families concerned is not infertility. It advised that the first cycle is the most costly as it includes the genetic testing and development of the specific genetic probe, and that 1-2 further cycles would increase the chances of pregnancy and make the best use of the genetic probe development. It also stipulated that adequate genetic counselling should be provided (7).

Of the 152 organisations surveyed, 28 responded. It was found that most did not have a written policy for handling funding requests, but handle requests on a case by case basis, often through Individual Funding Request panels. The decisions on funding varied considerably, as did the number of treatment cycles funded, sometimes even within the same region. Many organisations stated that they assess PGD on the same criteria as IVF. Table 2 collates data from the responses of the PGD providers (3).

The centres voiced concern over lack of education about PGD among the general public and staff within PCTs, particu-

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**Table 1:** Taken from EMSCG policy to demonstrate relative costs of PGD versus lifetime care of a child affected with a genetic condition

<table>
<thead>
<tr>
<th>Description</th>
<th>Associated costs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Potential average lifetime costs of one Cystic Fibrosis patient</td>
<td>40 years x £14,500 = £580,000</td>
</tr>
<tr>
<td>Potential average lifetime costs of 1 Haemophilia patient</td>
<td>70 years x £100,000 = £7,000,000</td>
</tr>
<tr>
<td>Average PGD costs per patient</td>
<td>£7,000 for one cycle of treatment</td>
</tr>
<tr>
<td>Potential numbers to be offered treatment each year</td>
<td>50 patients</td>
</tr>
<tr>
<td>Overall yearly cost of PGD based on above figures for 1 cycle</td>
<td>£350,000</td>
</tr>
<tr>
<td>Potential cost avoidance over 5 years based on prevalence rates of 21 babies born with CF in the East Midlands</td>
<td>4 years x £14,500 x 21 = £1,218,000 (assumption that no savings will be made in year 1)</td>
</tr>
<tr>
<td>Potential cost avoidance over 5 years based on prevalence rates of 1% per year increase in patients with Haemophilia in the East Midlands</td>
<td>4 years x £100,000 x 2.5 = £1,000,000 (assumption that no savings will be made in year 1)</td>
</tr>
</tbody>
</table>

**Table 2: PGD statistics for the year 2008.** Data taken from Human Genetics Commission funding survey (3)

<table>
<thead>
<tr>
<th>PGD Centre</th>
<th>Number of Requests</th>
<th>NHS funding</th>
<th>Private funding</th>
<th>Cycles started</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>180</td>
<td>78</td>
<td>34</td>
<td>157</td>
</tr>
<tr>
<td>2</td>
<td>12</td>
<td>4</td>
<td>8</td>
<td>10</td>
</tr>
<tr>
<td>3</td>
<td>12</td>
<td>5</td>
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<td>0</td>
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<td>4</td>
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<td>0</td>
<td>0</td>
</tr>
<tr>
<td>5</td>
<td>150</td>
<td>2</td>
<td>148</td>
<td>32</td>
</tr>
<tr>
<td>Totals</td>
<td>354</td>
<td>89</td>
<td>190</td>
<td>199</td>
</tr>
</tbody>
</table>
called for further education on the benefits of PGD, the cost effectiveness, and the success rates of treatments (3).

The Human Genetics Commission advised commissioners to review the evidence presented, and to consider the need for guidance on PGD within their own PCTs (3). In June 2009, the DoH encouraged commissioners to consider PGD when considering their genetics services (16).

Some regions have responded to this; the East Midlands brought out a revised specialised commissioning policy for PGD on 1st April 2011 (2). Their new policy allows wider access to PGD. Couples who meet the necessary criteria will now be funded for unlimited cycles. The new policy makes PGD available to couples who already have a child or children who are not affected with a genetic condition. It also allows couples who have previously self funded for PGD to have PGD on the NHS (2). Regional differences in funding policies in the UK have a considerable effect on the availability of PGD for individual couples (17).

Summary

PGD is a controversial treatment which evokes different moral & ethical opinions. It is currently being funded on the NHS in the UK in some circumstances, however the decisions leading to funding do not appear to be consistent. Funding is currently dependent upon PCT’s own policies or individual opinions of members of Individual Funding Requests panels. Given the likely increase in awareness of PGD and increase in funding requests over the coming years, national commissioning guidance would be useful to help the funding of PGD to be more equitable and consistent across the United Kingdom.

Acknowledgments

With thanks to: Dr Kathryn Millard, NHS Warwickshire for her contribution to this report.

REFERENCES


SummaryofPGDengagementresponsesseposéndoutSept10.doc


