

Results of the follow-up of the FCE activities 2006-2015 and comparison with European countries

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Embryo research in Belgium

- Research on embryos donated for science is allowed
- Creation of embryos for research is allowed if this is necessary to obtain knowledge

Prohibitions on

- Experiments and research for the selection or improvement of non-pathological genetic features of the human species, i.e. eugenic features or enhancement
- Reproductive cloning
- Social sexing
- Creation of chimaeras and hybrids

All projects have to be approved by a local Ethics Committee and by the Federal Commission on Research on Embryos in vitro.

Data collection

Data collection turned out to be more complicated than originally expected. The reasons will become clear in what follows.

Special thanks to Velichka Kontozova-Deutsch, Seppe Segers and the members of the working group.



Types of embryos

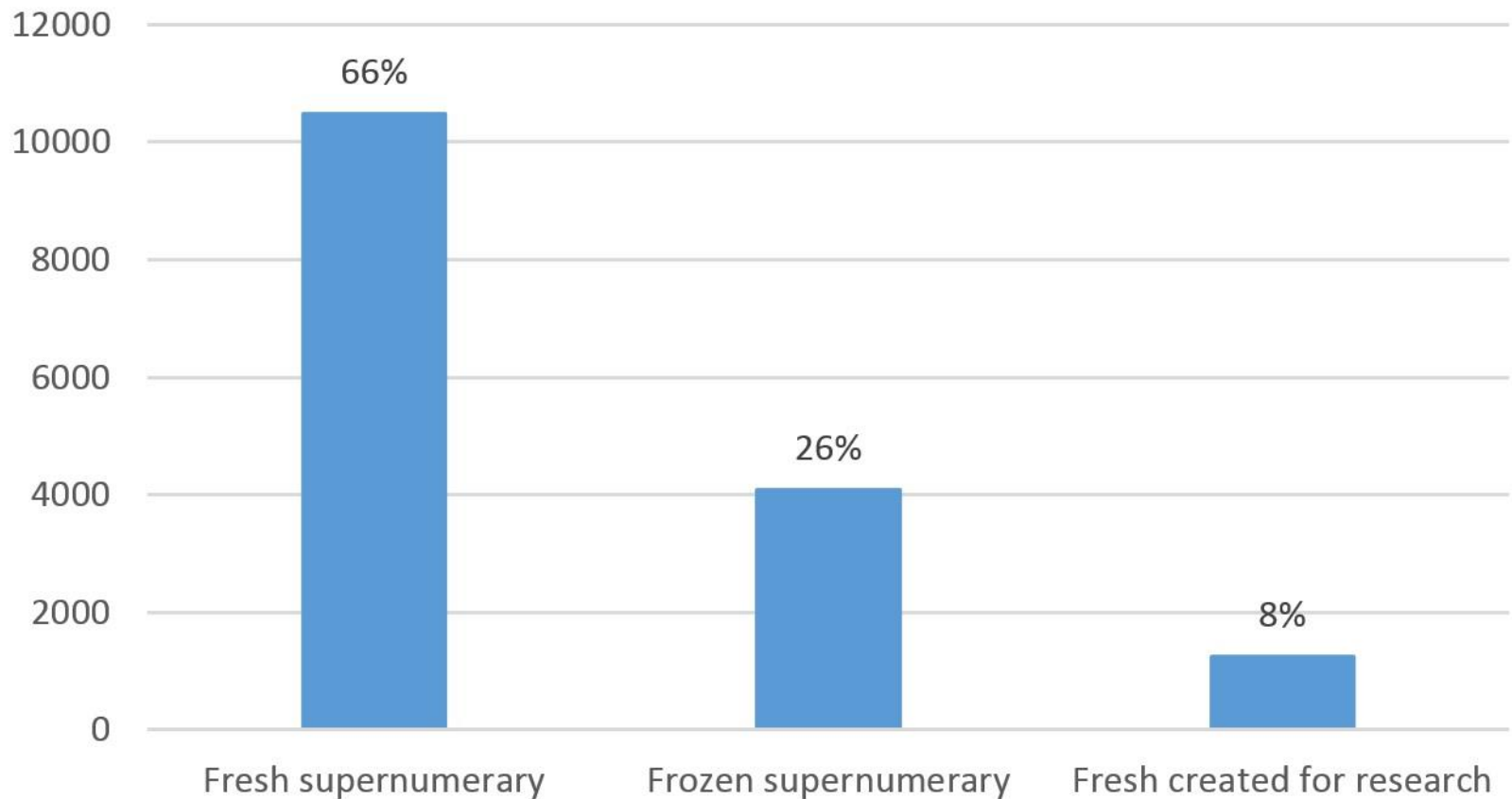
1. Fresh supernumerary embryos: unfit for transfer or freezing because of inferior quality, abnormal fertilisation, chromosomal abnormalities.
2. Frozen supernumerary embryos: good quality embryos, presumably healthy but no longer needed in the original parental project
3. Fresh embryos created for research: were never part of a parental project.
- [4. Frozen embryos created for research: embryos that for whatever reason could not be used directly in a research project]

Types of embryos

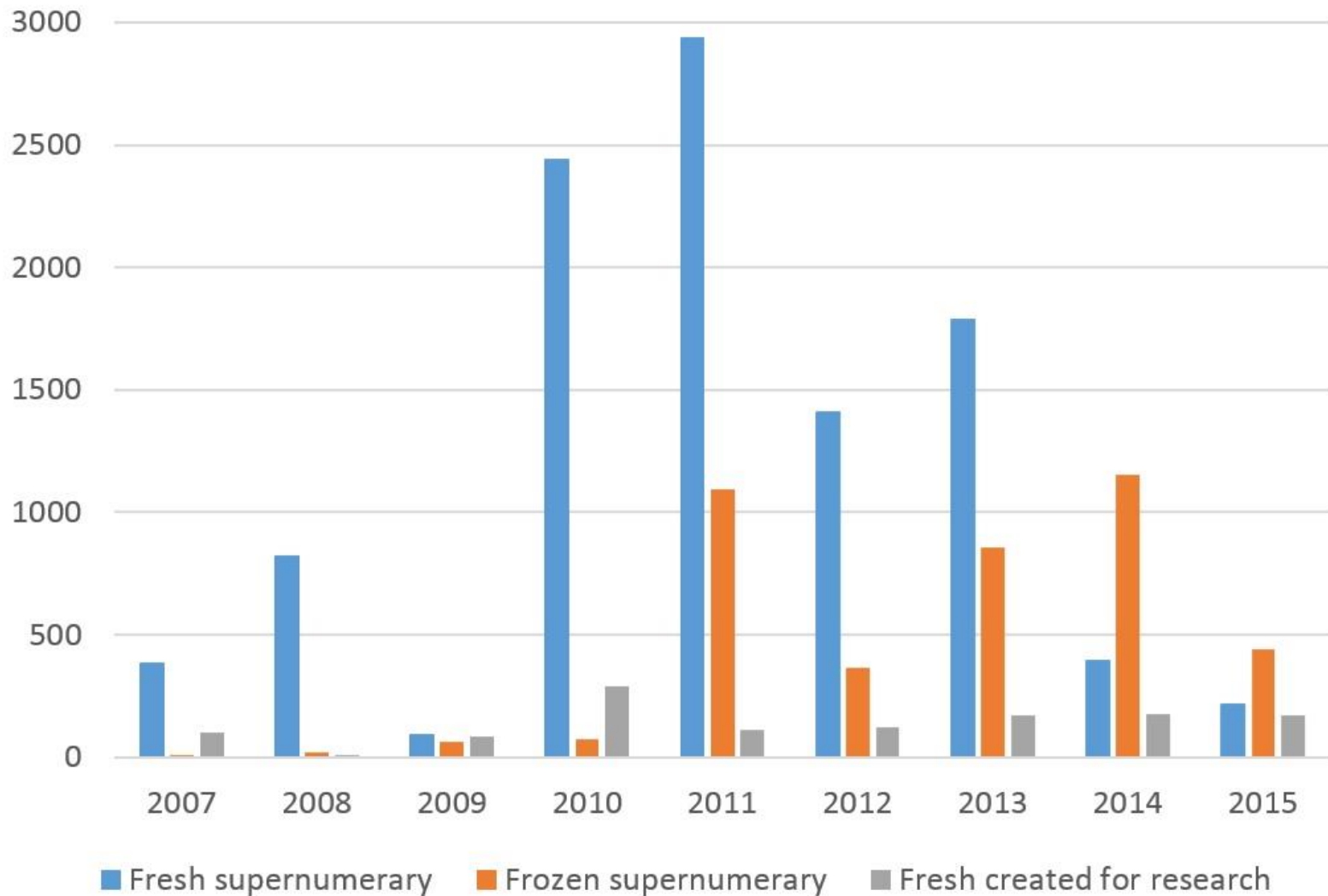
Attention: the numbers mentioned are the total number of embryos that were used in the research. A certain percentage will not have been actually used for research because they did not qualify (bad quality, did not survive freezing etc.)

The embryos mentioned in this report were not replaced. The research projects that were purely observational were classified as 'clinical management' by the FCE. See further on definition of research.

Number of embryos used per type 2007-2015



Types of embryos used per year



Embryo research in Belgium

Due to the short time period it is difficult to detect trends. Nevertheless, two points:

- the number of fresh supernumerary embryos is going down, and
- the number of frozen supernumerary embryos is going up.

Destination	Number of embryos in storage on 31/12/2014
IVF or ICSI	73802
Donation to others	1921
Scientific research	5082
Autologous storage for medical reasons	5941

FAGG, 2015



Embryo research in Belgium

About half of the IVF patients (51%) choose donation for research as the final destination for their supernumerary embryos (Provoost et al., 2012).

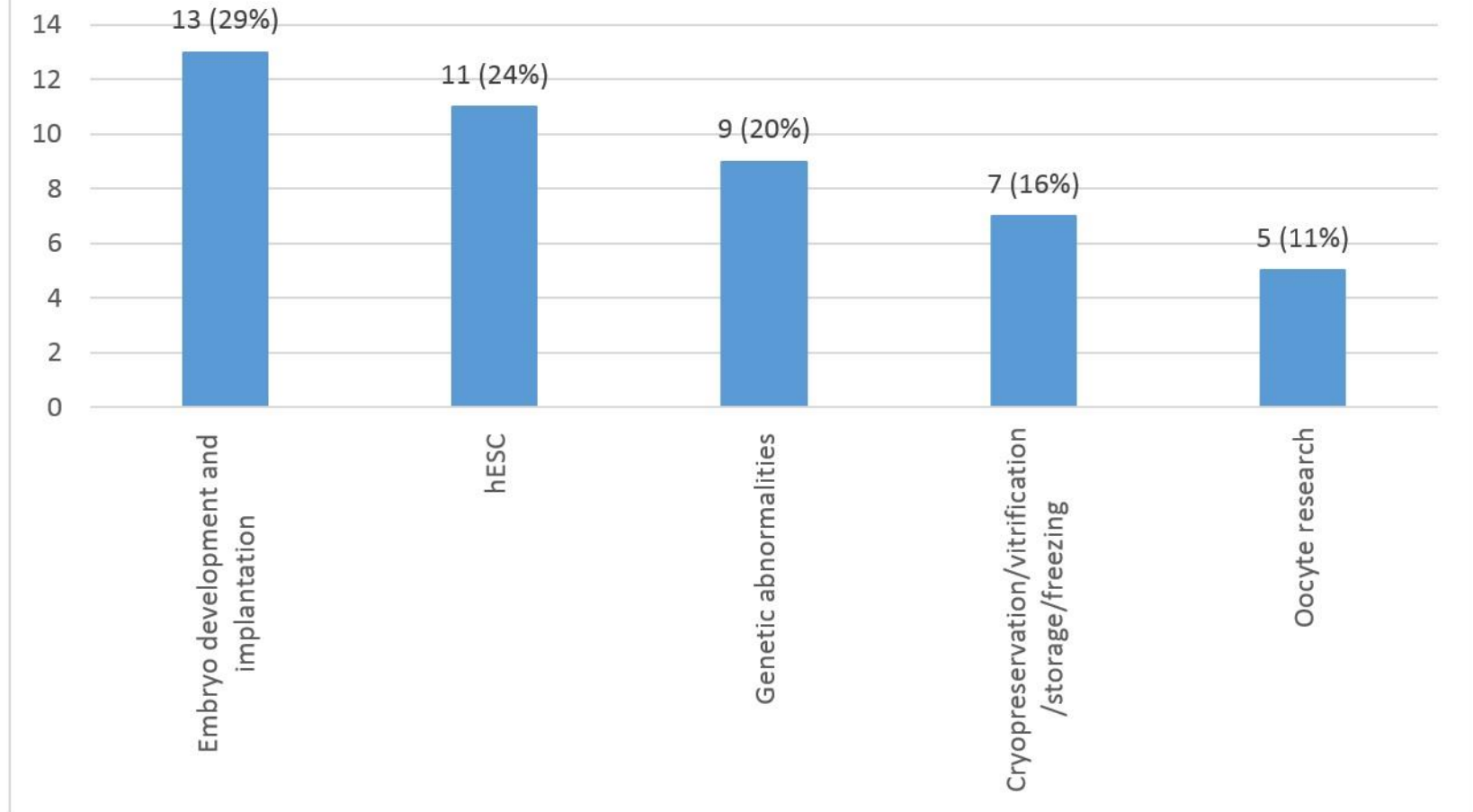
Important developments:

- freezing at blastocyst stage (day 5): fewer early cleavage stage embryos available.
- throphectoderm biopsy for PGD + cryopreservation: no fresh good quality genetically abnormal embryos available.

Possible consequence: more embryos will have to be created for early embryo studies.



Areas of research 2007-2015

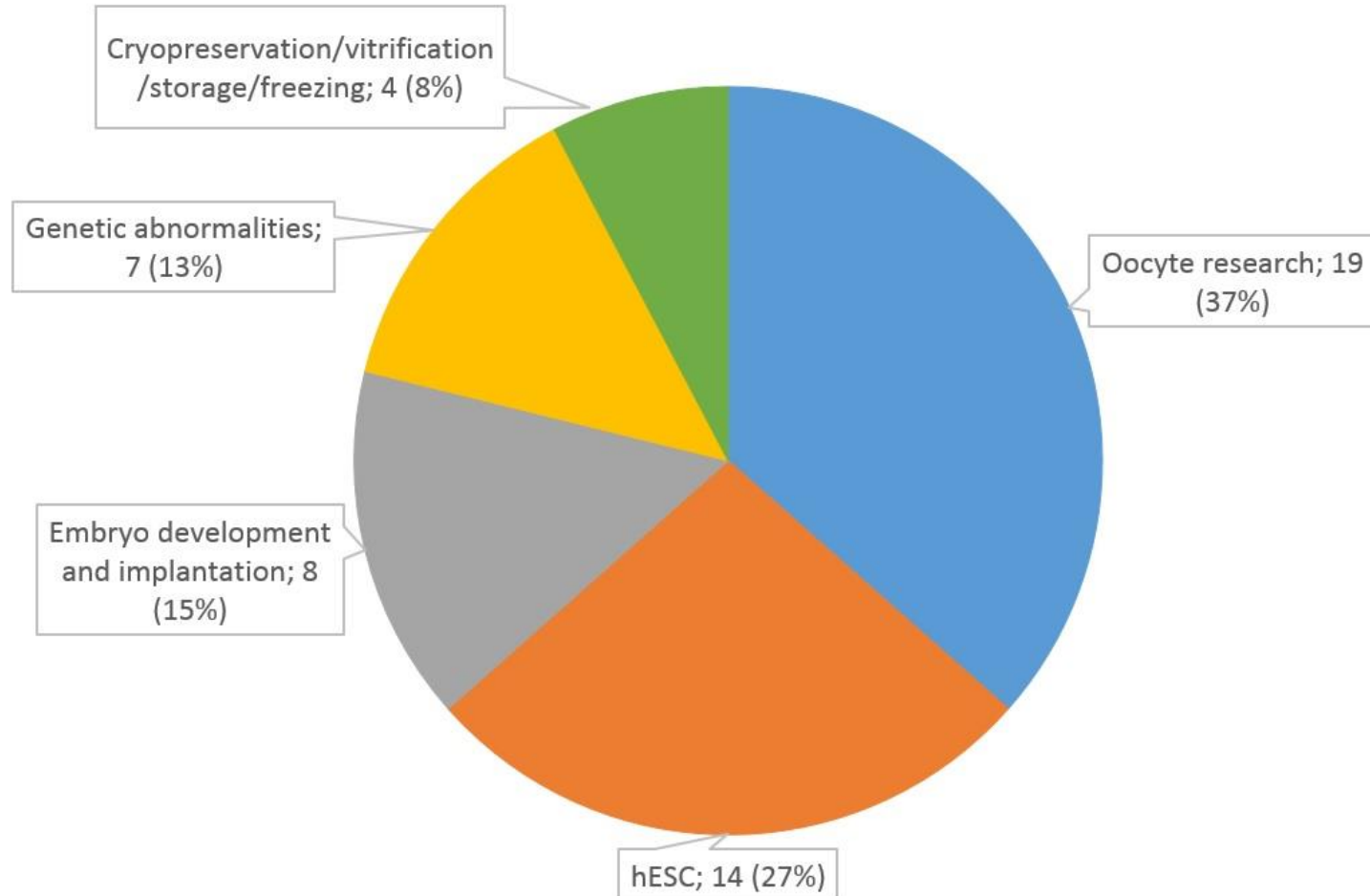


Several projects belonged to two areas of research.

Type of embryo in combination with type of research

- fresh supernumerary embryos: 63% hESC research; 32% embryo development
- frozen supernumerary embryos: 70% hESC research; 70% embryo development (45% overlap)
- research embryos: 33% embryo development, 33% oocyte research; 31% oocyte cryopreservation

Scientific output based on researchers' reporting



Definitional problems

Two major conceptual problems: 'research' and 'embryo'

RESEARCH

- no clear definition could be found: activity directed at the systematic collection of scientifically new information
- distinguish research from clinical management
ex. new incubator, new culture medium ...
- distinguish research from training (practicing skills)
ex. biopsy, ICSI ...
- no research if testing is conducted with existing devices, according to standard methodology that is internationally recognised (established method)
ex. vitrification

Definitional problems

RESEARCH

Art. 5: embryos subjected to research cannot be replaced except when the intervention has a therapeutic purpose for the embryo or when it concerns an observation method that does not harm the integrity of the embryo.

Problem: experimental intervention on a gamete (like genome editing), then creation of an embryo with these gametes and (after observation) replacement in a uterus. Not 'research on embryos'.

ex. mitochondrial transfer to rejuvenate the oocyte

ex. genome editing

Problem: should observational studies also fall under 'research' and not under 'clinical management'?

Definitional problems

EMBRYO

Definition in the law: a cell or a bundle of cells with the potential to grow into a human being.

- parthenote? Other things might be able to grow into a human being if enough manipulations are performed.
- 0PN, 1PN and 3PN: abnormally fertilized embryos? Unfertilized oocytes?
- low quality embryos
- genetically abnormal embryos

Comparison with other countries

General problem: no, little or incomplete information available

- The Netherlands: CCMO (Central Commission Human Research): some very general information on projects is available but no specific data.
- Sweden: Local Ethics Committees: some general information on research projects is available on request but no specific data. On the basis of publications: embryos created for research in 2003 111; 2004 249 (+239?); 2005 379; 2007 365. Fresh supernumerary from PGD: 2008 338; 2009 166. Remarkable: many research embryos.
- Spain: National Cellular Lines Bank & Spanish Commission on non-reproductive research on human embryos & Spanish Commission on Assisted Reproductive Technologies: 10 projects between 2006 and 2014, each with 50 to 100 embryos.



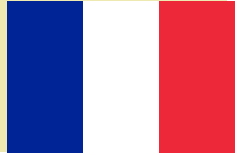
Embryo research in France

Use of supernumerary embryos for research is allowed.

Year	Total number of embryos frozen	Number of embryos for research
2009	165.591	13.804 (8.3%)
2010		17.503
2011		17.667
2012		18.309
2013	191.845	19.335

Between 2004 and 2010: 1,087 embryos were used for research (80% hESC lines and 20% early embryo development).

Embryo research in France



Very little research is performed and many embryos donated for research remain in the freezer. Reasons?

The Ethics Committee of INSERM (Institut national de la santé et de la recherche médicale) criticised the Agence for too many restrictions and too many barriers.

Not one single authorisation for embryo research has been given since 2008.

What will they do with the embryos donated for research? Keep them frozen indefinitely? Destroy them?

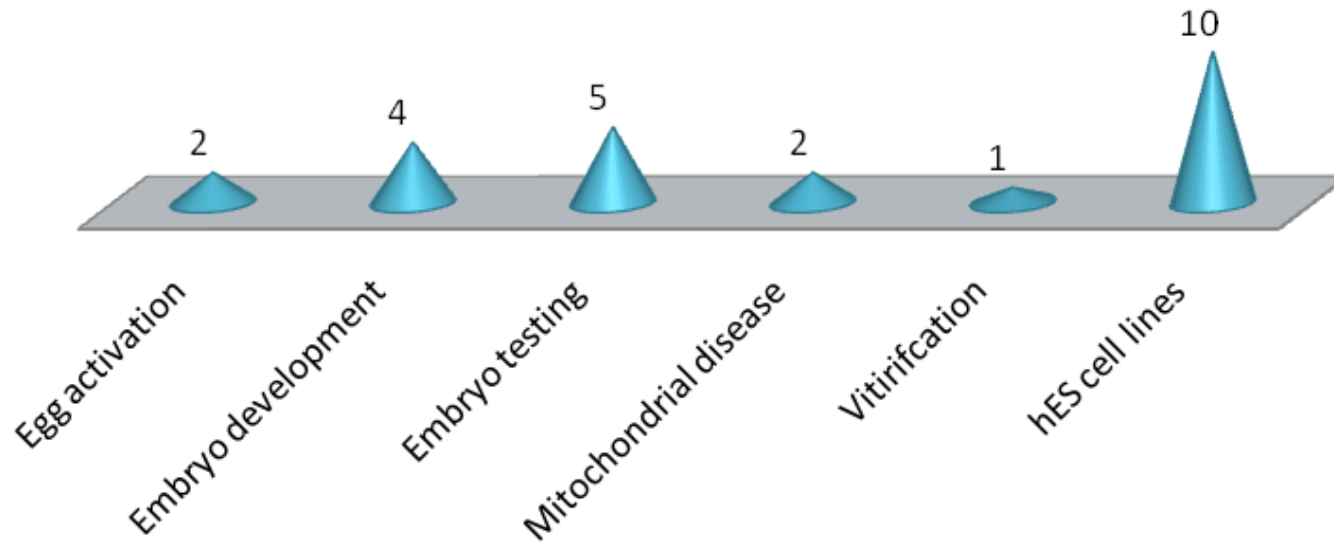
Question: is it a form of deception of the patients when they are offered to direct their embryos to research while at the same time, no action is taken to make research possible?



Embryo research in the UK



Fig. 2: Areas of research



HFEA, 23 research projects in 2010

Around 50% of the projects are on hES cells while only around 25% in Belgium (but over 8 years).



Embryo research in the UK



Use of supernumerary and created embryos is allowed.
Only partial data is available: 2006-2007, 2010 and 2011.

Centre No.	No. of projects	No. of embryos donated	No. of embryos received / thawed	No. of embryos used	No. of embryos allowed to perish	No. of embryos created	No. of created embryos used
TOTAL 2010	18	6462	6002	4925	2818	174	117
TOTAL 2011	17	4911	4120	2629	2719	74	74

HFEA, 2010; 2011.

Embryo research in the UK



Year	Embryos stored for patient use	Embryos stored for donation	Embryos stored for research	Total
1999	43467	168	<5	43638
2000	47980	133	43	48156
2001	49078	170	33	49281
2002	45804	168	39	46011
2003	43597	144	20	43761
2004	44676	159	25	44860
2005	45678	206	21	45905
2006	50770	70	39	50879
2007	48687	98	352	49137
2008	51852	88	1706	53646
2009	50918	70	1597	52585
2010	51095	111	1253	52459
2011	50572	47	776	51395
2012	49755	73	535	50363
2013	60103	12	372	60487
Totals	949955	2264	6814	959033

Embryo research in the UK



70% of embryos used in research are fresh embryos, compared to 66% in Belgium.



Embryo research in the UK



1. The number of frozen embryos donated for research goes down steadily since 2008. Explanation?
2. No information is available yet on the number of embryos used for projects for mitochondrial transfer.
3. The difference in frozen embryos and embryos used in research shows that, like in Belgium, the majority of embryos used in research are fresh supernumerary embryos.

Embryo research: conclusions

1. A number of countries (Spain, France) have legislation permitting embryo research but very little or no research is being performed. It is worthwhile to look closer to find out what the reasons / causes are.
2. In most countries, no information on embryo research is publicly available.
3. In most countries, data collection is poor or non-existent.
4. Collecting data as well as evaluating projects is a laborious process. If legislators claim that embryo research is important, they should provide the means to ensure the proper performance of these tasks.
5. Numerous problems remain to be solved in data collection but this is an ongoing process.
6. Transparency regarding research can help to increase trust by the public and the patients.