# European Society of Human Reproduction and Embryology


## COURSE 7

## Ethics and public funding for assisted reproductive technology in Europe

## Special Interest Group Ethics and Law

**18 June 2006**
**Prague - Czech Republic**

# Contents

## Course 7 - Pre-congress course organised by the Special Interest Group Ethics and Law

## "Ethics and public funding for assisted reproductive technology in Europe"

## PROGRAM

**Course coordinator:** G. Pennings (B)

**Course description:** The course considers the major questions involved in public funding of infertility treatment. The first questions regard the status of infertility treatment within the general health care system and the implications in terms of justice. A presentation of the systems of reimbursement both in western and central European countries is given in order to have an idea of the diversity. The second part treats the economics of assisted reproduction. The jargon (need, demand, cost-effectiveness) is explained within the field of infertility treatment. The final question is whether the information and views from both ethics and economics may lead to an optimal system for reimbursement.

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|---|---|
| 09.00 - 09.30: | Disease, disability or just disadvantage: the status of infertility and its implications for funding - **G. Lockwood (UK)** |
| 09.30 - 09.45: | Discussion |
| 09.45 - 10.15: | Distributive justice in assisted reproduction - **G. de Wert (NL)** |
| 10.15 - 10.30: | Discussion |
| *10.30 - 11.00:* | *Coffee break* |
| 11.00 - 11.30: | Overview of different systems: access and the law – **F. Shenfield (UK)** |
| 11.30 - 11.45: | Discussion |
| 11.45 - 12.15: | Overview of public funding in central European countries – **T. Mardesic (CZ)** |
| 12.15 - 12.30: | Discussion |
| *12.30 - 13.30:* | *Lunch* |
| 13.30 - 14.00: | Needs, demand and availability: a short guide to economic jargon – **M. Granberg (S)** |
| 14.00 - 14.15: | Discussion |
| 14.15 - 14.45: | Evidence based cost-effectiveness in IVF - **Ch. Bergh (S)** |
| 14.45 - 15.00: | Discussion |
| *15.00 - 15.30:* | *Coffee break* |
| 15.30 - 16.00: | Need, demand and services in infertility treatment - **K. Nygren (S)** |
| 16.00 - 16.15: | Discussion |
| 16.15 - 16.45: | An outline of an optimal reimbursement system for assisted reproduction - **Y. Englert (B)** |
| 16.45 - 17.00: | Discussion |

## Disease, Disability or just Disadvantage?

The status of infertility and its implications for funding

**Dr Gillian Lockwood**
**Medical Director**
**Midland Fertility Services**
**Aldridge**
**UK**

**www.midlandfertility.com**

# Fertility:

## Lifestyle choice or medical problem?

**'Erewhon' Samuel Butler (C19th author and artist)**

**If we accept the implications of a deterministic Universe then the sick could be in prison and the wicked in hospital....**

## Female Age, Socio-biology and Infertility in Europe

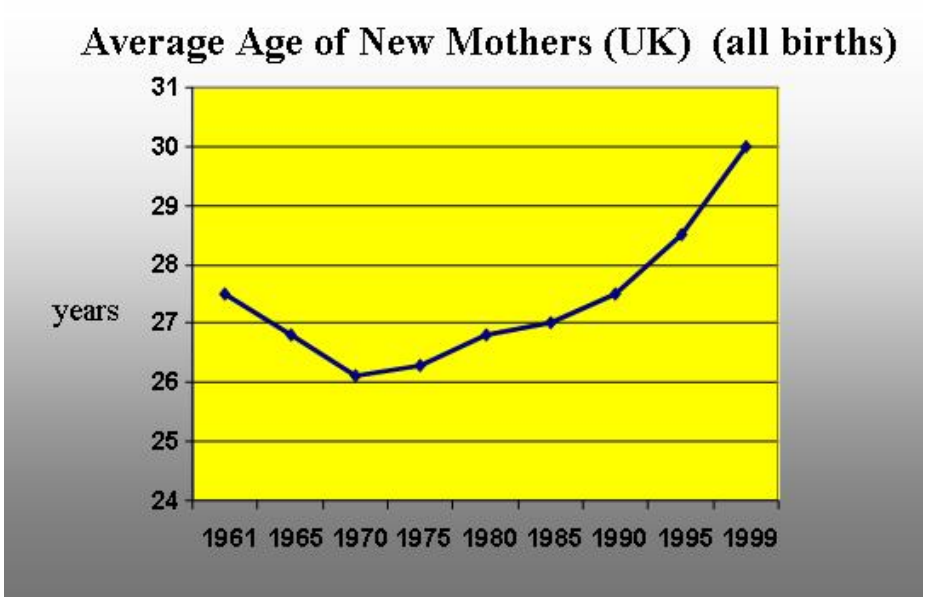
**The average age of first maternity in the UK has risen from 23 to 29 years in one generation**

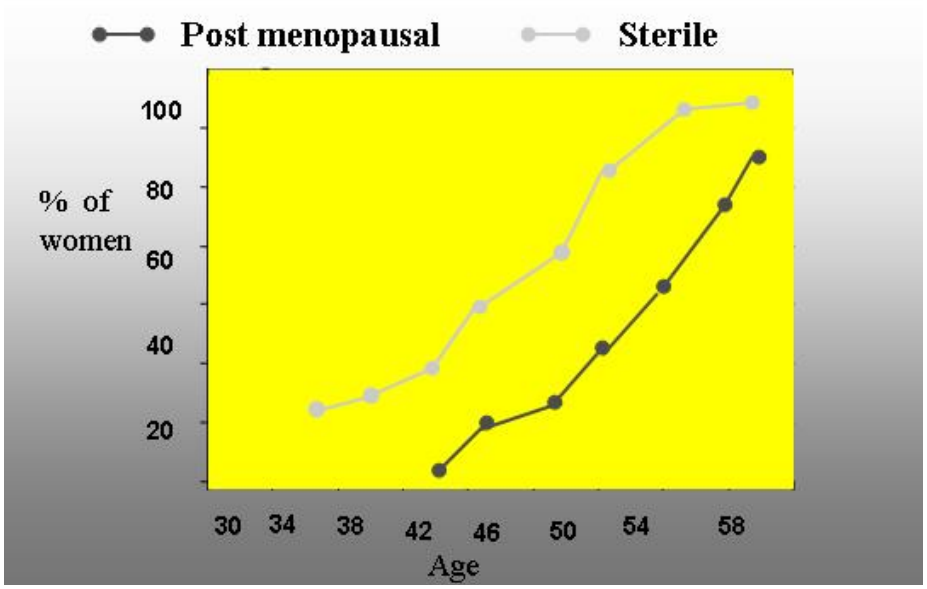
**The average number of babies per woman in the EU is 1.5**

**50% of UK women aged 30 who expressed a desire for motherhood failed to achieve by 40**

**20% of UK women are childless**

**Age-related sub-fertility is the fastest growing cause of infertility referred for treatment**




## The public perception of 'chance'

- Some chance/low chance/ no chance….
- UK National lottery: 1 in 14 million
- IVF < 39 years : 1 in 4 (take home baby rate)
- IVF > 40 years : 1 in 15 (take home baby rate)
- How low can we go?
- When is it reasonable to say 'No!'

## Technology to 'fix' the problems caused by 'brute biology'

- Subfertility judged on a 'medical' scale....
- Can a QUALY analysis help?
- Cost Benefit Analysis.. Introducing Macroeconomics
- Rights versus Duties. Human Rights Implications
- When is it reasonable (for governments) to say 'No!'

## The special case of fertility patients:

- Fertility patients are not ill
- Fertility patients 'volunteer' for treatment
- Success rates are objectively 'low'
- Society is generally unaware or unsympathetic
- Fertility patients have to pay!

## The psychological impact of infertility:

- frustration
- anger
- lowering of self-perception
- interpersonal difficulties
- anxiety
- depression (Moller and Fallstrom 1991)

## What influences how patients cope?

- Duration of infertility
- Diagnosis
- Previous failure
- Pre-existing depression

## Low chance and no chance:

- The repeated IVF failure
- The 'late starter'
- The '*a priori*' low-chance couple

## Exit Counselling:

- Only half of all couples referred to an IVF clinic will end up with a baby…..
- Good practice is judged by how the 'unlucky' 50% + perceive themselves to have been treated

## Pressures on the Sub-fertile Couple

- The 'technological imperative'
- Media coverage of 'celebrity' pregnancies
- Pressure from family…. " I'm ready to be a Grand-Mother now! "
- The clinic staff have been so kind & positive….

## Offspring of Older Mothers:

- Obstetric risks for mother and child
- Neonatal outcome
- Childhood development
- Positives and negatives

## Maternal Medical Risks

- Pre-eclampsia- women > 40 years are TWICE as likely to develop PET
- Gestational Diabetes - 4.1% in mothers > 35 years (1.7% in mothers <35)
- Miscarriage- 1st trimester risk: 25 - 40% > 40 years (12 - 15% < 25 years)
- Chromosomal abnormalities- 1 in 66 (aged 40) compared to 1 in 476 (ages 24)

## The Demographic Time-Bomb

- A baby girl born today in Europe today will live to be 87
- On current trends she will have her menarche at 10
- She will have 1.1 children
- Her health care/pension costs will exceed her lifetime tax contribution

## The Reality for Fertility Patients

- The majority reported that the outcome of treatment was 'the most important thing in their lives'
- The majority had or would make significant financial sacrifices to access treatment
- The majority regarded their infertility/subfertility as a medical problem

# Distributive justice in assisted reproduction

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## Learning objectives

This presentation should help the participants to identify and to weigh the various arguments pro and con the public funding of assisted reproduction, more in particular in vitro fertilization (IVF) and pre-implantation genetic diagnosis (PGD).

## 1. Introduction

In the ethical debate on assisted reproductive technologies (ART), one may discern at least three types of normative questions. A first question is whether ART should be allowed, and if so, on what conditions. Objections include religious objections (e.g. the argument that reproduction should not be separated from sexual intercourse), the 'fetalist' objection ('one should not waste pre-implantation embryos'), health and safety objections, the 'radical' feminist critique ('ART reinforce pronatalist ideologies which enforce women to have children'), the 'disability rights' critique (cfr. *infra*), and the slippery slope argument. A second question is whether these technologies should be publicly funded, i.e. included in a comprehensive health care package available to all. Do applicants for ART have a legitimate claim against society for help? And a third question is whether or not people with a medical indication have the right to get access to ART. Do doctors have an unqualified obligation to provide ART to all applicants who have a medical indication? Clearly, these types of questions are related, but not identical. If a specific reproductive technology should not be allowed, it should not be funded, but it does not follow that if ART are allowed, they should be funded. Furthermore, if allowed-and-funded, this is not to say that applicants have an unqualified right to get access to treatment; taking into account possible risk factors for the woman or for the welfare of the future child, there may well be a contra-indication for medical assistance in reproduction.
This presentation focuses on the second question. In debates on funding of ART, these technologies are often presented as one single category. In fact, of course, at least two categories of ART should be discerned, namely
1. fertility treatments, including IVF;
2. technologies for 'selective' reproduction, especially PGD.

## 2. Arguments for/against public funding

### 2.1 IVF

*For*

Brock has identified three different moral arguments for access to ART (esp. infertility treatment) (Brock, 1996). He argues that a full account of the moral basis of that access must incorporate all these three lines of argument. Firstly, people's interest in self-determination. This is a highest-order interest, based in people's capacity to form a plan of life. Others things being equal, the more central and far-reaching the impact of a particular decision will have on an individual's life, the more substantial the individual's self-determination interest in making it. Few decisions are more personal than reproductive decisions. Secondly, individual good or well-being. Clearly, securing access to ART for infertile couples will generally contribute to people's happiness, it typically makes a substantial positive impact on their well-being. And thirdly, justice. One of the arguments that is relevant here focuses on how access for infertile persons serves equality of opportunity. For most people, the opportunity to become a parent is on of the most important parts of their lives. Norman Daniels has argued that the importance for health care for justice lies in its securing and protecting for individuals access to the normal range of opportunities in their society (Daniels, 1985). ART often represent the means by which the opportunity to bear and raise children can be restored to infertile persons. The moral importance of doing so depends largely on the relative importance of parenting within the life plans of most people.

*Against*

One may discern contingent objections on the one hand and principled ones on the other. A contingent objection is that IVF is inefficient in view of its low/moderate take home baby rate (THBR). Clearly, this objection is debatable; one may seriously doubt whether it is reasonable to request that the success rate of IVF should be substantially better than the (moderate) success rate of natural conception in humans in order to qualify for funding. Anyway, if the efficiency of IVF would significantly improve in the future - e.g. by the successful introduction of in vitro maturation (IVM) of oocytes - the current objection may well dwindle. The principled (partially overlapping) objections include the following:

a. 'Subfertility is not a disease'

There is no consensus regarding the definition of disease. If we accept Daniels' definition - diseases are 'physical or mental conditions of an organism that result in deviations from normal species functioning' - infertility may well be qualified as a disease (Daniels, 1985). For others, however, this definition, and, as a consequence, the status of infertility, is problematic. Following Holm, infertility is best qualified as a disability or handicap (Holm, 1996). The conceptual question as to whether infertility is a disease/handicap or not, has important performative aspects, in that an affirmative answer generates a legitimate *prima facie* claim against society for help.

b 'There is no fundamental need, in view of the alternative ways to have children'

Even if we accept, as we should, that subfertility is a handicap, it does not follow immediately that we should provide IVF to subfertile applicants. The decisive question is

whether IVF meets a fundamental need. Some critics argue that an argument for the societal provision of ART will have to show that these technologies meet fundamental needs *that are not met by, for instance, adoption*. 'No doubt', so Holm argues, 'that the desire to beget, bear and rear a child that is genetically related to oneself can be a strong desire, but it is difficult to see how it could be a rational preference or a fundamental need, all things considered.' (Holm, 1996) He adds that, paradoxically, the mere existence of a societal provision of reproductive techniques may itself create a fundamental need for their continued provision. The treatment process itself seems to reinforce the desire to become pregnant and to generate 'a situation in which the final frustration of the desire to conceive a child may cause serious psychological harm. This does seem to create a valid claim for further assistance, but such a claim is not extendable to new couples seeking treatment.' I have some doubts about the validity of this reasoning, for two reasons. First, if the criterion for funding is the harm/probability ratio, i.e. the probability and magnitude of psychological harm caused by the frustration to have a genetically related child, it is difficult to see why only people who already are in the process of infertility treatment could have a strong claim for assistance. After all, it is well-know that for many infertile people (who are not yet in this process) parenting a biological child is of paramount importance. Secondly, critics of funding tend to disregard or play down the practical barriers regarding adoption. The number of infertile people far outruns the number of children available for adoption, adoption is expensive and parents applying for adoption have to meet rather strict criteria. It is unjustified to argue against the societal provision of ART on the basis of a simplistic referral to this - to a large extent unrealistic - alternative.

c. 'IVF is not curative'

Most types of ART do not remove the specific cause of infertility - they 'just circumvent' it. This, however is similar to many other treatments that are covered by basic health insurance packages (think of insulin for diabetes patients). One should not selectively (mis-)use this argument in the debate about ART.

d. 'People can pay for themselves'

According to some commentators, only those treatments/interventions that cannot be financed by people themselves, should be publicly funded: 'People who can afford to raise a child – the costs involved are approximately 100.000 Euros in The Netherlands – should (be able to) pay the costs of IVF.' No doubt, for at least some people, the costs of IVF would be prohibitive – and would *de facto* prevent them from having a child. Furthermore, the argument that only those interventions that people can not finance themselves should be funded, is used *selectively* against the funding of IVF. This double standard probably masks value judgments about the status of infertility and/or IVF.

## 2.2 PGD

What about public funding for PGD? The arguments pro and con differ substantially from the arguments regarding the funding of IVF:

*For*

Brock's second and third argument for funding IVF (cfr sub 2.1), need some modification in this context: the main argument in favor of funding is that PGD may prevent serious

harm for (prospective) parents *and* future children - the 'argument form well-being' regards both the applicants and progeny. And the 'argument from justice' can be re-formulated as follows: PGD gives people at high risk of having an affected child (people who have had bad luck in the genetic lottery) an equal opportunity to have a healthy (genetically related) child; for some of them there would be no other alternative but to refrain from having children at all.

*Against*

Arguments against are, again, contingent as well as principled. A contingent objection is that PGD lacks efficiency, at it depends on IVF/ICSI, technologies that have only a moderate success rate. The latter objection has already been questioned (cfr above). Principled objections include the following:

a. 'Presumed disorders/disabilities are *de facto* a social construction'

According to some critics, handicaps are a social construction; the problems that handicapped people encounter, basically result from social prejudices and barriers for their integration in society. We should 'change society, not people' – an exhortation to modify society to enable those who are now disabled to function effectively in society. (Funding of) PGD, then, could be seen as a misguided effort. No doubt, this critique rightly points to the fact that impairments sometimes become disabilities in one sort of social environment, but not in others. To argue, however, that disabilities per se have a social nature (that the problems of the handicapped can be *reduced* to the social context) simply is a *non sequitur*.

b. 'Public funding for PGD is unsound in view of the disability rights critique'

This critique may take several forms (Buchanan et al., 2000). One variant holds that PGD, like prenatal diagnosis/selective abortion, expresses the view that people with handicaps are second class citizens. This variant is untenable as is disregards that embryos/fetuses are not yet human persons. A second variant, the 'loss of support argument', holds that lower numbers of people with handicaps will undermine societal efforts to improve the condition of the handicapped. This variant is debatable as well, e.g. because there is no evidence for this adverse effect. Funding PGD, then, need not conflict with the rights and interests of the handicapped.

c. 'Public funding for PGD is unjustified as there are less expensive alternatives'

One might, again, point to adoption (cfr above, however, for a critical note). Another alternative - that would meet people's preference to have a genetically related child - would be prenatal diagnosis/selective abortion. We should realize, however, that for some people this alternative is unacceptable for moral, emotional and/or religious reasons. Furthermore, the dominant view in our society is that a fetus has a higher moral status/symbolic value than a pre-implantation embryo. Shouldn't this be taken into account when making decisions about the funding of PGD? And finally, just taking the genetic risk to have an handicapped child may well impose more financial costs/burdens on society.

Irrespective of whether we think that assisted reproduction should be included in the basis health care package available to all who need it or should be covered by a complementary health insurance, decisions have to made about conditions to be imposed.

## 3. Conditions

### 3.1 IVF

Possible conditions include:

*No funding in case of 'self-inflicted' infertility?*

The theme of personal responsibility is being used partly to justify the view that people should pay themselves the costs of medical care when their lifestyle results in medical problems. Veatch argues that even people who accept an egalitarian view of social justice should accept that people only have the right to an equal opportunity for a chance to be as healthy, insofar as possible, as other people (Veatch, 1980). The *cause* of medical needs, then, is ethically relevant. *In principle*, Veatch sees nothing wrong with the view that those who have not used fairly their opportunities receive inequalities of outcome. Clearly, this view may be relevant for the current issue, in so far as it regards infertility caused by unsafe sex/sexually transmittable disorders (STD), more in particular chlamydia: 'shouldn't people whose infertility is caused by STD pay themselves for infertility treatment?'

Veatch rightly acknowledges that his view could only be applied to people who truly voluntarily engaged in risky behaviors. Needless to say that this qualification raises difficult questions. What about the 15-old girl who felt pressurized to engage in sexual activities while her boyfriend 'forgot' to use a condom? And what about the professor in biomedical ethics who delayed childbearing for professional reasons – to discover at the age of 38 that she needed IVF? Veatch also points to another problem: if all voluntary risks ought to be treated alike, what do we make of the fact that only some of the behaviors are visible/monitorable? Finally, the consistent application of this policy would imply a complete erosion of privacy.

Interestingly, the majority of Dutch doctors and citizens seems to refute the idea that applicants whose infertility is cased by unsafe sex should pay themselves – but considers it to be justified that *sterilized* people who (regret and) opt for IVF should be excluded from social provision of IVF (Wolleswinkel et al., 2006). Apparently, the fact that infertility was deliberately chosen, makes a difference.

*A minimum of effectiveness?*

Clearly, if an infertility treatment it (almost) futile, funding would be absurd. In some cases, the THBR of IVF is (very) low – and, as a consequence, funding becomes questionable. A first controversy regards women with a (very) high Body Mass Index (BMI). There is dissent among experts regarding the precise cut-off point to be used for access to IVF. The case is complicated by the fact that concerns about increasing maternal risks, increasing risks for progeny and a decreasing THBR are interwoven. Decisions about funding should be separated from doctors' decisions about possible medical contra-indications. Would it be morally justified not to fund IVF for women who did not succeed in loosing weight (in cases where the THBR is decreased, but not close to zero)? (De Beaufort et al., 2006) And, secondly, what about maternal age? In view of the age-related decreasing THBR, the funding of IVF for women >40/42 seems to be unjustified (unless, of course, a biological parameter would indicate a reasonable success

rate in individual cases). For older women, IVF with donor eggs could be an option (cfr. however, below).

*Naturalness?*
Many people will agree with Brock, that a qualification must be put on the claim that infertility is a disease (because a deviation from normal species functioning), namely that this holds only for *the natural period* of childbearing years for women (Brock, 1996). There is an ongoing debate about the question as to whether IVF with donor oocytes in women over, say, 45, can be justified. Even among liberals, there is hardly any support for funding in these cases (as is clearly illustrated in a recent survey in the Netherlands) (Wolleswinkel et al., 2006). It is remarkable, however, that 'the argument from Nature' is used *selectively*; the funding of IVF with donor oocytes for 40-45-year-old recipients is considered to be acceptable by many people, whereas many of these women will suffer from a natural, age-related decline of fertility (Dondorp, 2006; Kortman, et al., 2006). Apparently, the notion 'medical indication' is somewhat flexible - 'a practical normative construct in which medical and social justifications are woven together' (Bateman Novaes, 1998).

*A limited number of treatments?*
An unlimited funding would be problematic or even unjust in view of other fundamental needs that have to be met both within and outside of health care. While justice does not request that applicants get unlimited access to infertility treatments, the question where to draw the line (2 IVF cycles for all applicants, 3 or maybe even 4?), is difficult to answer in the abstract. Nevertheless, the higher the number of infertility treatments/IVF cycles people have had, the weaker the claim for funding of additional treatments/cycles becomes.

*A limited number of children?*
Do infertile parents have the right to get funding for assisted reproduction? Do they have a fundamental need to have *another* (second, third, etc.) child? No doubt, the higher the number of children people already have, the weaker claims for funding (additional) infertility treatments become. But maybe this view needs some qualification, as the context of the applicants' request for infertility treatment may be relevant. Take the case of a widow and her new partner, both having one child from their former marriage, who want to have a child *together* and apply for ICSI because of secondary infertility. Would it be (un-)fair not to fund ICSI in this case because they already have two children?

**3.2 PGD**
Possible conditions include:

*Only for infertile couples (at-risk)?*
Should PGD be funded only when people already have an indication for IVF because of their infertility? Some argue that IVF was not *meant* for fertile couples. This 'essentialist' argument is, however, rather weak: many interventions are 'multifunctional' - what matters is whether fertile couples at high-risk have a fundamental need to IVF/PGD. The arguments in favor of funding PGD (cfr.2.2) equally apply to infertile and fertile couples

at high risk, as members of both groups may feel that they have no real reproductive alternative.

*Only for severe diseases?*
The ethics of PGD focuses to a large degree on the indications to be set, taking into account the severity of the disease/handicap. This is, in fact, a *pars pro toto*, as it covers *various* morally relevant variables, including the severity of the disorder, the penetrance of the relevant mutation(s), and the age of onset of the disease (De Wert, 2006). Likewise, these variables should play a role in deciding about the funding of PGD. The question '*where precisely to draw the line?'* is notably difficult to answer. Anyway, to collectively fund PGD of low-penetrant susceptibility genes for e.g. non-syndromal cleft lip and palate (CLP) or multifactorial late-onset Alzheimer's disease would be unjustified/unjust in view of the more serious health needs and – risks of other applicants (Steinbock, 2002; De Wert, 2006).

*No funding of PGD beyond the medical model?*
A few examples may illustrate that this category is in fact highly diverse (hybrid), which complicates univocal answers. Firstly, sex selection for non-medical reasons. Needless to say that this application is highly controversial in itself. But what if sex selection for family balancing would be morally justified – should it be collectively financed? The answer is, of course, 'No', as this is not part of the decent minimum of health care that should be available to all (Pennings, 2002). Secondly, so-called *intermediate* cases of PGD, i.e. cases which would not identify risk factors for the future child's health (and are, therefore, at odds with the medical model *stricto sensu*), but characteristics which are relevant for the health of 'third parties' (De Wert, 2005). One example is PGD/HLA-typing in order to save a child suffering from e.g. Fanconi anemia. Clearly, there are good arguments for collective funding in this case. Maybe even critics of funding regular IVF and/or PGD in situations which fit into the medical model would readily accept funding of IVF/PGD in this intermediate case, in view of the principle of proportionality (the procedure is life- giving and *life-saving* at the same time) and the principle of subsidiarity: there is no alternative to save the diseased child. Furthermore, people who would reject the funding of IVF when applicants already have a specific number of children, may consider this argument to be irrelevant when ART is needed to save an actual child.

## 4. Conclusions

1. It is remarkable that the debate about the public funding for ART focuses almost exclusively on infertility treatments, more in particular on IVF. It is important to realize that ART covers various categories of reproductive technologies and to take into account the specifics when discussing the implications of distributive justice for the provision of ART.
2. The view that both IVF and PGD should not be publicly funded *at all*, is difficult to justify – especially in relatively affluent societies.
3. It is not unjust to have a mixed or a two-tiered system, where applicants have to pay part of the costs of ART themselves or need to have a complementary insurance to cover

part of the costs. In view of the divergent views about distributive justice in assisted reproduction, a mixed system may well be a workable compromise. Distributive justice requires us, however, to check whether mixed systems do not *de facto* block access to ART for those individuals who really can not afford to pay part of the costs themselves or to have a complementary insurance

4. The conditions suggested in the literature for collective funding and/or coverage by complementary health insurance are highly diverse. Some are difficult to justify (like the exclusion of infertility caused by 'self-inflicted' STD), others hide difficult issues which need further debate (what about naturalness, what is a medical indication, how to demarcate the medical model?).

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## Overview of different systems: access and the law

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### Learning objectives

To be aware of the different types of legislation in ART in Europe and other major countries; to understand the difference between hard law and soft law systems, or positive law and jurisprudence; to have an overview of fair and unfair access to ART, with an understanding of the difference between the legal and ethical principles of justice

### Lecture summary

Speaking after G De Wert, the ethical under pining of the notion of justice should be clear. The major question is of course whether “Justice “ with a capital “J”, or the law in general is as ethically based, than it purposes to be semantically. The ambivalent answer to this question is provided by Bernard Dickens (1), emeritus Prof of Law in Toronto, and member of FIGO’s ethics committee: "Law and ethics operate in unavoidable interaction with each other
..as different systems of normative ordering…that sometimes overlap and sometimes conflict". The purpose of this presentation is to give examples of both propositions, especially concentrating on how the law restricts or allows access to ART treatments to infertile patients, and also to provide sources of comparative legislation in ART. First, means of enhancing and achieving overlap rather than conflict, between the ethical and legal concept of justice start with the knowledge of the intimate logic of the legal system.

### The role of the law, and the different systems

The two major systems are the anglo -saxon approach or natural law system, and the civil law system.
" Systems reflecting the Anglo-Saxon common law tradition are based on customary practices within their communities. The ethical principle of justice that like cases be treated alike has introduced the concept of binding precedent, but legislatures may change common law precedents in order to give effect to evolving ethical values. ...The law and legislation are usually regarded as morally neutral and often permit conduct that may be considered immoral." (1)
Thus often the principle of liberty is strongly upheld. You may do this (eg treating patients with IVF, , offering donor insemination to single women or lesbian couples), as long as there is no harm demonstrated to others (libertarian theory), although sometimes “public interest” is invoked in order to restrict personal liberty for the sake of society’s interest.

As for civil law systems, sometimes described as positive law systems, they tend to reflect the legal tradition "of Continental Europe since the Code Napoléon of 1804 locates all rights in a comprehensive national code that governs all legal claims. Any claimant to a right must first answer the question of where the right is contained within a provision of the code since no legal right can exist outside the code”.

Furthermore "continental codes often show strong influences of moral values, since historically they were developed under guidance of religious teachings".
Furthermore, even in countries of soft law tradition, in many cases hard law has replaced professional codes of practice, although the situation is far from homogeneous even in Europe, as the legislative process can easily be overwhelmed by party politics. However, the democratic process involves an interaction between either society as a whole and the agents involved in this particular matter; or delegates (eg parliamentary bodies). But even in countries with anglo- saxon legal tradition, there may be transition from soft law to hard law reflecting societal evolution. A prime example is the UK with the HFE Act (2): nevertheless, it is still an Act where what is not forbidden is allowed, contrary to the French laws in ART, part of the "bioethics laws"(3), which need for instance a "decret d'application", giving guidance as to the practical implementation of its different injunctions with regards to embryo research or PGD for instance.
Finally, since the end of the second world war, there is a recognised international framework, where national law .has to fit within a specific frame , this of international human rights . A recent case will be used to illustrate the importance of Human rights in contemporary law, as in the UK where the European Convention on HR has been integrated in English law as the Human Rights Act 1998 (4). In spite of the clear HFE Act which requires joint consent for embryo transfer, Ms Evans used all the steps to reach the European court of HR in order to claim her right to ET, when her ex husband had refused (5,Lockwood, 2006). She argued that it may be against a "right to privacy and family life", but the British judgment (refusal of ET) was confirmed: one cannot force a putative father to become the father of the child born when there are cryopreserved E present, and the law clearly insist on joint consent to give them a possibility to become legal person(s) by transfer. This also makes clear that most Human Rights are in the realm of negative rather than positive rights, and that to benefit from the protection of privacy of family life, the pre requisite is to have a family life, something to which Ms Evans was aspiring to by the hoped for transfer, but did not actually have at the time of her claim.
Thus international Human Rights may be seen as the wished for context of national law, but their relevance to the many faceted local systems is not necessarily as simple as it may seem. Let us now analyse the diversity of European ART laws and how they may enable or restrict access to treatment.

**Sources of legal data**

There are already several sources of legal data in our field, and they can make dry reading, although extremely valuable as a source of facts. One of these useful sources is the series of "IFFS Surveillance", started by J Cohen and H Jones in 1998, and published every 3 years since (6). The 1998 data were presented to the national delegates who had participated in the 1998 survey at the International Federation of Fertility Societies meeting in San Francisco, and covered the following subjects : types of constraints (eg, legislation and guidelines (surveillance)), insurance coverage (very relevant to the interaction between justice and access in our specialty), requirement of marital status in ART, legal limits to the number of embryos to transfer per cycle (or to the number of oocytes which may be fertilised as exist in Italy now), cryopreservation conditions, donation of gametes, micromanipulation, conditions ( for instance ICSI with testicular sperm is forbidden in the Netherlands), Oocyte maturation, welfare of the Child conditions (about which there has been a major revision recently in the UK, the only country where it is explicitely written into

the legislation, fetal reduction conditions (usually under abortion law), Preimplantation genetic diagnosis, IVF surrogacy, Experimentation on the embryo, Cloning, GIFT, and Status of the conceptus.
Indeed the first three headings of this survey expose already the main means of restricting patients' access to ART either by the requirement of marriage , or living together as a (subfertile) couple for the for a minimum amount of time, or indeed by qualifying for the legal terminology of being in a couple, which may mean "heterosexual only" in several countries. The other means of restricting access is financial, either by direct access restrictions which stem from public health policy, or by insurance cover variables. The aim here is not to give a list of countries, with their different criteria for access, but to illustrate such cases. Indeed, the first way of limiting access, with a great deal of disparity in Europe and elsewhere, is to make conditions about the couple's (or "women undergoing treatment") situation before they are legally allowed to have assistance to their plight. The second way is to restrict funding at the national health system level (whatever its name, or mechanism ); this funding may be generally free at the point of use (as in the UK), or refunded with a national insurance system, as in France; or it may indeed be practically inexistant.

**Examples of restriction to access: marital status, information giving, or insurance.**
Whilst in the UK, any woman may be offered treatment as long as the "welfare of the future child" is taken into consideration, in France (heterosexual) couples must be married or live together for 2 years before qualifying for reproductive health treatments. At a time where more and more countries are allowing homosexual marriage, and sometimes adoption, it may seem unfair or old fashioned that DI is not available to lesbian couples in France, leading to the well known "trans border reproductive treatment" (7) seen between France an Belgium for that very purpose. In the same spirit, changes in the anonymity status of sperm donor in Sweden 20 years ago have led to trans border treatment in Denmark by couples wishing to keep the option of an anonymous donor; the UK implemented identical changes from April 1st 2006, and similar exodus may follow (Belgium is of easy access), as well as the more dangerous use of (unregulated) internet sample access. More complex is the question of buying samples from abroad, when conditions of use of samples may be differ from the initial conditions of donation, which renders the consent of the donor nil and void.

Restriction by funding and insurance cover: cases of "double iniquity!" (8)
Several generous systems, allow complete financial coverage ( France, Germany, Belgium (under the recent criteria, which will be detailed in our last presentation today) the Czech Republic ( for IVF only), Slovenia (four cycles), and Israel (until the birth of two children). In the UK, there is one cycle of IVF for all below the age of 40, a ministerial decision taken although NICE had recommended 3 attempts for all women below 40, but in practice we still face a post code lottery, a situation where the waiting is sometimes very long in someareas.
Some countries rely totally on the private sector, with little or no insurance coverage, so the situation is extremely un homogeneous. Indeed the latest EIM figures reported in Human Reprod (9) show the disparity of cycles per million population, and the explanatory comment/discussion highlights the relationship of cycles' incidence to the state's generosity, with Denmark the most generous state in Europe.

**Conclusion**

The majority of techniques of assisted reproduction raise the issue of whether their use should be governed by laws, or be left to individual, professional or institutional ethical judgment. Again to quote Dickens, one may have an ethically ambivalent view of the law in general: "At first view, law may appear a more powerful instrument than ethics, because its provisions are more authoritatively and accessibly stated by political legislatures and courts, more publicly and systematically exposed, more practically enforceable by legal professional and police officers, …and more instrumentally changeable. As against this, however, law .. (without).. ethical dimension, (is) at best crudely pragmatic
and at worst ethically bankrupt, is impoverished in its capacity to educate and inspire ... to distinguish right conduct from wrong. "
The law is a frame ...(for).. ethical choices but ethics frame the limits within which law is voluntarily obeyed and respected as an expression of the values of the society in which it applies".
. Dickens also argues that much of the ART legislation is discriminatory when he says that: "discrimination on grounds of race, religion and, for instance, sex, tends to be legally condemned according to human rights laws applied at international and national levels, but reproductively impaired people have not customarily been regarded as specially susceptible to unlawful discrimination. Legislation is usually proposed in order to restrict access to ART". This was written 5 years ago, and in spite of progress in many states, the example of Italy shows just the opposite.

As for Sheila Mc Lean, professor of medical law in Glasgow, she asserts (10), when commenting on the proposed revision of the HFE Act 1990, which is expected in 2008 at the earliest, that "If we assume, with J.S. Mill, that the sole reason for the state to interfere in the lives of individuals is that their behaviour may harm others, then it is possible to argue that we are currently over-regulated in the area of the provision of assisted reproduction. That is, the provision of treatment services is of no interest to the state, or is of no more interest than the provision of any other therapeutic intervention. Although at the time the Act was being debated there may have been reasons for concern about possible harms, for example to potential children and to women/families, it does appear that ARTs have become a standard part of therapy, and that these fears are unsubstantiated. Certainly, there may still be risks for women associated with techniques such as IVF, but these are risks, which fall within the common law parameters of what adults can lawfully consent to. In a real sense, then, absent evidence that children are harmed by being born as a result of assisted reproduction, there is no justification for the level of intervention currently undertaken by the state in what is arguably private behaviour". One may agree or not with this statement, but I would qualify it with the paramount importance of the welfare of the future child (9 taskforce 12, ESHRE website). That the law may be there to protect the weak and vulnerable is surely an aspiration which may be naïve, but represents our professional and personal responsibility which as a practitioner I prefer to the libertarian attitude which assumes unrealistic equality of citizens present and future.

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**Overview of public funding in central European countries**

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**Objectives:**

- to provide an insight into background (demographic development) of ART reimbursement policy in central europen countries
- to document ART position and results in central europen countries
- to discuss the future of ART in central Europe

The development of methods of assisted reproductive technology (ART) has been a major breakthrough in the treatment of infertile couples. One of the basic human rights is that of a woman to be able to decide when and how to conceive. However, since there are not even two countries where regulations are similar in different countries different regulations induce important implications for patiens.

The introduction of assisted reproduction in daily medical practice posed a number of challenges to health care services, mainly deciding on:

- what resources can be allocated to ART services
- defining who can have access to such services
- striking the right balance between investment in prevention and in cure

The reimbursement – total or partial – of the costs of ART by medical insurance determines the choice (and accessibility) of many couples. Chances for a couple to have access to IVF are therefore variable, sometimes opposite in two countries sharing the border, leading to situations which have generated so called cross-border procreative medicine.

The reasons which have led to such contrasting situations are linked to the social, cultural and moral evolution of each country:

1/ religous tradition : in countries, where Roman catholics are a majority, the Church beeing opposed to IVF, laws are generally restrictive (in central Europe the example of Poland: no reimbursement at all, another example is Italy with its restrictive law limiting the daily practice in assisted reproduction)

2/ historical experience and cultural tradition: in Germany (and other german speaking countries) the memory of philosophy from World War II has led to a very restrictive policy limiting any possibility for embryo selection and embryo research

3/ the politicians: knowing mostly nothing about ART they often wish only to please to potential voters and they are concerned mostly about the cost of the supplies of government services and try to reduce them.

These differences created by the politicians and regulators have logically resulted in a sizeable traffic of infertile couples seeking treatment across the border.

However, current demographic situation in most european countries makes IVF babies more and more valuable and assisted reproductive technologies are becoming also an important political issue in many countries.

Declining birth rates can be seen in many european countries. This can be easily demonstrated on example of czech figures where the decline in birth rates after 1989 was unprecedently quick, unprecedently deep and (still lasting) unprecedently long. On top of that women are postponing their first births what in the near future will unevitably leed to the increased number of couples in their late reproductive age seeking help in clinics specialized in reproductive medicine (Table 1, Table 2).

In the situation of declining birth rates the IVF babies are more and more visible representing a growing group of newborns in many countries (Table 3).
The public funding significantly influences the accessibility (the overall number) of IVF treatments. In most central european countries mostly allowing couples to have a fair access to ART treatments this represents 800-1000 cycles per 1 million inhabitants (Table 4).

***Table 1***
***Births and deaths in Czech Republic 1920-2000***

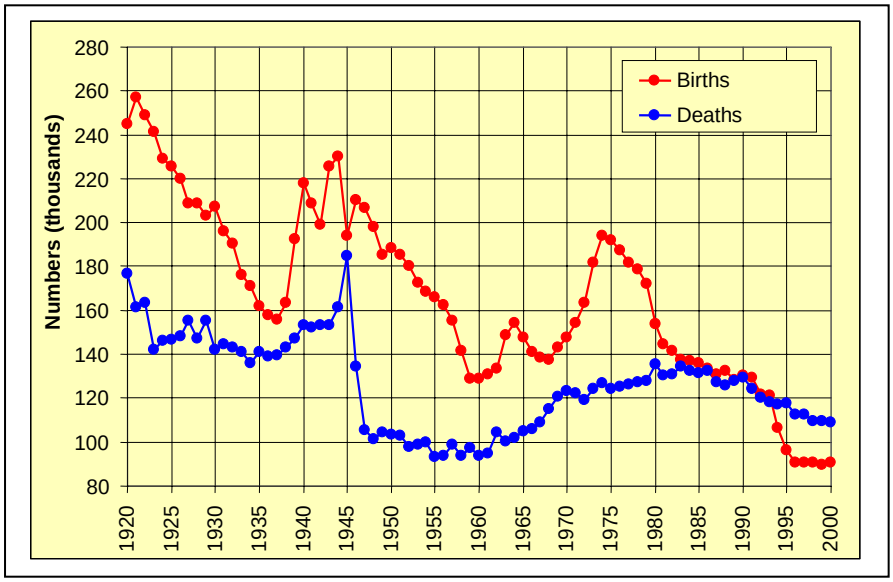
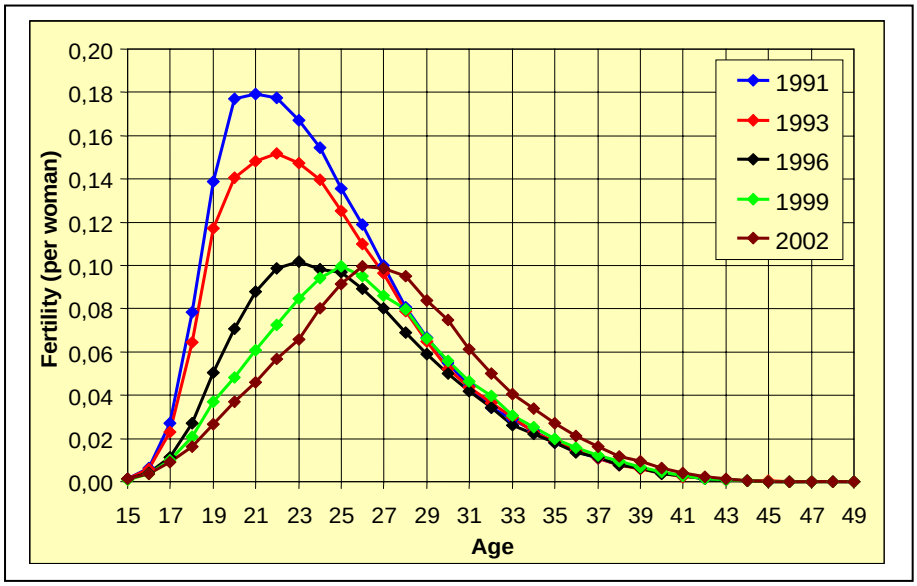



***Table 2***
***Fertility per woman (Czech republic 1991-2002)***



***Percentage of IVF babies in selected european countries***

| **Country** | **1997** | **2000** | **2003** |
|---|---|---|---|
| Denmark | 2,63 | 3,7 | |
| France | 1,21 | 1,4 | |
| Czech republic | 1,97 | | 3,1 |
| Slovenia | | | 4,0 |
| Hungary | | | 1,7 |

***Table 4***
***The numer of IVF cycles per 1 million of inhabitants in selected european countries***

| **Country** | **1997** | **2000** | **2003** |
|---|---|---|---|
| Denmark | 1448 | 1830 | |
| France | 780 | 961 | |
| Sweden | 952 | 1038 | |
| Czech republic | 778 | | 854 |
| Slovenia | | | 998 |
| Hungary | | | 621 |

***Table 5***
***Overview of public funding in reproductive medicine in central Europe***

| **Country** | **Public funding** |
|---|---|
| Czech Republic | Yes, 3 IVF cycles up to 39 |
| Hungary | Yes, 5 IVF cycles |
| Slovak Republic | Yes, 3 IVF cycles up to 38 |
| Poland | No |
| Slovenia | Yes, 4 cycles, after delivery another 4 cycles |

**Conclusions:**
In majority of central european countries (with exception of Poland) IVF is reimbursed partially or totally by medical insurance (by government). Facing the demographic, economic and political necessities, governments are acting to facilitate the evolution of reproductive medicine - in many of central european countries these babies represent a sizeable cohort of newborns. Most of the couples in central Europe have fair acces to ART treatments with very good chance for conception and birth of a heathy child.

**Needs, demand and availability: a short guide to economic jargon.**

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## Introduction

Two features are said to characterise an economic evaluation. Firstly, that it deals with both costs and consequences of activities. Before deciding to pay for a health service, both the price that have to be paid and what form of beneficial outcome will be the result needs to be known. Secondly, that it concerns itself with choices because resources are scares and the fact is that it is not possible to produce all desired outputs and therefore choices of what outputs to prioritise have to be made. These characteristics lead us to define economic evaluation as *the comparative analysis of alternative courses of action in terms of both their costs and consequences*. The specific techniques that are used to make these appraisals primarily differ in the extent to which the benefits are measured and valued.

## Costing

In economic literature, cost is often defined as the consumption of a resource that otherwise could have been used for another purpose. The opportunity to use the resource for this other purpose is lost and therefore, the next best use is called the opportunity cost. In the allocation of resources within health care systems, there are almost always several choices to be made and hence, several opportunity costs. One of the goals for health economics is to help identify these opportunity costs and to provide guidance in the best use of the allocated resources.

The methods related to costing in economic evaluations involve identifying, measuring and valuing all resource changes that occur as a certain health care intervention is carried out.

### *Costs and tariffs*

The difficulty to determine the true value of different resources within the health care sector is apparent because of the fact that many of the resources are not priced in a transparent and competitive market. Depending of the purpose of a study, the level of detail in the costing method can be varied. “Cross-costing”, using global cost-indicators (such as existing tariffs or diagnosis-related-groups) provides better opportunity for generalisation, but at the expense of the level of precision. “Micro-costing” on the other hand includes details of all separate cost-items involved. When tariffs are used, there is need for critical review on whether they reflect true (opportunity) costs or merely are financial parameters set by hospital or health care authorities.

**Perspective and methodology**
Depending on the choice of perspective of a study, different types of costs may be included or excluded. The study can have the perspective of the patient, the health provider or have a societal view. The choice of method for the analysis may also influence the costs to be included. It is for example more common to include costs of patient time and productivity in a cost-benefit and cost-utility analysis than in a study of cost-effectiveness. Another question might be for how long time period costs should be tracked and included. The agreement amongst analysts is that for therapy-specific costs, the follow-up period should not bias the analysis in favour of one intervention over another. The main objective for all of these choices should be to avoid misleading the user of the analysis.

**Cost-identification analysis**
When the effectiveness of competing interventions is already known and found to be equally effective in all respects of importance to consumers, the economic analysis is used to identify the cost for each of the interventions. A cost-identification analysis simply asks the question: What is the cost? Cost-identification studies can also be useful in quantifying the economic burden of a disease or of the treatments that are needed.

**Cost-effectiveness analysis**
In the field of health economics, studies of cost-effectiveness (CE) are the most frequent type of analysis. In CE analysis only costs are measured in monetary units and effectiveness in conventional clinical outcomes such as cases treated and life-years gained. With CE analysis you have the advantage of examining the possibility of improved outcomes in exchange for the use of more resources. In the assessment of new medical technology this fact is of importance and it makes cost-effectiveness the more suitable method to use. It is also the favoured method for the pharmaceutical industry when performing cost analysis in combination with randomised controlled trials for new drugs.

*Outcome*
The purpose of a CE analysis is to maximise the health effects for a given amount of resources, or in simpler words to show which treatment gives the best value for money. The CE study always involves a comparison between two or more methods that can be used to treat the same condition or illness. The outcome in a CE analysis is single, programme-specific and unvalued. This effectiveness measure should, in general relate to a final output. For the analysis to be of value for the audience, the effectiveness measure should also be relevant for the users of the analysis, such as authorities and other decision-makers.

*Effectiveness data*
The availability of effectiveness data is as crucial to the final analysis, as the availability of cost data described above. CE analysis are sometimes criticised more for the quality and handling of effectiveness data, than for the economics. Even with solid effectiveness data available, there may still be a need for judging the relevance of the data before applying it to the cost calculations. Ideally, the data used in economic evaluations should

be data on effectiveness rather than on efficacy. The economic analysis always seeks to estimate costs and consequences as they would occur in clinical practice.

*Mathematical models*
Several mathematical models can be used to perform economic evaluations in complex care processes involving multiple decision points and assumptions (Markov, Monte Carlo, Decision tree). When creating the model, assumptions and estimates play a major role in determining the outcome. It is therefore critical that these assumptions are based on the best available evidence and that bias is minimised. In order for the analysis to be seriously recognised by the audience (e.g. clinicians, health providers, decision-makers) the endpoint must also have clinical relevance and be well described and established in the medical literature.

*Analysis alongside clinical trials*
Another source of data for measurement of effectiveness is when economic analysis is performed alongside clinical trials. This has become increasingly popular and it is now very frequent to incorporate economic components in any randomised trial**.** When performing this type of analysis there are several practical and methodological questions to consider that highlights the differences in interest between the clinical researcher and the economist. These include design of the trial, collection of data on resources of use (costing), collection of outcome data and interpretation and extrapolation of results.

*Sensitivity analysis*
If good clinical evidence is lacking, one solution is to perform a sensitivity analysis to test the economic outcome to different assumptions of the effectiveness measurements. This should also be considered when mathematical models have been used to perform the economic evaluation or when it has been performed alongside randomised trials. The sensitivity analysis is in contrast to classical statistical analysis rarely data driven and it allows for considerable analyst discretion.

*Incremental cost ratios*
In choosing a comparator between mutually exclusive treatment alternatives, most guidelines on performing CE studies recommend using an incremental analysis, i.e. comparing the new intervention to the best current alternative. The incremental CE ratios reveals the cost per unit of benefit of switching from one treatment strategy to a another, whereas the average CE reflects the cost per benefit of the new strategy independent of alternative strategies. To obtain incremental CE ratios, the difference in cost between two options is divided by the difference in effectiveness. This provides us with the number of extra units of outcome we will receive for each extra unit of money spent.

The fact that the CE study does not require an explicit valuation of health in monetary units does not mean that the problem can be totally avoided. Some authors argue that CE analysis is a rather powerless tool. From a societal point of view and in order to utilise the result of a CE analysis in priority settings, either an explicit or implicit decision must be made as to the price per outcome that the society is willing to pay in connection with this patient group. On the other hand, if the differences in clinical effectiveness are very large

between two treatment options, a physician will have difficulties to simply compare the expenditure per unit of improved outcomes to guide clinical decision making.

**Cost-utility analysis**

The same basic data for cost analysis is used in both cost-utility (CU) and CE analysis but the outcomes in a CU analysis are expressed differently. The CU analysis focuses particular attention on the quality of the health outcome, and measures the utility of a particular health status and the length of life lived under that state. This utility is expressed as “quality-adjusted-life-years”, QALY. A QALY is obtained by multiplying life-years with a weight that reflects the quality of those years. Because of the many similarities between CU and CE analysis many authors consider CU analysis to be a subset of CE analysis, but from the societal perspective.

**Cost-benefit analysis**

In cost-benefit (CB) analysis both costs and consequences of a health care project are measured and valued in monetary units. The goal of CB analysis is to identify if the benefits emanating from a project are excessive to the cost of implementing that project, i.e. to identify the projects that have a positive net social benefit indicating that those projects are worthwhile. CB analysis can also shed light on whether the projects concerned are worthwhile when compared to other projects and have thus a larger scope than CE and CU analysis. It can assign relative values to both health and non-health related goals and is able to address questions of resource allocation. In theory it is the most powerful of the techniques for economic evaluation.

In other economic evaluations, the effects that spill over to other persons, positive or negative, in economics known as externalities, can not be captured as they can be in CB analysis. In areas such as transport and environmental economics, CB analysis has been used for many years, and is the most widely used form of economic evaluation. In health care, the need to value human life and quality of life in monetary units is controversial and this requirement can be seen as the major disadvantage of CB analysis.

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# Evidence based cost-effectiveness in IVF

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ESHRE 2006, Prague

ctive single embryo transfer versus double embryo transfer in
tro fertilization *Thurin et al, NEJM 2004, 351;23: 2392-2402*

| | |
|---|---|
| • Sahlgrenska Göteborg | 291 |
| • Fertilitetscentrum Göteborg | 77 |
| • Sophiahemmet Stockholm | 23 |
| • Linköping | 104 |
| • Falun | 22 |
| • Rigshospitalet Köbenhavn | 41 |
| • Herlev Köbenhavn | 16 |
| • Hvidovre Köbenhavn | 9 |
| • Odense | 12 |
| • Haugesund | 50 |
| • Trondheim | 16 |
| Total number: | 661 |

## Aims of the study

1. Equivalence concerning live birth

2. Reduction multiple gestation

# The hypothesis

## 1 + (1) = 2 + 0

### Sample size

- Primary outcome; rate of pregnancy resulting in at least one live birth
- If the true live birth rate in the two groups 1+(1) or 2+0 embryos is 0.30, then the probability is 0.80 that the upper limit of the 95% CI for the difference in probability of live birth between the groups, is lower than 0.10 if 330 patients are included in each group
- Equivalence study
  Equivalence was defined as: The 95% CI for the difference in live birth rates between groups is less than 10%,
  two-sided test

## Results *(ITT analysis)*

| | eSET (1+1) n=330 | DET (2+0) n=331 | p-value | 95% CI for the diff |
|---|---|---|---|---|
| Live births, n (%) | | | | |
| -only fresh | 91(27.6) | 142 (42.9) | <0.001 | |
| -only thawed | 29 (16.4*) | | | |
| -spontaneous pregnant | 8 | | | |
| cumulative | 128 (38.8) | 142 (42.9) | | -3.4 - 11.6 |

*calculated on the number of thawed cycles

## Results *(per protocol analysis)*

| | eSET (1+1) n=307 | DET (2+0) n=327 | p-value | 95% CI for the diff |
|---|---|---|---|---|
| Live births, n (%) | | | | |
| -only fresh | 91 (29.6) | 142 (44.0) | <0.001 | |
| -only thawed | 28 (15.9#) | | | |
| -cumulative | 119 (38.9) | 142 (44.0) | | -3.0 - 12.3 |

# Calculated on the number of thawed cycles

## Results *(ITT and per protocol analysis)*

| | eSET | DET | p-value |
|---|---|---|---|
| Multiple live births, n (%) | 1 (0.8) | 47 (33.1) | <0.001 |

## Maternal complications and caesarian sectio

| | SET n=128 | DET n=142 | p-value |
|---|---|---|---|
| Gestational diabetes | 1 | 5 | 0.22 |
| Pre-eclampsia | 9 | 11 | 1.0 |
| PPROM<br>Prem labour | 1<br>2 | 12<br>22 | 0.003<br><0.0001 |
| Haemorrage before, during and after partus | 21 | 39 | 0.039 |
| Other severe complications | 3 | 5 | |
| Caesarian section | 31 | 49 | <0.0001 |

## Neonatal outcome;gestational age of live born children

| | SET cumulative n=129 | DET n=189 | p-value |
|---|---|---|---|
| Days; mean (SD) | 276 (16.7) | 265 (26.0) | <0.0001 |
| Low gestational age (<37 weeks) n (%) | 15 (11.6) | 55 (29.1) | 0.002 |
| Very low gestational age (<32 weeks) n (%) | 3 (2.3) | 14 (7.4) | 0.07 |

## Birth weight of live born children

| | SET cumulative n=129 | DET n=189 | *p-value* |
|---|---|---|---|
| Gram;mean (SD) | 3439 (721) | 2938 (850) | <0.0001 |
| Low birth weight (<2500g) n (%) | 10 (7.8) | 52 (27.5) | <0.0001 |
| Very low birth weight (<1500g) n (%) | 5 (3.9) | 14 (7.4) | 0.23 |

## Neonatal outcome; children treated in neonatal ward/NICU

| | SET cumulative n=129 | DET n=189 | *p-value* |
|---|---|---|---|
| Treated NICU; n (%) | 23 (17.8) | 64 (33.9) | 0.002 |
| Days;mean (SD) | 4.9 (15.3) | 9.9 (24.3) | 0.002 |

*Thurin Kjellberg A, Carlsson , Bergh C. Randomized single versus double embryo transfer: obstetric and paediatric outcome and a cost-effectiveness analysis. Hum Repr 2006;21:210-16*

- Actual cost IVF treatment, drugs and complications
- Cost of sick-leave during treatment and pregnancy
- Cost maternal health care
- Cost hospitalization during pregnancy and delivery
- Cost of maternal complications after delivery (6 months)
- Cost neonatal care and first 6 months
- Documentation number of dead or severely impaired children and number of children with major malformations
- Questionnaires covering life quality parameters (SF-36;SPSQ)

## Health economy; methods

- Cost-miniminization analysis: medical effect is identical between the studied alternatives. Only costs need to be assessed.
- Cost-effectiveness analysis: Aims to relate the marginal cost of the more expensive alternative to what is gained in marginal health effect.

## Health economy; methods

- Cost-utility analysis: When many different effects occur or the treatments cannot be compared, adjustment of possible increases in life expectancy or life quality is made into ”quality adjusted life years”, QALYs
- Cost-benefit analysis: Costs and effects are assessed in the same unit, i.e. Euro. The measurement of health effects in money creates a number of methodological problems.

## Health economy; cost-effectiveness analysis

- Purpose: maximize the health effects obtained for a given budget.
- All relevant costs and effects related to the investigation during a certain time period into considerarion.

## Health economy; ICER

- When the more costly of two mutually exclusive alternative treatments is also more effective, then an incremental cost-effectivness ratio (ICER) may be calculated.
- The difference in cost is divided by the difference in effect.

## Health economy and the SET study

- To compare the outcomes and total costs to society for two IVF strategies, cumulative SET and DET, until six months after delivery, and to conduct a partial cost effectiveness analysis by relating costs to delivery with at least one live born child.

## Results

| | | SET | | DET | p-value |
|---|---|---|---|---|---|
| | n | mean | n | mean | |
| Total cost maternal health care (Euro) | 330 | 6857 | 331 | 6767 | 0.677 |
| Sum | | 2262952 | | 2239800 | |
| | | | | | |

## Results

| | | SET | | DET | p-value |
|---|---|---|---|---|---|
| | n | mean | n | mean | |
| Total cost loss of productivity (Euro) | 330 | 1602 | 331 | 2359 | 0.022 |
| Sum | | 528711 | | 780706 | |
| | | | | | |

## Results

| | | SET | | DET | p-value |
|---|---|---|---|---|---|
| | n | mean | n | mean | |
| Total cost cost for pediatric health care (Euro) | 128 | 2445 | 142 | 5551 | <0.0001 |
| Sum | | 807036 | | 1837355 | |
| | | | | | |

## Results

| | | SET | | DET | p-value |
|---|---|---|---|---|---|
| | n | mean | n | mean | |
| Total cost for maternal and pediatric health care (Euro) | 330 | 9303 | 331 | 12318 | 0.003 |
| Sum | | 3069989 | | 4077155 | |
| | | | | | |

## Results

| | | SET | | DET | p-value |
|---|---|---|---|---|---|
| | n | mean | n | mean | |
| Total cost for loss of productivity and maternal and pediatric health care (Euro) | 330 | 10905 | 331 | 14676 | 0.001 |
| Sum | | 3598699 | | 4857861 | |
| | | | | | |

## Cost-effectiveness analysis

Total health care cost

SET group 3 069 989 Euro

DET group 4 064 837 Euro

Mean health cost per randomized woman

SET group 9 309 Euro

DET group 12 318 Euro (p=0.002).

## Cost-effectiveness analysis

- The difference, i.e. the additional cost for the DET group : 994 848 Euro.
- The difference in number of deliveries with at least one live-born child: 14
- The incremental cost effectiveness ratio (ICER) 73 307 Euro per extra delivery with live-born child in the DET group.
- Including also productivity losses, ICER 91 702 Euro

## Cost-effectiveness analysis

- A fixed budget for IVF (e.g.4 million Euro, comparable to the total health care cost for DET)
- An extensive list of couples waiting for IVFtreatment.

## Cost-effectiveness analysis

- DET strategy: 331 women treated and 142 deliveries (28 712 Euro per delivery)
- SET strategy: 437 women treated and 170 deliveries (23 984 Euro per delivery)

| | SET delivery/child | DET delivery | DET child |
|---|---|---|---|
| Total costs maternal-neonatal (Euros) | 23 984 | 28 712 | 21 572 |
| +costs for loss of productivity (Euros) | 28 115 | 34 210 | 25 703 |
| Per randomized woman | 9 309 | 12 318 | |

*Thurin Kjellberg et al, Hum Reprod 2006*

## Discussion

- Definition of "effectiveness"; deliveries or number of children?
- What is a healthy child?
- How much is a child worth? For itself? To the parents? To the society?
- Ethical problems when calculating the costs for children with severe impairments.
- Why does society not perceive the outcome of IVF in times of life gain equal to life year gained in treatment of severe diseases?

# Summary

With a defined budget

Demand exceeding supply in IVF treatments

SET superior to DET, when number of deliveries with at least one live born child and complications are considered.

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# Conclusions

- ✓The SET strategy reduces the multiple birth rate dramatically while achieving a live birth rate that is not substantially lower than achieved with double embryo transfer, in women under 36 years of age
- ✓SET reduces the rate of severe maternal complications during pregnancy
- ✓SET reduces the rate of low birth weight babies and the rate of preterm delivery
- ✓SET reduces the need for ward at NICU
- ✓SET reduces severe neonatal complications
- ✓SET seems cost-effective in comparison to DET

# Need, demand and services for infertility treatments

KG Nygren
ECOTASK, SQUART and EIM for ESHRE

ESHRE 2006

## A Research Project:

Health Service Research in infertility
to identify casual factors
behind the large differences observed
between and within countries
of the availabilty of infertility services.

## Holy Bible, Genesis. 30:1

Rachel said unto Jacob:

"Give me children, or else I die!"

## N-D-A developments:

Need
Demand
Services available

## Need

- Need is the basic underlying occurence in a society of unwanted infertility.
- Appr 15%.
- Much higher in some contries.
- Secondary more than primary.
- Variation over time.

## Demand

- Demand comes from need transformed by cultural, social, economical factors and by available alternatives for family goals and personal choices of life.
- Personal neutral, negative or disasterous consequences of remaining childless ("the continuum of consequences")

## Differences of treatment availability

IVF treatment cycles per million inhabitants:

| | |
|---|---|
| Denmark: | 2.100 |
| Sweden: | 1.250 |
| U.K.: | 625 |
| U.S.A.: | 250 |

## Availability of services

- Public (governmental) respons to the level of national confidence in treatments.
- Regulation, restrictive or permissive.
- Allocation of public resources, restictive or generous.
- Available techniques.
- Private sector.

## Trends in the N-D-A chain

- Need.
- Geografical.
- Demografical.
- Cultural.
- Technical.
- Clinical.
- Surveillance.
- Stakeholder´s position.

## Trends in Need

- Increasing infertility for women:
  Life style factors: age, smoking, stress, STD (chlamydia), BMI

  For men: less so ?

## Geographical trends

- Europe 60%
- Japan 10 %
- USA 10%

- Rapid increase in Asia. Less so in Latin America.
- Total 500.000 cycles per year, rapidly increasing

## Demographical trends

- 4 % of all children born in Denmark come from IVF
- 6 % from any medical treament.
- Potential > 10 % ?

- General birth rates declining or low.

## Cultural trends

- Restictive:
- The catholic church
- Latin America
- Italy

- Permissive:
- Northern Europe
- Middle East
- Asia

## Technical trends

- Vitrification
- PGD-S
- IVM
- Soft IVF
- Drugs
- etc

## Clinical trends

- Decrease multiple pregnancies.
- Increase freezeing and thawing.
- SET
- Soft IVF
- Wider indications
- Lower cost??

## Trends in surveillance

- Clinical equipments and software
- National registers
- Regional register
- World reports.
- Economical health research.
- Reginal oversights

## Stakeholder´s position

- Patient groups
- Governments
- NGOs
- WHO
- IFFS, FIGO, ICMART
- The public/ the media

## Conclusions, so far

Factors that drives the Need-Demand-Availability-chain can be identified and differences are indeed large between (and within) countries.

National research to identify and quantify such factors may give strong arguments for the promotion of a much needed increase the availablitiy of infertility services

## An outline of an optimal reimbursement system for assisted reproduction

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### Learning objectives

- **To assess the level of costs of IVF for the patient and/or the community**
- **To learn how much multiples pregnancies are an adverse effect in IVF**
- **To estimate the cost of multiple pregnancies as part of the IVF cost**
- **To learn from the Belgian public reimbursement policy how treatment cost effectiveness can be improved by linking public funding and the multiple pregnancy prevention policy**

### Lecture summary

The Belgian social security system is a sophisticated system based on a reimbursement per medical act for more than 90% of the Belgian population.
Funds for reimbursement are collected from the workers, the employers and from the state.

IVF was part of the system since its introduction in Belgium but in a very partial manner, probably mainly because of the ethical debate within the country. Most of the drugs were already available before the IVF treatment being taken into account and some new ones were introduced and reimbursed. A sort of gentleman's agreement has been made between the non confessional political parties willing to support a treatment perceived as a progress and the catholic political parties reluctant to cover a procedure condemned by the church. So new drugs were refunded, like buseriline, the increase in the sales of gonadotrophins were also supported within the budget and egg collection procedures initially through laparoscopy, later by echography, were reimbursed. But the lab procedures either for eggs, sperm or embryos were at the cost of the patients until recently.

The change of the political majority in the early 2000's transformed the debate from an ethical conflict into a budget problem. The health minister was ready to discuss funding the lab procedures thus making IVF treatment accessibility similar to other medical procedures but at the condition of a cost control.

The agreement negotiated between the medical field and the state included the single embryo transfer debate as a tool to strongly limit multiple pregnancies seen as a frequent cause of low medical quality and as an expensive complication in terms of premature birth, ICU admission and long term brain damage with high sufferings and social costs.

Negotiation were held between health minister's counsellors and members of the college of physicians for reproductive medicine; a quality oriented body hosted by the ministry of health but only composed of clinicians and laboratory physicians representatives from the field. A three steps' procedure has been followed.

Firstly, assessment of costs and objectives

- calculation of cost benefit of various set strategies in terms of MP decreasing
- calculation of costs of ICU stays by samples of hospitalised twins in three ICU of the country
- calculation of costs of the usual IVF laboratory

Secondly, consensus negotiations within the field of IVF centres itself around an acceptable set strategy

- consensus meetings with external undisputable speakers under the auspices of the college of physicians for reproductive medicine
- circulation of the protocol draft for set strategy to the centres for comments and suggestions.

Thirdly, negotiations on the economic aspects of the deal with the Minister representatives.

- globalisation of the laboratory costs
- inclusion of a limitation in gonadotrophin consumption

After three years of efforts, the new reimbursement policy was initiated in July 2003.

In the field, reimbursement induced a significant increase in IVF cycles for the first year of use. The second year data shows a clear stabilisation.

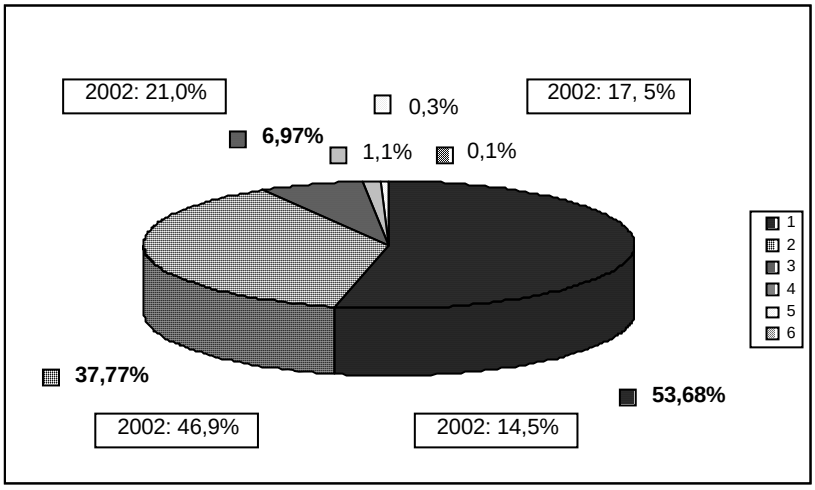
The multiple pregnancy rate dropped from 26% twins to 10% without a significant change in delivery rate.

**Conclusions**

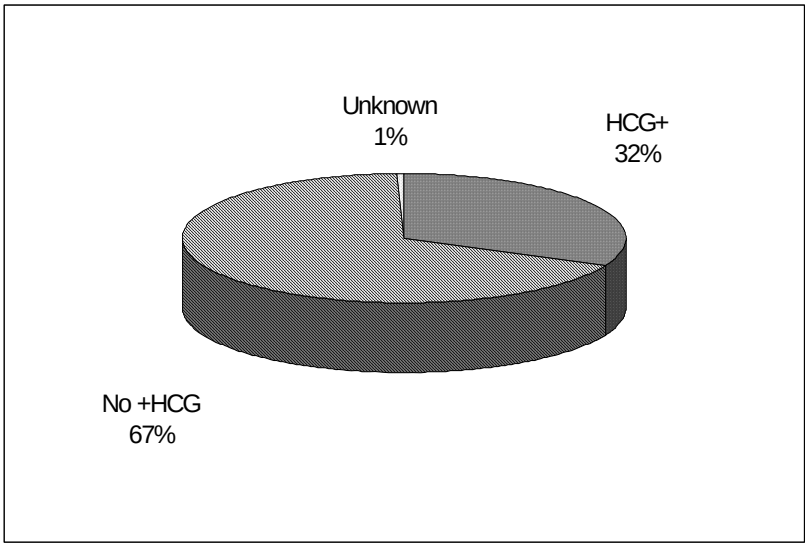
The economic dimension cannot be excluded from quality analysis in reproductive medicine, due to the high costs of the procedure but it may be used as a significant and efficient tool for improving treatment quality.

## DATA FROM THE FIRST YEAR OF THE NEW POLICY

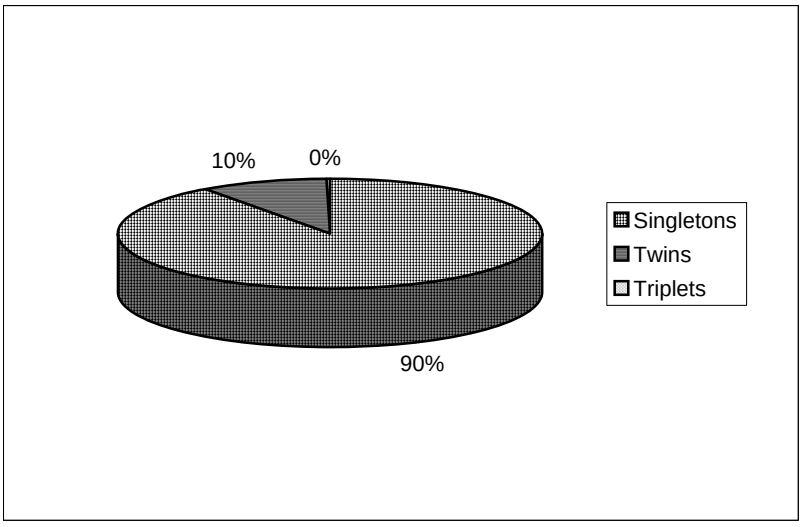
### Number of Embryos Transferred




### Transfer Outcome




### Deliveries

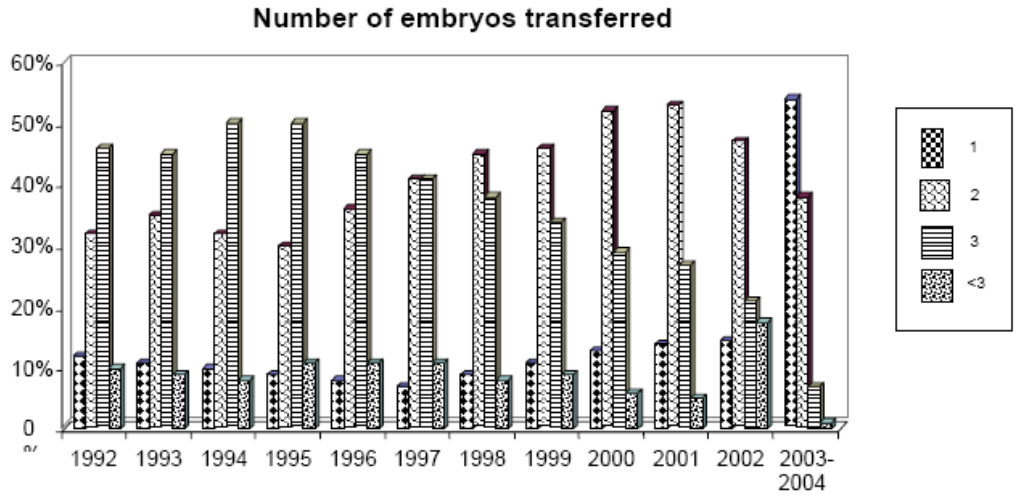



* Source: College of physicians in reproductive medicine. Brussels, February 2006

**Evolution of transfer policy from 1992 to 2004 (%)**

* Source: College of physicians in reproductive medicine. Brussels, February 2006

| No of ET | 1992 | 1993 | 1994 | 1995 | 1996 | 1997 | 1998 | 1999 | 2000 | 2001 | 2002 | 2003-2004 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | 12 | 11 | 10 | 9 | 8 | 7 | 9 | 11 | 13 | 14 | 14,5 | 54 |
| 2 | 32 | 35 | 32 | 30 | 36 | 41 | 45 | 46 | 52 | 53 | 47 | 38 |
| 3 | 46 | 45 | 50 | 50 | 45 | 41 | 38 | 34 | 29 | 27 | 21 | 7 |
| >3 | 10 | 9 | 8 | 11 | 11 | 11 | 8 | 9 | 6 | 5 | 17,5 | 1 |




**Evolution of single and multiple deliveries from 1992 to 2004(%)**

* Source: College of physicians in reproductive medicine. Brussels, February 2006

| Deliveries | 1992 | 1993 | 1994 | 1995 | 1996 | 1997 | 1998 | 1999 | 2000 | 2001 | 2002 | 2003-2004 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Singleton | 60 | 68 | 66 | 71 | 66 | 67 | 70 | 75 | 76 | 73 | 73 | 90 |
| Twins | 35 | 30 | 29 | 26 | 29 | 28 | 29 | 24 | 23 | 26 | 26 | 10 |
| Triplets | 5 | 2 | 5 | 3 | 5 | 5 | 1 | 1 | 1 | 1 | 1 | 0 |