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REPORT

Between politics and clinics—the many faces of biomedical policy in Europe

Analysis of drivers and outcomes of Assisted Reproductive Technologies policy

Volume II: Three country case studies

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Preface

Since the birth of the first "test tube baby" in 1978, several million children have been born through in-vitro fertilisation (IVF). IVF and other assisted reproductive technologies (ART) are now commonly practised and they seem to have been accepted by society in most industrialised countries. But assisted reproduction continues to feature in the media, and it is high on the political agendas in many countries in Europe. Despite European integration and a movement towards evidence-based health policy, ART policy in Europe is highly heterogeneous.

The report is organised into two volumes. Volume 1 presents the findings and analysis of a comparative study on ART policy in three European countries. Volume 2 is an overview of the evidence and a collection of the information collated for these three case studies, and a comparative analysis of the health outcomes in these countries. These case study reports all follow a similar format based on the conceptual model and provide a rich and detailed narrative on ART systems in these countries.

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Glossary of abbreviations and key terms

Agence	Agence de la biomédecine
AI	artificial insemination - the introduction of donor sperm into the vagina, the cervix or womb itself
ANAES	Agence d'accréditation et d'évaluation
ART	Assisted Reproductive Technology/ies - the collective term for all artificial techniques used to assist infertile women and men to conceive children including in vitro treatment (e.g. IVF, ICSI, FER, ED, GIFT, ZIFT) or in vivo treatment (e.g. IUI-H, IUI-D)
CCNE	Comité Consultatif National d'Éthique
Cell	basic unit of all living organisms. Complex organisms such as humans are composed of somatic (body) cells and germ line (reproductive) cells
Chimera	type of interspecies embryo injection created through the injection of single cells from one species into the embryo of another
CNAMTS	La Caisse Nationale d'Assurance Maladie des Travailleurs Salariés
CNT	Central Nazionale Trapianti
Cryopreservation	storage of gametes or embryos by freezing at low temperatures
Cytoplasmic hybrid embryos	A form of interspecies embryo where the nucleus of a human cell is inserted into the egg of an animal that has had its nucleus removed. Genetic material is therefore estimated to be 99.9 per cent human
DHA	District Health Authorities
DPR	Decreto del Presidente della Repubblica
DWP	Department for Work and Pensions

Egg or oocyte	The gamete produced by a woman during her monthly cycle
Egg donation	Donation of eggs by a fertile woman for the treatment of others or for research
Embryo	A fertilised egg that has the potential to develop into a foetus
Embryo transfer	The replacement of embryos back into the female patient
ESHRE	European Society of Human Reproduction and Embryology
ET	embryo transfer
FER	frozen embryo replacement
Fertilisation	penetration of an egg by a sperm resulting in the formation of an embryo. Naturally fertilisation occurs in the woman's body (in vivo), but it can also occur in the laboratory (in vitro)
Gamete	a mature reproductive cell, either a sperm cell or an egg cell
GIFT	gamete intrafallopian transfer - the procedure in which eggs are retrieved from a woman, mixed with sperm and immediately replaced into one of the woman's fallopian tubes, so fertilisation occurs inside the body (in vivo)
Gonadotrophins	hormones that may be used as part of medically induced ovulation
HFEA	Human Fertilisation and Embryology Authority
Hybrid embryos	generic term for embryos created through mixing genetic material of humans and other species
ICSI	intracytoplasmic sperm injection - technique where a single sperm is directly injected into the egg
Infertility	diminished or absent fertility; does not imply as irreversible condition as sterility. No conception in one year or more of regular unprotected coitus (Di Renzo et al., 1996)
IUI	intrauterine insemination – a procedure in which a doctor places a small amount of concentrated and 'washed' sperm directly into the uterus through the vagina and cervix using a catheter
IUI-D	intrauterine insemination with donor sperm

IUI-H	intrauterine insemination with partner sperm
IVF	in-vitro fertilisation - a technique whereby human eggs and sperm are mixed together in a laboratory to achieve fertilisation outside the body (in vitro). The embryos produced may then be transferred into a female patient
LHU	local health units
Microarray	a technology that can be used for selecting the viability of gametes for IVF treatment
Multiple birth rate	percentage of all births in which more than one baby was born
Multiple birth	when a multiple pregnancy actually results in the birth of two or more babies
Multiple embryo transfer (MET)	transfer of two or more embryos into the uterus
Multiple pregnancy	a pregnancy where two or more foetuses develop at one time in the uterus (womb)
Neonatal death	death of a baby within 28 complete days of delivery
NHS	National Health Service (UK)
NICE	National Institute for Clinical Excellence
Nucleus	Part of a cell with the majority concentration of its genetic material
OHSS	ovarian hyperstimulation syndrome - a serious complication following medical stimulation of the ovaries (the female reproductive organ producing oocytes from hormone-stimulated germ cells
OI	ovulation induction
Oocyte	egg cell before maturation, produced by the woman each month in a follicle in her ovary
PCT	Primary Care Trust
PGD	pre-implantation genetic diagnosis - the removal of one or two cells from an embryo to test for specific genetic disorders/characteristics prior to embryo transfer
PGS	pre-implantation genetic screening - the removal of one or two cells from an embryo, for testing to ensure the chromosome number is correct (euploidy) and not more or less than usual (aneuploidy)
RCOG	Royal College of Obstetrics and Gynaecologists

Saviour sibling	the use of tissue typing in conjunction with PGD to select an embryo for implantation which, if all goes well, will become a brother or sister capable of donating life-saving tissue to an existing child
Sex selection	the sex of an embryo is determined using PGD, in order to avoid sex-linked congential diseases
SET	single-embryo transfer - the transfer of a single embryo into the uterus
SSN	Servizio Sanitario Nazionale
Sterility	bearing no progeny (absence of fecundability); incapable of conception (Di Renzo et al., 1996)
Treatment cycle	one complete licensed treatment, commencing with drug administration or first insemination
USL	Unità Sanitarie Locali
Welfare of the child	the social and ethical considerations used when considering the well-being of an individual under the age of 18
ZIFT	zygote intrafallopian transfer - transfer of embryos to the Fallopian tubes for purposes of achieving a pregnancy. Embryos are transferred at the fertilised egg stage
Zygote	the fertilised egg cell through the fusion of the male (sperm) and female gamete (ovum), before division begins

Executive summary

There is a striking variation among policy frameworks for assisted reproductive technologies (ART) in Europe. However, public policy does not take place in a vacuum. The structure and effects of regulatory systems are shaped by the wider environment in which they are set. In the case of a policy domain as controversial as that of ART, it is likely that a wide set of cultural values and ethical considerations will have shaped, and will continue to shape, regulatory frameworks across Europe.

This report aims to shed light on the substantial differences in the way governments have shaped their ART policy, based on case studies of three countries: the United Kingdom, France and Italy. The ART policy frameworks in these countries have been studied in detail from four perspectives: a regulatory context, an economic context, their clinical practice, and the wider welfare and healthcare tradition. In this executive summary, we address the five research questions that have guided this study.

Question 1: What are the differences in the ART policy framework, its underlying goals and context between the three countries?

The case studies uncovered that ART policy frameworks are clearly set within a wider socio-political and economic context, unique to each country. From each of the four perspectives analysed, there are differences in the ART systems between the countries in terms of the rules of access, financing and the extent and nature of regulation. But there are also some similarities. Below, we explore each of these perspectives: regulatory, economic, clinical, and wider healthcare and welfare tradition.

Regulatory context: ART regulation has many faces despite common EU directives

The case studies have showed clearly that there are differences between the countries in their respective rules and conditions of access to ART services. All three countries have enacted legislation to regulate reproductive technologies; in the three countries they span a spectrum from fully comprehensive and liberal access (France), across to more moderate but moving towards liberalising access (UK), to a highly restrictive law (Italy). This legislation refers to the techniques that are allowed, but also to the eligibility criteria for treatment. Since 2004 Italy has recently moved along this spectrum from an unregulated "laissez faire" regime to one of the most restricted policy frameworks in Europe. The UK appears to be the most lenient country with respect to techniques available and also to parental relationship status; the government proposed to drop the "need for a father" and

same-sex female couples are, in law, equally eligible for ART treatment to heterosexual couples.

Moreover, despite all three European countries being subject to a new European directive protecting the quality and safety of human tissues and cells (and two Commission Directives related to implementing the quality and safety directive), including reproductive cells, there are differences between France, Italy and the UK in the implementation of the Europe-wide regulatory context. Italy for example seems to be lagging, particularly in its arrangements regarding the reporting of serious complications.

Economic context: there are considerable differences, but all have a proportion of individual payment

In principle, the regulations for financing ART services in each of the three countries studied are similar, although they differ with respect to how costs are shared between the state and individual couples. Financing of ART services in Italy is dominated by a high level of personal payment. In France ART is largely funded through social security via the national health system. The French society seems more willing than those of other two countries to accept the fact that a comprehensive national healthcare system will inevitably be costly and the cost may be expected to increase. However, as in the other countries, there are additional fees for treatment in private clinics. The audit culture in the UK is reflected in a focus on "value for money", where clinical guidelines aim not only at good clinical practice, but also at cost-effectiveness. Furthermore, autonomous Primary Care Trusts (PCTs) are not legally bound by national guidelines. They have regional autonomy to allocate the healthcare budget on the basis of local health priorities, and hence there is a high proportion of personal payment for ART treatment. Similar regional disparities may also be observed in Italy.

Clinical practice: ART treatment does not always reflect good clinical practice

Despite European integration and a movement towards health policy derived from evidence-based best clinical practice, the differences between the countries in clinical practice and consequent clinical and health outcomes are surprisingly large.

A common trend in all countries is the marked increase in the use of intracytoplasmatic sperm injection (ICSI). Although this technique – mainly used when sperm count is low – is similar to IVF, it is more expensive and does not necessarily have higher success rates. Literature suggests that in Europe ICSI treatment is not always in accordance with good clinical practice. Furthermore, despite good practice guidelines, the proportion of multiple-embryo transfers is still relatively high in the UK and Italy. As multiple pregnancies are associated with adverse health outcomes for both mother and child, the clinical community agrees that a shift to more single-embryo transfers (SET) is desirable. Although there is a shift away from transferring three or more embryos, 2-embryo transfers still dominate clinical practice in the UK. The proportion of multiple-embryo transfers in Italy is the largest of all three countries, and has increased since the introduction of the new law. Italian regulation requires that all embryos created must be transferred to the uterus, despite the increased health risks.

Wider healthcare and welfare tradition: ART has a distinct status, but its policy system is shaped by a tradition of healthcare and welfare services

We have found that the wider welfare and healthcare tradition also contributes to the distinct characteristics of ART policy frameworks. France's generous funding of ART treatment for infertile patients reflects the principles of its Bismarckian welfare system, based on solidarity with disadvantaged individuals. Furthermore, ART services in France are provided within the organisational framework of the healthcare system, and accreditation of infertility clinics is similar to that of other healthcare institutions. However, ART reimbursement stands out as a generous scheme. In Italy's Southern system, access to welfare benefits and social security payments has traditionally been fragmented and coverage has not been comprehensive. The types of benefits vary by occupation, the length of contribution and region. As with ART, limited access to certain services, therefore, is not unusual in the Italian welfare state. However, because of the absence of an explicit designation of infertility as an illness, ART does not fall within the national health service (Servizio Sanitario Nazionale, SSN) in Italy. The status of infertility within the National Health Service (NHS) in the United Kingdom is also ambiguous. Owing to this status, infertility services are characterised by considerable involvement of the private sector, which is otherwise not common in Britain. Other aspects are more in line with its wider tradition. The reluctance to provide general access to ART services reflects the principle of providing a basic protection rather than generous coverage in UK's Anglo-Saxon welfare system.

Question 2: Can these differences be explained by the different contexts in which they have been designed?

Based on analysis of these three countries, we have identified a number of contextual factors that shape the policy frameworks for ART and their outcomes. As this sample consists of the three case studies only, we do not purport to identify any causal relationships; rather, relationships are exploratory.

The reimbursement of ART and the medical practice have a crucial impact on ART outcomes.

In addition to the desire of infertile couples to become pregnant, we see the explanatory factors or drivers of ART policy clustering around the key link between the financing of ART treatment, the medical practice of ART (choice of techniques) and the clinical outcomes. Various factors within a society influence willingness to make ART treatment accessible to a wider population and to reimburse those who use it. The mechanisms and level of reimbursement in turn substantially shape the incentives to use certain medical techniques and adopt certain practices. Effective regulation and implementation of best practice guidelines may, however, limit how far these financial incentives translate into treatment decisions. At the same time, both reimbursement and medical practice are influenced by a multitude of intervening factors in the different contexts.

Definition as an illness is a crucial factor influencing ART policy

The most crucial determinant that influences reimbursement for ART in the three countries has been whether infertility is defined as an illness that is analogous to other medical conditions. This determines whether ART treatment is seen as a conventional medical intervention (France) rather than as a means to support the right to have children

(UK), or a health privilege of the more affluent couples (Italy). In France this biomedical labelling decision led to a full integration of ART treatment into the healthcare system. In contrast, funding of ART is patchy both in Italy and the UK because of the absence of such a label.

A driving force behind this determinant is the power of the country's medical profession relative to other stakeholder groups and the subsequent mechanisms to incorporate stakeholder perspectives in decision-making. Drivers behind the willingness to reimburse ART treatment include: fragmentation of healthcare budget allocation, the attention to accountability and value for money in public sector expenditure, and the guiding principles underlying the social security system (needs-based versus universal healthcare).

Clinical practice of ART is driven by funding, law and clinicians

We found three main driving factors in ART clinical practice. Firstly, funding arrangements drive the practice of ART. For example, multiple-embryo transfers are more common in environments characterised by a high degree of individual payment. Secondly, our review uncovered substantial differences in the ethical regulation of ART treatment, which influences the selection of treatments available, the application of certain techniques and eligibility criteria. The laws are very much an expression of how different stakeholders were able to shape the public debate about the regulation. Most striking here is Italian regulation, whereby all embryos created must be transferred because of the Roman Catholic dictum that life begins at conception, despite the increased risk of multiple pregnancies and births to the health of both mother and child. Finally, the importance of best practice guidelines in the ART system is that they shape medical practice as such. As these guidelines are usually not legally binding, they can be circumvented under the pressure of other strong incentives, in particular financial ones.

Question 3: To what extent have these differences led to variable outcomes in different domains?

The differences between ART policy frameworks have consequences for their outcomes. We have linked the characteristics of certain ART policy systems to the direct and indirect, intended and unintended consequences.

ART policy and the extent of ART provision are closely linked

At its most basic level, legislative restriction of treatment has an impact on access to ART services. Prohibiting access to certain technologies or relating the eligibility for treatment to certain conditions (such as relationship status, gender or age) reduces the number of people who can access ART services. Additionally, the level of funding – and the amount of individual payment – is an important driver of the demand for infertility treatment. The direct outcome of increased ART treatment is that couples with fertility problems have the opportunity to conceive biological offspring. It would be an oversimplification, however, to argue that increasing the provision of ART leads to a positive outcome *per se* as ART cycles may be inappropriate for certain couples, or could have been avoided.

A direct impact of increasing ART provision is the incumbent costs. These costs consist of a number of components. The burden of the direct costs of treatment, depending on the reimbursement regime, is borne by patients and those contributing to the social security system or insurance scheme. The indirect costs include infrastructure costs, equipment

costs, opportunity costs of lost employment, and so on. Furthermore, when ART treatment is successful, and especially when it results in multiple pregnancy, the inherent maternal and neonatal healthcare costs are absorbed by the public or private health system.

The unintended consequences of restriction and individual payment

In the case of Italy, we learned that some regulations which are the result of moral considerations and ethical debates may conflict with what the clinical community considers good clinical practice. While protecting the embryo was the original aim of this legislation, doing so tends to threaten the health of both mother and subsequent children.

Furthermore, we concluded that restriction of treatment and limiting financial compensation for ART may have unintended consequences. Firstly, when certain ART services are not available to couples in their native country, they increasingly travel abroad to undergo treatment in a country where it is available. Although cross-border ART may be seen as an opportunity to enjoy moral pluralism, it raises domestic issues of inequality of access to healthcare as the ability to undergo treatment abroad depends upon the financial means of infertile couples. It also raises complex issues of audit, standards, quality clinical practice, legal remedies in cases with adverse outcomes and accountability.

Secondly, the case studies seem to confirm that a high proportion of personal payment is an incentive to couples to prioritise a high pregnancy rate over best clinical practice. In the UK, for instance, the multiple birth rate is surprisingly high for a system with such a tradition of emphasising good clinical practice.

In addition to these indirect outcomes, ART may have longer term externalities, for example demographic impacts, that have so far hardly been considered in policymaking.

Question 4: How could these outcomes be interpreted, given the context differences?

Even though their outcomes may not all be equally desirable, it is difficult to challenge the foundations of these different ART policy frameworks. They are grounded in their country-specific contexts and are usually the outcome of a legitimate democratic process. However, the implementation of these principles in clinical regulations may be at odds with good clinical practice, as is the case in Italy. The unintended outcomes of Italy's ART system need serious consideration and should be addressed.

ART policy, particularly the definition of infertility, is a complicated matter. Not being able to conceive may be a medical condition, but may also be bad luck. Or, infertility may also be due to wider public health issues such as rising age at first pregnancy, sexually transmitted diseases, obesity, smoking, etc. If infertility is defined as an illness, ART will be imbedded in the wider healthcare framework. Sizeable public expenditure on ART in this context is merely an element of the entire healthcare system. If infertility is not explicitly defined as an illness, as is the case in the UK and Italy, principles for provision of care and access to treatment may deviate from those of the national health system. Countries have different approaches to addressing these issues; in Italy and the UK the decisions to address inequality of access to treatment vary regionally.

If citizens' financial means become an important determinant of their ability to afford infertility treatment, a treatment decision may lead to unnecessary health risks for mother

and child. These risks have to be addressed regardless of the societal context – not simply because in Europe the costs of these risks will eventually have to be met by society.

Question 5: Can we make some broad recommendations to address the challenges of ART policy, while taking account of their context-specific requirements?

We have assumed that a policy framework is largely defined by the context in which it is based. Taking account of these context-specific requirements, we have formulated several recommendations that can help in addressing the challenges to ART policy identified:

- Monitor and evaluate the implementation of the EU tissues and cells regulatory framework to ensure its rigour and equitable distribution across Europe;
- Address the negative consequences (health and economic) of multiple-embryo transfers, and consider compensation of the marginal reduction of success rates following a shift to single-embryo transfer (SET) through a number of strategies, including selection of high quality embryos and oocytes, preservation of high quality embryos, and funding of research into human reproduction and embryology. Implementation of these strategies will depend on the acceptability in local context;
- Cost containment through targeted ART funding, for example target good prognosis patients, means-testing of reimbursement schemes, co-payment. This could involve only subsidising the younger infertile patients as age is the best prognosis factor, or bringing age limits down, or choosing only to fund cycles with a certain likelihood of success (e.g. over 10%);
- European co-ordination of cross-border ART. This could take a similar form as the mediation and allocation of organ donation procedures by the international organisation, Eurotransplant. Furthermore, the extent of cross-border ART should be monitored through improved data collection at European level; and,
- Critically examine ART policy in its wider environment of trends and drivers of infertility (such as the increasing age of motherhood, consumption of alcohol and tobacco, prevalence of obesity, and sexually transmitted diseases and infections), and consider promoting a Europe-wide co-ordinated public health campaign for primary prevention of infertility; for example through detection and treatment of STDs/STIs, prevention of obesity, work-friendly family policies that incentivise earlier motherhood for working women, etc.

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CHAPTER 1 Introduction

This second volume of the report, compiled to accompany Volume I: Synthesis report, provides the evidence base for the analysis provided in the synthesis report. In each country it examines the current state of ART in its clinical, economic and policy context, and looks at ART provision in its national historical and legislative context. It reviews prominent debates and controversies in each country, and concludes by outlining the likely future outlooks for ART provision in each separate nation. The case studies are presented country by country. This is followed by a chapter of direct evidence-based comparison between the UK, France and Italy in the period between 1997 and 2004, using data reported by the European Society of Human Reproduction and Embryology. The report also contains an appendix of comparative tables of ART provision between France, Italy and the UK, based on the analytic framework we have devised for this report.

To avoid bias, we developed a predetermined case study template for the three country studies to facilitate the information collection process. During the process, we found that not all the information we sought to collect was indeed available or accessible to us. This template is constructed based on the main components of our analytical framework in which we distinguish four perspectives or contexts from which to consider ART policy: regulatory context, economic context, clinical context, and the wider health care and welfare tradition. Information collected for the case studies is organised around dimensions for inputs, processes, outputs (short-term) and outcomes (long-term) of key activities. Tables 1.1, 1.2 and 1.3 list the information attributes of this template for the first three perspectives. In order not to lose out on important determinants of the ART system in these countries that are not necessarily captured in one of the three context domains, we included space to report on these additional issues (see Table 1.4). Furthermore, in order to contextualise our research findings, we supplemented the first three perspectives with a fourth one: the healthcare and welfare systems of each country (see Appendices for further details).

In brief, our information and data collection relied primarily on the following:

- a review of the published academic literature on ART policy in the country of interest as well as on the wider healthcare system (using search engines such as PubMed and Google Scholar and referring to hard copies of published articles);
- a review of publically accessible grey literature in the country of interest such as: government documentation (ministries of health and/or competent authorities in

ART, for example the Human Fertility and Embryology Authority, HFEA, and Agence de la Biomédecine); professional society reports and websites; specific hospital or clinic information centre websites; World Health Organization (WHO) datasets and reports; and, in some cases, patient organisation reports or websites;

- an analysis of yearly reports on ART in Europe from 1997 to 2004 by the European Society for Human Reproduction and Embryology (ESHRE); and,
- Eurostat age-specific population data for each country for the same time period as the ESHRE reports.

In the main, we found the most difficult type of information to locate was treatment cost data and/or healthcare budgets with dedicated line items for ART services. In particular, we found little information available on the differences in cost of ART treatment provided by public versus private institutions. Italy appears to be the only country of the three for which we found some data published in a well-known national newspaper. Thus, to supplement our country case studies, we sought expert opinion in each of the countries.

Table 1-1 Information attributes for clinical context

	Dimension	Example indicators
Input	Prevalence of infertility	Estimated proportion of population with infertility problems
	Availability of skilled staff	Number of ART consultants/clinicians per million population
	Capacity of ART treatment	Number of public/private clinics (per million population) Average waiting time for ART treatment Number of IVF doctors
	ART history	Experience with different techniques Medical progress in ART treatment
	Clinical guidelines	Existence of national best practice guidelines Eligibility criteria for publicly funded ART
Process	Patient population	Number of patients reporting to ART clinics
	ART uptake	Number of patients with drug treatments started Number of patients undergoing ART treatment Total number of ART cycles by technique (IVF, ICSI, cryotransfer, etc) [see ESHRE] region age distribution [see ESHRE] citizenship numbers of embryos transferred [see ESHRE]
	Clinical guidelines	Adherence to national (or international) good practice guidelines
Output	Pregnancies	Number of ART pregnancies Efficacy (success rates) by age life-style indicators (smoking, overweight, etc) clinic Embryos transferred
	Pregnancy complications	Incidence of ovarian hyperstimulation other oocyte retrieval complications ectopic (extra-uterine) pregnancies multiple pregnancy miscarriage other fetal reductions etc.
	Births	Number of ART deliveries per year Efficacy (success rates) by age life-style indicators (smoking, overweight, etc) clinic Number of couples/single patients with more successive ART deliveries
	Multiple births	Number of ART singletons born Number of ART twins born Number of ART triplets born Number of ART quadruplets born
Outcome	Birth complications	Number of preterm ART births Number of ART stillbirths Number of ART neonatal deaths Number of ART perinatal deaths
	Neonatal complications	Number of neonates requiring intensive care or special care Number of neonates with low (implausible) birth weight
	Maternal complication	Maternal death ART mothers requiring extended postnatal hospital stay (eg longer than 7 days) Other
	Long-term health effects	Cerebral palsy Blindness Learning difficulties

Table 1-2 Information attributes for economic context

	Dimension	Example indicators
Input	Cost of different ART treatment	Costs of one cycle by technique IVF ICSI FER ED IVM PGD etc Costs of medication
	General healthcare budget	Health expenditure per capita (by category)
	Advertising and donor recruitment regulations	Is it allowed to advertise clinics or recruit egg or sperm donors via national press etc?
	Compensation for egg donation	Price per oocyte
	Reimbursement by state	Proportion of X cycles [See policy context]
	Reimbursement by health insurance	Proportion of X cycles [See policy context]
Process	Uptake of publicly funded treatment	Number of couples seeking and receiving publicly funded treatment
	Uptake of privately funded treatment	Number of couples seeking and receiving privately funded treatment
	Uptake of donor funded treatment (e.g., in the UK, it is possible to receive discounted IVF treatment at a private clinic if you are willing to donate an eggs to another couple (so-called “egg sharing”). In Germany, this is illegal)l	Number of couples seeking and receiving treatment funded through donation of sperm or eggs.
	Expansion of clinics (trends over time)	Number of clinics (with annual numbers of patients) 15, 10, 5 years ago Number of clinics (with annual numbers of patients) to date. Have there been a few growing bigger, or have numbers proliferated (or stayed the same, limiting supply?)
	Market behaviour of clinics competition between clinics etc	Price differences Advertising budgets
	Rewards for IVF clinicians	Fertility specialists’ salaries Other personnel
	Opportunity costs	Number of patient work days lost through treatment
	Cross-border ART (“reproductive travel”) export: native citizens going abroad import: foreigners undergoing treatment	Number of patient cycles with foreign residence Drug treatment for otherwise ”forbidden” techniques
Output	Public expenditure on ART	Total national ART cycle reimbursement Total national ART medication reimbursement Other public expenditure on ART
	Health insurance expenditure on ART	Total sum of insurance expenditure on ART treatments
	Private expenditure on ART	Cost of ART to individuals
	Over and under supply of treatment opportunities	Average waiting time for public clinics Average waiting time for private clinics Estimates of the extend of cross-border ART
	Clinic economics	Reported expenditure (salaries, etc) Reported revenues

		Reported profits
	Drug manufacturer economics	Reported costs Reported revenues by product Reported profits
	Healthcare costs of ART births maternal neonatal	Cost of singleton prenatal care Cost of twin prenatal care Cost of triplet prenatal care Cost of singleton/twin/triplet delivery Proportion of multiple births Premature births Proportion of births with low birth weight Maternal days in hospital Costs of 1 maternal hospital day
Outcome	Long-term healthcare costs	Long-term health effects premature births multiple births maternal complications Neonatal complications
	Tax revenues from ART industry	Clinics Drug manufacturers Staff
	Employment	Clinics Drug manufacturers

Table 1-3 Information attributes for political context

	Dimension	**Example indicators**
Input	History of ART policy and wider biotech policy	Stability and change of regulation approach over time
	Regulation of medical practice	Tradition of evidence-based policy Influence of non-scientific factors in regulating medical practice
	Healthcare system within welfare state public/private insurance	Type of healthcare and welfare state regime Recent reforms
	Society's demand and support religious groups patients insurer clinicians	To what extent is ART an issue? What is the degree of contention in society? How do stakeholder groups influence the debate?
	Media coverage	Salience of the issue on the public agenda Incidence in the media What are the issues covered in the media? Debate supporting or opposing ART Change of debate over time
	Funding available for ART services: public/private	Comparative overall funding Change over time Public budget for ART
Process	Lobbying	Activities of interest groups Parliamentary debates and hearings
	Governmental policymaking Regulatory framework Prioritising Allocating Monitoring	Definition of the issue Responsibility within government Salience of the issue within governmental policymaking Integration into other policy issues
	Decision-making by self-regulatory bodies	Role of self-regulatory bodies Link to government (delegation, negotiation, ignorance)
	Basis of ART regulation	Evidence-base for regulation Other

Output	Organisational design Responsible institutions	Ministry Agency Self-regulatory body
	Regulation of access (eligibility)	Access to techniques Definition of infertility Health and lifestyle requirements Gender and marital status
	Implementation of clinical guidelines	Adherence to clinical guidelines
	Financial coverage	Reimbursement (full, half, number of cycles) Eligibility criteria (marital status; age; sexual orientation)
Outcome	Beliefs and incentives	Attitude towards ART Knowledge of ART Interest in ART treatment
	Scale of ART	Type and number of treatments prohibited/enabled
	Access	Number of patients denied/allowed
	Clinical practice	Type and number of treatments reimbursed

Table 1-4 Other dimensions affecting Assisted Reproductive Technology systems

Possible dimensions
Perceptions of technological and biomedical threats
Public confidence in regulating science
Mobilised religious organisations Perceived need for children (pronatalism)
Public/government demographic anxiety
Awareness of age-related fecundity decline
Patient empowerment/patient group mobilisation
Influence of pharmaceutical/biotechnology industry
Media influence

To gain a better understanding of the country differences, we contextualise our research findings for the first three perspectives by examining a wider perspective of each country's bundle of welfare, social and healthcare policies, using typologies of welfare states developed in the political science literature (see Table 1-5 for a brief overview, and see Appendices for further detail). However, we refined these typologies by stressing the importance of the institutional set up of healthcare systems. The template for information collection on the fourth perspective through characterisation of the wider welfare and healthcare systems is provided in Table 1-6 and Table 1-7.

Table 1-5 Ferrera (1996) typology of welfare states

Typology	Country examples	Explanation
Scandinavian	Norway, Sweden Denmark, Finland	These countries are characterised by universal coverage for the risks of life. The right to social protection is attributed on the basis of citizenship.
Anglo-Saxon	Ireland, United Kingdom	This family of welfare states is also characterised by a highly inclusive social security coverage, but only in the area of healthcare can one speak of fully universal risk coverage. Also flat-rate benefits and means testing play an important role.
Bismarckian	Germany, Austria Belgium, France, Luxemburg, Switzerland Netherlands	The Bismarckian model is build around the social insurance system, an thus the relationship between social security entitlements, a person's labour market status and role within the family (breadwinner or not) is still clearly visible. Contributions play an important role in financing the various schemes. Almost everybody has social insurance coverage through their own or derived rights.
Southern	Italy, Portugal, Spain, Greece	The social protection systems of Southern countries are highly fragmented and, although there is no articulated net of minimum social protection, some benefits levels are very generous (such as old age pensions). Moreover, in these countries healthcare is institutionalized as a right of citizenship. However, in general, there is relatively little state intervention in the welfare sphere. Another important feature is the high level of particularism, with the state directing individual welfare provision with regard to cash benefits and financing.

Table 1-6 Information attributes for the welfare state characterisation

Dimension	Example Indicators
Rules of access	Equality of access/conditional on work/family position/means tested/subject to clientelism
Benefit formulae	Universal/means tested
Financing regulation	Funded through contributions/fiscal revenue
Organisational-managerial arrangements	Single social security system/regionally fragmented

Table 1-7 Information attributes for the healthcare system characterisation

Dimension	Example indicators
Healthcare provision	Public provider mixed (public + private) Private provider
Financing	Contributions Taxation Mixed (public + private) Private

CHAPTER 2 France

This chapter examines the particular case of France. A tradition of a Catholic population, state secularism, public welfare provision, and lavish medical provision are several of the characteristics that spring to mind when considering the case of France. The aim of this study is to describe the relative importance of these and other factors, and to provide an overview of the current provision of ART in France, with a view to informing an overarching analysis of options to integrate ART policies across Europe.

2.1 Current state of Assisted Reproductive Technologies in France

2.1.1 Regulatory context

Infertility[2] is classified as an illness in France, and hence the cost of ART treatment, including IVF, is fully covered through the collectively funded health insurance system.[3] While this medical label does not reflect the broader international concept of reproductive health[4] as defined by the United Nations (United Nations, 1995), we raise this point because of the political interpretation that implicates financing and reimbursement of ART services in the country cases.

In principle, ART is accessible to all, regardless of personal financial means. However, this access is tied to a number of conditions: recipients must be of normal reproductive age (up to the age of 42 years for women), part of a stable couple of two years' or more standing, heterosexual and in proven medical need of the treatment (McGregor and Dreifuss-Netter, 2007, and Agence, 2007b). Single women in France are not eligible to receive ART treatment.

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[2] An important distinction is made between sterility and infertility. Whereas sterility is defined as the impossibility of having a child by natural means, infertility refers to certain problems of sterility which can be resolved by ART. See Agence de la biomédecine, 2008b.

[3] Since 1994, the Public Health Code defines ART as 'the entirety of clinical and biological practices allowing the conception in vitro, the transfer of embryos and artificial insemination, as well as any technique of equivalent effect which allows procreation outside the natural process' (Gèneéthique, 2008).

[4] According to the United Nations (1995), the concept of reproductive health is defined as: "a state of complete physical, mental and social well-being and not merely the absence of disease and infirmity, in all matters relating to the reproductive system and to its function and processes. Reproductive health therefore implies that people are able to have a satisfying and safe sex life and that they have the capability to reproduce and the freedom to decide if, when and how often to do so."

ART is strictly regulated by the law on bioethics (Loi No.2004-800, 2004), which was first drawn up in 1994, and underwent an extensively debated, if not substantial (in the area of ART), revision in 2004 (McGregor and Dreifuss-Netter, 2007). Further revisions are scheduled to take place at five year intervals, and discussion of the 2009 version is under way. The law takes a comprehensive approach to the ethical frontier of biomedicine, dealing, for example, with organ donation and stem cell research as well as with ART.

In France, ART treatment is administered in co-operation between two groups of professionals operating in separate establishments: on the one hand, doctors based at "clinical centres", on the other hand, biologists in laboratories at "biological centres". In order to be able to practise, both types of centres, as well as the professionals working there, require authorisation. Formerly the responsibility of the Ministry of Health, all clinical and biological activities on ART are authorised by the recently established Agence de la biomédecine (hereafter referred to as the Agence).

The Agence directly oversees the authorisation of professionals, whereas centres are approved by the Regional Hospitalisation Agencies (Agences régionales de la hospitalisation), based on site visits and a review of local results. As of 31 December 2007, there were 107 clinical centres and 214 biological laboratory centres authorised to practise ART (Agence, 2008a). Of these, 45 authorised clinical centres in mainland France are private and 58 are public or semi-public (Agence, 2008c). In addition to authorising ART activity, the Agence has also authorised 293 laboratories and multi-disciplinary centres to practise prenatal genetic diagnosis or preimplantation diagnosis (Agence, 2007a).[5]

The law requires that the authorised practice of ART be guided by good practice rules (MES, 1999). The Agence has been charged by the legislature with the mission of inspection to control national concordance with regulations on ART activities and to analyse the potential risks of ART practice. As all clinical and biological centres are required to report outcome figures to the supervising Agence, there is a lively debate and concern over potential discriminatory practices of clinics, driven by competition between centres, which may reject patients with a lower likelihood of successful treatment to improve outcome figures (Desmarescaux, 2003). With the mission of inspection and in an effort to improve both the comprehensiveness and comparability of reported data, the Agence recently began performing systematic quality control through surprise inspections of all authorised centres (MES, 1999, and Agence, 2007a).

Egg and sperm donation for money is illegal in France. Donors, who must remain anonymous and unpaid, are only compensated for the inconvenience of travel, workdays lost and the like. Accordingly, advertisements to recruit donors are not allowed to offer financial incentives. Nevertheless, there are rumours of an active internal black market where eggs are offered for considerable sums, as well as rumours of couples paying for gametes available abroad. There is concern that the supply of donor eggs and gametes will dwindle if the anonymity of donors is lifted, with critics pointing to recent experiences in

[5] A key difference to note between these two types of activities is that preimplantation diagnosis concerns tests on embryos out of the woman's body (with the consequences correlating to non-insertion), whereas prenatal diagnosis involves tests on samples from a continuing pregnancy (with the consequences correlating with a termination of affected embryos/pregnancies).

the UK. Surrogate motherhood is illegal, as is the use of gametes from a deceased partner (Agence, 2008d).

Although anonymous, unpaid donation of both sperm and eggs is legal, a number of conditions still apply: namely, age limit; requirement to have had at least one child; and the consent of the donor's partner (Jones, 1988). The combined use of donated egg and sperm is not permitted; sterile couples can, however, receive embryos donated by another couple having undergone IVF treatment. Further options for surplus embryos (unused by infertile couples) are their destruction or donation for research purposes.

There is evidence of French patients circumventing these rules by seeking ART abroad (*tourisme procréatif*), with high profile cases of surrogate motherhood and post-menopausal conception stimulating the political and public debate of the boundaries and sanctioning of ART practice. In particular, neighbouring Belgium (and increasingly Eastern Europe) is regarded as a favourite destination for cross-border ART ("reproductive travel") on account of its liberal rules on ART techniques: for example, pre-implantation diagnostics and surrogate motherhood. (Mladovsky, 2006). In the 2006 annual report, the recently established Agence was in the course of collecting relevant information to better understand both the volume and motives of cross-border ART by French couples (Agence, 2007a).

The high profile court case regarding the right of the British widow Diane Blood to be inseminated with the sperm of her deceased husband established that in accordance with the Treaty of Rome, patients who go to another EU country to seek treatment illegal at home cannot be prosecuted if the treatment is lawful where it was administered. (*R v Human Fertilisation and Embryology Authority, ex parte Blood*, 1997, and McGregor and Dreifuss-Netter, 2007, pp. 125–126). In France, the principle was exemplified in 2001 by the "*affaire Draguignan*" involving a 61-year-old who successfully conceived with the help of a donor egg, and sperm donated by her brother, implanted at a clinic in the U.S. (Grabinski, 2001). As the procedure had taken place abroad, no charges were pressed. However, as will be explained below, in the case of certain techniques French patients may face severe complications regarding the legal status of the child.

France shows policy coherence in assisted reproduction with the European tissues and cells regulatory framework

At the European level, there are three legal directives concerning human tissues and cells which have relevance to the field of assisted reproduction (see Table 2-1). As of 30 May 2008, progress in France on implementing the European tissues and cells regulatory framework was assessed, in a recent survey (European Commission DG SANCO, 2008), on a number of indicators such as transposition; organisational structure and competences; accreditation; third party agreements; inspections; import/export of haematopoietic stem cells; serious adverse events and reactions; testing requirements; and sanctions.

In France, all three directives have been transposed into national law by Order 2007-613 (26 April 2007), and there are multiple designated competent authorities[6], but only the

[6] France has three designated competent authorities relevant to setting standards for quality and safety in human tissues and cells, which are: (1) Health Ministry; (2) French health products and safety Agency; (3)

Agence de la biomédecine is responsible for human reproductive tissues and cells (European Commission DG SANCO, 2008). Some elements of the quality and safety directive were already transposed into law in France (European Commission DG SANCO, 2007). It is interesting to note, moreover, that the transposition of the Commission Directives did not occur without a range of difficulties[7] in the reproductive field specifically, as outlined by the Agence de la biomédecine in the DG SANCO 2008 recent survey on implementing the European Tissues and Cells regulatory framework. Indeed, the survey provides for 'additional comments' where the Agence notes that the directive "is not fitted to the reproductive field. Some requirements can't be applied to ART activities or are not relevant. There is also a significant financial impact" (European Commission DG SANCO, 2008). The Agence commented in the 2008 survey that one of the key difficulties in the reproductive field is the definition of the processes which have to be authorised. This concern might explain the observed difference between France and the UK in regards to the UK including more activities in the accreditation of reproductive tissues and cells preparation processes (European Commission DG SANCO, 2007).

Accreditation of reproductive tissues and cells establishments in France is based on an inspection process, and there are some inspectors for each region in local Agencies part of the Health Ministry. In 2007, 101 regular inspections were conducted in assisted reproduction centres (one IVF received a license on 31 December 2007) (European Commission DG SANCO, 2008). An earlier survey by DG SANCO showed that all reproductive tissue establishments were fully accredited in February 2006 (which was not case for either Italy or the UK) (European Commission DG SANCO, 2007). Notably, the inspection scheme does not interact or overlap with French systems for the inspection of other activities such as blood, pharmaceuticals etc.

An important indicator of both the implementation of the European Tissues and Cells regulatory framework as well as the government's concern with patient safety is the existence of a system, with well defined criteria, for the reporting of serious adverse events and reactions. Indeed, as we have noted elsewhere, France has an established ART vigilance system (AMPvigilance) and forms for reporting serious adverse events and reactions are available for downloading from the home page of the Agence.

Finally, quality and safety of reproductive tissues and cells is also an issue relevant to cross-border ART. However, France does not appear to offer any figures on gamete imports/exports although the country reported no unauthorised imports or exports of reproductive cells, according to the earlier DG SANCO survey (European Commission

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Agence de la biomédecine. The latter of these is the competent authority responsible for human reproductive tissues and cells (European Commission DG SANCO, 2008).

[7] The specific difficulties with the transposition in France of the three European directives in assisted reproduction include the following: (1) the absence of a unique European coding system for non partner reproductive cells and embryos; (2) the requirement concerning air quality in the laboratory, despite the lack of "evidence of transmission of infectious disease that can be attributed to air quality"; (3) repeat screening for HIV and hepatitis at the time of donation even in partner donation, where the test in France is considered valid for 12 months; (4) the authorization of the processes, when there is no clear definition of what a process is in ART; and, (5) the requirement for inspection of the tissue establishment every 2 years , for which there is a human resource deficit (European Commission DG SANCO, 2008).

DG SANCO, 2007). As of 7 February 2007, France was elaborating a law on the import and export of gametes (European Commission DG SANCO, 2007), but no further information on this issue was provided in DG SANCO's October 2008 survey.

Table 2-1 The European tissues and cells regulatory framework consists of three Commission Directives

Name	Full Reference
Directive 2004/23/EC: setting standards on quality and safety directive.	Commission Directive No. 2004/23/EC of 31 March 2004, on setting standards of quality and safety for the donation, procurement, testing, processing, preservation, storage and distribution of human tissues and cells, *Official Journal of the European Union,* No. L. 294/32, 25 October 2006
Directive 2006/17/EC: technical requirements directive.	Commission Directive No. 2006/17/EC of 8 February 2006, on implementing Directive 2004/23/EC of the European Parliament and of the Council as regards certain technical requirements for the donation, procurement and testing of human tissues and cells, *Official Journal of the European Union,* No. L. 294/32, 25 October 2006
Directive 2006/86/EC: traceability and notification of serious adverse reactions and events directive.	Commission Directive No. 2006/86/EC of 24 October 2006, on implementing Directive 2004/23/EC of the European Parliament and of the Council as regards traceability requirements, notification of serious adverse reactions and events and certain technical requirements for the coding, processing, preservation, storage and distribution of human tissues and cells, *Official Journal of the European Union,* No. L. 294/32, 25 October 2006

2.1.2 Economic context

As noted above, the cost of ART treatments is fully reimbursed by the publicly funded social security system (*Sécurité sociale*), if treatment is provided in a public clinic or hospital. Services in private facilities are covered up to the public amount and then patients pay the difference. Although the additional fee is not reimbursed, many patients can apply for a subsidy by a privately funded supplementary insurance fund (*mutuelle*). Doctors are required to inform patients about all such additional costs before treatment starts.

There are no restrictions on the number of cycles. However, it is recommended to limit IVF and ICSI with embryo transfer to four cycles, if no pregnancy is achieved (Sorenson, 2006b). At present, the public health insurance system funds up to six attempts at artificial insemination, provided that the woman patient is less than 42 years of age (Agence, 2007b).

In 2004, the individual cost of artificial insemination with conjoint sperm was approximately €460 per cycle (University of Toulouse Hospital Information Centre, 2005), and the individual cost of IVF and ICSI ranged between €2,500 and €3,000, depending on the techniques used (FIVNAT, 2005).

Public financing for the social security system in France is guaranteed yearly by the relevant *projet de loi de financement de la Sécurité sociale* (PLFSS) (Ministère du Budget, 2008). National health expenditures are covered by different regimes of the social security system: namely, the general regime (*Régime général*) for employees in industry and commerce, and the obligatory basic regime (*Régime obligatoire de base*) for any person residing regularly in France for more than three months. The majority of the population in France (four out of five people) are covered by the *Assurance maladie* (*Régime général*), which finances 75 per cent of the nation's health expenditures.

As one of four autonomous branches of the *Sécurité social*, the *Assurance maladie* gives financial assistance to beneficiaries (employees) for costly life events related to maternity, paternity, disability, death, work accidents and occupational health risks. Unlike employees in France, foreigners or French residents "*sans resource*" (with limited or no income) benefit from the universal health coverage called *Couverture maladie universelle* (*Régime obligatoire de base*), which ensures that their medical expenses are covered by France's *Aide médicale d'État* (AME). We provide further details of France's budgeted expenditures for the two respective regimes, illustrating the growth in national health expenditures, in section 2.3.2 below.

2.1.3 Clinical practice: a strong emphasis on guidance by best clinical practice

One in seven women of reproductive age will seek consultation on problems of infertility and it is estimated that each year 60,000 couples will consult a gynaecologist for reasons of reproductive difficulty (Cohen et al., 2000). The causes of infertility in France are fourfold: sperm quality (42 per cent of sperm donation candidates are refused); ovulation; female and male genital anatomy; and incompatibility of sperm in the female genital environment (Agence, 2006). Problems with ovulation account for 32 per cent of the causes of female infertility. Male infertility constitutes 10 per cent to 20 per cent of all infertility and 30 per cent of sterility among couples. It is estimated that male infertility leads to over 500,000 IUI-H (artificial insemination with husband sperm), over 200,000 IVF and less than 100,000 ICSI treatments (Cohen et al., 2000). How these numbers translate to per capita provision is explored for IVF and ICSI below.

Legal practice of ART in France is strictly guided by good-practice rules formulated in 1999 and encoded in national law (MES, 1999). Notably, promoting the quality of care provided and the evaluation of medical practice only became visible issues in the mid-1990s (Sandier, Paris and Polton, 2004). These issues were addressed in practical terms by establishing and disseminating a system of practice guidelines, and increasing the emphasis on continuing medical education. Furthermore, as it is considered a medical intervention, ART is operating within a well-provisioned and highly respected medical system. However, there are some areas where implementation of regulation deviates by region or by clinic. These variations may be to the result of lack of clarity about regulation, or by other mechanisms such as economic drivers. Several of these are discussed below.

The latest ART figures for 2006 published by the Agence (2008a) in its 2007 annual report of activities indicate that ART accounted for 20,757.2 live births, representing 2.4 per cent of all 830,288 births (live and stillbirths) registered in France in 2006 – the same percentage as in 2005 (Agence, 2007a, and 2008a). Among the ART live births, 6 per cent were realised after gamete donation (sperm and oocyte) – a decrease of 0.8 per cent from 2005 (Agence, 2007a, and 2008a). Notably, the number of oocyte donations increased nearly 30 per cent between 2005 and 2004, but the total demand for oocyte donation was over 1,343 with 564 new requests over the course of 2004 (Agence, 2007a).

Differences in clinic density among regions favour more populated areas

French couples in need of medical assistance for infertility have, in theory, the choice of seeking treatment in either a public or semi-public hospital, or a private clinic. However, in practice, couples' choices are limited by the geographical distribution of clinical centres

among the 26 regions of France. For example, the densely populated Île de France (Paris) currently accounts for 24 licensed clinical centres in France (n=103[8]), whereas only one centre exists in Limousin and in Bourgogne (Agence, 2008c) – both regions are in the centre of France. Notably, Limousin is the second least populated area in France thus it is not surprising that it has only one clinical ART centre. Furthermore, we examined the most recent numbers of licensed ART establishments (clinics and/or laboratories) to determine if there was a particular geographical clustering. Instead, we found that the regions with the highest numbers of ART licensed clinics and/or laboratories were also the regions whose population is in the top five of the country.[9] Thus, in the aggregate, recruitment can be said to be very homogeneous between ART centres in France, except for the region of Paris (Pouly and Larue, 2007).

Some variation among clinics in clinical practice

Waiting times for ART treatment vary between centres, and by technique (University of Clermont-Ferrand Hospital Information Centre, 2005). The shortest "technical waiting time"[10] is 4 months for artificial insemination with husband sperm, and the longest is 16 months for AI and IVF or ICSI with donor sperm. Between cycles, the typical waiting time can range between 2 to 9 months, depending on the type of ART technique. Due to a severe shortage of oocyte donors, couples requiring donor eggs are advised not to expect treatment in less than *two years*. Some centres have been known to fast track couples when they bring with them an egg donor to the clinic, if not directly to the couple recruiting (University of Clermont-Ferrand Hospital Information Centre, 2005). This practice has been viewed with suspicion due to its discriminative potential, but has not actually been banned in France (Desmarescaux, 2003).

French law limits access to IVF to couples of normal reproductive age (19 to 42 years) in order to prevent IVF-aided conception by women significantly beyond child bearing age, as exemplified by the case of a 65-year-old grandmother successfully treated in Italy (to public dismay). However, there is uncertainty over how this provision should be interpreted in clinical practice, especially with regard to the question of where the line should be drawn for men in couples with a significant age difference, given that a couple's fecundity is less dependent on male age than female age. Individual clinics take different approaches to resolving this question, with some adding the ages of both partners and rejecting couples reaching a combined age of over 100. Furthermore, as the law does not regulate the number of embryos to be implanted, individual clinics are also left to make this decision according to the merits of each basis (Desmarescaux, 2003).

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[8] As of 31 December 2007, the Agence provides an updated list of clinic and biological establishments authorised to conduct medical activities related to ART.

[9] Ile de France (population ranked 1st) has 24 ART licensed establishments; Rhones-Alpes (ranked 2nd) has 11; Provence-Alpes-Cote d'Azur (ranked 3rd) has 8; Nord Pas-de-Calais (ranked 4th) has 6; and Pays-de-la-Loire (ranked 5th) has 7. Population rankings for the top seven regions in highest number of ART licensed establishments were retrieved from Service-Public: Le portail de l'administration française, at http://lessites.service-public.fr/cgi-bin/annusite/annusite.fcgi/loc1?lang=uk (on 11 November 2008).

[10] The University Hospital Centre of Clermont-Ferrand makes a distinction between 'technical' waiting time for receiving specific ART techniques and the waiting time for consultation with the biomedical technicians and gynaecologists of the ART team, which can be, on average, two and three months, respectively.

Another concern in the clinical context of France pertains to sustaining a sufficient supply of qualified doctors and biologists to ensure that ART procedures are accessible in all parts of the country. Some centres are currently debating strategies to counter the risk of much needed specialists migrating to other clinics. A recent action plan to deal with this problem highlights the need for local career opportunities for junior scientists, as well as a maximum number of staff accreditations given that institutional licences to practise ART sometimes hinge on a few individuals (Desmarescaux, 2003, and FC-Santé, 2006).

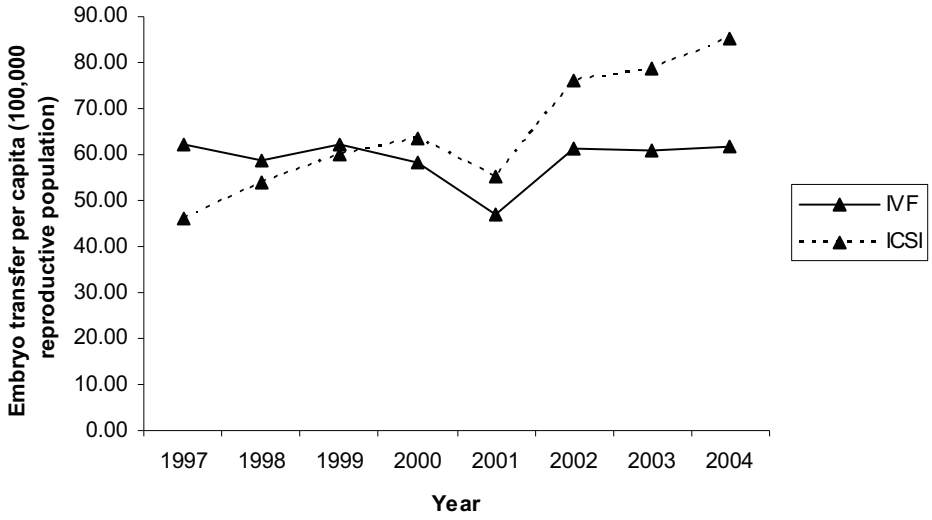
IVF provision has remained relatively stable, while ICSI is on the rise

In France, maternal age at first birth, across all levels of education, is lower than in a number of other European countries (Ekert-Jaffe et al., 2002, and Rendall et al., 2005), and the country's total fertility rate (1.91) is among the highest in Europe. Yet, there remains a sizeable demand for ART treatment among French couples.

Over time, the total number of IVF clinics in France has remained relatively stable, fluctuating between 92 in 1997 and 95 in 2003 and then reaching 100 in 2004 (data not shown). With a high demand for ART from infertile French couples, it is not surprising that the absolute number of embryo transfers in France after ART has increased from 32,684 in 1997 to 43,821 in 2004 (around 30% in 7 years), which is to be expected given underlying population growth. However, such an increase is not an illuminating indicator of ART provision; rather, it is more important to examine the number of embryo transfers per capita (100,000 population aged 15–49).[11]

In Figure 2-1, we see that the trend in embryo transfers after IVF has remained relatively constant whereas the trend for the same period shows a doubling in embryo transfers after ICSI – a similar technique to IVF, where a sperm cell is injected directly into the egg cell, which partly addresses the contribution of male infertility.

[11] To calculate the denominator figure, we used Eurostat age-specific population data for each country for each year during the time period of 1997 to 2004 for reported ESHRE data. Eurostat provides total population figures for each country as well as the proportion of the population aged 15–24 and the proportion of the population aged 25–49. Although the countries we studied require a minimum of 18 years of age to be eligible for ART treatment, we decided that our analysis warranted the inclusion of these two age strata to produce the most appropriate reproductive age population denominator in our subsequent per capita calculation.



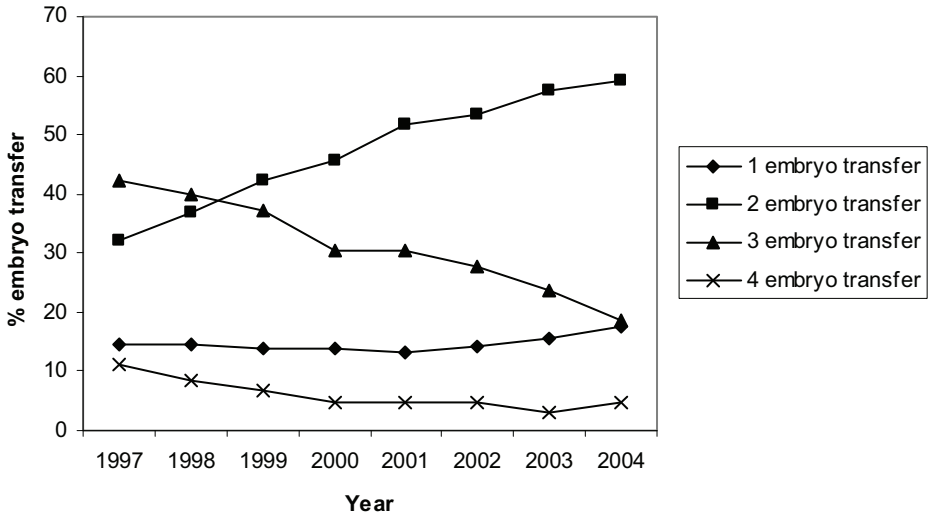
SOURCE: Nygren and Nyboe Andersen (2001a, 2001b, 2002) and Nyboe Andersen et al. (2004, 2005, 2006, 2007, 2008) and Eurostat (2008)

Figure 2-1 Total transfers of of ICSI and IVF per 100,000 reproductive women in France (1997-2004)

Embryo transfers to fewer in number

From 1997 to 2004, there is a consistent decline in 3-embryo transfers (from 42.3 per cent to 18.7 per cent) in France and a parallel rise in 2-embryo transfers (from 32.1 per cent to 59.1 per cent). The two trends intersect early on in this period (1998) and show a large divergence from each other by 2004. For 4-embryo transfer, the trend shows a proportionately greater decrease from 11 per cent towards 3–5 per cent of all transfers after IVF and ICSI. Conversely, France had a moderate rise in the percentage of 1-embryo transfers from 14.5 per cent to 17.5 per cent. On average, France has 1.8-embryo transfers, regardless of which ART technique is used.

The trends illustrated in Figure 2-2 indicate an important change in the process of providing ART treatment to infertile couples as the number of embryo transfers can impact on the risk of higher order pregnancies with all the associated maternal and child harms.



SOURCE: Nygren and Nyboe Andersen (2001a, 2001b, 2002) and Nyboe Andersen et al. (2004, 2005, 2006, 2007, 2008).

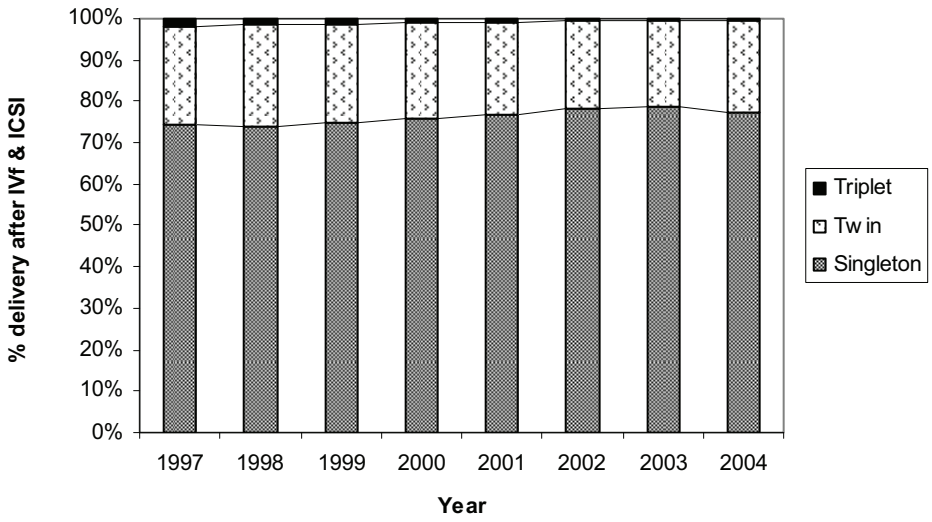
Figure 2-2 Embryo transfers after IVF and ICSI in France (1997-2004)

2.1.4 Assisted Reproductive Technologies outcomes: France shows positive trends in health outcomes over time

A relatively stable proportion of multiple births from Assisted Reproductive Technologies in France

Despite a marked decrease in the proportion of multiple-embryo transfers over the last decade, the decline in the proportion of multiple deliveries (per delivery) – that is, twins, triplets or quadruplets – was marginal. Between 1997 and 2004, as we see in Figure 2-3, the lowest proportion of multiple births was in 2003 (21.30 per cent). The figure in 2006 for ICSI using donated sperm (data not shown) was 18.8 per cent. The more interesting data is that of triplets during the 7-year time period: the proportion of triplet deliveries dropped from 1.81 per cent in 1997 to 0.5 in 2004.

Since half of all twins and ninety per cent of all triplets can be expected to be low birth weight babies (HFEA, 2007a), we can crudely assume that 19 per cent of ART babies in France suffer from these poor conditions – a figure much higher than the country's naturally occurring prevalence. The recent 2007 annual report of the Agence laments the fact that, despite adopting a policy of more prudent embryo transfer in all the centres (around 2 embryos per transfer on average), the percentage of multiple pregnancies remains above 20 per cent (Agence, 2008a, p. 218).

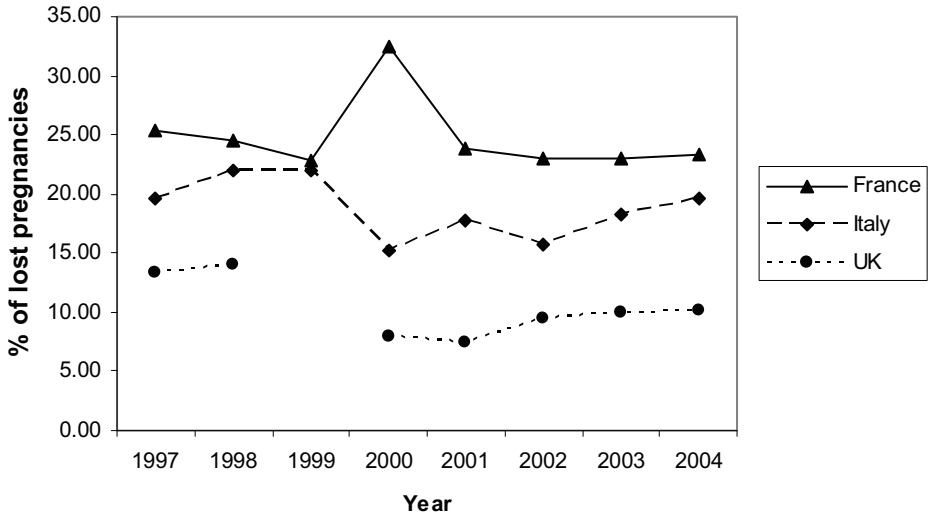


SOURCE: Nygren and Nyboe Andersen (2001a, 2001b, 2002) and Nyboe Andersen et al. (2004, 2005, 2006, 2007, 2008).

Figure 2-3 Proportion of singletons, twins and triplets in France (1997-2004)

Success rates are relatively low and vary considerably between clinics

Of these patients who have sought treatment, 80 per cent have become pregnant from IVF and gamete intrafallopian transfer (GIFT) within four attempts, however 20 per cent to 25 per cent of these pregnancies do not result in delivery (Cohen et al., 2000), which compares unfavourably with both Italy and the UK as seen in Figure 2-4. The figures for France have not changed much in 2006, when the percentage of reported miscarriages and terminations pregnancy per pregnancy ranges from 16.4 per cent to 25.2 per cent, depending on the technique and source of gamete used (Agence, 2008a).



SOURCE: Nygren and Nyboe Andersen (2001a, 2001b, 2002) and Nyboe Andersen et al. (2004, 2005, 2006, 2007, 2008).

Figure 2-4 Proportion of lost pregnancies after IVF and ICSI is highest in France, compared to Italy and the UK (1997-2004)

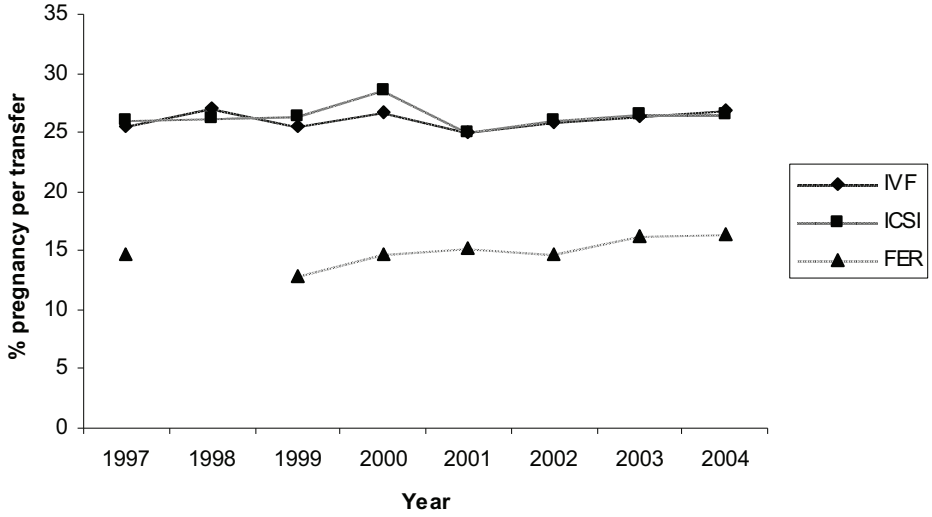
Assisted Reproductive Technologies success rate in France differs between clinics by a factor of 2.5

In a recent analysis of ART results in France, Pouly and Larue (2007) argue that the outcomes in a number of clinics are alarmingly poor. As the authors discuss, these outcomes cannot be explained by either the recruitment of patients or clinical practice. For example, despite the quite homogeneous recruitment between clinical ART centres in France, the success rate differs between the ten best and the ten worst centres by a factor of 2.5: whereas two or three French ART centres contribute nearly 10 per cent of the country's ART pregnancies, a quarter of centres contribute fewer than 14 per cent of all pregnancies. Although a critic might consider that the poorer performing centres have either a higher prevalence of older women or fewer embryo transfers – both known determinants of ART success – the authors comment that pregnancy rates by centre are independent of the mean age and the number of embryo transfers.

In response to documenting some of France's health disparities in its ART system, Pouly and Larue (2007) suggest that research into the causes of such general mediocrity, and their remedies, ought to be a national emergency in France that other countries have addressed. Yet, while an examination of the underlying social determinants of health outcomes is a laudable goal of ART policy research, it is worth considering that the average chance of getting pregnant after IVF, ICSI and FER (frozen embryo replacement) transfers in France has been relatively constant from 1997 to 2004, as shown in Figure 2-5.[12]

[12] The denominator, total embryo transfers, was chosen due to incomplete ESHRE data on the percentage of pregnancies per cycle, which may be more appropriate given that success rate is equal to the proportion of live births to total cycles.

Similarly, France also demonstrates a relatively constant rate of the percentage of deliveries per transfer after IVF, ICSI or FER (except for 2001).



SOURCE: Nygren and Nyboe Andersen (2001a, 2001b, 2002) and Nyboe Andersen et al. (2004, 2005, 2006, 2007, 2008).

Figure 2-5 Proportion of clinical pregnancy per transfer after IVF, ICSI and FER in France (1997-2004)

Furthermore, the comparatively low success rates can possibly be explained by the demographic characteristics of those seeking ART treatment. As funding for infertility treatment is accessible for everyone, income level is not a barrier to treatment. Therefore, the social profile of French ART patients may be more representative of the total population than in countries where patients pay out-of-pocket (partly or wholly). Since the prevalence of, for example, smoking and obesity – factors associated with lower success rates[13] – tend to be higher among lower income groups (Sundquist and Johansson, 1998, and Power et al., 2005), success rates in France could be affected by their patient population.

France's Assisted Reproductive Technologies system sits within a strong healthcare vigilance system

While lost pregnancies are a partial measure of ART success and overall good quality of care (healthy births of babies being the best measure of success), infections are another measure of poor health outcomes after ART. Although France reported no infections after ART between 1999 and 2001, the country shared a large portion of the reported infections after ART in Europe: France had 88 per cent of the total reported infections (199/227) in 2002 and 83 per cent (299/362) in 2004. France reported 95 infections in 2003, but a

[13] Both smoking and overweight unfavourably affect the live birth rate after IVF. The impact of smoking on the live birth rate in IVF treatment is comparable with an increase in female age of >10 years from age 20 to 30 years (Lintsen *et al.,* 2005). For an overview of smoking and fertility, see a report by The Practice Committee of the American Society for Reproductive Medicine (2004). And, for a systematic review on overweight and obesity and ART outcome, see Maheshwari et al. (2007).

proportion could not be calculated as the ESHRE did not report a figure for all European countries reviewed that year (n=28).

We urge caution in interpreting these figures for France because France has a very robust national reporting and learning system specifically for healthcare-acquired infections, created in 1996. Moreover, we found that only in France is there an explicit reference to an ART-specific vigilance system (*AMP-vigilance*) or a procedure for *évènements indésirables* (adverse events and reactions) (Agence, 2007a; Toulon laboratory centre quality assurance web page). Hence, the high numbers of infections reported for ART after the establishment of the Agence in Law No. 2004-800 (2004) is very likely to be a consequence of an established framework of reporting infections related to healthcare provision as a wider health policy intervention to improve quality of care and patient safety in the country.

High Assisted Reproductive Technologies activity in France does not translate to high health complications

As a key measure of complications and over-enthusiasm in ART services is the extent of Ovarian Hyperstimulation Syndrome (OHSS). It is important to note that, although France had an increase in absolute numbers of reported OHSS complications from 188 in 2001 to 297 in 2004 (an increase of similar magnitude to the increase in total ICSI transfers for the same time period), the country has consistently had less than 0.5 per cent of OHSS relative to all transfers (after IVF, ICSI and FER) (Nyboe Andersen et al., 2005, 2006, 2007 and 2008). The low occurrence of this negative health outcome after ART preparation might be explained by the fact that financing of ART in France is covered by the universal healthcare system, thereby relieving the financial pressure on individual couples to maximise their potential for harvesting a high number of eggs (which would increase the risk of OHSS and its complications).

2.2 Contextual factors for Assisted Reproductive Technologies policy in France

2.2.1 Historical overview of Assisted Reproductive Technologies practice and regulation

Before the Bioethics Law of 1994 was passed, ART had been practised under self-regulation for two decades. The earliest procedures were carried out at centres for the study and preservation of eggs and sperm (*Centres d'étude et de conservation des oeufs et du sperme*, CECOS), founded in 1973 to collect and preserve sperm and eggs for artificial insemination with donor gametes, an intervention authorised in the same year. In 1982, four years after the birth of the world's first IVF baby in Britain, Amandine, the first French IVF baby, was born.

In the aftermath of this breakthrough, discussions on how to ensure the ethically sound use of new reproductive technologies took off in professional and intellectual circles, outlining the key areas of dispute. The French government took first steps to address the issue following the creation in 1983 of the pioneering national ethics council: the National Consultative Bioethics Committee for Health and Life Sciences (*Conseil consultatif national d'éthique pour les sciences de la vie et de la santé*, CCNE) (CCNE, 2006). At the request of

the government, the Committee produced an expert report on the subject of ART, which was published in 1986 (Mehl, 1998).

The early years' debate revolved around the moral status of the embryo and the risk of reproductive technologies being used for eugenics, but also around the choice between continued self-regulation and a legislative framework issued by Parliament. However, even though professionals worked to define and follow common standards, self-regulation failed to provide a comprehensive set of rules for all ART techniques. Moreover, as both the government and parts of the medical community favoured legislation, the compass was set for a formal policy (Engeli, 2004).

A preliminary design, the so-called Barzach decrees, was launched in 1988. Among other things, it confirmed the legality of the practice of artificial insemination and IVF. This was followed by the submission of two bills on bioethics to the National Assembly and the Senate. The realisation of these fairly permissive proposals, however, was halted by the 1993 national elections causing the parliamentary majority to shift towards the right. The new government took a step back in the legislative process and, having conducted an extensive consultation of selected stakeholders, drafted a considerably more restrictive law. Once a compromise had been negotiated between the two chambers, the *Loi relative à la bioéthique* was passed in the summer of 1994 (Engeli, 2004). Although the law stipulated revisions every five years, legislative mechanisms delayed the promulgation of the next version until 2004.[14] While this revision of the law brought only minor modifications, it marked a new milestone in the creation of the Agence de la biomèdicine to oversee the practice of ART, as well as organ donation. (Gène éthique, 2005).

2.2.2 Motives for supporting Assisted Reproductive Technologies

The key characteristic of French public support of ART treatments, full coverage of costs through the social security system (*sécurité sociale*) within the limits of specific criteria, reflects the fact that infertility is regarded as an illness, and that France runs a welfare state where the ill are entitled to help. Sufferers – an appropriate term to use since the classification of an illness requires the recognition of possible pathological disorders associated with infertility – are entitled to the solidarity of the general public, which is the governing principle of the *sécurité sociale.*

Before the Bioethics Law of 1994 was passed, treatment of sterility was therefore already fully reimbursed. By the same logic of medical indication, however, individuals seeking treatment for other reasons, for instance the desire to conceive a child within a same-sex female couple[15], do not qualify for any support for, or indeed any access to, ART treatment

[14] For a detailed chronology of events, see La Documentation Français, 'La loi de bioéthique de 2004'.

[15] We distinguish between two different groups of homosexual, or more accurately, "same-sex" couples for the following reasons. First, there are very different needs/wants of female same-sex couples (which can be comprised of both lesbians as well as bisexual female-only partners) from male same-sex couples. In particular, female same-sex couples who want to become parents only require sperm donation (which can be an informal arrangement or via ART). The pregnant woman will automatically be the legal mother and likely look after the baby. By contrast, male-only couples need both an ovum donation and a surrogate uterus/mother, followed by some kind of separation/ adoption arrangements as the baby is transferred away from its birth (if not genetic) mother, thus bringing in other distinct potential child harms (e.g. not breast-feeding). Another difference

(Mehl, 1999, and Engeli, 2004). As McGregor and Dreifuss-Netter highlight, this sets the French approach in stark contrast to the concept of reproductive rights or procreative liberty used in debates about access to ART in the United States (McGregor and Dreifuss-Netter, 2007, p. 126).

The dominant idea that ART exists to cure infertility within stable heterosexual couples (rather than to provide a path to parenthood for all) explains why the current legal framework is at the same time comparatively exclusive, and comparatively generous. Current discussions of the next revision of the Bioethics Law have put the issue of same-sex couples' rights to parenthood via ART back on the negotiating agenda. However, while equality may turn out to be a potent driver for liberalisation, demographic motives, that is, the prospect of achieving more overall births through ART, have not been a prominent feature of the debate.

2.2.3 Determinants of the current legislative framework

The current Bioethics Law is the result of the political processes described above, but its roots reach far beyond the parliamentary process. The current legislative framework for ART in France is the direct heir of previous frameworks, filtered by restriction. As Engeli points out, "current regulation on ART does not contradict previous rules, but considerably enlarges their restrictive scope" (Engeli, 2004, p. 146.) The first policy design of 1988 was substantially informed by existing self-regulation. In all subsequent iterations and revisions, this self-regulation's basic premise, that artificial insemination and IVF should be allowed, was never challenged. (Engeli, 2004, p. 146).

The current ART legislative framework evolved within a wider political environment of existing regulation in related fields, and was informed by fundamental concepts developed in the context of other, previously debated issues. Importantly, legislation on abortion already had to deal with the question of how to consider the embryo, whose endowment with current legal status would have conflicted with the lawfulness of terminations (Law on the Interruption of Pregnancy, 1975, and Engeli, 2004, p. 146).

The banning of particular ART techniques – both surrogacy and posthumous insemination (or embryo transfer) – can be similarly traced back to already accepted norms and legal practicalities. From a normative perspective, the ban on surrogacy relates directly to the non-negotiable concept of human dignity, which was confirmed as a constitutional value by the *Conseil constitutionnel* in 1994. Surrogacy is viewed as a form of exploitation because the surrogate mother functions as an instrument to produce another couple's child; the practice therefore infringes the surrogate's human dignity (McGregor and Dreifuss-Netter, 2007, p. 120). From a legal practice perspective, the concept of surrogacy is incompatible with established rules on parenthood and inheritance in France. As already discussed, French law considers the woman giving birth to a child as its biological mother, even if she is a surrogate and not genetically related. Couples with a child produced through surrogacy therefore are not able to register the child as their own, nor are they able to adopt it as this would be considered to be a fraudulent action (McGregor and Dreifuss-

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between the groups is the fact that, while there may be a societal shift for female-only couples, one can challenge the view that the same has occurred for public acceptance of male-only parenting via ART.

Netter, 2007, pp. 120–121). As a couple involved in a high profile case of this kind pointed out to France's *Le Monde* (1 November 2006), surrogacy children therefore are "*sans papiers*", a term used for illegal immigrants (Chemin, 2006).

Furthermore, the ART technique of posthumous insemination has also been banned in France because it conflicts with the moral refusal in France's Bioethics Law to use ART to create orphans (a term also used in France for children with a surviving parent). In addition, this technique is banned to avoid the practical legal problem of settling inheritance claims when additional offspring may be born some time after a parent's death. It was this latter consideration which in 2004 decided the French Senate against allowing the transfer of IVF embryos to the widowed Madame Pires, after the proposition had been accepted by the National Assembly (Cour de cassation, 1996; McGregor and Dreifuss-Netter, 2007, p. 122).

2.2.4 Key players

Current legislation on ART was substantially informed by previous practice, as well as the extensive public consultation preceding the 1994 design. As Engeli points out, the selection of groups for consultation contributed significantly to the configuration of influential actors within the designing process. This selection may have effectively facilitated consensus building by privileging traditional societal actors such as religious leaders and professionals while excluding non-traditional interest groups such as feminists or same-sex female couples as well as ART patients themselves (Engeli, 2004, pp. 149–50).

The medical profession in France is an important force driving ART regulation as it currently exists in the country. In recognising this key actor, two important facts must be highlighted. First, the medical profession enjoyed a special position of authority in the designing process because its self-regulation had already delivered a legislative blueprint for the handling of ART. Second, as France has no single body representing the medical community, various associations and hierarchical levels were given their own voice in the consultation (Hassenteufel, 1997). Thus, the presence of the medical profession as a whole was enhanced, but there was also disproportionate influence given to smaller medical groups such as ART specialists (Engeli, 2004, pp. 149–50.)

Not surprisingly, a key point of disagreement among these groups revolved around the degree of autonomy to be retained by the profession in ART provision. To the degree that all the groups were active in the consultation process, this served as an important catalyst for compromise and consequently resulted in a relatively flexible proposal for ART regulation. However, medical practice was subsequently put under closer supervision under the more restrictive approach adopted by the right-wing government which followed in 1993 (Engeli, 2004, p. 149). Such conservative government supervision across the profession contrasts with the more permissive approach of the socialist leadership of the previous legislature favouring medical self-regulation, whereby the means of representation for legitimacy of clinical practice was *de facto* selective of dominant experts and stakeholders.

More substantively, the views on ART of the political left and right contrasted not only in terms of the degree of medical autonomy, but also in terms of the professional freedom to conduct research on the embryo. While the left wing was willing to allow such research, as

well as pre-implantation diagnostics, the right favoured strict controls or even, within the Catholic right-wing camp, an outright ban of such practice.

The latter identifies the second key player in ART in France: the Catholic religion. Even though polls suggest that the flock of the avowed faithful has been diminishing is recent decades – while in the 1990s, 80 per cent of the population declared themselves Catholic, the number had dropped to 51 per cent in early 2007 (CSA, 2006) – the Catholic Church remains France's leading religious institution. Deeply opposed to the practice of ART, it participated in the discussions preceding the design of the Bioethics Law, and continues to play a prominent role in the public debate of bioethical issues, and indeed challenge the current regulation.[16] Recently this was evidenced by a much publicised controversy about the 2005 *Téléthon*, a media fundraising event whose proceeds were partly destined for embryo research (Slama, 2006).

France's particular combination of traditional Catholicism and low individual religiosity has been identified as the reason why rules on embryo research are relatively strict, and yet it was possible to agree to a comprehensive Bioethics Law. This unique feature of France (low individual religiosity in a country with a strong church presence) marks its divergence with other countries, like the U.S. (or equally Italy), where high individual religiosity is believed to have stood in the way of reaching a formal agreement on legislation (Fink, 2004, and 2005).

Finally, a third key player in ART in France is the country's ethical authority, the aforementioned CCNE. The CCNE played a powerful role; this novel institution had already been approached for expert advice in the earliest stages of state-led scrutiny of ART regulation. An important contribution to the first legislative proposal was the definition of the embryo as a potential human being, as opposed to the Catholic Church view as a full human being. The CCNE has continued to deliver important input in the evolving debate of ART regulation, reflecting new questions and recent controversies, such as giving ongoing opinions in the context of revisions of the Bioethics Law to reflect newly emerging points of ethical controversy and uncertainty. Thus, in early 2006, the CCNE published a comprehensive report on the subject of the anonymity of gamete donors (CCNE, 2006).

2.2.5 Channels of influence

As has been shown, current ART regulation in France has been shaped mainly through the channels of professional fora, public consultation, the CCNE and the political process at large. Regarding the role of political parties, and by extension the electorate, candidates' positions on ART have not been a priority issue in election campaigns. Rather, these positions derive from more widely advertised attitudes and values across the political spectrum. Nevertheless, it should be noted that in the recent presidential elections, all three candidates endorsed the principle of anonymous, free gamete donation (Hasendahl, 2007).

[16] The French Catholic catechism concedes that research to cure infertility is desirable in principle, but it condemns the practice of ART. Use of such techniques is described as 'gravely indecent' (*gravement déshonnête*) when involving a donor or surrogate, and still 'morally impermissible' (*moralement irrecevables*) within a married heterosexual couple, as it detaches conception from the loving act of the parents, and allows technology to dominate over the destiny of the human being, Catéchisme de l'Église Catholique, no. 2,374–2,378 (Intratext, 2008).

In addition, Ségolène Royal, the socialist candidate, called for a re-examination of the Bioethics Law to consider the access of same-sex female couples to ART (Mallevoüe, 2007).

Interest groups have been actively working to bring about shifts in public attitude, but their actual influence is difficult to quantify. Media coverage of individual experiences pushing the boundaries of traditional and legal norms, such as same-sex female partners suing for the right to paternity leave, or couples returning to France with surrogacy-produced children, has certainly raised public awareness of the reality beyond the margins of the current system (Chemin, 2006, and Le Monde, 2007).

2.3 Healthcare and welfare systems

2.3.1 Regulatory

France has encoded in law the provision of healthcare services to its citizenry. France enacted a national health insurance (*Assurance maladie*, or *Régime général*) in 1928, which retained the earlier mutual aid funds[17] of craftsmen and workers as the carriers. Although many countries experience a common problem of resistance from the medical profession when statutory health insurance is designed and enacted, the French national health insurance in particular has had a constant and ongoing struggle between the health insurance system and the medical profession due to the fact that the doctors in France have been historically individualist and secretive (Glaser, 1994). This latter point suggests that the influence of the medical profession groups in designing ART regulation in France was to be expected.

Ranked number one in the world by the WHO (WHO, 2000), the French healthcare system is characterised by the complexity that has resulted from many political compromises made in order to achieve incremental change in a system that is fundamentally based on three principles: the principle of social solidarity, the principle of healthcare as a public good, and the principle of a liberal, pluralistic attitude towards healthcare.

In brief, the political compromises produced a governmentally enacted and administered arrangement with a complex structure. Based on the French mood after the wartime trauma of social solidarity and universal participation, the comprehensive legislation of the postwar government in 1945 resulted in health coverage of almost the entire population of France under a general regime[18] (for all employees). The legislation also obligates the population to join a sickness fund and to pay a percentage-of-earning payroll taxes. The

[17] As in Germany and the rest of Europe, craftsmen and workers had many mutual aid funds that provided cash benefits during unemployment, illness and retirement. Some maintained health centres and employed doctors, but most reimbursed subscribers after visits by independent physicians.

[18] The general regime includes hundreds of local offices (*caisses d'assurance maladie*) throughout France. The local offices enrol members, receive the money from the special social security tax machinery, pay the hospitals for members' stays, reimburse the members who have paid doctors, monitor providers in the locality, and represent the members in case of disputes (Glaser, 1994). As Glaser notes, the *caisses d'assurance maladie* are public corporations governed by boards, the evolution of which is described in further detail in his article.

elderly, disabled and unemployed remain with full coverage and normal benefits. Premiums are deducted from their cheques. However, one compromise led to the creation of special regimes that apply to the self-employed, farmers and farm workers, railroad managers and workers, miners and several others – with their own rules about taxes and benefits.

Overall, the organisation and management of insurance schemes for social protection and healthcare provision in France are mainly governed by unions and employer organisations. Importantly, the organisational structure and management of France's healthcare system was profoundly affected by the Juppé reform of 1996, which introduced parliamentary control over the healthcare system and its resources as well as reinforcing the role of regions with new institutions created at the regional level (Sandier, Paris and Polton, 2004).

France, according to Glaser (1994), has more cost-sharing than any other national health insurance system – the sickness funds reimburse the ambulatory patient less than the primary care doctor's charges and hospitalisation requires a charge. Perhaps not surprisingly, then, France has a very large private insurance industry (about 3,000 exist today), whereby the mutual aid funds (the *mutuelles*) from before World War II have survived by filling new niches (eg the payment of all patient cost-sharing). In France, 100 companies specialise in life insurance, which offer health insurance (supplemental coverage) as well as coverage in work accidents, auto accidents and short-term disability.

The insurance carriers in France are diverse. For example, six are nationalised companies legally owned by the French national government, 58 are for-profit stock companies and 16 are mutual insurance companies. The six nationalised companies are very large and sell half of France's life insurance.

2.3.2 Reimbursement and financing

The key elements of the French welfare state are financed through social insurance contributions that are paid as a percentage of the salary and shared between employers and employees, with the employers paying a larger share. These contributions are supplemented by a generalised social insurance contribution not belonging to the individual schemes and taxes in cases of overruns, as guaranteed yearly by the relevant *Projet de loi de financement de la sécurité sociale* (PLFSS) (MBCF, 2008).

National health expenditures are covered by different regimes of statutory health insurance. The three main schemes are:

- The general scheme (*Régime général*) covers employees in commerce and industry and their families (about 84 per cent of the population) and the universal disability insurance (*Couverture Maladie Universelle*, CMU) beneficiaries (estimated on 30 November 2001 to be 950,000 people or 1.6 per cent of the population).
- The agricultural scheme (*Mutualité sociale agricole*) covers farmers and agricultural employees and their families (about 7.2 per cent of the population).
- The scheme for non-agricultural self-employed people (*Caisse Nationale d'Assurance Maladie des Professions Indépendants*,CANAM) covers craftsmen and self-employed people, including self-employed professionals such as lawyers (about 5 per cent of the population) (Sandier, Paris and Polton, 2004).

France is the fourth highest-ranking country in terms of national health expenditures (Minogiannis, 2003). Total expenditure on health per capita is 3,406 (Int.$, 2005)[19] and total expenditure on health as a percentage of GDP (2004) is 11.2 (WHO, 2008a).

As described above, there are two main types of healthcare coverage in France: the comprehensive and basic coverage (*Assurance maladie*) and the supplemental coverage (through life insurance). In terms of the sources of financing, in general, sickness funds which administer the comprehensive and basic coverage of healthcare pay for almost 74 per cent of total health expenditures; supplemental coverage accounts for another 6 per cent of expenditures; and out-of-pocket payments contribute another 19 per cent. Direct government payments for healthcare services are around 1 per cent (Minogiannis, 2003).

Public financing for the social security system in France is guaranteed yearly by the relevant PLFSS (MBCF, 2008). National health expenditures are covered by different regimes of the social security system: the general regime (*Régime général*) for employees in industry and commerce, and the obligatory basic regime (*Régime obligatoire de base*) for any person residing regularly in France for more than three months. The majority of the population in France (four out of five people) are covered by the *Assurance maladie (Régime général)*, which finances 75 per cent of the nation's health expenditures. As one of four autonomous branches of the *Sécurité social*, the *Assurance maladie* gives financial assistance to beneficiaries (employees) for costly life events related to maternity, paternity, disability, death, work accidents and occupational health risks. Unlike employees in France, foreigners or French residents *sans resources* (those with limited or no income) benefit from the universal health coverage called *Couverture maladie universelle (Régime obligatoire de base)*, which ensures that their basic medical expenses are covered by France's *Aide médicale d'État* (AME).

Table 2-2 summarises the budgeted expenditures for the two respective healthcare regimes of France's social security system which well illustrates the fiscal growth in national health (and welfare) expenditures. We note, however, that while there is indeed a rise in the budgeted expenditures, the proportion of health expenditures to the total remains effectively constant over the three years, at 43 per cent and 50 per cent for the *Régime obligatoire de base* and the *Régime général*, respectively.

Table 2-2 Summary of budgeted expenditures for France's social security system

	Régime obligatoire de base de sécurité sociale		*Régime général de sécurité sociale*	
Date	**All branches**	**Maladie branch**	**All branches**	**Maladie branch**
2006	€389.2 billion	€166.0 billion	€286.6 billion	€143.4 billion
2007	€406.9 billion	€173.4 billion	€299.6 billion	€149.7 billion
2008	€422.5 billion	€179.6 billion	€311.1 billion	€155.2 billion

SOURCE: MBCF (2008).

Every hospital in France has its own unique budget and, because of private clinics, France has a dual system of hospital finance. During the 1980s, France enacted "global

[19] International dollars refer to purchasing power parity exchange rates (to the dollar) and these are used by the WHO to standardise country-specific healthcare expenditures, measured in 2005 as the reference year; hence, Int.$ 2005.

budgeting"[20] for all public hospitals and for a few non-profit charitable organisations that were "assimilated into the public services" (Glaser, 1994). Each year, then, each hospital fills out a line-item report describing its past and current services and costs, and it requests a total budget for next year. A local representative of the Ministry of Health screens the prospective budget carefully based on the assumption that all hospitals exaggerate their needs and clinical plans and overstaff wastefully.[21] The local sickness funds then send lump sums to the hospitals every month, proportional to their shares of the patient numbers that they cover.

By contrast, the private clinics are regulated for safety but have much more discretion in their operational costs and budgeting. That is, they do not submit cost reports and prospective budgets to government regulators but rather negotiate their rates with the general offices of the *Caisse nationale de l'assurance maladie des travailleurs salariés* (CNAMTS; headquarters for the general regime). Unlike for public hospitals, the sickness funds are not obligated to ensure that private clinics operate within the national health insurance's yield of payroll taxes.

2.3.3 Clinical practice

In 2006, physician density (per 10,000 population) in France was 34; nursing and midwifery personnel density was 80 and pharmaceutical density was 11 (WHO, 2008b). Yet, despite universal access to care, disparities in the distribution of doctors at regional level have existed in France for a long time with the density of medical capacity for specialists varying from 1 to 2.2 without any justification in terms of different health needs (Sandier, Paris and Polton, 2004). The north of France (with the exception of Paris) has a lower supply of doctors than the southern regions.

In terms of promoting quality of care in the hospital setting, for example, the 1996 Ordinances in France obligate all healthcare institutions to be accredited in order to continue providing medical treatment and services. This accreditation procedure, carried out by the Agence d'accréditation et d'évaluation (ANAES), is an external evaluation of the quality and safety of the healthcare provided within an institution, based on the implementation of a certain number of procedures and compilation of quality indicators. In addition, France has a national reporting and learning system to improve patient safety in hospital settings by greater vigilance through systematic analysis of hospital associated infections.

Another clinical practice issue of relevance to understanding the health outcomes for ART services in France is the concern of future shortage of licensed ART staff. In general, the number of doctors in France has more than trebled since 1960 and the numbers have

[20] The purpose of replacing the per diem by global budgeting in France was to discourage long hospital stays and discourage the avoidance of expensive admissions. According to Glaser (1994), the new method seems to have succeeded in that long-term patients, for example, are no longer kept in the acute beds of hospitals but are transferred to the associated long-term care hospitals or are treated at home.

[21] It is worth noting that national and regional regulators screen hospital budgets, examining the finances and staffing of each type of hospital. It is increasingly the case in France that the ministries in Paris send strict expenditure targets so that the country's national health insurance can operate within the yield of payroll taxes and ultimately keep the national government's budget from running excessive deficits (Glaser, 1994).

stabilised since implementing a policy to reduce the *numerous clausus* (closed number). Moreover, despite the forecasting of a significant decrease in the numbers of doctors generally, the intake of students in some specialities known to have difficulty in recruiting doctors, in particular obstetrics and gynaecology, has been raised once again (from 3,850 in 1998 to 4,100, 4,700 and 5,200 in 2002–2003, depending on the speciality) and may be raised even further in the future (Sandier, Paris and Polton, 2004). Hence, the concern that ART practice may continue to exhibit under-performance unless more efficient measures of quality control, coordination and training are put into place seems to contradict the activities of the French government to address the issue of staff shortages in specialist areas affecting ART services and maternal and child health: namely, by reserving a number of places for certain specialities in the entrance exams.

Finally, the WHO provides some useful reproductive health data in the Monitoring and Evaluation (MAE) database on the lifetime risk of maternal death in France in 2000, at 1 in 2,700; low birth weight prevalence, at 6.7 per cent (reduced from 7 per cent in 1996); and perinatal mortality rate, at 6 per 1,000 (WHO, 2006a). The top two causes of death for neonates in France (2000 data) were congenital anomalies (35 per cent) and preterm birth (26 per cent) (WHO, 2006b). Unfortunately, the most recent data in the WHO's reproductive health MAE database does not provide any maternal and perinatal health indicators for antenatal care coverage (for more than one or more than four visits), nor for the availability of basic or comprehensive essential obstetric care. These indicators are important to provide the clinical context of maternal and child healthcare in France's system.

2.3.4 Organisation and management

The post-war government of France planned a simple set of funds that would administer all social welfare benefits – pension, health, family allowances, accidents and disability – for all occupations. Benefits, in cash or in kind, depend on the contribution to the scheme and the membership in the occupational groups. Despite the fact that the population acceded to the policy of *universal social security*, several important groups feared losing benefits to the mass membership (Glaser, 1994). Thus, in France, pensions, health insurance and family allowances are supported by different payroll tax rates and are administered separately.

Importantly, despite the structural differences, all the regimes belong to a single social security system supported by taxes. As Glaser (1994) explains, funds with surpluses transfer money to funds with lower-income subscribers, sicker subscribers and deficits – in particular, money has long been transferred from the family allowance funds. The separate pension funds make special payments to the headquarters for the general regime (CNAMTS) to cover certain long-term care programmes for the elderly.

Ultimately, the rules of access to France's Bismarckian type welfare state, according to Ferrera's typology, are characterised by a strong link between work position (and/or family state) and social entitlements.

As a Bismarckian type welfare system, the social welfare system in France provides reasonably substantial social assistance benefits that are financed through contributions.

2.4 Outlook: future trends and possible developments

We conclude this study with an outlook on prominent issues, as well as relevant wider developments likely to influence the future policy, economic and clinical context of ART. As a technology and a field for ethical choices, ART will remain inevitably in flux, in France as elsewhere. However, the current basic parameters of ART regulation and practice in France – notably, its firm foundation on the idea of illness – entail specific challenges and issues for future debate, as do the evolution of the skills and financial base that are indispensable for giving effective and timely help to patients in practice.

2.4.1 Regulatory context: prominent points of debate

Many aspects of ART lend themselves to different and opposing viewpoints. ART regulation is inseparable from an evolving political and socio-economic context; it is also influenced by what is possible and allowed in other countries. As the debate of the next revision of the Bioethics Law begins, the following areas are likely to be at the centre of attention.

Assisted Reproductive Technologies for same-sex couples

We have already highlighted that in the run up to the recent elections, Ségolène Royal, the left-wing presidential hopeful, challenged the existing framework by suggesting that the case of access to ART for same-sex couples should be examined afresh. By contrast, her right-wing rival Nicholas Sarkozy, since elected president, distanced himself from any such proposition.

In its 2006 expert opinion on the anonymity of gamete donors, the CCNE included a short discussion on the subject in which it expressed concern that donors may not wish their gametes to be used for single or same-sex recipients. The report also observed that any such reform would signify a fundamental shift from the current idea of ART as medical therapy to an instrument to realise an individual right to a child, and warns that this may unduly prioritise individual interest over collective interest (CCNE, 2006). Given the opposition of both the ruling political faction and the CCNE as ethical authority, reconsideration of the requirement for heterosexual couples may not be realised as part of the next revision. However, the fact that it has been vividly discussed demonstrates that the issue is set to remain part of the debate for the years to come.

Anonymity of gamete donors

Since the foundation of the CECOS centres for the collection and preservation of donated gametes, donation has been governed by the principle of anonymity. In France, parental anonymity is not a phenomenon that only appeared with ART, but women have long had the option to give birth anonymously under a procedure known as *l'accouchement sous X*. However well established, both practices pose an ethical problem in that they deny the child knowledge of its biological descent. Indeed, in the UK, anonymity was recently lifted in acknowledgement of this very consideration, with the result of a dwindling number of donors. In June 2006, Valerie Pécresse, Member of Parliament for Yvelines, and 90 fellow *députés* proposed a bill to lift the anonymity of sperm donors for their decendants in France, a move strongly opposed by the *Académie de medicine* and CECOS (Petinicolas, 2007).

Organisations pleading the right of children to know their origins, as enshrined by an international convention signed by France among other countries, are thus pitted against those who oppose what they see as an inappropriate confusion of biological origins and parenthood, and a serious threat to the future supply of donor gametes. The CCNE's expert opinion on the subject acknowledges this dilemma, wondering whether interest in the subject has been intensified by an ever stronger urge for transparency, or more common use of genetic family information. As has already been mentioned, in the 2007 presidential elections, all three major candidates endorsed continued donor anonymity. The CCNE also recommends that donors should remain anonymous, but that the child should at the same time be informed about the mode of its conception. However, the committee has also called for a "genuine public debate" to explore the deep questions of identity and parenthood at stake.

2.4.2 Economic context

In terms of economic forces at play, two trends already visible are set to increase in force in the near to mid term. First, French ART centres will continue to compete with foreign clinics for those patients that can afford to forego the full reimbursement of costs associated with treatment within the country in order to achieve shorter waiting times, or undergo forms of treatment illegal in France. As in France, patients seeking treatment legal in other EU countries are not prosecuted; cross-border procreation (or, "reproductive travel"), already much referred to in debates, results in tangible ART access advantage for the wealthy, even though at the national level, an egalitarian system of access and costs is in operation for those who qualify for treatment (Tain, 2003). Second, the national system faces severe strain as its traditionally lavish healthcare needs to cater for an increasing burden of medical need, with rising costs for interventions and an ageing population. Within the specific field of ART practice, pressure on resources has been rising in recent years, meaning that future liberalisation of access of ART may be curtailed for economic reasons as well as reasons of principle.

2.4.3 Clinical practice

In France, maternal age at first birth, across all levels of education, is lower than in a number of other European countries (Rendal et al., 2005). At the same time, the country's birth rate is higher. However, even if policy thus appears to have achieved a certain degree of success in minimising age-related infertility, there remain a sizable number of couples in need of ART treatment. The large variation in the country's success rates suggests that there is much room for improving the quality of ART treatment given to French patients by investigating the underlying causes of within-country disparities. Some critics have blamed the situation on insufficient standards and a culture of division between the doctors and biologists who administer ART. Clinics themselves have voiced concern about a future shortage of licensed staff, and a lack of local career opportunities for budding ART specialists. It remains to be seen, therefore, whether the government's plans to increase the supply of specialist doctors can address this concern. The future of clinical practice of ART in France must remain vigilant regarding regional disparities in care provision and outcomes as well as active in stemming the possible tide of skilled workforce migration to ART centres abroad.

CHAPTER 3 Italy

This chapter examines the particular case of Italy. The Italian example clearly shows that ART policy is strongly influenced by the cultural and political context of a country. The long debate in the country on the regulation of assisted reproductive treatments in Italy, dating back to 1958, concerned the legal status of the child, whose natural father was not identical with the husband, and the potential interpretation as adultery (which was at that time legally prohibited) (Soldano, 2003). Prior to the recent enactment of a very restrictive law 40/2004, Italy was described as the "far west" of assisted reproductive technologies and Italian doctors enjoyed a high level of autonomy in practising ART. But despite now having a regulatory framework, secularists argue that the law has not provided a satisfactory solution.

3.1 Current state of Assisted Reproductive Technologies in Italy

3.1.1 Regulatory context

In Italy, sterility is not recognised as an illness (Soldano, 2003). Consequently, the Italian healthcare system does not, in principle, reimburse ART treatment. However, while no law has as yet introduced the financial coverage of ART at national level, there exist a number of partial reimbursement schemes that have been introduced by Italian regions within their autonomy. These schemes vary significantly (discussed below in Section 3.1.2).

The specific cultural footprint of Italy, with the strong influence of the Catholic Church and a fragmented political system, has had significant impacts on the long and controversial discussions of a law regulating ART (see Section 3.2). Under the current law – the highly disputed Law 40/2004 (Legge 19 febbraio 2004, n. 40), which entered into force in 2004 – the Italian system prohibits certain types of assisted reproductive treatments. For example, cryopreservation of human embryos,[22] the use of donated eggs (oocytes) or sperm, and pre-implantation genetic testing of embryos[23] are prohibited under Italian law. Furthermore, a maximum of three oocytes can be fertilised within one ART cycle, and all embryos created must be transferred into the woman's womb.

[22] However, embryos that were frozen before the new law was enacted can still be used.

[23] However, a recent decision by an Italian court has allowed the pre-implantation testing of an embryo if the parents suffer from a genetically transmissible illness. (De Bac, 2007).

Box 1 Requirements in Italy for Assisted Reproductive Technologies

- Heterosexual couple (marriage is not required)
- Both partners of the age of 18 years or older and within the fertile age group (attested by doctors)
- Certification of infertile by the doctor.

Despite the fact that ART treatment falls outside the remit of services covered by Italy's healthcare system, one of the requirements for receiving ART treatment is the certification of infertility by any doctor authorised to practise medicine (Annex to the Law, 2004, and Taccani, 2005) – a seeming contradiction of the role of medical professionals in determining the state of ART in the country compared with the strong and consistent influence of this group in France, for example. The Italian guidelines for ART use the terms sterility and infertility synonymously, and define infertility as "12 to 24 months of unprotected intercourse without conception" (Annex to the Law, 2004).

Tripling of cross-border Assisted Reproductive Technologies since the 2004 policy change

As a result of the limited and varying availability of funding due to the Italian policy not to define infertility as a medical condition for inclusion in its health system, many infertile Italian couples travel across country borders for ART treatment (Turone, 2004). The introduction of the new law on reproduction in 2004 has made it more difficult for couples who have infertility problems to receive ART treatment in Italy. In fact, the number of couples engaging in cross-border ART has increased significantly since the new law entered into force: a survey by the Osservatorio sul Turismo Procreativo showed that the number of couples crossing the border to undergo ART has significantly increased after the law entered into force (see Table 3-1).

Table 3-1 Italian cross-border Assisted Reproductive Technologies

Countries	Italian couples treated annually prior to the new law (2003–2004)	Italian couples treated annually subsequent to the new regulation (2004–2005)
Switzerland	649	1,150
Spain	114	960
Belgium	279	580
France	117	128
United Kingdom	35	175
United States	40	78
Austria	15	340
Israel	0	35
Greece	28	120
Slovenia	38	44
Total	**1,315**	**3,610**

SOURCE: Osservatorio sul Turismo Procreativo (2007).

NOTE: Figures relate to a sample of 53 foreign clinics.

The survey that compared cross-border ART of Italians before (2003–2004) and after the enactment of the Italian law (2004–2005) in a sample of 53 foreign clinics found that the number had nearly tripled. Among the Italian infertile couples who obtained ART in foreign countries, 32 per cent went to Switzerland; because of the vicinity and the common language they went mostly to the Canton Ticino. The survey showed also a certain trend towards Eastern European countries and Greece, which may be driven by the

lower prices for treatments (data not shown). An update of this survey for the period 2005-2006 showed that the increases in cross-border ART continued. The 27 foreign clinics contacted for the latest survey reported that a total of 4,173 Italian couples had undergone ART at their institutions in the period 2005–2006 (Osservatorio sul Turismo Procreativo, 2008).

The quality and safety of reproductive tissues and cells in Italy falls outside the remit of the designated competent authority under the Commission Directives

Of the three Commission Directives relevant to assisted reproduction, Italy has only transposed one of them into its national law (as of 30 May 2008) which is the setting standards of quality and safety directive. The other two directives are expected to be transposed by the end of 2008, according to the most recent survey by the European Commission's Directorate-General for Public Health (European Commission DG SANCO, 2008). The reason for delay in transposition is the "many competing priorities for legislators" in Italy (European Commission DG SANCO, 2008).

Despite having multiple competent authorities in Italy aimed at implementing the European Tissues and Cells regulatory framework - Italian National Transplant Center, Italian National Blood Center and Regional Health Authorities – none of them is responsible for reproductive tissues and cells; rather, the organisation responsible is the National Health Institute in the Ministry of Health (European Commission DG SANCO, 2008). This fact probably explains why there were no regular inspections conducted in 2007 in assisted reproduction centres reported by the competent authorities designated to implement the European Tissues and Cells regulatory framework (European Commission DG SANCO, 2008). Since there is also no interaction or overlap in Italy with systems for the inspection of other activities (e.g. blood, pharmaceuticals) (European Commission DG SANCO, 2008), it is unclear how the European standards for quality and safety of human tissues and cells in the reproductive field will be guaranteed in the interest of ensuring a high standard of human health. Similarly, Italy had no measures in place to verify the quality of imported reproductive tissues and cells as of February 2007, although the country does prohibit all imports and exports of human cells (Sorenson, 2006a).

In an earlier DG SANCO survey (2007), it was reported that a single authority in Italy, the CNT, carries out both the inspections and accreditation process of human tissues and cells establishments. Indeed, as of February 2007, Italy did not have an accreditation procedure in place for establishments that deal with reproductive tissues and cells (European Commission DG SANCO, 2007). Since then, however, Italy reports 282 reproductive tissues and cells establishments (semen, egg cells) had received accreditation on 31 December 2007 but 56 establishments were not yet accredited by then (European Commission DG SANCO, 2008). These figures are therefore confusing in light of the above information. Furthermore, while there may be an accreditation process for reproductive tissues and cells establishments, there is no system in place for the reporting of serious adverse events and reactions in the reproductive field. Not in there defined criteria for reporting of either adverse events or adverse reactions, it is only tissue banks in Italy that are required to have a procedure in place and compliance is verified by the CNT. Notably, one certificate was revoked following a serious adverse event.

Thus, Italy is not only lagging in its implementation of the European Tissues and Cells regulatory framework, but the structure responsible for doing so is not responsible for ensuring the quality and safety of reproductive tissues and cells in Italy.

3.1.2 Economic context

While the general healthcare budget is not dedicated to the direct financing of the individual ART treatment costs, €6.8 million of the national health budget was allocated to ART in 2005. This amount was distributed to the regions for any activity related to the "improvement of ART services", such as appointing new staff to help shorten the waiting time for patients, and renewing the technical infrastructure to improve the treatments provided by clinics (Ministero della Salute, 2006).

The actual cost of ART treatment in Italy depends on the type of provider and the type of technique. In private institutions, according to an article published in July 2007 in one of the major Italian newspapers, *La Repubblica*, the costs of ART services range between €2,000 and €4,500; in public institutions (or private institutions adhering to a convention with Servizio Sanitario Nazionale (SSN) treatments, they are around €1,500 (Amato, 2007). For specific techniques, the Centro Mahre, a clinic in Rome offering ART, estimates the costs for IVF to be around €3,500; for ICSI, around €4,000; and for pre-treatment assessment, around €200–300 (in public institutions) and up to €3,000 (in private institutions) (Amato, 2007).

As mentioned, ART treatment is not covered by the Italian healthcare system and no national law has introduced coverage for ART because sterility or fertility is not considered an illness in Italy. Nevertheless, infertile Italian couples can seek some reimbursement for their costs within their region as the Italian regions have, within their autonomy, partly introduced reimbursement schemes for clinics accredited to operate under the public convention. Already in 2005, a year after the introduction of the new ART law, several regions had introduced specific provisions foreseeing (some kind of) financial coverage of ART. In addition some professional associations, like the association of teachers (Ordine degli Insegnant), provide healthcare coverage for ART treatments at private institutions to their members (membership in these associations normally depends on a monthly fee).

Given their regional basis, these different reimbursement schemes result in a very fragmented picture of the economic context of ART in Italy. In Tuscany the regional administration had introduced a reimbursement scheme that left couples with expenses of only €36 per cycle. In Lombardia – if provided by a public healthcare facility – the treatment was completely covered, and according to a conference held by the Lombardian institutions accredited to perform ART in February 2007, no limitation of cycles has been introduced yet. In Piedmont, where only few hospitals adhered to the SSN convention, the private contribution was limited to €1,000 for IVF and €1,300 for ICSI. In Veneto, the hospitals adhering to the convention provided their services for free, with the exception of a co-payment of €50 for prenatal ultrasounds. However, the more southern regions of Italy were falling behind in this respect, often agreeing only with a few hospitals on reimbursable services (Porciani, 2005).

3.1.3 Clinical practice: value-laden clinical practice trumps international guidance

The central regulation and the guidelines at federal level based on this law provide the general framework of ART in the Italy. The D.P.R. (Decreto del Presidente della Repubblica, 1997) establishes the basic requirements for all public and private institutions that provide healthcare services, while there are regional regulations which further specify the concrete requirements for institutions providing ART in their territory.[24] Unlike in France, minimal requirements for the specific clinical practice of ART in Italy are established by an inter-regional agreement (Gruppo Tecnico Interregionale, 2001).

The minimum requirements for clinical practice of ART, set by the inter-regional technical group, are divided, on the one hand, into three categories (structural, technical and organisational requirements) and, on the other hand, differentiated for the three different levels of ART treatments (Gruppo Tecnico Interregionale, 2001). Of the 330 clinics authorised to perform ART treatment, roughly 40 per cent practise the so-called first level treatments (stimulation of egg production, and insemination), while the other 60 per cent practise second and third level treatments (IVF, GIFT, ICSI, FER etc) (Ministero, 2007).

In brief, Italy is different from France to the degree that Italy's law does not proscribe the minimum requirements for the clinical practice of ART whereas best practice in France is encoded in law at the federal level. This difference is important in the wider context of the country's healthcare system: since it is not considered a medical intervention, ART in Italy operates outside the country's healthcare system and therefore the government has less control over quality of care provided and less ability to enforce patient safety improvement practices. The health impact of this disconnection between ART services and Italy's healthcare system is explored below.

Regional variation in clinic density and waiting times

There are considerable regional differences in the density of clinics providing ART second level services. There are between 0.4 and 3.5 ART clinics in Italy per 100,000 women aged 15 to 49 (see Table 3-2). While 34.1 per cent of public clinics are located in the North West and 28 per cent in the North East, there are only 15.9 per cent of clinics in the central regions, and 22 per cent in the South. Private clinics seem to balance this gap; 34.8 per cent are located in the South, 28.1 per cent in the central regions, and only 21.9 per cent in the North East and 15.2 per cent in the North West (Ministero, 2007, p. 39). The regional distribution of IVF and ICSI treatments (per million of population) also shows a marginal decline from the north to the south.

[24] See Deliberazione n. VII/20790, 16 February 2005, for the autonomous region of Trento and Bolzano, Giunta Regionale, for example.

Table 3-2 Regional distribution of IVF and ICSI cycles per million inhabitants

Region	Treatment cycles/1 million population	Clinics (private and public) performing second and third level treatment (ICSI, IVF etc)
North West	**683**	**43**
Aosta Valley	773	1
Liguria	336	3
Lombardy	894	28
Piedmont	448	11
Nord East	**717**	**42**
Bolzano	1,700	3
Trentino-Alto Adige	74	2
Emilia-Romagna	873	11
Friuli-Venezia Giulia	735	4
Veneto	542	22
Centre	**562**	**46**
Marches	117	3
Lazio (Latium)	647	31
Tuscany	718	11
Umbria	170	1
South and Islands	**407**	**67**
Abruzzi	356	4
Apulia	372	6
Basilicata	137	1
Calabria	7	2
Campania	564	24
Molise	252	1
Sardinia	394	4
Sicily	473	25

SOURCE: Ministero (2007, pp. 40 and 45, graph 2.1.5).

NOTE: Based on data from 174 centres and clinics performing second and third level treatments.

There is no fixed scheme for waiting times in Italy, which suggests that, in practice, there could be as many different waiting times as there are clinics in Italy. One estimate from the region of Reggio Emilia indicates that couples have to wait around 12 months for their first visit (i.e. interview). If the couple is subsequently registered on the waiting list, they have to wait again between five and seven months for the actual treatment (Informa Famiglie & Bambini Regione Emilia-Romagna, 2007). To bypass waiting times in public clinics in regions with reimbursement schemes, couples often resort to individually financing their ART treatment at private clinics in Italy or travel to undergo ART abroad.

Italy provides Assisted Reproductive Technologies to more older women than elsewhere

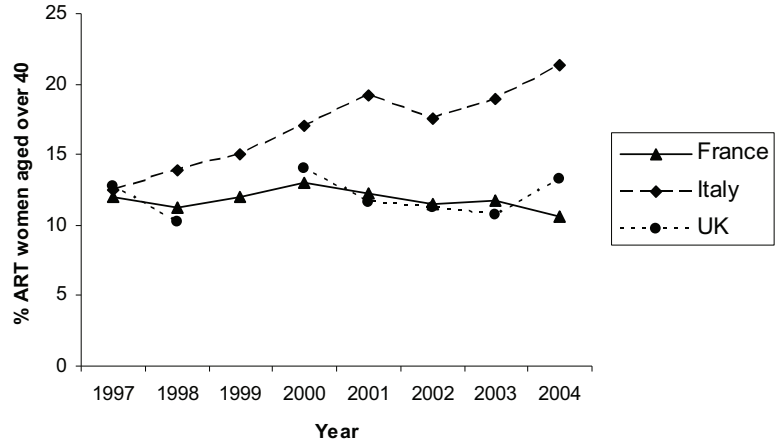
Unlike in France, Italy only prohibits ART to infertile individuals of reproductive age who are under the age of 18, but there is no upper limit. Thus, women over 45 years old can and do receive ART in Italy – a restriction in France. ART given to women older than 45 is but a small proportion of all women receiving ART (1.6 per cent) (see Table 3-3). Nonetheless, compared with France and the UK, Italy has consistently had a higher proportion of women >40 years treated with IVF or ICSI from 1998 to 2004 (see Figure 3-1).

Table 3-3 Cycles initiated by age group

Age Group	Total	Percentage
<29	3,304	10.1
30–34	9,590	29.3
35–39	13,100	40.0
40–44	6,265	19.1
>45	510	1.6
Total	32,769	100.0

SOURCE: Ministero (2007).

Note: 475 initiated cycles at 4 institutions, are missing.



SOURCE: Nygren and Nyboe Andersen (2001a, 2001b, 2002) and Nyboe Andersen et al. (2004, 2005, 2006, 2007, 2008).

Figure 3-1 Proportions of women older than 40 years in Assisted Reproductive Technology treatment in France, Italy and the UK (1997-2004)

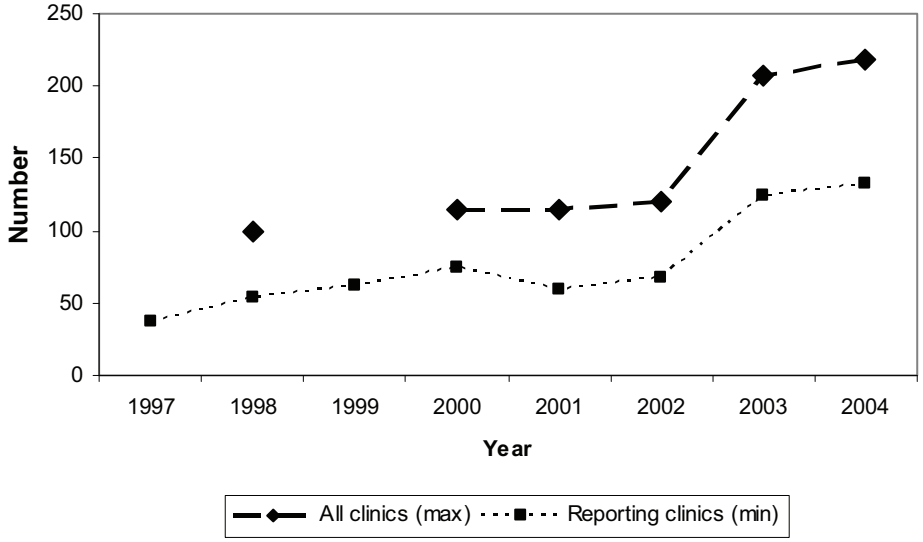
Assisted Reproductive Technologies provision in Italy has improved over time

Italy has the fourth largest population in Europe (according to the European Commission) and recent estimates show that one in five Italian couples has infertility problems[25] – a higher proportion than in either France or the UK.

Given such a high demand for ART services from 20 per cent of Italian couples (a number that increases in absolute terms with population growth), we found that the total number of IVF clinics in Italy more than doubled between 1997 and 2004 (see Figure 3-2). Similarly, the number of embryos transferred after ART in Italy increased nearly threefold from 6,296 in 1997 to 18,521 in 2004 (see Figure 3-3). Maximum and minimum trend lines for the period are given in the figure because there are more clinics known to be licensed for ART in Italy (according to an ESHRE monitoring programme) than there are

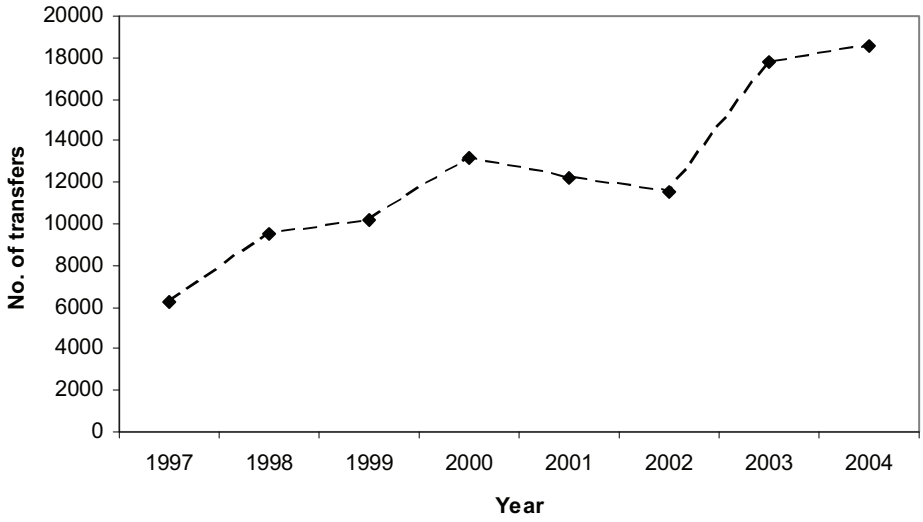
[25] This estimate was given in a 2007 report of the Instituto Superiore di Sanità (ISS), prepared for the Italian Ministry of Health.

IVF clinics reporting to the country's National Registry (between 51 per cent and 65 per cent). Data was not available on the clinics reporting for the years 1997 and 1999, hence the trend line is not complete.



SOURCE: Nygren and Nyboe Andersen (2001a, 2001b, 2002) and Nyboe Andersen et al. (2004, 2005, 2006, 2007, 2008).

Figure 3-2 Number of IVF clinics in Italy (1997 and 2004)

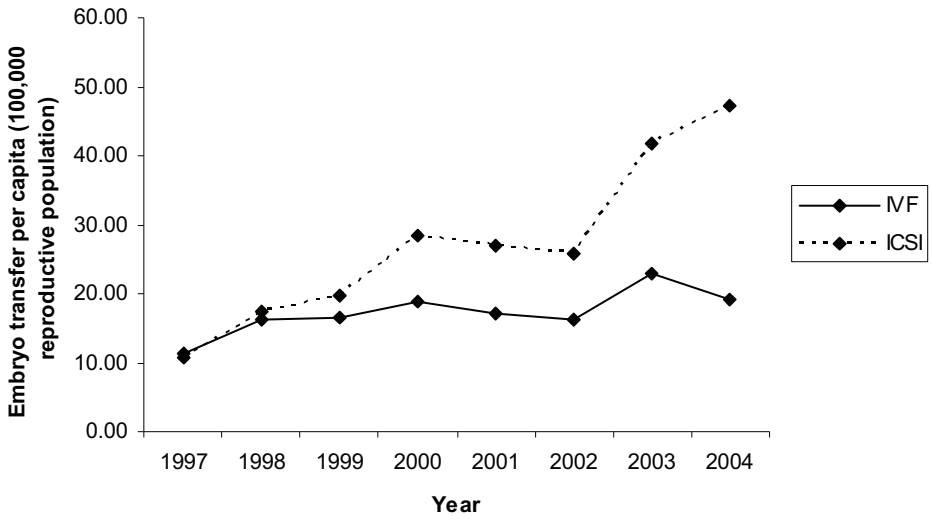


SOURCE: Nygren and Nyboe Andersen (2001a, 2001b, 2002) and Nyboe Andersen et al. (2004, 2005, 2006, 2007, 2008).

Figure 3-3 Number of embryo transfers after IVF and ICSI in Italy (1997-2004)

Italy is peculiar compared with other European countries of similar population size because the total number of clinics has increased and yet the average number of treatments per clinic has decreased (Nyboe Andersen et al., 2006, and Ministero, 2007). Thus it is possible that the absolute growth in IVF clinics and embryo transfers may not translate to real improvements in ART provision. To determine this more accurately, we examined the per capita measure of embryo transfers after IVF and ICSI.[26] Indeed, we found that ART provision has improved in Italy over time, particularly ICSI (see Figure 3-4). More specifically, the trend in embryo transfers after IVF per 100,000 reproductive population (aged 15–49) has increased slightly over time while there is a five-fold rise in per capita embryo transfers after ICSI in Italy (similar to France).

It is clear, moreover, that the ICSI technique is used significantly more often in Italy than in France or Britain. Moreover, the dominance of ICSI is particularly strong in private clinics (82.1 per cent of all cycles are after ICSI), compared with public clinics (72.8 per cent of all cycles are allocated to ICSI treatments) (Ministero, 2007: pp. 63 and 67).



SOURCE: Nygren and Nyboe Andersen (2001a, 2001b 2002), and Nyboe Andersen *et al.* (2004, 2005, 2006, 2007, 2008) and Eurostat (2008)

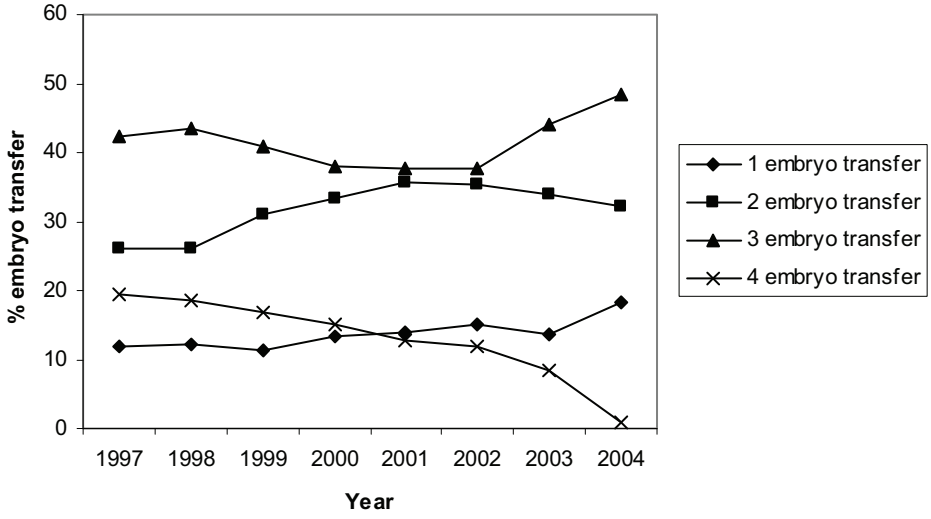
Figure 3-4 Provision of ICSI in Italy has increased recently (1997-2004)

A moderate reduction in transfers of three or more embryos

One positive trend we see in Italy is the trend away from high numbers of embryo transfers, which increase the risk of higher order pregnancies and their incumbent health harms. Between 1997 and 2004, the percentage of 4-embryo transfers after IVF and ICSI conducted in Italy among all embryo transfers after IVF and ICSI reduced from 19.5 per cent to 0.9 per cent (see Figure 3-5). By 2005, the percentage of 4-embryo transfers after IVF and ICSI dropped to zero (Ministero 2007, p. 73, table 2.3.18).

[26] It should be noted that other ART techniques, such as GIFT, are rarely practised in Italy so the influence on the figures is negligible. For example, GIFT constituted only 0.1 per cent of all cycles in 2005 and resulted in only eight pregnancies that year (Ministero, 2007, p. 5).

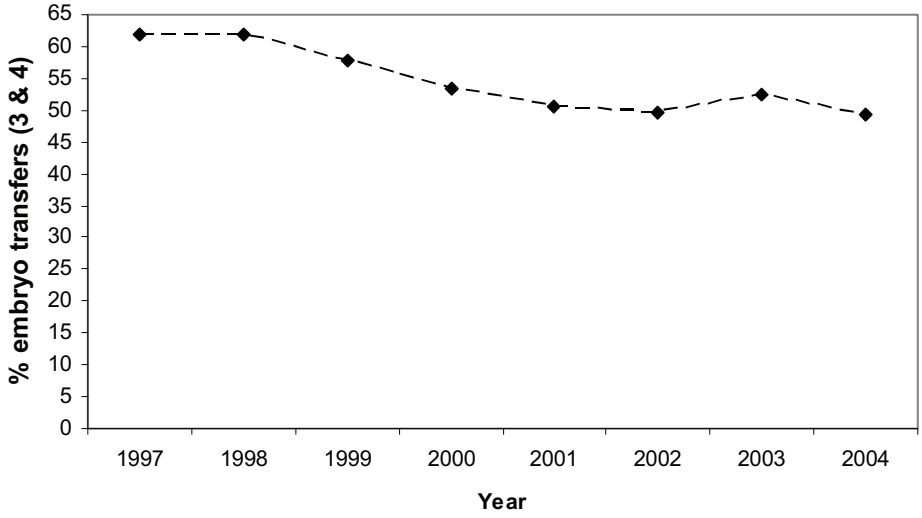
A similar decreasing trend also occurred with 3-embryo transfers – from 42.3 per cent in 1997 to 37.7 per cent in 2002. But after 2002 this proportion increased again to 48.5 per cent in 2004 (see Figure 3-5). In 2005, the Ministry of Health reported that 3-embryo cycles after IVF and ICSI increased even further to 49.5 per cent and 50.4 per cent (reported separately) (Ministero 2007, p. 73, table 2.3.18). Given the Italian law obligating the transfer of all three egg cells that developed into embryos (a maximum of three eggs can be used for one cycle), the political context of ART in Italy would therefore seem to be clearly reflected in the reported increases in the number of 3-embryo transfers for ICSI (the most dominant ART treatment in Italy) and IVF.



SOURCE: Nygren and Nyboe Andersen (2001a, 2001b, 2002) and Nyboe Andersen et al. (2004, 2005, 2006, 2007, 2008).

Figure 3-5 Proportions of 1-, 2-, 3- and 4-embryo transfers in Italy (1997-2004)

Nonetheless, there is clearly a move away from 4-embryo transfers and, to explain this change, we hypothesised that the opposing trend lines for higher order embryo transfers in the above Figure may be a sign of a shifting in clinical practice from 4- to 3-embryo transfers such that the overall effect may still be an increase in 3-embryo transfers in Italy. But this does not appear to be the case. When we add the percentage of 3- and 4-embryo transfers together, we see the net effect is still a marginal decline for the period studied (see Figure 3-6).



SOURCE: Nygren and Nyboe Andersen (2001a, 2001b, 2002) and Nyboe Andersen et al. (2004, 2005, 2006, 2007, 2008).

Figure 3-6 Clinical practice in Italy moves towards a net reduction in higher order embryo transfers

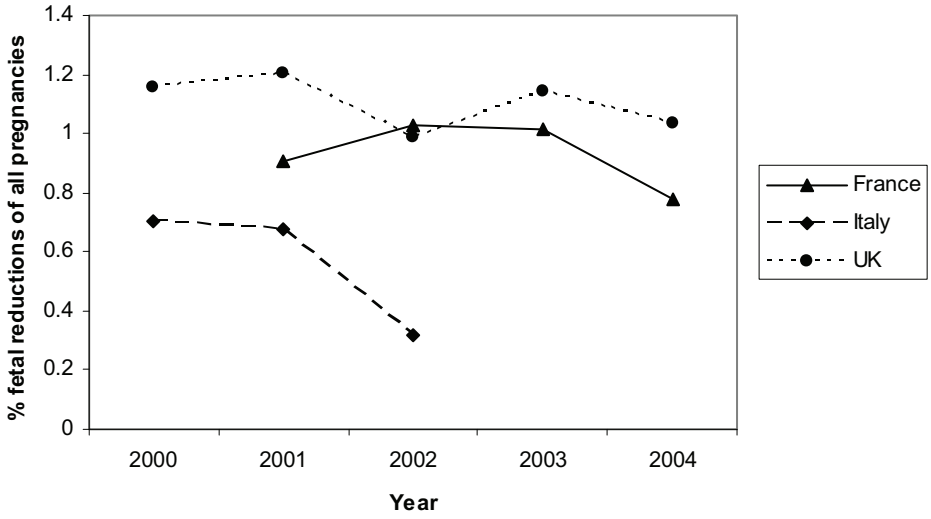
So, rather than a substitution as an explanation for the change in trends, there is likely a real change in clinical practice in Italy of *reducing* higher order embryo transfers. Indeed, this improvement is supported by the parallel increase in the percentage of 1- embryo and 2-embryo transfers after IVF and ICSI Italy over time: in 1997, 11.8 per cent of transfers were 1 embryo and 26 per cent were 2 embryo, but in 2004 18.3 per cent were 1 embryo and 32.3 per cent were 2-embryo transfers (see Figure 3-5). Additional data for the year 2005 suggests that 1-embryo transfers are continuing to increase (19.1 per cent after IVF and 19.3 per cent after ICSI), but 2-embryo transfers are not (31.4 per cent after IVF and 30.4 per cent after ICSI) (Ministero, 2007, p. 73, table 2.3.18).

Clinical practice in Italy moves away from fetal reductions to limit multiple pregnancies

It seems clear that the value-based ART policy in Italy trumps the clinical importance of limiting multiple pregnancies – ART treatment in Italy requires the transfer of all viable embryos even at the risk of higher order pregnancy outputs and consequent poor health outcomes for mother and child. There is another aspect of Italian clinical practice that may contribute to an increased number of multiple pregnancies: the percentage of reductions to all ART pregnancies in Italy are reduced two-fold over 3 years (from 0.71 per cent in 2000 to 0.32 per cent in 2002) and data after 2002 is absent from ESHRE reports (see Figure 3-7). Moreover, since the new 2004 law on assisted reproduction, there are two known cases of fetal reduction in Italy and both required a court ruling. In one case, the court ruled that a twin pregnancy be reduced to a singleton due to a congenital disorder prevalent in the pregnant woman's region, and the other case involved an 11-week triple pregnancy in which the mother's life would be at risk (Arie, 2004).

The observation that clinical practice in Italy has moved away from fetal reductions to limit multiple pregnancies is consistent with the fact that the technique of fetal reduction is normatively at odds with Italy's value-based regulation aimed at preserving the rights of the

embryo. The main reason is that reduction, as a potential form of eugenics, adds a new dimension of controversy beyond the existing controversial nature of abortion. Abortion, however, is legal in Italy up to 90 days into the pregnancy and later if there are health risks (Arie, 2004). Nevertheless, with growing international best practice to limit high numbers of embryo transfer and reduce higher order pregnancies, it is perhaps not surprising that the percentage of fetal reductions in France and in the UK has been higher than in Italy.



SOURCE: Nygren and Nyboe Andersen (2001a, 2001b, 2002) and Nyboe Andersen et al. (2004, 2005, 2006, 2007, 2008).

Figure 3-7 Clinical practice of Assisted Reproductive Technologies in Italy moves away from fetal reductions to limit multiple pregnancies

The success of Assisted Reproductive Technologies in Italy may be diminishing in recent years

Clinicians were allowed to fertilise more oocytes in order to select the most viable zygotes. Critics of the 2004 law voiced the expectation that the legislative requirement to transfer all three embryos – without a prior health check of the embryo – would reduce the success rate because doing so would lead to an increased rate of multiple pregnancies and hence poorer health outcomes for the mother and any surviving babies (Ragni et al., 2005). It is possible that this is the case: the first public data from the Italian health minister on the effects of the restrictive law show a decrease in the percentage of pregnancies obtained per extraction of eggs from 24.8 per cent in 2003 to 21.2 per cent in 2005 (see Table 3-4). Prior to the 2004 law, the chance of getting pregnant after IVF and ICSI stayed relatively constant between 1997 and 2004 (fluctuating around 25 per cent), and increased slightly after FER treatment in that time period (from 16.4 per cent to 18.5 per cent) (see Figure 3-8).

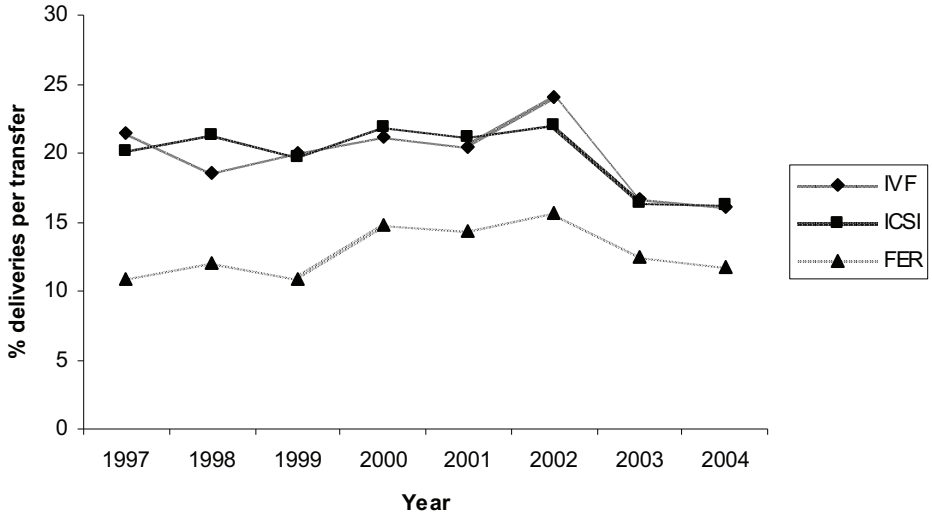
In addition, the delivery rate after ART in Italy shows a bleaker picture; despite an earlier trend of an increasing delivery rate (deliveries per transfer), there is a sharp decline after 2002 in the delivery rate in Italy after IVF, ICSI and FER – a trend that appears to

continue in 2005 after the new law.[27] Data from the Italian registry also shows a decrease in the delivery rate after the new law to 18 per cent in 2005, compared with 22 per cent in 2003 (Ministero, 2007; Bartolucci, 2008).

Table 3-4 Comparison of Assisted Reproductive Technology clinical practice (IVF and ICSI) in Italy in 2003 and 2005

	2003	2005
Clinics participating	120	169
Pregnancies	4807	6235
Average pregnancies per clinic	40.1	36.9
Pregnancies per eggs extracted	24.8%	21.2%
1-embryo transfers	13.7%	18.7%
2-embryo transfers	34.4%	30.9%
3-embryo transfers	30.9%	50.4%
Cycles	22.517	33.244
Pick up	19.962	29.380
Transfers (fresh and cryopreserved)	17.829	25.402
Total of pregnancies	4.914	6.235
Pregnancies/transfers	27.6%	24.5%
Delivery rate	22%	18%

SOURCE: Ministero (2007, p. 100).



SOURCE: Nygren and Nyboe Andersen (2001a, 2001b, 2002) and Nyboe Andersen et al. (2004, 2005, 2006, 2007, 2008).

Figure 3-8 Change in proportion of deliveries to all transfers after Assisted Reproductive Technology treatment in Italy (1997-2004)

[27] Data from the Italian registry shows that a decrease in the delivery rate after the new law to 18 per cent in 2005, compared with 22 per cent in 2003 (Ministero, 2007, and Bartolucci, 2008). However, as this data is not fully representative of all clinics due to incomplete reporting to the National Registry, the values are somewhat biased and were not comparable with the rest of the ESHRE data used to generate the trends.

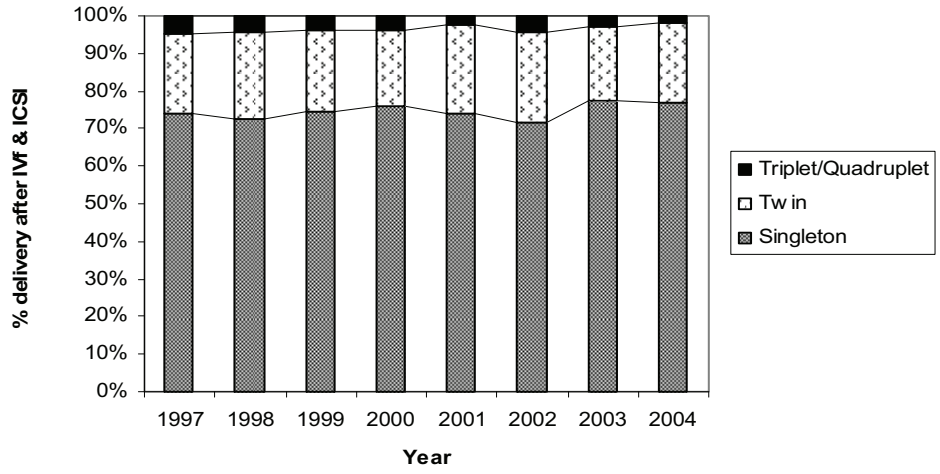
Although these figures appear to support the concerns of critics, caution is urged when interpreting these trends. The reasons for this decline in delivery rate after ART are many since this measure is more indicative of the influence of the safety and quality of maternal and perinatal care within the wider healthcare system of the country, than of ART services per se.

3.1.4 Assisted Reproductive Technologies outcomes: health outcomes are comparatively poor in Italy

Triplets after IVF and ICSI have always been a significant proportion of higher order pregnancies

While the majority of deliveries after IVF and ICSI in Italy between 1997 and 2004 were singleton (as in France), Italy is distinct in the trends of higher order pregnancies (twins, triplets, quadruplets). In general, due to the requirement of transferring all three embryos (irrespective of whether they are adequate or not), the number of pregnancies in relation to treatments in Italy is relatively low compared with other countries. On the other hand the number of multiple births is relatively high (Ministero, 2007, pp. 84–85).

As can be seen in Figure 3-9, the proportion of triplet (or quadruplet – reported between 1997 and 2000) deliveries remains a significant proportion of higher order pregnancies in Italy, and the proportion of twin deliveries fluctuates by a few percentage points from year to year, ranging from a high of 24.1 per cent (2002) to 19.3 per cent (2003).



SOURCE: Nygren and Nyboe Andersen (2001a, 2001b, 2002) and Nyboe Andersen et al. (2004, 2005, 2006, 2007, 2008).

Figure 3-9 Triplet and quadruplet deliveries are a significant proportion of higher order deliveries in Italy over time

Recent Italian ministerial data on 2005 shows multiple births after IVF and ICSI increased since the new law to 24.3 per cent multiple births, compared with 22.7 per cent multiple births in 2003 (Ministero, 2007, p. 100). One can speculate that this rise might be attributed to the legal obligation to transfer all three embryos should they develop from fertilised eggs, given certain caveats about reporting bias, according to Dr Giulia Scaravelli, the head of the registry at Italy's ISS (Sinclair, 2007). But, given past variation, more

longitudinal data will be necessary to determine adequately the true impact of the new law on increasing multiple pregnancies – a trend that would be worth monitoring in the future given the negative health and economic impact.

Here, we note the different impacts of multiple pregnancies. For women, higher order pregnancies frequently require hospitalisation and caesarean delivery, and many give birth to premature, low-weight babies or suffer miscarriage. For the future child, short- and long-term complications include increased risk of perinatal mortality, mental retardation, learning disabilities and behavioural problems (ESHRE, 2003). More specifically, multiple pregnancies incur a 40 per cent higher risk of premature delivery and neonatal malformation (Robertson, 2004). From an economic perspective, multiple births from Italian ART regulation equally affect Italian families by introducing financial hardship – beyond the additional costs of caring for multiple children, there is also no routine financial or social support made available to parents of newborn twins or even triplets – in addition to producing a higher incidence of maternal depression and marital problems (Braude, 2006), which also have known negative impact on child health and development. Finally, multiple pregnancies and births have been shown to generate higher costs than single births as a result of greater need for antenatal, obstetrical and neonatal treatment and long-term disability services (Goldfarb et al., 1996, and Katz et al., 2002).

Health outcomes have worsened since the 2004 policy change

Italy's new law also requires transferring all created embryos irrespective of their quality. Quality of eggs for fertilising is clearly a significant issue given that, in Italy, there is no transfer in 22.5 per cent of initiated ART treatments, due to the lack of embryonic development (Ministero, 2007, p. 73, table 2.3.18). The consequence of this legal obligation is that multiple embryos may be transferred to women for whom a single embryo would have been appropriate. The increase in multiple-embryo transfers since 2004 was therefore expected to have adverse consequences for both maternal and neonatal health. Indeed, nearly a fifth of infertile couples will lose a clinical pregnancy after receiving ART treatment in Italy – a chance that has fluctuated by 6.8 percentage points between 1997 and 2004 but appears to be increasing since the new law to 22.5 per cent in 2005 (compared with 18.4 per cent in 2003) (Bartolucci, 2008).

The Ministry's data indeed report an increase in the number of multiple births from 22.7 per cent to 24.3 per cent (see Table 3-5). Although there is no definitive evidence for causality, it is not unlikely that this is a direct consequence of the implementation of the 2004 law (Robertson, 2004). Additionally, the data report that "negative outcomes" from ART services in Italy have increased since the new law came into force into 2004 – rising from 23.4 per cent in 2003 to 26.4 per cent in 2005 (Ministero, 2007, p. 100). However, we are not aware of how this category was defined.

It is worth noting that not all clinics have provided data for the Ministry's report, and that due to Italian privacy law there is an insufficiency of follow-up data available publicly (e.g. on the number of cycles women had undergone before getting pregnant or stopping their attempts), according to Dr Giulia Scaravelli, who is head of the registry at the Instituto Superiore di Sanita (Sinclair, 2007). Nonetheless, the health outcome data from the latest Ministry report ART is partially indicative of the health impact of the 2004 policy change. Furthermore, as a proxy indicator of poor health outcomes, we can crudely assume that

21% of all ART babies born in Italy will suffer from prematurity and low birth weight (among other prematurity-associated health conditions), given that this is the reality for 50% of twins and 90% of triplets who are born (HFEA, 2007a).

Table 3-5 Comparison of health outcomes (IVF and ICSI) in Italy in 2003 and 2005

	2003	2005
Cycles	22.517	33.244
Delivery rates (%)	22	18
Miscarriages (%)	18.4	22.5
Multiple births (%)	22.7	24.3
Negative outcomes (%)	23.4	26.4

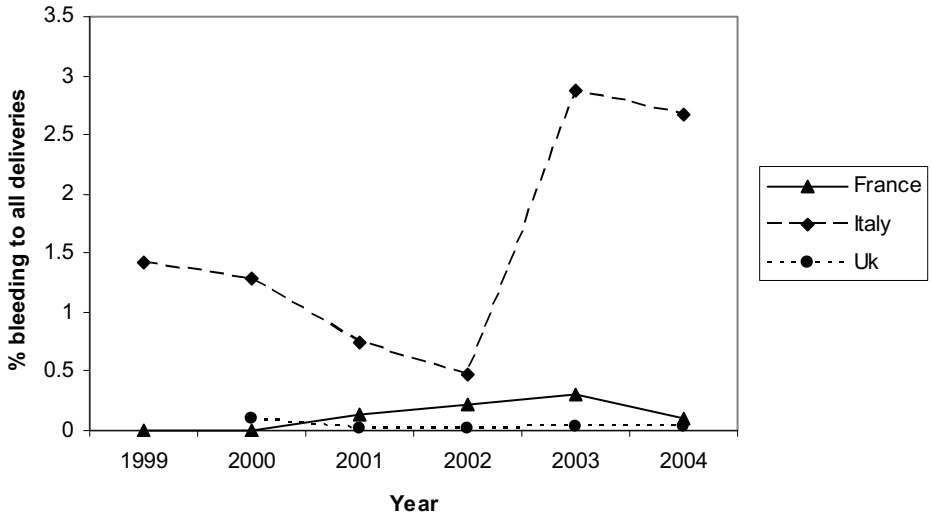
SOURCE: Ministero (2007).

Health outcomes after Assisted Reproductive Technologies already compared unfavourably with other countries

Clearly the loss of a clinical pregnancy is a negative outcome for the 20 per cent of women becoming pregnant after receiving ART in Italy. But the most dramatic negative health outcome of ART is reported maternal death. Between 2000 and 2004, for which ESHRE data was collected and available, Italy was one of four European countries (n=29) in 2004 to report one maternal death after ART. It is unlikely that this is due to Italy's general poor maternal health since, according to 2006 data in the WHO's Department of Reproductive Health and Research Monitoring and Evaluation (MAE) database, Italy has a much lower lifetime risk of maternal mortality (1 in 13,900) than either France (1 in 2,700) or UK (1 in 3,800). These indicators might suggest that the one country to report maternal death in the population receiving ART is the one least likely of the three country cases to have this risk in its general population. Although the lifetime risk of maternal death in Italy may have increased from 2000 and 2004, it is unlikely that any natural increase would overtake either France or the UK.[28] Hence, we might suggest that the socio-political context in Italy leading to the regulatory change in ART in 2004 may have contributed to unsafe clinical practice such as higher-order embryo transfers that would lead to such poor health outcomes as maternal death after ART.

Another indicator of poor health outcomes after ART is the chance of bleeding to total ART deliveries. Here again, Italy stands out with the highest percentage of the three countries and with a sharp rise in this value after 2002 to above 3 per cent (see Figure 3-10).

[28] We note here that we have not investigated further the underlying assumptions and data used to produce these measures and it is possible that there may be under-reporting of lifetime risk of maternal death in Italy and/ or different reproductive rates might contribute to maternal mortality rates. There is also the problem of not knowing how many pregnant women conceived using ART if they do not self-report as such, especially if ART was sought in a foreign country.



SOURCE: Nygren and Nyboe Andersen (2001a, 2001b, 2002) and Nyboe Andersen et al. (2004, 2005, 2006, 2007, 2008).

Figure 3-10 The chance of bleeding among all Assisted Reproductive Technology deliveries is highest in Italy, compared with France and the UK (1999-2004)

Finally, and unexpectedly, the percentage of Ovarian Hyperstimulation Syndrome (OHSS) complications after ART in Italy has been decreasing in recent years to 0.82 per cent in 2004 from a high of 1.64 per cent in 2000 (data not shown). This trend is difficult to explain since, on the one hand, it would be expected that there is a financial incentive in Italy for couples to maximise the number of oocytes retrieved for fertilisation, since many pay out of pocket for ART treatment. On the other hand, Italian regulation limits the number of oocytes to be fertilised, which might counter-balance a need for over-stimulating a women's ovary to retrieve a greater number of eggs – a practice that clearly comes with a risk of complications.

3.2 Contextual factors for Assisted Reproductive Technologies policy in Italy

3.2.1 Historical background

Prior to the Law 40/2004 on ART, Italy was described as the "far west" of assisted reproductive technologies. Given the regulatory vacuum, Italian doctors enjoyed a high level of autonomy in practising ART. Only a few specific activities were regulated by ministerial regulations, while doctors had freedom with respect to medical and ethical decisions in non-regulated areas.

The political debate on the regulation of assisted reproductive treatments in Italy dates back to 1958, when two MPs addressed the issue and its regulation for the first time in their text on the prohibition of the artificial insemination and its legal regulation (*Divieto della inseminazione artificiale e sua disciplina giuridica*). The issue of the debate was the potential use of donor sperm regarding simple insemination. The main concerns revolved

around the legal status of the child, whose natural father was not identical with the husband, and the potential interpretation of this as adultery (which was at that time legally prohibited) (Soldano, 2003).

The issue re-emerged when the first IVF baby was born in Italy in 1983. Numerous proposals put forward by individual MPs or small groups of MPs entered the debate. However, as no proposal had a solid supporter base, none succeeded in becoming a formal item on the agenda in parliamentary sessions. Nevertheless, in 1985, a governmental Commission was established to elaborate a proposal. The second proposal put forward by this Commission determined that only married couples could undergo ART, prohibited the use of donated gametes and allowed IVF only if the couple had previously undergone unsuccessful GIFT. This very restrictive proposal, which was not adopted, showed that the debate on ART was not driven by the clinical and technical issues but rather by ethical concerns. The moral protection of the classical concept of the family prevailed over medico-ethical considerations about the health impact on women (GIFT is an invasive technique with low success rates), and the need to take into account complete infertility (i.e. sterility) which would not be solved without allowing for gamete donation (Soldano, 2003).

A decade later, in 1998, the Chamber's Social Affairs Committee issued a relatively liberal proposal (e.g. the donation of gametes was allowed, cohabitant couples could also resort to ART), which the Assembly strongly revised and reshaped into a much more restrictive text, allowing, for example, only homologous treatments (using the gametes of the couple). Once approved by the Chamber this text was submitted to the Senate where the predominant centre-right majority managed to revise the text again towards more permissive provisions (eg the donation of gametes was again included). The destiny of this proposal, which was at the end not adopted, exemplifies the difficult socio-political process that has dominated this debate.

That the line of demarcation in this debate cuts across all stakeholder groups can also be seen in the fact that the opinions on ART adopted by the National Bioethics Committee, a permanent governmental committee established in 1990, were rarely unanimous and it struggled to put forward recommendations (Ramjoué and Klöti, 2004).

The controversy over ART issues, not only within the parliament and the government but in society as a whole, has led to a standstill of more than a year and a re-launch of the debate with no conclusive agreement till the Chamber and the Senate agreed finally in 2004 on the first comprehensive law regulating ART in Italy (Law 40/2004).

The adoption of this first comprehensive law has triggered severe criticisms. Secularists campaigned against its restrictive regulation of ART, considering the decision whether or not to undergo ART as part of their personal freedom. Furthermore, the law was criticised against the background of a potential brain drain caused by the limitation of research in this area, which compared with other European countries is very restrictive and drives scientists to accept offers from abroad.

Some legal experts have questioned the law, saying it conflicts with Italy's constitution, which explicitly protects the health of its citizens. But criticism has also occurred at

international level, attacking the excessive concern with the status of embryos and disregard for the interests of women and infertile couples (Robertson, 2004).

Given the fact that the Italian legal system foresees only the possibility of referenda to abrogate a law, opponents immediately launched the initiative of a referendum (the request was deposited at the Supreme Court, Corte di Cassazione, in September 2004).

Box 2 Questions posed by the referendum

Should the law be amended to:

- lift the ban on embryo research and freezing?
- lift the ban on fertilisation of more than three eggs at a time?
- lift the obligation of doctors to implant immediately all embryos created by in vitro fertilisation into the womb (without the possibility of pre-implantation diagnosis)?
- lift the ban on the use of donated eggs and sperm?
- cancel the section of the law that deferred the same rights to the embryo (or more precisely already the fecund egg cell) as to the other involved parties (mother)?

Most of the scientific community supported the referendum appealing to voters to vote "yes". However, confronted with such an opponent as the Catholic Church, which supported the law, the promoters of the referendum did not succeed in their efforts. The church appealed to Italian citizens not to vote. It aimed to keep the turnout below the quorum, and emphasised that these issues were too complex to be understood and decided by a popular vote.

In general the centre left politicians supported the referendum, while the centre right was in favour of the law. However, there have been several exceptions on both sides with the president of the rightwing Alleanza Nazionale, Gianfranco Fini (at that time deputy prime minister and foreign affairs minister), supporting the referendum, while Francesco Rutelli, Minster for Cultural Affairs in Prodi's centre left government, campaigned against it.

The referendum was held on 12–13 June 2005. With only one out of four Italians voting in the referendum (25.9 per cent) the required quorum of more than 50 per cent was not met. Participation was higher in the North and big cities such as Rome and Milan, while the South and the more rural areas showed minimal participation. Some surveys indicated that the majority of voters had a high educational background, and that around 78 per cent of the actual voters voted in favour of zygote donations, while 90 per cent sustained all other points (Turone, 2004).

The failure of the referendum was seen as a result of the abstention from the vote which was promoted by the opponents (in particular the Catholic Church), the biased media coverage, and the complexity of the issues which were hard to explain to the broad public.

A survey of 4,000 people undertaken prior to the referendum (equally divided by gender, age, geographic area of residence and demographic class) found that 27.4 per cent did not know the content of the law 40/2004, 32.7 per cent of the Italians were not even aware of the fact that a referendum would be held, and of the ones who knew about the planned

referendum, 18.5 per cent did not know what the referendum was about (Malagutti, 2005).

The debate on a more secular regulation is still on the agenda and causes strong reactions. And the ruling by an Italian court in September 2007, which permitted pre-implantation testing of an embryo given the parents were suffering from a genetically transmissible illness, might initiate re-evaluation of the law relating to the prohibition of pre-implantation genetic testing. Given the Ministry is in the process of assessing the current version of the guidelines issued on the basis of the ART law, it might consider amendments in this direction (De Bac, 2007).

3.2.2 Legislative framework

Before the law 40/2004, the three circulars (only valid until a law regulates the area) and three ordinances (temporary measures) were the only acts with relevance to the area. These were only adopted in response to an urgent need and had therefore rather specific remits. The most prominent, the *Degan Circolar* of 1985, remained the most comprehensive authoritative decision on ART, although it addressed only the question of which ART should be covered by the SSN.

The *Degan Circolar* (Ramjoué and Klöti, 2004) envisaged

- non-separated married couples could in agreement request ART to overcome infertility
- the prohibition of the creation and cryopreservation of embryos for deferred implantation, industrial use and research
- the prohibition of ART using donated gametes, and of cryoconservation

As this regulation addressed only the public provision, almost no prohibitions existed in the private sector in Italy. Therefore, for those few infertile Italian couples with the necessary financial means, there was a broad spectrum of treatments they could access (including egg and sperm donation), whereas only limited treatments were accessible to everyone.

In the "non-regulated" area, some weak self-regulation took place. Following some scandals in the area of ART, the Federation of the Orders of Doctors and Dentists amended its Code of Medical Ethics prohibiting surrogacy, treatment after the menopause, post-mortem ART, the embryo production for research, and the commercial use of gametes and embryos. Furthermore, access to ART was restricted to heterosexual couples. As the Code did not have a legally binding status, no common interpretation existed on whether or not adhering to these guidelines would be followed by a severe sanction (such as the exclusion from the Order). Another attempt to establish a (non binding) self-regulatory code was launched by several research institutions, patient groups and ART clinics associations; this resulted in the adoption of the Code of the Forum for the Protection of Assisted Reproduction (Ramjoué and Klöti, 2004). In addition the non-for-profit association Centro Studio e Conservazione Ovociti e Sperma Umani (CECOS) Italia had established a kind of self-regulation codex for the institutions applying ART.

After a decade of debate, on 19 February 2004 the law 40/2004 (*Norme in materia di procreazione medicalmente assistita*) regulating ART was adopted; it entered into force one month later in March 2004. "The promulgation of this law [Law 40/2004] is the end

point of a long and troubled journey that has seen many bills come and go, all of which have failed. The law consists of a whole set of regulations that will have a great impact on health and on society in general" (Fineschi, Neri, and Turillazzi, 2005).

Box 3 Prohibited treatments

- Freeze or destroy human embryos
- Use of donated sperm
- Use of donated eggs
- Pre-implantation genetic testing of embryos
- Scientific research on embryos
- Fertilisation of more than three oocytes within one ART cycle
- Not transferring all embryos created into the woman's womb (this means in practice that if the fertilisation of all three oocytes was successful all three embryos have to be transferred, which increases the risk for multiple births)
- Post-mortem insemination

3.2.3 Key players

Although the battle on whether and how to regulate ART has found its arena in both parliament and government (and several of its commissions such as the Chamber's Social Affairs Committee or the National Bioethics Committee) – where many proposals have gone through the lifecycle of being issued, criticised and revised, and at the end rejected – the debate in these political bodies has only reflected the strong contrasts between secular groups and groups following the doctrine of the Catholic Church.

The Church has played and continues to play a major role in the discussion revolving around ART regulation. Its influence has been exerted not only indirectly by the fact that many Italian politicians follow the Church's doctrines but also by explicitly taking a stance in the debate (eg asking the population not to participate in the referendum).

Promoters of a more secular and liberal regulation included several civil society and patient groups, and associations of ART clinics. Surprisingly, despite their strong representation in parliament and government (partly by the lobbying of their Federation of Orders, partly given that many government officials and MPs are doctors), medical doctors did not take a strong consolidated stance.

Prominent critics of the restrictive position included a number of Nobel laureates (Rita Levi-Montalcini, Renato Dulbecco, Giovanni Berlinguer), a long-term parliamentarian and former President of the National Bioethics Committee, as well as the famous Italian oncologist and former Minister of Health Umberto Veronesi. Nevertheless, it has to be mentioned that there were also scientists supporting the law (e.g. biologist Angelo Vescovi and geneticist Bruno Dalla Piccola).

3.2.4 Channels of influence

As is the case in most contemporary public debates, the media have been an important channel for discussion, even with criticisms of publishing biased information. The Church

has used various channels of direct and indirect influence: on the one hand, directly addressing the population (such as over the referendum) and, on the other hand, using its influence on the politicians and its significant role within the Italian socio-political system.

Immediately after its adoption, opponents of the restrictive law resorted to the legal instrument of calling for a referendum (as discussed above). The organisers included among others the Partito Radicale Associazione Luca Coscioni, Democratici di Sinistra, Socialisti Democratici Italiani, Rifondazione Comunista and some exponents of other parties.

3.2.5 Prominent controversies

Several characteristics of, and tensions in, the Italian social and political system help understand why the adoption of a comprehensive regulation on ART was so cumbersome and took so long, and that the outcome is still highly controversial. First of all Italy, its value system and also its politics, has historically been strongly influenced by the Catholic Church. Although the Church did not succeed in completely blocking the adoption of a regulation, with its direct and indirect pressure it succeeded in gaining a very restrictive regulation. A more liberal regulation of ART would have focused on the clinical aspects and the protection of the health of all individuals involved as requested by the secularists, rather than taking ideological considerations into account (Ramjoué and Klöti, 2004).

The influence of the Church can hardly be contested when looking at the recent successes in promoting its values; not only did it manage to make sure that the law on ART is allowing ART only in a very restrictive form, but its public appeal to abstain from the subsequent referendum on the abrogation of some of the most restrictive clauses succeeded and the referendum failed to meet the required quorum. Finally it managed to get the centre-left coalition to drop the issue of extending the legal rights to unmarried (including same-sex) couples from its priority list (Economist, 2007).

The disintegration of the most important Catholic party (Democrazia Cristiana; DC) in the aftermath of the big political "tangentopolis" bribery scandal of the 1990s did not harm the political influence of the Church especially given that it also led to the dissolution of the ideological opponent of the DC (and the Catholic Church), the Italian Communist Party. Rather then losing influence, promoters of Catholic values can nowadays be found in nearly every party including the leftists. This has also hindered the adoption of a more liberal law under centre-left governments, and has allowed for the adoption of the restrictive law under the centre-right government by a strong majority in the Senate.

A third aspect that hindered a quick adoption of a law is that Italian legislation is based on perfect bicameralism, meaning that both houses of the parliament (the Chamber and the Senate) have identical rights. Any legislation must therefore be approved in the identical version by both houses. If a legislation approved by the Chamber is subsequently revised by the Senate, this version has to go back to the Chamber for adoption, a procedure which can lead to long iterations of a bill before its approval.

3.3 Healthcare and welfare systems

3.3.1 Regulatory

The Italian healthcare system, Servizio Sanitario Nazionale (SSN), is a regionally based national health service that, in principle, provides universal healthcare coverage free of charge at the point of service. Different from a pure NHS, these services are provided by not only public facilities but also private facilities. If private facilities adhere to a convention with the SSN, healthcare services can also be covered by public funding; otherwise, they need to be paid for by the individual patient. In order to bypass long waiting lists, patients often resort to private payment for health services. As a result of increased co-payments to the public system, and growing use of private providers with direct out-of-pocket payments, privately financed healthcare expenditures are significant, however.[29] Private medical insurance is, on the other hand, not very common in Italy.[30]

Prior to the debated reforms in 1978, healthcare in Italy was offered to all but about 3 million Italians by several occupation-based sickness funds (seven of which covered 98 per cent of the insured population). Given the historical political context in which Italy's central government has been reluctant to standardise benefits and enrolment practices among the funds and to regulate their financial affairs, Lawrence Brown (1984) has noted that coverage varied widely across occupational groups; some categories of employees gave up larger shares of their incomes than did others for coverage and some citizens remained outside the system altogether. In other words, regional disparities were superimposed on social groups, creating an "inequitable, uncoordinated and needlessly fragmented" system, according to Brown.

The law in 1978, establishing the Italian national health service, Servizio Sanitario Nazionale (SSN), spelled out a wide range of personal health services that were to be provided by the newly created local public health units (Unità Sanitarie Locali, USL), which would replace the sickness funds. Healthcare was to be provided to all citizens (universal coverage) free of charge at the point of service (Brown, 1984). Different from a pure NHS where all healthcare facilities are public entities, such as in the UK, private facilities also may provide public healthcare services in Italy (Assistudio, 2008). In other words, Italians were to have both free access to a fine new public system and a strong private sector continuing alongside it.

As described by Brown (1984), the political idealism of the new law was quite ambitious: bringing new coverage to 3.5 million Italians; expanding entitlements for all citizens; emphasising equality, uniformity, absence of fees; reducing regional disparities; and insisting on decentralising and consumer participation within a context of regional and central planning and budgeting. Unfortunately, Italy's NHS seemed doomed to numerous difficulties from its inception since reformers had not invented a practical way to link

[29] In 1999 private financing accounted for 33 per cent of total healthcare expenditure according to Donatini et al., 2001.

[30] According to a study by Ania Trends (Associazione Nazionale fra le Imprese Assicuratrici) commissioned by Banca Italia in 2002, only 0.9 per cent of the private contributions to the healthcare system were financed by insurance policies; see Assistudio, 2008.

central planning and global budgets with local control, leaving few changes as the USLs were "left floundering" in stagnation.

In brief, two key elements of the Italian NHS are worth mentioning here: first, the new system was formulated by a coalition whose members were drawn to it for dissimilar ideological reasons (institutionalised local party competition characterised by changes and counter-changes); and second, Italy's NHS was created in a unique normative context of public sentiment that healthcare in Italy was essentially a waste of money, costed too much and delivered too little.

With a set of reforms in 1992, the regional level gained considerable influence and independence in the provision of healthcare services. They are in charge of legislation, management and regional planning of healthcare services, as well as for monitoring the quality and efficiency of local health units (LHUs), and public and private hospitals (Donatini et al., 2001). Since 1992, the organisational framework of Italy's SSN has profoundly changed by the gradual introduction of an elaborated system of user co-payments and the ambitious plans of the 1994 Italian government to partially dismantle public universal insurance (Ferrera, 1995).

3.3.2 Reimbursement and financing

For the financial period 2007–2009 the national budget in Italy has allocated €300 billion to the SSN (Ministero, 2007). Total expenditure on health per capita is 2,494 in 2005 purchasing power parity (i.e. Int. $, 2005) and total expenditure on health as a percentage of GDP is 8.9 (WHO, 2008a).

If private facilities adhere to a convention with the SSN, healthcare services can also be covered by public funding; otherwise, they need to be paid for by the individual patient. In order to bypass long waiting lists, patients often resort to private payment for healthcare services. As a result of increased co-payments to the public system throughout the 1980s and early 1990s, both in terms of the amount and the types and levels of care (Ferrera, 1995) as well as the growing use of private providers with direct out-of-pocket payments, privately financed healthcare expenditures are significant in Italy.[31] Yet, perhaps surprisingly, private medical insurance is not very common.[32] Specialist outpatient visits, for example (such as maternity care), had relatively high co-payments and contributed to the picture of general citizen dissatisfaction in the mid- to late-1990s (Donatini et al., 2001).

3.3.3 Clinical practice

In Italy, physician density (per 10,000 population) was 37 in 2006; nursing and midwifery personnel density was 72; and pharmaceutical personnel density was 8 (WHO, 2008b). Despite the fact that Italy has probably the highest level of medical staffing in the world, the number of active physicians is not stabilise with more than 11 per cent of the

[31] In 1999 private financing accounted for 33 per cent of total healthcare expenditure according to Donatini et al. (2001).

[32] According to a study by Ania Trends (Associazione Nazionale fra le Imprese Assicuratrici) commissioned by Banca Italia in 2002 only 0.9 per cent of the private contributions to the healthcare system were financed by insurance policies (Assistudio, 2008).

profession unable to find work at all and a great number without a full-time position (Calcopietro, 2002). Added to this supply–demand mismatch, the organisation and management of Italy's healthcare system (and social protection more broadly), as already discussed, is inherently unequal in its regional disparities in healthcare coverage and differences in access to care based on ability to pay. Surprisingly, the physician–population ratio is lower in the northern provinces where the per capita GDP is much higher than in the South – a feature that underscores the role of non-economic factors in shaping the geographic distribution of health workforce (Calcopietro, 2002).

The decentralisation of Italy's SSN is also evident in the oversight of the quality of healthcare delivery in the country. As Donatini et al. (2001) describe, quality of care is governed by a regionally based accreditation process, which must respect the clinical and accreditation guidelines defined at central government level. The Ministry of Health is responsible for technically regulating healthcare activities in various areas and its monitoring activity includes authorisation of drug use and research. Under the executive functions of regional governments, the regional health departments of Italy regulate the provision of care by private and public providers through the authorisation and accreditation system. That is, the regional health departments in Italy are responsible for applying national framework rules to define the criteria for authorising and accrediting public and private healthcare settings in the region. But while institutional accreditation is a regional responsibility based on specific criteria related to structure, process and outcome, accredited status does not automatically confer the right to deliver healthcare services funded by the NHS. By the new millennium, seven regions in Italy formed a regional agency for health responsible for assessing the quality of local healthcare; these included Emilia-Romagna (1994), Friuli-Venezia Giulia (1995), Campania (1996), Marche (1996), Piedmont (1998), Lazio (1999) and Tuscany (2000). In addition, the role of user groups in Italy has grown in recent years and various consumer associations are involved in monitoring the quality of care provided both by private and public providers. Finally, Italy's National Health Plan for 1998–2000 envisaged the development of a National Programme on Health Care Quality aimed at steering the SSN towards continuous and systematic improvement, assessment and monitoring of all dimensions of quality.

Despite the re-distribution of responsibility for accreditation of health personnel and quality assurance across all levels of government in the National Health Plan, it remains unclear to what extent the available institutional mechanisms can guarantee similar quality of healthcare across Italy's regions (Donatini et al., 2001). In this context, it is important to note that Italy is not among the top performing European countries in policy areas aimed at improving patient safety – the country is among others which do not have a national reporting and learning system to monitor and analyse the incidence of adverse events and reactions in healthcare settings, nor an established fair redress mechanism (Conklin et al., 2008).

Finally, Italy's maternal and perinatal healthcare services can be assessed based on WHO's reproductive health MAE data (2000). In Italy, in 2000, the lifetime risk of maternal death was 1 in 13,900; low birth weight prevalence was 6 per cent (the same as it was in 1996); and, the perinatal mortality rate was 8 per 1,000 (WHO, 2006a). In 2000, the top two causes of death for neonates in Italy were preterm birth (48 per cent) and congenital anomalies (29 per cent) (WHO, 2006c). Unfortunately, the most recent data in WHO's

reproductive health Monitoring and Evaluation database does not provide any maternal and perinatal health indicators for antenatal care coverage (for more than one or more than four visits); births attended by skilled personnel (as per the UN Millenium Development Goals); nor the availability of basic or comprehensive essential obstetric care (per 500,000). These indicators are important to provide the clinical context of maternal and child healthcare in Italy's system.

3.3.4 Organisation and management

In Ferrera's typology of welfare states in Europe, Italy has a "Southern" type of welfare state in which its rules of access are governed by a fragmented system of income linked to work position. This reality is perhaps a reflection of the overall normative context of Italy where the country's solidaristic principles tend to "treat equality as synonymous with uniformity of benefits" (Brown, 1984) such that access to the benefits of social care and healthcare reflect to some degree the economic status and ability to contribute of various occupational sectors. The point that Brown makes regarding Italy's healthcare reform in terms of the normative context of Italy is important for understanding public impressions of Italy's public system more broadly: compared with the UK, or even France, the sense of class grievance is fairly muted and the sense of social justice is more subdued in Italy, leading to a greater public interest in a strong private sector (certainly for healthcare).

The financing of Italy's "Southern" welfare system occurs through contributions and fiscal revenues. However, there is a high level of regional particularism with regard to cash benefits and financing, which is expressed in high levels of private service clientelism.

3.4 Outlook: future trends and possible developments

The Italian example clearly shows that ART policy is strongly influenced by the cultural and political context of a country. After a long debate, the enactment of the very restrictive law 40/2004, has, according to the secularists, not provided a satisfactory solution. Rather the recently published first report on the implementation of the law has stimulated new debates.

The current regulation foresees the re-evaluation and potential amendment of the guidelines for ART (issued on the basis of the law 40/2004) in the light of new technical and scientific developments, every three years. The first re-evaluation is currently on its way and the Ministry of Health has asked the Consiglio Superiore di Sanità to provide recommendations on possible amendments of the guidelines. The recommendations issues on 19 July 2007 included: recognising sexually transmittable illnesses such as Chlamydia as a risk factor for infertility; allowing cryoconservation (and later use) of more then three eggs; improving the regional access to ART to counter the migration of infertile couples to other Italian regions; and collecting disaggregated data to provide a more complete picture of the implementation of ART. These recommendations are not binding but provide some information on the most probable future developments in Italian ART policy.

The requests for amendments issued by other associations, civil society groups and parties, patient groups and medical professionals go somewhat further.

Box 4 Examples of amendments requested by critics of the current law[33]

- Recognition of sexually transmittable illnesses such as HIV as a condition of infertility
- Fertilisation of more than three eggs
- Cryoconservation of eggs
- Pre-implantation testing
- Transfer of less than three embryos into the woman's womb even when the fertilisation of more eggs was successful
- Heterologous treatments
- Declare sterility and infertility as being an illness

In September 2007 a ruling of the court of Cagliari has shown that developments can also be driven by the judiciary. The court permitted pre-implantation testing of an embryo given the parents suffered from a genetically transmissible illness, a decision that has been welcomed by those groups asking for a less restrictive regulation, while having been strongly criticised by the Catholic Church and the supporters of the law.

But individual initiatives may also impact the practice of ART provision in Italy. According to an article published in the Italian newspaper *Corriere della Sera* in September 2007, couples suffering from infertility have started to adopt strategies to undermine some of the most controversial aspects of the law. To avoid multiple pregnancies, which according to the medical opinions cited incur a 40 per cent higher risk of premature delivery and neonatal malformation, couples undergoing ART have started to oppose the obligation of transferring all three embryos, by issuing written statements denying their agreement to this. Given that the transfer of embryos into the woman's womb is not enforceable this tactic has led to the return of the legally prohibited cryoconservation of the superfluous embryos in many Italian hospitals, putting them into a difficult position given the contradictory legal provisions (Ravizza and Sargentini, 2007).

While Italy was governed by a short-lived centre-left coalition there appeared a good chance that assessment of the guidelines would lead to the adoption of some of the proposed changes; however, a return to power of the centre-right coalition in May 2008 rendered this less likely. Even with the left in power, a fundamental revision of the law itself would have been unlikely, especially considering the experience of the complicated and controversial debate preceding the adoption of the current law.

Issues such as ART for same-sex female couples that are on the horizon in other countries seem to be far too controversial in the light of the strong influence of the Catholic Church, to be adopted in the Italian framework in the near future.

[33] See for example Associazione Luca Coscioni, *Appello dei parlamentari: a tre anni dalla legge 40 ripartiamo dalle linee guida*, 17 October 2007 (Associazione Luca Coscioni, 2007).

CHAPTER 4 United Kingdom

The UK has the longest history of ART provision of any country in the world, with a tradition in the pioneering of controversial biomedical research and techniques. The UK also has a moderate system of regulation whereby an oversight body issues licences to fertility clinics, providing recommendations in the form of a code of good practice. The body has the power to take into consideration a clinic's adherence to the prescribed standards when reissuing licences, which it has the power to revoke. The provision of ART also varies significantly across the UK, a situation that is often referred to as a "postcode lottery". This disparity of access is due to the relative autonomy of regional funding bodies varying in their policy to ART treatment, and the absence of an adequately forceful central directive. This chapter case study will explore the regulatory, cultural and economic landscape of ART use in the UK, and discuss its characteristics and performance in a comparative context.

4.1 Current state of Assisted Reproductive Technologies in the UK

4.1.1 Regulatory context

The UK has a nationalised health system, the National Health Service (NHS), under which there is an independent licensing authority, the Human Fertility and Embryology Authority (HFEA), created by the relevant 1990 Act to regulate and license clinics and laboratories to perform certain ART practices. The HFEA is made up of medical professionals and lay people (including religious officials, social workers, reporters and individuals who have experienced infertility) who consider the regulation of ART twice-yearly (based on changes in technology and the evolving ethical landscape), and inspects and licenses ART clinics. While the HFEA is a regulatory body, the UK-based National Institute for Clinical Excellence (NICE) issues guidelines on patient access to ART in the NHS in England and Wales. These guidelines, however, are only recommendations. Individual clinics – in co-operation with Primary Care Trusts (PCTs) if they are National Health Service (NHS) funded – make decisions about which clinical services they choose to offer, and about access to those services.

NICE has defined infertility as "failing to get pregnant after two years of regular unprotected sex,", though it has not explicitly defined infertility as an illness (NICE, 2004). Moreover, there is no UK-wide standard for who can receive ART procedures, due to the degree of regional autonomy of both the different countries within the UK, and the PCTs within the NHS. Only Wales has centrally established eligibility criteria for ART

services. By contrast, PCTs in England, Scotland and Northern Ireland may have divergent definitions of infertility; and waiting times can also differ markedly (Infertility Network UK, ca. 2008). Resulting from this differing access is a sort of "postcode lottery," most pronounced in England, where one PCT offers coverage of ART treatment, while the neighbouring one does not (BBC Health, 2008).

Each PCT decides the scope of its ART funding and associated eligibility criteria. Almost a quarter of PCTs in the UK did not fund ART at all in 1998. For example, the Cambridgeshire Primary Care Trust had not previously provided ART services, which its board had declared a low priority for resources (Birenbaum-Carmeli, 2004). In a subsequent shift of policy, the NHS East of England (covering Cambridgeshire PCT) announced that from April 2009 it would implement NICE's 2004 guidelines of funding three full cycles of IVF to clinically eligible couples: that is, where the woman is aged 23–39, and the couple have been having regular unprotected sex for three years (Henderson, 2008b). Most of the local PCTs claim the reason behind any non-provision of ART is its expense and "lack of necessity". For PCTs looking at budget shortfalls, it is much easier to justify cutting ART programmes than, for instance, downsizing or eliminating cancer programmes.

Despite local differences in who is eligible for public funding of ART, there are some requirements common to all PCTs. Until recently, all PCTs required applicants to be in stable relationships for at least two or three years and have no existing children. In November 2007 the government introduced the Human Fertilisation and Embryology Bill into Parliament with the aim of updating existing legislation, including removing the reference of the "need for a father" in respect of the "welfare of the child". In May 2008 a parliamentary vote rejected an amendment with cross-party support seeking to maintain the "need for a father" reference, effectively ensuring that the Bill would pass into law (Department of Health, 2007b, and Watt, 2008). Requirements in respect of "welfare of the child" include the proven ability to provide a caring environment for the child and an absence of child-related convictions or offences related to domestic violence.

Potential ART patients are encouraged to undergo counselling by fertility clinics – a recommendation of the HFEA, though some clinics require this, while others do not – to determine: (1) the patient's age and likely future ability to look after or provide for a child's need; (2) the couple's commitment to having and bringing up a child; (3) their economic status and ability to provide for the child; (4) mental and physical health of the parents; and (5) need of the potential child to know about their origin (IVF-infertility, 2008). This last point led to the 2004 change in regulations that previously required gamete donation to be an anonymous activity. Under the new ART guidelines, donors are required to consent to their name being released to the child on their 18th birthday (if it is requested).

While British law is relatively liberal regarding the practice of most ART treatments, there are two major exceptions: surrogacy and Preimplantation Genetic Diagnosis (PGD). The 1985 Surrogacy Arrangements Act seeks to regulate surrogacy so that there is no commercial dimension: advertising is forbidden for both parties and commercial third-party brokering is illegal (Surrogacy UK, 2008a; 2008b). Voluntary surrogacy agencies do, however, exist in the country such as COTS (Childlessness Overcome Through Surrogacy

UK). While surrogacy arrangements themselves cannot be legally binding, COTS attests that 98 per cent of surrogate pregnancies reach a successful conclusion (COTS, 2008a; 2008b). Both sperm and egg donation are likewise regulated against being commercialised, allowing only for "reasonable expenses" incurred in the process of donation to be reimbursed (HFEA, 2008d). The one exception is for so-called "egg-sharing" where discounted IVF can be obtained for egg donation to another infertile couple.

The UK also limits PGD and Preimplantation Genetic Screening (PGS) to monitor spontaneously occurring genetic defects and other serious diseases. The technique is also allowed for tissue sampling to determine whether a potential child could be a donor to an ailing sibling. But, its use for sex selection is generally forbidden, unless it is to avoid sex-selective genetic disorders. The HFEA licenses the testing of certain genetic conditions permitted for testing with PGS (HFEA, 2008h).

While the UK has made progress on implementing the EU tissues and cells regulatory framework, the designated authority is not responsible for reproductive tissues and cells

All three Commission Directives related to human tissues and cells have been transposed into national law in the UK, and some elements of the setting standards for quality and safety directive were already transposed into national law as of February 2006 (European Commission DG SANCO, 2007). Similar to Italy, the designated competent authority under the EU Tissues and Cells Directive, the Human Tissues Authority (HTA), is responsible for all tissues and cells for human application other than reproductive cells. Hence, the HTA reports in the 2008 DG SANCO survey that no reproductive tissues and cells establishments were accredited on 31 December 2007. However, in a previous survey, the country reported that it was still in the process of accrediting the remaining 100 establishments in accordance with Directive 2004/23/EC, including reproductive tissue establishments (European Commission DG SANCO, 2007).

Notably, accreditation of all (non-reproductive) tissues and cells establishments is based on an inspection process that is risk-based and, while the HTA has the power to suspend or revoke licences where there has been a serious breach of licence conditions, it has never yet revoked a licence – it has laid down penalties for infringements of the national provisions pursuant to the Directive (European Commission DG SANCO, 2008). Importantly, third party agreements of tissue establishments in the UK are also examined as part of any on-site HTA inspection of a tissue establishment (ibid.). But again, no inspections by the HTA were conducted in assisted reproduction centres since it is not the designated competent authority responsible for reproductive tissues and cells (European Commission DG SANCO, 2008). Nevertheless, an earlier DG SANCO survey (2007) listed a number of activities included in the UK's accreditation of reproductive tissues and cells preparation processes that were not explicitly listed for authorisation in France, such as procurement and distribution (European Commission DG SANCO, 2007).

In 2007, moreover, the UK's existing regulatory framework for human tissues and cells already provided for a control system to ensure that all gametes and embryos coming into the UK for use in treatment had been handled to the same standards applicable to UK establishments – the import/export controls applied equally to imports from EU Member States as they did to non-EU countries (European Commission DG SANCO, 2007). Furthermore, among the three country cases, only the UK has reported figures on gamete

(sperm and egg cell) imports/exports in another Commission document (DG SANCO, 2006).

Finally, the availability of data on cross-border exchange of reproductive tissues and cells is important in the wider context of improving patient safety both at home and abroad because without such data one cannot monitor progress in this area. Indeed, the UK has an established electronic system for the reporting of serious adverse events and reactions as well as for the submission of analysis reports from tissue establishments following their investigation into the serious adverse event or reaction (European Commission DG SANCO, 2008). Similar to France, the UK has clearly defined criteria for reporting, using the definitions of each term given in the Directive 2004/23/EC as well as providing additional term specifications. However, one difference between the two countries in regards to their reporting systems is the fact that the UK has explicitly reported data on such reports (16 in 2007) and also undertook analysis of the reports from licensed tissue establishments (European Commission DG SANCO, 2007).

4.1.2 Economic context

According to Birenbaum-Carmeli (2004), most UK health authorities treated several dozens of couples each (36–119) in 1999, at an average cost of €5,872–7,130 per cycle. While it is often difficult to obtain reliable data for the cost of ART treatment, costs clearly vary greatly by type of treatment. For example, IVF costs around €4,194 per cycle, ICSI between €6,770 and €11,510 per cycle, GIFT around €7,689 per cycle, and ZIFT between €10,150 and €13,540 per cycle. A somewhat dated cost-effectiveness study found that an ongoing IVF pregnancy costs on average roughly €12,580–15,380 (Sykes et al., 2001). In the UK, 44 per cent of ART cycles are ICSI and the rest are conventional IVF; about 25 per cent of IVF treatments are paid for by NHS (Ledger et al., 2006).

NICE guidelines suggest that the NHS should pay up to three cycles of ART treatment for women aged 23–39 with an identified cause of infertility, or those who have not conceived after three years of regular unprotected sex (the official NICE definition of infertility actually refers to couples who have not conceived after two years of unprotected sex) (NICE, 2004, and HFEA 2008j). NICE recommends that it is appropriate to fund IVF treatment when the chances of success are more than 10 per cent (HFEA, 2008i). In February 2004 the government announced that it would be asking PCTs to provide all women with appropriate clinical need *at least one cycle* of treatment paid for by the NHS, starting 1 April 2005.

In March 2005 the National Infertility Awareness Campaign (NIAC), alongside the All Party Parliamentary Group on Infertility (APPGI), conducted a survey of PCTs' progress towards the April 2005 deadline, and found significant differences both in eligibility for treatment as well as access to NHS funding (Infertility Network UK, ca. 2008). While inequality of access clearly exists in the UK, progress towards a minimum provision of at least one NHS funded cycle has been made. In 2007 the Department of Health conducted a survey of PCTs in England (with 100% response rate), finding that only four offered no form of IVF, which was a marled improvement from the figure of 14 in 2006 (with only a 50 per cent response rate to the survey) (Department of Health, 2008).

The UK has also suffered from a shortage of donated gametes in the past (Murray and Golombok, 2000). In 1999 the Glasgow Royal Infirmary was even required to import sperm from Denmark, due to a regional shortage. Although donors received compensation for "reasonable expenses," such as loss of time at work and transportation costs, there is currently a debate over whether there should be an increase in the financial incentive of donation (to thousands of pounds), an idea that anti-ART groups have opposed, equating it with "buying a life". The number of egg and sperm donors had been dropping fairly steadily, going from 325 sperm donors and 1,242 egg donors in 2000 down to 259 and 956 in 2005, respectively (HFEA, 2007d). Further adding to the shortage of male gamete donors, the HFEA has limited the number of children a single sperm donor can father to 10, in order to limit the incidence of accidental incest. In Denmark, the number is 25, while in France the limit is 5 (Deech, 2003). Finally, while it has been suggested that another factor contributing to the shortage of gamete donation in the UK is the recent changes to the anonymity of donors, this does not appear to be the case for sperm donors (Day, 2007). Rather, the latest figures of HFEA show that the number of men registering as sperm donors rose by 6% in the year following the law removing donor anonymity (HFEA, 2007d).

Egg donors have historically not been compensated, other than for travel expenses. There is some discussion of changing this to offer women more compensation for what is, indisputably, a more invasive donation procedure carrying greater risk of surgical complications to the donor than the donation of semen (BBC News, 2004). Indeed, the former head of the HFEA suggested in 2004 that women should be compensated much more for donating their eggs. In some cases in the UK, clinics have offered women free IVF treatment if they also donate some extra oocytes ("egg-sharing"). The HFEA remains concerned about this practice, however, especially in the case that IVF does not work for the donor herself, but is successful for another recipient of her eggs (Murray and Golombok, 2000). Most egg donors are identified through patient recommendations and advertising in local press. However, in the 12 months leading up to Murray and Golombok's study, 76 per cent of clinics reported that no resources were spent on recruiting egg donors, 12 per cent spent between €14 and €419, and another 12 per cent spent between €1,400 and €4,190. Asked why there are so few egg donors, 82 per cent of respondents in the study said that the main reasons were concerns about medical risks and a lack of knowledge about the need for oocyte donation.

A shortfall in gamete donation is one reason for why British couples engage in cross-border ART (or, "reproductive travel"), going to countries such as Spain. Women in Spain can receive around €900 for egg donation and there is no regulatory limit to the number of eggs that may be inseminated. Another common destination for reproductive travel by British couples is Eastern Europe, where there is concern among British doctors about the poor regulation of ART clinical practice (Henderson, 2004, and Monaghan, 2008). The lack of harmony in ART policy across Europe was a driving force in the enactment of the recent EU Legislative Directive on Protecting the Quality and Safety of Tissues and Cells.

4.1.3 Clinical practice: Assisted Reproductive Technologies practice is variable, but with minimum good practice standards

National regulation of ART in the UK means that it can only be practised legally under the accreditation of (and regular auditing by) the country's independent competent authority: the Human Fertilisation and Embryology Authority (HFEA), which licenses clinics and laboratories to perform certain ART practices, as noted above. Moreover, the quality of care provided throughout ART treatment is guided by good clinical practice guidelines, produced by the Royal College of Obstetrics and Gynaecologists (RCOG) and commissioned by HFEA, but which are not legally binding (implementation is discretionary).

Since HFEA is the implementation body of a European Commission (2004) Legal Directive on Tissues and Cells, the provision of ART services in the UK operates within a wider vigilance system for ensuring the quality and safety of human tissues and cells, including the handling and processing of oocytes and sperm at infertility centres. However, there is no clear separation in the oversight of care quality between public and private institutions as there is some overlap between public and private clinics which may accept either type of payment. That is, there are 60 public, NHS clinics offering IVF services and 49 private clinics, but some NHS clinics accept private payment, and vice versa) (HFEA, 2008a). This point is important given the fact that ART services may not always be provided in the UK within the established NHS, particularly in those regions where PCTs do not offer financial coverage of ART, thereby forcing many infertile couples to seek private care.

Table 4-1 shows the regional distribution of clinics offering ART in the UK. Licensed ART clinics are primarily concentrated in the South East (13) and in London (24).

Table 4-1 Clinics offering Assisted Reproductive Technologies in the UK, by region

Region	Public	Public, but can pay for unfunded treatment	Private	Private, but also accepts NHS patients	Total	Total public	Total private
East Midlands	1	3	0	3	7	4	3
East of England	1	0	1	3	5	1	4
London	2	8	7	7	24	10	14
North East	0	6	2	1	9	6	3
Northern Ireland	1	1	1	0	3	2	1
North West	1	6	1	2	10	7	3
Scotland	3	3	2	1	9	6	3
South East	1	4	0	8	13	5	8
South West	4	4	1	3	12	8	4
Wales	1	1	0	1	3	2	1
West Midlands	1	5	1	2	9	6	3
Yorkshire and the Humber	0	3	0	2	5	3	2
UK Total					109	60	49

SOURCE: HFEA (2008a).

Assisted Reproductive Technologies provision in the UK varies widely at the local level

It is estimated that approximately one in seven UK couples suffer from infertility (HFEA, 2008e). In 1998 the NHS funded an average of 10.8 IVF cycles per 100,000 persons; Ledger et al. (2006) estimate that the NHS funds only 25 per cent of IVF treatment in the

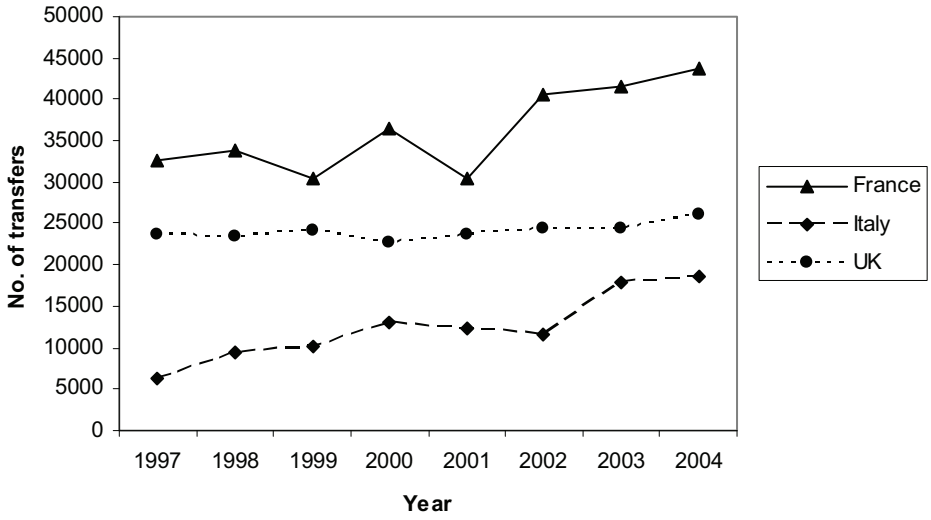
UK. However, the regional breakdown of infertility and its treatment gives a different picture (HFEA, 2008c). More specifically, this average has a wide spread in real ART provision at the local level, ranging widely between 0.3 and 21.5 women per 100,000 population, depending on the PCT (College of Health, 1997). Added to the unequal distribution of funded IVF cycles, over half of the PCTs in the UK have had waiting times of over one year for infertile couples (Birenbaum-Cameli, 2004).

Due to restrictions or lack of access to some types of ART, some UK couples desiring IVF may travel outside the country to receive lower cost treatment or treatment that is not allowed in the UK. However, there are currently no reliable sources of data on the true prevalence and incidence of such cross-border travel to ART clinics abroad.

Access to Assisted Reproductive Technologies in UK is among the lowest in Europe

Over a decade ago, the UK had the second highest provision of ART in Europe; with 23 per cent, it was second to France (32 per cent) in terms of total numbers of embryo transfers after IVF and ICSI among 18 European countries. By 2004, it was third among the same European countries, after France and Germany (Nyboe Andersen et al., 2008). In 2006, the country was still the third largest provider of ART services in Europe, with 37,000 cycles per year (HFEA, 2006).

Over the last several years, the number of IVF clinics in the UK has remained relatively constant over time (ranging between 72 and 80 from 1997 to 2004). Moreover, while the total number of embryo transfers after IVF and ICSI in the UK has increased from 23,553 in 1997 to 26,092 in 2004 (with some variation between the years), this increase is relatively small compared with the steeper rise in these figures for France and Italy (see Figure 4-1).

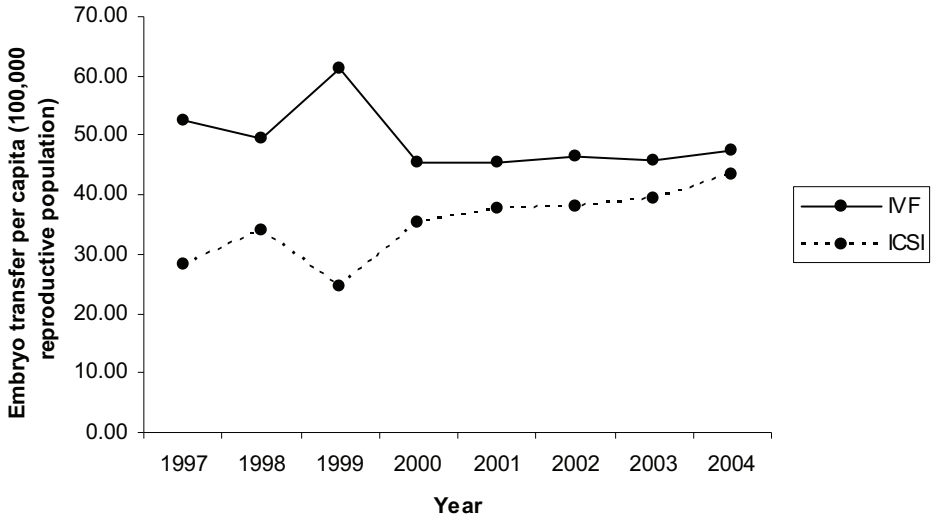


SOURCE: Nygren and Nyboe Andersen (2001a, 2001b, 2002) and Nyboe Andersen et al. (2004, 2005, 2006, 2007, 2008).

Figure 4-1 Total number of embryo transfers in the UK is stable over time relative to France and Italy

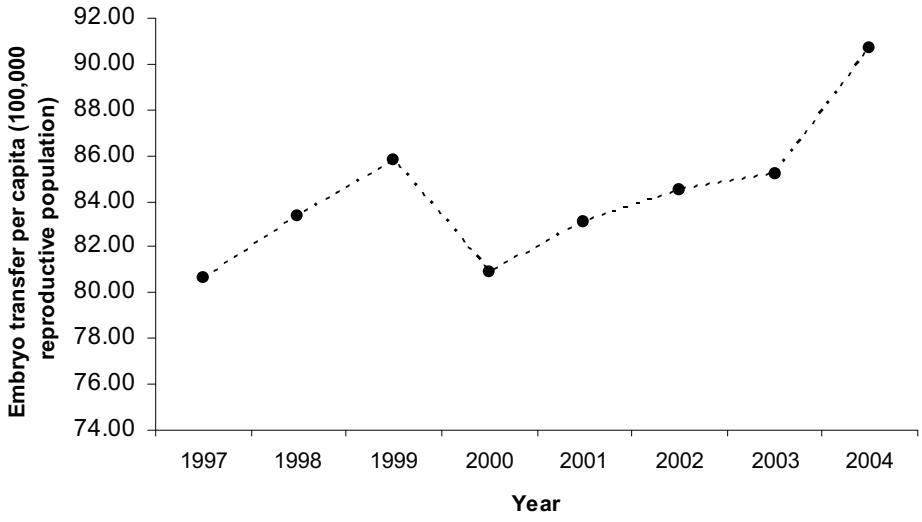
More problematically, when accounting for population growth, per capita ART provision in the UK is also among the lowest in Europe. Of those countries surveyed by ESHRE in 2004 and which reported to a National Registry, only Latvia (0), Austria (2) and Macedonia (1) had fewer cycles than the UK (3 per thousand women of reproductive age) (Nyboe Andersen et al., 2008). This further supports the concerns of Professor Ledger of Sheffield University that, despite being the third largest provider of ART, the UK is a country with one of the poorest rates of access to IVF treatment with only 600 cycles per 1 million women (Ryan, 2006a; see also Nyboe Andersen et al, 2006). This figure can be compared with 2,031 cycles of IVF per million people in the Danish population, the highest in Europe (Ryan, 2006b).

In terms of the different types of ART treatments in the UK, we see an interesting convergence of IVF and ICSI provision by 2004 to, respectively, 47.34 IVF and 43.34 ICSI transfers per 100,000 women of reproductive age (see Figure 4-2). The trends for these two types of ART treatment seem to be mirroring another, suggesting there could be a substitution effect between ICSI and IVF. In sum, however, the net effect of IVF and ICSI provision in the UK is a fluctuating increase of 10 additional embryo transfers per capita between 1997 and 2004 (see Figure 4-3).



SOURCE: Nygren and Nyboe Andersen (2001a, 2001b, 2002), Nyboe Andersen et al. (2004, 2005, 2006, 2007, 2008), Eurostat (2008).

Figure 4-2 Per capita provision of IVF and ICSI embryo transfers in the UK (1997-2004)



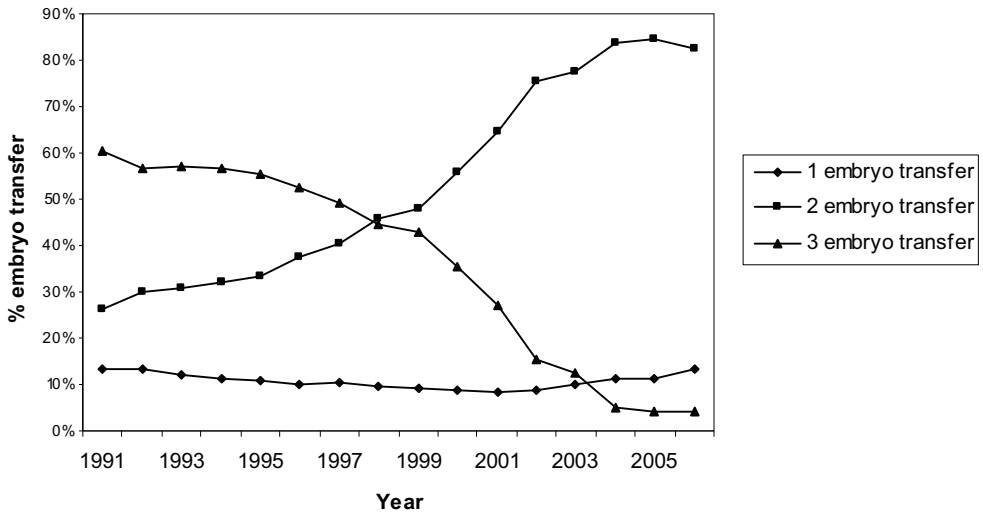
SOURCE: Nygren and Nyboe Andersen (2001a, 2001b, 2002) and Nyboe Andersen et al. (2004, 2005, 2006, 2007, 2008).

Figure 4-3 Assisted Reproductive Technology provision in the UK shows an overall increase over time

Transfers of three embryos are being phased out

Between 1991 and 2006, the UK showed a large decline in 3-embryo transfers (from 48.8 per cent to 5.5 per cent) with a concomitant rise in 2-embryo transfers (from 42.1 per cent to 85.1 per cent) (see Figure 4-4). This pattern is also seen in France, but the change there is less dramatic. The transfer of more than 3 embryos has not been practised in the UK

because it is illegal. At the same time, the proportion of 1-embryo transfers in the UK is very low (less than 10 per cent), and has only marginally increased over the last few years.



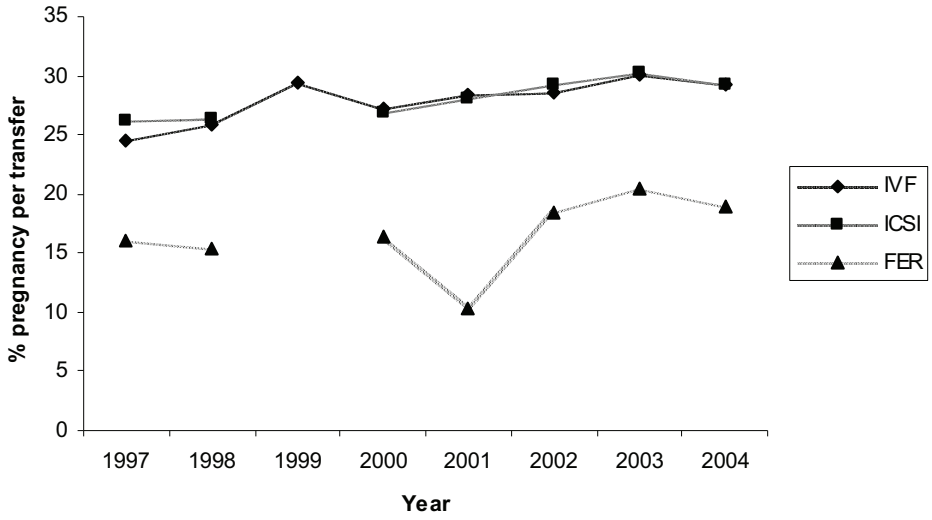
SOURCE: HFEA (2007b).

Figure 4-4 Proportions of 1-, 2-, 3- and 4-Embryo Transfers in the UK (1991-2006)

As multiple births are known to be associated with adverse health outcomes, both the HFEA and NICE have advocated that no more than 2 embryos be transferred per cycle, in order to cut down on multiple births (Ledger et al., 2006). Although this limit is not yet a legally binding requirement, the UK recommendation reinforces an international trend of good clinical practice that is known to improve maternal and child health after ART treatment.

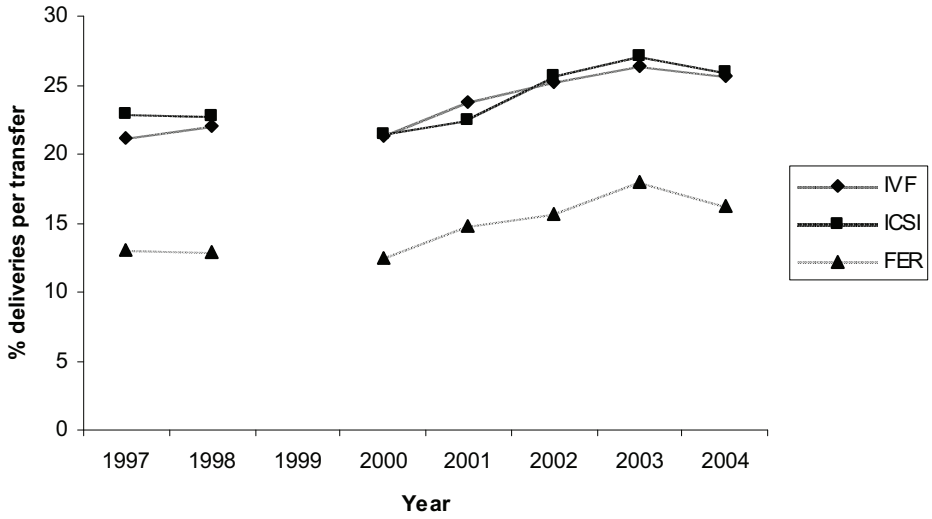
Success rates are increasing slowly

The pregnancy rate after ART in the UK has consistently increased by approximately 3 per cent since 1997 (see Figure 4-5), and the proportion of transfers that result in delivery has also improved by approximately 5 per cent in the same period examined (see Figure 4-6).



SOURCE: Nygren and Nyboe Andersen (2001a, 2001b, 2002) and Nyboe Andersen et al. (2004, 2005, 2006, 2007, 2008).

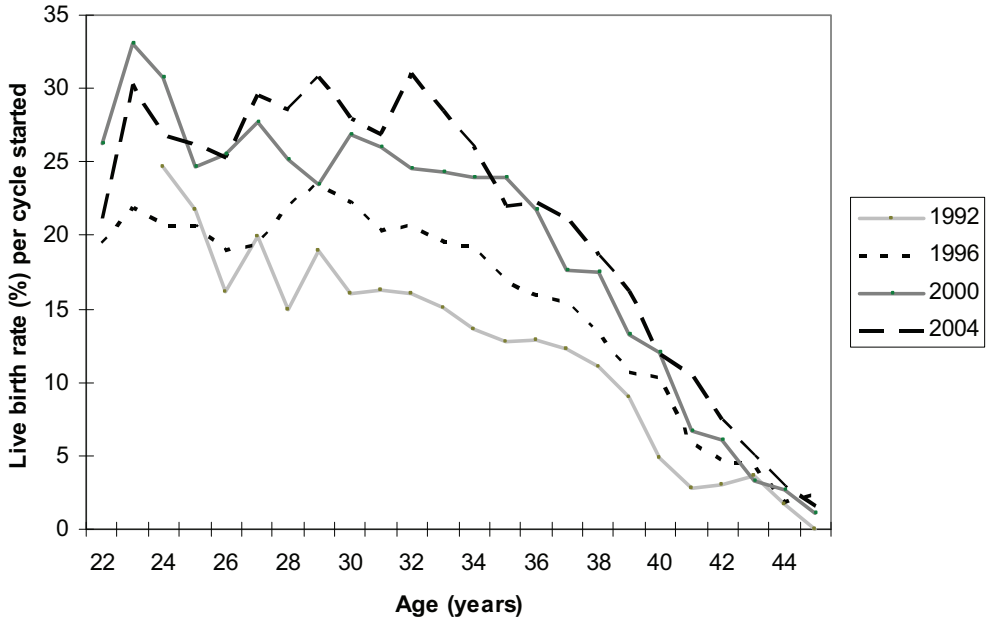
Figure 4-5 Pregnancy rate per embryo transfer after ART in the UK (1997–2004)



SOURCE: Nygren and Nyboe Andersen (2001a, 2001b, 2002) and Nyboe Andersen et al. (2004, 2005, 2006, 2007, 2008).

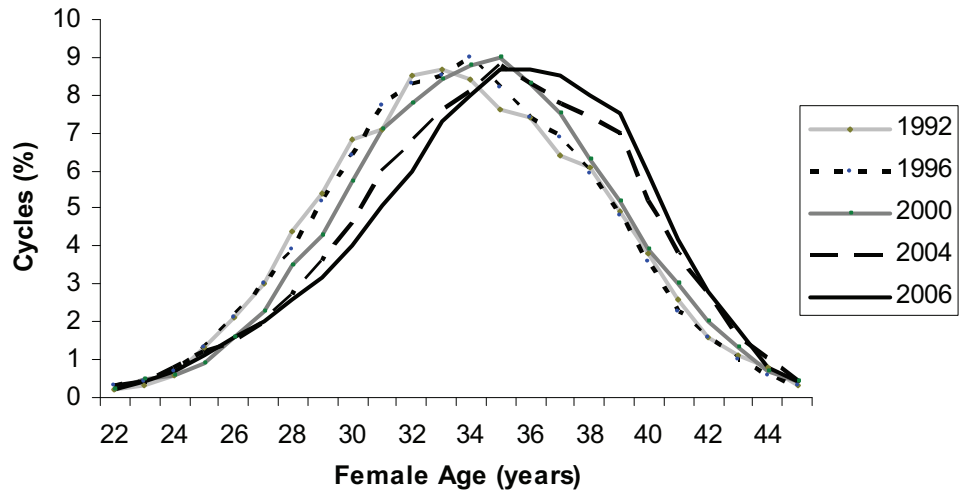
Figure 4-6 Delivery rate per embryo transfer after ART in the UK (1997–2004)

As Figure 4-7 illustrates, success rates decrease considerably after the female age of 35. Ironically, it is women aged between 35 and 40 that increasingly form the dominant age group among British infertility patients seeking treatment in recent years (see Figure 4-8). Despite the increasing proportion of older women undergoing ART, aggregate success rates have improved over time, particularly for women under 35-40 years old.



SOURCE: HFEA (2007b).

Figure 4-7 Overall success rate of IVF and ICSI in the UK, by age (1992; 1996; 2000; 2004)



SOURCE: HFEA (2007b).

Figure 4-8 Age distribution of women in the UK undergoing ICSI or IVF (1992; 1996; 2000; 2004; 2006)

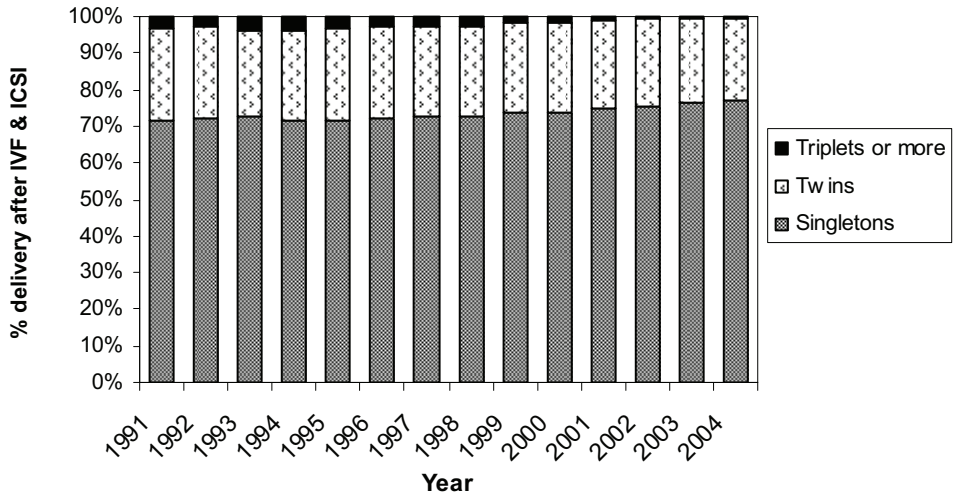
Bearing in mind that these are aggregated figures, in order to better understand how these improvements in clinical practice come about, it would be useful to disaggregate the figures along more variables, such as primary diagnosis, and health behaviours (e.g. smoking or drinking behaviour) that are also known to affect the outcomes of ART.

4.1.4 Assisted Reproductive Technologies outcomes: changing health outcomes in the UK over time

Triplets after Assisted Reproductive Technologies are becoming rare in the UK

The proportion of deliveries after ICSI and IVF that are multiple births fluctuates in the UK between 25 per cent and 30 per cent over the time period examined. Nevertheless, there is an overall trend of reducing significantly the proportion of triplet deliveries from 3.7 per cent to 0.3 per cent between 1991 and 2004 (see Figure 4-9). By contrast, twin deliveries in the UK have fluctuated around 24–25 per cent between 1991 and 2004, but there seems to be a marginal downward trend in recent years.

In parallel, we see a modest increase of 5 per cent in the proportion of all ART births that are singleton in the UK. This is a small change in clinical practice given that one in four IVF births are multiple (compared with the incidence of one in eighty multiple deliveries of naturally conceived births in the UK) (HFEA, 2008b and 2008g).



SOURCE: HFEA (2007b).

Figure 4-9 Proportions of singletons, twins and triplets after IVF and ICSI in the UK (1991-2004)

The proportion of multiple deliveries after IVF and ICSI is a useful proxy for assessing the extent of adverse health outcomes after ART treatment. Among multiple pregnancies, around 20 per cent of mothers carrying twins suffer from induced hypertension (high arterial blood pressure), compared with only 1 per cent to 5 per cent of mothers of singletons (Oneatatime.org, 2008b). Moreover, given that 50 per cent of twins and 90 per cent of triplets will be born prematurely and suffer low birth weight (HFEA, 2007a, and Oneatatime.org, 2008a), we can expect that 20% of all ART babies in the UK will suffer these health problems. In order to limit triplet births, the HFEA guidelines stipulate a maximum of 2 IVF embryos be re-implanted, other than in exceptional circumstances (HFEA, 2001). In this context, the phasing out of 3-embryo transfers in the UK shows an improvement over time towards fewer triplets associated with ART. The effect on twins has been much less pronounced.

Thus, the HFEA maintains that the current rate of multiple births in the UK is unacceptably high. From October 2005, the HFEA conducted a multiple births and single embryo transfer review, commissioning an expert group to review the available evidence. Their recommendations, published in October 2006, focused on the development and wider implementation of eSET (elective single embryo technology) as the most effective means of reducing multiple births. The group drew on evidence suggesting that if good prognosis patients are carefully selected (they are relatively young women who do not have a history of failed IVF attempts), single embryo transfer can be as successful as multiple embryo transfer.

The HFEA also advised that this transition must be accompanied by a significant injection of state investment to finance both frozen embryo storage facilities and *three* full cycles of eSET treatment, in recognition that patients are unlikely to be enthusiastic about single embryo transfer if only one cycle is offered as they would perceive this as providing merely "one chance" at pregnancy. The recommendations therefore underlined the need to implement the NICE guidelines on funding of three cycles. They also suggested that the Department of Health should issue a statement that acknowledges the benefits of eSET. It is estimated that offering eSET to 50 per cent of IVF patients will lead to a twin rate of less than 10 per cent. By contrast, the most recent available data indicates a twin rate of 24 per cent in 2005 (HFEA, 2008g).

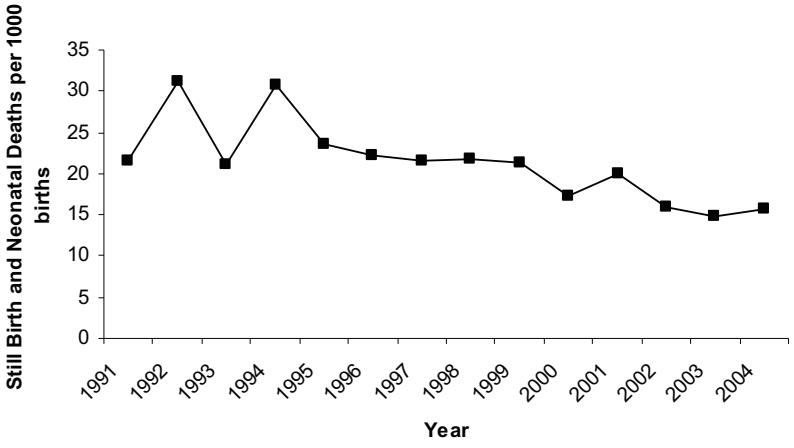
It is in recognition that multiple births are the single biggest health risk associated with IVF treatment that guidelines promoting the use of eSET have been issued. As recently as September 2008, the British Fertility Society (BFS) and Association of Clinical Embryologists (ACE) issued guidelines strongly advocating moves towards more widespread implementation of eSET, estimating that the short term increases in cost would be offset by money saved from otherwise treating the longer term health problems associated with multiple births. However, it is worth emphasising that the increase in cost of treatment falls largely on the presently private patients (as a majority), whereas the costs of treating pregnant women and premature babies falls almost entirely on the NHS. Once again, it was emphasised as "absolutely critical" that "the Department of Health issues strict guidance to Primary Care Trusts to fully implement the NICE guidelines on fertility treatment" (British Fertility Society, 2008). That eSET is now a viable form of ART indicates how much scientific progress has been made since the beginning of IVF treatment. Moreover, as these technologies continue to improve, the cost of ART facilitated pregnancies is likely to decrease, making limited funding of eSET less of a constraint.

Although the HFEA's general clinical guidelines are based on careful and thorough bi-yearly review, there have been documented cases of poor adherence to them. The HFEA's own regulatory procedure has, however, itself been met with controversy, as the HFEA was forced to withdraw its January 2007 assessment report of UK clinics after a high-profile London fertility doctor, who had been criticised for poor adherence to HFEA guidelines in spite of the highest pregnancy success rate of any clinic in the country, issued a High Court challenge to the legitimacy of the HFEA's assessment methodology (Henderson, 2007).

Adverse events after IVF and ICSI are rare in the UK, except for OHSS

Among the many care quality and patient safety indicators, the UK appears to show better health outcomes. Without investigating the extent of reporting bias, we note that only one infection after IVF and ICSI reported in the UK in 2004 (compared with 299 in France that year), and very few reports of bleeding between 2000 and 2004 (compared with double-digit figures in Italy and France over this time period) (data not shown), according to published data reported to the ESHRE. By contrast, annual numbers of still births and neonatal deaths after IVF and ICSI have ranged widely between 65 and 104 in total. However, accounting for population growth, the rate of these events per 1,000 births shows a marginal downward trend in recent years (see Figure 4-10). Furthermore, the proportion of pregnancies after IVF and ICSI that are lost over time in the UK is lower than in France and Italy by a factor of approximately two (see Figure 5-21).

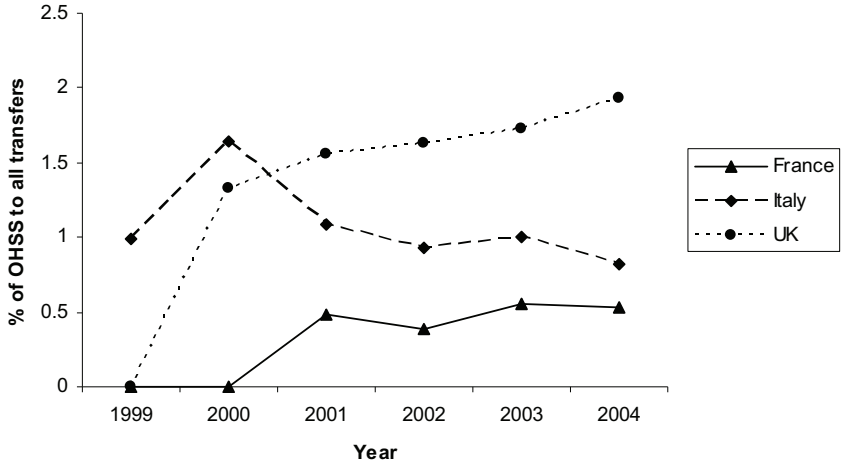
In the wider healthcare context, it is important to note here that the UK, like France, has a national reporting and learning system for adverse events and reactions to improve patient safety. However, the vigilance system in the UK includes a variety of adverse events, whereas the French system only reports on infections in the country's hospitals.



SOURCE: HFEA (2007b).

Figure 4-10 Still births and neonatal deaths per 1,000 births in the UK decline (1991-2004)

Although there are few health complications in Britain after IVF and ICSI, there is a relatively high incidence of Ovarian Hyperstimulation Syndrome (OHSS) complications, compared with France and Italy. This serious complication is the consequence of an overdose of gonadotrophins (drugs for medically induced ovulation), which may cause enlargement of the ovaries, fluid-retention and weight gain. Not only do OHSS complications occur at least twice as frequently as in France or Italy, the incidence of this condition is also increasing in recent years (see Figure 4-11).



SOURCE: Nygren and Nyboe Andersen (2001a, 2001b, 2002) and Nyboe Andersen et al. (2004, 2005, 2006, 2007, 2008).

Figure 4-11 Proportions of OHSS to all transfers in the UK, compared with France and Italy (1997-2004)

This trend could be the consequence of a pressure to produce as many viable oocytes as possible, due to financial constraints. If couples have to pay out-of-pocket, they have an incentive to produce as many oocytes as possible. Additionally, the anecdotal evidence that some clinics offer discounted (or free) IVF in return for oocyte donation (in a so-called "egg sharing" arrangement) may be contributing to this trend.

4.2 Contextual factors for Assisted Reproductive Technologies policy in the UK

4.2.1 Historical background

In July 1978, the world's first IVF baby, Louise Brown, was born in the UK (HFEA, 2008j). This achievement gave rise to an intense round of soul searching for the UK medical community, and by March 1979 the Medical Research Council had convened a committee to discuss the policy and ethical issues of Assisted Reproductive Technologies (ART). In 1981 the Medical Research Council approved public funding for IVF research, and in 1982 the ethics committee reconvened to explore the changes in the ethical landscape. This first committee focused the discussion on technical capabilities, but also addressed the right of all couples to have children, a position opposed by the British Council of Churches and others (Blank, 2004, and Priest, 1988).

Initially, politicians were loath to deal with the extremely controversial issues brought up by the technical developments in ART, but spurred by public pressure in 1982 they established a Committee of Inquiry under Dame Mary Warnock. The Warnock Committee convened for two years and in that time considered policies and safeguards that should be applied to ART and developed relevant policy recommendations. The Committee reviewed submissions by 252 health authorities, research councils, colleges of medicine, religious bodies, medical charities and university departments, aiming to take

into account the full spectrum of public opinion and research (to "discover the public good in its widest sense") (Blank, 2004).

One recommendation of the Committee was a statutory licensing authority that would regulate the practices permitted by the PCTs. They suggested that this authority should have significant lay presence and that there be criminal prosecutions for unauthorised ART research or clinical procedures. They also recommended for data to be collected by all clinics on the service and outcomes experienced by individuals seeking treatment.

The country was split in its feelings about the report, with a variety of stakeholders taking positions against it. Those who opposed it include the following: the Medical Research Council, the British Medical Association (BMA), the Royal Society and the Church of England supporting it, and the Roman Catholic Church, the Society for the Protection of the Unborn Child and other anti-abortion groups. As a result, the report's results were largely ignored (being too controversial) and the UK was left without formal regulation until 1986 (Blank, 2004).

Between 1982 and 1986 there was much debate among policymakers, the public, religious groups and advocacy organisations, as well as within professional societies, about what the best form of regulation would be. In 1986 the government released a consultation paper entitled *Legislation on Human Infertility Services and Embryo Research*, which asked stakeholders to decide on a regulation mechanism – either voluntary self-regulation, direct control of procedures by the Secretary of State, or the statutory licensing authority proposed by the Warnock Committee. Stakeholders – the Catholic Church, SPUC, LIFE and professional medical groups – voted overwhelmingly in favour of regulation via the licensing authority (Blank, 2004).

In 1990, the Human Fertilisation and Embryology Act 1990 (c. 37) created the relevant regulatory body, the Human Fertilisation and Embryology Authority (HFEA), to design a system of national regulations and license individual clinics to perform ART (Blank, 2004). It was the first statutory body of its type in the world. The HFEA developed a Code of Practice for clinics, which is reviewed every two years to keep abreast of changes in technology and the state of bioethics in ART services (Blank, 2004, and HFEA, 2008f).

4.2.2 Legislative framework

The legislative framework in the UK was developed through the political process previously described, but it was also based on the conclusions by the ethics committees of various professional organisations, such as the Royal College of Obstetricians and Gynaecologists and BMA, which produced guidance documents on the use of ART for their members. Many of these professional ethics committees came to similar conclusions as the Warnock Committee.

While most of the medical community preferred self-regulation, they saw that this was unlikely to happen, given the political climate. Likewise, many anti-ART interest groups recognised that they were not going to win the push for state control, so both sides in the end decided to agree to the Licensing Authority route of regulation. In this way, both stakeholder groups could participate in the process and progression of regulation. While anti-ART groups did not generally come out ahead in the arguments, they did get some important concessions, such as the initial requirement that IVF-receiving couples be

heterosexual, and the provision of extensive counselling and screening to ensure that parents could provide a stable and supportive environment for their children.

4.2.3 Key players

At the beginning of the policy process in the 1980s, decision-making was dominated by corporate interests, particularly medical associations. The first inquiries into the ethical questions produced by Louise Brown's birth were spearheaded by the Medical Research Council and the Department of Health and Social Security, which had a mainly professional medical membership. The medical community clearly holds significant sway in the HFEA's decisions on permissible techniques and applications of ART in the UK.

Opposition groups have achieved few concessions, and as time goes on even these concessions are being curtailed. The requirement that couples be heterosexual has, for instance, now been explicitly lifted: as discussed in section 4.1, same-sex female couples are now by law eligible for ART on the NHS.

Churches in England have been split in support and opposition to ART. The (Anglican) Church of England is generally more moderate in its stance on social issues such as homo/bisexuality and bioethics. The Catholic Church, on the other hand, has historically been staunch in its opposition to ART. Nonetheless, it is of historic note that the Church of England had once vehemently opposed gamete donation that, within a decade, became authorised practice in the UK.

4.2.4 Channels of influence

When the first IVF baby was born in the UK, newspapers all over the world announced her arrival and, as the British public became more aware of what was going on in UK scientific laboratories, the influential media came to demand that the government look at the moral and ethical dimensions of this scientific revolution.

Lobbying groups and the public were also very influential in getting political action on IVF on both sides of the debate. There was public demand for ART as well as public demand for its regulation. Public interest lobbying groups, such as SPUC and LIFE, pressed hard for parliamentary action, and achieved some parliamentary representation in the form of Enoch Powell's 1985 Unborn Child (Protection) Bill, which would have effectively outlawed all research on human embryos. In spite of failing to be enacted, Powell's Bill nevertheless contributed to a firmer regulatory strategy for ART (Doran, 2008).

4.2.5 Prominent controversies

Two particularly controversial fertility cases exist in the UK: first, the case of Diane Blood who was a plaintiff in a civil case arguing to use her deceased husband's frozen sperm to become pregnant; and second, the case of Michelle and Jayson Whitaker, who fought for the right to use PGD (tissue typing) to choose an embryo that was free of the disease Beta Thalassemia and could serve as a "saviour sibling" for a child that was already suffering from the debilitating condition.

In 1997 Diane Blood won her court case against the HFEA, which had denied her the right to use her deceased husband's sperm samples for insemination because he did not consent to their use in this particular way. The Court of Appeal overturned a ruling by the

High Court that had denied her use of the sperm. However, the ruling required that she have the procedure done in Belgium, rather than in the UK. The HFEA reported, "the Court of Appeal has confirmed that the principle of informed written consent is an essential part of English law and that the posthumous storage or use of sperm or eggs without such consent is unlawful in this country in all cases" (Deech, 2003, and HFEA, 1997). They nevertheless stressed that this was a one-off case, and that it should not be made a precedent for a permissible change in the rules on the subject.

A third possible controversy pertains to the perceived need for children in the UK in the face of the looming demographic issues of an ageing population. While the total fertility rate of 1.9 in 2007 (National Statistics Online, 2008) is well above the EU average of 1.5, it still remains below the minimal rate of 2.1 required to replace the current reproductive generation. At odds with this perception is the strong opposition from church and anti-ART groups on the grounds that having children should not be a universal right. Thus, the tension between the powerful medical community and the religious community will continue to be a driver of controversy surrounding new ART treatments in the UK.

4.3 Healthcare and welfare systems

4.3.1 Regulatory

In 1911 the UK's Liberal government enacted a very limited programme of national health insurance, which made a few official improvements to the pre-existing private system of 19th century mutual aid funds for English industrial and urban workers. During World War II the national coalition government made one of its aims to improve healthcare and social protection generally and major improvements were pledged in the famous Beveridge Report and the White Paper *A National Health Service*, although the precise structure was not described therein.

With the nationalising of healthcare by the 1945 Labour government, the entire population in the UK is covered by the National Health Service (NHS), with all contributing taxes in some fashion. All persons have the same benefits and rules. Hospitals have since been the property of the state and institutional and physician services have been financed from the general budget of the national government. Some healthcare has remained private, such as long-term care for the elderly. It is important to note that the driving force behind the creation of Britain's NHS in the post-war era was a strong sense of social justice (Brown, 1984).

Importantly, the UK's NHS differs from national health insurance in other countries where members of different regimes vary in payroll tax rates and correlated benefits, and where some classes may remain completely uncovered as in France, for example. Unlike France, uniformity in the operations of the NHS structure and in the delivery of NHS services throughout the UK has always been sought through the framework of laws of Parliament, the regulations from the Ministry, the monitoring of the providers' reports about their expenditures and performance, and the nationwide contracts between the Ministry of Health and its NHS executives, on the one hand, and the labour unions and professional associations representing providers and employees, on the other (Glaser,

1994). In its entirety, the NHS is but one of several programmes within the UK's Ministry of Health.

There is a small private market for healthcare services in the UK which is limited primarily to speciality care services. A small private sector also exists within NHS establishments, such as "pay beds" for consultants (independent specialists) who, guaranteed by the original contracts when first joining the NHS, have the right of part-time private practice on the premises of NHS hospitals (Glaser, 2002).

National health insurance initially covered drugs prescribed by GPs without patient co-payments but, as costs become too high, co-payments were introduced in 1951 and have become substantial by now in the context of an otherwise free-at-the-point-of-service healthcare system (Glaser, 2002). Since the NHS is a monopoly buyer and can therefore dictate drug prices, the NHS negotiates with drug companies the wholesale prices for individual drugs that are meant to be sufficient to cover the companies' costs and profits.

4.3.2 Reimbursement and financing

Social security coverage in the UK is not universal and, eligibility partly depends on prior contributions. The system consists of three types of financing (European Commission, 2007):

- Contributory benefits: funded by the National Insurance (NI) Fund, which is financed by compulsory contributions based on current income and paid by most workers and employers (e.g. Retirement Pension);
- Non-contributory benefits: financed from general taxation and dependent on individual circumstances (e.g. disability, children); and,
- Income-related benefits: also funded from general taxation and act as a safety net (e.g. Housing Benefit, Income Support and Pension Credit).

By contrast, the UK's NHS is universal, taxpayer-paid-in-full and has always been inexpensive compared with other developed countries, characterised predominantly by shorter stays in hospitals than the European hospitals paid by per diems. This fact has remained true even in the context of Thatcher government reforms to bring market competition and entrepreneurial behaviour into government structure and into public finance, including the NHS.

In the past, an NHS hospital was an integral division of the district health authorities (DHAs) whereby the DHA administered a global budget to each hospital and dictated the plans for service provision. Since the innovative entrepreneurial reforms of the Thatcher government, NHS hospitals became an autonomous "Trusts" such that the hospital could develop its own services, set its own employment rules and attract patient referrals from outside the hospital's district. Although it might be expected that Thatcher's innovative reforms would cause a cost explosion, this has not occurred in the NHS because the DHAs collectively cannot pay out more than Parliament's annual appropriations (Glaser, 1994).

The total budget of the NHS in 2007–08 was £90 billion, equivalent to approximately €124.7 billion[34] (HM Treasury, 2007). Health expenditure per capita in the UK is approximately €2,095.[35] Of this per capita cost, 87.1 per cent of health spending is by the government and the remaining (12.9 per cent) is spent by private means (WHO, 2008b). Total expenditure on health per capita in the UK is 2,597 (Int. $, 2005), which constitutes 8.2 per cent of the region's GDP (WHO, 2008a). Table 4-2 illustrates UK health spending in 2005.

Table 4-2 UK health spending in 2005 (as per cent and PPP in Int. €)

General government expenditure on health as percentage of total expenditure on health (%)	87.10
General government expenditure on health as percentage of total government expenditure (%)	16.20
Out-of-pocket expenditure as percentage of private expenditure on health (%)	92.10
Per capita government expenditure on health (PPP int. EU)	2,819.04
Per capita total expenditure on health (PPP int. EU)	2,089.36
Private expenditure on health as percentage of total expenditure on health (%)	12.90
Total expenditure on health as percentage of gross domestic product (%)	8.20

SOURCE: WHO (2008b).

At the Trust level, a hospital trust's budget to cover its operating costs originates from patient revenue, provided by several DHAs and from groups of doctors with purchasing funds, as well as some infrastructure support from its own DHA. NHS hospital trusts can also raise capital privately in addition to government grants. Although the hospital-trust methodology of Thatcher may have introduced some "market behaviour" into the UK's healthcare services, the Ministry can issue executive orders to reduce or close hospital facilities if they seem over-bedded and inefficiently used. In other words, because the UK government cannot risk large cost overruns or bankruptcies and because public money and patients' needs are involved, the regional and district tiers of the NHS monitor and regulate the trusts' economic operations – a situation aptly phrased as "managed competition" (Glaser, 1994).

4.3.3 Clinical practice

Of the three country cases, the UK has the greatest density of overall health workforce. Although the physician density (per 10,000 population) in the UK in 2006 was only 23 (lower than France and Italy), the country's nursing and midwifery personnel density was 128, and "other services providers" (an additional category not shared by the other two country cases) density was 112 per 10,000 population that year – which does not include the UK's pharmaceutical personnel density (5 per 10,000 population) (WHO, 2008b).

Under the NHS universal coverage and financing, every person in the UK registers with a general practitioner (GP) who gives patients primary care and writes prescriptions. If there is a need for more specialist care, UK patients must be referred by their GP and cannot go directly to a consultant (independent specialist), unless they consult one privately. Apart from the unequal option for some in the UK to receive healthcare privately, the public

[34] Currency conversion from £ to € calculated using oanda.com, 'FX History: Historical Currency Exchange Rate', using 631 day average of £1 = €1.38592 between 1 January 2007 and 22 September 2008.

[35] Calculated using NHS budget forecast in the HM Treasury spending review (HM Treasury, 2007). The UK population is estimated to be 60,852,828 (Eurostat, 2008).

provision of healthcare is known to have substantial disparities between different locations within the UK. The term "postcode lottery" has often been used in the UK to describe the experience of differential provision of healthcare services in the NHS. As a criticism, the recent *Next Stage Review of the NHS* appeals to "patient choice" in deciding where to receive specialist care that is not dependent on one's local residence.

Ensuring proper standards in the practice of medicine is independently regulated by accreditation from the UK's General Medical Council (GMC). The four functions of the GMC, under the Medical Act 1983, which aim to protect, promote and maintain the health and safety of the public, include *inter alia* controlling entry to the medical register and setting the educational standards for medical schools, as well as employing its strong and effective legal powers to deal firmly and fairly with doctors whose fitness to practise is in doubt. (This can involve removing the doctor from the register and removing their right to practise medicine in the UK.) In addition to the GMC, the UK has a National Patient Safety Agency, which leads and contributes to improving safe patient care by providing a National Reporting and Learning Service, a National Clinical Assessment Service and a National Research Ethics Service.

However, quality of care also depends on the availability of a healthcare workforce. Like in France, there is a concern about a chronic shortage of junior medical staff in the NHS in England (BBC News, 2008). Thus, despite having an institutional framework for quality and safety of clinical practice in the UK, the BMA has recently warned that patient care quality is being threatened in this way (Carvel, 2008). According to the BMA, a reform of medical training introduced in the NHS system in 2007, which changed recruiting of junior doctors to training posts leading to consultant positions, has meant the end of staggered start dates for the training posts. This change has resulted in there now being gaps in hospital staffing rotas in England when junior doctors are promoted to consultant or leave. Young doctors used to fill the locum posts in between their official training positions. At present, the Department of Health is asking regional health chiefs to investigate this problem, which seriously impacts upon the quality of patient care in the UK (Carvel, 2008).

Finally, the practice of medicine, particularly reproductive medicine, in the UK can be assessed to a certain extent by some useful WHO health data (2000) from the Reproductive Health and Research Monitoring and Evaluation (MAE) database. More specifically, the lifetime risk of maternal death in the UK in 2000 was 1 in 3,800; low birth weight prevalence was 8 per cent; and the perinatal mortality rate was 8 per 1,000 (WHO, 2006a). The top two causes of death for neonates in 2000 in the UK were preterm birth (56 per cent) and congenital anomalies (24 per cent) (WHO, 2006d). It is interesting to note that preterm birth in the UK is 30 per cent higher than in France and 8 per cent higher than in Italy as a cause of death for newborns, whereas the UK has the opposite trend for congenital anomalies compared with France (35 per cent) and Italy (29 per cent). A possible explanation of this observation may be a difference in demography (ethnic minority and low socio-economic status being prime predictors of infant prematurity) for deaths of newborns, and different strategies for detection of abnormality (high abortion rates leading to less congenital anomaly causes of perinatal mortality).

4.3.4 Organisation and management

Based on the work of Ferrera in his typology of welfare states in Europe, the UK belongs to the "Anglo-Saxon" type in terms of its provision of social protection and can therefore be understood broadly to have a "fairly high welfare state cover". That is to say, welfare coverage in the UK is largely inclusive but is not universal (as is the case for healthcare coverage) insofar as inactive citizens and workers whose revenue is inferior to certain threshold figures do not have access to the benefits of the country's National Insurance. The UK's National Insurance benefits are of a fixed amount and much more modest than benefits in Scandinavian type welfare states. In addition, the range of the benefits of assistance granted on the means test is a lot more spread in the UK.

In the UK's Anglo-Saxon type welfare system, the regulations to finance social protection are characterised by a mixed system of financing whereby healthcare is taxpayer-paid-in-full but cash benefits for social protection (and in particular those that depend on insurance) are in large part financed by social contributions.

4.4 Future trends and possible developments

4.4.1 Regulatory context

The UK is at the forefront of legislative action in many of the controversial issues related to ART that are still being debated in other countries. In particular, the UK recently enacted two major policy initiatives with the Human Fertilisation and Embroyology Bill of 2008: namely, allowing single women and lesbians to receive ART treatment, and authorising new stages of research into human–animal hybrid embryos.

In December 2006 the HFEA released a white paper updating its position on a number of controversial rules that were part of its original 1990 charter; the white paper formed the basis of the Human Fertilisation and Embryology Bill 2008 (Department of Health, 2006). One of the most controversial changes to be announced was to remove the "need for a father" when assessing the welfare of the potential child. This clears the way for lesbians and single women to have equal access to IVF through the NHS, a move lauded by many human rights activists and those in the gay, lesbian, bisexual, transgender and queer (LGBTQ) community as an end to an unnecessarily moralizing stance on the part of the British government. While religious groups were unequivocally opposed to liberating same-sex female couples from the constraints of heterosexual biology in order to conceive, political opponents across party lines decried the move as having wider symbolic value in endangering the well-being of children by marginalising the role of fathers in society more broadly (Callan et al, 2008). The need for a "father figure" was put forward for inclusion as part of the attempted amendment to the Bill and, in the end, it was rejected.

The White Paper also declared a ban on creating human and animal hybrid embryos *in vitro*, unless under licence (Department of Health, 2006). Subsequent consultation with a joint parliamentary committee produced recommendations that the HFEA be allowed to judge which scientists could create hybrids and what type of hybrids may be created (Department of Health, 2007a). An HFEA consultation concluded in September 2007 that individual research teams would be able to undertake cytoplasmic hybrid research, if researchers could "demonstrate to the satisfaction of an HFEA licence committee, that

their planned research project is both necessary and desirable" (HFEA, 2007c). Research on other types of hybrid of embryos, such as chimera (involving the injection of cells or genetic material from one species into the embryo of another), would not be issued a licence owing to an inadequate evidence base, and "no desire" on the part of the scientific community to pursue this avenue of research "at present" (*ibid.*).

The subsequent Bill before Parliament permits the Secretary of State power to liberalise regulation "in the light of developments in science or medicine" (Human Fertilisation and Embryology Bill, 2008). The parliamentary debate over this Bill began when scientists at Newcastle University announced the creation of a cytoplasmic hybrid embryo in April 2008; this was legal to do because their creation had been permitted by the HFEA's 2007 consultation which the Bill before Parliament would legally formalise. The embryo was created by taking the nucleus of a human cell and inserting it into the reproductive cell of a cow that had had its nucleus removed (a technique known as cytoplasmic hybrid method). The genetic material is therefore 99.9 per cent human (Henderson, 2008a). Further debate about these issues is likely to persist, particularly as their as yet undetermined outcomes unfold.

The HFEA acknowledged in its consultation that public opinion on hybrid and chimera research is finely divided, accepting that any future expansion of these policies is likely to be contentious. While opposition from religious leaders has been widespread and oftem dogmatic (one Catholic cardinal described the notion of human–animal hybrid embryos as "Frankenstein Science" (Sugden, 2008)), the HFEA itself acknowledges the "clear demand from people to know more about what researchers are doing and their plans for future work" in respect of hybrid embryo research. In addition, HFEA highlights "the need for better communication about science and research from both the scientific community and ourselves as regulator" (HFEA, 2007c).

4.4.2 Economic context

The development of microarrays for embryo selection (discussed below) is likely to decrease the cost of IVF by cutting the number of cycles. Additionally, the decision of the HFEA to actively discourage multiple births for safety and health reasons may have economic consequences in the future if this new recommended policy of transferring no more than 2 embryos leads to an increased number of cycles. More far reaching consequences would occur if all PCTs were legally obligated to implement the NICE guidance of three full cycles provided by the NHS. As previously discussed, combined with a move towards eSET, this could drastically change access to and outcomes of ART provision in the UK. However, it is unlikely to happen any time in the immediately foreseeable future.

The avoidance of multiple births is a serious cost consideration for the NHS and its funding of ART. Ledger et al. (2006) produced a study estimating the yearly costs of multiple births to the NHS (see Table 4-3). These costs included routine care costs and the costs of stays in hospital neonatal units. It did not include the costs due to other co-morbidities associated with the very low birth weight babies that result from multiple births. Neither does the study include the cost of maternal health complications associated with ART, of which Ovarian Hyperstimulation Syndrome (OHSS) is the most common adverse event (Nyboe Andersen et al., 2006).

Table 4-3 Estimated cost (in €) to the NHS of multiple births

	Singleton	Twin	Triplet
Estimated maternal cost (€)	4,366	8,469	16,125
Estimated neonatal cost (€ per family)	267	4,283	29,106
Total cost per family (€)	4,632	12,753	45,231
Number of IVF births in UK[36]	4,621	1,579	109
Costs of IVF births to the NHS (€)	21,402,503	20,136	4,930,167

SOURCE: Ledger et al. (2006).

NOTES: Twin and triplet figures are number of sets, rather than individual babies

4.4.3 Clinical practice

The HFEA cited two scientific developments likely to occur in the next three years that would create major changes in fertility treatment in the UK:

- **Microarrays for more effective embryo selection**: A microarray, sometimes called a "gene chip", would take the place of manual methods to assess the viability of IVF embryos. Clinical outcomes would include a higher probability of IVF success, fewer cycles and a lower risk of multiple births; and,
- **In vitro growth of eggs**: It may soon become possible to use ovarian tissue to grow eggs outside the body for use in IVF treatment or research. This is primarily intended to help to preserve the fertility in cancer patients (by decreasing the use of stimulatory drugs which can exacerbate cancer), but the technique may also have wider applications and associated ethical implications.

The Horizon Scanning Panel of the HFEA also raised several other issues that may become viable or visible in the future:

- the production of human chimeras, in particular to allow lesbian partners to contribute equally to the genes of a child; and,
- the ethics of using IVF to select for desirable characteristics in children; currently this is prohibited in the UK, except in the case where it is used to avoid known heritable genetic diseases

The HFEA and UK government will continue to make decisions based on the welfare of the child (a stated perspective for all recent regulatory changes in fertility treatment, and for child health more generally). While anti-ART groups will continue to argue that changes, both proposed and enacted, may compromise the welfare of the child, these groups have not won many battles yet. Moreover, it appears that the HFEA's and other clinical bodies' current direction of promoting more liberal access to ART treatment is unlikely to alter without a sea-change in opinion among not only the medical and political establishment, but also the hundreds of thousands of would-be parents desiring every possible access to the assistive reproductive technologies permitted by modern scientific advances.

[36] Twin and triplet figures are number of sets, rather than individual babies

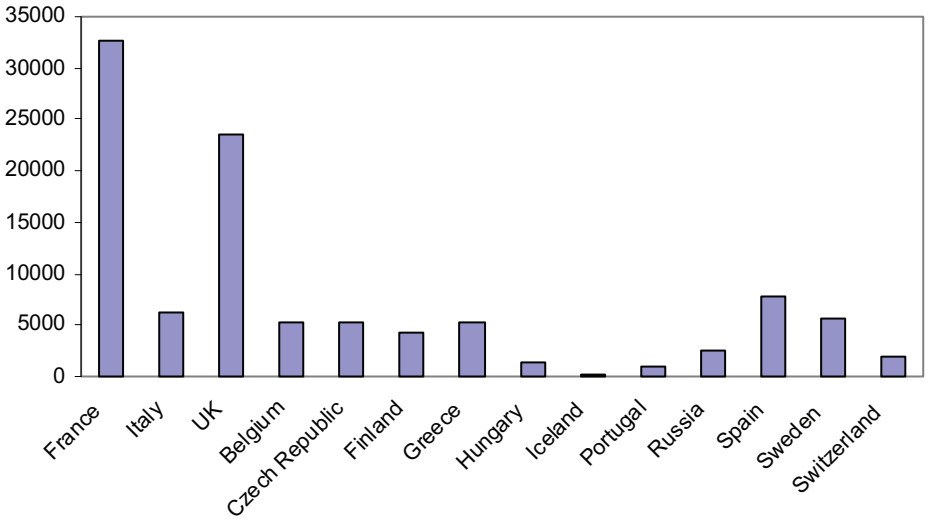
CHAPTER 5

Comparison of Assisted Reproductive Technologies in France, Italy and the UK between 1997 and 2004

This chapter presents our discussion and comparative analysis of population trends in the ART systems of France, Italy and the UK. To generate the figures and trends for this discussion, we draw primarily on ESHRE reported data for the years 1997 to 2004 (a separate report is published for each year). The main reason for using this source was to ensure uniformity of data source to create more reliable comparisons. However, as the ESHRE cautions in its respective reports, country data may reflect reporting bias from incomplete data and other inherent inaccuracies due to different methods of data collection using different definitions in different countries. Some of our analysis required independent calculations as some of the values we use for comparative purposes were not provided in the ESHRE reports (in cases where data was incomplete or unavailable) Thus, we present a few graphs that show gaps in the trend lines we generated. Moreover, the denominator used in some of the comparisons may not always reflect the existing literature, but we chose the best possible alternative with the most complete data in order to ensure data comparability. Finally, we note that most of the data we use pertain to only two types of ART treatment, IVF and ICSI, for two reasons: first, these are the two types for which ESHRE presents the most amount of country data; and second, while IVF was the earliest type of ART treatment, ICSI is in greater use more recently and it addresses the male factor of infertility. Therefore we hope our comparison can highlight important changes in the evolution of ART systems both within the three country cases as well as between them for the time period examined in the ESHRE reports. For clarity of reasoning, we present the data below according to a logic model of inputs, process, clinical outcomes (as primary ART outputs) and health outcomes.

5.1 Assisted Reproductive Technologies inputs

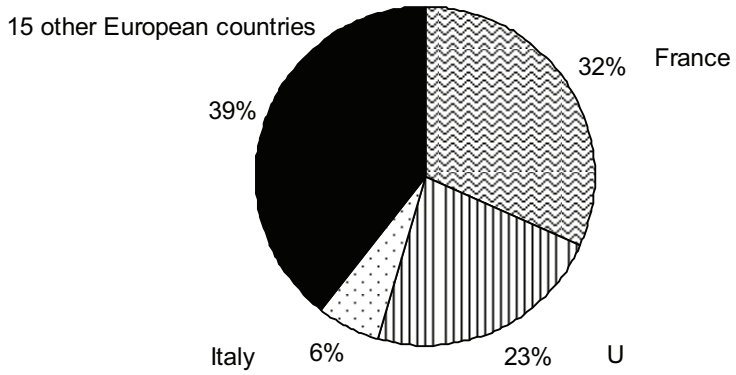
Over a decade ago, France and the UK were the two European countries (n=18) with the highest level of ART activity, in terms of the absolute number of embryo transfers after IVF and ICSI, in 1997 (see Figure 5-1).



SOURCE: Nygren and Nyboe Andersen (2001a, 2001b, 2002) and Nyboe Andersen et al. (2004, 2005, 2006, 2007, 2008).

Figure 5-1 Number of embryo transfers after IVF and ICSI in 1997, by country

As a proportion of the overall services in Europe in 1997, more than half (55 per cent) of all embryo transfers after IVF and ICSI in the examined European countries came from France and the UK (see Figure 5-2).

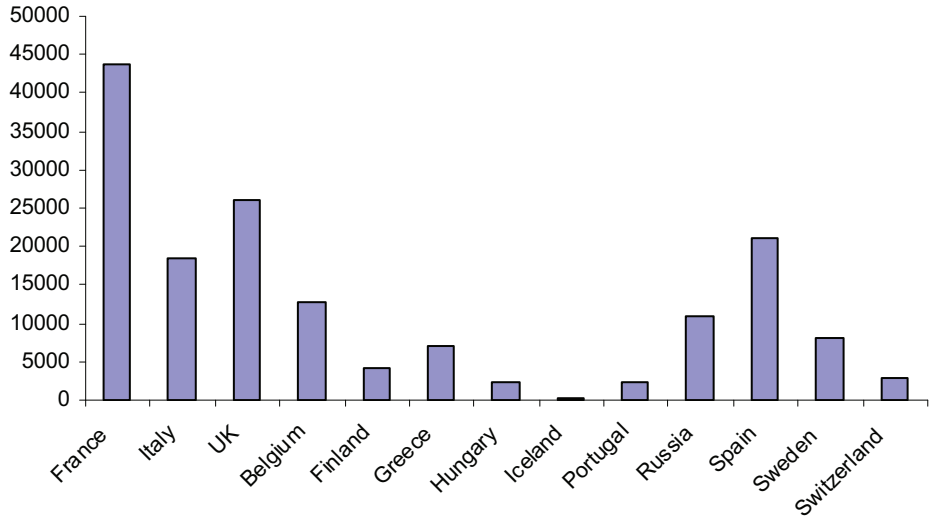


SOURCE: Nygren and Nyboe Andersen (2001a, 2001b, 2002) and Nyboe Andersen et al. (2004, 2005, 2006, 2007, 2008).

Figure 5-2 Proportions of embryo transfers after IVF and ICSI in France and the UK in 1997, relative to other countries in Europe

Although this lion's share of ART inputs by France and the UK decreased over time to about 31 per cent of all embryo transfers after IVF and ICSI in 29 European countries examined by ESHRE in 2004 (data not shown), France continues to have the highest total number of embryo transfers of all these countries. The decline in the relative contribution

of France and the UK by 2004 can be explained by the addition of 11 European countries in the denominator. Thus, for comparability, Figure 5-3 for data on ART inputs in 2004 includes the same 18 countries as those examined in 1997. What is not shown in this figure is the fact that, in 2004, Germany is second to France in the number of embryo transfers after IVF and ICSI, followed by the UK, Spain, Italy and then Russia.

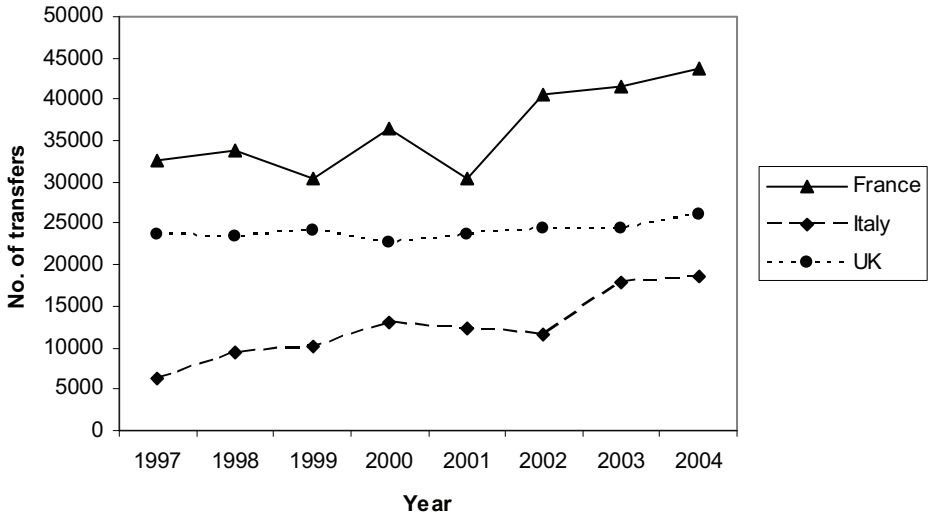


SOURCE: Nygren and Nyboe Andersen (2001a, 2001b, 2002) and Nyboe Andersen et al. (2004, 2005, 2006, 2007, 2008).

Figure 5-3 Number of embryo transfers after IVF and ICSI in 2004, by country

In turning to a comparison of our three case study countries, we see in Figure 5-4 that, overall, the absolute number of embryo transfers after IVF and ICSI has increased in France and Italy and stayed constant in the UK[37] from 1997 to 2004. In fact, only in Italy has the number tripled between 1997 and 2004. More surprisingly, the trend in the UK appears to contradict a public notion that provision of ART has increased drastically over the last decade.

[37] In the ESHRE report for 1999 there was incomplete data on the UK due to technical problems with reporting to the UK's HFEA that year. We therefore had to create a reasonable estimate of the number of ICSI transfers by multiplying the total number of ICSI cycles reported by a factor of 0.94.



SOURCE: Nygren and Nyboe Andersen (2001a, 2001b, 2002) and Nyboe Andersen et al. (2004, 2005, 2006, 2007, 2008).

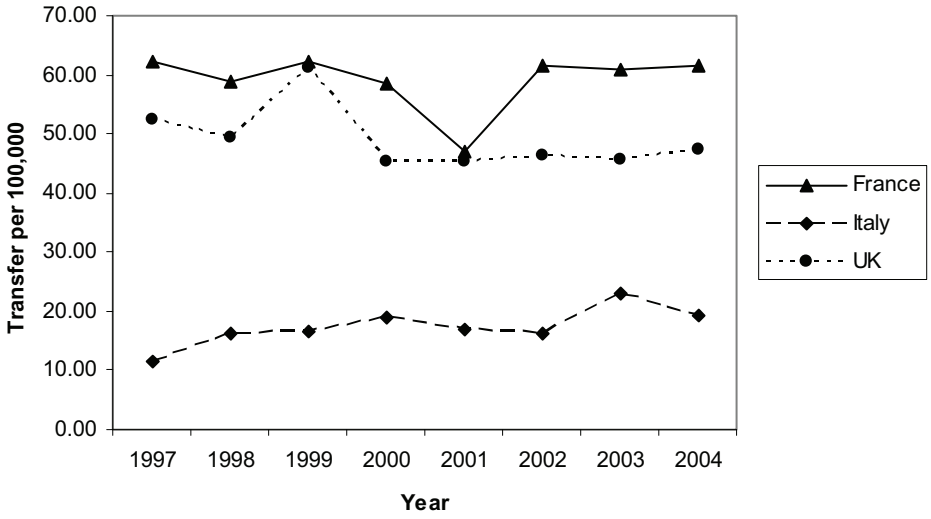
Figure 5-4 Number of embryo transfers after IVF and ICSI in France, Italy and the UK (1997–2004)

However, an increase in absolute numbers is not very informative of the extent of national-level growth in the provision of ART services over time in each of the three European countries studied, because one would expect to see a growth in the absolute number of embryo transfers in each country over time in response to natural population growth. Hence we present two figures showing the per capita (100,000 reproductive population)[38] transfer of embryos after IVF (Figure 5-5) and ICSI (Figure 5-6), respectively, for each country over time. Although not revealing anything surprising, we summarise some of the main empirical observations from a comparative perspective:

- France is well above either Italy or the UK in the per capita transfer of embryos after IVF and ICSI, respectively.
- Per capita transfer of embryos after IVF increases only in Italy and there is a small decline in the UK over time.
- Per capita transfer of embryos after ICSI increases in all three countries from 1997 to 2004. However, the magnitude of increase in France (slope=5.58) and in Italy (slope=0.93) is 13 times and 2.2 times the increase seen in the UK (slope=0.42), respectively.

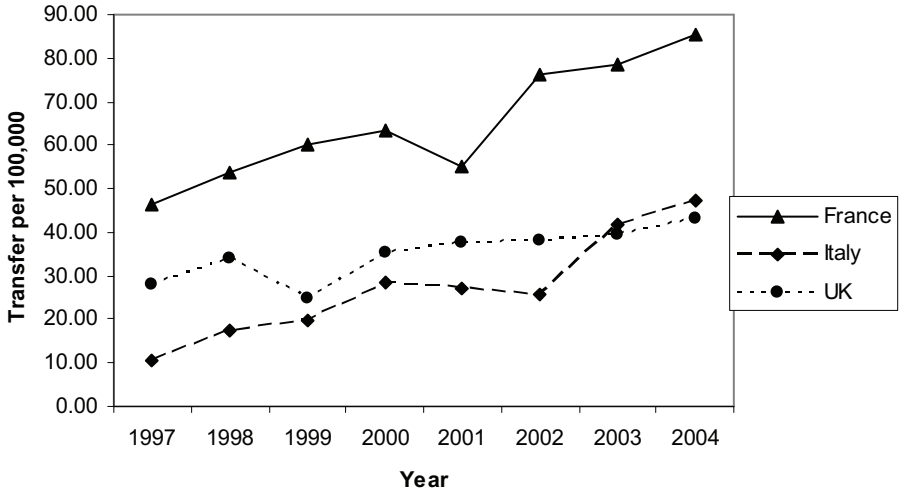
[38] In calculating the per capita number of embryo transfers after IVF and ICSI, respectively, we first determined the most relevant denominator (the country's population of reproductive age). To establish this figure, we conducted a series of additional calculations using Eurostat data on (1) total population of each country for each year and (2) proportion of population aged 15–24 years and aged 25–49 years. The final figure is still only partially accurate for two reasons: first, the value includes some age groups that are not eligible to receive ART (e.g. under 18 and over 45); and second, the Eurostat population data is not mid-year but reflects the number at the start of the year for which population data is provided (1 January), and not mid-year figures. Standard epidemiological practice of calculating standardised populations uses mid-year population data to adjust for births conceived in the previous year.

- Whereas the UK started off in 1997 having a higher per capita transfer of embryos after ICSI than in Italy, the sizeable increase in Italy means that Italy surpasses the UK in 2003 and 2004 in the per capita transfers of embryos after ICSI.



SOURCE: Nygren and Nyboe Andersen (2001a, 2001b, 2002), Nyboe Andersen *et al.* (2004, 2005, 2006, 2007, 2008), and Eurostat (2008).

Figure 5-5 Per capita transfers of embryos after IVF in France, Italy and the UK (1997–2004)



SOURCE: Nygren and Nyboe Andersen (2001a, 2001b, 2002), Nyboe Andersen *et al.* (2004, 2005, 2006, 2007, 2008), and Eurostat (2008)

Figure 5-6 Per capita transfers of embryos after ICSI in France, Italy and the UK (1997–2004)

These figures clearly provide the empirical evidence for the growing prominence in ICSI provision in all three countries. The latter observation may reflect the increasing recognition of the "male factor" of infertility, for which ICSI is a potential solution.

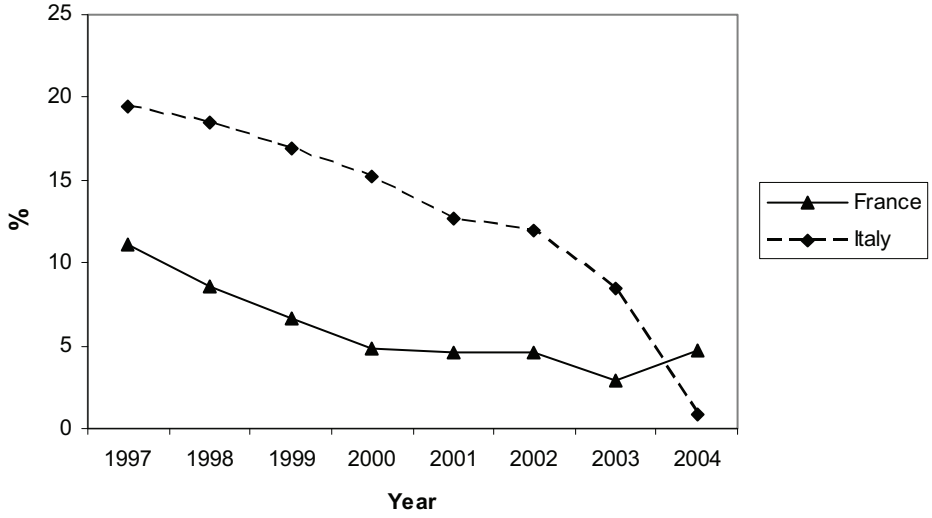
The finding that per capita transfer of embryos after IVF shows marginal to no increase in either France or the UK appears to parallel the relatively constant trend in the total number of IVF clinics in these two countries, over the same period (data not shown). By contrast, Italy demonstrates a consistent rise in the total number of IVF clinics in the country during the period examined such that, by 2004, Italy had between 133 IVF clinics reporting to a National Registry and 218 IVF clinics determined by the European IVF-monitoring programme (EIM),[39] compared with 100 in France and 74 in the UK.

Although there may be an association between the number of IVF clinics and the per capita transfers of embryos performed after IVF (and ICSI), the direction of the causal effect is unknown; that is, we cannot know from this data whether the number of IVF clinics drives the number of embryo transfers per 100,000 reproductive population, or vice versa.

5.2 Assisted Reproductive Technologies process

The UK does not allow 4-embryo transfers, and none were reported after IVF and ICSI from 1997 to 2004. By contrast, there is a downward trend in France and Italy towards a smaller percentage of 4-embryo transfers (to total transfers after IVF and ICSI) (see Figure 5-7). In France, the trend is from 11 per cent towards 3–5 per cent and in Italy the trend is more dramatic from 20 per cent to 1 per cent. The decline in the percentage of 4-embryo transfers after IVF and ICSI in Italy is evidently greater in magnitude than the decrease in France. However, until 2004, the percentage of 4-embryo transfer in Italy was almost twice as high as that in France. Given this massive decline in Italy, one might soon expect to find visible changes in the negative health outcomes (discussed below in section 5.4).

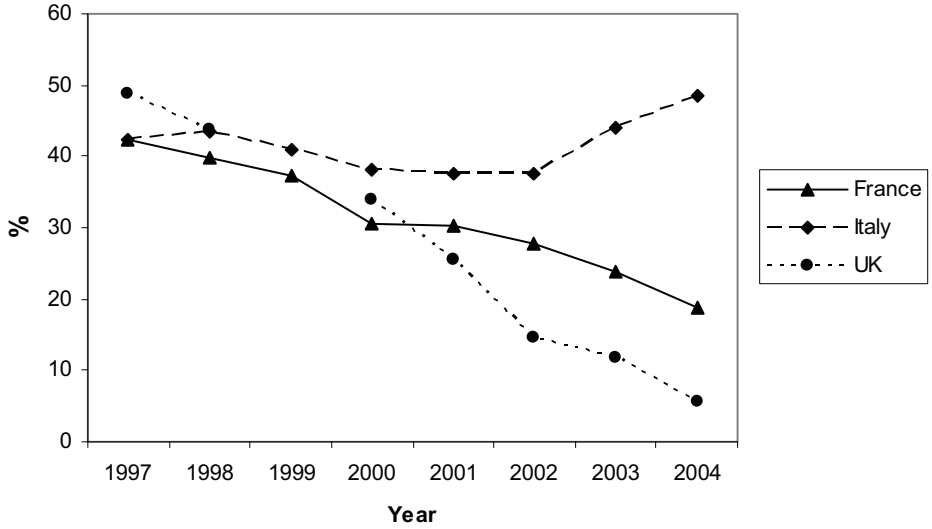
[39] Although IVF clinics in France and the UK are fewer in absolute number than those in Italy, only half (ranging from 51 per cent to 65 per cent) of the existing IVF clinics in Italy formally reported to the country's National Registry during the period from 1997 to 2004. By contrast, all of the existing clinics in France and the UK reported to a National Registry during that period.



SOURCE: Nygren and Nyboe Andersen (2001a, 2001b, 2002) and Nyboe Andersen et al. (2004, 2005, 2006, 2007, 2008).

Figure 5-7 Percentage of 4-embryo transfers after IVF and ICSI in France and Italy (1997–2004)

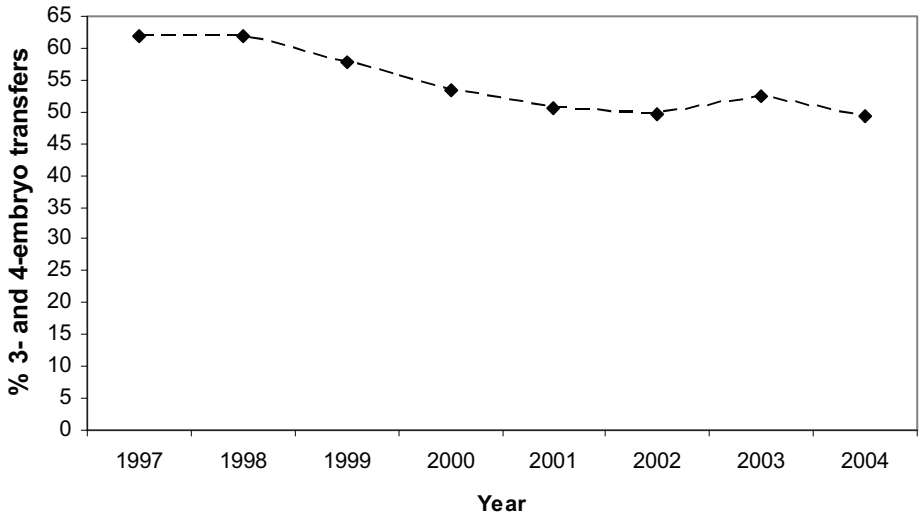
But, while Italy's trend may appear to be a positive move away from the greater risk of higher order pregnancies, it is still the only country to increase the percentage of 3-embryo transfers after IVF and ICSI (up to 49 per cent) in the latter part of this period, compared with the less than 20 per cent trend in both France and the UK (see Figure 5-8).



SOURCE: Nygren and Nyboe Andersen (2001a, 2001b 2002) and Nyboe Andersen et al. (2004, 2005, 2006, 2007, 2008).

Figure 5-8 Percentage of 3-embryo transfer (of total tansfers) after IVF and ICSI in France, Italy and the UK (1997–2004)

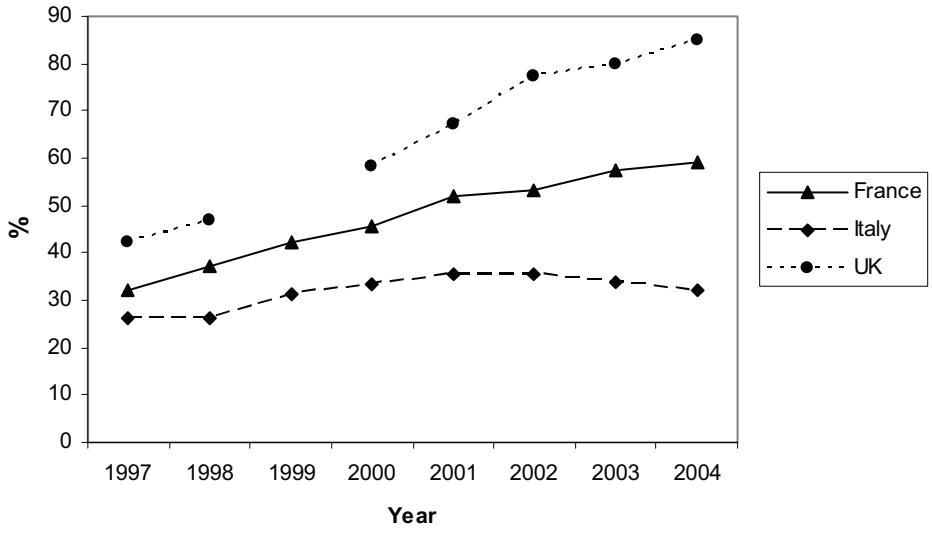
It seems that the decrease in 4-embryo transfer in Italy occurring over the same time period as the increase in 3-embryo transfer in Italy could reflect a substitution of the former for the latter. However, the sum of the two percentages over time suggests that there is a marginal decline in the percentage of higher order embryo transfers after IVF and ICSI in Italy over time, which diminishes our substitution hypothesis (see Figure 5-9).



SOURCE: Nygren and Nyboe Andersen (2001a, 2001b, 2002) and Nyboe Andersen et al. (2004, 2005, 2006, 2007, 2008).

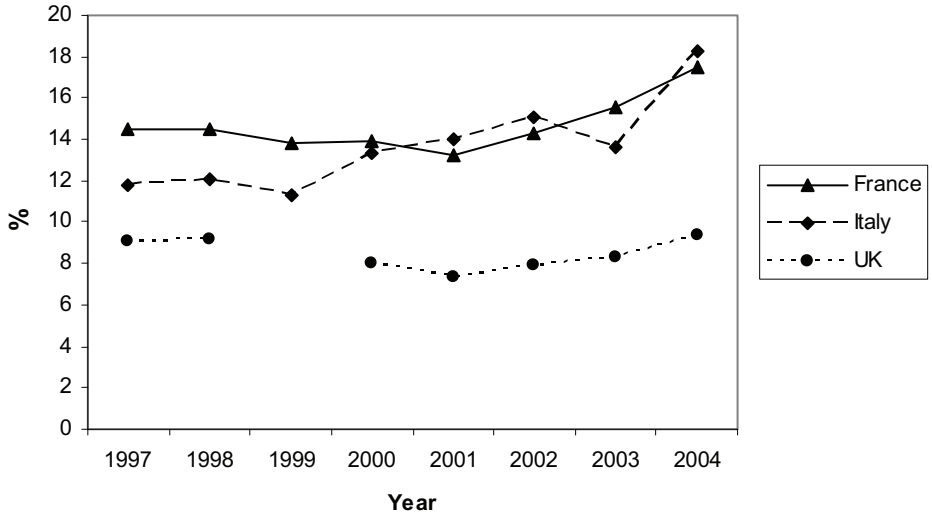
Figure 5-9 Percentage of 3- and 4-embryo transfers after IVF and ICSI in Italy (1997–2004)

Interestingly, Figure 5-10 shows that the percentage of 2-embryo transfer after IVF and ICSI has remained relatively constant in Italy over the same period. France demonstrates a trend of gradual increase over time and the UK is noticeably higher than the general European trend (data not shown), reaching 85 per cent in 2004 in the UK compared with 55 per cent in France and in 26 other European countries for the same year. This observation for the UK is perhaps explained by the significant decrease in 3-embryo transfer and consistently low (less than 10 per cent) 1-embryo transfer (see Figure 5-11) in a country that has also never conducted 4-embryo transfer after IVF and ICSI.



SOURCE: Nygren and Nyboe Andersen (2001a, 2001b, 2002) and Nyboe Andersen et al. (2004, 2005, 2006, 2007, 2008).

Figure 5-10 Percentage of 2-embryo transfers after IVF and ICSI in France, Italy and the UK (1997–2004)



SOURCE: Nygren and Nyboe Andersen (2001a, 2001b, 2002) and Nyboe Andersen et al. (2004, 2005, 2006, 2007, 2008).

Figure 5-11 Percentage of 1-embryo transfer after IVF and ICSI in France, Italy and the UK (1997–2004)

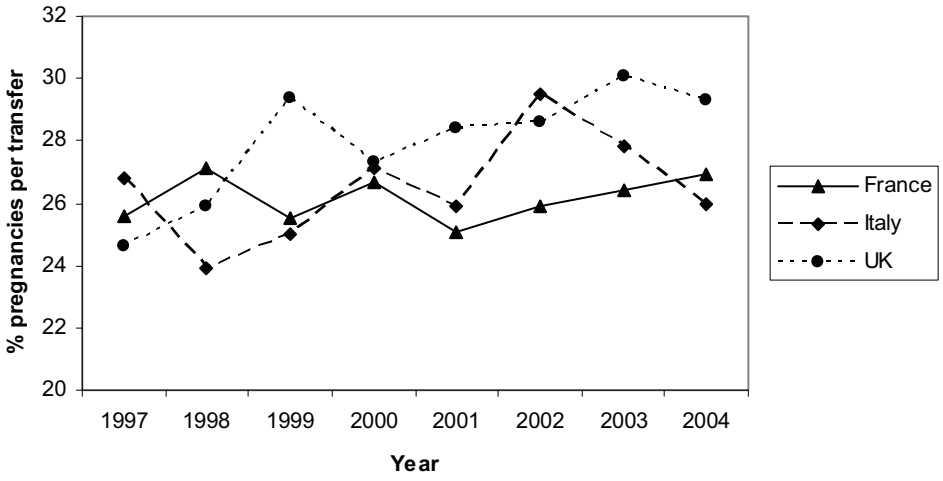
Of the three countries, Italy appears to fluctuate the most over this period: 1-embryo transfer fluctuates but increases sharply in 2004; 2-embryo transfer has marginally decreased; 3-embryo transfer increased significantly (40 per cent); and 4-embryo transfer is phased out. It could be that there is some unrest among infertile couples and clinicians, or

a build up towards the 2004 policy change. It is worth investigating further whether 3-embryo transfers were free of charge, more generously reimbursed in those regions with schemes, and hence infertile couples would take advantage of such an opportunity before the more restrictive policy regime in 2004. This build up phenomenon may also be the case for other indicators discussed below.

5.3 Assisted Reproductive Technologies clinical outcomes (outputs)

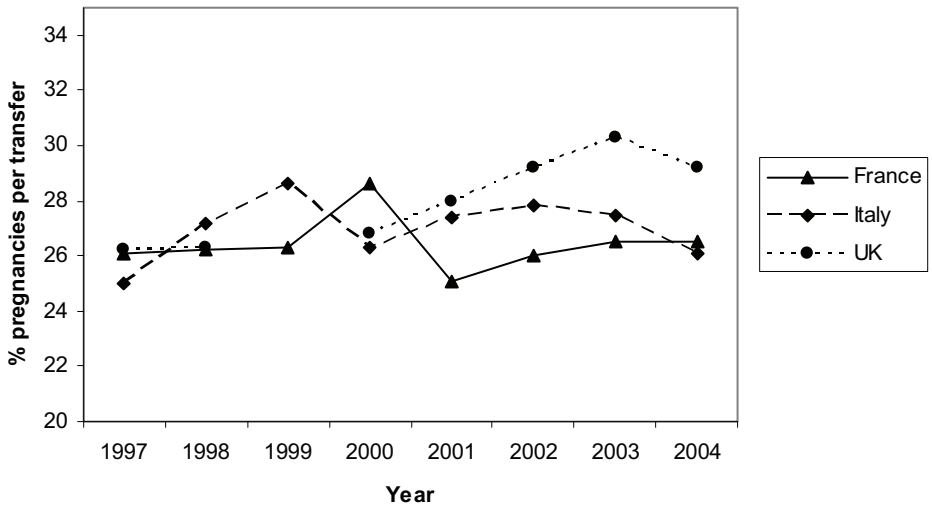
For infertile couples, having a baby is clearly the most relevant clinical outcome of ART and thus a high percentage of deliveries per embryo transfers is an important measure. However, the likelihood of a delivery from an ART pregnancy is not only dependent on good ART technique alone. Thus, it is also important to examine pregnancy rate after ART as a more direct measure of the treatment's clinical outcome. Below we present both types of clinical outcomes of ART treatment in all three case study countries.

There is minimal variation in the percentage of pregnancies to all transfers after IVF and ICSI between the three countries, ranging from 20 per cent to 30 per cent. However, what is most striking is the extent of *within*-country variation over time for each of the three countries (see Figure 5-12 and Figure 5-13). Note that to better illustrate this variation, the scale of the y-axis has been artificially adjusted (i.e. the scale begins at 20 per cent and not at zero). The UK shows the most increase over time of the three countries in the percentage of pregnancies to all transfers after IVF and ICSI, and despite some increases in Italy within this same period, there is a marked declined from 2002 to 2004.



SOURCE: Nygren and Nyboe Andersen (2001a, 2001b, 2002) and Nyboe Andersen et al. (2004, 2005, 2006, 2007, 2008).

Figure 5-12 Percentage of pregnancies per transfer after IVF in France, Italy and the UK (1997–2004)

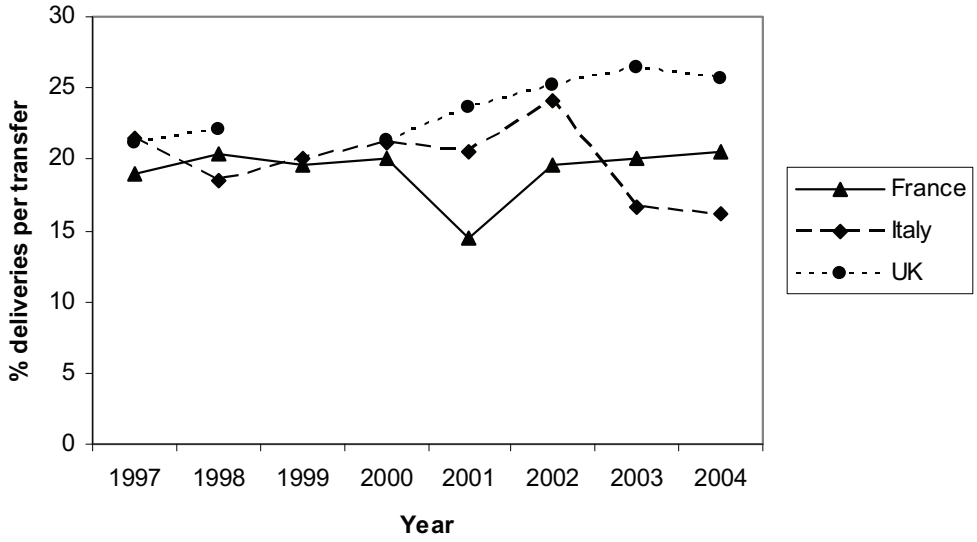


SOURCE: Nygren and Nyboe Andersen (2001a, 2001b, 2002) and Nyboe Andersen et al. (2004, 2005, 2006, 2007, 2008).

Figure 5-13 Percentage of pregnancies per transfer after ICSI in France, Italy and the UK (1997–2004)

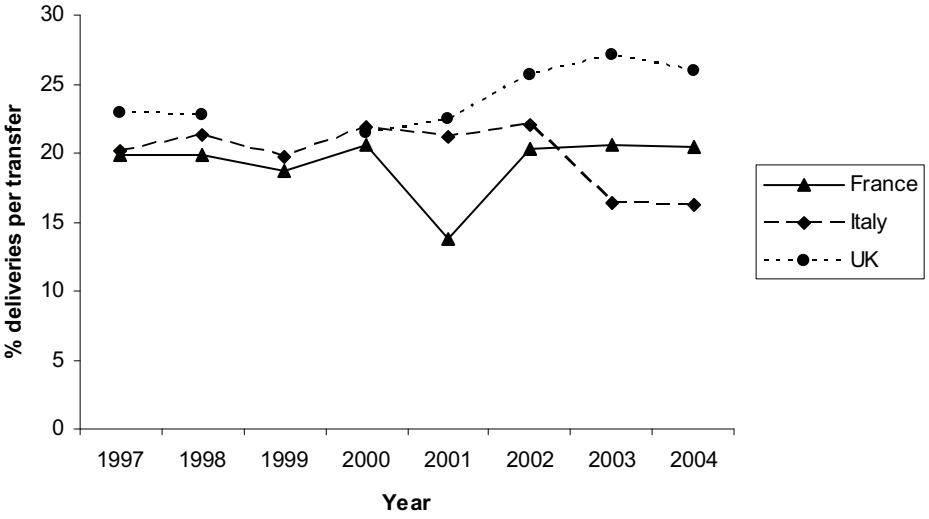
The proportion of successful deliveries per transfer is more varied between the three countries as well as within each country, as can be seen in Figure 5-14 and Figure 5-15. For both IVF and ICSI, the UK stands out above France and Italy in terms of reaching nearly 25 per cent deliveries per transfer by 2004. France showed a marked drop of its deliveries per transfer for both IVF and ICSI to 14 per cent in 2001. However, France appears to have recovered its poor performance in 2001 to a level similar as in 1997. Yet, despite this return to its earlier rate, the delivery rate in France remains approximately 5 percentage points lower in deliveries per transfer after both IVF and ICSI than the UK.

Italy also shows some interesting trends. In Italy's case, the IVF and ICSI success rate, respectively, as the percentage of deliveries per transfer, was closely comparable to the figures for the UK (until 2002) and France (until 2001). More recently ART success in Italy has remarkably declined to 10 percentage points below the UK's success rate. However, the drastic drop between 2002 and 2003 in the IVF and ICSI deliveries per transfer in Italy may not be fully representative for the whole country as this observation could be an effect of selection bias by the reporting clinics, which may be in poorer regions of the country with a greater risk of poorer health outcomes related to the underlying determinants of health in those areas.



SOURCE: Nygren and Nyboe Andersen (2001a, 2001b, 2002) and Nyboe Andersen et al. (2004, 2005, 2006, 2007, 2008).

Figure 5-14 Percentage of deliveries per transfer after IVF in France, Italy and the UK (1997–2004)



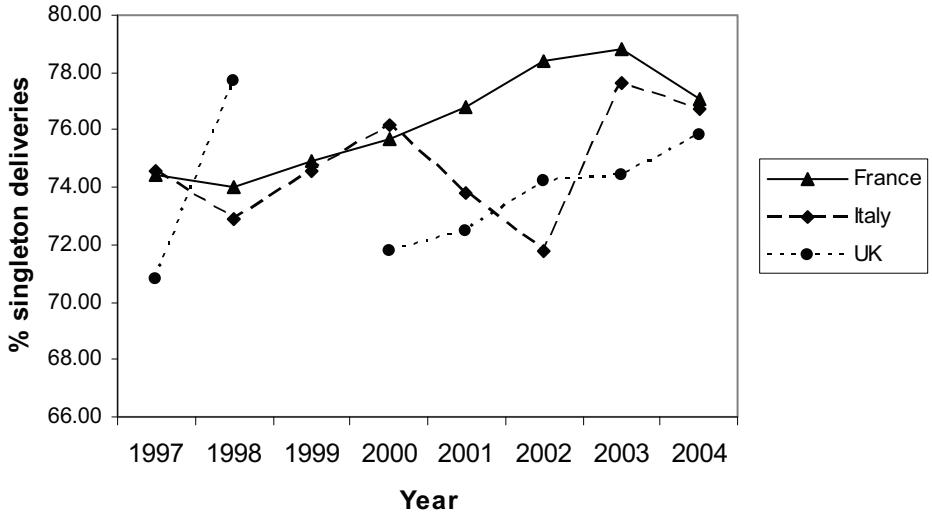
SOURCE: Nygren and Nyboe Andersen (2001a, 2001b, 2002) and Nyboe Andersen et al. (2004, 2005, 2006, 2007, 2008).

Figure 5-15 Percentage of deliveries per transfer after ICSI in France, Italy and the UK (1997–2004)

Finally, the key clinical outcome of ART services is the delivery of a healthy infant, whether the delivery is of a single child, twins, triplets or more. Ideally, the best health outcome is for the highest percentage of deliveries after IVF and ICSI to be singleton or twins. The main reason is that triplets, quadruplets or more have known serious

consequences for maternal and child health in the short and long term, much more so than is the case for twins.

With variability over time, all three countries are within a few percentage points of a general trend towards a high percentage of singleton deliveries (of all deliveries after IVF and ICSI) in the period of 1997 to 2004 (see Figure 5-16)[40]. However, the natural variation in all three countries makes it unclear which of the three countries is "doing better" than the others and the real difference is difficult to know from this figure.[41] Despite the gap in the UK's trend, there was clearly a decrease from 1998 to 2000, followed by a gradual increase in the percentage of singleton deliveries after the two ART techniques in that country. Yet, the UK has the lowest figures for singleton deliveries compared with France and Italy and this is a direct reflection of the UK having the lowest percentage of 1-embryo transfers among the three countries.



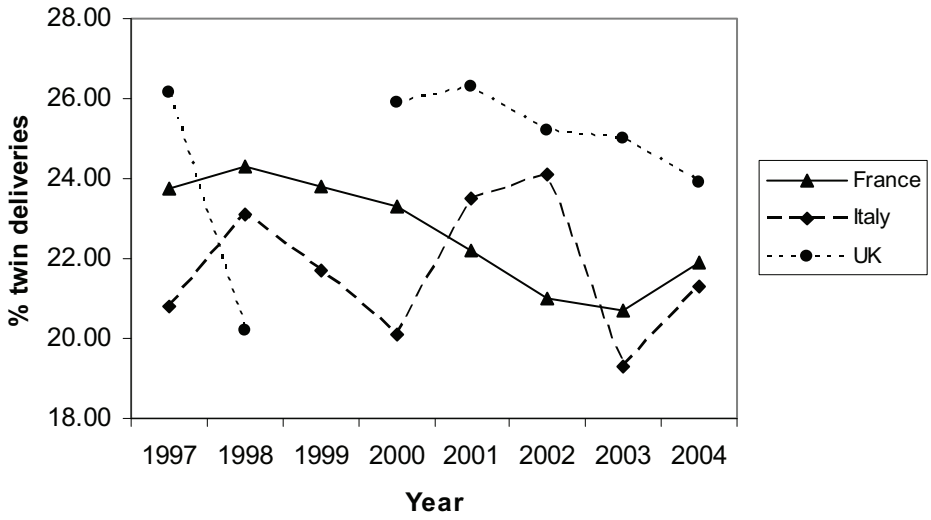
SOURCE: Nygren and Nyboe Andersen (2001a, 2001b, 2002) and Nyboe Andersen et al. (2004, 2005, 2006, 2007, 2008).

Figure 5-16 Percentage of singleton deliveries in France, Italy and the UK (1997–2004)

Similarly, the UK had the highest percentage of 2-embryo transfers and thus has a greater percentage of twin deliveries, among the three countries examined for the same period (see Figure 5-17). This observation may be explained by the fact that there is a relatively high proportion of self-funding in the UK which creates an incentive among infertile couples to maximise embryo transfers for better clinical outcomes (healthy infant born).

[40] The gap in the UK's trend at year 1999 is due to incomplete data reported to ESHRE as a result of technical problems with the UK's HFEA.

[41] The scale of the y-axis has been adjusted to better demonstrate this country-specific variability.

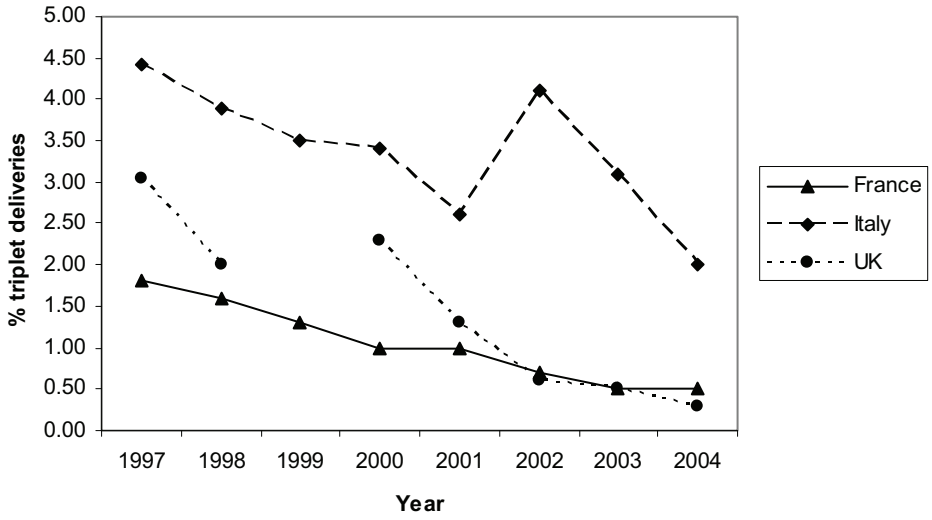


SOURCE: Nygren and Nyboe Andersen (2001a, 2001b, 2002) and Nyboe Andersen et al. (2004, 2005, 2006, 2007, 2008).

Figure 5-17 Percentage of twin deliveries after IVF and ICSI in France, Italy and the UK (1997–2004)

The percentage of triplet and quadruplet deliveries is a more critical clinical outcome because such higher order deliveries (and pregnancies) are known to substantially increase the relative risk of serious health outcomes for both mother and infant. Thus, while the percentage of triplet deliveries, for example, is generally quite low compared with the percentage of twin or singleton deliveries after IVF and ICSI, Italy seems to be the "poorest performer" in this regard.

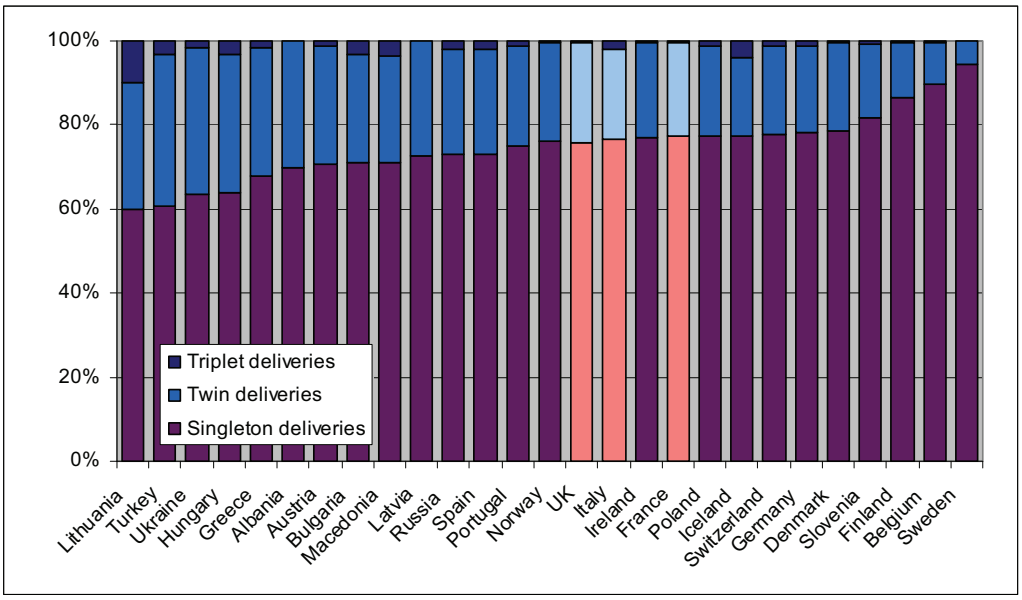
As we see in Figure 5-18, France has the lowest percentage of triplet deliveries and falls most consistently over time of all three countries. The UK started off worse than France in 1997 but ends up having a lower percentage of triplet deliveries than France. Finally, Italy also shows a decrease in the percentage of triplet deliveries, yet the gap between Italy and the other two countries remains enormous (the difference is fivefold and nearly sevenfold compared with France and the UK, respectively).



SOURCE: Nygren and Nyboe Andersen (2001a, 2001b, 2002) and Nyboe Andersen et al. (2004, 2005, 2006, 2007, 2008).

Figure 5-18 Percentage of triplet deliveries after IVF and ICSI in France, Italy and the UK (1997–2004)

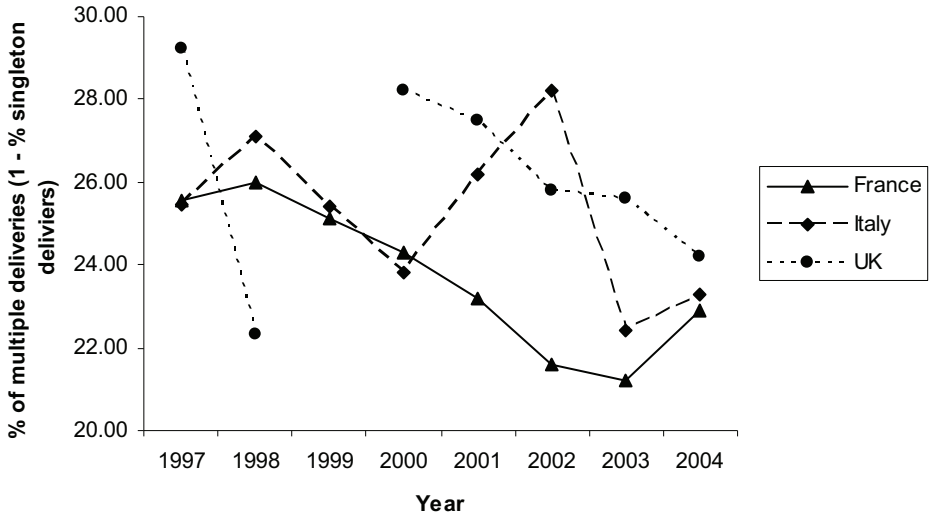
Here, we note that among the three countries, only Italy has reported quadruplet deliveries after IVF and ICSI, varying from 0.61 per cent in 1997 to 0.3 per cent in 2000. The figures after this date are unknown and may reflect an absence of reporting or a real change in clinical practice towards reducing higher order pregnancies. In presenting data on multiple births in the three country cases, we remind the reader that all three of these countries cluster around the European average, as can be seen below (Figure 5-19).



SOURCE: Nygren and Nyboe Andersen (2001a, 2001b, 2002) and Nyboe Andersen et al. (2004, 2005, 2006, 2007, 2008).

Figure 5-19 Proportions of singleton, twin and triplet deliveries in Europe in 2004, by country

It is often assumed that a move from multiple to single embryo-transfer implies a reduction in the success rate of ART. Rather, in recent years, there is growing empirical evidence from Finland, Sweden and UK demonstrating the fact that single embryo transfer (SET) can be introduced on a national level without a decline in the ongoing pregnancy rate, but with a marked reduction in the proportion of multiple pregnancies (Braude, 2006). Legislation obligating national implementation of SET in Belgium, for example, has succeeded in achieving near-complete avoidance of triplet births while the prevalence of twins has declined to approximately 7 per cent. To achieve a similar outcome in the UK, the HFEA report suggests targeting good prognosis patients (young women without previous failed IVF attempts) and effective embryo freezing (cryopreservation) programmes. This has not been implemented and the UK continues to have a higher percentage of multiple births over time than either France or Italy (see Figure 5-20). Italy, moreover, has no legal restrictions that would undermine either of the UK's HFEA recommendations for implementing SET on a national scale. But Italy is clearly a country with the widest yearly variation in multiple deliveries after ART, which suggests that there are more factors than clinical evidence at stake in ART practice in Italy.



SOURCE: Nygren and Nyboe Andersen (2001a, 2001b, 2002) and Nyboe Andersen et al. (2004, 2005, 2006, 2007, 2008).

Figure 5-20 Percentage of multiple deliveries after ART in France, Italy and the UK (1997–2004)

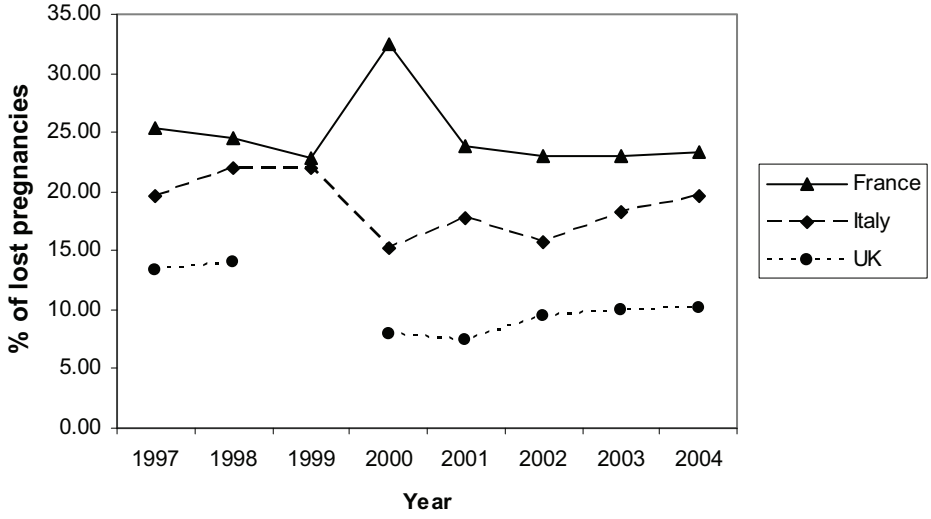
Since it is known that 50 per cent of twins and 90 per cent of triplets can be expected to be premature and therefore have low birth weight (HFEA, 2007a), we can crudely estimate the proportion of ART births that are low birth weight in each of these countries for comparison with the country prevalence in the general population. In making the conservative assumption that only 50 per cent of ART deliveries are premature, we know that 11.5 per cent of ART deliveries in France are low birth weight; 11.7 per cent are in Italy; and 12.1 per cent are in the UK. These proportions are much higher than the prevalence of low birth weight in each of the countries, which are 7 per cent in France in 1998, 6 per cent in Italy in 1998, and 8 per cent in the UK in 2000 (WHO, 2008b). The largest within-country disparity is in Italy.

5.4 Assisted Reproductive Technologies health outcomes

The most telling data for health outcomes is the trends for pregnancy loss after IVF and ICSI as well as for complications and other adverse events or reactions associated with ART procedures. Based on the ESHRE reported country data on pregnancy loss after IVF and ICSI, we calculated a crude estimate for the percentage of miscarried or lost pregnancies. This estimate may offer insight into the quality of care as a component of ART success rate in each country. First and foremost, among the three countries examined, France has the highest estimated proportion of lost pregnancies from the total number of clinical pregnancies – a figure that has remained constant over the period examined (1997 to 2004), with one year (2000) as an exception.[42] The lowest estimated percentages of lost

[42] This exception in 2000 explains the drop in the percentage of pregnancies and deliveries after IVF and ICSI in France in 2001.

pregnancies are found in the UK, with Italy between the two countries but its figures are closer to those in France (see Figure 5-21).



SOURCE: Nygren and Nyboe Andersen (2001a, 2001b, 2002) and Nyboe Andersen et al. (2004, 2005, 2006, 2007, 2008).

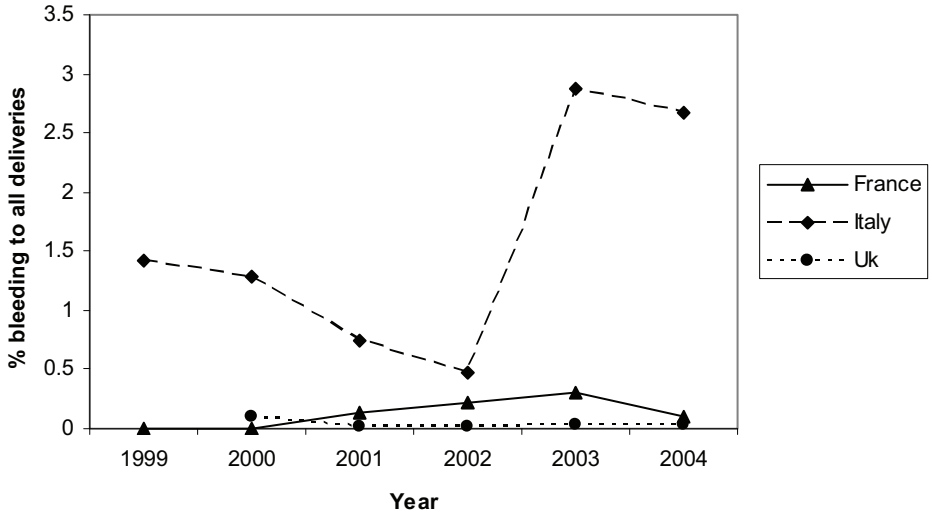
Figure 5-21 Percentage of documented pregnancies lost after IVF and ICSI in France, Italy and the UK (1997–2004)

Apart from the more direct poor health outcome of ART – lost pregnancies – there are a number of other health states by which to measure the experience of ART services in each of the three countries, such as maternal death. As discussed in the relevant chapter, Italy was one of four European countries (n=29) in 2004 to report maternal death after ART (the only two other deaths after ART were reported for the year 2002, but none occurred in any of the three countries we studied here). According to the most recent WHO reproductive health Monitoring and Evaluation (MAE) database from the three countries in 2000, France had the highest lifetime risk of maternal mortality (1 in 2,700), followed by the UK (1 in 3,800) and then Italy (1 in 13,900). These indicators might suggest that the one country to report maternal death in the population receiving ART is the one least likely to have this risk in its general population. However, we urge caution in this interpretation of the data for reasons given at the start of this chapter. Although the lifetime risk of maternal death in Italy may have increased from 2000 and 2004, it is unlikely that any natural increase would overtake either France or the UK. Hence, we might suggest that the socio-political context in Italy leading to the regulatory change in ART in 2004 may have contributed to unsafe clinical practices such as higher-order embryo transfers that would lead to such poor health outcomes as maternal death after ART.

Infections are another measure of poor health outcomes after ART. The UK has had no infections reported since 1999 with the exception of one infection reported in 2004. Similarly, there were no infections in France between 1999 and 2001. However, France had 88 per cent of the total reported infections (199/227) in 2002 and 83 per cent (299/362) in 2004. France reported 95 infections in 2003, but a proportion could not be

calculated as the ESHRE did not report a figure for all European countries reviewed that year (n=28). In Italy, the number of infections is significantly lower in absolute number than in France. But it is worth noting that Italy had reported infections each year since 1999, ranging from a high of 10 in 2000 to a low of 3 in 2004. We suggest caution in interpreting these figures for France because France has a very robust national reporting and learning system, created over a decade ago, specifically for healthcare-acquired infections (Conklin et al., 2008). Hence, the high numbers of infections reported for ART is very likely to be a consequence of an established patient safety culture which informed the recently creation of the ART-specific vigilance system.

In addition, reports of bleeding after ART indicate another negative health outcome for women undergoing such treatment. Figure 5-22 shows the percentage of bleeding to total deliveries in France, Italy and the UK in 1999 to 2004, illustrating nearly 3 per cent of all deliveries after IVF, ICSI and FER resulted in bleeding in Italy in 2003 and 2004. We suspect this observation may be associated with a build-up effect to the new policy in Italy, with infertile couples rushing to have 3-embryo transfer before the new law enters into force. A more detailed examination of this hypothesis was not possible in the available time and resources of the project.

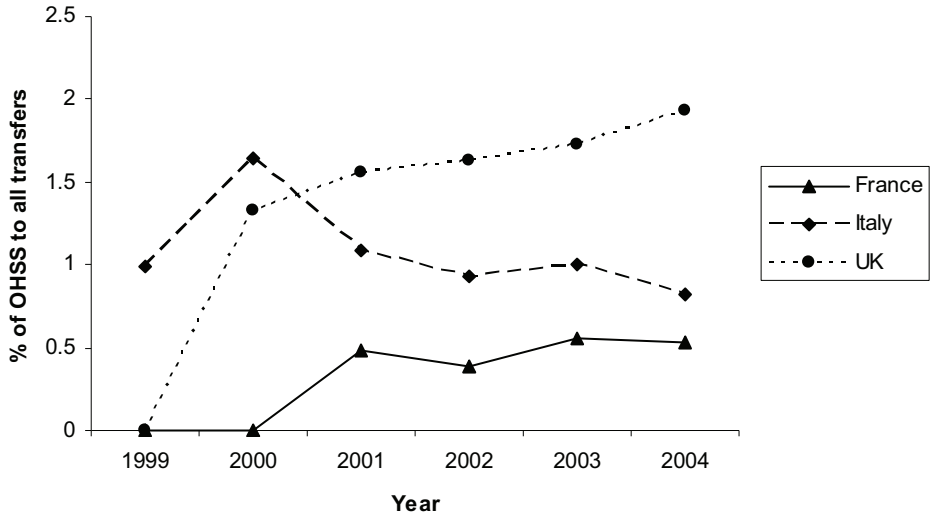


SOURCE: Nygren and Nyboe Andersen (2001a, 2001b, 2002) and Nyboe Andersen et al. (2004, 2005, 2006, 2007, 2008).

Figure 5-22 Percentage of bleeding to all deliveries after IVF, ICSI and FER in France, Italy and the UK (1997–2004)

Among the many types of complications that can result from oocyte retrieval in the process of providing ART services to infertile couples are complications related to Ovarian Hyperstimulation Syndrome (OHSS), such as ovarian torsion, ovarian rupture, thrombophlebitis and renal insufficiency. Although most cases of OHSS are mild and resolve within one to two weeks, a small proportion are severe, and potentially life-threatening (NHS Direct, 2008).

Figure 5-23 illustrates how France has consistently had the lowest percentage (0.5 per cent) of OHSS relative to all transfers after IVF, ICSI and FER.[43] As we can see, from 2000 to 2004, the UK has the highest percentage of OHSS of all ART transfers compared with the other two countries, reaching nearly 2 per cent in 2004. Moreover, whereas France and the UK show an increase over time, the percentage of OHSS of all transfers in Italy has stayed relatively constant over time with a small peak in 2000. The trend in the UK may be explained by the economic context of ART in the country creating an incentive to harvest a greater number of eggs and a greater clinical focus on selection of the best 1 or 2 embryos for more prudent transfer. But since this explanation could also be applied to Italy more readily, it is unclear why Italy does not demonstrate a similar trend.



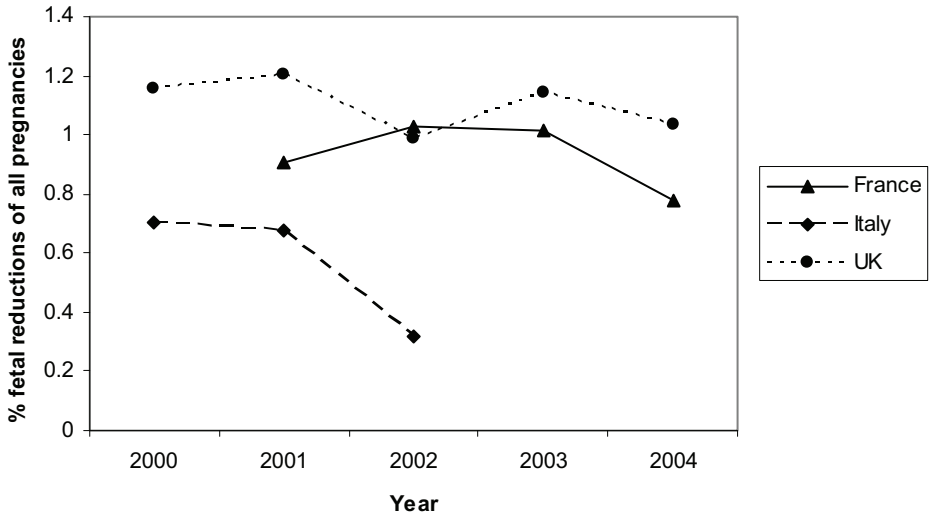
SOURCE: Nygren and Nyboe Andersen (2001a, 2001b, 2002) and Nyboe Andersen et al. (2004, 2005, 2006, 2007, 2008).

Figure 5-23 Percentage of OHSS to all transfers after IVF, ICSI and FER in France, Italy and the UK (1997–2004)

Finally, one interesting observation is the fact that the percentage of fetal reductions relative to all pregnancies after IVF, ICSI and FER is greater in France and the UK, compared with Italy where there was a decline from 2000 to 2002 (see Figure 5-24).[44] As we noted above, the UK had the lowest percentage of triplet deliveries in 2004. Although there may be a correlation between the above outcome and the greater percentage of fetal reductions of all pregnancies in the UK for that same year, it is difficult to make any suggestions of the direction of this relationship – but note that it is one worth further investigation.

[43] The graph shows 0 per cent for the years 1999 and 2000 but this is an artefact of unavailable data. Similarly, there was no data on OHSS for the UK in 1999.

[44] No ESHRE data was reported by Nyboe Andersen et al. (2007, 2008) in Italy for the years 2003 and 2004 and no explanation was given in the relevant tables for these data points. It is possible that, even if the practice occurred in some clinics in Italy, none would report this to the National Registry because of its controversial nature.



SOURCE: Nyboe Andersen et al. (2004, 2005, 2006, 2007, 2008).

Figure 5-24 Percentage of fetal reduction of all pregancies after IVF, ICSI and FER in France, Italy and the UK (1997–2004)

We end by suggesting that the decline in fetal reductions in Italy and the absence of data for later dates could reflect the fact that there is a value-based rather than evidence-based clinical practice of ART in Italy: ART treatment in Italy requires the transfer of all viable embryos even at the risk of higher order pregnancy outputs and consequent poor health outcomes for mother and child. Thus, the technique of fetal reduction is at odds with Italy's value-based regulation to the degree that reduction, as a potential form of eugenics, adds a new dimension of controversy beyond the existing controversial nature of abortion. With growing international best practice to limit embryo transfer and reduce higher order pregnancies, it is perhaps not surprising that the number of fetal reductions in France and in the UK has increased from 2000 to 2004.

REFERENCES

Reference list

Agence de la biomédecine, *Rapport annuel: bilan des activités de l'Agence de la biomédecine 2006*, Saint-Denis La Plaine, Cedex, France: Agence de la biomédecine; Autumn 2007a.

— *Le guide de l'assistance medicale a la procreation*, Saint-Denis La Plaine Cedex, France: Agence de la biomédecine; 2007b. As of 6 November 2008: http://www.procreationmedicale.fr/dl/2008/02/guideamp-bd.pdf

— *Rapport annuel de l'Agence de la biomédecine 2007*, Saint-Denis la Plaine Cedex, France: Agence de la biomédecine; 2008a. As of 22 October 2008: http://www.agence-biomedecine.fr/fr/experts/chiffres-rapport.aspx#

— *Lexique: stérilité*, home page, 2008b. As of 30 September 2008: http://www.agence-biomedecine.fr

— *Liste des établissements de santé autorisés au 31 décembre 2007: activités cliniques d'assistance médicale à la procréation*, Saint-Denis la Plaine Cedex, France: Agence de la biomédecine, 28 January 2008c. As of 9 October 2008: http://www.agencebiomedecine.fr/fr/experts/doc/AMP-clinique31122007.pdf

— *Pour en savoir plus sur l'assistance médicale à la procréation*, Saint-Denis la Plaine Cedex, France: Agence de la biomédecine, 2008d. As of 30 September 2008: http://www.agence-biomedecine.fr/project/amp/amp.html

Amato, Rosaria, "Il business della fecondazione - ecco i costi di cure e farmaci," *repubblica.it*, home page, 17 May 2007. As of 30 September 2008: http://www.repubblica.it/2005/e/sezioni/politica/dossifeconda/dossifeconda/dossifeconda.html

Annex to the Law 40/2004 based on Article 7 of the law: *Linee guida contenenti le indicazioni della procedure e delle tecniche di procreazione medicamente assistita*, Art. 7 – Legge no. 40/2004.

Arie, S., "Woman forced to have three embryos implanted is allowed fetal reduction to save her life," *British Medical Journal*, Vol. 329, 2004 (10 July), p. 71. As of 12 November 2008: http://www.bmj.com/cgi/content/full/329/7457/71-c

Assistudio SRL, "Polizze sanitarie: ancora poche in Italia," home page, ca. 2008. As of 30 September 2008: http://www.assistudio.sm/modules.php?name=News&file=article&sid=15

Associazione Luca Coscioni, "Appello dei parlamentari: a tre anni dalla legge 40 ripartiamo dalle linee guida," *lucacoscioni.it*, home page, 17 October 2007. As of 30 September 2008: http://www.lucacoscioni.it/appello_dei_parlamentari_a_tre_anni_dalla_legge_40_ripartiamo_dalle_linee_guida

Bartolucci, R., "Restrictive laws in Italy: Impact on couples," presentation at *The 9th International ICSI Conference*, Budapest, 23 February 2008

BBC Health, "Is Access to Fertility Treatment Fair?" home page, ca. 2008. As of 30 September 2008: http://www.bbc.co.uk/health/fertility/bigissues_access1.shtml

BBC News, "Egg and sperm donor cash proposal," home page, 11 November 2004. As of 30 September 2008: http://news.bbc.co.uk/2/hi/health/4002829.stm

— "NHS Facing Locum Doctor Shortage," home page, 29 February 2008. As of 21 October 2008: Online at: http://news.bbc.co.uk/2/hi/health/7271029.stm

Birenbaum-Carmeli, D., "'Cheaper Than a Newcomer': On the Social Production of IVF Policy in Israel," *Sociology of Health and Illness*, Vol. 26, No. 7, 2004, pp. 875–1,049.

Blank, R., "The United Kingdom: Regulation Through a National Licensing Authority," in Ivar Bleiklie, Marlcolm Goggin, and C. Rothmayr, eds., *Comparative Biomedical Policy: Governing Assisted Reproductive Technologies*, London, UK: Routledge, 2004, pp. 120–137.

Braude, P., *One Child at a Time: Reducing Multiple Births after IVF. Report of the Expert Group on Multiple Births after IVF*, London, UK: Human Fertilisation and Embryology Authority, October 2006.

British Fertility Society, "New Guidelines for Elective Single Embryo Transfer in IVF Treatment," home page, 3 September 2008. As of 30 September 2008: http://www.britishfertilitysociety.org.uk/news/pressrelease/08_09-SingleEmbyoGuidelines.html

Brown, L., "Health Reform, Italian Style," *Health Affairs*, Vol. 3, Fall 1984, pp. 75–101.

Calcopietro, M., "Medical Doctors in Italy: A Situation Analysis," *Cahiers de sociologie et de démographie médicale,* Vol. 42, No. 1, Jan–Mar 2002, pp. 113–148.

Callan, S., B. Almond, R. Bensted et al., *Father's Not Included: A Response to the Human Fertilisation and Embryology Bill*, London: Centre for Social Justice Assisted Reproduction Working Group of the Family Law Review, 2008.

Carvel, J., "Doctor Shortage Is Threat To Care, Warns BMA," *Guardian*, 31 March 2008. As of 21 October 2008: http://www.guardian.co.uk/society/2008/mar/31/nhs.health

Chemin, A., "Né de mère porteuse, enfant de personne," *Le Monde*, 1 November 2006. As of 10 October 2008 (by private subscription): http://www.lemonde.fr/cgi-bin/ACHATS/acheter.cgi?offre=ARCHIVES&type_item=ART_ARCH_30J&objet_id=964143

Childlessness Overcome Through Surrogacy (COTS), "Do Surrogates keep the baby?", home page, [no date], ca. 2008a. As of 23 September 2008: http://www.surrogacy.org.uk/FAQ4.htm

— "Is Surrogacy Legal in the UK?", home page, [no date], ca. 2008b. As of 23 September 2008: http://www.surrogacy.org.uk/FAQ1.htm

Cohen J, P. Madelenat and R. Levy-Toledano (eds.) *Gynécologie et santé des femmes: Quel avenir en France?* Paris: Eska publishers, 2000, pp. 156-162. As of 7 November 2008: http://www.cngof.asso.fr/d_cohen/coB_24.htm

College of Health, *Report, Fifth National Survey of Funding and Provision of Infertility Treatment*, London, UK: College of Health, 1997.

Comité consultatif national d'éthique pour les sciences de la vie et de la santé (CCNE), *Accès aux origines, anonymat et secret de la filiation, No. 90*, CCNE, 25 Janvier 2006. As of 29 August 2007: http://www.ccne-ethique.fr/francais/start.htm

Conklin, A., A.M. Vilamovska, H. de Vries, and E. Hatziandreu, *Improving Patient Safety in Europe: Assessing the Expected Effects of Three Policy Areas for Future Action*, Santa Monica, CA: RAND Corporation, 2008. TR-596-EC (in press).

Conseil constitutionnel, decision no. 94-343-344 DC 27 juillet 1994.

Cour de cassation, Bulletin d'information no. 440, 1 December 1996. Fr. Dreifuss-Netter (Paris: Dalloz, 1996, no. 27, p. 376). Note sous Civile I, 9 janvier 1996, Bulletin 1996, I, no. 21, p. 13 – *Assistance médicale à la procréation. – Fécondation in vitro.– Embryons. – Article 9 de la loi du 29 juillet 1994. – Embryons préexistants à la date de promulgation de la loi. – Destination*

CSA – Le Monde des Religions, *Portrait des Catholique, sondage de l'institut CSA, No. 0601224*, home page, October 2006. As of 30 September 2008: http://www.csa-fr.com/dataset/data2006/opi20061025d-portrait-des-catholiques.htm

Day, M., "Number of sperm donors rises despite removal of anonymity in UK," British Medical Journal, Vol. 334, 12 May 2007, p. 971

De Bac, M., *Fecondazione, si al testo preventiv*, corriere.it home page, 25 September 2007. As of 5 September 2008: http://www.corriere.it/Primo_Piano/Cronache/2007/09_Settembre/25/fecondazione_test_embrione.shtml

Decreto del Presidente della Repubblica, *Approvazione dell'atto di indirizzo e coordinamento alle regioni e alle province atuonome di Trento e di Bolzano, in material di requisiti strutturali, tecnologici ed organizzativi minimi per l'esercizio della attivita sanitarie da parte delle strutture pubbliche e private* (G.U. 20 febbraio 1997, no. 42, S.O.), 14 gennaio 1997. As of 28 September 2008: http://www.asvap.it/LEGGI%20NAZIONALI/DPR_14_1_97%20Requisiti.pdf

Deech, R., "Reproductive Tourism in Europe: Infertility and Human Rights," *Global Governance*, Vol. 9, 2003, pp. 425–432.

Department of Health, *Review of the Human Fertilisation and Embryology Act: Proposals for Revised Legislation (Including Establishment of the Regulatory Authority for Tissue and Embryos)*, Cm 6989, London, UK: Department of Health Publications and Statistics, 14 December 2006, pp. 9–11 and pp. 24–25. As of 23 October 2008: http://www.dh.gov.uk/en/publicationsandstatistics/publications/publicationspolicyandguidance/dh_073098

— *Government Response to the Report from the Joint Committee on the Human Tissue and Embryos (Draft) Bill*, Cm 7209, London, UK: Department of Health Statistics and Publications, 8 October 2007a. As of 23 October 2008: http://www.dh.gov.uk/en/Publicationsandstatistics/Publications/PublicationsPolicyAndGuidance/DH_079127

— *Impact Assessment of the Human Fertilisation and Embryology Bill (2008)*, London, UK: Department of Health Publications and Statistics, 8 November 2007b. As of 23 September 2008: http://www.dh.gov.uk/en/Publicationsandstatistics/Legislation/Regulatoryimpactassessment/DH_080209

— *PCT Survey – Provision of IVF in England 2007*, London, UK: Department of Health Publications and Statistics, 23 June 2008. As of 7 October 2008: http://www.dh.gov.uk/en/Publicationsandstatistics/Publications/PublicationsPolicyAndGuidance/DH_085665

Desmarescaux, S., *Rapport d'information fait au nom de la délégation du Sénat aux droits des femmes et à l'égalité des chances entre les hommes et les femmes sur le projet de loi, adoptée par l'Assemblée Nationale, relatif à la bioéthique (no. 189, 2001–2002)*, *No. 125, Sénat session ordinaire de 2002–2003, annexe au procès-verbal de la séance du 14 janvier 2003*. As of 30 September 2008: http://www.fc-sante.org/sros/SROS%20PDF/06%20Assistance%20medicale%20a%20la%20procreation.pdf

Di Renzo G.C., E. V. Cosmi and G. Caserta, "Control of human reproduction: a clinical perspective on bioethical problems," in *Creating the child: The ethics, law and practice of assisted procreation*, D. Evans (ed.), The Hague: Martinus Nijhoff Publishers, 1996

Donatini, A., A. Rico, M. Giuseppina D'Ambrosio, A. Lo Scalzo, L. Orzella, A. Cicchetti, and S. Profili, *Health Care Systems in Transition – Italy*, edited by Ana Rico and Teresa Cetani, Brussels, Belgium: European Observatory on Health Care Systems 2001, EUR/01/5012667 (ITA), Vol. 3, No. 4, 2001.

Doran, A., "20 Years of Regulation: Law, Science and Society," speech delivered at ACE annual conference, Manchester, UK, 3 January 2008. As of 29 September 2008: http://www.hfea.gov.uk/docs/Alan_Doran_speech_to_ACE_Annual_Conference_3_Jan_2008.pdf

Economist, "By Hook or by Crook; Italy and the Catholic Church," New York, NY: *The Economist* (US edition), 2 June 2007.

Ekert-Jaffe, O, H. Joshi, K. Lynch, R. Mougin, M.S. Rendall, "Fertility, Timing of Births and Socio-Economic Status in France and Britain: Social Policies and Occupational Polarization," *Population*, English ed.; Vol. 3, 2002, pp. 475–508.

Engeli, I., "France: Protecting Human Dignity While Encouraging Scientific Progress," in *Comparative Biomedical Policy: Governing Assisted Reproductive Technologies*, Ivar Bleiklie, Marlcolm Goggin, and C. Rothmayr (eds.), London, UK: Routledge, 2004, pp. 139, 140, 146, 147, 149, 150.

European Commission, "Directive 2004/23/EC of the European Parliament and of the Council of 31 March 2004 on setting standards of quality and safety for the donation, procurement, testing, processing, preservation, storage and distribution of human tissues and cells," *Official Journal of the European Union*, L 102/48, 7 April 2004. As of 23 October 2008: http://europa.eu/eur-lex/pri/en/oj/dat/2004/l_102/l_10220040407en00480058.pdf

— *Social protection in the Member States of the European Union, of the European Economic Area and in Switzerland. Organisation of Social Protection Charts and Descriptions*, MISSOC, Brussels, Belgium, 2007.

European Commission DG SANCO, *Report on the Regulation of Reproductive Cell Donation in the European Union – Results of Survey,* Directorate C – Public Health and Risk Assessment, C6 – Health Measures, February 2006. As of 24 October 2008: http://ec.europa.eu/health/ph_threats/human_substance/keydo_tissues_cells_en.htm

— *Summary Table of Responses from Competent Authorities: Questionnaire on the transposition and implementation of the European Tissue and Cells regulatory framework. SANCO C6 CT/gcs D (2007) 360045*. Brussels, Belgium: DG SANCO, 6 February 2007. As of 24 October 24 2008: http://ec.europa.eu/health/ph_threats/human_substance/keydo_tissues_cells_en.htm

— *Summary Table of Responses from Competent Authorities*: *Questionnaire on the transposition and implementation of the European Tissue and Cells regulatory framework. SANCO C6 EFZ/PS D (2008).* Brussels, Belgium: DG SANCO, October 2008

European Society of Human Reproduction and Embryology (ESHRE) Task Force on Ethics and Law, "Ethical Issues Related to Multiple Pregnancies in Medical Assisted Procreation," *Human Reproduction*, Vol. 18, No. 9, 2003, pp. 1,976–1,979.

Eurostat Data Navigation Tree, "Population," home page, ca. 2008. As of 8 October 2008: http://epp.eurostat.ec.europa.eu/portal/page?_pageid=1996,45323734&_dad=portal&_schema=PORTAL&screen=welcomeref&open=/populat/pop&language=en&product=EU_MASTER_population&root=EU_MASTER_population&scrollto=122

Ferrera, M, "The Rise and Fall of Democratic Universalism: Healthcare Reform in Italy, 1978—1994," *Journal of Health Politics and Law*, Vol. 20, No. 2, 1995, pp. 275–302.

Fineschi, V., M. Neri, and E. Turillazzi, "The New Italian Law on Assisted Reproduction Technology (Law 40/2004)," *Journal of Medical Ethics,* Vol. 31, 2005, pp. 536–539.

Fink, S., "Live and Let…? Measuring and Explaining the Strictness of Embryo Research Laws in 21 Countries," paper prepared for the EPCR General Conference, Budapest, 8–10 September 2005.

— "Why Do Some States Regulate Embryo Research While Others Don't? The Impact of Parties, Institutions, Economic Interests and Religious Factors," paper presented at the workshop *Die Konstruktion und Interaktion globaler, europäischer und nationaler Ordnungen*, Graduiertenkolleg Märkte und Sozialräume in Europa, Otto-Friedrich-Universität, Bamberg, Germany, 14–15 October 2004.

FIVNAT, *La prix de la PMA*, home page, last updated 6 May 2005. As of 30 October 2008: http://perso.orange.fr/fivnat.fr/gpprixfiv.htm

Franche Comité Santé (FC-Santé), Schema régional de l'Organisation Sanitaire de Troisième Génération, *Assistance médicale à la procréation et diagnostic prenatal*, FC-Santé, 2006. As of 27 September 2008: http://www.fc-sante.org/sros/SROS%20PDF/06%20Assistance%20medicale%20a%20la%20procreation.pdf

Gène éthique, *Assistance médicale à la procréation: code de la santé publique Article L. 152-1,* home page. As of 30 September 2008: http://www.genethique.org/doss_theme/dossiers/amp/codes.asp

— *Décret n. 2005-420 du 4 mai 2005 relatif à l'Agence de la biomédecine et modifiant le code de la santé publique (partie réglementaire)*, No. 65, May 2005. As of 22 October 2008: http://www.genethique.org/parus/lettres/2005/lettre_mai.htm#2

Glaser, W. A., "Doctors and Public Authorities: The Trend toward Collaboration," *Journal of Health Politics, Policy and Law,* Vol. 19, No. 4, Winter 1994.

— "How do Other Countries Do It?" *HealthPAC Online,* January 2002. As of September 30, 2008: http://www.healthpaconline.net/rekindling/Articles/Glasser.htm

Goldfarb, J.N., C. Austin, H. Lisbona, B. Peskin, and M. Clapp, "Cost-Effectiveness of In Vitro Fertilization," *Obstetrics and Gynecology*, Vol. 87, 1996, pp. 18–21.

Grabinski A., *À propos de "l'affaire de Draguignan" (1): ménopause et procréation médicalement assistée*, Paris, France: Institut national de la santé et de la recherche médicale, 2001. As of 22 October 2008: http://www.ethique.inserm.fr/ethique/Ethique.nsf/397fe8563d75f39bc12563f60028ec43/7a6c092c407daf1a80256ac5003ebc93?OpenDocument

Gruppo Tecnico Interregionale, *Requisiti strutturali, strumentali e di personale per l'autorizzazione delle strutture che erogano prestazioni di procereazione medicalmente assistita*, Riunione, 12 July 2001.

Hasendahl, S. de, "L'AMP dans la loi de bioéthique," *Le Quotidien du Médecin*, 3 August 2007. As of 30 September 2008: http://www.genethique.org/revues/revues/2007/mars/20070308.3.asp

Hassenteufel P., *Les médecins face à l'état: une comparaison européenne*, Paris: Presse des sciences politiques, 1997.

Henderson, M., "Britain's Fertility Tourists 'Go East for Cheaper IVF'," *Timesonline.co.uk*, home page, 1 July 2004. As of 29 September 2008: http://www.timesonline.co.uk/tol/news/uk/health/article452041.ece

— "'Flawed' Report on IVF Clinics Recalled After Court Challenge," *Timesonline.co.uk*, 22 March 2007. As of 30 September 2008: http://www.timesonline.co.uk/tol/news/uk/science/article1550916.ece

— "We Have Created Human Animal Embryos Already, Say British Team," *Timesonline.co.uk*, 2 April 2008a. As of 30 September 2008: http://www.timesonline.co.uk/tol/life_and_style/health/article3663033.ece

— "Infertile Couples to Be Priority for NHS IVF Treatment," *Timesonline.co.uk*, 22 August 2008b. As of 23 September 2008: http://www.timesonline.co.uk/tol/life_and_style/health/article4583272.ece

HM Treasury, "Annex D2: Department of Health," in *2007 Pre-Budget Report and Comprehensive Spending Review: Meeting the Aspirations of the British People*, London, UK: HM Treasury, 9 October 2007. As of 23 October 2008: http://www.hm-treasury.gov.uk/d/pbr_csr07_annexd2_197.pdf

Human Fertilisation and Embryology Authority (HFEA), "Explanation of Court of Appeal's Judgement in the Diane Blood Case," HFEA Document No. CE(97)01, 17 February 1997.

— "Use of Gametes and Embryos: CH(01)10," 3 August 2001. As of 30 September 2008: http://www.hfea.gov.uk/en/567.html

— "What You Need to Know About Using Donated Sperm, Eggs or Embryos in Your Treatment," 14 February 2006. As of 29 September 2008: http://www.hfea.gov.uk/docs/What_you_need_to_know_about_using_donated_sperm_eggs_or_embryos.pdf

— "The Risks of Multiple Births: Background and Statistics," home page, March 2007a. As of 21 October 2008: http://www.hfea.gov.uk/docs/2007-03-27_The_risks_of_multiple_births_-_background_and_statistics_stat_sheet_for_launch.pdf

— "A Long Term Analysis of the HFEA Register Data 1991–2006," HFEA Long term data, version 1, revision 2, saved 11 July 2007b [an updated version of the full report was made available from 18 June 2008].

— "Statement on Its Decision Regarding Hybrid Embryos," home page, 5 September 2007c. As of 22 October 2008: http://www.hfea.gov.uk/en/1581.html

— "Facts and Figures: Number of sperm and egg donors," home page, updated 4 December 2007d. As of 11 November 2008: http://www.hfea.gov.uk/en/1459.html

— "Clinics at a Glance," home page, [no date], ca. 2008a. As of 29 September 2008: http://guide.hfea.gov.uk/guide/pdf/AtAGlance.pdf [Figures found at this URL are continuously updated and hence may not reflect data cited in this report].

— "Report of the Expert Group on Multiple Births after IVF: Executive Summary," home page, [no date], ca. 2008b. As of 29 September 2008: http://www.hfea.gov.uk/docs/MBSET_executive_summary.pdf

— "Regional Breakdown of Infertility and Treatment – 2005," home page, 3 January 2008c. As of 29 September 2008: http://www.hfea.gov.uk/docs/2008-02-25_Regional_clinic_statistics_2005_including_couples_experiencing_infertility.pdf

— "FAQs for Donors," home page, last updated 18 January 2008d. As of 23 September 2008: http://www.hfea.gov.uk/en/1205.html (as of 23 September 2008).

— "Facts and Figures: The Scale of Fertility Problems," home page, last updated 7 April 2008e. As of 29 September 2008: http://www.hfea.gov.uk/en/406.html

— "FAQs about HFEA," home page, last updated 13 May 2008f. As of 30 October 2008: http://www.hfea.gov.uk/en/385.html#What_is_the_HFEA_Register

— "Multiple Births and Single Embryo Transfer Review," home page, last updated 12 June 2008g. As of 30 September 2008: http://www.hfea.gov.uk/en/483.html

— "FAQs – Preimplantation Genetic Diagnosis," home page, last updated 2 September, 2008h. As of 23 September 2008: http://www.hfea.gov.uk/en/910.html

— "Facts and Figures: Treatments and Success," home page, last updated 8 October 2008i. As of 8 October 2008: http://www.hfea.gov.uk/en/406.html#Treatment_and_success

— "History of IVF in the UK," home page, last updated 22 October 2008j. As of 30 October 2008: http://www.hfea.gov.uk/en/1737.html

Human Fertilisation and Embryology Bill [HL] (2007–08) Part 1, Section 4A, Part (10), UK Parliament home page, revised 13 June 2008. As of 30 September 2008: http://www.publications.parliament.uk/pa/cm200708/cmbills/120/08120.1-5.html#j254

Infertility Network UK, "Key Messages – Regional Funding," home page, [no date], ca. 2008. As of 23 September 2008: http://www.infertilitynetworkuk.com/?id=1160

Informa Famiglie & Bambini Regione Emilia-Romagna, "Fecondazione assistita," helath ministry home page, [no date], ca. 2008. As of 30 September 2008: http://www.municipio.re.it/retecivica/urp/retecivi.nsf/code/684B8C5666B4CA30C1256F6D00418FF8?opendocument

Institut national de la statistique et des études économiques (INSEE), *La situation démographique en 2004 – mouvement de la population*, home page, [no date], ca. 2008. As of 30 September 2008: http://www.insee.fr/fr/ppp/ir/accueil.asp?page=SD2004/dd/SD2004_fecondite.htm

Intratext.com, *Catéchisme de l'Église Catholique, no. 2,374–2,37*', home page. As of 30 September 2008: http://www.intratext.com/IXT/FRA0013/_P81.HTM

IVF-Infertility.com, "United Kingdom Regulations," home page, last updated 10 September 2008. As of 23 September 2008: http:www.ivf-infertility.com/ivf/standard/regulations4.php

Jones, D.J., "Artificial Procreation, Societal Reconceptions: Legal Insights from France," *American Journal of Comparative Law*, Vol. 36, No. 3, 1988, pp. 525–545.

Katz, P., R. Nachtigall, and J. Showstack, "The Economic Impact of the Assisted Reproductive Technologies," *Nature Cell Biology and Nature Medicine*, 4 (Suppl.), 2002, pp. S29–S32. As of 21 October 2008: http://www.tu-cottbus.de/BTU/Fak4/AllgOeko/erm/reprotox/fertil/ncb-nm-fertilitys29.pdf

La Documentation Français, "La révision des lois de bioéthique: chronologie," home page, [no data], ca. 2008. As of 14 November 2008: http://www.ladocumentationfrancaise.fr/dossiers/bioethique/chronologie.shtml

Law No. 75-17 of 18 January 1975, concerning the voluntary termination of pregnancy, as amended by Law 79-1204 of 31 December 1979, *Journal officiel de la République française*, No. 1, 1 January 1980, p. 3.

Law No. 82-1172 of 31 December 1982, concerning the extension of social security coverage to 70 per cent of the costs of care and hospitalisation associated with lawful non-therapeutic termination of pregnancy, *Journal officiel de la République française*, Edition des Lois et Decrets, No. 1, 1 January 1983, p. 15.

Le Monde, "Congé paternité: la Halde apporte son soutien à un couple d'homosexuelles," home page, 17 September 2007. As of 10 October 2008: http://www.lemonde.fr/cgi-bin/ACHATS/acheter.cgi?offre=ARCHIVES&type_item=ART_ARCH_30J&objet_id=1005253

Ledger, W., D. Anumba, N. Marlow, C. Thomas, and E. Wilson, "The Costs to the NHS, of Multiple Births after IVF Treatment in the UK," The Cost of Multiple Births Study Group (COMBS) Group. *British Journal of Obstetrics and Gynecology*, Vol. 113, 2006, pp. 21–25.

Lintsen, A.M.E., P.C.M. Pasker-de Jong, E.J. de Boer, C.W. Burger, C.A.M. Jansen, D.D.M. Braat and F.E. van Leeuwen, 'Effects of subfertility cause, smoking and body weight on the success rate of IVF', *Human Reproduction,* Vol. 20, No. 7, 2005, pp. 1867–1875.

Loi de bioéthique n°2004-800 du 6 août 2004, titre VI ch. II art. 24. As of 28 September 2008: http://www.service-public.fr/accueil/loi_bioethique_2004.html

Maheshwari, A., L. Stofberg, S. Bhattacharya, "Effect of overweight and obesity on assisted reproductive technology," *Human Reproduction Update*, Vol. 13, 2007, pp. 433-444

Malagutti, M., "Ginecologia ecco i quesiti," *dica33.it* home page, 31 May 2005. As of 30 September 2008: www.dica33.it/argomenti/ginecologia/fecondazione/assistita.asp

Mallevoüe, D. de, "*Le débat sur l'homoparentalité s'invite dans la campagne présidentielle,*" *Le Figaro.fr* home page, 30 January 2007. As of 30 September 2008: http://www.lefigaro.fr/debats/20070130.FIG000000028_le_debat_sur_l_homoparentalite_s_invite_dans_la_campagne_presidentielle.html

McGregor, J., and F. Dreifuss-Netter, "France and the United States: The legal Legal and Ethical Differences in Assisted Reproductive Technology (ART)," *Medicine and Law*, Vol. 26, No. 1, Mar 2007, pp. 117–135.

Mehl, D., *Naître? La controverse bioéthique*, Paris: Bayard Editions, 1999, pp. 338–349.

Mehl, D., "Bioéthique – Révue de presse," in: *Les procréations médicalement assistées: vingt ans après*, R. Frydman, M. Flis-Trèves, and B. Koeppel (eds.), Paris: Odile Jacob, 1998.

Ministère de l'Emploi et de la Solidarité (MES), *Arrêté du 12 janvier 1999 relatif aux règles de bonnes pratiques cliniques et biologiques en assistance médicale à la procréation, NOR: MESP9920284A*. As of 21 October 2008: http://admi.net/jo/19990228/MESP9920284A.html

Ministère du Budget, des comptes publics et de la fonction publique (MBCF), *Projet de loi de financement de la sécuritéé sociale pour 2008, République Française, NOR: BCFX0766311L/B1*. As of 22 October 2008: http://www.securite-sociale.fr/chiffres/lfss/lfss2008/071011_plfss_2008.pdf

Ministero della Salute, *Norme in materia di procreazione medicalmente assistita (Legge 19)*, home page, Febbraio 2004, No. 40, Art. 2. As of 30 September 2008: http://www.ministerosalute.it/imgs/C_17_normativa_454_allegato.pdf

— *Legge finanziaria e patto per la salute. Una sanità dalla parte dei cittadini*, home page, 2006. As of 30 September 2008: http://www.ministerosalute.it/ministero/sezDettaglioDiario.jsp?id=26&anno=2006

— *Realazione del ministro della salute al parlamento sullo stato di attuazione della legge contenente norme in materia di procreazione medicalmente assista (legge 19*), home page, Febbraio 2004, no. 40, Art. 15, 28 June 2007. As of 7 October 2008: http://www.ministerosalute.it/imgs/C_17_pubblicazioni_662_allegato.pdf

Minogiannis, P., *European Integration and Health Policy*, New Brunswick, NJ: Transaction Press, 2003, pp. 189–237.

Mladovsky, P., "ART treatment in the EU: IVF and Reproductive Tourism," *Euro Observer: Health Policy Bulletin of the European Observatory on Health Systems and Policies*, Vol. 8, No. 4, Autumn 2006, p. 5.

Monaghan, G., "Irish head to Europe for Egg Donation," *Timesonline.co.uk*, home page, 10 August 2008. As of 29 September 2008: http://www.timesonline.co.uk/tol/news/world/ireland/article4494228.ece

Murray C. and S. Golombok, "Oocyte and Semen Donation: A Survey of UK Licensed Centres," *Human Reproduction*, Vol. 15, No. 10, October 2000, pp. 2,133–2,139.

National Institute for Clinical Excellence (NICE), *Fertility: Assessment and Treatment for People with Fertility Problems*, London, National Institute for Clinical Excellence, No. 465, 2004, p. 10. As of 22 September 2008: http://www.nice.org.uk/nicemedia/pdf/CG011niceguideline.pdf

National Statistics Online, "Rise in UK Fertility Continues," homepage, 21 August 2008. As of 29 September 2008: http://www.statistics.gov.uk/cci/nugget.asp?ID=951

NHS Direct, "Health Encyclopaedia: Ovarian Hyperstimulation Syndrome," home page, last updated 4 August 2008. As of 7 October 2008: http://www.nhsdirect.nhs.uk/articles/article.aspx?articleId=214&sectionId=6

Nyboe Andersen, A., L. Gianaroli, and K.G. Nygren, "Assisted Reproductive Technology in Europe, 2000. Results Generated from European Registers by ESHRE," *Human Reproduction*, Vol. 19, No. 3, 2004, pp. 490–503.

Nyboe Andersen, A., L. Gianaroli, R. Felberbaum, J. de Mouzon, and K.G. Nygren, "Assisted Reproductive Technology in Europe, 2001. Results Generated from European Registers by ESHRE," *Human Reproduction*, Vol. 20, No. 5, 2005, pp. 1,158–1,176.

— "Assisted Reproductive Technology in Europe, 2002. Results Generated from European Registers by ESHRE," *Human Reproduction*, Vol. 21, No. 7, 2006, pp. 1,680–1,697.

Nyboe Andersen, A., V. Goossens, L. Gianaroli, R. Felberbaum, J. de Mouzon, and K.G. Nygren, "Assisted Reproductive Technology in Europe, 2003. Results Generated from European Registers by ESHRE," *Human Reproduction*, Vol. 22, No. 6, 2007, pp. 1,513–1,525.

Nyboe Andersen, A., V. Goossens, A.P. Ferraretti, S. Bhattacharya, R. Felberbaum, J. de Mouzon, and K.G. Nygren, "Assisted Reproductive Technology in Europe, 2004. Results Generated from European Registers by ESHRE," *Human Reproduction*, Vol. 19, No. 3, 2008, pp. 490–503.

Nygren, K.G. and A. Nyboe Andersen, "Assisted Reproductive Technology in Europe, 1997. Results Generated from European Registers by ESHRE," *Human reproduction*, 2001a; Vol. 16, No. 2, 2001, p. 384–391.

— "Assisted Reproductive Technology in Europe, 1998. Results Generated from European Registers by ESHRE," *Human Reproduction*, Vol. 16, No. 11, 2001b, pp. 2,459–2,471.

— "Assisted Reproductive Technology in Europe, 1999. Results Generated from European Registers by ESHRE," *Human Reproduction*, Vol. 17, No. 12, 2002, pp. 3,260–3,274.

Oneatatime.org, "Risks to the Child," home page, [no date], ca. 2008a. As of 30 September 2008: http://www.oneatatime.org.uk/37.htm

— "Risks to the mother," home page, [no date], ca. 2008b. As of 30 September 2008: http://www.oneatatime.org.uk/38.htm

Osservatorio sul Turismo Procreativo, "Turismo procreativo: fotografia di una realtà," by Cecos Italia and the Osservatorio sul Turismo Procreativo, Press Conference, Hotel Capo d'Africa, Rome, 25 May 2007. As of 30 September 2008: http://www.tecnobiosprocreazione.it/UserFiles/Media/approfondimenti/PressRoom/Turismo%20Procreativo%20fotografia%20di%20una%20realt.pdf

— "Turismo procreativo: sempre più coppie cercano la cicogna all'estero. raccolta dati a cura di chiara fornasiero, biologa e ricercatrice," Osservatorio Turismo Procreativo, Hotel Capo D'Africa, Rome, 30 November 2008. As of 28 September 2008: http://www.tecnobiosprocreazione.it/UserFiles/Media/approfondimenti/PressRoom/Osservatorio%20Turismo%20Procreativo.pdf

Petinicolas, C , "La révision de la loi de bioéthique en débat," Le figaro.fr, home page, 8 février 2007. As of 14 November 2008: http://www.lefigaro.fr/sciences/20070208.FIG000000038_la_revision_de_la_loi_de_bioethique_en_debat.html

Porciani, F., "Dove il figlio è gratuito," *corriere.it* home page, 7 May 2005. As of 30 September 2008: http://www.corriere.it/Rubriche/Salute/Diritto_alla_salute/2005/05_Maggio/07/ART_fecondazione_centri_080505.html

Pouly, J.L. and L. Larue, "Résultats de l'assistance médicale à la procréation en France: sommes-nous si mauvais?," *Gynécologie, Obstétrique et Fertilité,* Vol. 35, No. 1, 2007, pp. 30–37.

Power, C., H. Graham, P. Due, J. Hallqvist, I. Joung, D. Kuh, and J. Lynch, "The Contribution of Childhood and Adult Socioeconomic Position to Adult Obesity and Smoking Behaviour: an International Comparison," *International Journal of Epidemiology,* Vol. 34, No. 2, 2005, pp. 335–344.

Priest, J.A., "Assisted Reproduction: Developments in England," *International and Comparative Law Quarterly*, Vol. 37, No. 3, July 1988, pp. 535–550.

R v Human Fertilisation and Embryology Authority, ex parte Blood, *All English Law Reports 1997,* 6 February [1997], No. 2, pp. 687–704.

Ragni, G., A. Allegra, P. Anserini, F. Causio, A.P. Ferraretti, E. Greco, R. Palermo, and E. Somiglianal, on behalf of the Società Italiana della Riproduzione (S.I.d.R.) study group on the impact of the law 40/2004, "The 2004 Italian Legislation Regulating Assisted Reproduction Technology: A Multicentre Survey on the Results of IVF Cycles," *Human Reproduction*, Vol. 20, No. 8, 2005, pp. 2,224–2,228.

Ramjoué, C. and U. Klöti, "ART Policy in Italy. Explaining the Lack of Comprehensive Regulation," in: *Comparative Biomedical Policy: Governing Assisted Reproductive Technologies*, I. Bleiklie, M. Goggin, and C. Rothmayr (eds.), London, UK: Routledge, 2004, p. 53.

Ravizza, S. and M. Ricci Sargentini, "Fecondazione: si torna a congelare embrioni," *corriere.it* home page, 7 September 2007. As of 30 September 2008: http://www.corriere.it/Rubriche/Salute/Medicina/2007/09_Settembre/07/fecondazione_legge_aggirata.shtml

Rendall, M.S., C. Couet, T. Lappegard, Trude, I. Robert-Bobée, M. Ronsen, and S. Smallwood, "First Births by Age and Education in Britain, France and Norway," *Population Trends*, Vol. 121, 2005, pp. 27–34.

Robertson, J.A., "Protecting Embryos and Burdening Women: Assisted Reproduction in Italy," *Human Reproduction*, Vol.19, No.8, 2004, pp. 1,693–1,696.

Ryan, C., "IVF 'Good for the British Economy'," *www.bbc.co.uk*, home page, 19 June 2006a. As of 29 September 2008: http://news.bbc.co.uk/2/hi/health/5095884.stm

— "More Than 3m Babies Born from IVF," *bbc.co.uk*, home page, 21 June 2006b. As of 29 September 2008: http://news.bbc.co.uk/2/hi/health/5101684.stm

Samuel, H., "France 'No Longer a Catholic Country'," *Telegraph.co.uk*, home page, 10 January 2007. As of 30 September 2008: http://www.telegraph.co.uk/news/main.jhtml?xml=/news/2007/01/10/wfra10.xml

Sandier S., V. Paris, and D. Polton, *Health Care Systems in Transition: France*, Brussels, Belgium: WHO Regional Office for Europe on Behalf of European Observatory on Health Systems and Policies, 2004.

Sinclair, K., "Italian Reproduction Law Increases Multiple Pregnancies," *Ivf,net* home page, 16 July 2007. As of 30 September 2008: http://www.ivf.net/ivf/index.php?page=out&id=2822

Slama, A.G., "Bioéthique: les limites de la loi," *Le Figaro.fr* home page, 11 December 2006. As of 30 September 2008: http://www.lefigaro.fr/debats/20061211.FIG000000156_bioethique_les_limites_de_la_loi.html

Soldano, M., "*Storia di una legge nata male: quaderni del Circolo Fratelli Rosselli no 1/2003*," reprinted in: *Una questione di liberta: procreazione assistita tra lege e desiderio*, Valanzuolo, I. (ed.), womennews.net home page. As of 30 September 2008: http://www.womenews.net/spip3/IMG/pdf/pma.pdf

Sorenson C. "ART in the European Union," *Euro Observer: Health Policy Bulletin of the European Observatory on Health Systems and Policies*, Vol. 8, No. 4, Autumn 2006a, pp. 1–4

— "IVF/ART Funding and Reimbursement," *Euro Observer: Health Policy Bulletin of the European Observatory on Health Systems and Policies*, Vol. 8, No. 4, Autumn 2006b, p. 6–7.

Sugden, J., "Religious Leaders' Attack PM's Endorsement of Embryo Bill," *timesonline* home page, 18 May 2008. As of 8 October 2008: http://www.timesonline.co.uk/tol/news/uk/article3957232.ece

Sundquist, J. and S.-E. Johansson, "The Influence of Socioeconomic Status, Ethnicity and Lifestyle on Body Mass Index in a Longitudinal Study," *International Journal of Epidemiology,* Vol. 27, No. 1, 1998, pp. 57–63.

Surrogacy UK Organisation, "Surrogacy Arrangements Act 1985, Chapter 49," home page, [no date], ca. 2008a. As of 23 September 2008: http://www.surrogacyuk.org/surrogacyact1985.pdf

— "Surrogacy UK Website – Legal Information for Members," home page, [no date], ca. 2008b. As of 23 September 2008: http://www.surrogacyuk.org/legalities.htm

Sykes, D., H. J. Out, S. J. Palmer, and J. van Loon, "The Cost-Effectiveness of IVF in the UK: A Comparison of Three Gonadotrophin Treatments," *Human Reproduction*, Vol. 16, No. 12, December 2001, pp. 2,557–2,562.

Taccani, C., "La procreazione tra scienza e tecnica – il desiderio di un figlio e le risposte della medicina," *pastuninovara.it* home page, 21 March 2005, pp 2–3. As of 30 September 2008:

http://www.pastuninovara.it/nuovo_sito/attivita/grandi_dibattiti/procreazione/documenti/scienzaetecnica.pdf

Tain, L., "Health Inequality and Users' Risk-Taking: a Longitudinal Analysis in a French Reproductive Technology Centre," *Social Science and Medicine,* Vol. 57, 2003, pp. 2,115–2,125.

The Practice Committee of the American Society for Reproductive Medicine, "Smoking and infertility," *Fertility and Sterility*, Vol. 82 (Suppl. 1), 2004, pp. 62-67

Toulon laboratory centre, *Assurance de qualité*, home page, [no date], ca. 2008. As of 26 September 2008: http://www.labo-billiemaz.fr/pma/assurance_qualite.html

Turone, F., "Italy to Pass New Law on Assisted Reproduction," *British Medical Journal*, Vol. 328, 3 January 2004, p. 9. As of 30 September 2008: http://www.bmj.com/cgi/content/full/328/7430/9-a?maxtoshow=&HITS=10&hits=10&RESULTFORMAT=&fulltext=turone+%2B+reproductive+law&searchid=1&FIRSTINDEX=0&resourcetype=HWCIT

University of Clermont-Ferrand Hospital Information Centre (CHU-ClermontFerrand), "A.M.P: Delais d'Attente," home page on waiting times, last updated 4 September 2008. As of 26 September 2008: http://www.chu-clermontferrand.fr/reproduction/05_AMP_delai.htm

University of Toulouse Hospital Information Centre (CHU-Toulouse), home page on artificial insemination with conjoint sperm, last updated 5 April 2005. As of 30 October 2008: http://www.chu-toulouse.fr/spip.php?rubrique381

Watt, N., "MPs Reject 'Need For Father' in IVF Bill," *guardian.co.uk/politics*, home page, 20 May 2008. As of 23 September 2008: http://www.guardian.co.uk/politics/2008/may/20/health.health

World Health Organization, *The World Health Report 2000 – Health systems: Improving Performance*, Geneva: WHO, 2000. As of 30 September 2008: http://www.who.int/whr/2000/en/

— Department of Reproductive Health and Research Monitoring and Evaluation (MAE) Database, home page, updated as of 31 July 2006a. As of 10 September 2008: http://www.who.int/reproductive_indicators/countrydata.asp?page=1

— "Mortality Country Fact Sheet 2006: France," home page, 2006b. As of 22 October 2008: http://www.who.int/whosis/mort/profiles/mort_euro_fra_france.pdf

— "Mortality Country Fact Sheet 2006: Italy," home page, 2006c. As of 22 October 2008: http://www.who.int/whosis/mort/profiles/mort_euro_ita_italy.pdf

— "Mortality Country Fact Sheet 2006: United Kingdom," home page, 2006d. As of 22 October 2008:: http://www.who.int/whosis/mort/profiles/mort_euro_gbr_unitedkingdom.pdf

— *World Health Statistics 2008*, Geneva: WHO Press, 2008a.

— "Core Health Indicators," *WHO Statistical Information System (WHOSIS)*, home page, 2008b. As of 22 October 2008: http://www.who.int/whosis/data/Search.jsp

APPENDICES

Appendix A: Comparative tables

Here we present three summary tables as follows:

A-1. Political, Social and Legal Context on ART in the UK, France and Italy (Abbreviations: HS = Health care system; LHAs = Primary care trusts)

A-2. Clinical and Health Care System Context on ART in the UK, France and Italy (Abbreviations: ISS = Istituto di sanità; DI = Donor Insemination treatment; Avg. = Average)

A-3. Economic Context on ART in the UK, France and Italy

Table A-1Summary of indicators for political, social and legal context on ART in three EU countries (UK, France, Italy).

Dimension	Example Indicator	UK	France	Italy
Input – Media coverage	Driving forces in debate on ART	Initially ethical concerns produced by Louise Brown's birth and two controversial legal cases: Diane Blood (use of deceased husband's frozen sperm) and Michelle & Jayson Whitaker (right to use PGD for "saviour sibling"); tensions between powerful medical community and religious and interest groups (Catholic church, SPUC, LIFE) Recently passed two big issues: • allow single women and lesbians to have ART • ban on human–animal hybrid and chimeras Other issues: • shortage of donation • no compensation to women donors • fear of health risks • microarrays for effective embryo selection • *in vitro* growth of eggs	High profile cases of surrogate motherhood and post-menopausal conception (affaire Draguignan, 2001), via cross-border ART – cannot be prosecuted if treatment abroad is legal but legal status of child is severely complicated How outcome figures should be reported – concern to improve figures may lead to discriminatory practices for patients with lower likelihood of successful treatment Concern over decreasing donation rates due to anonymity requirement Problem of strategies to counter risk of needed specialists migrating to other clinics – need local career opportunities for junior scientists and max. number of staff accreditations Tensions between clinical and biological centres preventing integrated ART centres	Ethical concerns over: • status of embryo • protecting the classical concept of family
Input – Reimbursement	Public financing for ART	Scope of funding determined by PCTs (ranges from 1 to 3 cycles) → "'postcode lottery" in access	Cost of ART, incl. IVF, is fully covered by *Sécurité Sociale* for public and private treatments Limitations: AI: 6 attempts, pregnancy IVF-ICSI: 4 attempts, pregnancy for women <43 yrs Transfer of frozen embryos are not considered as new attempts	No national financial coverage Partial reimbursement schemes within regions (large variations) for accredited clinics → fragmented picture
Process – Regulatory framework	National law(s) regulating ART	Human Fertility and Embryology Act (1990) (c. 37)	*Loi relative à la bioethique* (Law on Bioethics), 1994; revised in 2004	First comprehensive Law 40/2004 entered into force March 2004
	Nature of the law(s)	Moderate, but moving towards liberalising access	Comprehensive approach	Restrictive
	Authoritative regulatory body	Human Fertility and Embryology Authority , independent licensing authority: bi-yearly regulation of ART and inspects and licenses ART clinics	Both clinical centres and biological centres must be authorised by Agence de la biomédicine (formerly by the Minister of Health) and approved by regional hospitalisation agencies (Source: Agence	National Bioethics Committee (1990), permanent governmental body

Dimension	Example Indicator	UK	France	Italy
			de la Biomédicine)	
Output – Regulation	Status of fertility problems	Infertility is not explicitly defined as an illness	Subfertility is an illness	Sterility is taken as a synonym for infertility and is *not* an illness
Output – Regulation of access	Eligibility criteria Age Marital status Fertility status Other requirements	1. Assessed in counselling 2. All PCTs require no existing children and measures of ability to provide care– no ”need for a father” 3. No country-wide standard for infertility (some PCTs require three yrs of infertility) → each PCT decides eligibility criteria 4. Ability to provide caring environment	Access limited to couples of normal reproductive age – costs not refunded for women 42 years and over (Uncertainty about men in couples with significant age difference – eg rejecting couples reaching combined age of over 100)	Both partners of ≥ 18 yrs Marriage not required, but must be heterosexual couple Only certified infertile in fertile age group (attested by a doctor)
	Definition of infertility	“Failing to get pregnant after two years of regular unprotected sex.” Regional differences exist due to autonomy of Primary Care Trusts	« Incapacity to conceive after two years of unprotected sex »	“Between 12 and 24 months of unprotected intercourse without conception”
Output – Implementation of clinical guidelines	Adherence to or use of guidelines	1 in 5 clinics fails to meet basic standards expected	All authorised ART clinics and laboratories comply with the good practice guidelines as mandated by law and as a requirement for authorisation by the Agence de la Bioemédicine which continually monitors all ART activities in France	
Outcome – Scale of ART	Types of ART prohibited, or restricted IVF ICSI FER Cryopreservation GIFT ZIFT PGD/PGS	Surrogacy (unless clinical/health need or reasons) Preimplantation genetic diagnosis and screening (PGDS) (unless looking for spontaneous genetic defects)	Illegal: • combined use of donated egg and sperm (sterile couples can receive embryos from another IVF couple) • surrogate motherhood • gamete donation for money • posthumous insemination	Freeze human embryos Use of donated gametes (eggs or sperm) PGD (but recent court ruling allowed PDG in a specific case in which both parents suffer from congenital illnesses) Scientific research on embryos (stem cell) Post mortem insemination
	No. of oocytes that can be fertilised within 1 ART cycle	Recommended 2, but some PCTs allow up to 3	All available frozen embryos must be used before new cycle No. of embryos implanted not regulated	Max. 3 (and *all embryos* created must be transferred to uterus)

Table A-2 Summary of indicators for clinical and healthcare system context on ART in three EU countries (UK, France, Italy)

Dimension	Example Indicator	UK	France	Italy
Input – Clinical context and prevalence	Total fertility rate	1.84 in 2006	Birth rate in 2004: 1.90 TFR in 2007: 1.98 (Source:INSEE)	
	Rate of fertility problems	1 in 7 couples	1 in 7 (~15%) women consult for infertility (CGNOF, November 2007)	1 in 5 couples (2007 ISS report)
Input – Capacity of ART treatment	Total no. of clinics authorised to perform ART 1 per country	60 public (some of which allow private patients) NHS clinics and 49 private (some of which allow NHS-funded cycles)	60 public or semi-public; and 47 private clinics (Source: Agence, 2008c); four of these clinical centres exist outside mainland France Regional disparities: • Ile de France: 24 licensed clinical centres • Limousin: only one licensed centre	330 clinics in national registry: 132 practise 1st level ART; 198 practise 2nd and 3rd level ART
	Waiting time for ART treatment	In over 50% of PCTs, waiting times are > 12 months	Varies between centres; can be longer than recommended 2 to 6 months (eg 9 months between attempts at Clermont-Ferrand in Auvergne)	In one region (Reggio Emilia) first visit/interview: 12 months Begin treatment: 5–7 months
	State of gamete donation	Decrease between 2000 to 2005: • egg donation: 1,242 to 956 • sperm donation: 325 to 259	Oocyte donation: 281 IVF attempts performed thanks to oocyte donations in 2005; no accurate data available on the number of egg donation. Sperm donation in 2005: 410 candidates; 238 donors; 15,797 sperm straws (or *paillette*) (Source: Agence, 2007*a*)	
Input – Clinical guidelines	Existence of guidelines	[Warnock Committee – policy recommendations] HFEA – *Code of Practice*, Appendix B – "Guidelines and information for good practice" NICE – *Feritlity: Assessment and Treatment for People With Fertility Problems* (Clinical Guideline 11, Feb. 2004); full guidelines © RCOG	1. Ministère de l'Emploi et de la Solidarité, *Arrêté du 12 janvier 1999 relatif aux règles de bonne pratique cliniques et biologiques en assistance médicale à la procréation*, NOR: MESP9920284A (1999) 2. Ministère de la Santé, *Arrêté du 10 mai 2001modifiant l'arrêté du 12 janvier 1999 relatif aux règles de*	1. Federation of the Orders of Doctors and Dentists – *Code of Medical Ethics* 2. Interest groups (several research institutions, patient groups, ART clinics associations) – *Code of the Forum for the Protection of Assisted Reproduction*

Dimension	Example Indicator	UK	France	Italy
		RCOG – *Standards of Care in Infertility* and *Generic Standards for Provision of Gynaecology Services* British Fertility Society – *Response to the HFEA Public Consultation on the 7th Edition of the Code of Practice* Association of Clinical Embryologists – *Code of Professional Conduct* (2nd ed., Aug. 2003)	*bonne pratique cliniques et biologiques en assistance médicale à la procréation*, NOR: SANP0121721A 3. Ministère de la Santé, *Arrêté du 19 juillet 2002 portant modification à l'arrêté du 10 mai 2001 modifiant l'arrêté du 12 janvier 1999 relatif aux règles de bonne pratique cliniques et biologiques en assistance médicale à la procréation*, NOR SANP0222478A	3. CECOS Italia – *Codex for institutions applying for ART*
Process – Clinical guidelines	Adherence to or use of guidelines	1 in 5 clinics fails to meet basic standards expected	All authorised ART clinics and laboratories comply with the good practice guidelines as mandated by law and as a requirement for authorisation by the Agence de la Bioemédicine, which continuously monitors all ART activities in France	
Process – ART uptake	Type of ART treatment most common	**ICSI is dominant** (44% of ART cycles), rest are IVF	**Artificial insemination** dominates (45% of all ART using parental gametes)	**ICSI is dominant**: 72.8% of all cycles in public structures 82.1% of all cycles in private clinics
	Rate of ART treatments: IVF ICSI FER Cryopreservation GIFT ZIFT PGD/PGS	10.8 IVF cycles per 100,000 persons – national provision [UK is 3rd largest provider of IVF but one of the poorest for access to fertility treatment] Local provision ranges from 0.3 to 21.5 per 100,000		3.5 to 4.0 per 100,000 women (2nd & 3rd level treatments) [Low number of treatments despite high number of clinics]
	No. of couples engaging in cross-border ART		Couples mainly go to Belgium, Spain or Greece depending on the reason justifying cross-border ART: same-sex couples, IVF with oocyte donation, age limit; but there is no accurate information to confirm this point	Increase from 1,066 to 4,173 of Italian couples treated by foreign clinics; data from sample clinics surveyed indicate strong increase after the adoption of the law.

Dimension	Example Indicator	UK	France	Italy
	Avg. no. of ART cycles	In 2003: 37,116 cycles (623 cycles per 1m population) In 2004: • 30,818 patients underwent 40,115 IVF cycles, yielding 8,275 births and 10,175 babies • 2,951 patients underwent 6,888 cycles of DI, giving 708 births and 750 babies	In 2003: 60,681 ART cycles (978 cycles per 1m population) In 2004: • 53,310 artificial insemination • 60,076 IVF cycles In 2005: • IUI: 57,777 attempts • IVF: 22,012 attempts • ICSI: 29,897 attempts • Frozen embryo transfer: 13,314 attempts (Source: Agence de la Biomédecine, *Rapport annuel*, p. 188)	568 cycles per 1m population [Regional distribution shows North–South decline in numbers]
	No. of ART cycles per type of provider	25% of ART cycles are provided by NHS, the rest are private		North: 74.9% public provision Central: 54.7% public provision South: 43.3% public provision
	Age distribution of cycles	2003 (**IVF**): >45 yrs: 0.9% 40–44 yr olds: 13.8% 35–39 yr olds: 40.6% 30–34 yr olds: 33.5% ≤ 29 yrs: 11.2% 2003 (**ICSI**): >45 yrs: 0.5% 40–44 yr olds: 10.2% 35–39 yr olds: 37.5% 30–34 yr olds: 36.8% ≤ 29 yrs: 15.0%	2003 (**IVF**): >45 yrs: 0.8% 40–44 yr olds: 16.2% 35–39 yr olds: 33.7% 30–34 yr olds: 36.1% ≤ 29 yrs: 13.2% 2003 (**ICSI**): >45 yrs: 0.4% 40–44 yr olds: 11.3% 35–39 yr olds: 28.4% 30–34 yr olds: 39.4% ≤ 29 yrs: 20.6% 2004 (**IVF**): >45 yrs: 0.3% 40–44 yr olds: 15.3% 35–39 yr olds: 34.3% 30–34 yr olds: 36.2% ≤ 29 yrs: 13.9% 2004 (**ICSI**):	2003 (**IVF**): >45 yrs: 2.2% 40–44 yr olds: 15.6% 35–39 yr olds: 38.9% 30–34 yr olds: 31.4% ≤ 29 yrs: 11.9% 2003 (**ICSI**): >45 yrs: 2.9% 40–44 yr olds: 16.0% 35–39 yr olds: 37.2% 30–34 yr olds: 30.8% ≤ 29 yrs: 13.1%

Dimension	Example Indicator	UK	France	Italy
			>45 yrs: 0.2% 40–44 yr olds: 10.4% 35–39 yr olds: 27.9% 30–34 yr olds: 39.5% ≤ 29 yrs: 22.0% (Source: FIVNAT 2005) 2005 **(IVF + ICSI)** ≥ 42 yrs: 1,949 cycles 39–41 yr olds: 6,475 cycles 33–38 yr olds: 19,929 cycles ≤ 32 yrs: 18,733 cycles No info about age: 3221 cycles (Source: Agence de la Biomédecine, *Bilan activité 2002–2005*)	
Output – Pregnancies	No. of embryos transferred per type of ART treatment	2003: combined IVF & ICSI 1-embryo transfer: 8.3% 2-embryo transfer: 79.9% 3-embryo transfer: 11.8% 4+-embryo transfer: 0.0%	2003: combined IVF & ICSI 1-embryo transfer: 15.6% 2-embryo transfer: 57.6% 3-embryo transfer: 23.8% 4+-embryo transfer: 2.9% 2004: IVF 1-embryo transfer: 17.6% 2-embryo transfer: 59.4% 3-embryo transfer: 19.0% 4+-embryo transfer: 4.2% 2004: ICSI 1-embryo transfer: 17.6% 2-embryo transfer: 58.6% 3-embryo transfer: 19.7% 4+-embryo transfer: 4.1% (Source: FIVNAT, 2005)	1-embryo transfer: – 19.1 % of IVF – 19.3% of ICSI 2-embryo transfer: – 31.4 % of IVF – 30.4 % of ICSI 3-embryo transfer: – 49.5 % of IVF – 50.4% of ICSI 2003: combined IVF & ICSI 1-embryo transfer: 13.6% 2-embryo transfer: 34.0% 3-embryo transfer: 44.0% 4+-embryo transfer: 8.4%
	% of ART pregnancies per cycle and per transfer	**IVF:** 24.1% per cycle 30.1% per transfer	**IVF:** 22.1% per aspiration (cycle) 26.4% per transfer	**IVF:** 21.1% pre cycle 24.4% per aspiration 27.8% per transfer

Dimension	Example Indicator	UK	France	Italy
		ICSI: 28.4% per cycle 30.3% per transfer	**ICSI:** 23.6% per aspiration (cycle) 26.5% per transfer **IVF 2005:** 23.0% per cycle 27.3% per transfer **ICSI 2005:** 24.4% per cycle 27.3% per transfer (Source: Agence de la Biomédecine, *Bilan activité 2002–2005*)	**ICSI:** 22.2% per cycle 27.5% per transfer 24.5% of transfers result in pregnancies (6,243 of 33,244 cycles in 169 institutions)
	Efficacy (success rates) of clinics – conception rate (no of pregnancies/no. of embryos transferred)	Avg. conception rate for "best IVF" clinics is 32%	IVF success rate near 30% (22% for IVF and 23.4% for IVF with ICSI)	
Output – Births	No. of ART deliveries per year % of ART deliveries per cycle % of deliveries per transfer	**IVF:** 1. Yearly, 800 babies born using donated sperm, eggs or embryos (2004: IVF live births was 19.3) 2. 21.2% per cycle 3. 26.4% per transfer **ICSI:** 25.4% per cycle 27.1% per transfer	**IVF:** 1. 2004: 2.3% of live births from ART 2. 16.8% per aspiration 3. 20.0% per transfer **ICSI:** 18.3% per aspiration 20.6% per transfer **IVF births in 2005:** 4,313 babies 17.3% deliveries/cycle 20.5% deliveries/transfer 75.3% deliveries/pregnancy **ICSI births in 2005:** 6,675 babies 18.9% deliveries/cycle 21.1% deliveries/transfer 77.4% deliveries/pregnancy (Source: Agence de la Biomédecine,	**IVF:** 1. 74.4% of ART pregnancies resulted in births (3,385 babies from 3,603 pregnancies) 2. 12.7% per cycle 3. 16.7% per transfer **ICSI:** 13.3% per cycle 16.4% per transfer

Dimension	Example Indicator	UK	France	Italy
			Bilan activité 2002–2005)	
	Efficacy (success rates) of clinics – birth rate (no. of live births/no. of ART pregnancies)		IVF success rate near 30% (22% for IVF and 23.4% for IVF with ICSI)	
Output – Multiple Births	Multiple birth rate (no. of multiple and total births) • no. of singletons • no. of twins • no. of triplets • no. of quadruplets	**After IVF & ICSI:** 1. 74.4% singleton 2. 25.0% twin 3. 0.5% triplet **After FER:** 1. 84% singleton 2. 15.5% twin 3. 0.6% triplet Singleton rate is 70% & 25% of ART births are multiple (1 in 4 cases); in 2004, multiple birth rate was 22.9	**After IVF & ICSI:** 1. 78.8% singleton 2. 20.7% twin 3. 0.5% triplet **After FER:** 1. 86.1% singleton 2. 13.4% twin 3. 0.5% triplet **After IVF with intraconjugal gametes (2005):** 1. 78.8% singleton 2. 20.5% twin 3. 0.4% triplet **After ICSI with intraconjugal gametes (2005):** 1. 78.8% singleton 2. 20.6% twin **After frozen embryo transfer with intraconjugal gametes (2005):** 1. 87.8% singleton 2. 11.3% twin 3. 0.4% triplet (Source: Agence de la Biomédecine, *Bilan activité 2002–2005*)	**After IVF & ICSI:** 1. 77.6% singleton 2. 19.3% twin 3. 3.1% triplet **After FER:** 1. 85.9% singleton 2. 13.9% twin 3. 0.3% triplet Relatively high
Outcome – Complications and fetal reductions (2003)	OHSS	1999: n/a 2000: 376 2001: 457 2002: 492 2003: 525	1999: n/a 2000: n/a 2001: 188 2002: 198 2003: 291	1999: 118 2000: 255 2001: 155 2002: 128 2003: 208

Dimension	Example Indicator	UK	France	Italy
		2004: 631	2004: 297	2004: 170
	All complications to oocyte retrieval	2000: 120 2001: 52 2002: 68 2003: 55 2004: 85	2000: n/a 2001: n/a 2002: 220 2003: 125 2004: 309	2000: 51 2001: 27 2002: 19 2003: 100 2004: 90
	Bleeding	1999: n/a 2000: 6 2001: 1 2002: 1 2003: 3 2004: 2	1999: n/a 2000: n/a 2001: 7 2002: 21 2003: 30 2004: 10	1999: 33 2000: 41 2001: 21 2002: 14 2003: 95 2004: 87
	Infection	1999: n/a 2000: 0 2001: 0 2002: 0 2003: 0 2004: 1	1999: n/a 2000: n/a 2001: 0 2002: 199 2003: 95 2004: 299	1999: 4 2000: 10 2001: 6 2002: 5 2003: 5 2004: 3
	Maternal death	2000: n/a 2001: 0 2002: n/a 2003: n/a 2004: n/a	2000: n/a 2001: 0 2002: n/a 2003: n/a 2004: 0	2000: 0 2001: 0 2002: 0 2003: 0 2004: 1
	Fetal reduction	2000: 82 2001: 87 2002: 80 2003: 98 2004: 92	2000: n/a 2001: 80 2002: 126 2003: 130 2004: 106	2000: 28 2001: 25 2002: 12 2003: n/a 2004: n/a
Outcome – Long-term health effects	• Cerebral palsy • Blindness • Learning difficulties • Other		% impairment IVF and ICSI: 2.9% (pooled data 2000–2004) (Source: FIVNAT 2005)	

Table A-3 Summary of indicators for economic context on ART in three EU countries (UK, France, Italy)

Dimension	Example Indicators	UK	France	Italy
Input – General health budget	NHS budget	£105.6 billion (2007–8) 16.7% per capita cost is private	€155.2 billion (2008, health branch of *Régime général*, financing 75% of national's health expenditures), and €179.6 billion (2008, Health branch of *Régime obligatoire*)	€300 billion (2007–9)
	National health care budget dedicated to ART	About 25% of IVF paid for by NHS → at least 1 cycle funded		€6.8 million (2005) Used to "improve services" not direct financing of individual treatment costs
Output – public expenditure on ART	Cost of ART (avg.) per cycle per type of service	For IVF, €4,194 (in total, €12,580–15,380 per ongoing IVF pregnancy) For ICSI, €6,770–11,510 For GIFT, €7,689 For ZIFT, €10,150–13,540	For AI, €500 For IVF, €2,500–3,000	For IVF, €3,500 For ICSI, approx. €4,000 For preliminary analysis, €200–300 (public) and €3,000 (private)
	Avg. cost per cycle	€5,872–7,130 in public		€1,500 in public institutions
	Regional differences in costs			**Tuscany**: ART coverage leaves couples paying €36 per cycle **Lombardia**: complete coverage (no cycle limitations) **Piemont**: private pay up to €1,000 for IVF and €1,300 for ICSI **Veneto**: only co-pay of €50 for echography
Output – health insurance expenditure on ART	Avg. cost per cycle		Private clinics may charge additional fee, partly covered by supplementary insurance fund (*mutuelle*)	€2,000–4,500 in private
Output – Private expenditure on ART	Cost of ART to individuals		In 2004, the individual cost of AI was approximately €500; for IVF the individual cost ranged between €2,500 and €3,000, depending on the techniques used (University of Toulouse Hospital Information Centre, 2005, and FIVNAT, 2005)	

Appendix B: Typology of welfare states and healthcare systems

B.1 Welfare state typologies

To establish the most appropriate typology of welfare states, we explored a number of typologies in the existing political science literature.[45] One of the many alternative typologies of welfare states is provided by Maurizio Ferrera.[46] We chose Ferrera's typology for the main reason that it offers a greater level of granularity between types of welfare states which facilitates our comparative analysis than Esping-Anderson's model.[47] Ferrera argues that welfare states can be grouped according to their positions on four dimensions (as opposed to two as in Esping-Andersen's work, for example) of welfare statism: namely, (1) the rules of access (eligibility); (2) the benefit formulae used to determine benefits; (3) the regulations to finance social protection; and, (4) the organisational and administrative structures. Ferrera notes that there are several other discriminating parameters, but these four were deemed to be the most important in the context of his analysis.

Applying these four dimensions to existing welfare systems in Europe, the following table can be constructed:

[45] For a comprehensive overview of existing typologies, see Arts and Gelissen (2002). Three worlds of welfare capitalism or more? A state-of-the-art report. *Journal of European Social Policy*, 12: 137.

[46] Ferrera M. 1996. Modèles de solidarité, divergences, convergences: perspectives pour l'Europe. *Swiss Political Science Review*, 2 (1), 1-72

[47] Esping-Andersen. *The Three Worlds of Welfare Capitalism*. Oxford: Polity Press; 1990

Table B-1 Summary of Ferrera's typology of welfare states in Europe as the basis for our analysis

Dimension / Type	Rules of access	Benefit formulae	Financing Regulation	Organisational-managerial arrangements
Anglo-Saxon (UK)	Fairly high welfare state cover	Social assistance with a means test	Mixed system of financing	Highly integrated organisational framework entirely managed by a public administration
Bismarck/ Continental (France)	Social insurance system Strong link between work position (and/or family state) and social entitlements	Benefits proportional to income	Financing through contributions; reasonably substantial social assistance benefits	Insurance schemes mainly governed by unions and employer organisations
Scandinavian	Social protection as a citizenship right	Universal coverage	Relatively generous fixed benefits for various social assistance benefits; financing mainly through fiscal revenues	Strong organisational integration
Southern (Italy)	Fragmented system of income guarantees linked to work position; healthcare as a right of citizenship though	Generous benefits (such as old age pensions) without articulated net of minimum social protection	Financing through contributions and fiscal revenues;	However, in general, little state intervention in the welfare sphere; high level of particularism with regard to cash benefits and financing, expressed in high levels of clientelism

SOURCE: Ferrera (1996)

Briefly, the four models of welfare statism can be explained further as follows:

1. The Scandinavian countries are characterised by universal coverage for the risks of life. The right to social protection is attributed on the basis of citizenship.
2. The Anglo–Saxon family of welfare states is also characterised by a highly inclusive social security coverage, but only in the area of healthcare can one speak of fully universal risk coverage. Also flat-rate benefits and means testing play an important role.
3. The Bismarckian model is build around the social insurance system, an thuse the relationship between social security entitlements, a person's labour market status and role within the family (breadwinner or not) is still clearly visible. Contributions play an important role in financing the various schemes. Almost everybody has social insurance coverage through their own or derived rights.
4. The social protection systems of Southern countries are highly fragmented and, although there is no articulated net of minimum social protection, some benefits levels are very generous (such as old age pensions). Moreover, in these countries healthcare is institutionalized as a right of citizenship. However, in general, there is relatively little state intervention in the welfare sphere. Another important feature is the high level of

particularism with regard to cash benefits and financing, expressed in high levels of clientelism.

B.2 Healthcare systems

However, within welfare states there is not necessarily consistency in how different strands of the system are organised. In particular healthcare systems might be organised differently, as the "odd case" of the United Kingdom shows, which combines universal healthcare coverage with otherwise mostly means-tested social benefits. Thus, differentiating between the wider welfare state context and the healthcare system promises to generate additional analytical mileage.

On a very general level, healthcare systems can be distinguished along two main dimensions: financing and provision of healthcare services. Both can be either public or private. Furthermore, public financing can either take the form of a direct tax subsidy or be based on a public health insurance model. The table below provides a typology based on those distinctions. Both the United Kingdom and Italy have a tax financed national health service and rely heavily on public providers for healthcare. Although moving more towards a more universal healthcare system, the French system is still strongly routed in its health insurance tradition; with multiple health insurance funds financed through contributions cover medical costs. In contrast to Italy and the United Kingdom, healthcare services are delivered by a multitude of private, private not for profit, and public providers.

Table B-2 Typology of OECD healthcare systems, 1994

Financing	Healthcare provision		
		Mixed (public + private)	Private provider
Public: contributions		Belgium, **France**, Germany, Austria, Luxemburg, Japan	
Public: taxation	Ireland, Spain, Denmark, Finland, Greece, **Italy**, Portugal, Norway, Sweden, **United Kingdom**	Australia, New Zealand	Canada
Mixed: Public and private		Turkey, Korea	Netherlands, Mexico
Private			United States, Switzerland

SOURCE: OECD, Health Care Reform: The Will to Change, Paris: OECD, 1994