Funding in vitro fertilization treatment for persistent subfertility: the pain and the politics

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Objective: To consider the arguments for and against funding for in vitro fertilization (IVF) and to explore potential avenues for policy change.

Design: Narrative literature review, policy analysis.

Setting: University Department of Obstetrics and Gynecology.

Patient(s): Sub-fertile women and men.

Intervention(s): Fertility treatments, in particular IVF.

Result(s): The two main arguments used against funding for IVF are that [1] subfertility is a social, not a medical problem, and therefore its treatment is not medically indicated or necessary, and [2] the clinical effectiveness of IVF is unproven. These and other major arguments are critiqued.

Conclusion(s): Dismissing IVF as medically unnecessary seems premature because medical necessity has not been operationally defined. Demonstrating IVF effectiveness through a randomized trial has not been done but is feasible: a multicenter trial is currently underway in Canada. Dealing with the concern that subfertility treatment challenges the role of women in society, as well as with questions of cost-effectiveness, are more difficult challenges that deserve further debate. The potential for unethical uses and broader social implications of IVF add to its dubious status and provide a convenient rationale for refusing to pay. However, none of these concerns is unique to IVF: many currently covered health services are susceptible to the same criticisms. For all services, judgments of eligibility for coverage should be consistent and transparent and should explicitly separate the issues of cost from other factors. (Fertil Steril 2001;76:431–42. ©2001 by American Society for Reproductive Medicine.)

Key Words: IVF, ethics, effectiveness, cost-effectiveness, policy, reproductive choice, technology assembly, rationing, de-insurance, insurance benefits

Thirty years ago, subfertility was a more private and stigmatic problem than it is today. People often chose to accept their lot rather than seek medical treatments, which were relatively limited and ineffective. The advent of human IVF in 1978 expanded both medical intervention and public debate. Since then, many aspects of subfertility have become more openly discussed and actively managed. In the eyes of some, IVF has been a significant advance in favor of couples who might otherwise remain childless. However, the widening use of technology to resolve subfertility has also triggered much concern and criticism, especially with regard to ethical implications, cost, proof of effectiveness, and safety.

In most countries, these concerns have hindered public and private insurance coverage. Confined to a market-driven setting, the evaluation of effectiveness through randomized controlled trials is even more problematic than it might have been in the public sector; so much so that the need for and feasibility of an adequate randomized controlled trial has been questioned by practitioners (1, 2). This article considers the complex matrix of medical, social, and ethical issues that influence decisions on public funding for IVF.

OBJECTIVES

This narrative review addresses two main questions:

1. Why is the cost of treating subfertility with in vitro fertilization (IVF) borne largely by
TABLE 1

Regulation and reimbursement by country as reported by national consumer support groups as of June 2000.

<table>
<thead>
<tr>
<th>Country</th>
<th>Regulation and reimbursement for IVF and other fertility treatments</th>
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<tbody>
<tr>
<td>Argentina</td>
<td>No legislation or reimbursement for fertility treatments</td>
</tr>
<tr>
<td>Australia</td>
<td>Reproductive Technology Accreditation Committee (RTAC) ensures standard of care, in conjunction with relevant statutes in three states. Since November 2000, no restriction on lifetime use of IVF treatment. Only country in the world with unlimited government reimbursement for infertility treatment. However, to qualify for reimbursement, treatment must be seen legally as “clinically relevant” to comply with the Commonwealth Health Insurance Act (1973).</td>
</tr>
<tr>
<td>Austria</td>
<td>ART law passed in 1991. Since January 2000, approximately 70% of IVF treatment including medication, publicly funded for women aged &lt;40, men aged &lt;50 with tubal dysfunction or male infertility.</td>
</tr>
<tr>
<td>Canada</td>
<td>No legislation governing ART. All IVF procedures privately funded except in the province of Ontario, where up to three cycles, lifetime, publicly funded for women with completely occluded fallopian tubes. If live birth is achieved, three more publicly funded cycles available.</td>
</tr>
<tr>
<td>Denmark</td>
<td>Egg donation forbidden. Publicly funded IVF available through hospitals but waiting time ≥2 years. Private clinics now established, avoiding long wait for treatment.</td>
</tr>
<tr>
<td>Finland</td>
<td>No legislation governing infertility treatment. Sixty percent to 75% of infertility and IVF treatment costs covered by the National Pension Institute.</td>
</tr>
<tr>
<td>France</td>
<td>Public funding for up to 100% of fertility treatment, if done in a public hospital; up to six artificial inseminations and four IVF treatment cycles. If live birth achieved, same treatment options available for a further pregnancy. Postmortem transfer of embryos prohibited. Fertility treatment not provided for single or lesbian women.</td>
</tr>
<tr>
<td>Germany</td>
<td>1990 Embryo Protection Act prohibited several ART procedures. Public funding for 14 inseminations, two GIFT, and four IVF cycles. No health insurance reimbursement for ICSI. Couples’ criteria for reimbursement include married or de facto relationship, no previous male sterilization. Donor insemination not reimbursed.</td>
</tr>
<tr>
<td>Southern Ireland</td>
<td>No legislation governing assisted reproduction. There are two private health insurers in Ireland, neither of which covers infertility treatment but do cover several diagnostic tests.</td>
</tr>
<tr>
<td>Israel</td>
<td>National Health Bill does not provide public funding for medication or treatment.</td>
</tr>
<tr>
<td>Italy</td>
<td>No legislation governing ART. Reimbursement for treatment inconsistent.</td>
</tr>
<tr>
<td>Latvia</td>
<td>No legislation or public funding for ART.</td>
</tr>
<tr>
<td>The Netherlands</td>
<td>Commercial surrogacy prohibited; moratorium on microsurgical epididymal sperm aspiration (MESA)/testicular sperm aspiration (TESA). Public funding for three IVF cycles and most other fertility treatments. Most private insurance companies also pay for three IVF cycles but charge a co-payment. Most medication for infertility publically funded.</td>
</tr>
<tr>
<td>New Zealand</td>
<td>Two bills currently before Parliament for regulation of ART. Public funding depends on geographic location. In some areas, drugs are funded and in others, copayment is required. Waiting lists vary from one to three years.</td>
</tr>
<tr>
<td>Norway</td>
<td>Legislation controls infertility treatment, limiting it to heterosexual couples. Egg donation, surrogacy, and embryo research prohibited. Public funding available for fertility treatment but only in public hospitals.</td>
</tr>
<tr>
<td>Sweden</td>
<td>Within IVF, egg and sperm donation prohibited. Legislation governs donor insemination; prohibited for single or lesbian women and only performed in public hospitals. Children born after donor insemination have access to the identity of their genetic father once they reach age of majority. Public funding available for IVF but varies from one to three cycles, depending on geography. Waiting list, 2 to 8 years; private clinics compete, reducing waiting time.</td>
</tr>
<tr>
<td>United Kingdom</td>
<td>HFEA, a statutory licensing organization, controls standard of care through Code of Practice. Reimbursement complicated: in Scotland, up to three IVF cycles publically funded. Elsewhere, individual health authorities may choose not to provide coverage.</td>
</tr>
<tr>
<td>United States</td>
<td>No federal legislation governing ART. Insurance coverage varies greatly. Thirteen states have mandates for infertility treatment coverage. Most couples pay out of pocket.</td>
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patients rather than health insurers in many jurisdictions?

2. What key elements would have to change to allow IVF to become a funded benefit?

BACKGROUND

For those who are unable to have a child, subfertility may be the most protracted and painful problem of their lives. A “willingness-to-pay” study suggests that to have a healthy child, subfertile couples may accept a 20% risk of death and give up 29% of their income (3). Although many subfertile adults would sacrifice much to have a child, the broader community’s view of the problem is far less committed.

IVF is the most intensive and final treatment for subfertility, used when less intensive approaches have failed. Many countries provide basic fertility services through public funding, whereas IVF coverage may be limited or absent (Table 1). For example, in Canada, where most medical care is publicly funded, IVF is purchased privately by patients at $3,000–$5,000 per treatment cycle (4). This limits access to those with substantial financial resources, although legislation mandates the provision of reasonable access to medically necessary services without financial or other barriers (5, 6). This paradox highlights the subjectivity of the term medical necessity (7, 8). Although this has not been defined, one of the principle argu-
Arguments for and against public funding of IVF.

<table>
<thead>
<tr>
<th>Arguments for public funding of IVF</th>
<th>Arguments against public funding of IVF</th>
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<tbody>
<tr>
<td>Subfertility is a medical problem deserving medical treatment</td>
<td>Subfertility is not a medical problem but a social one. Treatment is therefore not medically necessary</td>
</tr>
<tr>
<td>IVF is effective, based on evidence from large case series</td>
<td>IVF effectiveness is unproven. No RCT of adequate size has been done</td>
</tr>
<tr>
<td>Risks to women from treatment are acceptable</td>
<td>Risks to women are significant and hidden: ovarian hyperstimulation syndrome; increased chance of multiple births; possible ovarian cancer risk; objectification</td>
</tr>
<tr>
<td>No evidence exists suggesting increased rates of anomalies in IVF offspring</td>
<td>Multiple-pregnancy risk is clearly increased, resulting in prematurity.</td>
</tr>
<tr>
<td>The need for IVF is relatively small and would cost as little as 0.003% of total health care expenses (4)</td>
<td>Long-term follow-up needed</td>
</tr>
<tr>
<td>Equity: IVF should not only be available to the rich</td>
<td>Commons issue: basic community needs have to be met first. Oregon’s rationing exercise rated IVF last</td>
</tr>
<tr>
<td>Other less effective fertility treatments are funded, such as tubal surgery</td>
<td>With limited resources, IVF cannot be community supported</td>
</tr>
<tr>
<td>Adoption difficult and expensive</td>
<td>Other less effective treatments should also be de-insured</td>
</tr>
</tbody>
</table>

The true value of medical treatments for subfertility is poorly understood, in part because there are many possible measures of quality or effectiveness. Although studies of

### What Is Subfertility?

Failure to conceive after 12 months of unprotected intercourse is the most commonly used medical definition of infertility. Adopting this arbitrary, time-based definition serves to identify approximately 15% of young adults for whom advice and resources might hasten the birth of a healthy child. Between 50% and 70% of such couples will ultimately conceive (13–15), highlighting the fact that most subfertile couples are not sterile. Because the term *infertile* may be confused with the complete inability to conceive, or *sterility*, it is largely avoided in the discussion that follows; instead, the term *subfertile* is used. This may be defined as a perceived delay or difficulty in conception or carrying a baby to term.

### Subfertility Demographics

Population-survey data from American women aged 15 to 44 provide insight into the prevalence of subfertility over the last 20 years. The proportion of those surgically sterilized has remained relatively stable: 25% in 1982 and 27% in 1995. However, the proportion of women with *impaired fecundity*, defined as “women of any marital or cohabitation status having problems with conceiving or carrying a pregnancy, as well as being unable to conceive after three years of unprotected intercourse,” rose from 8.4% in 1982 and 1988 to 10.2% in 1995 (16). Although this increase may seem trivial, in absolute terms, it is highly significant.

The total number of women with impaired fecundity actually grew between 1982 and 1995 by about 35%, from 4.6 million to 6.2 million, reflecting both increased prevalence and growth in the total U.S. female population aged 15–44 years over this period. The proportion of women aged 35–44 with no previous pregnancy also increased from 24% in 1982 to 37% in 1995, likely as a result of delayed marriage and childbearing (17). The proportion of first-time mothers who were 30 or older increased from 4.1% to 21.2% during the same time period (17). Similar prevalence rates have recently been reported in Canada, although a different definition of subfertility was used (12). Three telephone surveys of women aged 18–44, cohabiting or married (n = 1,412), were sponsored by the Royal Commission in 1992. After 1 year, 8.5% of respondents had not conceived, and at 2 years, the proportion had fallen to 7.0%.

### Accessing Treatment for Subfertility

Although it has been argued that labeling couples as *infertile* on the basis of 12 months of unprotected intercourse without conception might push them into intensive and perhaps unnecessary medical treatment, this is not usually the case (18). Only about 5% of “infertile” Canadian women ultimately choose IVF (4). However, because the chance of live birth declines with advancing age, women in their late 30’s may indeed move more rapidly through less intensive treatment to IVF. The Oxford family-planning cohort study suggests that cycle fecundity of women aged >35 years is 50% of that seen in women aged 25 to 27 (19). The rising risks of miscarriage and genetic abnormality in offspring are other important factors considered by couples seeking medical help for subfertility as they pass through their fourth decade (20).

### Evolution and Effectiveness of IVF

The true value of medical treatments for subfertility is poorly understood, in part because there are many possible measures of quality or effectiveness. Although studies of
IVF effectiveness generally focus on pregnancy rate per treatment cycle, there is a far more complex weave of secondary issues to consider. These include neonatal and infant outcomes, short and long-term maternal complications, and the medical concept of physiologic health versus the more humanistic one of well-being. They are further complicated by the medicalization of normal events such as menopause through the availability of donor egg IVF.

The 1996 average rates of delivery per treatment cycle commenced and per embryo-transfer in North America were 26% and 28%, respectively (21). Intracytoplasmic sperm injection (ICSI) was performed in approximately one third of these cycles and produced similar rates of delivery to those seen after standard IVF with normal sperm (21). The safety of both approaches will be considered below.

In this 1996 US cohort, 32% of all deliveries were twin, 6.5% triplet, and 0.6% higher order pregnancies. Because of this high risk of multiple pregnancy, the number of embryos transferred has already been limited to two in many European countries, markedly reducing the risk of triplets and higher order pregnancy (22, 23). Single-embryo transfer is increasingly common in women with a good prognosis, further minimizing the risk of twin pregnancy (24).

**IVF Funding in North America**

IVF is a privately funded treatment in most of North America. Reasons for IVF insurance coverage refusal in the United States include arguments that the treatment is not medically necessary to preserve the patient’s health, that IVF is experimental, or that infertility constitutes a pre-existing condition (25). Only 14% of large plans and 16% of preferred plans offer IVF coverage (25). Only 12 states have mandated private insurance coverage for subfertility services (25). When covered, limitations often apply in terms of the number of cycles allowed or source of sperm. Connecticut, California, and Texas demand that private insurers must offer coverage for infertility services, but employers may choose not to pay for this. In California, insurers do not have to offer IVF but do have to include GIFT, a procedure that is now widely considered to be less effective than IVF. Even in Clinton’s otherwise comprehensive health security act, IVF was explicitly excluded from standard health benefit.

Paradoxically, in Canada, one province provides partial public funding, but only for women with complete, bilateral fallopian tube occlusion (BTO). They represent approximately 1% of the subfertile population (26); this subgroup qualifies for up to three publicly funded IVF treatment cycles, excluding costs of drugs. The Ontario government’s initial decision to provide resources for bilateral fallopian tube occlusion was not based on evidence of effectiveness from randomized controlled trials. Instead, assumptions and “biological evidence” were cited in the recommendation that for bilateral fallopian tube occlusion, IVF is the most appropriate treatment (12).

Before 1994, the Ontario Health Insurance Plan covered all IVF services for all clinically qualified recipients, but that year, the Ministry of Health reviewed and deinsured IVF for indications other than bilateral fallopian tube occlusion. This decision was rationalized on the basis of IVF’s questionable medical necessity and clinical effectiveness. However, these criteria were not defined or consistently applied, and cost savings were clearly a driving concern (27).

Bonnicksen (28) suggests that if 100% of American couples were subfertile, fertility treatment would be that country’s number one health priority. Whether or not this is true, the outstanding question remains: with about 10% of young adults affected, how should individuals, health-care providers, and policy makers respond? The tension between the drive of an individual to have a child and society’s broader priorities for health in the context of rapidly evolving technologies provides a dynamic framework for debate.

**WHY IS IVF AN UNFUNDED SERVICE IN MANY JURISDICTIONS?**

Is Subfertility a Medical or a Social Problem?

The question of whether failure to conceive a wanted pregnancy is a medical or social problem is central to the debate over who should pay for treatment. Public debate currently tends to follow two separate themes. The first concerns whether *subfertility in general* is a legitimate problem for social subsidy via medical insurance. Again, using Canada as an example, the answer to this question has been relatively uncontroversial: both the Royal Commission on New Reproductive Technologies and provincial ministries of health have explicitly affirmed subfertility as a legitimate medical concern and subfertility treatment as legitimate medical care for public funding (12). Indeed, “lower-tech” subfertility treatments such as ovulation induction and tubal surgery have been covered without contest by health insurance in many jurisdictions. Clearly, IVF has raised new concerns.

The second theme concerns whether *IVF in particular* is more than just a treatment for subfertility. Are the diverse applications of IVF, such as surrogacy, medically insurable and socially acceptable, and does IVF unduly medicalize social and personal problems? Indeed, IVF techniques have introduced a number of reproductive options and practices besides the simple opportunity to bear a child. These include sex selection of embryos, the identification of certain genetic abnormalities before implantation, the ability to contract out one’s biological child bearing to a surrogate, the creation of a market for human ova and the advent of childbearing after menopause. These raise serious ethical questions, including who should be obliged to pay for such choices if they are to be allowed at all. Crucial policy questions include whether such ethical challenges are integral or incidental to IVF technology and whether IVF coverage can be limited to...
address more conventional understandings of subfertility without supporting a plethora of socially questionable uses of the technology.

If the social and economic impacts of IVF are controlled by restricting it to medically necessary applications, how should medical necessity be defined? Hurley et al. (7) have argued that objectivity in distribution of limited resources may be improved by focusing on the concept of benefit and deciding whether this should encompass outcomes of both physiologic health and well-being. Another approach would be to admit that defining medical necessity is impossible. Rather than continuing to use this concept to defend potentially unjust and inconsistent decisions, attention should be focused on improving health and well-being. These themes will be pursued in the final section of this article, on key elements for change.

The social and medical elements of IVF are also seen in the tension between an individual’s claim to effective treatment for subfertility and the community’s broader concern that such treatment may cause harm to offspring and lead to commodification of reproduction and exploitation of women. In deliberating these emotionally charged ethical issues, the Canadian Royal Commission attempted to be as objective and transparent as possible (12). Its members formulated “an explicit and consistent ethical approach to examining the implications of NRT for all concerned, and making decisions and ensuring that the reasoning behind recommendations were clear.” Although a single overarching ethical theory was rejected, an “ethic of care” was outlined, based on eight components:

1. Individual autonomy;
2. Equality of community members;
3. Respect for human life and dignity, including all human tissues, specifically reproductive ones;
4. Protection of the vulnerable;
5. Noncommercialization (for profit) and commodification (human tissues “as a means to an end, not as ends in themselves”);
6. Appropriate use of resources—definition of public policy priorities;
7. Accountability—responsibility of those in power;
8. Balancing of individual and collective interests.

These relatively complex principles were chosen because they were intended not just to deal with caregiver-patient relationships but also public policy. Using this framework, the Commission set out to balance the needs of the subfertile with the obligation of society to weigh the broader implications of supporting reproductive technology and to monitor and regulate health care so as to ensure the safety of the population and future generations (12).

Is IVF Effective?

Data from IVF registries in North America and Europe suggest that the results of treatment have improved significantly over the last 10 years (21, 29, 30). Because historically, IVF/ICSI success has increased by an additional 2%–3% per annum, the 1999 average delivery rate per retrieval is likely to be approximately 30%. This does not appear to be secondary to favorable changes in the population undergoing treatment.

The proportion of women aged ≥40 years commencing treatment has actually increased from 15.6% in 1991 to 19.7% in 1996 (21, 31). The most recent published North American data describe the outcomes of >30,000 IVF and 14,000 ICSI treatment cycles in 1996 (21). Although not analyzed by diagnostic group, other studies suggest that there is no significant difference between the success of IVF in women with tubal occlusion, tubal disease, and other diagnoses (32).

Although these results are encouraging, more rigorous and definitive evaluations through large, well-designed randomized trials are not available. The only two trials of IVF effectiveness are relatively small and were published before many significant advances in technique. Both come from McMaster University (33, 34). They had insufficient power to adequately assess the results of treatment in individual diagnostic groups and were done when the success of treatment was <15% per cycle (33, 34).

The most recent trial included a total of 245 couples with a mean age of 32 years and a mean duration of 5 years who were undergoing treatment between 1990 and 1991. In that study, one stimulated-treatment cycle (without embryo freezing) was compared with a 6-month period of conventional therapy in the control group. The overall pregnancy rate per cycle was only 13% in the IVF group versus 8% in controls. Among those with all types of tubal disease, 3 of 35 (8.6%) IVF cycles were successful, compared with 3 of 42 (7.1%) control cycles. In a subgroup analysis, of these, 2/15 (13%) women with tubal occlusion and 0/30 (0%) women in control cycles were successful. This subgroup analysis yielded the only statistically significant finding of the study (P = .04). Clearly, these results do not prove the effectiveness of IVF in any diagnostic group.

The next best level of evidence available, comparing IVF success with no treatment, comes from observational studies reporting IVF-associated and treatment-independent pregnancies among women before or after IVF treatment. Three such studies reported data collected between 1981 and 1986, in the very early days of IVF (2, 35, 36). All were retrospective analyses of comparatively primitive IVF techniques. The use of operative laparoscopy at the time of the oocyte retrieval for some patients with tubal disease further confounds the evaluation of subsequent treatment-independent pregnancies. Bearing these factors in mind, all three studies reported significant spontaneous rates of conception in IVF failure patients (0.3%–0.9% conception per month), with or without subsequent treatment, during a follow-up period of 1 to 30 months (Table 3).
Two more recent studies suggest a highly positive treatment effect. A retrospective cohort study of 202 couples on an IVF waiting list between 1988 and 1992 demonstrated a treatment-independent cycle fecundity of 0.9% and a pregnancy rate per IVF cycle of 17% (1). During the same time period, Evers et al. (37) reported a spontaneous conception rate of approximately 0.5% per month in couples with unexplained and male factor infertility. Again, 18% of these patients conceived with a single cycle of IVF (Table 3). Since these studies were conducted, major advances in technique have lead further widened the gap between treatment-dependent and independent pregnancy rates.

In evaluating treatment effectiveness, two major problems remain: [1] the real effect size of IVF may be smaller than that suggested by nonexperimental studies, the results of which may be biased by selective inclusion of “good-prognosis” patients; and [2] the standard analysis of IVF ignores the benefits and burdens experienced by the couple undergoing the treatment. A more complete assessment would include the value placed on increasing the couple’s chances of having a child. Describing positive and negative experiences through successful and unsuccessful treatment would add to the understanding of its cost and value.

### Risks for Women

In addition to the perceived societal risks for women as a group, assisted reproductive technologies (ARTs) present some risks to the individual undergoing treatment. Ovulation induction agents must be used with caution to minimize the risk of severe ovarian hyperstimulation syndrome (OHSS) (38, 39). This may affect 2% to 5% of women undergoing treatment, some of whom require hospital admission and anticoagulant therapy to minimize the risk of thromboembolic disease. At least two deaths have been reported as a result of this phenomenon (40).

Concern has also been raised regarding ovarian cancer risk associated with fertility medications (41). Although clomiphene citrate use for >12 months has been cited as a potential source of increased risk, more recent data, including follow-up of approximately 30,000 Australian women, are reassuring (40, 42–44). Maternal risks of multiple pregnancy are also significant: severe ovarian hyperstimulation syndrome, pre-eclampsia, antepartum and postpartum hemorrhage, gestational diabetes, and cesarean section are all more common than with single gestations (45).

A less visible risk to women might be summed up as the existential cost of going through IVF (46). Loss of personal control, objectification, and medicalization have all been linked with IVF (47). These may best be measured by women who have gone through treatment but have not conceived; they have an appreciation of the many costs of IVF that successful patients and society as a whole do not. Also, the cost to women of being denied access to treatment bears consideration.

The burden of illness from unresolved persistent subfertility is substantial. The individual women and men who experience this often bear tremendous personal and psychological pain. Some scholars argue that this suffering does not originate only from individuals’ frustrated dreams but also from broader cultural, social or economic imperatives to procreate: this suffering is a product of a pronatal society, which values women largely for their ability to bear children (48). These imperatives in turn, contribute to the overvaluation of women as child bearers, which historically has perpetuated oppression and suffering that extends far beyond the realm of ART.

Some feminists argue that IVF and other technological opportunities, to bear children implicitly strengthens the imperative to have children, to the further detriment of women’s status. This argument is perhaps best answered by individual women dealing with subfertility themselves. In industrialized Western societies, it seems paternalistic indeed to assume that women seeking infertility treatments act out of a sense of external obligation rather than out of authentic, self-interested desire. It is an empirical question whether the increased availability of assisted reproduction makes women in general more expected or obligated to bear children and whether this in turn undermines their power or status. There are many arguments—feminist as well as conventional—both in favor and against this possibility.

### Risks for Offspring

The most important risks to offspring result from multiple pregnancy. The rates of premature delivery increase from approximately 7% with a single gestation to 41% with twins and to 93% with triplets (49). Registry data from the United Kingdom show a dramatic increase in perinatal mortality: 1.4% for singletons, 5.8% for twins and 9.1% for triplets (50). In response to this problem, many IVF programs have begun to reduce the number of embryos transferred and thus the risk of multiple pregnancy (51, 52). Although this approach is
becoming more popular, particularly in Europe, the incidence of high-order multiple pregnancy (triplets, quads), has continued to rise in the United States. The proportion rose by 14% from 1996–1997 and by a further 13% in 1998 (53).

The incidence of congenital and chromosome anomalies seems similar in IVF and naturally conceived offspring of singleton pregnancies (54). In both groups, between 2% and 2.5% have minor or major congenital anomalies. This risk is not increased in pregnancies after transfer of thawed embryos. However, it is influenced by female age and multiple pregnancy.

Concerns have been raised around the safety of ICSI in two main areas: genetics and child development. Men with abnormal sperm production have an increased rate of sex chromosome anomalies (55). Karyotypes from 1,007 men who had severely abnormal sperm showed structural chromosome anomalies in 6.5%. Half of these were XXY, presumably increasing the potential for transmission of sex chromosome anomalies to offspring. Of 491 ICSI offspring karyotyped, 5 had sex chromosome anomalies (1%), the expected rate being 0.2% (56). On the basis of these studies, male karyotyping is now recommended by many IVF programs before ICSI, when total motile sperm counts are significantly reduced. The risk of other congenital anomalies does not appear to be increased after ICSI.

Further genetic concerns include an increased risk of transferring a Y-chromosome microdeletion. A portion of the long arm of the Y chromosome (DAZ) is deleted in 13% to 17% of oligospermic men (57). Although this has no phenotypic impact, the microdeletion and the resultant fertility problem are likely to be inherited by all male offspring.

Oligozoospermic and azoospermic men also have an increased risk of carrying a cystic fibrosis mutation (CFTR). In men with congenital bilateral absence of the vas, 80% have one or two CFTR mutations (58). Twenty percent of oligospermic men have one mutation (58). Again, the use of ICSI without prior screening in such patients may increase the risk of transmission of CF to offspring.

Child development is a further concern. No difference has been noted between IVF offspring and the general population up to the age of 13 years (59). However, data from ICSI offspring are conflicting. A small study from Australia suggested that the Bayley score at 1 year is statistically significantly lower after ICSI-conceived compared with IVF-conceived and naturally conceived children (60). Data from Belgium show no such difference at 2 years in a sample of 201 children (61).

Is IVF Cost-Effective?

Whether or not a treatment is considered cost-effective depends on the chosen methods for assessing cost and the outcomes. Cost-effectiveness analyses of medical treatments assess whether resources are used most efficiently, in other words, are yielding the greatest gain for expense. This approach hinges on the opportunity cost of a treatment: the value of alternative uses of the resources required for the treatment.

In evaluating IVF, the wide range of indirect treatment costs such as time off work, the psychosocial and social stress of IVF procedures, the savings achieved by avoiding alternative treatments, and neonatal intensive care for multiple pregnancies also deserve consideration. It was recently estimated that in the year 2000, the cost of multiple birth after IVF and ICSI in North America ($640 million) would actually exceed the cost of treatment ($470 million) (62). Variation in drug and private treatment costs, which are market driven, and the difficulties of measuring the impact of remaining childless on physical and mental health are additional and complex challenges. Bearing these constraints in mind, estimates for the direct cost of a single IVF cycle range between $8,000 and $10,500 (63).

Before a cost per delivery can be calculated, the success rate of IVF must be measured. Neumann et al. (63) based their calculations on a rate of only 9%–12% per cycle, estimating the cost of delivery at $66,000 for the first cycle, increasing to $114,000 for the sixth. More recent estimates put the cost at $31,597 for women aged 30 years and $89,981 for women aged 38 years (64). How does this compare with alternative treatments? A recent evaluation of National Health Services from the United Kingdom suggested that IVF was superior to alternatives for women with severe tubal disease and endometriosis but was not as efficient as stimulated IUI or ovulation induction for women with less severe conditions (65). What is not made clear in the latter analysis is that the patients receiving these different treatment options have different prognoses. The IVF group, having tried and failed less intensive treatments, are a filtered subgroup of the population and would likely have a worse prognosis than those succeeding with less intensive therapy.

Mol et al. (66) recently addressed this concern using regression analysis, taking into account several prognostic factors. The cost-effectiveness of IVF was compared with no treatment, using estimates for untreated outcome based on data from the Canadian Infertility Treatment Evaluation Study (67). In vitro fertilization outcomes were based on 1994 data from the United Kingdom registry (68). Female age, duration of subfertility, presence of tubal or ovulation factor, primary or secondary subfertility, and the number of previous IVF cycles were included in these regression models.

The cost of a single IVF cycle was estimated at $8,000 (63). Hospital admission and subsequent neonatal care for multiple pregnancy was estimated at $38,000 (69). The cost of long-term care of handicapped offspring was not taken into consideration. On the basis of these assumptions, for a woman aged 30, with a subfertility duration of 2 years, immediate treatment with three cycles of IVF would result in a 3-year cumulative live-birth rate of 54%. The performance of three IVF cycles in couples who did not achieve a spon-
taneous pregnancy after 2.5 years of observation would result in a cumulative live-birth rate of 50%. This translates into a cost per live birth of $85,000 when IVF is done immediately and of $68,000 when done after 2.5 years of further observation. Clearly, an additional benefit in this relatively young group is that a significant proportion will conceive spontaneously and thus avoid the many costs of IVF.

However, the mean age undergoing treatment and mean duration of subfertility may be higher than 30 and 2 years, respectively (70). Performing IVF immediately under these circumstances seems more cost-effective than delayed intervention.

Although these data suggest that IVF may be on balance less costly than other treatments for subfertility, the problem of limited healthcare resources remains: costs in the absolute sense, rather than cost-effectiveness in the relative sense. The “willingness-to-pay” model suggests that IVF is highly valued, at least by subfertile women and men.

DeZoeten et al. (71) reported that of 80 infertile couples in the Netherlands, two thirds said they would undergo IVF even if it had only a 2% chance of success. In a British survey, members of the general population reported their willingness to pay 29% of their after-tax income for a 50% chance of having a child and to risk a 20% chance of death to have a child (3). Neumann and Johannesson (72) reported in 1994 that Boston residents would pay an average of $17,730 for a cycle of IVF if they were infertile and the procedure had a 10% chance of success. They would pay $865 for a lifetime insurance policy that gave them a 10% chance of the procedure working.

Individuals were also willing to pay substantial amounts so that others would have access to the procedure. The average was $32 per year in taxes, for a hypothetical public program that would provide 1,200 cycles per year in Massachusetts with a 10% chance of pregnancy per cycle. This far exceeds the real cost of providing the service (63). Collins et al. (4) recently estimated that the additional annual cost to employee health plans would be only $3.14 at the current level of IVF utilization and $9.41 if this increased by 300% because of improved access to treatment.

In considering these data, it should be remembered that willingness to pay is a controversial method for incorporating community values into public policy-making because results may be colored by peoples’ income and ability to imagine their real choices. An individual with a subsistence income may be unable to spend any money on a service that she might strongly desire. The same individual may be unable to imagine the impact of persistent subfertility and its treatment.

Although willingness-to-pay data suggest that many communities support and value IVF services, the perspective of the evaluator, the apparent effectiveness of treatment at the time of assessment, the untreated disease outcome, the costs of the program and whether these are expressed as amounts of money or in comparison to other medical services, and the socioeconomic status of respondents all influence conclusions. Assessors polled in Oregon’s rationing experiment placed IVF treatment at the bottom of a broad list of services (73). A random sample of 80 community members from Hamilton between 1987 and 1990 also rated IVF next to last in a selection of 12 program choices, only ahead of prenatal classes (74). In both of these examples, however, it should be remembered that IVF was in its very early stages of development, with ongoing pregnancy rates of only 11.8% per retrieval, compared with 4.1% of their conventional or no-treatment controls. After a further decade of development, with ongoing pregnancy rates of approximately 30% and perhaps a shift in societal perceptions of IVF from an experimental to a more therapeutic procedure, a repeat analysis of this type might produce different results.

Equity: the Individual Versus the Community

Is the allocation of IVF subsidies fair and equitable? Equity refers to the imperative to distribute health resources fairly across different groups and individuals within a community. The private funding of IVF creates a potential maldistribution of resources along two population dimensions: between the subfertile and those without fertility concerns and between the wealthy and the poor. The first equity dilemma is whether those without a subfertility problem should subsidize fertility treatment for others. If subfertility is understood to be a medical problem or if “a responsible and caring society should seek ways to recognize and support the desire of individuals to have children” (12), then a publicly funded system should enforce solidarity between the fertile and subfertile, just as it does between the healthy and the sick for any number of conditions. Subfertility care was routinely underwritten in many countries before the advent of IVF. Reluctance to pay for IVF thus seems to depend on issues other than the legitimacy of the claims of the subfertile to medical treatment for their condition.

The second equity dilemma is whether IVF should be more accessible to the wealthy than to the poor. Currently, the private expense of IVF effectively reserves it for the wealthy or impoverishes those with limited resources who choose to pursue treatment. Public insurance of physician and hospital services for IVF would make the service more accessible to the poor. However, in the absence of equitable drug coverage policies or a national pharmacare program, the out-of-pocket cost of drugs remains formidable at approximately $3,000 per cycle (75).

A related but somewhat different issue from whether resources are distributed fairly between subpopulations is the question of whether resources are distributed fairly between technologies or services. These all have their own characteristics and constituencies in patients, providers, and others. In vitro fertilization has become a high-profile, highly- scrutinized technology for many reasons, including the fanfare around its
breakthrough clinical and scientific developments, its high costs, and its ethical challenges. For these and other reasons, IVF is often selected as a comparator with other treatments that have a wider popular and emotional appeal, such as cancer therapy or cardiac surgery (76). It may thus be disfavored.

Ad hoc rationing is now a reality in many countries. The Oregon experiment provided a graphic example of how fickle the process may be. When a boy died while waiting for a de-insured bone marrow transplant, media and community outrage lead to a broader, more systematic approach to determining publicly insured services. However, even when more reason was applied to the Oregon debate, large constituents with strong lobbying power managed to remove their programs from the pool of services under review (73). After mental and child health, as well as services for the elderly, were removed from the frame of comparison, only 30% of the total budget was left on the rationing table. Services, such as IVF, that are easily defined, poorly understood, serve a minority group, and whose effectiveness is considered unproven remain vulnerable to this type of process. Ways of improving community input, a key element of the national debate, are considered in the final section on opportunities for change.

Consistency: Should Other Less Effective Fertility Treatments Be Funded, but not IVF?
Less effective treatments such as tubal surgery and ovulation induction are publicly funded in many jurisdictions. Access to these treatments is not based on proof of effectiveness. In particular, tubal surgery has not been tested through randomized trials and seems to be less cost-effective than IVF for severe tubal disease and endometriosis (65). A conservative response to this concern might be to de-insure these other less effective fertility treatments, which would in turn set a precedent for de-insuring “unproven” services in other medical fields. A more practical approach would be to broadly review the policy process used in assembly of treatments for comparison before decision making in the rationing of all medical services (76).

Adoption
It has been argued that rather than use intensive and expensive fertility treatments to achieve a pregnancy, couples with persistent subfertility should adopt a child. The reality of this option is difficult and challenging. Newborn adoption is increasingly rare with therapeutic abortion currently used to terminate approximately 20% of all pregnancies in the United States (53). Between 1989 and 1995, only about 1% of babies born to never-married women were relinquished for adoption, compared with 9% before 1979 (77). International adoption is only accessible to those with significant resources. The average cost for such a venture is estimated at between $10,000 and $20,000.

WHAT HAS TO CHANGE FOR IVF TO BE FUNDED?

Defining Medical Necessity
The term medical necessity has been invoked inconsistently, using it as a coverage exclusion criterion to control IVF’s fiscal impact. It has also been used to draw attention to the nature of infertility treatment and in particular, its social rather than medical aspects. The term is ambiguous and difficult to apply for the purpose of screening insurable services: determining which belong in medical rather than social sectors. We are unlikely to achieve fair evaluation and coverage of IVF by looking for improved definitions of medical necessity. Instead, issues such as effects, effectiveness, and cost should be examined and debated on their own merits. Community input is essential in this debate. By putting aside personal biases of current health (90% of the population is fertile) and wealth (some have adequate personal resources to access IVF privately), a more balanced approach is possible. Focus may then move away from the mirage of medical necessity and toward the provision of benefit where it is truly needed and desired.

Subfertility Treatment as a Challenge to the Status of Women
Reproduction is a social and political construct or matrix, with significant tension between the interests of the individual and the community. On one hand, the autonomy of an individual woman must be valued, but on the other, does an individual’s choice to use fertility treatments affect the lot of women who do not need or choose them? A major concern here is that once on the slippery slope of acceptance, IVF may lead directly or indirectly to exploitation of women, commodification of gametes and embryos, and many other unethical practices. Licensing authorities such as Human Fertilization and Embryology Authority (HEFA) in the United Kingdom may help to allay such fears by controlling standards of practice. More vocal input from subfertile women and men is also essential to challenge the position that fertility treatment, and IVF in particular, threatens rather than empowers the status of women.

Demonstrating Effectiveness
Although nonexperimental studies suggest that IVF is effective, the need for an adequate randomized trial of IVF versus no treatment has been underlined (12). Although the feasibility of such a study has been questioned (1, 2), a multicenter randomized trial is ongoing in Canada (78). The purpose of the expectant management versus IVF (EMVI) trial is to assess the effectiveness of IVF in women with at least one patent fallopian tube in terms of live birth per cycle start and serious morbidity. Eligible couples undergoing their first treatment cycle in six IVF programs in Ontario and British Columbia are being randomized to receive early IVF (within 90 days of randomization) or an observation period of 90 days prior to IVF. Randomization is stratified, based on
female age and presence of abnormal sperm. Follow-up at 4, 6, 9, and 12 months will assess outcomes, including live birth in each group. The associated morbidity of both options will also be determined. This up-to-date and valid assessment of IVF effectiveness will provide vital information for policy makers, clinicians, and patients in making decisions about IVF treatment.

CONCLUSIONS

In vitro fertilization is both the most potent and controversial treatment available for persistent subfertility. Many arguments have been used to support and deny access. Health system administrators in some countries, including Canada, currently lean heavily away from public funding. Several key issues require attention in order to effect change. Effectiveness and cost-effectiveness must be demonstrated. The societal view of subfertility as a medical as well as a social problem must change. Last but not least, the tension between the autonomy of an individual woman seeking treatment and the broader concerns of the community of women that IVF challenges their status must be addressed.

Although a rigorous clinical trial has been established to determine whether IVF “works” to produce pregnancies and babies, judgments of effectiveness also include the enumeration and understanding of IVF’s important effects. An appraisal of these effects must be based on values, as well as evidence. Studying the effects of IVF and other forms of reproductive care on the general well-being of women, men, children, and families would provide further meaningful information for the policy debate. This should include consideration of values relating to disability and its place in the community. Perfect health is the ideal outcome in children conceived naturally and through subfertility treatment, but this is not always achieved. Many seemingly clinical questions about IVF’s effectiveness thus blur into philosophical and moral questions about what it means to have children, or even about life itself.

In dealing with the social dimensions of IVF, it may be more realistic and meaningful to understand the service in terms of both medical and social functions, rather than playing one against the other. In fact, some applications of IVF are medically quite conventional, for example, overcoming poor sperm quality or fallopian tube occlusion, especially when viewed in the broader context of other forms of subfertility care. Some aspects of IVF might also be considered socially conventional, especially when viewed in the broader context of rights to reproductive self-determination and privacy. However, some other IVF applications are medically or socially avant garde and ethically alarming.

Accepting that technologies can carry political and social agendas (2, 3), we should nevertheless avoid “throwing the baby out with the bath water” by characterizing IVF technology as a monolith rather than an array of decisions and purposes. Instead of bluntly rejecting all uses and purposes of IVF, coverage policies should be crafted to support legitimate goals, without implicitly condoning or subsidizing less legitimate ones.

How can public views and values help to define what is legitimate health care and health need and thus more fully inform the coverage debate? Ideally, public views should be regularly explored and used to guide policy. However, in practice, the public’s role in determining service coverage policies has not been well established. Jurisdictions in the U.S., Canada, the United Kingdom, and elsewhere have been developing methods for more publicly and explicitly deliberating coverage. These exercises range from one-off surveys and public consultations to formally structured and institutionalized decision making fora such as resource allocation committees or citizen’s juries.

Until acceptable processes are in place for subjecting all health services to public judgment, it is unlikely that putting IVF forward as a test case for public debate will yield fair and meaningful policy directives. Because IVF is highly visible and complex, it tends to become caricatured in the public imagination and readily symbolizes broader issues such as reproductive rights and high technology (1, 4). Social science research could generate useful information on how to frame questions about IVF and similarly controversial new technologies, helping to interpret and use the answers for wise policy making.

What is the real problem with IVF? Economic worries have driven much of the debate about whether it should qualify for public insurance coverage. Its unit cost and potential demand may be considered high. Unproven effectiveness, the potential for unethical uses, and broader social implications add to the questionable status of IVF and provide a convenient rationale for refusing to pay. However, none of these concerns is unique to IVF. Many currently covered health services are susceptible to the same criticisms. For all of them, judgments of eligibility for coverage should be consistent, transparent, and should explicitly separate the issues of cost from other concerns.

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