commentaries

The economic impact of the assisted reproductive technologies

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Thousands of cycles of *in vitro* fertilization (IVF) are performed each year. In the US, multiple births occur after 39% of IVF cycles, whereas in Europe, the figure is 26%. Indeed, multiple births are a major factor in the costs attributable to IVF. Reducing the multiple birth rate may reduce the overall costs of IVF, and providing insurance coverage of IVF may contribute to lowering multiple birth rates. The use of IVF is likely to expand in response to increases in infertility and scientific advances.

The birth of Louise Brown in 1978, arguably the most publicized medical event of the century, heralded an era of technology-driven reproductive interventions that shows no signs of abating. Jointly referred to as assisted reproductive technologies (ART), the annual number of *in vitro* fertilization (IVF), gamete intrafallopian transfer (GIFT) and zygote intrafallopian transfer (ZIFT) procedures performed in the US has increased from 2,389 in 1985 to 61,284 in 1998; IVF (with and without intracytoplasmic sperm injection (ICSI)) accounts for approximately 96% of these procedures[1,2]. In European countries in 1998, 193,111 cycles of IVF (with and without ICSI) were initiated (Fig. 1)[3]. Including frozen embryo transfers and oocyte donations increases the number of procedures performed to 79,698 in the US and 232,443 in Europe. ARTs represent the best chance for some couples to conceive a child, but success rates still average only 24.7% in the US across all procedures and age groups, and European delivery rates are generally lower (Fig. 2). Although approximately 13% of American women will receive infertility services during their lifetime[4], only 1–2% will undergo treatment with ART. However, IVF continues to generate controversy and debate, including questions about the cost-effectiveness of ART treatment, the impact of age and multiple births on costs, and inequities in access to infertility services.

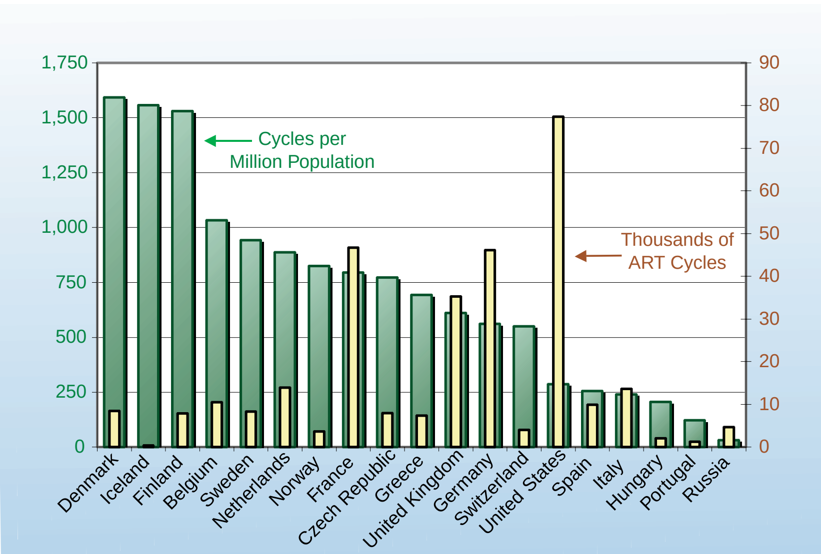

Figure 1 **An international comparison of assisted reproductive technology rates.** The number of ART cycles performed in the US and European countries in 1997 (yellow) and the number of ART cycles per million population (green) are shown. Data reproduced from refs 2 and 3.

Several studies have examined the cost-effectiveness of IVF by estimating the cost for each live birth that results from treatment[5–11]. These estimates range from $16,998 for women under 30 (ref. 10) to a highly publicized estimate of $800,000, which included neonatal care for high-risk infants[6]. Studies in Massachusetts and Iowa found that expenses for infertility (including IVF) accounted for 0.4–0.8% of total healthcare costs, at a cost of $8.04–20.52 per person per year[12,13], whereas expense estimates in New Zealand (1995) and Great Britain (1992) range from $2.40–4.68 per person per year[14,15]. In the Nordic countries, IVF accounted for 0.08–0.16% of total health care costs[16]. Recently, Collins estimated

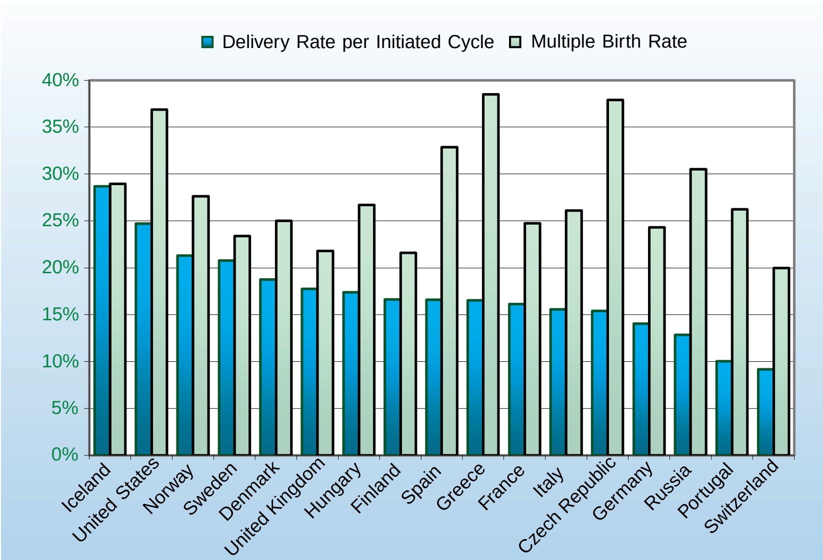

Figure 2 **An international comparison of ART delivery and multiple birth rates.** The delivery rates per initiated ART cycle (blue) and multiple birth rates (green) for the US and European countries are shown. Data reproduced from refs 2 and 3.

the median cost per IVF cycle in 2001 in the US to be $9,226, and the cost per live birth to be $56,419, whereas non-US costs were significantly lower, at $3,531 for IVF (based on data from 25 countries) and $20,522 per live birth (based on data from 8 countries)[11]. The reasons for the higher costs in the US are not clear. Indirect economic costs associated with infertility diagnosis and treatment, such as time lost from work, child care expenses or debt incurred to pay for treatment, are more difficult to quantify, but may add to the financial burden assumed by individuals undergoing infertility treatment.

In 1998, the median age of women undergoing IVF in the US was 36, with 12% of women being treated over the age of 40 (ref. 1). Because pregnancy rates decline and miscarriage rates rise with age, IVF costs per live birth are more than three times higher for women aged 40 and older, compared to women aged 30 or younger[17]. IVF pregnancy rates depend predominantly on the age of the oocytes, so older women may elect to use oocytes retrieved from younger donors to increase their chance of a live birth. Use of donor oocytes also lowers the average cost of a live birth for women over the age of 39 (ref. 10). Although this practice is increasingly popular, it has raised ethical concerns about the recruitment of young women as egg donors, with especially heated debate over the appropriate level of oocyte donor compensation.

The effect of multiple births

Multiple births may occur after IVF treatment, when more than one embryo is transferred to increase the likelihood of pregnancy. In the US in 1998, three or more embryos were transferred in 80% of ART cycles and in 47% of cycles, four or more embryos were transferred[1]. In contrast, three or more embryos were transferred in 51% of European cycles, and four or more were transferred in only 9% of cycles, although in practice there is wide variation[3]. In 1998, the percentage of IVF births that were multiples was higher in the US than in Europe. Over one-third of the IVF births in the US were multiples (32% twins, 7% triplets or more), compared with 26% in Europe (24% twins, 2% triplets or more; see Fig. 2)[1,3]. Furthermore, in the US, 57% of children born from IVF were multiples, compared to 43% in Europe[1,3].

Multiple births generate higher costs than singleton births, as a result of the higher incidence of antenatal, obstetrical and neonatal complications associated with the pre-term labour and delivery of low birth-weight premature infants[18]. Mothers carrying multiple foetuses frequently have repeated hospitalizations (often with prolonged bed-rest) and higher rates of Caesarean delivery[19]. The average triplet infant is born six weeks prematurely and weighs less than 2500 g, or only half as much as a typical single baby. Infants with birth-weights less than 2500 g are five times more likely to be admitted to a neonatal intensive care unit and forty times more likely to die in early infancy[20]. It has been reported that average hospital charges for a twin delivery were four times higher than for a singleton, whereas charges for a triplet delivery were eleven times higher, averaging over $100,000 (ref. 18). Obstetrical and neonatal costs of quadruplets have at times exceeded $1,000,000 (ref. 21). Rarely addressed are the increased costs related to long-term complications, including mental retardation, cerebral palsy, chronic problems with lung development and learning disabilities, which increase in frequency with prematurity[19–22]. Perhaps even more troubling is recent evidence showing that even singleton infants born as a result of IVF are at increased risk for low (less than or equal to 2500 g) and very low (less than or equal to 1500 g) birth-weight and major birth defects[23,24], and thus their attendant costs.

Access to fertility treatment

With a few exceptions, most notably the US, developed countries have recognized that infertility is a medical condition and have made provisions within national health policies to cover infertility treatment, including IVF. For example, Australia, Austria, Denmark, Finland, France, Germany, Iceland, The Netherlands, Norway and Sweden provided public funding for IVF as of June 2000 (ref. 25). In the US, the health insurance

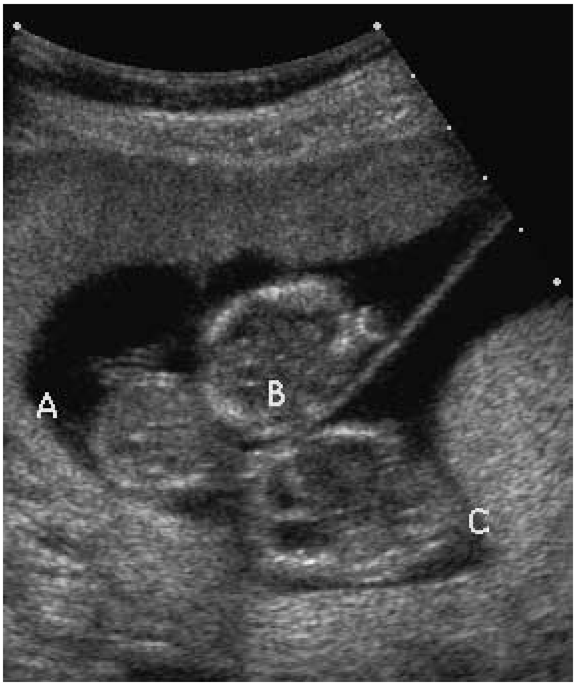

Figure 3 **Ultrasound of triplet IVF pregnancy.** The letters identify the three foetuses.

Figure courtesy of R. A. Filly, Department of Radiology, UCSF.

industry views infertility as a "socially constructed need" rather than a disease or medical condition[26], and IVF has been labelled as "experimental" and thereby excluded from coverage. The effect of these policies has been to create tremendous inequities in the availability of infertility treatment. In the US, the costs of infertility treatment are usually borne by infertile couples, including an estimated 85% of the cost of IVF[27]. Perhaps for this reason, fewer than half of infertile American women seek medical treatment, and those that do are generally Caucasian, older, married and with middle- to high-incomes[4]. In the US, 14 out of 50 states have mandated that minimum levels of infertility coverage be available, but do not necessarily mandate that employers should offer such coverage, or that IVF should be covered.

The use of IVF is greater in countries that subsidize expenses (Fig. 1). For example, in 1998, per capita use of IVF was about three times greater in France, the Netherlands, Norway and Sweden than in the US, and five times greater in Denmark, Finland, and Iceland (Fig. 1). Although the use of IVF increased when insurance coverage was mandated in Massachusetts, there was no evidence of overuse by poor-prognosis patients[13]. It was estimated that even with a fivefold increase in the utilization of IVF, the additional premium cost of adding IVF services to a typical employer health plan would be $15.69 per person per year[27].

Reducing the incidence of multiple births

Multiple births are a major factor in the overall costs attributable to IVF. Collins recognized the dilemma of decision-making in IVF almost a decade ago: "...the procedures are so costly that there is pressure to maximize success, and sadly, this response generates more adverse effects and further costs" (ref. 28). Pressures to increase pregnancy rates have resulted in the practice of implanting multiple embryos, which has caused a proliferation of multiple gestational pregnancies. Multiple gestational pregnancies are associated with much higher costs and a much greater risk of poor neonatal and pediatric outcomes.

The tension between maximizing pregnancy rates and increasing the risks of multiple birth may be addressed at several levels. Many couples have little understanding of the risks of multiple gestation and may even express a desire for a multiple birth. Patients need to be better informed of the risks associated with multiple gestation. Howard Jones, the 'father' of IVF in the US, recently advocated the abandonment of clinic-specific reporting of IVF pregnancy rates, if it can be shown that they increase pressure on physicians to transfer an excessive number of embryos to achieve an attractively high pregnancy rate[29].

The serious medical and social consequences of multiple gestation have resulted in a world-wide appeal to transfer fewer embryos. In 2001, the International Federation of Fertility Societies (IFFS) reported that 37 out of the 39 member-countries had passed national legislation (15 countries) or guidelines (22 countries) addressing the number of transferred embryos[30].

Advocates for ART may have a better chance of securing public funding/insurance coverage if the multiple birth rate decreases. Even if a pregnancy occurs as a result of infertility treatment (which may or may not be covered), insurers or the national health service bear many costs. These include prenatal care, labour and delivery and post-natal care, including the costs associated with preterm and multiple births, and maternal, obstetric and perinatal complications, which may exceed the cost of multiple IVF cycles. In fact, in the United Kingdom, there are now calls for private IVF clinics to pay toward the NHS bill for multiple births for just this reason[31]. If health insurance were expanded to pay for IVF, couples and physicians may feel less pressured to take chances with multiple births, particularly as "to the patient, the financial risk is in having an unsuccessful IVF cycle, not in the often exorbitant costs of the resultant multiple gestation" (ref. 32). Conversely, coverage of IVF may be the best chance to lower the overall costs for IVF, through regulations or legislation that specify the number of embryos that can be transferred. There is evidence from the US to suggest that coverage of IVF services results in a lower multiple birth rate[33], and in Europe, where a number of countries provide public funding, the number of embryos transferred per cycle and the multiple birth rate are lower than in the US.

Increasing access to infertility treatment

The high cost of ART is an international problem that affects many countries and many different health systems. Per capita use of IVF is higher in countries where IVF is covered either by public funding or health insurance. The US stands out in terms of the relationship between the number of IVF cycles performed compared with the size of its population (Fig. 1), illustrating the lack of access to IVF for many in the US. The costs and lack of insurance coverage put infertility treatments, particularly IVF, completely out of reach for many in the US, and create financial hardship for many others. As a result, US infertility services are used primarily by Caucasian, middle- to high-income individuals, even though the rates of infertility are equivalent, or greater, in other segments of the population. Payment for infertility treatment by health insurers or coverage by national health services may reduce some of the inequities in access, and, at least in the US, may drive down the overall costs of these procedures. As noted by Gerris and Van Royen, we still do not understand the reason that "...IVF cost(s) 10,000 US dollars in New York, 3000 US dollars in London, and 2000 US dollars in Antwerp (for similar results)" (ref. 34).

Clinical trials of IVF may provide additional evidence of its efficacy, but the underlying attitude toward infertility and its treatment may need to shift before policy changes are enacted. In a recent international survey, only 38% of those surveyed perceived infertility as a disease[35]. When told that leading medical societies recognized infertility as a disease, and that three cycles of IVF cost about the same as a hip replacement operation, 70% supported reimbursement of IVF. Public education may then be the key to increased coverage of IVF.

Insurance coverage for IVF may be seen as providing an incentive to pursue medical treatment when consideration of adoption may be more realistic for some couples[36]. However, if financial resources are exhausted during the course of multiple unsuccessful IVF attempts, adoption may no longer be an option. Therefore, a focus on family building that would provide employer and tax incentives and decrease social barriers for adoption may balance the incentives to pursue medical treatments.

Conclusions

Although IVF and other ARTs may provide the only means to have a biologically linked child for some couples, these procedures and their obstetrical, perinatal and potential long-term sequelae are associated with high costs. However, it is almost certain that the use of IVF will continue to increase in response to both a projected increase in the incidence of infertility[37] and advances in scientific knowledge and technical sophistication. Until recently, IVF was applied almost exclusively to the reproductive problems of women, yet the introduction of ICSI has made IVF available for the treatment of even severe male infertility. The not-too-distant future of IVF includes the potential for an unprecedented application of pre-implantation genetic diagnosis by couples without fertility problems who are seeking to avoid an ever-widening array of medical problems. As the use of reproductive technologies expands, concerns about cost and equitable access are likely to increase. ❑

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