

# Limitations of infertility treatment: psychological, social and cultural

Valerie L Peddie<sup>†</sup> &  
Maureen Porter

<sup>†</sup>Author for correspondence  
Department of Obstetrics and  
Gynaecology, University of  
Aberdeen, Foresterhill,  
Aberdeen, UK  
Tel.: +44 122 455 4874;  
Fax: +44 122 468 4880;  
E-mail: v.peddie@abdn.ac.uk

Having children is part of most people's expectations of life. Failing to have them, or failing to have them when planned, causes emotional distress and a (sometimes painful) re-ordering of life's priorities. This article reviews selected studies of the experience of infertility and its treatment and related advances in Western and some underdeveloped countries, and focuses on the psychological, social and cultural limitations identified. Stressful as infertility is for those in developed countries, it is generally acknowledged that it is worse, particularly for women, in many developing countries where limited treatment options are available and fewer opportunities for personal fulfilment outside the family exist. New reproductive technologies may have increased the chances of infertile men and women in developed countries having children, but they are not without limitations. In the context of stark differences in the availability of treatment and reproductive opportunities between the UK and sub-Saharan Africa, this paper highlights: the areas of common experience; the largely unacknowledged limitations of treatment failure and access to existing fertility treatment and its technological developments; and cultural expectations that place limitations on the possibilities for childless couples who are at the mercy of societal opinion and policy.

Infertility is a problem of global proportions that is predicted to increase considerably in the future as the prevalence of sexually transmitted diseases increases [1,2] and couples delay parenthood until past their fertile prime [2–4]. Nachtigall estimates that infertility affects 80 million people worldwide [2], with approximately one in six couples of reproductive age having problems conceiving a baby [5] or seeking medical advice in the UK [6]. In sub-Saharan Africa, up to a third of couples are infertile [7], and relatively few have access to such treatment as is available in private centers. Studies from a number of countries indicate that approximately 50% of infertile couples make use of infertility services including *in vitro* fertilization (IVF) and intracytoplasmic sperm injection (ICSI) [2,4]. Estimated rates of primary infertility vary widely between countries, ranging from less than 6% in China, Malawi, Tanzania and Zambia, 9% in the Philippines, less than 10% in Finland, Sweden and Canada and 18% in Switzerland [8,9]. Secondary infertility often goes unreported and rates are less reliable [10]. HIV/AIDS has been cited as an important factor affecting fertility in sub-Saharan Africa.

Wherever the geographical location, those who experience difficulty conceiving will have psychological, social and cultural privations, which have been examined in a large number of studies. This article will selectively review those

works, highlighting the limitations on infertility treatment that the authors believe have resulted. The availability and treatment of infertility in the UK is contrasted with sub-Saharan Africa and the similarities imposed by legislation in two European countries are discussed. The UK's advanced fertility services are inaccessible to many, and Italy's restrictive legislation has placed limitations on infertile couples' ability to safely access treatment. Attention is also drawn to the limitations of research on reproductive technologies, in particular pre-implantation genetic diagnosis (PGD) and stem cell research (SCR). We have not attempted to cover every aspect of fertility treatment, but to highlight those that have resulted from or imposed psychological, social and cultural limitations.

## Infertility in the developing world: sub-Saharan Africa

Most adults take it for granted that they will have children at some time in their lives [11–13]. When pregnancy does not occur, the expectations of the women and men concerned and those of other society members are disturbed [14]. The social and family pressure on infertile couples in both developed and developing countries to reproduce is immense, but van Balen and Gerrits suggest that the negative consequences of childlessness in developing countries are much

Keywords: culture, infertility, psychology, reproductive technologies

future medicine part of fsg

stronger than in Western societies [15]. Where childlessness is stigmatized, it may lead 'to profound social suffering' [2], exclusion and even death [7].

Daar and Merali estimate that, across sub-Saharan Africa, up to a third of couples are infertile [16] and Pilcher that male infertility in Africa accounts for up to 40% of childlessness [17]. Yet, discussion of male infertility is traditionally forbidden and women are generally blamed for the infertility in a society where they are dependent on children for economic survival [2]. Aboulghar reports that infertile women in Nigeria are despised or perceived as 'evil beings' and excluded from societal events, often leading to neglect or physical abuse [2,18]. In a qualitative study by Dyer and colleagues, women verbalized intense emotions when talking about their childlessness: 'burning pain', anger, deep sadness, bitterness, guilt, loneliness and desperation were feelings frequently described [19]. To add to the psychological upheaval caused by involuntary childlessness, a woman's worth is largely defined by her fertility. Thus, many women engage in promiscuous behavior and risk contracting HIV in an attempt to have a child [2]. According to Favot and colleagues, women with fertility problems have a higher HIV prevalence, which justifies such women receiving more attention in the context of AIDS programs [20]. Unmet fertility expectations were also examined in a qualitative study in Malawi, which showed women seeking treatment and engaging in risky sexual behavior, including the traditional practice of becoming pregnant by a husband's brother in order to meet the demand for high fertility rates [17].

According to Collins, out of the 191 member states of the WHO, only 48 provide IVF, covering 78% of the world's population [21]. However, given that the typical cost of an IVF cycle in Africa is nearly 42-times the average monthly salary, the estimate is that only 5–10% of those who could actually benefit from treatment can afford to pay [7]. One African woman who was thrown out of her family home because of her inability to conceive a child realized there was a need for female counselling and education and, in 2000, set up a society to help childless women become financially independent and to fight prejudice through rural workshops on infertility [17]. Central to the delivery of effective infertility care is an understanding of the experiences and implications of involuntary childlessness and of the religious and cultural context in which these experiences occur [19]. Although infertile women in sub-Saharan

Africa may lack access to services and alternatives to childlessness, some of their experiences are comparable with women in the west.

### Infertility in the West

Although not so extreme, there is evidence that infertile women in developed countries also suffer stigma and report a hostile response from the public whether involuntarily [22,23] or voluntarily childless [24]. Mueller and Yoder found that those who did not conform to the 'norm' of two or three children, whether they had too many or too few, were stigmatized [25]. Most couples who have difficulties conceiving seek medical help [6] and usually undergo a protracted course of physically and emotionally demanding investigation and treatment, during which time they may or may not conceive. Since the birth of Louise Brown in the UK in 1978, the experience of infertility in developed countries has been partially mitigated by the ability of modern technology to treat infertility successfully. But there are three major limitations to the 'available technology': unexpected failure, inaccessibility and psychological and other effects.

### *Infertility treatment: expectations versus reality*

Van der Steeg and colleagues have shown that only approximately 30% of those seeking medical assistance would have become pregnant within a year without receiving such help [26]. As IVF and ICSI yield only a 20–25% chance of a live birth per cycle, many will leave the IVF clinic childless [12] and having to make psychological adjustments to their feelings about their lives and relationships [11,27]. Yet, Leiblum and colleagues say that most have not considered 'the possibility of IVF failure and its consequent impact on emotional, marital and sexual functioning' [28], embarking on IVF programs with unrealistically optimistic expectations [29–32]. Although positioned as an 'innocuous solution within narratives of hope and promise' [33], IVF treatment in the West appears to have a significantly negative impact on lifestyle and cultural acceptance [12,34]; yet, infertility treatments are rarely spoken of as problematic for women who are subject to, or who can afford them:

"The possibility that the procedures themselves might contribute to the level of human misery endured by infertile women is silenced by their location in infertility discourse as a mere procedure, the 'hero' – the 'miracle' or 'breakthrough' that 'relieves' the suffering caused by infertility" [34].

Media ‘hype’ creates an illusion that doctors can work ‘miracles’ and that assisted conception should ‘know no limits’ [33]. IVF clinics may inadvertently create a ‘false sense of security’, both raising patients’ hopes and setting no limits on the number of attempts for those who can afford it. This, combined with rising ages deemed acceptable for IVF, gives such treatment a ‘never enough’ quality, meaning that women do not know when to stop [12]. As ‘success’ is only measured in terms of live babies, many women are doomed to ‘fail’ despite their repeated attempts [35]. Most cultures place a high value on heterosexual couples bearing children and, consequently, may be less than supportive to those who ‘do not comply’ or cannot fulfil this expectation. Becker explored the connection between bodily distress and the social order ‘advocating social change to broaden cultural ideologies that impose a limited view on life possibilities’, which ‘results in social and emotional pain for those who cannot comply’ [34].

Many couples accessing infertility services lead professional and successful lives outside treatment and, ‘when pregnancy does not occur as expected, their ability to control this part of their lives is challenged’ [13]. In an ethnographic study, Allan reported that, ‘patients believed that infertility had brought chaos or disorder to their everyday lives and that they had lost control over a part of their lives in which they had previously assumed they had control’ [36]. Although women may wish to control their experiences of fertility, their expectations of choice and control are frequently an illusion [13], especially if they lack financial resources or have a child borne from a previous relationship.

#### **Barriers to accessing infertility services**

The apparent availability of assisted reproductive technology (ART) in the West may mask *de facto* limitations in access, with many couples finding themselves excluded or ‘limited’ by age, marital status, children from a previous relationship, geographical area or inability to pay [37]. Inequality in the provision of National Health Service (NHS)-funded fertility services within the UK may exacerbate the pain of childlessness [37]. It has been suggested that those who fund their own treatment – common in the UK, unlike parts of Europe, such as Israel and Scandinavia, where ‘complete and equitable access to treatment’ is standard [2] – may attempt to ‘push the boundaries’ that apply to IVF provision. Becker

found similarities in the USA where, “...women and men anticipated a prompt solution to their childlessness and were unprepared for the lengthy and often complex series of medical procedures in which they gradually became immersed if they had the financial resources” [34]. Despite the obvious limitations that funding poses for infertility treatment, Collins and colleagues point out that few clinical studies of infertility include data on socioeconomic or educational status [38].

The regulation of ART from the late 1980s has imposed further limitations. The Human Fertilisation and Embryology Authority (HFEA) in the UK regulates clinics providing IVF, determines the number of embryos that can be transferred and decides who can receive treatment and what types are available. Couples complying with the legislation have had to submit to the ‘welfare of the child clause’ and prove themselves ‘economically and socially viable’ to parent a child. Italy recently introduced restrictive legislation that allows only heterosexual couples of fertile age access to ART, disallows gametes or embryo cryopreservation and obliges the woman to have all fertilized eggs, normal or abnormal, replaced in the uterus [39]. The law has been criticized, both in and outside the country, because of its disregard for the interests (and rights) of women [40]. It places excessive limitations on access to ART, challenging freedom of choice and adding to the psychological upheaval of involuntary childlessness. It is reported that Italy’s restrictive legislation has forced couples to seek treatment abroad [41,42], increasing their own stress and undermining the viability of the remaining Italian centers. Spar dubbed the practice of seeking a child abroad that is genetically their own, ‘reproductive tourism’, arguing that: “Many desperate couples are at the forefront of a quiet but burgeoning market that stretches around the globe and already encompasses thousands of people. Soliciting for gametes, illegal surrogacy and even ‘buying’ babies is a realistic possibility” [42]. There is no doubt that the Italian legislation adds another dimension to the psychological limitations of infertility and its treatments.

#### **Psychological & other effects**

Many studies report that both men and women experience psychological effects from infertility, such as depression [18,43–45], although this may pre-date the infertility [46]. Surveyed regarding the psychological effects of IVF, couples often

describe infertility as the most upsetting experience of their lives [11]. This finding is reiterated by Domar and colleagues, who found that women with infertility are significantly more distressed than fertile women, and that the disruption of the expected life course leads many to experience grief and loss [14,45,47,48]. Chen and colleagues reported that depression and anxiety were 'highly prevalent' among women attending an ART clinic [49] and Souter and colleagues found that one in three such women are at risk [50]. Some studies report that infertile women suffer more psychologically than men [27,44,51–53], others that there is no difference [52,54], although there are variations within the group [55]. Many studies use standardized measures of psychological effects, such as the Hospital Anxiety and Depression Score (HADS), which are perhaps unlikely to detect subtle differences induced by the experience of infertility and may even limit expression of the specific problems represented by infertility and its treatment [56]. The Infertility Reaction Scale [57] is perhaps a more appropriate tool with which to gauge negative and positive reactions to infertility. Using the Fertility Problem Inventory to measure perceived infertility-related stress, Folkman and Lazarus revealed differences in the number and type of strategies employed by men and women to cope with their infertility [27,53,58–60]. Peterson and colleagues found that women experienced higher levels of distress during IVF than men and, as a result, used more self-coping strategies [53,61].

Where qualitative studies have been used, it has been reported that couples sometimes found it necessary to seek professional intervention to help heal the damage that had been done to their sex lives as a consequence of their infertility [54], or that they should have sought help, but did not [11,12]. Whereas Cox and colleagues found that previous exposure to IVF treatment does not negatively affect psychological wellbeing during pregnancy [62], Hjelmstedt and colleagues suggest that IVF mothers are more anxious about losing the pregnancy [63]. Colpin and Soenen found parenting abilities of those who conceived through IVF did not differ from a control group [60], but others have reported a negative effect [29]. Interestingly, those who become parents as a result of infertility treatment through adoption or surrogacy do not feel the same as biological parents who conceive naturally, and perceive themselves to be both 'lesser' or 'other' [64,65]. Thus, sociological

evidence suggests that the 'technological fix' to infertility is not always the complete solution couples were seeking.

Other studies have examined the effects of infertility and its treatment on a couple's quality of life (QoL) and relationship. QoL is usually measured by means of standardized instruments, such as EUROQOL [66] and SRF36 [67], which attempt to examine the effect of (ill) health or symptoms on various aspects of life – social, physical and mental. Using such means, some studies report that infertile women are less healthy or have a poorer QoL than those who have children [68] and others that there is no difference [30,69,70]. Clearly, multiple parenthood (which is an additional limitation of fertility treatment) complicates the measurement of QoL [71], yet it is rarely investigated.

Since the 1970s, twin birth rates have been increasing worldwide, mainly as a result of ART [72]. More than one in four IVF pregnancies result in multiple births [73] compared with one in 25 natural conceptions [201]. Not only are women's bodies subjected to extreme drug regimes whose long-term effects are questionable [74], but they frequently agree to accept more than one embryo in the hope that it will increase their chances of conceiving [75]. Multiple birth is the single biggest risk to the health and welfare of children born as a result of IVF. As twin and higher-order pregnancies are more problematic [75,76] and children are more likely to be born 'damaged' [77], this choice seems likely to also take its toll on the families concerned. The available literature suggests that parenting twins or higher-order multiples may negatively affect the emotional wellbeing of the mother [73,78]. However, relatively few studies have examined long-term effects or compared parenting singletons and twins. In our opinion, the increased risk of multiple pregnancy from ART and long-term consequences place social limitations on couples who decide to have more than one embryo replaced.

Evidence regarding the effect of infertility on couples' relationships is varied, with some studies reporting that infertile patients have marital and sexual problems that endure after the end of treatment [11,45,56], that there was a significant negative impact on their marriage [28], and others that there is no difference in the long term, especially if they develop alternative life goals to parenthood [31]. Several papers have discussed the long-term effects on sexual [28,79] and marital relationships [11,28,56,80], and Berg and Wilson

report that marital adjustment deteriorated after the third year of unsuccessful treatment [81]. Holter and colleagues [56] and Hammarberg and colleagues [30] found that, after treatment follow-up, those who conceived were less depressed and more positive about their relationship. Domar and colleagues reported that where infertile women participated in cognitive behavioral therapy, they experienced less psychological distress overall [45]. Those who moved on to consider adoption or donor insemination (DI) were more optimistic and appeared to resume normal marital relations when ‘founding a family’ by alternate means [82]. Clearly, some research instruments may be too crude to pick up the subtle differences in the relationships of those with and without children or the profound effect that parenthood can have on QoL.

### **New reproductive technologies**

As long ago as the 1980s, feminist writers were complaining that infertile couples, and particularly women, were being treated as guinea pigs by the (sometimes well-intentioned) medical profession and drug companies who managed their treatment [83]. In our opinion, little has changed since then, except that the opportunities for exploitation have increased as new technologies offering ‘hope against the odds’ have become available in Western countries. More recent advances in reproductive technology have ethical as well as social and psychological limitations for new parents and their children [62].

Where it is enacted, legislation removing the anonymity of gamete donors has resulted in drastic shortages of gametes, sometimes forcing infertile couples to seek treatment abroad or search the internet where less rigorous safety standards exist [40]. The UK also forbids payment beyond ‘reasonable expenses’ for egg donors, resulting in delays, often of 1–2 years, for treatment. In some countries, there has been a proliferation of private organizations that put donors and recipients in contact for financial reward [84]. Even in the USA, where young egg donors are paid to donate either anonymously or ‘known’ to the recipient, the infertile may benefit only as a result of exploiting poorer women. In the USA, donor websites appear to be cash-driven, allowing recipients to choose their optimal donor from a list.

### **Research linked to treatment**

Most clinics in Western countries operate in the context of ongoing research aimed at developing and improving diagnostic and therapeutic

techniques to help childless couples achieve parenthood. Couples receiving infertility treatment, particularly IVE, may be asked to participate in various trials and studies that may further exacerbate emotional distress. Studies show that many couples participate in research because of a desire to help others or to give something back [12], but there is also evidence that they do not understand the terminology [85], are uncomfortable with concepts such as ‘randomization’ [86] and may feel pressured into giving consent. There is also evidence that infertile women may participate in research for its ‘therapeutic’ effect [87], supporting Greil’s theory that ART exacerbates emotional distress [44].

Research embedded in reproductive medicine has led to scientific advances in ART offering not only the chance of genetic inheritance (in cases of severe male-factor infertility), but eradication of certain genetic diseases and, more recently, the possibility of cures for debilitating conditions. Therefore, the boundaries of fertility treatments, in particular IVE, which offer hope for childless couples, have become inextricably linked with potentially ‘life-saving’ technologies derived from the procedure itself. The advances of SCR have become embedded in, and dependent upon, fertility practices [88], possibly adding to the psychological burden carried by couples and, in our view, requiring that limitations be placed on those responsible for recruiting couples to such research.

### **Pre-implantation diagnosis**

Infertile couples, who are often characterized as ‘desperate’, are willing to endure extremely invasive treatment [74], such as IVE, ICSI and PGD, and take risks with their health that those conceiving naturally might not countenance. The recent development of more reliable techniques for examining embryos to determine sex-linked or genetic defects potentially offers prospective parents (who are known carriers of a genetically inherited disease) an increased chance of having ‘the child they desire’. PGD is a technique used to biopsy and analyze a single cell from an embryo created through IVF to select those unaffected by a mutation or chromosomal abnormality associated with serious illness [89]. While this procedure offers the potential for life without suffering, it also invites debate regarding the limitations and ethics of selecting certain embryos and discarding others [90].

More contentious has been the possible use of PGD for selecting the sex of a child in order to ‘balance’ a family [90] or ‘replace’ a deceased child. In the UK, the HFEA has published the findings of a wide-ranging review of sex-selection regulation and technology, including public opinion. Sex selection for social reasons was largely viewed unfavorably as it would not benefit families or society [91]. By contrast, sex selection remains legal for social reasons in the USA and certain parts of Europe. Yet, this ‘advance’ carries moral implications for the potential parents whose views about the embryos discarded during PGD have not been widely studied, although Parry has showed a difference in perceptions between parents and scientists [88].

### Stem cell research

Couples undergoing IVF in the majority of the European member states are frequently asked to consider donating their unused (poor grade) or ‘spare’ embryos [92,93] for embryonic SCR (eSCR). Within the USA, eSCR has been slowed by political opposition and is limited to a small number of cell lines that qualify for federal funding. Such innovative health technologies, including therapeutic cloning, are thought to have the potential to diagnose, treat and possibly even prevent disease [94]. Much current debate focuses on whether other sources of stem cells, such as blood from the umbilical cord removed at birth, might obviate the need to destroy embryos [95,96]. However, the scientific consensus so far is that embryos remain the best research resource [92].

For the couples concerned, eSCR raises important ethical issues and anxieties regarding the direction of scientific and medical research [88]. Additional information and requirements to consent may add to the distress infertile couples face during the course of their IVF treatment and further reduce their sense of control [97]. An early study by Miller-Campbell and colleagues demonstrated that the more control women perceived they had over their infertility and treatment, the less depressed they were [98]. McMahon and colleagues reported that couples donating ‘spare’ embryos for eSCR were motivated by their desire to help infertile couples, and/or to advance scientific knowledge [99]. Nevertheless, several papers have highlighted embryos being viewed as ‘a potential child’ and couples perceiving a lack of control over the type of research to be carried out [88,99,100].

Researchers in Edinburgh (Scotland, UK) found that many did not have spare embryos to donate and what the scientists considered to be spare was intertwined with the suitability of an embryo for reproduction [88]. Stem cell lines may be derived from IVF treatment cycles that do not result in pregnancies, potentially adding to donors’ distress. Thus, the request to donate precious embryos for eSCR may involve reflection on very personal feelings related to the pain of infertility, the struggle to conceive and the meaning invested in the embryos, which are viewed as potential and highly sought-after children [88,99].

### Oncology & ART in Western countries

The improved long-term survival of young men and women treated for cancer has resulted in new techniques to preserve fertility. Where possible, men have had their sperm cryopreserved prior to treatment for later use [101]; however, poor results with freezing either ovarian tissue or eggs means that this is not usually an option for women [102]. Young women with cancer represent a group who not only have particular concerns regarding their future fertility and the possibility of a premature menopause [102], but the additional psychological upheaval of coming to terms with their own mortality. However, the risk of reseeding cancer by ovarian transplantation imposes a limitation on this promising treatment [101]. Similarly, although ICSI affords some infertile men – who might previously have been offered only donor sperm – the chance of their own genetic offspring, it has its limitations. There is still concern about the possible transmission of foreign genetic material, the use of immature germ cells and the association between genetic disorders, and some forms of male infertility [103].

### Conclusion

This selective review serves as a reminder that infertility is a problem of global proportions. The literature suggests that psychological distress experienced as a result of infertility and/or its treatments is comparable between countries in the West and underdeveloped countries in sub-Saharan Africa. Although cultural views and expectations have certain similarities, the social exclusion and treatment of childless women in sub-Saharan Africa is certainly worse. In the West, reproductive research has resulted in technological advances that have improved women’s chances of conception. They have also created a

society with enhanced expectations and possibly result in an increasingly 'willing but susceptible audience for overly optimistic practices' [28]. We feel that fertility specialists may have pushed the boundaries of what was previously acceptable practice to limits that are potentially unacceptable. The clinical application of fertility treatment is a powerful tool, but professionals and researchers should ensure that the technology is used to enhance, rather than limit, individual freedom, welfare and choice in vulnerable infertile couples. What is needed now is thorough consideration of the cultural differences worldwide that undoubtedly impose a limited view on the possibilities for childless couples who, as individuals, appear to be at the mercy of societal opinion and policy.

### Future perspective

Research into infertility and potential cures for debilitating diseases seems likely to rely increasingly on technological developments. Techniques such as IVF and ICSI will be refined, producing greater success rates combined with fewer multiple pregnancies. However, it is unlikely that these advances will be available to all but the wealthy few in developed countries. Meanwhile, the use of frozen and discarded embryos to develop stem cell lines, with the potential for overcoming many debilitating and relentlessly progressive diseases, such as Parkinson's and motor neurone disease, is likely to continue. In the UK and many parts of Western Europe, a generously funded public initiative looks set to be dependent on a 'low priority' fertility service. Inevitably, scientists will have to work more closely with regulatory authorities in the future and gain public acceptance for more controversial advances in science. Parthenogenesis, which literally means 'virgin conception' and which involves neither fertilization with sperm nor cloning, is one example. This ethically challenging research will result in 'hybrid' embryos, leaving scientists wide open to criticism from pro-life groups. Couples who may or may not have been successful and who have often self-funded their IVF treatment will continue to be asked to donate 'spare' embryos for such life-saving research. It is unlikely that funds will be available to help such couples adjust to infertility and cope with their loss, although the internet and voluntary groups may increasingly fill this void in the future.

### Executive summary

- Infertility is a stressful life event with short- and long-term implications for the social relationships and psychological wellbeing of those affected.
- Few men and women receive help in coming to terms with remaining childless or finding alternative sources of self esteem or satisfaction, the consequences of which are worse in developing countries.
- Many barriers – financial, physical and legislative – remain, preventing couples in various parts of the world from accessing effective treatments, such as *in vitro* fertilization and intracytoplasmic sperm injection.
- New advances in fertility research, such as pre-implantation genetic diagnosis and oocyte or ovarian tissue freezing, may have helped some of those suffering inheritable diseases or cancer to become parents. However, they may also have falsely raised the hopes of others, and added to any trauma experienced by those using assisted reproduction techniques.

### Bibliography

1. Karinen L, Pouta A, Hartikainen AL *et al.*: Association between *Chlamydia trachomatis* antibodies and subfertility in the Northern Finland Birth Cohort 1966 (NFBC 1966), at the age of 31 years. *Epidemiol. Infect.* 132(5), 977–984 (2004).
2. Nachtigall RD: International disparities in access to infertility services. *Fertil. Steril.* 4, 871–875 (2006).
3. Goto A, Yasumura S, Yabe J, Reich MR: Addressing Japan's fertility decline: influences of unintended pregnancy on child rearing. *Reprod. Health Matters* 14(27), 191–200 (2006).
4. ESHRE Capri Workshop Group: Social determinants of human reproduction. *Hum. Reprod.* 16(7), 1518–1526 (2001).
5. Panagopoulou E, Vedhara K, Gaintarzi C, Tarlatzis B: Emotionally expressive coping reduces pregnancy rates in patients undergoing *in vitro* fertilization. *Fertil. Steril.* 86, 672–677 (2007).
6. Hull M, Glazener C, Kelly N *et al.*: Population study of causes, treatment and outcome of infertility. *BMJ* 291, 1693–1697 (1985).
7. Editorial: Cheap IVF needed. *Nature* 442, 958 (2006).
8. Liu J, Larsen U, Wyshak G: Prevalence of primary infertility in China: in-depth analysis of infertility differentials in three minority province/autonomous regions. *J. Biosoc. Sci.* 37(1), 55–74 (2005).
9. Lunenfeld B, Van Steirteghem A, Bertarelli Foundation: Infertility in the third millennium: implications for the individual, family and society: condensed meeting report from the Bertarelli Foundation's second global conference. *Hum. Reprod. Update* 10, 317–326 (2004).
10. Al-Inany H: Female infertility. *BMJ Clin. Evid.* 15, 2465–2487 (2006).
11. Daniluk JC: Reconstructing their lives: a longitudinal, qualitative analysis of the transition to biological childlessness for infertile couples. *Couns. Dev.* 79, 439–449 (2005).
12. Peddie VL, van Teijlingen E, Bhattacharya S: A qualitative study of women's decision-making at the end of IVF treatment. *Hum. Reprod.* 20(7), 1944–1951 (2005).
13. Earle S, Letherby G: Whose choice is it anyway? Decision making, control and conception. *Hum. Fertil.* 5(2), 39–41 (2002).

14. Becker G: *Disrupted Lives: How People Create Meaning in a Chaotic World*. University of California Press, CA, USA (1997).
15. van Balen F, Gerrits T: Quality of infertility care in poor-resource areas and the introduction of new reproductive technologies. *Hum. Reprod.* 16(2), 215–219 (2001).
16. Daar AS, Merali Z: *Infertility and Social Suffering: The Case of ART in Developing Countries*. World Health Organisation (2001).
17. Pilcher H: IVF in Africa: fertility on a shoestring. *Nature* 442(7106), 975–977 (2006).
18. Aboulghar MA: The importance of fertility treatment in the developing world: commentary. *BJOG* 112 (9), 1174–1176 (2005).
19. Dyer SJ, Abrahams N, Hoffman M, van der Spuy ZM: ‘Men leave me as I cannot have children’: women’s experiences with involuntary childlessness. *Hum. Reprod.* 17(6), 1663–1668 (2002).
20. Favot I, Ngulala J, Mgalala Z, Klokke AH, Gumodoka B, Boerma JT: HIV infection and sexual behaviour among women with infertility in Tanzania: a hospital-based study. *Int. J. Epidemiol.* 26(2), 414–419 (1997).
21. Collins JA: Cost effectiveness of *in-vitro* fertilisation. *Semin. Reprod. Med.* 9, 279–289 (2002).
22. Whiteford LM, Gonzalez L: Stigma: the hidden burden of infertility. *Soc. Sci. Med.* 40(1), 27–36 (1995).
23. Woollett A: From ‘inside/out’ to ‘outside/in’ *Fem. Psychol.* 6, 74–78 (1996).
24. Park K: Stigma management among the voluntarily childless. *Sociol. Perspect.* 5, 21–45 (2002).
25. Mueller K, Yoder J: Stigmatization of non-normative family size status. *Sex Roles* 41, 901–909 (1999).
26. van der Steeg JW, Steures P, Eijkemans MJ *et al.*: Pregnancy is predictable: a large-scale prospective external validation of the prediction of spontaneous pregnancy in subfertile couples. *Hum. Reprod.* 22(2), 536–542 (2006).
27. Hjelmstedt A, Andersson L, Skoog-Svanberg A, Bergh T, Boivin J, Collins A: Gender differences in psychological reactions to infertility among couples seeking IVF- and ICSI-treatment. *Acta Obstet. Gynecol. Scand.* 78(1), 42–48 (1999).
28. Leiblum SR, Aviv A, Hamer R: Life after infertility treatment: a long-term investigation of marital and sexual functioning. *Hum. Reprod.* 13, 3569–3574 (1998).
29. Eugster A, Vingerhoets AJ: Psychological aspects of *in vitro* fertilization: a review. *Soc. Sci. Med.* 48(5), 575–589 (1999).
30. Hammarberg K, Astbury J, Baker H: Women’s experience of IVF: a follow-up study. *Hum. Reprod.* 16(2), 374–383 (2001).
31. Verhaak CM, Smeenk JM, Evers AW, Kremer JA, Kraaijaat FW, Braat DD: Women’s emotional adjustment to IVF: a systematic review of 25 years of research. *Hum. Reprod. Update* 13, 27–36 (2007).
32. Newton R, Hearn MT, Yuzpe AA: Psychological assessment and follow-up after *in vitro* fertilisation: assessing the impact of failure. *Fertil. Steril.* 54(5), 879–886 (1990).
33. Franklin S: Deconstructing ‘desperateness’: the social construction of infertility in popular representations of new reproductive technologies. In: *The New Reproductive Technologies*. McNeil M, Varcoe I, Yearley S (Eds). Macmillan, London, UK 29 (1990).
34. Becker G: *Healing the Infertile Family: Strengthening Your Relationship in the Search for Parenthood*. University of California press, CA, USA (1997).
35. de Lacey S: IVF as lottery or investment: contesting metaphors in discourses of infertility. *Nurs. Inq.* 9(1), 43–51 (2002).
36. Allan HA: ‘Good enough’ nurse: supporting patients in a fertility unit. *Nurs. Inq.* 8(1), 51–60 (2001).
37. Ashcroft A: The true cost of infertility. *Pract. Nurs.* 9(20), 34–36 (1998).
38. Collins JA, Burrows EA, Willan A *et al.*: Occupation and the clinical characteristics of infertile couples. *Can. J. Public Health* 85(1), 28–32 (2004).
39. Fenton RA: Catholic doctrine versus women’s rights: the new Italian law on assisted reproduction. *Med. Law Rev.* 14(1), 73–107 (2006).
40. Robertson JA: Protecting embryos and burdening women: assisted reproduction in Italy. *Hum. Reprod.* 19(8), 1693–1696 (2004).
41. Heng BC. ‘Reproductive tourism’: should locally registered fertility doctors be held accountable for channelling patients to foreign medical establishments? *Hum. Reprod.* 21(3), 840–842 (2006).
42. Spar D: Reproductive tourism and the regulatory map. *N. Engl. J. Med.* 352(6), 531–533 (2005).
43. Ozkan M, Baysal B: Emotional distress of infertile women in Turkey. *Clin. Exp. Obstet. Gynecol.* 33(1), 44–46 (2006).
44. Greil AL: Infertility and psychological distress: a critical review of the literature. *Soc. Sci. Med.* 45(11), 1679–1704 (1997).
45. Domar A, Clapp D, Slawsby EA *et al.*: Impact of group psychological interventions of pregnancy rates in infertile women. *Fertil. Steril.* 73, 805–811 (2000).
46. Meller W, Burns LH, Crow S, Grambsch P: Major depression in unexplained infertility. *J. Psychosom. Obstet. Gynaecol.* 23(1), 27–30 (2002).
47. Baram D, Tourtelot E, Muechler E, Hang KE: Psychological adjustment following unsuccessful *in-vitro* fertilisation. *J. Psychosom. Obstet. Gynaecol.* 9, 181–190 (1988).
48. Möller A, Fällström K: Psychological consequences of infertility: a longitudinal study. *J. Psychosom. Obstet. Gynecol.* 2, 27–45 (1991).
49. Chen TH, Chang SP, Tsai CF, Juang KD: Prevalence of depressive and anxiety disorders in an assisted reproductive technique clinic. *Hum. Reprod.* 19(10), 2313–2318 (2004).
50. Souter VL, Hopton JL, Penney GC, Templeton A: Survey of psychological health in women with infertility. *J. Psychosom. Obstet. Gynaecol.* 23(1), 41–49 (2002).
51. Kowalcek I, Wihstutz N, Buhrow G, Diedrich K: Coping with male infertility. Gender differences. *Arch. Gynecol. Obstet.* 265(3), 131–136 (2001).
52. Edelmann RJ, Connolly KJ: Gender differences in response to infertility and infertility investigations: real or illusory. *Br. J. Health Psychol.* 5, 365–375 (2000).
53. Peterson BD, Newton C, Rosen KH, Skaggs GE: Gender differences in how men and women who are referred for IVF cope with infertility stress. *Hum. Reprod.* 21(9), 2443–2449 (2006).
54. Boivin J, Andersson L, Skoog-Svanberg A, Hjelmstedt A, Collins A, Bergh T: Psychological reactions during *in-vitro* fertilization: similar response pattern in husbands and wives. *Hum. Reprod.* 13(11), 3262–3267 (1998).
55. Filetto JN, Makuch MY: Long-term follow-up of women and men after unsuccessful IVF. *Reprod. Biomed. Online* 11(4), 458–463 (2005).
56. Holter H, Anderheim L, Bergh C, Moller A: First IVF treatment–short-term impact on psychological well-being and the marital relationship. *Hum. Reprod.* 21(12), 3295–3302 (2006).



57. Newton CR, Sherrard W, Glavac I: The fertility problem inventory: measuring perceived infertility related stress. *Fertil. Steril.* 72(1), 54–62 (1999).
58. Folkman S, Lazarus RS, Dunkel-Schetter C *et al.*: Dynamics of a stressful encounter: cognitive appraisal, coping and encounter outcomes. *J. Pers. Soc. Psychol.* 50, 992–1003 (1986).
59. Hsu YL, Kuo BJ: Evaluations of emotional reactions and coping behaviors as well as correlated factors for infertile couples receiving assisted reproductive technologies. *J. Nurs. Res.* 10(4), 291–302 (2002).
60. Colpin H, Soenen S: Parenting and psychosocial development of IVF children: a follow-up study. *Hum. Reprod.* 17(4), 1116–1123 (2002).
61. Peterson BD, Newton C, Rosen KH, Schulman RS: Coping processes of couples experiencing infertility. *Fam. Relat.* 55, 227–239 (2006).
62. Cox SJ, Glazebrook C, Sheard C, Ndukwe G, Oates M: Maternal self-esteem after successful treatment for infertility. *Fertil. Steril.* 85(1), 84–89 (2006).
63. Hjelmstedt A, Widstrom AM, Wramsby H, Collins A: Emotional adaptation following successful *in vitro* fertilization. *Fertil. Steril.* 81(5), 1254–1264 (2004).
64. Letherby G: Other than mother and mothers as others: the experience of motherhood and non-motherhood in relation to ‘infertility’ and ‘involuntary childlessness’. *Womens Stud. Int. Forum* 22, 359–372 (1999).
65. Ross E: The gift of a child. *Reprod. Health Matters* 7, 65–68 (1999).
66. Euroqol Group: EuroQol – a new facility for the measurement of health-related quality of life. *Health Policy* 16(3), 199–208 (1990).
67. Ware J, Snow G, Kosinski M *et al.*: *SF-36 Health Survey Manual and Interpretation Guide*. New England Medical Centre, Health Institute Boston, MA, USA (1993).
68. El-Messidi A, Al-Fozan H, Lin Tan S, Farag R, Tulandi T: Effects of repeated treatment failure on the quality of life of couples with infertility. *J. Obstet. Gynaecol. Can.* 26(4), 333–336 (2004).
69. Ragni G, Allegra A, Anserini P *et al.*: The 2004 Italian legislation regulating assisted reproduction technology: a multicentre survey on the results of IVF cycles. *Hum. Reprod.* 20(8), 2224–2228 (2005).
70. Bringhentti F, Martinelli F, Ardeni R, La Sala GB: Psychological adjustment of infertile women entering IVF treatment: differentiating aspects and influencing factors. *Acta Obstet. Gynecol. Scand.* 76(5), 431–437 (1997).
71. Ellison MA, Hall JE: Social stigma and compounded losses: quality-of-life issues for multiple-birth families. *Fertil. Steril.* 80(2), 405–414 (2003).
72. Pinborg A: IVF/ICSI twin pregnancies: risks and prevention. *Hum. Reprod. Update* 11, 575–593 (2005).
73. Glazebrook C, Sheard C, Cox S, Oates M, Ndukwe G: Parenting stress in first-time mothers of twins and triplets conceived after *in vitro* fertilization. *Fertil. Steril.* 81(3), 505–511 (2004).
74. Crowe C: Whose mind over matter? Women, *in-vitro* fertilisation and the development of scientific knowledge. In: *The New Reproductive Technologies*. McNeil M, Varco I, Yearly S (Eds). Macmillan, London, UK (1990).
75. Thurin A, Hausken J, Hillensjo T *et al.*: Elective single-embryo transfer versus double-embryo transfer in *in vitro* fertilization. *N. Engl. J. Med.* 351(23), 2392–2402 (2004).
76. Bergh T, Ericson A, Hillensjo T, Nygren KG, Wennerholm UB: Deliveries and children born after *in-vitro* fertilisation in Sweden 1982–95, a retrospective cohort study. *Lancet* 354(9190), 1579–1585 (1999).
77. Yokoyama Y, Shimizu T, HayaKawa K: Incidence of handicaps in multiple births and associated factors. *Acta Genet. Med. Gemellol.* 44, 81–91 (1995).
78. Thorpe K, Golding J, MacGillivray I, Greenwood R: Comparison of prevalence of depression in mothers of twins and mothers of singletons. *BMJ* 302(6781), 875–878 (1991).
79. Beaupreire J, Jones M, Thiering P, Saunders D, Tennant C: Psychosocial adjustment to infertility and its treatment: male and female responses at different stages of IVF/ET treatment. *J. Psychosom. Res.* 38(3), 229–240 (1994).
80. Slade P, Emery J, Lieberman BA: A prospective, longitudinal study of emotions and relationships in *in-vitro* fertilisation treatment. *Hum. Reprod.* 12, 183–190 (1997).
81. Berg BJ, Wilson JF: Psychological functioning across stages of treatment for infertility. *J. Behav. Med.* 14(1), 11–26 (1991).
82. Peddie VL: *Decision-Making at the End of in-vitro Fertilisation*. Unpublished MSc Thesis. University of Aberdeen, UK (2004).
83. Arditti R, Klein R, Minden S: *Test Tube Women: What Future for Motherhood?* Pandora, London, UK (1984).
84. Craft I, Johnson MH, Sauer MV: Should egg donors be paid? *BMJ* 314(7091), 1400–1403 (1997).
85. Featherstone K, Donovan JL. “Why don’t they just tell me straight, why allocate it?” The struggle to make sense of participating in a randomised controlled trial. *Soc. Sci. Med.* 55(5), 709–719 (2002).
86. Porter M, Bhattacharya S: Investigation of staff and patients’ opinion of a proposed trial of single embryo transfer. *Hum. Reprod.* 20(9), 2523–2530 (2005).
87. Peddie VL, Porter M, Van Teijlingen E, Bhattacharya S: Research as a therapeutic experience? an investigation of women’s participation in research on ending IVF treatment. *Hum. Fertil.* 9(4), 231–238 (2006).
88. Parry S: (Re)constructing embryos in stem cell research: exploring the meaning of embryos for people involved in fertility treatments. *Soc. Sci. Med.* 62(10), 2349–2359 (2006).
89. Thomas C: Preimplantation genetic diagnosis: development and regulation. *Med. Law* 25(2), 365–378 (2006).
90. Grant VJ: Sex predetermination and the ethics of sex selection. *Hum. Reprod.* 21(7), 1659–1661 (2006).
91. Scully JL, Banks S, Shakespeare TW: Chance, choice and control: lay debate on prenatal social sex selection. *Soc. Sci. Med.* 63(1), 21–31 (2006).
92. Devolder K: Creating and sacrificing embryos for stem cells. *J. Med. Ethics* 31(6), 366–370 (2005).
93. Landry DW, Zucker HA: Embryonic death and the creation of human embryonic stem cells. *J. Clin. Invest.* 114(9), 1184–1186 (2004).
94. Williams C, Kitzinger J, Henderson L: Envisaging the embryo in stem cell research: rhetorical strategies and media reporting of the ethical debates. *Sociol. Health Illn.* 25(7), 793–814 (2003).
95. Fernandez CV, Gordon K, Van den Hof M, Taweel S, Baylis F: Knowledge and attitudes of pregnant women with regard to collection, testing and banking of cord blood stem cells. *CMAJ* 168(6), 695–698 (2003).

96. Sanberg PR, Willing AE, Garbuzova-Davis S *et al.* Umbilical cord blood-derived stem cells and brain repair. *Ann. NY Acad. Sci.* 1049, 67–83 (2005).
97. Rotter JB: Generalized expectancies for internal versus external control of reinforcement. *Psychol. Monogr.* 80(1), 1–28 (1966).
98. Miller-Campbell S, Dunkel-Schetter C, Peplau LA: Perceived control and adjustment to infertility among women undergoing *in-vitro* fertilisation. Cited in: Stanton AL, C Newton CR, Hearn MT, Yuzpe AA: Psychological assessment and follow-up after *in-vitro* fertilisation: assessing the impact of failure. *Fertil. Steril.* 54(5), 879–886 (1991).
99. McMahon CA, Gibson FL, Leslie GI, Saunders DM, Porter KA, Tennant CC: Embryo donation for medical research: attitudes and concerns of potential donors. *Hum. Reprod.* 18(4), 871–877 (2003).
100. Bjuresten K, Hovatta O: Donation of embryos for stem cell research – how many couples consent? *Hum. Reprod.* 18(6), 1353–1355 (2003).
101. Zapzalka DM, Redmon JB, Pryor JL: A survey of oncologists regarding sperm cryopreservation and assisted reproductive techniques for male cancer patients. *Cancer* 86(9), 1812–1817 (1999).
102. Lutchman Singh K, Davies M, Chatterjee R: Fertility in female cancer survivors: pathophysiology, preservation and the role of ovarian reserve testing. *Hum. Reprod. Update* 11, 69–89 (2005).
103. Tournaye H: ICSI: a technique too far? *Int. J. Androl.* 26(2), 63–69 (2003).

**Website**

201. HFEA Report of the Expert Group on Multiple Births after IVF  
[www.hfea.gov.uk/cps/rde/xbcr/SID3F57D79B-](http://www.hfea.gov.uk/cps/rde/xbcr/SID3F57D79B-)