

Experiences of IVF - from a patient perspective -

by

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All real living is meeting
Martin Buber

Experiences of IVF - from a patient perspective -

Herborg Holter

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Gothenburg, Sweden, 2014

The overall aim of this thesis was to assess the quality of life and quality of care from a patient perspective, in relation to IVF treatment. This was done by:

- assessing infertile couples' short-term emotional responses to their first IVF treatment, the relationship between partners at different stages of the first treatment, and differences/similarities between the reactions of men and women as to whether or not a pregnancy was achieved
- investigating whether a male infertility diagnosis had any influence on men's experience of infertility and its treatment, view of life, relationships, self-image and psychological well-being, when compared with men in couples where the diagnosis was female, mixed or unexplained infertility
- developing a validated instrument (QPP-IVF) for measuring patient-centered quality of care in an IVF-programme for both men and women
- investigating patient-centered quality of care during IVF treatments as evaluated by men and women

Method: *Papers I and II* were part of a prospective, longitudinal study carried out between 1999 and 2002 at the Reproductive Medicine Unit, Sahlgrenska University Hospital.

Men and women answered questionnaires on three occasions during their first treatment. The questionnaires consisted of personal questions, including relationships with partners and social aspects of infertility and treatment. In *Papers III and IV* women and men undergoing IVF treatment between September 2011 and May 2012 at the Reproductive Medicine Unit at Sahlgrenska University Hospital and Fertility Centre of Scandinavia answered the QPP-IVF questionnaire used to measure quality of care from a patient perspective, developed and validated in *Paper III*. The measurement consisted of two kinds of evaluations, the rating of perceived quality of care and the rating of the subjective importance of various aspects of treatment. The quality of care was evaluated in separate answers to the questionnaire by men and women, within two weeks after IVF treatment (*Paper IV*).

Results: *Paper I:* The women reported stronger emotional reactions to their infertility than their partners. The men, however, reacted with the same emotional pattern as their partners when pregnancy was not achieved. The majority reported that the relationship improved during treatment.

Paper II: Men with a male infertility diagnosis reacted in a similar way as men in couples where the diagnosis was female, mixed or unexplained infertility at the time of the first IVF/ICSI treatment cycle.

Paper III: The QPP-IVF instrument seemed to be a valid and reliable way of measuring quality of care from a patient's perspective, for both women and men. The final questionnaire consists of 43 items for women and 42 items for men divided into ten factors; "Pain relief and physical care", "Waiting time", "Care room characteristics", "Information during treatment", "Information after treatment", "Participation", "Responsibility/Continuity", "The staff's respect/commitment/empathy", "Atmosphere and environment", "Availability" and one single item measuring overall medical care.

Paper IV: Women valued most aspects of care as significantly more important than men. Men and women evaluated however the importance of the different care factors in a similar pattern.

General Conclusion: The results of these studies support the idea of similar response patterns in men and women concerning both quality of life in relation to IVF treatment, and the evaluation of quality of care during treatment. Despite women reporting stronger emotional reactions to their infertility and valuing the care aspects in fertility treatment more importantly than men, women and men reacted with similar emotions when pregnancy was not achieved and valued similar aspects of quality of care.

Keywords: infertility/IVF/quality of life/quality of care/relationship/gender differences/male factor/measurement instrument

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Svensk sammanfattning

Det övergripande syftet med avhandlingen var att mäta upplevelsen av livskvalitet och vårdkvalitet ur ett patientperspektiv i relation till in-vitro fertilisering (IVF).

Syfte: *Delarbete I:* att undersöka kvinnor och mäns upplevelser av barnlöshet relaterat till första IVF behandlingen utifrån psykologiska aspekter, behandlingens effekt på parrelationen, skillnader och likheter mellan kvinnor och män och relaterat till behandlingsresultat. *Delarbete II:* att undersöka om manlig infertilitetsdiagnos påverkar mäns upplevelse av infertilitet, synen på livet, parrelationen, självbild och psykologiskt välmående jämfört med män i par där infertiliteten är av kvinnlig eller oförklarlig orsak. *Delarbete III:* att utveckla och validera ett mätinstrument Kvalitet Ur Patientens Perspektiv (KUPP-IVF) för mätning av patientcentrerad vårdkvalitet för kvinnor och män i samband med IVF behandling. *Delarbete IV:* att undersöka om bedömning och upplevelse av patientcentrerad vårdkvalitet under IVF behandling skiljer sig mellan män och kvinnor.

Metoder: *Delarbete I och II* var del av en prospektiv, longitudinell studie som pågick mellan 1999 och 2002 på Reproduktionsmedicin, Sahlgrenska Universitetssjukhuset. Män och kvinnor besvarade frågeformulär om psykologiska effekter, effekter på parrelationen och sociala aspekter av infertilitet och behandling vid tre tillfällen under deras första IVF behandling. *Delarbete III och IV* pågick mellan september 2011 och maj 2012 på Reproduktionsmedicin, Sahlgrenska Universitetssjukhuset och Fertilitetscentrum Göteborg, Carlanderska sjukhuset. Män och kvinnor evaluerade patientcentrerad vårdkvalitet under IVF behandling genom att besvara den webbaserade KUPP-IVF enkäten inom två veckor efter IVF behandlingen.

Resultat: *Delarbete I:* Majoriteten av män och kvinnor rapporterade att deras relation förbättrades under behandlingen. De flesta uppgav heller inga svårare negativa psykologiska effekter av den första IVF behandlingen. Kvinnor rapporterade starkare emotionella effekter av infertiliteten och behandlingen än vad deras partners gjorde. Män reagerade dock med liknande emotionellt mönster som deras partner vid utebliven graviditet. *Delarbete II:* Män rapporterade generellt god psykisk hälsa innan första IVF/ICSI behandlingen inleddes oberoende av infertilitetsdiagnos. Män med manlig infertilitetsdiagnos rapporterade liknande upplevelse av infertilitet, behandling, relation med partner och psykologisk välbefinnande jämfört med män i par med kvinnlig, blandat manlig och kvinnlig eller oförklarad infertilitetsorsak. *Delarbete III:* Vi har utvecklat och validerat ett användbart instrument för att mäta patientupplevd vårdkvalitet för män och kvinnor. KUPP-IVF enkäten består av 43 frågor för kvinnor och 42 frågor för män indelat i tio faktorer: "Smärtlindring och fysisk omvårdnad", "Väntetid", "Vårdrumskaraktäristika", "Information under behandling", "Information efter behandling", "Delaktighet", "Ansvar/kontinuitet", "Personalens respekt/engagemang/empati", "Atmosfär och miljö", "Tillgänglighet" och en enskild övergripande fråga "Medicinsk vård". Varje enskild fråga i enkäten bedöms på två sätt; dels upplevd realitet som speglar den faktiska upplevelsen av aspekter av vårdkvalitet ("så här var det för mig") och dels subjektiv betydelse, d.v.s. hur viktigt olika vårdaspekter värderas ("så här betydelsefullt var det för mig"). *Delarbete IV:* Trots att kvinnor värderade den subjektiva betydelsen av de flesta vårdaspekter signifikant högre än män, graderade män och kvinnor vårdaspekternas betydelse i ett liknande mönster. Den faktiska upplevelsen av de olika vårdaspekterna var likartad mellan kvinnor och män.

Generell slutsats: Kvinnor rapporterade starkare emotionella reaktioner och värderade vårdaspekterna som mera betydelsefulla än män, men mönstret i upplevelsen av livskvalitet i relation till IVF-behandling och bedömning av vårdkvalitet under behandlingen var likartad för män och kvinnor.

List of papers

This thesis is based on the following papers, which will be referred to by their Roman numerals in the text:

- I. Holter H, Anderheim L, Bergh C, Möller A. **First IVF treatment – short-term impact on psychological well-being and the marital relationship.**
Human Reproduction 2006;21:3295-3302.
- II. Holter H, Anderheim L, Bergh C, Möller A. **The psychological influence of gender infertility diagnoses among men about to start IVF or ICSI treatment using their own sperm.**
Human Reproduction 2007;22:2559-2565.
- III. Holter H, Sandin-Bojö A-K, Gejervall A-L, Wikland M, Wilde-Larsson B, Bergh C. **Quality of care in an IVF programme from a patient's perspective: development of a validated instrument.**
Human Reproduction 2014; 29:534-547.
- IV. Holter H, Sandin-Bojö A-K, Gejervall A-L, Wikland M, Wilde-Larsson B, Bergh C. **Patient-centered quality of care in an IVF-programme evaluated by men and women.**
Manuscript.

Abbreviations

ART	Assisted Reproductive Technology
DET	Double Embryo Transfer
ESHRE	European Society for Human Reproduction and Embryology
ET	Embryo Transfer
EFA	Exploratory Factor Analysis
FertiQoL	the Fertility Quality of Life
FSH	Follicle-Stimulating Hormone
FPI	the Fertility Problem Inventory
GnRH	Gonadotrophin Releasing Hormone
HRQoL	Health Related Quality of Life
hCG	Human Chorionic Gonadotrophin
HTLV	Human T-Lymphotropic Virus
ICC	Intraclass Correlation Coefficient
ICMART	International Committee for the Monitoring of Art
ICSI	Intracytoplasmic Sperm Injection
IMAP	International Medical Advisory Panel
IPPF	International Planned Parenthood Federation
ISO	International Standards Organization
IUI	Intra Uterine Insemination
IVF	In Vitro Fertilization
KMO	Kaiser-Meyer- Olkin measure
NRHC	Nordic Reproductive Health Council
Q-IVF	National Quality Register for Assisted Reproduction, Sweden
QoL	Quality of Life
QPP	Quality from the Patient's Perspective
QPP-IVF	Quality from the Patient's Perspective of In Vitro Fertilisation
PCC	Patient Centred Care
PCQ-infertility	Patient-Centeredness Questionnaire on Infertility
PGWB	Psychological General Well-Being Index
PREM	Patient Reported Experience Measures
PROM	Patient Reported Outcome Measures
SET	Single Embryo Transfer

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Introduction

This thesis deals with quality of life and quality of care from patients' perspectives, with regard to IVF treatment. The study developed from having its focus on the quality of life of men and women during their first IVF treatment, into focusing on quality of care in IVF treatments, in the course of which an IVF-specific instrument for both men and women was developed and validated.

Infertility

Reproductive health as an aspect of general health is defined by the World Health Organization as: "Within the framework of WHO's definition of health as a state of complete physical, mental and social well-being, and not merely the absence of disease or infirmity, reproductive health addresses the reproductive processes, functions and system at all stages of life. Reproductive health, therefore, implies that people are able to have a responsible, satisfying and safe sex life and that they have the capability to reproduce and the freedom to decide if, when and how often to do so", (www.who.int/topics/reproductive_health/en/).

This statement implies that the ability to reproduce is an aspect of good health. According to the WHO, infertility is a disability (an impairment of function), and thus access to health care falls under the Convention on the Rights of Persons with Disability. Infertility in women was ranked the fifth highest serious global disability

among populations below the age of 60 (World Report on Disability 2011, www.who.int).

The definitions of infertility vary. WHO defines infertility as "a disease of the reproductive system defined by the failure to achieve a clinical pregnancy after 12 months or more of regular unprotected sexual intercourse" (Zegers-Hochschild *et al.*, 2009).

The International Planned Parenthood Federation's International Medical Advisory Panel states that *primary infertility* is failure to conceive after two years of frequent unprotected intercourse and *secondary infertility* is failure to conceive after two years of unprotected intercourse (in the absence of breastfeeding or postpartum amenorrhoea), in a woman who has previously been pregnant (IMAP, IPPF Medical Bulletin, 2006).

The global prevalence of primary infertility was about 2.5 percent and of secondary infertility as high as 24 percent according to the latest IPPF Medical Bulletin (2006), mostly owing to sexually transmitted diseases (STDs), infections following childbirth and unsafe abortions. The prevalence and causes of infertility vary from area to area. In industrialised countries an important consideration is the tendency toward reduced family size and delayed birth of the first child. In younger couples, especially in Sub-Saharan Africa, the dominant cause of infertility is sexually transmitted diseases (IMAP, IPPF Medical

Bulletin 2006). Rutstein and Shah (2004) found rates of infertility to vary considerably from country to country. In developing countries more than one-quarter of married women of reproductive age were infertile because of primary or secondary infertility, and in Sub-Saharan Africa the secondary infertility rate was over 30 percent. In a recent study (Mascarenhas *et al.*, 2012) when estimating levels and trends of infertility in 190 countries over the time period 1990 to 2010, the researchers found 1.9 percent of women aged 20 to 44 could be classed as primary infertile, and 10.5 percent of women could be classed as secondary infertile (infertility here defined as being unable to conceive within five years). The researchers found that the levels of infertility were similar in 1990 and 2010, with only a slight overall decrease in primary infertility and a modest overall increase in secondary infertility. The findings suggest that in 2010, an estimated 48.5 million couples worldwide were unable to have a child after five years. In a review of 25 population studies and according to WHO's definition of infertility as an inability to conceive after 12 months, Boivin *et al.* (2007) estimated that as many as 72.4 million women in the world were infertile, including about 40.5 million seeking medical treatment for infertility. The current prevalence of infertility (after at least 12 months) is estimated at 9 percent worldwide, a rate which is now quite similar between more and less developed countries (Boivin *et al.*, 2007; ESHRE ARTfact sheet, 2010).

Infertility can be attributable to male or female factors or both. According to ESHRE (ARTfact sheet, 2010) 20 to 30 percent of infertility is caused by physiological male factors, 20 to 35 percent by physiological

female factors and 25 to 40 percent by both male and female factors. In 10 to 20 percent of couples no cause is found. Besides physiological factors, lifestyle factors such as smoking, body-weight and stress can impair fertility. Increasing age in the female partner is a common explanation today. Causes of male infertility are: abnormal spermatogenesis, disorders of secretory function (eg. hypogonadotropic hypogonadism), genital tract obstruction and sexual and erectile dysfunction. Causes of female infertility are: ovulatory disorders, tubal occlusion due to pelvic inflammatory disease (PID), endometriosis, and cervical and uterine factors (IMAP, IPPF Medical Bulletin 2006). Some of these disorders can be treated using hormone therapy or microsurgery, while assisted reproductive technology (ART) has developed as a superior method of treatment for most infertility disorders. ART is defined as all reproductive methods that involve the handling of human gametes outside the body. This study only covers standard in vitro fertilization (IVF) and intracytoplasmic sperm injection (ICSI).

In Vitro Fertilization (IVF) and Intracytoplasmic Sperm Injection (ICSI)

After more than twenty years of preclinical research, the first IVF baby was born in 1978 in England (Steptoe and Edwards, 1978). In Scandinavia the first child was born in Gothenburg in 1982. IVF has become a common and effective treatment for infertility in industrial countries. The development of the intracytoplasmic sperm injection (ICSI) technique in the early 1990s (Palermo *et al.*, 1992) represented a major

step forward in enabling infertile men to father a biological child. Before the introduction of ICSI, the only way for couples with severe male infertility to become parents was treatment with donor insemination. However, in 1992 the first child was born after ICSI (Palermo *et al.*, 1992) and one year later the first child in Sweden was born with this technique in Gothenburg. While the standard IVF technique combines the sperm with the aspirated oocytes in dishes in the laboratory, the ICSI technique injects a single sperm into an oocyte. Currently, ICSI is the most common fertilization technique in the world accounting for around two-thirds of all treatments, while conventional IVF accounts for around one-third (ESHRE ARTfact sheet, 2010). In Sweden, ICSI and conventional IVF technique are used to a similar degree (National Quality Register for Assisted Reproduction, Sweden 2013).

The use of ART is rapidly increasing, and in the whole world it is estimated that around 5 million babies have been born after IVF/ICSI. Around 1.5 million ART cycles are performed each year worldwide, with an estimated 350,000 babies born as a result. Of all reported ART cycles, 55 percent are carried out in Europe (ESHRE ARTfact sheet, 2010).

IVF/ICSI treatments in Sweden

Since the first IVF baby was born in Sweden in 1982, the use of ART has developed from being quite a controversial and exclusive form of treatment to being a common and straightforward way of conceiving children. In Sweden, a total of about 50,000 children

have been born after IVF (Statistics Sweden, 2013). During 2011, 18,057 cycles of ART were started, using own or donated gametes and including fresh and frozen cycles, resulting in 3,931 live births (National Quality Register for Assisted Reproduction, Sweden 2013). Thus, 3.6 percent of all children born yearly in Sweden are IVF children (Statistics Sweden, 2011).

Of the sixteen IVF clinics in Sweden today, six are publicly and ten are privately financed. With some exceptions in certain municipalities in Sweden, most public clinics offer infertile couples three complete treatment cycles, including transfer of frozen embryos. Public infertility clinics in Sweden offer treatments for couples without children in their current relationships. Most public clinics treat couples if the women are not more than 40 years old.

Legislation, guidelines and registration in Sweden

According to Swedish legislation, ART can only be carried out if there is no risk of transmission of infections caused by HIV, HTLV I, HTLV II, hepatitis B, hepatitis C or syphilis to the women or the child in the fertilization process, and there is no risk that a pregnancy, an infection or another disease can pose a risk to the woman's or the child's life or health. The National Board of Health and Welfare recommend that the woman's age should be within the normal fertile range, and the man should not be too old to be able to take parental responsibility throughout the whole childhood (National Board of Health and Welfare, 2002). The recommendations are quite general concerning ART with the couples' own gametes, while there are more

detailed guidelines for sperm and egg donation. Treatment with sperm and egg donation can only be done after an examination of suitability in each case (National Board of Health and Welfare, 2002; 2006). The judgement should consider both the partner's and the woman's capacity and capability to function as parents throughout the child's childhood and assessments should include medical, psychological and social testing. If there are any concerns about the couple's ability to become satisfactory parents, further investigations by other relevant professionals should be done before treatment is allowed (National Board of Health and Welfare, 2006). It is usual for Swedish infertility clinics, both public and private, to follow these recommendations for all ART treatments.

Since 2007, all infertility clinics in Sweden report treatments and results to the National Quality Register for Assisted Reproduction in Sweden (Q-IVF). Cycle-based data from all IVF units in Sweden, public as well as private clinics, are collected in Q-IVF. Before 2007 two other IVF registries existed in Sweden. One registry collected aggregated cycle-based data from all IVF units in Sweden on a yearly basis. Another registry included identified data on all deliveries after IVF from 1982 to 2006. Both these registries were managed by the National Board of Health. The results of IVF have also been included in the Swedish Medical Birth Register (National Board of Health and Welfare) since 1991.

According to the European Union Tissue and Cell Directive all clinics performing ART must undergo accreditation (Directive, 2004)

and in Sweden most infertility clinics, both public and private, are certified according to ISO 9001:2000 or 9001:2008 guidelines.

Single embryo transfer (SET)

The main complication associated with IVF is the high risk of multiple pregnancies and multiple births, with high frequency of premature deliveries and low birth weight. The most important factor influencing the rate of multiple births is the number of embryos transferred. Sweden has been one of the leading countries in seeking a solution to this problem. In the early 1990s the multiple birth rate was about 35 percent, and to reduce this high rate the IVF clinics in Sweden voluntarily started to restrict the number of embryos transferred from three to two. In 1999 the use of single embryo transfer (SET) started on a small scale after the results of a pioneering study in Finland on elective single embryo transfer (Vilksa *et al.*, 1999), which reported that in selected cases similar pregnancy rates could be obtained with one as with two embryos. In 2003, in Sweden the number of embryos to be replaced was regulated by new guidelines from the National Board of Health and Welfare. SET was to be the normal routine, and only when the risk of multiple births was considered to be low, could two embryos be replaced (National Board of Health and Welfare 2002). The increase in SET became pronounced and between 1991 and 2011 multiple birth rates decreased from 35 to 5.3 percent when fresh embryos were replaced (National Board of Health and Welfare, 2007; National Quality Register for Assisted Reproduction, Sweden 2011).

In a randomized multi-centre study in Scandinavia, Thurin *et al.* (2004) found the cumulative live birth rate after one fresh and one frozen SET not to be substantially lower than for one fresh double embryo transfer (DET), while the number of multiple birth rates decreased dramatically, from 33 percent to 0.8 percent. An observational study based on the annual reports from all IVF clinics in Sweden to the National Board of Health and Welfare between 1991 and 2004 found delivery rates to be maintained while multiple birth rates decreased dramatically with the use of SET (Karlström and Bergh, 2007). The authors concluded that the results ought to encourage other countries to introduce SET more widely, in order to decrease the obstetric and neonatal risks for children born after IVF treatment. In 2008, the results of assisted reproductive technology in Europe showed that Sweden was the leading country in Europe in this field with 69.5 percent SET, and also the only country with zero triple embryo transfers (Ferraretti *et al.*, 2012). In the ESHRE ART-fact sheet (2010) it is stated that Sweden has the lowest multiple delivery rates in the world (5.6 percent), with 73.3 percent of all cycles being a single embryo transfer.

Obstetric outcome

Numerous publications have reported increased risks of perinatal mortality, preterm birth, low birth weight and congenital malformations in children born after IVF, when compared to children born after spontaneous conception (Bergh *et al.*, 1999; Helmerhorst *et al.*, 2004; Jackson *et al.*, 2004). Most of these increased risks are explained by the higher multiple birth rate,

but also IVF singletons are more likely to have increased rates of poor obstetric outcome than spontaneously conceived singletons (Jackson *et al.*, 2004; Helmerhorst *et al.*, 2004; Mc Donald *et al.*, 2009; Pandey *et al.*, 2012). These rates remain significantly higher after adjustment for relevant confounders. There is no explanation for these findings; both maternal characteristics and treatment-related variables have been discussed. Current evidence suggests that certain maternal characteristics, and aspects of IVF treatment itself, may be involved.

Quality of life

Quality of Life (QoL) in general

One of the first-known attempts to define quality of life comes from Aristotle (384-322 bc). In the book *Nicomachean Ethics* he wrote: “Both the multitude and persons of refinement conceive ‘the good life’ or ‘doing well’ to be the same thing as ‘being happy’.” But what constitutes happiness is a matter of dispute; some say one thing and some another, indeed very often the same man says different things at different times: when he falls sick then he thinks health is happiness, when he is poor, wealth.” This statement still carries the ring of truth. Because of its multi-dimensionality there is no common definition of QoL; it means different things to different people, and differs due to circumstances. The World Health Organization Quality of Life (WHOQOL) Group defines QoL as: “people’s perception of their position in life in the context of the culture and value systems in which they live in relation to their objectives, expectations, standards and concerns” (WHOQOL group, 1994).

Definitions or indicators of QoL are associated with personal/psychological well-being and are measured with subjective indicators which include emotional functioning (such as absence of anxiety and depression), social functioning, self-esteem, morale, sense of coherence, physical functioning and absence of physical health problems (Bowling, 2005; Fayers and Machin, 2007).

The theoretical models of QoL are many and various. Different models are described in the literature (Bowling, 2001; 2005; Fayers and Machin, 2007) such as the *expectation* model of Calman (1984) which measures QoL as the difference between the individual's aims and goals in life, and how he or she actually perceives life in relation to hopes and expectations achieved. The *need* model relates QoL to the ability and capacity to satisfy deficiency needs (hunger, thirst, loneliness, security) and growth needs (learning, mastery and self-actualization). These are derived from Maslow's hierarchy of human needs (1954; 1962). Another related model is the *reintegration to normal living* model. Reintegration means the ability to do what one has to do or wants to do, but it does not mean being free of disease or symptoms of illness. A different model derived from decision-making theory is *patient-preference* measures, which uses *weighting* to reflect the importance patients give to specific dimensions, thereby ranking different values. The *existential* model means that QoL is dependent on the individual's value system and that a positive outlook on life can result in a high quality of life, regardless of the medical conditions. Fayers and Machin (2007) considered the different aspects of QoL, the different models and different views on how to measure QoL, as reflecting issues that are of

fundamental importance to patients' well-being. All these different concepts should therefore be considered and quantified.

In 1948, WHO defined health as "a state of complete physical, mental and social well-being, and not merely the absence of disease" and this statement included the three dimensions - physical, mental and social well-being in the context of health. Health is one of the most important dimensions in the overall QoL and the concept "health-related quality of life" (HRQoL) is based on a multi-dimensional perspective of health associated with physical, psychological, and social well-being according to the definition of WHO. The HRQoL concept includes health as well as quality of life, but HRQoL is like QoL in that it is a formally undefined term with varying aspects depending on the issue studied. Bowling (2001, page 6) defines HRQoL as ".. optimum levels of mental, physical, role (e.g. work, parent, career, etc.) and social functioning, including relationships, and perceptions of health, fitness, life satisfaction and well-being. It should also include some assessment of the patient's level of satisfaction with treatment, outcome and health status and with future prospects".

QoL related to infertility and treatment

"One of the important challenges an infertile couple faces is learning how to manage the infertility in relation to oneself as in relation with the partner and in the different social arenas" (Schmidt, 2006, p.6).

Psychological factors associated with infertility are well documented. Infertility has been ranked as one of the greatest stressors in life, comparable with divorce and death in the family (Baram *et al.*, 1988), and with somatic diseases such as cancer and

HIV (Domar *et al.*, 1993). Freeman *et al.*, (1985) found that half of the women and 15 percent of the men they studied reported infertility as the most upsetting experience in their lives. Infertility has been described in terms of “loss” - the loss of genetic continuity, the loss of the experience of pregnancy and birth, the loss of the identity as a parent, the loss of a “real” family and often the loss of the “ticket” to many social activities (Wirthberg, 1992).

Crisis is defined as a state where previous experience and learned patterns of behaviour are not sufficient for understanding and coping with the current situation (Caplan, 1964). Caplan identified four main phases of a crisis: shock (e.g. denial), reaction (e.g. anger, depression), adaptation (e.g. acceptance) and resolution (planning of solution). In a general traumatic crisis the reactive phase is usually about six weeks. *The crisis of infertility* follows the pattern of a general crisis situation, but the infertility crisis also differs from a general crisis in that it is seldom abrupt and total, but instead prolonged and repeated. An infertility crisis can be defined as a prolonged and repeated life crisis (Lalos, 1999), as a life-situation (Möller, 1985) or a life-grief (Johansson *et al.*, 2005) and lead to a state of prolonged chronic crisis (Lalos, 1986), associated with risk of depression, feelings of loss, guilt, isolation and meaninglessness, and sexual and marital problems (Möller and Fällström, 1991; Wirthberg, 1992; Mahlstedt, 1994). Möller and Fällström (1991) described the infertility crisis as a threat to the individual’s identity in three dimensions; affinity – abandonment, meaningfulness – meaninglessness, and a positive self-picture - self-rejection.

Domar *et al.* (1992) found infertile women to be significantly more depressed than a control group of fertile women, and Baram *et al.* (1988) found that 94 percent of the women, and 60 percent of the men in the 86 couples studied, reported somatic and psychological symptoms of depression and anxiety following IVF failure. However, it was also discovered that emotional adjustment got better as time passed after the last treatment cycle. More recent studies also report significant differences between involuntarily childless men and women and successfully treated couples or fertile control groups. Johansson *et al.* (2010) found both men and women reporting significantly lower QoL compared to successfully-treated couples in a follow up study some years after IVF treatment. Klemetti *et al.* (2010) found that infertile men had a significantly poorer quality of life compared to fertile men, but concluded also that on average infertile women and men reported only marginally poorer levels of psychological health and subjective well-being. One problem when studying the emotional impact of infertility is that almost all studies only investigate people seeking help or treatment for infertility. Thus there is little knowledge about the impact of infertility on the QoL in the larger population of infertile people, which includes people who do not seek help for their condition.

In a review of infertility and psychological distress, Greil (1997) concluded that in spite of all the significant differences observed in standardized measures of general psychological distress in infertile groups when compared to fertile groups, the results for infertile people still remained within the normal range. He also pointed out the differ-

ence in results in studies between those using control groups and general measures of psychological distress, and descriptive studies using measurements specifically designed to measure infertility distress. The latter type of study was shown to be much more sensitive. While the use of control groups leads to the question of whether infertile people are more or less distressed than others, the descriptive studies assert that infertility is a difficult situation to live in and tries to characterize the *situation* of being infertile without making general comparisons.

QoL in relation to life-long infertility

There are few studies dealing with the long-term effects of infertility and treatment, partly because most methods of infertility treatment are relatively new. Wirtberg *et al.* (2007) have interviewed 14 Swedish women, still childless, 20 years after unsuccessful infertility treatment with tubal surgery. The women reported childlessness to be the major negative factor in their personal, interpersonal, sexual and social lives. The issue of not having grandchildren was raised by all the women and the effects of childlessness increased in this phase of life. Not becoming a grandparent activated feelings of loss and isolation. It seems that there are two periods to the infertility crises, not becoming a parent and not becoming a grandparent, and the authors propose the introduction of the concept “grandchildlessness.” In spite of unsuccessful treatment, most of the women remembered the treatment as an important and positive period in life, although all but one expressed the desire for “someone to talk to.”

In a follow-up study 20 years after ended treatment, Sydsjö *et al.* (2011) found

relationships in couples to be generally good, both in couples who had become parents and couples who were still childless. Childless couples had higher positive levels of communication and the authors propose that this is because the challenge of childlessness trained the couples in communication. Men in the childless group also scored higher on “conflict resolution”. Interestingly 90.8 percent of all couples who had been treated 20 years earlier had become parents biologically or via adoption, and some other long-term studies also found the vast majority of people in this group lived with children in one or another way (Sundby *et al.*, 2007; Johansson *et al.*, 2010). A common problem reported with all long-term follow-up studies is the high dropout rate, which limits the generalizability of the results. In a ten year follow-up study after infertility treatments Wischman *et al.*, 2012 found quality of life to be high both in childless couples and couples who had become parents after fertility treatments. This study suggests further research is necessary into the problem of non-responders, suggesting one solution to be personal interviews of representative samples in prospective studies, instead of the use of anonymous questionnaires.

QoL specifically related to treatment

When investigating psychological reactions related to treatment, both past and recent studies in general find most people seeking IVF treatment to be well-adjusted (Connolly *et al.*, 1992; 1993; Edelman *et al.*, 1994a; Wishman *et al.*, 2001; Anderheim *et al.*, 2005) also compared with fertile groups (Hearn *et al.*, 1987; Edelman *et al.*, 1994a; Wishman *et al.*, 2001). Bringhenti *et al.* (1997) suggested that the infertile women’s higher level of anxiety compared to a control

group of mothers was a situational response to the stress of the treatment.

There are many factors related to the experience of treatment, but most studies focus on the psychological stress associated with IVF treatments. Boivin and Takefman (1995) investigated the impact of the IVF treatment process on emotional, physical and relationship variables by comparing 20 women's daily monitoring of a treatment cycle, and a menstrual cycle without treatment. They found the impact of stress (nervousness, pessimism, infertility stress and frustration) as a reaction to IVF treatment itself to be only a part of the treatment experience. Treatment stimulated optimism as there was a chance to become pregnant. Health, partner relationships and social networks were also affected by treatment, and the difference in stress levels between women in a treatment cycle and in a normal menstruation cycle without treatment, was not salient.

In a systematic review of how women adjust emotionally to the various phases of IVF treatments Verhaak *et al.* (2007a) postulated IVF to be a primary multi-dimensional stressor with the treatment itself likely to evoke anxiety. The unpredictable outcome of the treatment was regarded as another major stress factor likely to evoke feelings of depression. The review covered four phases of treatment with regard to the patients' emotional responses to IVF in terms of anxiety, depression and general distress. These emotions were registered before the start of the treatment, within one treatment cycle, before and after treatment cycles (comparing differences) and after abandoning treatment. Before the start of the treatment IVF patients in general did not

differ from norm groups concerning depression levels, whereas levels of anxiety differed between studies; some studies reported elevated anxiety levels in patients, other reported no difference compared to norm groups. Within one treatment cycle, oocyte aspiration and the pregnancy test were found to be the most stressful stages of the IVF cycle. When comparing differences in pre- and post-treatment emotional adjustment, the most consistent finding reported by three studies was an increase in depression after one or more unsuccessful treatment cycles. Concerning anxiety after unsuccessful treatment, the results differed. The authors call for longitudinal studies with regard to long term post-treatment emotional adjustment. Studies in emotional adjustment after successful IVF treatment showed no difference when compared with women who conceived naturally, indicating that IVF treatment itself evokes no long-term emotional problems. This systematic review also included women at risk of developing severe psychological maladjustments during treatments, an issue that will be discussed in detail in the discussion part of this thesis.

In a long-term perspective most women seem to manage the burden of unsuccessful infertility treatments. Leiblum *et al.* (1998) found, in a cross-sectional long-term investigation, that women who became biological mothers through IVF were significantly more satisfied with life than women who were unsuccessful in IVF and remained childless, but no differences in emotional status were observed.

Hammarberg *et al.* (2001) found in a follow-up study two to three years after treatment, that women who were not treated successfully tended to be more critical about the

experience of treatment, but their general health was no different from those who were successful. In a prospective longitudinal cohort study Verhaak *et al.* (2007b) investigated levels of psychological adjustment in 298 women, before they started IVF treatment, immediately after the last treatment, after six months, and then three to five years after finishing treatments. After unsuccessful treatments they found that anxiety and depression levels in women returned to baseline after an initial increase during treatment, but also that women whose successful treatment resulted in a birth showed a more positive long-term emotional status compared with the base line. Significant differences in anxiety and depression were found according to mode of adaptation three to five years after unsuccessful treatment. Those women who focused on new life goals or adoption three to five years after unsuccessful IVF showed significantly lower levels of anxiety and depression compared to those who persisted with medical treatment or were still longing for a biological child.

Relationship with partner

Previous studies report different findings and results in the relationship with partner as a result of infertility and treatment. In an overview of the literature and clinical practice regarding infertility and sexuality, Möller (2001) found great variations in the results. Between 10 and 60 percent of infertile couples reported that infertility provoked sexual problems, although the majority of these couples only experienced episodes of diminished sexual pleasure and were able to handle the problems. Most recent studies report no negative impact on relationships with partners due to infertility treatments, neither in the short or long terms,

and other studies actually indicate infertility treatments have a positive impact on the partner relationship (Greil, 1997; Hjelmstedt *et al.*, 1999; Hammarberg *et al.*, 2001; Schmidt *et al.*, 2005).

Claims indicating that the relationships of patients undergoing fertility treatments benefited during the treatment were investigated more thoroughly by Peterson *et al.* (2011). In a prospective longitudinal cohort study following 2,250 Danish fertility patients over a five-year period, they examined couples undergoing unsuccessful fertility treatments, focusing on the possible marital benefit related to coping strategies. They found one-third of the participants with unsuccessful treatments reported higher levels of marital closeness as a long-term positive effect of coping with this stressful life challenge. Marital benefit was measured by the response to two items relating to childlessness: the period “*has brought us closer together*” and “*strengthened our relationship*”. Coping strategies relating to infertility (the Copenhagen Multicenter Psychosocial Infertility Coping Strategy Scale) was categorized in four subscales; *active-avoidance strategies* (e.g. avoiding pregnant women or children), *active-confronting strategies* (e.g. showing feelings, asking others for advice), *passive-avoidance strategies* (e.g. hoping for a miracle) and *meaning-based coping* (e.g. growing as a person in a positive way, finding other goals in life). The use of meaning-based coping was the only coping strategy that had a significant positive effect from the point of view of marital benefit, for both men and women. It was also the only coping strategy that increased in use during the five years of the study period.

Gender differences

Most studies find women to react more strongly than men to infertility and its treatment (Beaupaire *et al.*, 1994; Hjelmstedt *et al.*, 1999; Newton *et al.*, 1999; Lee and Sun, 2001). In a retrospective cohort study comparing psychological distress between men and women preparing for IVF, Wichman *et al.* (2011) found women scored significantly higher than men for symptoms of depression, anxiety, infertility-specific distress and general perceived stress. However, they found infertility-specific psychological distress to be significantly higher in both men and women when compared to general measurements of psychological states. A longitudinal study by Verhaak *et al.* (2005) showed that women reacted with increased anxiety and depression after IVF failure, while no changes were observed among men, and Greil (1997) concluded in a literature review of infertility and psychological distress, that most researchers have found infertility to be a more stressful experience for women than men.

When using the terms quality of life and well-being in relation to the evaluation of self, marriage, intimacy and health, Andrews *et al.* (1991) found the negative effects on quality of life to be stronger for women than for their partners, and linked these findings to the explanation that treatment and its consequences affect women more than men. Different results have been reported when measuring gender differences in quality of life. While Huppelschotten *et al.* (2013a) and Ragni *et al.* (2005) found women reported lower quality of life than men, Chachamovich *et al.* (2009) found the quality of life of in both men and women similarly affected. In a systematic review investigating

QoL and HRQoL in infertility measured with validated general instruments, Chachamovich *et al.* (2010) found infertile women consistently to have lower QoL scores when compared to both infertile men and norm groups. In a recent study, Huppelschotten *et al.* (2013a) measured QoL and emotional status of women and their partners by using a QoL instrument (FertiQoL) and a screening instrument of risk factors for emotional problems (SCREEN-IVF). Both these instruments were specifically developed for infertility and IVF treatments (Verhaak *et al.*, 2010; Boivin *et al.*, 2011). Women had significantly lower levels of QoL than their partners, and more and different risk factors for developing emotional problems during and after treatment. The authors concluded that infertility impacts differently on women than on their male partners.

Many studies dealing with gender differences have only analysed differences at one single time, usually before or after treatment. When analysing the changes over time some longitudinal studies have found the pattern of psychological reactions in men and women to be similar, although women report stronger reactions. In a study monitoring daily emotional, physical and social reactions among men and women in couples undergoing one complete IVF or ICSI treatment cycle, Boivin *et al.* (1998a) found similar response patterns in both spouses. Women reported reactions at a more intense level, but the increase in reactions to oocyte aspiration, fertilization, embryo transfer and pregnancy testing was similar for both men and women in the relationship. The results clearly demonstrate the same patterns in levels of distress, intimacy and optimism in men and women in their reactions to the various IVF stages. These results are in line

with several other studies finding the pattern of emotional reactions to infertility treatments to be similar in both genders, but women to report significantly more infertility stress than men (Baram *et al.*, 1988; Wright *et al.*, 1991; Collins *et al.*, 1992; Jordan and Revenson, 1999; Schmidt, 2005).

Male infertility

Studies investigating the influence of a male infertility diagnosis on men's experience of QoL report equivocal results. Naghtigall *et al.* (1992) found that men with male infertility perceived a loss of physical potency, had poor self-esteem and experienced feelings of stigma, compared to men in couples where the female was infertile or there was an unexplained fertility diagnosis. Connolly *et al.* (1987; 1992) found elevated distress in cases of male infertility and assumed that male infertility could create particular difficulties for the couple. Newton *et al.* (1999) reported higher general stress and more social and sexual concerns in both men and women in couples with male infertility, than in couples with female infertility. Smith *et al.* (2009) measured personal, social, sexual and marital impacts of a male factor infertility diagnosis by the use of questionnaires and interviews with 357 men in infertile couples. They found men diagnosed with male factor infertility to have a significant lower QoL in sexual and personal domains compared to men in couples with female, mixed or unexplained infertility diagnoses. However, no significant differences were observed between the groups of men when it came to the impact on the marriage. When investigating the impact of male diagnosis on sexual desire and satisfaction as indicated by frequency of coitus, Ramezanzadeh *et al.* (2006) found no difference in sexual satisfaction in male

partners, regardless of infertility diagnoses. On the other hand, in a long-term follow-up study of men diagnosed with male factor infertility five years earlier, Hammarberg *et al.* (2010) found 25 percent of the men reported a negative impact on partner relationship and 32 percent reporting a negative effect on levels of sexual satisfaction. The authors concluded that even if most men did not report adverse effects to male infertility, the results suggest that male factor infertility affected relationships negatively in a significant sub-group of men.

Pook *et al.* (2002) and Pook and Krause (2005) found infertility diagnoses did not affect distress scores either among men attending an andrological clinic for fertility treatment, or at a follow-up some months later. In their study of couples undergoing insemination, Dhillon *et al.* (2000) found no difference in the psychological well-being and the ability to cope between fertile men with pregnant wives, and men with male, or unexplained, infertility. There were no differences between these groups in the mean scores for measures of depression, anxiety, anger or self-esteem. When studying men undergoing their first IVF or ICSI treatment with daily monitoring, Boivin *et al.* (1998b) found that the men's psychological reactions were similar, except that ICSI patients showed marginally more anticipatory anxiety on the days prior to oocyte aspiration, possibly because of the uncertainty of fertilization.

In a literature review of infertility and psychological distress, Greil (1997) reported that most studies have not found the relationship between gender and infertility distress to be affected by gender-specific factors.

However, some studies in this field suggest that men's experiences of infertility are associated with threats to their masculinity, potency and manhood as well as feelings of role failure (Naghtigall *et al.*, 1992; Mahlstedt, 1994; Edelman *et al.*, 1994b; Glover *et al.*, 1998). Hjelmstedt *et al.* (1999) found the most important aspect of infertility among women to be the desire to have a child, while for men the main aspect was the obligation to fulfil the male role and the social pressure of parenthood. These views might also be attributable to socially-constructed gender roles as well as biological reality.

Fisher and Hammarberg (2012) reviewed 73 studies investigating men's desire for fatherhood, and the associated psychological and social aspects of diagnosis and treatment. The studies indicated that fertile and infertile men, independent of their partner's wishes, wanted to experience fatherhood in a similar way as their female counterparts wanted to experience motherhood. Infertility-specific anxiety is elevated in men at the initiation of diagnostic investigations, confirmation of diagnosis and during treatment, but the overall prevalence of clinically significant symptoms of depression and anxiety is no higher than in the general population. Men experience grief when fertility treatments are unsuccessful and this can become an enduring sadness. Gannon *et al.* (2004) investigated media reports concerning male infertility and found that in the media, stereotypical masculinity and male infertility were conflated with impotence. The review of Fisher and Hammarberg (2012) found no indication of the popular beliefs about the conflation of virility and fertility to be true, but that men experience these issues to be separate aspects of their lives.

Overall, few studies in this field focus exclusively on men's experience of infertility and treatment; it is still mainly seen as a woman's problem.

Quality of care

Quality of care in general

"Our aim is to find out what patients want, need and experience in health care, not what professionals (however well-motivated) believe they need or get." (Through the Patient's Eyes. Gerteis *et al.*, 1993).

The Institute of Medicine (2001a) has defined quality of care as "the degree to which health services for individuals and populations increase the likelihood of desired health outcomes, and are consistent with the current professional knowledge." Patient-centered care is one of the six aims for improvement of the health care system, which are:

- *Safe*: Avoiding injuries to patients from the care that is intended to help them.
- *Effective*: Providing services based on scientific knowledge to all who could benefit, and refraining from providing services to those not likely to benefit.
- *Patient-centered*: Providing care that is respectful of and responsive to individual patient preferences, needs, and values, and ensuring that patient values guide all clinical decisions.
- *Timely*: Reducing waits and sometimes harmful delays for both those who receive and those who give care.
- *Efficient*: Avoiding waste, including waste of equipment, supplies, ideas, and energy.
- *Equitable*: Providing care that does not vary in quality because of personal characteristics such as gender, ethnicity, geographic loca-

tion, and socioeconomic status. (Institute of Medicine, 2001b).

Both the market-oriented approach to reforming the health care system according to efficiency and cost (the patient a customer) and the movement in clinical practice towards patient-centered care, are two forces focusing attention on patient perceptions of quality (Sofaer and Firminger, 2005). In the last two decades there has been an increasing conviction that patients' options have to be included in the evaluation of health care to achieve a more thorough and patient-centered reflection of quality of care (Jenkinson *et al.*, 2002). Patient-centeredness is ideally monitored by surveys measuring patients' specific experiences rather than by surveys measuring overall satisfaction (Cleary 1999, van Empel *et al.*, 2010b; Wilde Larsson and Larsson, 1999a; Wilde Larsson and Larsson, 2002). Responses to general questions give little guidance as to quality-enhancing measures, while measuring patients' experiences of specific aspects of care stimulates quality improvements (Jenkinson *et al.*, 2002; Sofaer and Firminger, 2005; Haagen *et al.*, 2008). Thus from a validity point of view, as well as from a practical quality improvement perspective, several specific questions are better than a few overall ones (Wilde Larsson and Larsson, 2002).

How to measure quality of life? Ask the patient. How to measure quality of care? Ask the patient. Observers are poor judges of patients' opinions. Many studies have shown that independent assessments by either healthcare professionals or patients' relatives differ from the responses obtained when patients complete self-reported questionnaires. Many studies have shown

that patients' opinions vary considerably from the expectations of both staff and relatives, and that observers tend to underestimate the impact of psychological aspects and tend to emphasize the importance of the more obvious symptoms. Therefore QoL and quality of care should be measured from the patient's perspective, using a patient-completed questionnaire. (Bowling, 2001; Sofaer and Firminger 2005; Fayers and Machin, 2007; Arts *et al.*, 2011a; van Empel *et al.*, 2011; den Breejen *et al.*, 2013).

In a review of patient perceptions of the quality of health services, Sofaer and Firminger (2005) examined 11 qualitative studies designed to determine patients' own definitions of quality of care. The categories defining quality of care were: "patient-centered care", "access", "communication and information", "courtesy and emotional support", "technical quality", "efficiency of care/organization" and "structure and facilities". For patients in the studies reviewed, quality defined in terms of "patient-centered care" included patients having their physical and emotional needs met; being involved in their own care, and in decisions involving them; receiving individualized care by respectful doctors, nurses and staff with personalized knowledge of the patient; patient privacy and confidentiality; having nurses to act as advocates for the patient; equal care for all patients; and family and friends being involved in the care of the patient.

Factors found to influence patient perceptions of quality are shown in the "conceptual model of development of patient perceptions of quality" (Figure1). On the left side in the model are the factors that influence the

patients' expectations (e.g. previous experiences, patient demographics, social and cultural norms, knowledge of what to expect) and on the right in the model are the patient's specific experiences of seeking and using healthcare services. The comparison between expectations and experience gives the patient's perception of quality.

The classical categorization of indicators for assessing the quality of healthcare, divided into structure, process and outcome by Donabedian (1966), are often used by health professionals and scientists. *Structure* measures the patient's rating of physical environment and facilities. *Process* measures the patient's ratings of interpersonal interactions (e.g. empathy, competence, availability). *Outcome* measures the patient's

rating of the result of the process (e.g. symptom reduction or resolution, improvement in functioning). When measuring quality of health care reported by patients, there are two different approaches to measurements used. While Patient Reported Outcome Measures (PROM) assess patient experiences of health results as an aspect of HRQoL, Patient Reported Experience Measures (PREM) assess patient experiences of health care. The need of PREM as a complement to PROM has been emphasized because while PROM includes *outcome* measures in terms of health or symptoms, PREM includes both *structure*, *process* and *outcome* assessments according to the experience of quality of health care (Promcenter, report 2013).

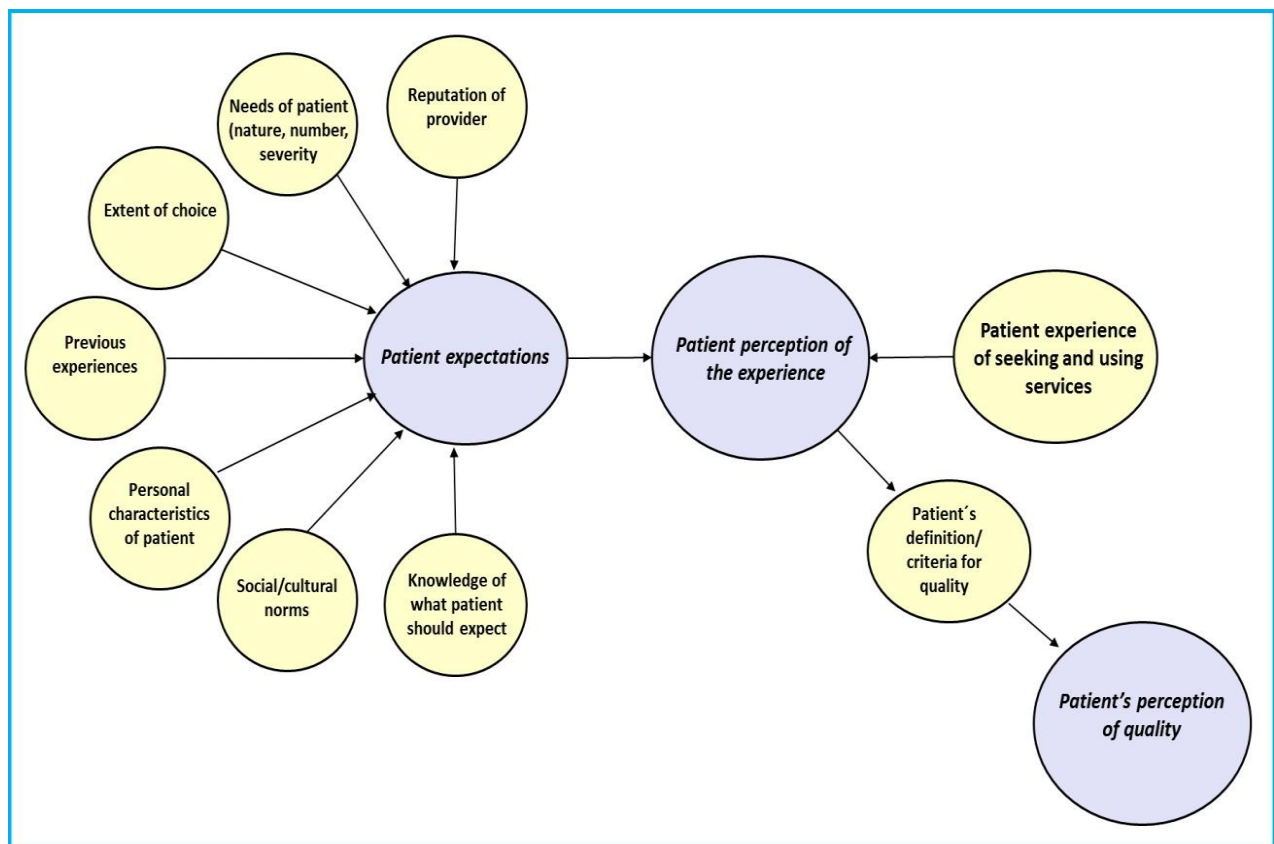


Figure 1. Conceptual model of development of patient perceptions of quality (reproduced from Sofaer and Firminger (2005) with permission from Annual Reviews).

Patient satisfaction is difficult to assess and define. In general, surveys reveal high levels of overall satisfaction with medical care, making it more difficult for practitioners and managers to prioritize areas for service development. Souter *et al.* (1998) concluded that women who responded to questionnaires were, in general, satisfied with their care and it was only when asking more specific questions that inadequacies in the service were identified. The differences in patient *satisfaction* versus patient *experience* have been widely discussed. The terms have often been used interchangeably. Patient satisfaction can be defined as fulfilling expectations, desires and needs (Sitzia and Wood, 1997) and thereby it follows that someone with low expectations may report themselves as satisfied while someone with high expectations would find the same care totally unacceptable. Crow *et al.* (2002) concluded that satisfaction does not imply superior service, only acceptable service, and that satisfaction is a relative concept. In studies measuring quality of care, the development has shifted from the ratings of patient satisfaction towards measuring patient experiences.

The term “patient-centered care” was originally coined by the Picker Commonwealth Program for Patient-Centered Care in USA, which subsequently became the Picker Institute in 1988. The Picker Institute is an independent nonprofit organization dedicated to the advancement of patient-centered care. From 1994, the Picker Institute began working with partner organizations in Europe and the Picker Institute Europe was established in 2000, (www.pickerinstitute.org).

Gertis *et al.* (1993) performed an extensive research of the patients’ experience of care, including a wide range of focus groups (patients, family members, physicians and non-physician hospital staff) combined with a review of the literature. They defined and presented the aspects of health care that were most important to patients in the famous book *Through the Patient’s Eyes*. These aspects are the basis for The Eight Picker Principles of Patient-Centered Care, used worldwide as guidelines when developing and validating new instruments for measuring patient-centered quality of care.

The Eight Picker Principles of Patient-Centered Care consists of dimensions related to *the relationship between individual patients and professionals*:

- involvement in decisions and respect for preferences
- clear, comprehensible information and support for self-care
- emotional support, empathy and respect

and *dimensions relate to services and systems*:

- fast access to reliable health advice
- effective treatment delivered by trusted professionals
- attention to physical and environmental needs
- involvement of, and support for, family and carers
- continuity of care and smooth transitions, (www.pickerinstitute.org).

From these dimensions, Jenkinson *et al.* (2002) developed and validated the Picker Patient Experience Questionnaire (PPE-15) by selecting questions from the bank of items from the Pickers Institute assessing quality of care. The questionnaire was tested on 62, 925 patients from countries in Europe and the USA. The PPE-15 is meant to be a basic core, to be incorporated in further optional instruments. Because the instrument was developed to be applicable in all hospitals and relevant to all patients, it can be used as a benchmark for national and international comparisons.

Quality of care related to infertility and treatments

In the field of assisted reproduction, criticism has been raised against the focus on effectiveness (e.g. pregnancy and live birth rates) when measuring quality, while less attention has been paid to patients' perceptions of quality of care (Alper *et al.*, 2002; Van den Broeck *et al.*, 2012). Efforts have been made to deal with this deficiency in reproductive medicine, and several instruments for measuring patients' perspectives on fertility care have been developed, although many have short-comings.

Instruments

“Developing a new instrument is a time-consuming task. In summary, our advice is: don't develop your own instrument – unless you have to. Wherever possible, consider using or building upon existing instruments. If you must develop a new instrument, be prepared for much hard work over a period of years.” (Fayers and Machin, 2007).

However, despite this warning there are groups of researchers in reproductive medicine that have taken on the task of fully developing and validating instruments for infertility patients. The main criticisms of many instruments measuring the quality of fertility care have been their lack of validation, and they have also been criticized for not having the examination of the patients' perspective as a primary aim (Dancet *et al.*, 2010). Recently, however, there has been a breakthrough in this field in Europe with the development of validated, specific, patient-centered instruments for patients undergoing IVF treatments, both measuring QoL and the quality of care. Some of the instruments will be mentioned below because of their valuable contributions to this field, while other instruments developed and validated for specific sub-groups of the infertile population (e.g. endometriosis, polycystic ovarian syndrome, testicular sperm extraction) will not be mentioned in this brief overview.

The patient-centered infertility care (PCIC) model

Influenced by the overall move in the healthcare system towards systematic investigation and categorization of dimensions in the quality of care from the patient perspective, Dancet *et al.*, (2010) examined the patients' perspective on fertility care in a review including 51 studies. Most studies reviewed used specific questionnaires developed for fertility care, but many had significant methodological problems, few had been validated and most instruments focused exclusively on women. They identified ten dimensions of care relevant to fertility patients, whereof eight

dimensions accorded to The Eight Picker Principles of Patient-Centered Care: (I) Access to care; (II) Respect for patients' values, preferences and needs; (III) Coordination and integration of care; (IV) Information, communication and education; (V) Physical comfort; (VI) Emotional support and alleviation of fear and anxiety; (VII) Partner involvement; (VIII) Continuity and transition. There are also two additional, newly-developed dimensions for fertility care; (IX) Fertility clinic staff, and (X) Technical skills. Later, in a qualitative study of the use of focus groups of infertility patients, both women and men, Dancet *et al.*, (2011) developed a model of patient-centered infertility care (PCIC) from the identified dimensions. The PCIC divided the dimensions into *system factors* ("information", "competence of clinic and staff", "coordination and integration", "accessibility", "continuity and transition", "physical comfort") and *human factors* ("attitude of and relationship with staff", "communication", "patient involvement and privacy", "emotional support") with a two-way interaction between the two factors. The PCIC model was then used in an international multilingual qualitative study to test whether patients from four European countries had similar views on patient-centered care (Dancet *et al.*, 2012). All specific care aspects important to the focus groups in the four European countries could be allocated a place in the dimensions of the PCIC model.

The fertility quality of life (FertiQoL)

An international instrument to measure both QoL and quality of care related to infertility and treatments, the fertility quality of life (*FertiQoL*), has been developed recently (Boivin *et al.*, 2011). The instrument was

validated with focus groups of infertility patients involved. The *FertiQoL* consists of two parts; one part that assesses core quality of life and one part that assesses treatment-related quality of life. The core *FertiQoL* module consists of 24 items covering four domains; "mind-body", "relational", "social", "emotional", and two additional items concerning overall life and physical health. The *FertiQoL* treatment module consists of two subscales, indexing treatment environment and treatment tolerability. The *FertiQoL* instrument can be used by both women and men, but is mainly directed to women. The core quality of life part in the *FertiQoL* instrument has been used in a Dutch study to confirm the negative relationship between emotional distress and quality of life in women undergoing fertility treatments (Aarts *et al.*, 2011b).

The patient-centeredness questionnaire-infertility (PCQ-infertility)

A Dutch study, (van Empel *et al.*, 2010a) identified weaknesses, strengths and needs in fertility care from the patient's perspective by using focus groups of patients. The dimensions of the needs identified in the focus group were "information and communication", "autonomy and respect", "continuity of care", "care organization", "emotional support" and "physical support." The qualitative results were converted into a questionnaire for both women and men, and distributed to patients in Dutch clinics. This questionnaire was later used to identify organizational determinants of patient-centered fertility care in a multilevel analysis (van Empel *et al.*, 2011). To better tailor fertility care to both women and men, a Dutch patient-centered questionnaire to be answered by the couple together was developed. It was generated by focus groups

of infertility patients (van Empel *et al.*, 2010b). The patient-centeredness questionnaire-infertility (*PCQ-infertility*) includes seven sub-scales that are “accessibility”, “information”, “communication”, “patient involvement”, “respect for patient’s values”, “continuity” and “competence.” The questionnaire included one “experience item” and one “importance item” for each aspect of care.

Both the FertiQoL tool and the PCQ-infertility instruments have been used to investigate how patient-centered care relates to infertile women’s quality of life, and the levels of distress they experience. A relationship between these variables was confirmed, indicating that improved patient-centered care can have an impact on the quality of life and positive well-being (Aarts *et al.*, 2012).

The fertility Problem Inventory (FPI)

The fertility Problem Inventory (FPI) assesses global infertility stress by measuring the impact of infertility on social, marital and sexual life and the importance of parenthood. It was developed by Newton *et al.*, (1999) and has been widely used. The instrument has recently been psychometrically tested and validated by confirmative factor analysis (Moura-Ramos *et al.*, 2012). The new model proposes that global infertility stress should be divided into two dimensions, “*impact on life domains*” including social, sexual and relationship concerns and “*representations about the importance of parenthood*” including a rejection of a childfree lifestyle and the need for parenthood. The instrument combines assessment of the infertility experience and the personal meaning of parenthood and childlessness at an individual

level for both men and women. It is suitable for assessing infertility-related stress and as a screening instrument prior to infertility treatments.

Tübinger Lebensqualitätsfragebogen für Männer mit Kinderwunsch (TLMK)

A QoL measurement for men experiencing involuntary childlessness caused by male infertility was developed and validated by Schanz *et al.*, (2005). Tübinger Lebensqualitätsfragebogen für Männer mit Kinderwunsch (*TLMK*) consists of 35 items divided into four dimensions; “Desire for a child”, “Sexual relationship”, “Gender identity”, and “Psychological well-being.” The instrument was developed from patient interviews with men who were attending andrological clinics, from literature research and general QoL measurements. It can be used to assess QoL from a male perspective, both as a base-line and during fertility treatments.

SCREENIVF

A screening instrument, *SCREENIVF*, for women at risk of emotional problems as a result of unsuccessful IVF treatments has been validated by Verhaak *et al.* (2010). The instrument covers risk factors for emotional maladjustment identified in an earlier study (Verhaak *et al.*, 2005) and consists of 34 items divided into scales assessing anxiety, depression, helplessness, lack of acceptance and perceived social support. All items are based on previously developed generic and infertility-specific instruments. Ideally the instrument should be used as a screening tool to identify women with a risk profile for emotional problems before starting IVF treatments.

Patient evaluation of infertility management

A short instrument based on quality management and in line with ISO 9001; 2008 guidelines has also recently been developed and validated by Van den Broeck *et al.* (2012). The instrument focuses on identifying possible weaknesses in fertility management on quality aspects selected by health professionals, but the development of the instrument also includes qualitative interviews with infertility patients in the validation phase. The instrument can be answered by both women and men, with 14 items covering four dimensions; “telephone access”, “reception”, “information” and “patient-centeredness”. Because of its “top-down” approach it is proposed it should be used in combination with other more “bottom up” instruments (e.g. instruments covering all dimensions of care important from the patient’s perspective).

Quality from the Patient’s Perspective (QPP)

A presentation of the general questionnaire “Quality from the Patient’s Perspective” (QPP) is appropriate in this thesis, due to the fact that QPP is the foundation for building the specific IVF instrument described in *Papers III* and *IV*.

The QPP instrument has been widely used in Sweden, most recently in intrapartal care (Wilde-Larsson *et al.*, 2010; Sandin-Bojö *et al.*, 2011). IVF-specific variations of the QPP have been used by several IVF clinics in Sweden over recent years, but without any validation.

The model, Quality of Care from the Patient’s Perspective, was developed using a grounded theoretical approach generated

from in-depth interviews with patients (Wilde *et al.*, 1993) and operationalized into the questionnaire, Quality from the Patient’s Perspective (QPP), using a conventional factor analytic approach (Wilde *et al.*, 1994). The QPP questionnaire was further developed by a dimensional analysis of all items using structural equation modelling (Larsson *et al.*, 1998), and a short version of the QPP has also been developed (Wilde Larsson and Larsson, 2002). The QPP is based on a theoretical model of quality of care from a patient perspective and all items can be traced back to specific dimensions of this model. They are: (1) the medical-technical competence of the caregivers, (2) the physical-technical conditions of the care organisation, (3) the degree of identity-orientation in the attitudes and actions of the caregivers and (4) the socio-cultural atmosphere of the care organisation (Wilde *et al.*, 1993). Quality of care can be understood in the light of two conditions, the resource structure of the care organisation and the patients’ preferences. The resource structure of the care organisation consists of person-related, as well as physical and administrative environment qualities. Patients’ preferences have both rational and human aspects. A diagram of the model is given in Figure 2.

When answering the questionnaire various aspects of care are evaluated in two ways; how important each aspect is for the patient (subjective importance) and how it was actually experienced (perceived reality).

In 2010, Swedish health authorities requested data on patient-reported quality of care to be added to The Swedish National Quality Register of Assisted Reproduction. There was no existing validated instrument for IVF patients at that time, either in Sweden or

Europe. The fact that the theoretical foundation of the QPP-instrument was based on patients' conceptions of quality of care, the evaluation of both subjective importance and perceived reality, and the fact that several

IVF clinics were familiar with the instrument, inspired us to use QPP when developing and validating a new instrument specifically for IVF treatments.

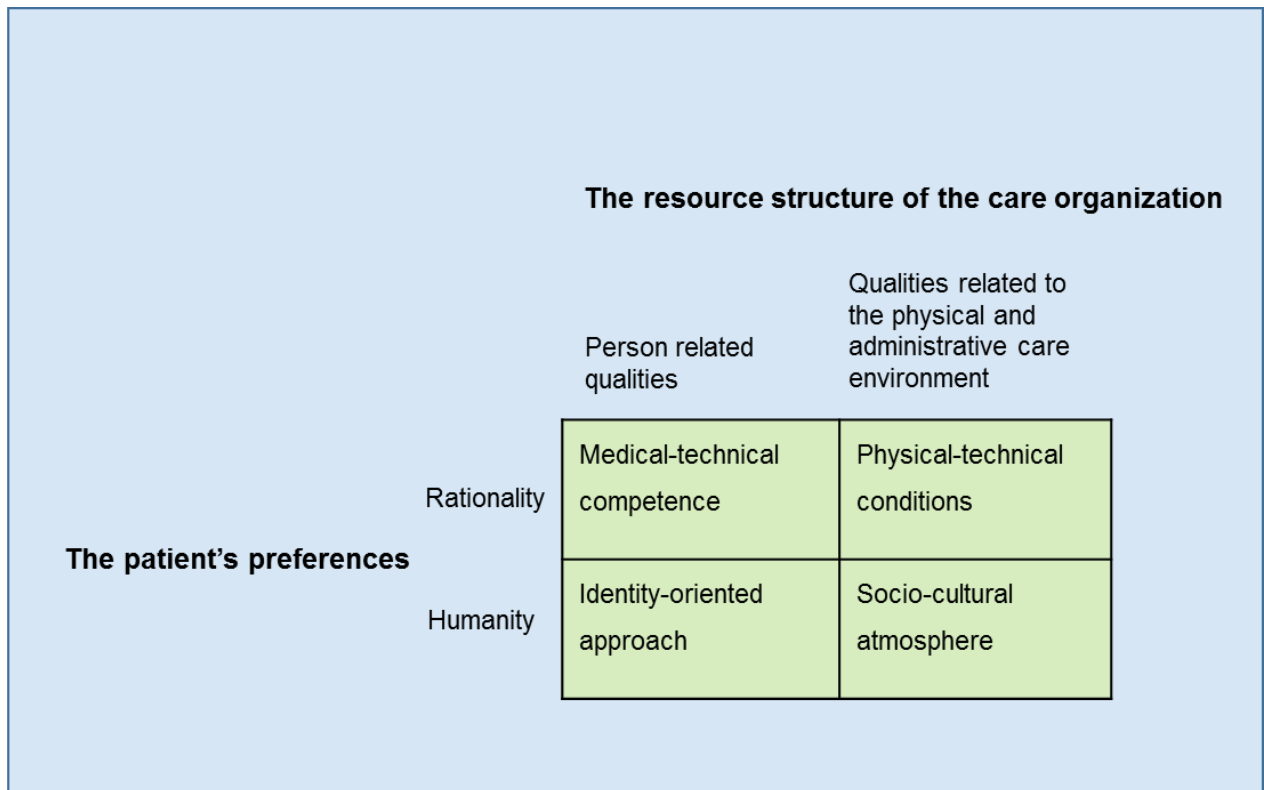


Figure 2. Model of quality of care from the patient's perspective. (Reproduced from Wilde *et al.*, 1993 with permission from Scandinavian Journal of Caring Sciences).

Aims of the thesis

- to assess infertile couples' short-term emotional responses to their first IVF treatment and their experiences of the marital relationship at different stages of the first treatment, and also to examine the differences/similarities between the genders as regards whether or not a pregnancy was achieved (*Paper I*)
- to investigate whether a male infertility diagnosis had any influence on men's experience of infertility and treatment, view of life, relationships, self-image and psychological well-being, when compared with men in couples where the diagnosis was female, mixed or unexplained infertility (*Paper II*)
- to develop a validated instrument for measuring quality of care in IVF-programmes for both men and women (*Paper III*)
- to investigate whether men and women differ in their evaluations of the importance of different aspects of quality of care, measured by the validated QPP-IVF instrument (*Paper IV*)

Methodological considerations

IVF treatment

Two different IVF stimulation protocols were used, either down-regulation with a GnRH agonist followed by ovarian stimulation, or ovarian stimulation in combination with a GnRH antagonist. Ovarian stimulation was performed with recombinant FSH or urine-derived human menopausal gonadotrophin. Stimulation was monitored by vaginal ultrasound and serum estradiol levels. Oocytes were retrieved 36 to 38 hours after hCG injection, using ultrasound guided puncture. The patient received a combination of intra-venous sedation and local anaesthesia. Fertilization was achieved by standard IVF or ICSI. In general, two embryos were transferred two or three days after oocyte retrieval for women (*Papers I and II*), and one embryo was transferred two to five days after oocyte retrieval for women (*Papers III to IV*). Additional embryos of good quality were cryopreserved and replaced later. Luteal support was given with vaginal or intramuscular progesterone.

Ethics

Ethical approval was obtained from the Ethics Committee of Gothenburg *Papers I and II*: Dnr L604-98, *Papers III and IV*: Dnr 417-11. All participants gave their written consent (*Papers I to IV*).

Settings, designs, participants and methods

Paper I

First IVF treatment – short-term impact on psychological well-being and the marital relationship

Paper II

The psychological influence of gender infertility diagnoses among men about to start IVF or ICSI treatment using their own sperm

Paper III

Quality of care in an IVF programme from a patient's perspective: development of a validated instrument

Paper IV

Patient-centered quality of care in an IVF-programme evaluated by men and women

Settings

Papers I and II were part of a prospective, longitudinal study at the Reproductive Medicine Unit at Sahlgrenska University Hospital in Gothenburg. *Papers III and IV* were a cross-sectional study at the Reproductive Medicine Unit at Sahlgrenska University Hospital and the Fertility Centre of Scandinavia, in Gothenburg, Sweden.

Table 1. Overview of designs, period and settings, participants and methods in Papers I to IV.

Study	Design	Period and setting	Participants	Methods
Paper I-II	Prospective longitudinal study	1999-2002 Reproductive Medicine Unit at Sahlgrenska University Hospital	117 couples (<i>Paper I</i>) 166 men (<i>Paper II</i>)	Paper questionnaire
Paper III-IV	Cross sectional study	2011-2012 Reproductive Medicine Unit at Sahlgrenska University Hospital/ Fertility Centre of Scandinavia, Gothenburg	363 women 292 men	Web questionnaire

Design

Papers I and II

These two studies were part of a large, prospective, longitudinal study in which couples (both men and women) were followed during their first IVF treatment by means of questionnaires administered on three occasions: before, during and after treatment. The patients were recruited between March 1999 and June 2002 at the Reproductive Medicine Unit, Sahlgrenska University Hospital, Gothenburg, Sweden.

All patients planning to start their first IVF/ICSI treatment received written information about the study a week before an information meeting held two to four weeks before the first treatment. Exclusion criteria were inadequate fluency in the Swedish language and participation in other studies. At the information meeting those who expressed an interest in participating in the study were asked to remain after the meeting in order to answer the first questionnaire.

Each partner was asked to answer the questionnaire separately after the meeting without communicating with his or her partner.

The second questionnaire was given to the couples to fill in about one hour before oocyte aspiration, and the third questionnaire was sent by mail in a stamped, addressed envelope, two weeks after menstruation or result of pregnancy test or two weeks after the termination of treatment for those who did not receive embryo transfer.

Two reminders were sent within two weeks.

Papers III and IV

The study group consisted of men and women (n=655) undergoing in vitro fertilisation (IVF) between September and November 2011, and April and May 2012, at the public Reproductive Medicine Unit at Sahlgrenska University Hospital and the privately-run Fertility Centre of Scandinavia, in Gothenburg, Sweden.

The men and women received oral and written information about the study from a midwife at the clinic when planning for oocyte aspiration. They were informed that participation was voluntary and confidential. Those who accepted the invitation to participate provided their e-mail addresses on consent, and the midwife responsible for the study sent the addresses, without names or identification numbers, to a company that administered the questionnaires (ImproveIT www.improveit.se). The questionnaire was sent to the patients' e-mail addresses five days after oocyte aspiration and had to be answered within two weeks (before the pregnancy test) to avoid the responses being influenced by the pregnancy results.

One reminder was sent by email after 3 days.

Participants

Paper I

A total of 117 couples participated in this part of the study. Of the 117 couples who agreed to participate and who answered the first questionnaire, 100 couples (200 men and women) answered all three questionnaires. Of the 17 couples who did not answer the third questionnaire, three couples had discontinued ovarian stimulation, one couple had separated during the time period, one couple reported psychological distress, and for the remaining 12 couples the reasons for not answering the third questionnaire are unknown.

Paper II

Of the total of 166 men who participated in the study, 65 were diagnosed with male infertility and 101 men were in couples with female, mixed or unexplained infertility. No

significant differences in patient characteristics were observed between the groups. No individual in either group had children in the current relationship. Three men in the male infertility group and two men in the female/mixed/unknown infertility group had undergone previous IVF treatment at other clinics. Eight men in the male infertility group and 10 men in the female/mixed/unknown infertility group had physical diseases i.e. asthma, epilepsy, gastrointestinal disorders and hypertension. Two men in the male infertility group and four men in the female/mixed/unknown infertility group had an ongoing psychological condition, i.e. depression or anxiety disorders. The pregnancy rate after the first treatment cycle was 36.9 percent in the male factor group and 33.7 percent in the female/mixed factors group.

Papers III and IV

Men and women undergoing IVF and ICSI (with own gametes), who had adequate fluency in the Swedish language, were invited to participate. Of the 994 persons invited to participate in the study 971 agreed, (489 women and 482 men). In total, 655 persons (response rate 67.5 percent) answered the questionnaire, 363 women (response rate 74.2 percent) and 292 men (response rate 60.6 percent). Reasons for not responding were mostly not known, but 20 participants contacted the clinics and reported that they had missed the deadline for answering the questionnaire. Five persons (three women and two men) who had not received an embryo transfer explained that their non-response was the result of the current experiences, which made it too sensitive for them to handle questions about treatment at that moment. An analysis of demographic variables was performed for

those who did not respond to the questionnaire. No major differences in demographic variables were noted between those who responded and those who did not respond but the proportion of men were higher in the non-responding than the responding group. Although the men and women answered the questionnaire individually via personal email, both partners in the couple were invited to participate, i.e. 497 couples. Of the 655 men and women who answered the questionnaire, 112 were from the woman only, 41 from the man only, and 502 answers were from both partners in the couple.

Measurements (All items in appendix)

The Psychological General Well-Being

Index (*Papers I and II*)

Psychological well-being during the weeks immediately before entering the study was measured using the Psychological General Well-Being Index (PGWB) (Dupuy 1984). The PGWB contains 22 items divided into six subscales – anxiety, depressed mood, positive well-being, self-control, general health and vitality. The index scores can be totalled to form a general overall score, and the scores can be divided into these six dimensions. Each item is ranked 1 to 6: the higher the value, the greater the well-being. Norm values from the Swedish population matched for age and gender are available (Dimenäs *et al.*, 1996). The PGWB has shown satisfactory reliability and validity (Dupuy, 1984; Wiklund *et al.*, 1995).

The strength of the child-wish (*Paper I*)

Experiences of childlessness were evaluated by means of four questions covering the

respondents' perceptions of the importance of having a child and the effects of childlessness. Visual analogue scale 0 to 10 was used, where 0=not at all and 10=very much.

The effects of infertility (*Papers I and II*)

Psychological effects of infertility were measured using 14 items (guilt, success, anger, contentment, frustration, happiness, isolation, confidence, anxiety, satisfaction, depression, powerlessness, competence and control). Twelve of these items were previously used by Connolly *et al.* (1987) and Edelman and Connolly (1998). These items seek to capture aspects of experiences often expressed by infertility patients. The items were formulated as questions such as: “*To what extent have you had the following feelings the last few days: guilt, success, etc?*” These items were both summarised and analysed separately. Each item was graded 1 to 5. The lower the value, the greater the well-being.

Relationship with partner (*Papers I and II*)

The respondent's relationship with his or her partner was evaluated by means of two questions: (i) “*Do you feel that childlessness has caused problems in your marriage?*” And (ii) “*Is talking to each other more difficult now than it was before infertility became an issue?*” These items were graded 1 to 5 where 1=not at all and 5=very much.

The effects of treatment on the respondent's relationship (*Paper I*)

Views of the way the relationship with partner was affected by treatment were evaluated by means of questions concerning affection, understanding, support, and time spent talking with one's partner about the treatment.

Differences between the ideal life situation and real-life (*Paper II*)

The congruence between the desired life and the present life situation was measured using seven items concerning the person's perceptions of the correspondence between how he/she wished life to be and how he/she thought it was in terms of work, leisure time, contact with friends and family, relationship with partner, sex life and life in general. Visual analogue scale 0 to 10 was used where 0=very good accord and 10=no accord.

Optimism versus pessimism (*Paper II*)

The outlook on life was captured using two questions: (i) "What do you think will be the result of the treatment you are about to start?" and (ii) "How do you describe yourself, as an optimist or a pessimist?" Visual analogue scale 0 to 10 was used where 10=absolutely optimistic and 0=absolutely pessimistic.

The meaning of reproduction (*Paper II*)

The man's perception of the point of reproduction was estimated using six items covering aspects of self-imagine, meaningfulness and affinity (Möller and Fällström, 1991). Visual analogue scale 0 to 10 was used where 0=no, not at all and 10=yes, much.

The influence of family's and friends' attitudes toward childlessness (*Paper II*)

The impact of the opinions of friends and family was evaluated using four questions i.e. "How important do you think it is to your parents that you have children?" and "How much are you influenced by your parents' attitudes?" Visual analogue scale 0 to 10 was used where 0=not at all and 10=very much.

Professional support (*Paper II*)

The need of professional support was covered by two questions: (i) "Have you ever had contact with a psychologist or other professional counsellor to talk about the strain of childlessness?" and (ii) "If not, do you think such contact would have been valuable?"

Openness about infertility and treatment (*Unpublished results related to the content of Paper II*)

The man's openness in relation to others about infertility and treatment was measured using the questions: "Who know about your infertility: Parents, siblings, friends, work colleagues?" and "Who know about your treatment: Parents, siblings, friends, work colleagues?"

Quality from the Patient's Perspective of In Vitro Fertilisation (QPP-IVF) (*Papers III and IV*)

A specific questionnaire for measuring men and women's experiences of quality of care during IVF treatment was developed and validated. The questionnaire is based on the theoretical foundation of the validated general instrument, Quality of Patient's Perspective (QPP), which has its origin in in-depth interviews with patients (Wilde *et al.*, 1993). The items of the QPP-IVF questionnaire are divided into ten factors (subscales); "Pain relief and physical care", "Waiting time", "Care room characteristics", "Information during treatment", "Information after treatment", "Participation", "Responsibility/Continuity", "The Staff's respect/commitment/empathy", "Atmosphere and environment", "Accessibility" and one item measuring general medical care. The final

questionnaire consists of 43 items for women and 42 items for men with two kinds of evaluations: the rating of perceived reality of care and the rating of the subjective importance of various aspects of treatment.

To measure the subjective importance of various aspects of treatment and care, each item relates to the statement, “*This is how important it was to me...*” and a four-point response scale is used for all items, ranging from (1) Of little or no importance to (4) Of the highest importance. To measure how the quality of care was perceived, each item relates to the statement, “*This is what I experienced...*” with a four-point response

scale: (1) Do not agree at all to (4) Completely agree.

The Fertility Quality of life (FertiQoL)
(Paper III)

The fertility quality of life (FertiQoL) tool (Boivin *et al.*, 2011) consists of two parts; one part that assesses core quality of life and one part that assesses treatment-related quality of life. In the present study the treatment-related part (the Optional Treatment FertiQoL module) was used, consisting of ten items assessing current thoughts and feelings directly related to fertility treatment. (For all items and scoring instructions see www.fertiqol.org.)

Questionnaire development (Paper III)

Quality from the Patient’s Perspective of In Vitro Fertilisation (QPP-IVF)

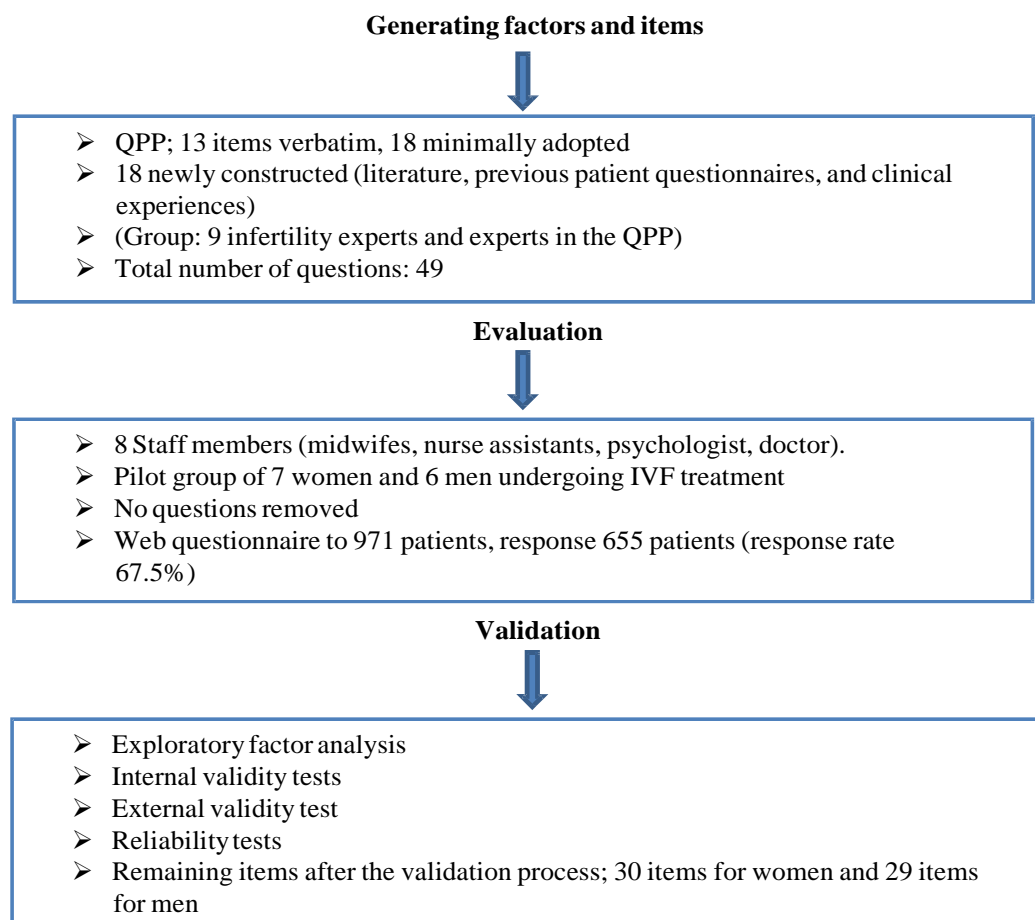


Figure 3. Flow cart of the development and validation of the QPP-IVF instrument.

Generating factors and items

The first step in the development of QPP-IVF was a selection of items from the long and short versions of the QPP questionnaire (Wilde *et al.*, 1994; Wilde Larsson and Larsson, 2002). This selection was made by a group consisting of infertility experts and experts in the QPP instrument (professors, doctors and midwives) who selected items suitable for infertility patients and ensured the retention of the theoretical frame of the original QPP.

The second step was to construct items designed to measure central aspects specific to IVF treatment which were not covered, or were only partly covered, by the original QPP. The newly constructed items were derived from the literature (Baram *et al.*, 1988; Sabourin *et al.*, 1991; Connolly *et al.*, 1993; Schmidt *et al.*, 1998; Souter *et al.*, 1998; Malin *et al.*, 2001; Schmidt *et al.*, 2003b; Gejervall *et al.*, 2007), as well as from previous patient questionnaires and clinical experiences. They covered aspects of care, support, privacy, availability, information and instructions before, during and after IVF treatment.

The items were evaluated by a group of infertility experts (n=6) consisting of doctors and midwives with long experience of clinical IVF. In total, 49 items were derived from these sources. Thirteen items were taken verbatim from the QPP questionnaire (e.g. *“I received good information regarding the drugs I needed, so that I understood their effects, and how they should be administered”* and *“I received this treatment within acceptable waiting time”*). Eighteen items were minimally adapted from the QPP questionnaire to an IVF context (e.g. *“My partner was treated well”* and *“I received*

effective pain relief during oocyte aspiration”), and 18 were newly constructed items (e.g. *“I received good information regarding the time between embryo transfer and pregnancy test”* and *“It was easy to get in contact with the clinic”*).

In addition, three open-ended questions, three background questions, two questions about waiting time for appointments and one question about whether embryo transfer was received or not, were added to the questionnaire. The participants also responded to three general questions concerning physical health, psychological well-being and attitudes towards re-visiting the clinic, all questions previously found to be related to perceptions of quality of care (Wilde *et al.*, 1994; Wilde Larsson and Larsson, 1999; Wilde Larsson and Larsson, 2009). The entire questionnaire consisted at this stage of 61 items for women and men.

Evaluation

Eight staff members tested the questions for content comprehensibility, which resulted in minor changes in wording. After this, thirteen infertile patients (seven women and six men) in treatment at the Reproductive Medicine Unit at Sahlgrenska University Hospital performed a pilot study of the new questionnaire and found that the items functioned on a cognitive level and were comprehensible and relevant. Then the questionnaire was sent by email to 971 patients and 655 answered (response rate 67.5 percent).

Index of measures (addition to Paper IV)

An index of measures was constructed at item level taking both subjective importance and perceived reality into account. This index, shown in Figure 5 (page 65) gives an overall picture of the responses and

compares men and women's views of issues in need of improvement. The responses are calculated at an individual level and merged into an overall picture at group level. High or low scores on both ratings of subjective importance and perceived reality indicate a state of balance (green). Low scores on both ratings indicate some deficiency (yellow). High scores on subjective importance and lower on perceived reality indicate a state of

deficiency and signals that actions need to be taken (red). Lower scores on subjective importance and higher on perceived reality point to a state of excess, indicating that these aspects should be given low priority (blue). In the bars of the index, the digits are number (n) and the width of bars represent the percent of responses in the different categories (state of deficiency, some deficiency, balance, excess) at group level.

Statistics

Table 2. Overview of statistical methods used in Papers I to IV.

Statistical Methods	Paper			
	I	II	III	IV
Descriptive Statistics				
Mean, SD, Median, Minimum and maximum for continuous variables	X	X	X	X
Number and % for categorical variables	X	X	X	X
Statistical Analysis				
For comparison between two groups:				
- Mann-Whitney U-test for continuous variables	X	X	X	X
- Mantel-Haenzsel Chi-Square test for ordered categorical variables			X	X
- Fisher's exact test for dichotomous variables	X	X		X
- Chi-Square test for non-ordered categorical variables				X
Interaction between group and time:				
Mann-Whitney U-test between groups for changes over time.		X		
Analysis within patients and within couples, eg changes over time: Wilcoxon Signed Rank Test	X		X	X
Repeated measures ANCOVA applied to man and woman within couple adjusted for age				X
Analysis within couples between man and woman ordered categorical variables: Sign test				X
Stepwise multiple linear regression analysis	X	X		
Univariate logistic regression analyses and stepwise multiple logistic regression analyses				X
Exploratory Factor Analysis			X	
Internal Validity: Cronbach's alpha, correlation item to scale corrected for overlap, Item discriminant analysis			X	
External Validity: Pearson correlation coefficient, Pitman's non-parametric permutation test			X	
Reliability: Test – retest: Distribution of changes, intra-individual SD, intra-class correlation coefficient for subscales and Weighted Kappa and percent agreement for single items			X	

Paper I

First IVF treatment – short-term impact on psychological well-being and the marital relationship

For descriptive statistics means, standard deviations, medians, ranges and 95% confidence intervals for mean were used for continuous variables and n (%) for categorical variables.

For comparison between two groups Mann-Whitney U-test was used for continuous and ordinal scale variables and Fisher's exact test for dichotomous variables. Wilcoxon signed rank test was used for paired comparison of continuous and ordinal scale variables. A stepwise multiple linear regression analysis was performed for each gender on the dependent variable "*The effects on infertility*" total score.

Paper II

The psychological influence of gender infertility diagnoses among men about to start IVF or ICSI treatment using their own sperm

For descriptive statistics means, standard deviations, medians and ranges were used for continuous variables and n (%) for categorical variables.

For comparison between two groups Mann-Whitney U-test was used for continuous and ordinal scale variables and Fisher's exact test for dichotomous variables. Interaction between groups and time was analysed with Mann-Whitney U-test on the changes over time.

A stepwise multiple linear regression analysis was performed on the dependent variable "*The effects on infertility*" total score.

The results are presented in two groups (i) men with male factor infertility and (ii) men in couples with all other infertility diagnoses. A sample size calculation was performed according to the following: Assuming a mean score of 30.0 and with a SD of 8.0 in "*The effects of infertility*" in the female/mixed factor group, it was possible to detect a difference in score of 4.0 if 64 patients in each group were included (β -level 0.20, α -level 0.05). Assuming a mean score of 107.0 and a SD of 12.0 in PGWB in the female/mixed factor group, it was possible to detect a difference in score of 6.0 if 64 patients in each group were included (β -level 0.20, α -level 0.05).

Paper III

Quality of care in an IVF programme from a patient's perspective: development of a validated instrument

Quality of In Vitro Fertilisation treatment from the Patient's Perspective (QPP-IVF).

In order to investigate whether the data was suitable for exploratory factor analysis (EFA) the Kaiser-Meyer-Olkin (KMO) measure of sample adequacy was calculated and Bartlett's test of sphericity was performed. The KMO statistic measures the relation between the correlations and the partial correlations. Bartlett's test of sphericity tests whether the variables are uncorrelated. In order to perform an EFA, the

KMO should be >0.5 and Bartlett's test of sphericity should be highly significant.

An exploratory factor analysis of all the items of subjective importance within each of the four dimensions of QPP-IVF was performed for women to test the relations among the items and how they cluster together to represent underlying factors. The number of factors was chosen based on scree plots. Items with loadings below 0.40 were excluded and an oblique rotation promax was used. Oblique rotation was chosen because of the expected interrelated aspects of quality of care, and the factor analysis of the perceived ratings of subjective importance was chosen because these scores were regarded as reflecting more general values than the perceived reality scores. Eigen value, explained variance and factor loadings, are given for each factor.

Validation

The scales received from this factor analysis were validated both internally and externally, for both men and women, and for both subjective importance and perceived reality variables.

Internal validity

The internal consistency of the subscales was assessed by Cronbach's alpha. Cronbach's alphas from 0.70 and higher were regarded as desirable; subscales with alphas lower than 0.60 were considered unacceptable. Correlations between each item and its own subscale corrected for overlap, item convergent validity, was accepted if > 0.40 . Item discriminant validity was assessed by correlations between the items within the subscale with the other scales. A scaling success was counted if the item was significantly ($p < 0.05$) higher correlated to its

own scale, corrected for overlap, than to all other subscales within the same QPP dimension. The subscales were calculated by means of the included items. All subscales were calculated within each of the four dimensions except for the newly constructed factor, "Availability", which consisted of two items.

External validity

Convergent validity was established, comparing calculated Pearson's correlation coefficient (r) between the factors of QPP-IVF and the Optional Treatment FertiQoL module with expected correlations between the QPP-IVF subscales and the FertiQoL (Boivin *et al.*, 2011). Pitman's non-parametric permutation test (Good, 2000) was used for the significance test of correlations.

Reliability

A subgroup of the participants was asked to answer the questionnaire on two occasions. Reliability was assessed by test-retest analysis with the distribution of the change, intra individual SD (s_w) and Intraclass Correlation Coefficient (ICC) for the subscales, and with weighted kappa and percent agreement for single-item scales. Wilcoxon Signed Rank test was used for the analysis of systematic changes between test and retest for subscales, and Sign test was used for single item scales. In 95 percent of the observations, the true value will be within $1.96 \times s_w$ of the measured value.

Sensitivity analyses were performed by known group analyses of the items which measured physical and psychological well-being and the item "visiting the clinic for future needs". The Mann-Whitney U-test was used for subscales and the Mantel-

Haenszel Chi Square Exact test in the case of single-item scales.

For descriptive statistics mean, standard deviation, median, quartiles, minimum and maximum were used for continuous variables and n (%) for categorical variables.

Paper IV

Patient-centered quality of care in an IVF-programme evaluated by men and women

Mean, standard deviations, median, minimum and maximum, were used for descriptive statistics of continuous variables, and for categorical variables n (%) was used. For comparison between men and women in the baseline table Mann-Whitney U-test was used for continuous variables, Fisher's Exact for dichotomous variables, Mantel-Haenszel Exact Chi-Square test for ordered categorical variables, and Chi Square test for non-ordered categorical variables.

For the comparison of subjective importance and perceived reality between men and women within couples, Wilcoxon Signed rank test was used for the scales and Sign test applied to the original ordinal values (1-4) for individual items. In these analyses only couples where both man and woman have answered was included.

In order to adjust for age an additional repeated measures ANCOVA applied to men and women within couple as time variable and with age as covariate was performed (Chachamovich *et al.*, 2009).

In order to select independent predictors to highest score of subjective importance univariable logistic regression analysis was first

performed for each of the baseline variables. Variables with $p < 0.15$ were then entered into a stepwise multiple logistic regression analysis.

All significance tests were two-sided and conducted at the 5% significance level for all papers.

Methodological comments

The main methodological strength of these studies is that methods are specifically designed for patients undergoing IVF treatments. When studying couples with infertility problems, it is of value to use specific methods of measurement related to the problem being studied, and not only generic instruments. According to a review of studies published from 1980 to 1997 on infertility and psychological distress (Greil, 1997), several studies with standardized measurements of psychiatric symptoms or psychological distress failed to show differences between infertile and control groups while descriptive studies showed the extensive negative psychological consequences of infertility. Other authors have also dealt with the problem of measuring infertility-related distress by the use of standardized psychiatric measurements, which may limit the expression of the specific problems represented by infertility and its treatment (Berg and Wilson, 1990; Newton *et al.*, 1999; Edelman and Connolly, 2000; Yong *et al.*, 2000).

Patient-centeredness is ideally monitored by surveys measuring patients' specific experiences rather than by surveys measuring general satisfaction (Souter *et al.*, 1998; Cleary 1999; Wilde Larsson and Larsson, 1999a; 2002; van Empel *et al.*, 2010a). A major criticism of the various scales

designed to measure patients' satisfaction with quality of care is their lack of theoretical foundation and validation (Rubin *et al.*, 1990; Wilde *et al.*, 1993; van Campen *et al.*, 1995; Mark and Wan 2005;), and the same criticism has been directed against specific IVF instruments (Dancet *et al.*, 2010). A major methodological strength (*Papers III* and *IV*) of this thesis is the thorough validation process of an instrument based on a theoretical foundation and developed specifically for patients undergoing assisted reproduction. Inclusion of both a public and a private clinic increases the generalizability of the results. A suggestion of further validation of the QPP-IVF instrument (*Papers III* and *IV*) would involve conducting a confirmatory analysis on new data.

The majority of studies in this field mainly focus on women, and the need for fully involving the male partner has been emphasized in several studies (Sabourin *et*

al., 1991; Laffont and Edelmann 1994; Souter *et al.*, 1998; Malin *et al.*, 2001, Haagen *et al.*, 2008; Dancet *et al.*, 2012; Boivin *et al.*, 2012). In these studies the inclusion of both men and women answering individually addressed questionnaires strengthens this thesis.

A methodological weakness is the discrepancy in the period between data collection of *Papers I* and *II* and *Papers III* and *IV*, which reduces the comparability of the emotional reactions to IVF treatment and the perception of care in IVF treatments in this thesis.

Another limitation is that only patients who had adequate fluency in the Swedish language participated in these studies. The methodological problems, such as performing a proper translation procedure and interpreting results, were regarded as too complex to include in the design of these studies.

Results and comments

Paper I

First IVF treatment – short-term impact on psychological well-being and partner relationship

Individual responses before, during and after treatment

Before starting the treatment, the participants as a group had high scores on the PGWB, indicating a high level of general well-being in the group, which considered together with the demographic factors, suggests that they were quite a homogeneous and well-adjusted group of people. Men scored significantly higher than women in total ($p < 0.01$), felt less depressed ($p < 0.001$), showed less anxiety ($p < 0.01$) and had better self-control ($p < 0.0001$). No significant differences between men and women were found in regard to quality of life, positive well-being, general health or vitality.

Overall, women expressed a significantly stronger child-wish than men. It was significantly more important for the women to have children ($p < 0.01$); they felt significantly more emotionally affected by their childlessness ($p < 0.0001$) and thought significantly more about their difficulty in having children ($p = 0.0001$).

The couples answered questions about the effects of infertility before, during and after treatment, and significant gender differences were found on all three measurement occasions. Women scored significantly higher than men on total score ($p < 0.01$) and on several items: anger, frustration, anxiety, depression, powerlessness and losing control.

However, the mean figures were low, indicating that most of the men and women felt quite well. Even one hour before oocyte retrieval, (second measurement occasion) a time we know is demanding for most patients, the mean figures for “The effects of infertility” were low, indicating relatively good psychological well-being.

Two weeks after the pregnancy test all participants answered “The effects of infertility” questionnaire for the third time.

Figure 4 shows the development of the psychological effects of infertility on men and women over the approximate eight weeks covered by the study. Not surprisingly, the results illustrate clearly that the women’s and men’s emotional reactions after their first IVF cycle are dependent on whether or not pregnancy was achieved. Those who failed to become pregnant rated their emotions as significantly more unhappy, while those who became pregnant rated their emotions as significantly happier than before treatment started. The women in the no pregnancy group felt significantly more guilt, isolation, depression and powerlessness and significantly less success, contentment, happiness, confidence and satisfaction after, than before, treatment. The men in the no pregnancy group felt significantly more anger, anxiety, powerlessness and significantly less contentment, happiness, satisfaction and control after treatment. Pregnant women felt significantly more successful, and experienced significantly less anger and frustration after treatment, and

men in the group whose partners became pregnant felt significantly less frustration after treatment than before.

The women seemed to have stronger emotional reactions to their infertility than their partners on all three measurement occasions. However, the pattern of reaction was similar for both partners (figure 3). The men reacted as strongly as their partners when pregnancy was not achieved. The mean figures were low, however, indicating relative well-being.

View of the relationship before, during and after treatment

In the short term, the relationship seems to be strengthened during the treatment process. Men felt that childlessness had caused problems in the relationship to a greater extent than women, both before and during treatment, but there was no difference after treatment in either the pregnancy group or the no pregnancy group. The vast majority (approximately 90 percent) answered “not at all” to the question: “Do you find it more difficult to talk to each other now than before childlessness became an issue?”

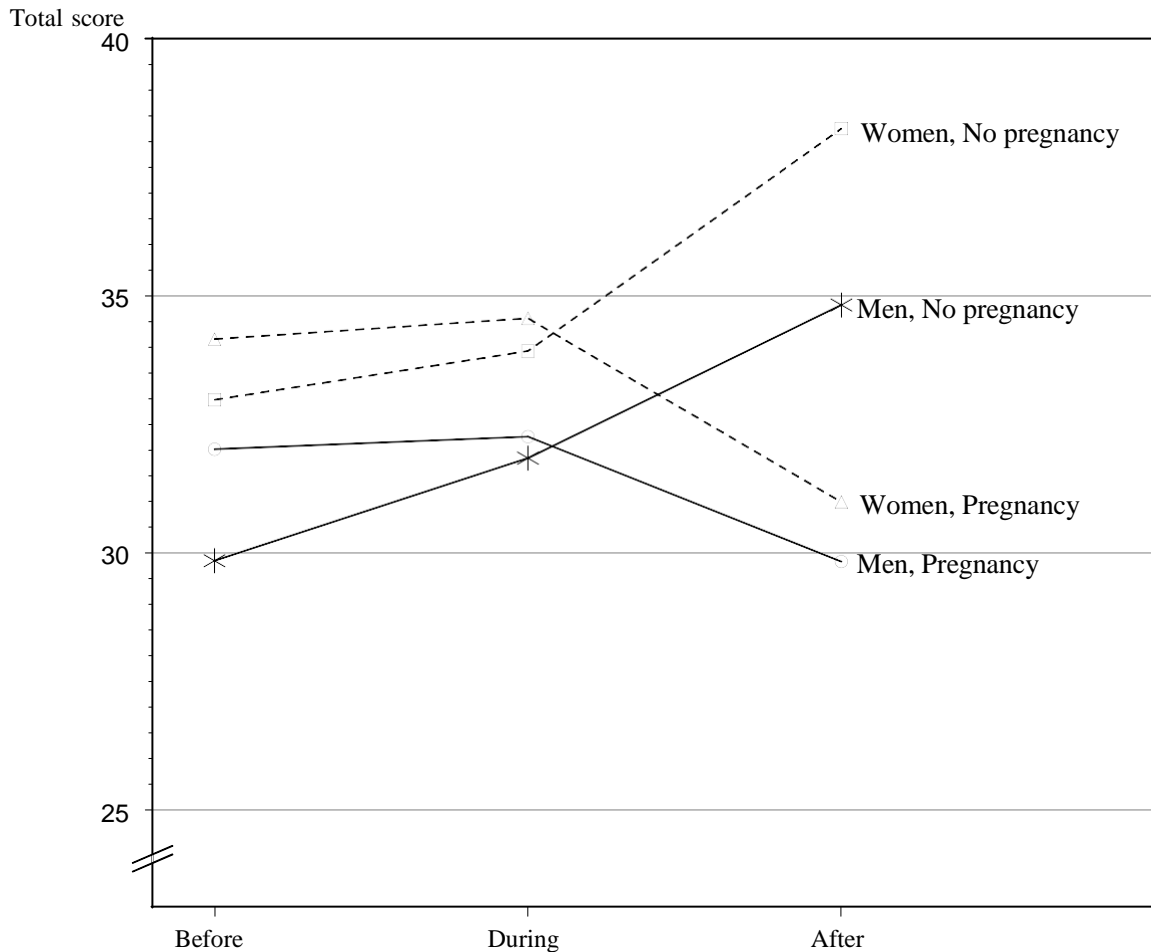


Figure 4. Total score (min 14, max 70) of “The effects of infertility” before, during and after treatment.

In the stepwise multiple linear regression analysis concerning the men, the variables pregnancy ($p=0.0006$), “The effects of infertility”, second measurement ($p=0.0022$) and PGWB ($p=0.0055$) significantly correlated with the dependent variable “The effects of infertility” third measurement. For the women, the variables pregnancy ($p<0.0001$) “The effects of infertility” first measurement ($p=0.0158$) and second measurement ($p=0.0033$) significantly correlated with “The effects of infertility” third measurement.

The effects of treatment on the relationship

There were no differences between the pregnancy and no pregnancy groups in answers to the question: “How did the infertility treatment process affect your relationship with your partner?” The majority in both the pregnancy and the no pregnancy groups answered that the treatment had affected the relationship in a positive way during the treatment process. The men and women in most couples gave the same answers. Two men in the pregnancy group and two couples in the no pregnancy group gave the answer “worse.” Seven people in the no pregnancy group gave double answers (that the treatment process had affected their relationship both to the worse and to the better).

There were no differences between men and women in either the pregnancy group or the no pregnancy group in answers to the questions: “Do you believe that your partner understood your feelings and provided emotional support?” “Do you think you understood your partner’s feelings and provided emotional support?” The majority of the couples felt that they understood and

could support each other, but in about 20 percent of the couples either the woman or the man or both answered “no” to these questions, and more women in the pregnancy group than in the no pregnancy group gave a negative answer.

In response to the question: “How much time have you and your spouse spent talking about the treatment?” the majority answered that they had spent a great deal of time talking to each other, and only two women and two men answered that they had not talked about it at all.

Most couples wrote in their personal comments that their relationship had always been close, and that the treatment process had brought them even closer.

One woman described her relationship like this:

“It feels like we have chosen each other, with or without children. We have talked so much with each other and gone through so much together and we have gotten to know each other in a new way, at a deeper level.”

“There are also things that have been damaged under certain periods of the treatment, our sex life, for example. But looking back I think even this had benefits. Now we can talk more openly about sex, and we know that things can be sorted out in a relationship if you just listen to each other and let it take time...”

Conclusions

Infertile couples undergoing their first IVF treatment are generally well-adjusted and can cope with the strain of treatment. Most couples who failed to achieve a pregnancy after IVF and experienced the associated

emotional pain were able to manage the attendant crisis in the short term.

Comments

The results clearly illustrate that the emotional reactions of both men and women after their first IVF cycle depend on the result of treatment. Those who failed to become pregnant rated their emotional status as worse, whereas those who became pregnant rated their emotional status as better than before treatment started. The women reported stronger emotional reactions about their infertility than their partners on all three measurement occasions. However, the pattern of reaction was similar for both spouses. When pregnancy was not achieved, the men reported their emotional status as worse on the third measurement occasion than on the first occasion, in a similar way to their partners. Some other studies have also found the same pattern in men's and women's reactions to infertility and treatment, although women have stronger reactions (Baram *et al.*, 1988; Boivin *et al.*, 1998a). Newton *et al.* (1990) found a significant increase in anxiety and depressive symptoms in both men and women after a first failed IVF cycle, although mean depression scores remained within the normal range.

Most studies, however, conclude that infertility and its treatments is a more stressful experience for women than for men (Greil, 1997; Jordan and Revenson, 1999; Hjelmstedt *et al.*, 1999; Verhaak *et al.*, 2005; Chachamovich *et al.*, 2010).

Women tend to be the focus of infertility studies, also in psychosocial infertility studies including both partners. Women are the more exposed partner during treatment

and men may see their role more as the supporting partner than as a participant in their own right. Men see their own problems as subordinate to the women's problems (Mahlstedt, 1994; Wirtberg, 1992), and this might have influenced the men's answers, despite the fact that they responded individually and anonymously.

IVF treatment did not have any negative influence on most of the couple's relationships during the period studied, regardless of the outcome of treatment. Instead, most couples were supportive and close to each other during and immediately after the IVF treatment. Men and women reported more variation in their view of the relationship before than after treatment. At the time of treatment relations seemed strengthened because of the treatment process. This finding is supported by other studies. Schmidt *et al.*, (2005) reported in a large epidemiological study that infertility patients frequently experienced high marital benefit, both before their first treatment and at follow-up twelve months later. Two-thirds of the participants reported that the infertility process had strengthened their relations and brought the partners closer together. Hjelmstedt *et al.* (1999) also found couples seeking IVF or ICSI treatment reported that their relationship had improved, because the problems related to the infertility had resulted in greater emotional intimacy. Some previous studies investigating couples undergoing other fertility treatments than IVF reported deterioration in marital relationships and increased sexual problems with repeated failures to conceive (Möller and Fällström, 1991; Lalos, 1985). Other studies investigating couples undergoing IVF treatments in the same space of time, found positive effects on the marital

relationship in regard to communication, support and closeness, both before IVF treatment (Hearn *et al.*, 1987) and after unsuccessful IVF (Baram *et al.*, 1988). More recent studies find couples stable in their relationships irrespective of the IVF results, even in the longer term (Hammarberg *et al.*, 2001; Sydsjö *et al.*, 2005; 2011). Wischmann *et al.* (2012) reports in a ten year follow-up study good psychological adjustments in both childless couples and parents after IVF treatments, with no statistically significant differences regarding overall life satisfaction, satisfaction with relationship with partner and sexual satisfaction.

We only studied the couples prior to and shortly after their first treatment, a period when the treatments still represent the possibility of a child and before the couples have been affected by the strain of further treatments. Some earlier studies report increased emotional strain and depression after long-term treatment (Berg and Wilson, 1991; Beaurepaire *et al.*, 1994) while Verhaak *et al.* (2007b) in a long-term follow up study found most women adjusted well psychologically after unsuccessful IVF. However, in a follow-up study four to five years after terminated IVF treatments, Johansson *et al.* (2009) found quality of life significantly lower among childless couples than couples who had undergone successful IVF, although there was no significant difference in the quality of life between women and men in the childless group (Johansson *et al.*, 2010).

Despite the short-term perspective of this study, it is good news that we did not find that the treatment resulted in harmful reactions. Even one hour before oocyte aspiration, a time we know is demanding and

frightening for some patients, the mean figures on the subscale measuring the effects of infertility were low, indicating relative psychological well-being. We regarded this as a positive evaluation of the care and support given by the staff during treatment. However, it could of course also indicate the lack of sensitivity of the measurement scales. Our findings are positive, in the sense that being infertile today does not seem to be very threatening to individuals' quality of life, at least not initially when starting IVF treatments. But the positive answers may also reflect a tendency to give positive answers to these kinds of psychological questions. Our impression was that most of the participants wanted to give as many true answers as possible in a situation that was of great importance to them. On the other hand, they probably also wanted to give a balanced impression as good future parents and good patients, at least at the start of the treatment, which might have influenced them to minimize problems.

The questionnaire consists of several measurements. Except for the validated instrument PGWB measuring general feelings of well-being, the other measurements were constructed specifically to address infertility and its treatment, and were mainly based on experience from clinical practice and research. The questionnaire was constructed to examine aspects of infertility as a threat towards identity, relationship with partner and social life. When investigating quality of life in relation to infertility, a strength of this study may be seen as its covering core aspects of infertility and its treatment, and not only general well-being. The main limitation of the questionnaire used in the study is that the majorities of the measurements were only partly validated, or

not validated, instruments. It is also possible that some of the significant differences found in this study are chance findings because of several comparisons which were performed without adjustment for multiple comparisons.

Paper II

The psychological influence of gender infertility diagnoses among men about to start IVF or ICSI treatment using their own sperm

Before treatment

Quality of life

Health-related quality of life, measured as psychological well-being using the Psychological General Well-Being Index (PGWB), indicated good psychological health both for men in the male infertility group and men in the female/mixed/unknown infertility group. There were no significant differences between the two groups concerning depressed mood, anxiety, positive well-being, self-control, general health or vitality before treatment (Table 3).

Men in both groups reported their quality of life to be good when comparing how they wished life to be with how it actually was. The aspects asked about were work, leisure time, contact with friends and relatives, their sex life and life in general. The only difference was found in contact with friends and acquaintances, where men in the male infertility group reported less congruence

between ideal life and real life than men in the female/mixed/unknown infertility group. Men in both groups reported a high level of agreement between their expectations and the reality of their relationships with their partners.

Regarding the outlook on life and results of treatment, there was no difference between the men in the male infertility group and the men in the female/mixed/unknown infertility group. Both groups had quite an optimistic attitude.

Experiences of infertility

No differences were found in perceptions of the meaning of reproduction. Men in both groups valued the need to have a child in order to feel happiness, to experience life as meaningful and to have goals in life fulfilled, in a similar way. The mean values for these were 5.1 to 5.9 on a visual analogue scale 0 to 10. The need to have a child to feel like a man among men was graded lower by all the men as 3.9 to 4.4.

Both groups reported that their parents, parents-in-law, relatives and friends had very little influence on their own attitudes toward childlessness. However the men in both groups rated the importance to their parents that they had children as high.

No significant differences were found between the groups when analysing the 14 items measuring the effects of infertility. The mean scores in both groups were low, indicating high levels of well-being.

Table 3. General psychological well-being as evaluated using the Psychological General Well-Being Index (PGWB) Graded 1-6.

	Male factor (n=65)	Female/mixed/ unknown factors (n= 101)	P- value
Depressed mood	16.4 (2.0)	16.4 (1.8)	0.629
Anxiety	23.9 (3.7)	23.3 (3.7)	0.295
Positive well-being	17.4 (3.2)	17.7 (2.6)	0.765
Self-control	15.6 (2.0)	15.7 (1.8)	0.844
General health	16.1 (1.9)	16.1 (2.2)	0.538
Vitality	17.4 (2.8)	17.5 (3.0)	0.667
Total score 1-22	106.8 (12.5)	106.8 (11.5)	0.843

Values are means, SDs and P-values. (Possible range of total score 22-132). High score indicates high levels of well-being.

In the stepwise multiple linear regression analysis, the variables working ($p=0.005$), part-time job ($p=0.008$), high score on PGWB ($p<0.000$) little influence of the attitudes of parents ($p=0.001$) and good accord between the ideal life and the real-life situation in relation in general with partner ($p=0.034$) showed significant positive correlations with low scores on the dependent variable “The effects of infertility”. The variable male infertility showed no independent correlation. Thus well-being, as measures by “The effects of infertility” was not significantly influenced by male factor infertility when adjusting for possible confounders.

During treatment

The day of oocyte aspiration for women and of giving a sperm sample for men is a day we would expect to be especially stressful for men with male infertility. With regard to the answers to the 14 items in “The effects of infertility” subscale, we did not find any significant differences in the answers given in the two groups this day.

Reactions after failed treatment

Two weeks after the pregnancy test after the first treatment cycle, the men answered the third questionnaire and a subgroup analysis was performed on the men in couples where no pregnancy was achieved. There were 41 men in the male infertility group and 67 men in the female/mixed/unknown infertility group. Small differences were found between the groups in this analysis, in both directions. Thus even after failure to achieve a pregnancy we found no indication that men with male factor infertility reacted more negatively than men in couples with other types of infertility.

There was no difference between the two groups in understanding and supporting partners during treatment. The majority (approximately 90 percent) of the men felt that they understood and could support their partners and that they received support and understanding from them. (Unpublished results).

The majority of men were open with family and close friends about their infertility and treatment (approximately 70 percent). Quite unexpectedly, the men in the male infertility group were open with their work colleagues about their childlessness (54 percent) to a significantly higher extent ($p=0.025$) than the men in female/mixed/unknown infertility group (29 percent). Men in the male infertility group had also informed their colleagues about their infertility treatment to a significantly higher extent ($p=0.048$). (Unpublished results)

Approximately 9 percent of all the men in this subgroup had experience of contact with a psychologist or other professional counsellor. Of those with no experience of such contact, 24 percent of the men in the male infertility group and 33 percent of the men in the female/mixed/unknown infertility group answered that they thought such contact would have been valuable.

Conclusions

A diagnosis of male infertility does not influence men's experience of infertility, view of life, relationship or psychological well-being at the time of the first IVF/ICSI treatment cycle. Men in couples where the fertility problem is of female or unexplained origin share the same scores. Men with the diagnosis of infertility are generally well-adjusted before they start their first infertility treatment, regardless of which partner has the infertility diagnosis.

Comments

The main findings of this study indicate no evidence for the hypothesis that male infertility influences men more negatively than men in couples with female/mixed/unknown infertility. We found that

men with the diagnosis male factor infertility reacted in a similar way as men in couples where the infertility was of female, mixed or unknown origin. Our findings are similar to previous prospective findings (Boivin *et al.*, 1998b; Dhillon *et al.*, 2000; Pook *et al.*, 2002; Pook and Krause, 2005). Hjelmstedt (1999) found that the cause of origin of the infertility had no effects on emotional reactions to infertility among either men or women. This finding is also supported in a literature review by Greil (1997).

Before the introduction of ICSI (Palermo *et al.*, 1992) some studies indicated that infertility affected men diagnosed with male factor infertility more negatively than it affected men in couples with female/mixed/unknown infertility (Connolly *et al.*, 1987; 1992; Naghtigall *et al.*, 1992). An explanation for not finding any differences among the men in couples with different infertility diagnoses could be the fact that male infertility is no longer synonymous with being unable to father a genetic child. The main problem - childlessness - and the possible solution - treatment - is the same for all the men studied, regardless of infertility reason. It is obvious that the introduction of ICSI has revolutionized the treatment of couples who are childless due to male infertility, and thereby probably also improved the psychological well-being of men with fertility issues. It could, however, be worth studying infertile men with azoospermia whose partners are about to undergo donor insemination or donor IVF. In a prospective study Indekeu *et al.* (2012) compared motives for parenthood, well-being and disclosure patterns between men in couples undergoing intra uterine insemination (IUI) where their own sperm was used, and men in couples where donor sperm was

used. They found men using donor semen had higher expectations of parenthood and reported less negative effects of infertility on sexuality. However, they also had lower self-esteem and felt more guilt compared to men who produced their own sperm. Men using donor sperm also planned to disclose the method of conception less frequently than men whose own sperm was used.

It is worth noting that in spite of no differences being observed between men with and without male factor infertility diagnoses, and in spite of no severe negative psychological reactions being observed in the subgroup of men studied after failed infertility treatment, 24 percent of the men in the male infertility group and 33 percent of the men in the female/mixed/unknown infertility group with no previous contact with a psychologist thought it would have been useful to receive counselling. Pook *et al.* (2001) suggest that one reason male patients seek counselling is that they feel responsible for the infertility. This may be true, but we interpreted the desire for counselling as a need for support when dealing with infertility and treatment, irrespective of the infertility diagnosis or gender of the patient. Even if the men and women seeking infertility treatment generally seem to function well psychologically, infertility and its treatments are still extremely demanding situations which take a lot of energy for couples to cope with, and they need support.

The reason we did not find any differences between the two groups of men may, of course, have to do with our methods of measurement. The questionnaires used may be more sensitive to female forms of expression. Edelman and Connolly (2000)

found no gender differences when studying response to infertility in infertility investigations, but suggested that: "Differences of this kind may be primarily a function of the methodology adopted, the findings reflecting simply a tendency for women to express their feelings more readily to a stranger than are their partners." (p.372). In an inductive thematic analysis of an online infertility support group for men, Malik and Coulson (2008) examined the male perspective on infertility. When analysing the communication, they found men to experience a range of negative emotions and difficulties as a result of infertility. They suggested that online support groups may be a good way for men to open up about their infertility problems and to freely discuss problems and experiences with other men with similar experiences rather than confining themselves to being the supportive and "silent" partner.

This study investigated only whether a diagnosis of male infertility influences men's experience of infertility at the time of the first IVF/ICSI treatment cycle, a short period when treatment still represents the possibility of a child. The results may be different in a long-term perspective. Pook and Krause (2005) found that distress increases significantly in men after treatment lasting more than 17 months and after experiencing treatment failure, while no impact was identified at the time of the diagnosis of male infertility. They concluded that treatment and the ongoing childlessness were the problems, not the diagnosis.

There is still a lack of studies of men's experience of infertility and treatment. Future research, investigating all aspects of gender roles in contemporary society, is needed.

Paper III

Quality of care in an IVF programme from a patient's perspective: Development of a validated instrument

Exploratory factor analyses

Kaiser-Meyer-Olkin measures of sample adequacy were between 0.62 and 0.81 and Bartlett's test of sphericity was significant with $p < 0.0001$ in the four dimensions, which indicates no objections against explorative factor analysis.

The Exploratory Factor Analysis (EFA) produced the following results. Two underlying factors (subscales) in the QPP dimension Medical technical competence were, "Pain relief and physical care" and "Waiting time". One factor in the dimension, Physical-technical conditions was, "Care room characteristics." Five factors in the dimension, Identity-oriented approach, were, "Information during treatment", "Information after treatment", "Participation", "Responsibility/Continuity", "The Staff's respect/commitment/empathy." One factor in the dimension, Socio-cultural atmosphere was, "Atmosphere and environment". The number of factors chosen for each dimension was based on scree plots.

One item from the original QPP model measuring general medical care in Dimension 1 (Medical-technical conditions) was included as a single item scale. This was because of its overall information "I received the best possible medical care (examinations and treatments) as far as I can tell".

One additional factor, Availability, consisting of the two items, "It was easy to get in contact with the clinic" and "It was easy to get an appointment at the clinic" was

included in the questionnaire despite being outside the four dimensions, because of its content validity and Cronbach's alpha 0.88. The scales built from the items of the factor analysis were calculated using mean score (1 to 4). When rating perceived reality, higher scores correspond to higher quality of care and when rating subjective importance, higher scores mean higher importance. There is no total score.

Descriptive statistics

Descriptive statistics on the QPP-IVF scales are presented as measurements of subjective importance and perceived reality of care, and include both men and women. The ratings of subjective importance were generally numerically higher than the evaluation of perceived reality except for the factor "Atmosphere and environment."

Internal validity

The exploratory factor analysis showed ten underlying factors with scaling success in all subscales and Cronbach's alpha above 0.70 for women in all subscales measuring subjective importance. For men, acceptable Cronbach's alphas, above 0.60 for all subscales, were found except for subjective importance in the factor "Participation" (Cronbach's alpha 0.49). However, the Cronbach's alpha for perceived reality for men was 0.69, so combined with the important content of the factor, it was accepted.

For female participants, the internal consistency of the items within each factor, subjective importance and perceived reality, are presented in Table 4. For men only, Cronbach's alpha of subjective importance and perceived reality are presented and show only small differences when compared to the

Table 4. Item scaling tests. Convergent and Discriminant validity, Scaling success, Reliability Cronbach's alpha for women by QPP-IVF dimensions, both for subjective importance and perceived reality. Cronbach's alpha subjective importance and perceived reality for men.

Dimensions and factors	No of items	Women Subjective importance				Women Perceived reality				Men Subjective importance	Men Perceived reality
		Item Convergent validity*	Item Discriminant validity**	Scaling success***	Cronbach's alpha	Item Convergent validity*	Item Discriminant validity**	Scaling success***	Cronbach's alpha	Cronbach's alpha	Cronbach's alpha
Medical-technical competence											
Medical care	1		0.21 – 0.27	2/2 (100%)			0.21 – 0.42	2/2 (100%)			
Pain relief and physical care	2	0.61 – 0.61	0.18 – 0.41	4/4 (100%)	0.76	0.56 – 0.56	0.15 – 0.50	4/4 (100%)	0.72		
Waiting time	2	0.80 – 0.80	0.19 – 0.40	4/4 (100%)	0.89	0.67 – 0.67	0.17 – 0.22	4/4 (100%)	0.80	0.85	0.88
Physical-technical conditions											
Care room characteristics	3	0.58 – 0.76			0.83	0.51 – 0.67			0.77	0.74	0.69
Identity-oriented approach											
Information during treatment	3	0.53 – 0.67	0.16 – 0.44	12/12 (100%)	0.76	0.41 – 0.53	0.27 – 0.45	12/12 (100%)	0.66	0.73	0.70
Information after treatment	2	0.59 – 0.59	0.14 – 0.38	8/8 (100%)	0.74	0.59 – 0.59	0.30 – 0.47	8/8 (100%)	0.75	0.86	0.81
Participation	2	0.59 – 0.59	0.22 – 0.42	8/8 (100%)	0.74	0.60 – 0.60	0.35 – 0.48	8/8 (100%)	0.75	0.49	0.69
Responsibility/continuity	4	0.63 – 0.72	0.09 – 0.39	16/16 (100%)	0.85	0.54 – 0.60	0.21 – 0.39	16/16 (100%)	0.77	0.84	0.79
Staff's respect/commitment/empathy	6	0.73 – 0.85	0.18 – 0.41	24/24 (100%)	0.93	0.59 – 0.71	0.18 – 0.55	24/24 (100%)	0.86	0.94	0.90
Socio-cultural atmosphere											
Atmosphere and environment	4	0.45 – 0.78			0.80	0.33 – 0.55			0.68	0.75	0.75

Bold indicates dimensions

*Item Convergent validity = Item Internal Consistency = Correlations between each item and its own scale corrected for overlap. (Range of correlations)

**Correlations between the items within the scale with the other scale. (Range of correlations)

***A scaling success is counted if the item to the own-scale was significantly ($p < 0.05$) higher than the correlations with other scales

women. All items showed significantly ($p < 0.05$) higher correlation to their own scale, corrected for overlap, than to all other subscales in the same QPP-dimension (scaling success). Scaling success was obtained in all subscales for both women and men and provided evidence that the subscales were measuring separate, although related, factors of quality of care in infertility treatment.

Of the 49 items derived from the initial content validity process, 30 items for women and 29 items for men remained after the factor analysis and internal validity process. Items were excluded mainly because of too much missing data, an evaluation of little or no importance by the participants or a too high correlation with other items. Two items were merged into one question; “I had examinations and interviews with doctors in private without disturbance” and, “I had examinations and interviews with midwives in private without disturbance.” Both had factor loadings of 0.93 and Pearson Correlation Coefficients of 0.90 between items and subscale, indicating that they measured the same option. In the final version they were therefore merged into one question, “I had examinations and interviews in private without disturbance.”

External validity: scale convergent validity

Convergent validity as a part of construct validity was analysed by estimating the correlation between QPP-IVF and FertiQoL using the Pearson correlation coefficient. Only women ($n=76$) answered the FertiQoL treatment module because the questionnaire is mainly directed at women.

The Optional Treatment FertiQoL module consists of ten items divided into two subscales; the Environment scale, where items reflect effects related to the treatment environment (e.g. access, quality, interactions with staff) and the Treatment tolerability scale, where items reflect effects due to consequences of treatment (e.g. physical effects, mood changes, daily disruptions). As expected, we found quite strong correlations (Pearson's correlation) between FertiQoL treatment environment scale and the QPP-IVF factors “Medical care” (0.46), “Information during treatment” (0.53), “Staff's respect/commitment/empathy” (0.67) and the factor, “Atmosphere and environment” (0.70). We had also expected a rather strong correlation between FertiQoL treatment and the factor, “Information after treatment”, but instead the correlation was weak (0.31). The correlations between FertiQoL and the other factors were as estimated.

Reliability

The results from the test-retest reliability analysis for perceived reality were estimated as the distribution of the change, intra-individual SD (s_w) and Intraclass Correlation Coefficient (ICC) for the subscales. Intraclass Correlation Coefficients (ICC) was satisfactory, with all factors above 0.60 for women. The subscale, “Information during treatment’ decreased significantly ($p=0.04$) between test and retest, mean change = -0.12 (SD 0.41), and the subscale “Responsibility/Continuity” increased significantly ($p=0.04$), mean change=0.15 (SD 0.51). For men, the result of the test-retest was acceptable with ICC above 0.60 for all factors except the factor “Responsibility/continuity” (0.52) and the factor “Availability” (0.57).

For the single item, “Medical care” weighted kappa was 0.64 for women with 78.9 percent agreement and no systematic changes were found ($p=1.00$). For men, the single item, “Medical care” weighted kappa was 0.69 with 85 percent agreement, and systematic changes cannot be excluded ($p=0.22$).

Sensitivity analyses

Known group comparisons were performed by dichotomizing the following additional three questions and comparing the sub-scales between the two groups: “Would you want to visit this clinic again (for future care needs)?”, “How would you rate your physical health now?” and “How would you rate your psychological well-being now?” Low scores on these three questions were associated with significantly lower scores in the majority of all subscales of QPP-IVF for both women and men, indicating a sensitive instrument. For the eleven men rating psychological well-being as bad, significantly lower scores were found on all subscales except “Care room characteristics”, “Information after treatment” and “Responsibility/Continuity.” Concerning physical health, only two men reported low ratings.

Conclusions

We have developed an instrument from the patient’s perspective, for both women and men, measuring the quality of care specific to IVF treatments. It is usable in making quality improvements and suitable for making national comparisons. The QPP-IVF is theory-based and has its roots in a patient perspective. The instrument has been psychometrically tested and validated.

Comments

In total, the final questionnaire consists of 43 items for women and 42 items for men. Apart from the 30 items for women and 29 items for men remaining after the factor analysis and internal validity process, the questionnaire contained 12 additional questions concerning background, general questions and open-ended questions. All items in the final questionnaire are presented in the Appendix.

Items were excluded mainly because of missing data, evaluated as being of little or no importance by the participants, or being too closely correlated to other items. Three of the items which were excluded from the statistical analyses because of psychometric difficulties (the majority answering the “not applicable” response alternative), will still be present in the questionnaire because of their important content (Souter *et al.*, 1998; Hammarberg *et al.*, 2001; Schmidt *et al.*, 2003b; Mourad *et al.*, 2010) “I had easy access to a psychologist if I needed it”, “I received good information about the reason why I did not get embryo transfer” and “I had good access to support after receiving this information.”

The external validity of the instrument was evaluated by comparing calculated Pearson’s correlation coefficient between the subscales of QPP-IVF and the Optional Treatment FertiQoL module with the expected correlations. The FertiQoL treatment module consists of two subscales, indexing treatment environment and treatment tolerability.

A recent large multi-centre study has shown a strong association between a high level of patient-centred care and favourable Ferti-QoL scores (Arts *et al.*, 2011), which made us assume that the instrument would be suitable for comparisons with QPP-IVF as well. As hypothesized, the QPP-IVF subscales correlated more strongly with the subscale environment than the complete treatment module. This was probably because of the personal, emotional approach of FertiQoL treatment tolerability subscale and the concrete approach of the QPP-IVF design. As expected, we found strong correlations between the FertiQoL Treatment Environment scale and the QPP-IVF subscales “Information during treatment”, “Staff’s respect/commitment/ empathy” and “Atmosphere and environment.” The single item “Medical care” correlated more strongly to the Optional Treatment FertiQoL module than the FertiQoL Environment subscale. This may be due to its overall character compared to the other subscales in QPP-IVF. We found an unexpectedly weak correlation between the QPP-IVF subscale “Information after treatment” and the FertiQoL Treatment Environment scale (0.31), which we have no explanation for. All subscales of QPP-IVF and the Optional Treatment FertiQoL module had significant correlations, except (as expected) the subscale “Waiting time,” indicating satisfactory external validity.

Reliability was examined by test-retest analysis of perceived reality, confirming a stable instrument with Intraclass Correlation Coefficients from 0.74 to 0.89 for women. The Correlation Coefficients were somewhat lower for men, but still acceptable. We considered the results of the test-retest satisfactory in respect to reliability, particularly since the time period for

responding was between embryo transfer and the result of the pregnancy test. This period is known to be very stressful for couples (Boivin and Takefman, 1995; Hammarberg *et al.*, 2001; Dancet *et al.*, 2012).

One way to assess the success of efforts to reflect the patient perspective on important dimensions in fertility care is to compare the new version of the QPP-IVF with dimensions of care identified as relevant to fertility patients by others. According to the model of the concept “patient-centred infertility care” (PCIC) from the patient’s perspective (Dancet *et al.*, 2011) the QPP-IVF covers all dimensions of care important from the patient’s perspective, which supports the content validity of the study.

We have developed a patient questionnaire specific to IVF treatments based on the theoretical foundation of the validated general QPP instrument. The items reflect all four quality dimensions which the QPP is based on, and some additional variables. The items are assessed in two ways; (1) ratings of perceived reality as well as (2) the subjective importance ascribed to the content of the given item. Many patient questionnaires observe the association between patients’ expectations and perceived reality. The present questionnaire design assesses the relationship between subjective importance and perceived reality, which in our minds is more relevant, and a major strength of this study. Subjective importance reflects how the person *wants* something to be, whereas expectancy ratings reflect how the person *thinks* it will be. A person may expect the quality of care to be low because of previous experience or poor reputation, and there is therefore a good degree of agreement between expectation and actual outcome,

despite the actual care being perceived as poor. Subjective importance ratings will reveal the discrepancy of needs and reality and is, in our opinion, a better marker when assessing quality of care from the patient's perspective (Wilde *et al.*, 1994). The combining of responses on perceived quality and subjective importance ascribed to the various aspects of care, offers the provider better guidelines, indicating which quality processes are in need of improvement. This concept has also recently been tested and validated in the Netherlands in the patient-centeredness questionnaire on infertility (PCQ-infertility) developed by van Empel *et al.* (2010b). The PCQ infertility questionnaire measures patients' specific experiences with one "experience item" and one "importance item" for each care aspect. The PCQ infertility questionnaire is designed for couples to answer together, while the QPP-IVF instrument is constructed for women and men to respond to separately.

A strength of the QPP-IVF instrument is that the questionnaire addresses women and men equally, as individuals with their own experiences of fertility care. Men are often the forgotten partners in IVF treatments and the vast majority of studies in the area of infertility focus only on women. There is a need to include men in future research (Dancet *et al.*, 2010; Verhaak *et al.*, 2010; Mourad *et al.*, 2010; Aarts *et al.*, 2011) and a need for further investigations into the specific perspective of male patients' perceptions of fertility care (van Empel *et al.*, 2010a; Boivin *et al.*, 2011).

Some limitations need to be discussed. First, only participants with adequate fluency in the Swedish language participated in the study, which limits the concept "quality of

care" to Swedish norms only. It was regarded as too complicated to include a proper translation process in the initial validation process of the questionnaire in this study. Further development of the instrument should address availability of other languages and establish the QPP-IVF as a valuable instrument for quality of care outside Sweden.

Another limitation of the study is the response rate for women of 74.2% compared to 60.6% for men. Although considered an acceptable response rate in questionnaire studies, this discrepancy might introduce a certain risk of selection bias. The reasons why men responded to a lesser degree than women ought to be investigated further.

For practical reasons, we only included heterosexual couples undergoing IVF and ICSI treatments in this study because of the analytical problems with too many subgroups in the validating process. Fertility treatments today offer a number of alternatives, like hormonal treatments, insemination, surgery, gamete donation and treatments for heterosexual as well as lesbian couples. The concept of a web-based instrument, like QPP-IVF, makes the instrument possible to adjust to all groups involved in fertility treatments and further development of the instrument should emphasize this aspect.

Measuring patients' experiences of specific aspects of care rather than overall satisfaction provides good guidance for stimulating quality improvements (Jenkinson *et al.*, 2002; Sofaer and Firminger, 2005; Haagen *et al.*, 2008) and is suitable for performing comparisons of clinics at a national level. The QPP-IVF is now used for

IVF patients at all IVF clinics in Sweden and was implemented in the Swedish National Quality IVF Register (Q-IVF) for the first time in the autumn of 2013. The inclusion of the QPP-IVF instrument in the Q-IVF has made it possible to monitor quality of care on a regular basis, in a similar way as live birth rates and other effectiveness data are monitored. The results are presented on the public website of Q-IVF (www.ucr.uu.se/qivf/).

At a clinical level, the QPP-IVF instrument presents a valuable tool for quality improvements. Future changes in clinical practice will focus on aspects receiving low scores for the rating of perceived reality but high scores for subjective importance.

Paper IV

Patient-centered quality of care in an IVF-programme evaluated by men and women

No significant gender differences were found in demographic variables except for men being significantly older than women ($p < 0.0001$).

Quality of care - factor level – Comparison men and women

QPP-IVF-scales for measurements of subjective importance and perceived reality of aspects of care of all participants (363 women and 292 men) and differences within the couple ($n=251$) are presented in Table 5. When comparing men and women within the couple corrected for age, women rated all factors significantly more important than men except for the factor “Responsibility/continuity”. The factor “Medical care” was given the highest score by both men and women, followed by the factor “Information

after treatment”. The factor “Responsibility/continuity” was given the lowest important rating by both genders.

For perceived reality the differences between women and men were as expected less as for subjective importance. Women evaluated the perceived reality of “Information during treatment” and “Atmosphere and environment” significantly better than their partner while men evaluated “Responsibility and continuity” as significantly better.

Quality of care – item level – Comparison men and women

At item level women rated the majority of items as significantly more important than men. No significant differences in subjective importance between partners in the couple were noted for the items “participation in decisions”, “having the same doctor”, “same midwife/nurse”, “partner well treated” and “pleasant waiting and treatment room.” For perceived reality on item level women scored significantly higher on many items, but men scored significantly higher for the following items: “responsible midwife/ nurse”, “same doctor” and “same midwife/ nurse”.

In the stepwise multiple logistic regression analysis for women the baseline variables "receiving embryo transfer" (adjusted OR 4.32; 95% CI 1.89-9.83, adjusted $p=0,0005$) and "short duration of infertility" (adjusted OR 0.83; 95% CI 0.68-0.998, adjusted $p=0.048$) were independently correlated to the highest score of importance on the factor "Medical care" (Area under the ROC-curve (AUC) = 0.70). “Number of previous cycles” (adjusted OR 1.36; 95% CI 1.16-1.61, adjusted $p=0.0002$) and "IVF as method" (adjusted OR 1.64; 95% CI 1.06-2.54, adjusted $p=0.027$) were independently

Table 5. Comparison of factors with regard to subjective importance and perceived reality, between woman and man within couple.

Variable	Subjective Importance					Perceived Reality				
	Women (n=363)	Men (n=292)	Difference Woman – Man within couple (n=251)			Women (n=363)	Men (n=292)	Difference Woman – Man within couple (n=251)		
				Un- adjusted p-value	Adjusted p-value				Un- adjusted p-value	Adjusted p-value
Medical care (single item)	3.89 (0.34) 4.00 (2.0; 4.0)	3.78 (0.45) 4.00 (2.0; 4.0)	0.120 (0.539) 0.0 (-2.0; 2.0)	0.0004	0.0008	3.54 (0.66) 4.00 (1.0; 4.0)	3.51 (0.65) 4.00 (1.0; 4.0)	0.084 (0.720) 0.0 (-2.0; 2.0)	0.0688	0.1937
Waiting time	3.71 (0.50) 4.00 (1.0; 4.0)	3.52 (0.57) 4.00 (1.0; 4.0)	0.181 (0.758) 0.0 (-3.0; 3.0)	<.0001	<.0001	3.29 (0.90) 4.00 (1.0; 4.0)	3.29 (0.86) 3.50 (1.0; 4.0)	-0.010 (0.875) 0.0 (-3.0; 3.0)	0.9576	0.3716
Information during treatment	3.67 (0.46) 4.00 (1.0; 4.0)	3.29 (0.59) 3.33 (1.0; 4.0)	0.362 (0.745) 0.33 (-2.3; 3.0)	<.0001	<.0001	3.45 (0.55) 3.67 (1.67; 4.0)	3.26 (0.59) 3.33 (1.33; 4.0)	0.194 (0.654) 0.17 (-1.67; 2.67)	<.0001	<.0001
Information after treatment	3.80 (0.41) 4.00 (2.0; 4.0)	3.61 (0.52) 4.00 (1.0; 4.0)	0.139 (0.626) 0.0 (-2.0; 2.0)	0.0017	<.0001	3.22 (0.85) 3.50 (1.0; 4.0)	3.20 (0.80) 3.50 (1.0; 4.0)	0.075 (0.875) 0.0 (-3.0; 3.0)	0.1915	0.3520
Participation	3.43 (0.71) 3.50 (1.0; 4.0)	3.25 (0.68) 3.00 (1.0; 4.0)	0.101 (0.940) 0.0 (-3.0; 2.5)	0.0513	0.0020	2.77 (0.92) 3.00 (1.0; 4.0)	2.87 (0.82) 3.00 (1.0; 4.0)	-0.048 (1.005) 0.0 (-2.5; 3.0)	0.4559	0.1572
Responsibility/Continuity	2.88 (0.79) 3.00 (1.0; 4.0)	2.79 (0.73) 2.88 (1.0; 4.0)	0.019 (0.951) 0.0 (-2.5; 2.3)	0.5750	0.1895	2.04 (0.81) 2.00 (1.0; 4.0)	2.33 (0.84) 2.25 (1.0; 4.0)	-0.283 (0.863) -0.25 (-3.0; 2.5)	<.0001	<.0001
The Staff's respect/commitment/empathy	3.72 (0.43) 4.00 (2.0; 4.0)	3.36 (0.63) 3.33 (1.0; 4.0)	0.339 (0.720) 0.17 (-2.0; 3.0)	<.0001	<.0001	3.55 (0.51) 3.67 (1.33; 4.0)	3.50 (0.54) 3.67 (1.5; 4.0)	0.096 (0.625) 0.0 (-1.8; 2.0)	0.0205	0.0817
Atmosphere and environment	3.55 (0.50) 3.75 (1.5; 4.0)	3.40 (0.47) 3.40 (1.6; 4.0)	0.156 (0.663) 0.05 (-2.5; 2.15)	<.0001	0.0001	3.67 (0.43) 3.75 (1.33; 4.0)	3.53 (0.47) 3.60 (2.0; 4.0)	0.156 (0.496) 0.0 (-1.25; 2.00)	<.0001	<.0001
Availability	3.67 (0.49) 4.00 (2.0; 4.0)	3.51 (0.52) 3.50 (2.0; 4.0)	0.120 (0.725) 0.0 (-2.0; 2.0)	0.0102	0.0009	3.12 (0.88) 3.00 (1.00; 4.0)	3.18 (0.81) 3.00 (1.0; 4.0)	-0.035 (0.905) 0.0 (-3.0; 3.0)	0.5657	0.6086

Mean (SD)/median (min;max) is presented.

Unadjusted analysis: Wilcoxon Signed Rank test.

Adjusted analysis: Repeated measurement ANCOVA applied on Woman vs. Men within couple adjusted for age.

correlated to the highest score of importance on the factor "Participation" (AUC=0.62). Further the "number of previous cycles" (OR 1.19, 95% CI 1.007-1.399) was independently correlated to the highest score on the factor "The staff's respect/commitment/empathy" (AUC =0.54).

Index of measures

The index of measures visualized the most deficient areas in quality of care, rated by both genders as "responsibility/continuity" (responsible doctor, responsible midwife/nurse, same doctor, same midwife/nurse) and "participation" (participation in decisions, my care was determined by my own requests and needs). The best functioning areas were rated as "doctors and midwives/nurses were respectful" and "privacy" (Figure 5).

Women rated aspects concerning "participation", "responsibility/continuity" and "staff's respect/commitment/empathy" as significantly more deficient than men, while men rated "treatment room" and "partner well treated" as significantly more deficient than women (data not shown).

Additional questions

Physical and psychological health

Men rated both their physical health and psychological well-being as significantly higher than women when responding to the questions: "How would you rate your physical health now?", "How would you rate your psychological well-being now?" while no significant gender differences were found in answers to the question: "Would you want to visit this clinic again (for future care needs)?"

Open ended questions

Interesting and extensive information was received from the open-ended questions, both from women and men. A rather striking tendency in men's personal comments was the feeling of being overseen and not included to the same extent as the women. Lack of information, especially concerning sperm samples, unsatisfactory conditions when delivering sperm samples, and a wish that the staff should focus attention equally on both partners during treatment were subjects often mentioned by men. One man expressed his feelings this way:

"...Furthermore, I was ignored as a man in the conversation. The staff talked to my wife and when the conversation was over they looked at me, in silence, and then the conversation continued between the staff and my wife. Honestly, I don't really care but I would rather have been either totally ignored or completely involved. As it was, it just felt ridiculous."

And another man wrote:

"I felt that I was in the way sometimes while my wife was taken care of. It felt sometimes as it was only she who was trying to have a baby and not us. The situation is a little bit sensitive."

Approximately 65 percent of all participants gave comments in response to the open-ended questions, responses that will be analyzed and presented in a separate paper.

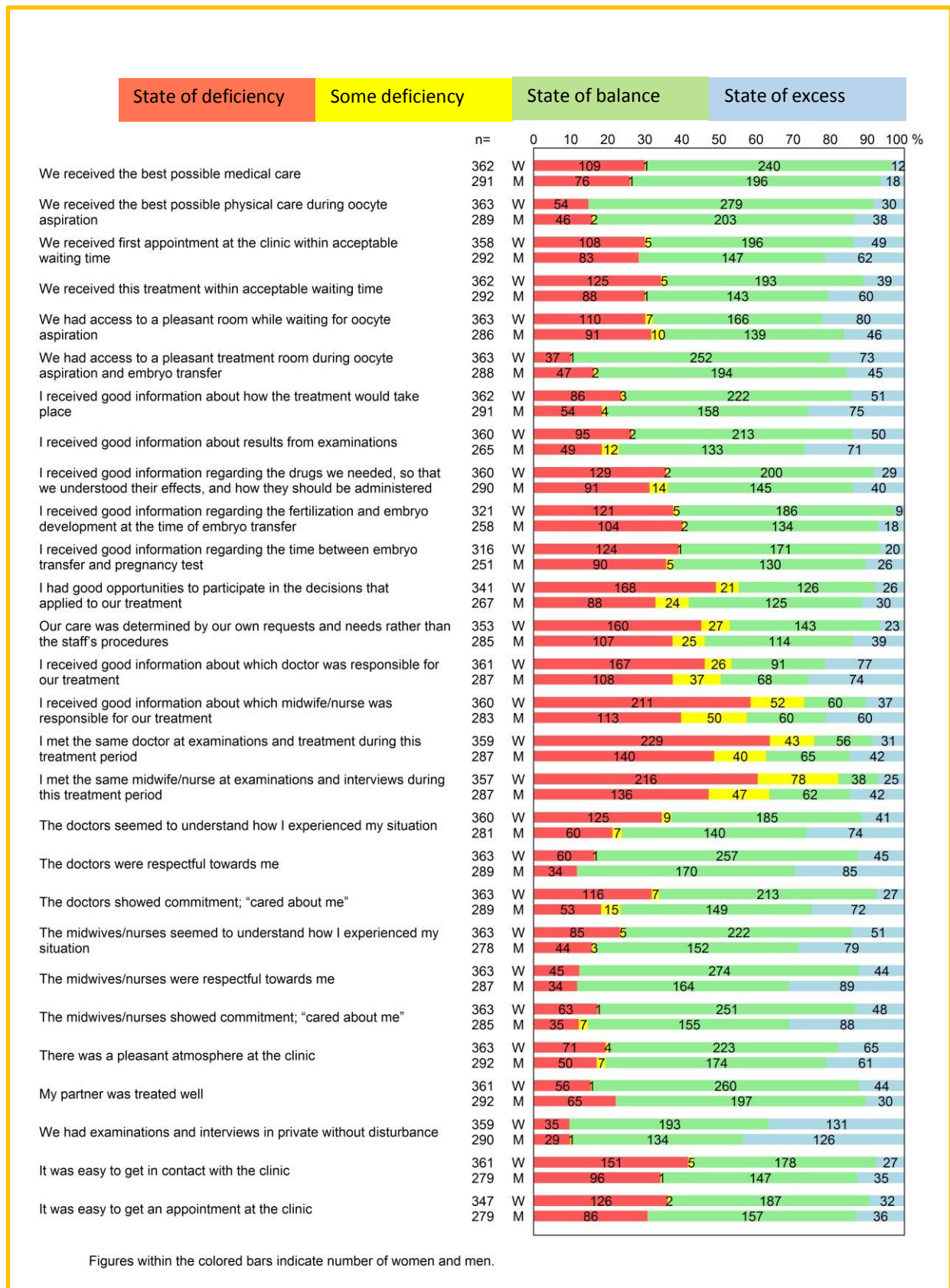


Figure 5. Index of measures.

Conclusions

Women valued most aspects of care as significantly more important than their partners. Men and women evaluated however the importance of the different care factors in a similar pattern. The factors “Medical care” and “Information after treatment” were given the highest importance score by both men and women. Perceived reality for most factors and items was similar rated by men and women in the couples.

Comments

The main finding of this study was that women rated all the aspects of care as more important than their partners. Significant differences between men and women were observed in the ratings of all factors except the factor “Responsibility and continuity”. Men and women evaluated however the importance of the different care factors in a similar pattern.

The overall single item “Medical care” was given the highest importance score by both men and women, followed by the factor “Information after treatment”. Information is reported to be one of the most important aspects of patient-centered care (Souter *et al.*, 1998; Schmidt *et al.*, 2003a; Mourad *et al.*, 2010). When developing the PCIC model, Dancet *et al.* (2011) found that the dimension “Information provision” received the highest importance ratings. In a further international multilingual qualitative study, Dancet *et al.* (2012) found information provision to be a top priority dimension in all patient focus groups. When developing guideline-based indicators of patient-centredness in fertility care, den Breejen *et al.* (2013) found both professionals and patients valued informa-

tion and communication in fertility care as most important.

In the present study the factor “Responsibility and continuity” received the least important ratings of all factors, but also the lowest scores of both men and women when evaluating perceived quality of care. In a qualitative study of patient-centered infertility care from the patient’s perspective, including women and men, Dancet *et al.* (2011) found patients appreciated continuity in staff, but the importance of such continuity differed between patients. In a study of professionals’ perceptions of patients’ experiences of fertility care, Aarts *et al.* (2011) found professionals overestimated the importance of continuity of care. The importance of accessibility, communication, patient involvement and competence was underestimated compared to patients’ ratings. On the other hand, van Empel *et al.* (2010a; 2010b) found that the main weakness in care was related to continuity of care and emotional support.

Perceived reality for most factors and items was similar rated by men and women in the couples. The factor “Atmosphere and environment” received the best ratings from both men and women followed of “The staff’s respect/commitment/empathy”. Other studies have also reported the contact with staff to be evaluated as a positive experience (Van Empel *et al.*, 2010b).

While gender differences regarding the psychological impact of IVF treatments have been studied to a great degree, gender differences concerning attitudes to quality of treatment and care have been much less reported. Schmidt *et al.* (2003a) investigated

gender differences in the motivation to seek assisted reproduction, and expectations about medical and psychosocial services, and found no differences between men and women. In a follow-up 12 months later, the participants were satisfied with medical and psychosocial services and there were almost no gender differences (Schmidt *et al.*, 2003b). In a recent study of couple's experiences of fertility care, measured with the PCQ-Infertility instrument (Huppelschoten *et al.*, 2013b) only slight differences between women and their partners were found. The results in the present study are consistent with the results of an earlier study of patients receiving medical and surgical care (Wilde Larsson *et al.*, 1999b). When comparing men and women's views on quality of care using the general origin QPP-instrument, women evaluated the importance of various aspects of care higher than men, while perceived care was rated similar by both genders. In the "Index of measures" (Figure 5) this pattern is visualized. The index shows that both men and women identified the same issues as in need of improvement, but women generally to a stronger degree than men. The most deficient areas defined by both men and women were items concerning "responsibility/continuity", "meeting the same doctor during treatment" and items concerning "participation." The idea behind the index is that various combinations of responses to the questions, both on subjective importance and perceived reality of aspects of quality of care, should provide guidelines regarding which aspects of quality of care need improvement. The Index has repeatedly been used as a tool for improvement of quality of care in Sweden and the computation and interpretation procedures have successively been refined and simplified over the years (Wilde *et al.*, 1993; 1994; Larson *et al.*, 1998; Wilde

Larsson and Larsson 2002; Larsson and Wilde Larsson 2003; 2004). The index of measures should ideally be used at a clinical level for practical improvements and for comparisons within and between clinics.

The questionnaire had to be answered before the pregnancy test to avoid the responses being influenced by the pregnancy test results. From a "quality of infertility care" point of view it is a deficiency not to have covered the need for support in this important matter. In a study of Dancet *et al.* (2012) investigating patients' views on patient-centred care across Europe, patients reported that they required support especially when they received the negative result of a pregnancy test.

A strength of this study is the use of couple based analyses. Partners in the couple are not independent of each other and a couple based analyses seems to give more trustworthy results when investigating similarities and differences in men and women's view of patient-centered fertility care.

A limitation of this study is the lower response rate of men compared to women (60.6 percent versus 74.2 percent), which may have influenced the results through selection bias. The lower response of men is a well-known problem in all surveys about fertility, and an explanation may be that IVF treatments are still directed more to women than men. Another limitation is that only patients who had adequate fluency in the Swedish language participated in the study. This may have disguised important information about different cultural needs in quality of care.

Studies have reported that men feel marginalized and overlooked in fertility care (Schantz *et al.*, 2005; Malik and Coulson 2008; Arts *et al.*, 2011; 2012). A rather striking tendency in men's personal comments in this study was the feeling of being overlooked and not included to the same extent as the women. A lack of information, especially concerning sperm samples, unsatisfactory conditions when

delivering sperm samples, and a wish that the staff should focus attention equally on both partners in treatment, were subjects often mentioned by men. The extensive information received from the open-ended questions indicates the need for qualitative methods and content analyses, as well as quantitative methods to gain a deeper insight into the male experience of infertility and treatments.

General discussion

Methodological issues

Quality of life

In *Papers I* and *II*, in order to investigate the emotional responses related the first IVF treatment of couples and men with a male infertility diagnosis, both a generic validated instrument PGWB, and infertility-related specific instruments, have been used. There were no validated instruments specific to patients undergoing IVF treatments suitable for our purpose at that time. The specific, infertility-related instruments used to gain knowledge about the impact of infertility and described in *Papers I* and *II* were partly developed on the basis of clinical experiences and other studies, and partly from the literature (Connolly *et al.*, 1987; Laffont and Edelman, 1994; Edelman and Connolly, 1998). The lack of proper validated instruments to assess issues of QoL as well as quality of care has also been a problem in other earlier studies. Even if most of the non-validated earlier specific instruments contain the same aspects as recently-validated specific instruments, indicating that they have captured the essential issues of QoL with respect to infertility, the results cannot be fully trusted. The need to develop validated instruments must be emphasized, in order to give trustworthy, reliable and comparable results (Dancet *et al.*, 2010; Boivin *et al.*, 2011).

Quality of care

In the literature, patient satisfaction questionnaires have been criticized because of their lack of sensitivity, power to discriminate, reliability and validity, and for their

extremely positive results (Hyrkäs *et al.*, 2000). In spite of carefully developed and validated instruments many patient satisfaction questionnaires fail to interpret the results and verify positive improvement trends because of the “ceiling effect” (Souter *et al.*, 1998; Hyrkäs *et al.*, 2000; Sofaer and Firminger, 2005; van Empel *et al.*, 2010a). Many studies find patient satisfaction with care in infertility treatments in general to be high (Sabourin *et al.*, 1991; Souter *et al.*, 1998; Haagen *et al.*, 2008; Mourad *et al.*, 2010), probably due to general questions suffering from the “ceiling effect.” Studying the answers given by the participants in *Papers III* and *IV*, the results revealed many aspects of care in need of improvement, and we regard this as proof of the sensitivity and discriminatory power of the QPP-IVF instrument. The use of subjective importance and perceived reality ratings instead of “satisfaction” ratings gives information which are valuable in indicating necessary improvements. It also guarantees, to a certain degree, that the patient perspective on the aspects being assessed is heard. The specific and concrete items in the QPP-IVF and the Index of measure gives practical information about which aspects of care need to be prioritized in clinical improvement projects.

Several factors are assumed to influence patient perspectives on quality of care. Studies have found older patients to be more satisfied with care while young and middle-aged patients are more critical (Hyrkäs *et al.*, 2000; Sofaer and Firminger, 2005) and well-educated people rate their satisfaction with care lower than less educated people

(Hammarberg *et al.*, 2010; Schmidt *et al.*, 2003a; 2003b). Satisfaction rates have been found to depend on the patients' background variables (age, gender, ethnicity, physical and psychological health, education level) or related to how the patient feels at a given moment (Hyrkäs *et al.*, 2000; Sofaer and Firminger, 2005). Fertility patients as a group could be anticipated to be educated at a higher level than the general population, as they are a young group and have generally good physical health. The infertility and its treatment concerns existential issues in their lives and it is not surprising to find their ratings of quality of care, when measured in a specific and concrete way, are quite critical. As a group, they are well-informed compared to other groups seeking health services, and are probably well aware of what to expect from treatments.

Quantitative versus qualitative research

Open-ended questions in contrast to closed questions can give information on patients' experiences on a deeper level, giving more critical and multi-content information (Hyrkäs *et al.*, 2000; Sofaer and Firminger, 2005).

On the other hand, in research associated with a patient satisfaction questionnaire Hyrkäs *et al.* (2000) found the answers to open-ended questions to be short and over positive, with poor content and offering no additional significant information. The authors propose that one explanation for the limited information revealed in the open-ended questions regarding healthcare could be because the patients answered the questionnaire in the clinic before they were discharged and may have tended to express gratitude and satisfaction rather than negative feelings, for fear of consequences. In contrast we found the open-ended answers contributed a lot of

information. Many participants gave long and extensive answers regarding positive and negative experiences of the quality of care and expressed many good ideas for improvements. We regard the chosen time for answering the questionnaire to be optimal, within two weeks after terminated treatment. The web administration of the questionnaire we judged as appropriate for the group studied (*Papers III and IV*) and it was an advantage that the questionnaire was answered at home and not at the clinic. Answers given at a clinic will probably give a higher response rate, but may also lead to superficial and more positive answers because the respondents are still in the clinical environment, creating a feeling of dependence and vulnerability.

The open-ended questions in both the QoL questionnaire used in *Papers I and II* and the quality of care questionnaire used in *Papers III and IV* offered extensive and important information not detected by the standardized questions in the instruments. Qualitative studies gain deeper insight and can thereby reveal important information which remains undetected with quantitative methods (Greil, 1997; Sofaer and Firminger, 2005; Wirthberg *et al.*, 2007; Dancet *et al.*, 2011). Unlike the time-consuming and complex methods used in qualitative studies (e.g. face-to-face interviews and focus groups), self-reported questionnaires are a cheap and easy way of gathering information from large groups. The disadvantage is that, compared to qualitative methods, the information is superficial and general, and influenced and limited by the instrument itself. To capture experiences affecting QoL and quality of care it is necessary to go deeper, using qualitative methods, and wider, using quantitative methods. In a review of the

research on the socio-psychological impact of infertility during the past ten years Greil *et al.* (2010) calls for an integration of the two research traditions. Combining qualitative and quantitative methods in mixed-method research will yield richer, more valid and reliable results, and further investigation of the patient's perspective of quality of life and care related to infertility and its treatment should benefit from closer cooperation between the two scientific methods.

Couple as a dyad or as individuals

There is a risk that ignoring the impact of gender roles may lead to insufficient knowledge about men's experience of infertility. Newton *et al.* (1999) indicated that potential gender differences in coping with infertility, and a potential lack of sensitivity to male concerns may complicate the assessment of infertility related stress. It has been suggested that the needs of men and women in relation to infertility have to be studied and treated separately (Glover *et al.*, 1998; Pook *et al.*, 2001). Previous studies have pointed out the need for counsellors to be aware of specific gender-related experience and to be gender-sensitive (Lalos *et al.*, 1986; Möller and Fällström, 1991; Wirthberg, 1992). In their review of studies of the patient perspective in fertility care, Dancet *et al.* (2010) found only three out of 51 studies focused specifically on the male perspective. This review considered a first step into gaining insight into the experience of fertility care among men to be the distribution of questionnaires separately to women and men. The review also addressed the need for qualitative research into the male perspective of care.

Some recent studies have highlighted the problem of research typically focusing on

individual's reaction to infertility and treatment without an examination of how the partner is reacting to the same conditions (Chachamovich *et al.*, 2009; Huppelschoten *et al.*, 2013). Infertility is a condition experienced by both partners in the couple and couples should be investigated as a single unit rather than individuals to capture the intra-couple effects. Chahamovic *et al.* (2009) found congruence regarding quality of life among infertile men and women in couple-based analysis measuring QoL with a generic QoL instrument, and suggests offering interventions to them as a dyad. However, when measuring the couple from a dyadic perspective using fertility specific instruments (FertiQoL and SCREENIVF) Huppelschoten *et al.* (2013a) found women had lower levels of QoL and more risk factors for emotional problems during and after treatment than their partners. In a systematic review of quality of life and health-related quality of life, Chachamovich *et al.* (2010) addressed the need for studies of the intra-couple effects of infertility, suggesting that intervention strategies should include both individual and couple approaches. Peterson *et al.* (2011) also used the couple as a unit of analysis to examine marital benefits experienced by men and women who were undergoing unsuccessful treatments. The same concept of using the couple as a dyad was used in a study of the association of severe pre-existing depressive symptoms and infertility distress (Peterson *et al.*, 2014), and the authors call for more studies at the dyadic level to better understand the complete picture of the infertility experiences. The PCQ-infertility questionnaire measuring patient-centeredness in fertility care (van Empel *et al.*, 2010a) was also developed for couples to answer together, rather than women and men

answering separately, thus capturing the dyadic view of patient-centeredness in fertility care. Huppelschoten *et al.* (2013b) have recently evaluated the level of patient-centered fertility care within the couple by the use of the PCQ-infertility questionnaire. They found only small differences in the evaluation of care between women and their partners indicating overall experiences with infertility care to be equal. The findings of a similar pattern regarding QoL and quality of care in relation to IVF treatments in our studies could also support the idea of assessing the couple as a dyad. With regard to the extensive literature stating significant differences between men and women's emotional reactions to infertility and treatment, we still find it important to study both the individual and the couples' responses to multi-dimensional experiences of infertility and treatments. In a meta-analysis of gender differences in coping with infertility, Jordan and Revenson (1999) concluded that there are more similarities than differences and that "it is important to understand the psychosocial issues in infertility from the woman's, the man's *and*, the couple's experience" (page 355).

The need for counselling

In spite of the results finding infertile couples undergoing their first IVF treatment are generally well adjusted and able to cope with the strain of treatment, we found approximately five percent of the couples in our study had very poor emotional statuses, even at the first measurement, before starting their treatment (*Paper I*). These persons reported serious problems in all fields studied: relationships, well-being, treatment, and view of a possible future without children, at all three measurements. Edelmann and Connolly (1998) found

participants with high initial scores on the psychometric measures more likely to show significant increases in distress/strain scores during a medical infertility investigation. Litt *et al.* (1992) reported that women with depressive symptoms prior to IVF treatment had the poorest rates of adaption to IVF failure and Newton *et al.* (1990) also found pre-existing anxiety and depressive symptoms in both women and men to be the most important predictors of anxiety and depression after failed IVF. Peterson *et al.* (2014) found severe depression symptoms prior to infertility treatment to be significantly associated with increased infertility-related stress at both the individual and partner level. It is of great importance to develop methods to identify these individuals early and offer them professional help (Fekkes *et al.*, 2003; Verhaak *et al.*, 2005: 2010; Volgsten *et al.*, 2008; Lund *et al.*, 2009; Klemetti *et al.*, 2010; Van den Broeck *et al.*, 2010; Wichman *et al.*, 2011; Peterson *et al.*, 2014). In their study "*Why are infertile patients not using psychosocial counselling?*" Boivin *et al.* (1999) found the most distressed patients gave practical reasons, such as not knowing who to contact, as reasons for not consulting a mental health professional even when the clinic had provided such information. The authors suggested that the contact ought to be initiated by the counsellor rather than the patient.

Even if relative well-being was reported by all men in our study (*Paper II*), 24 percent of the men in the male infertility group and 33 percent of the men in the mixed/female/unknown infertility group expressed the need for contact with a psychologist or other professional counsellor. When interviewing 100 infertile men, Laffont and Edelman

(1994) found almost one-quarter prepared to meet with a psychologist. El Kissi *et al.* (2013) found 77 percent of women and 48 percent of men in their study of 100 couples requested concomitant psychological treatment to accompany medical treatment of infertility, and Wischmann *et al.* (2009) reported 72.5 percent of women and 61.8 percent of men as being interested in psychological support during treatment. Hammarberg *et al.* (2010) found the most important source for emotional support by infertile men to be their partner, and the second most important source to be support by clinical staff, and the authors emphasize the importance of clinical staff being aware of their role as a source of emotional support. Support groups are reported by several studies to be the least preferred source of emotional support and information by infertile men (Laffont and Edelman, 1994; Hammarberg *et al.*, 2010; Wischmann, 2013). In a review of studies on counselling with focus on men's needs (Wischmann, 2013) two main questions was addressed: "Do men suffer less from infertility than women or do they suffer at all?" and "What is the psychological impact of male factor infertility on men?" He proposed the difference between men and women in their responses to infertility may reflect more general differences in response to stress rather than being specific to infertility, and that men have more difficulties in communicating their emotions than women. Men prefer an instrumental grieving style to regain a sense of control while women tend to use an intuitive grieving style, associated with an outward expression of feelings. The review concludes that future studies should differentiate between the psychological impact of infertility on women and men, and their respective abilities to communicate

about this distress. Peterson *et al.* (2012) point out the need for counsellors to understand the impact of traditional cultural patterns on gender roles, and how they influence interactions in the couple relationship. Masculinity, for example, is associated with emotional stoicism and interpersonal distance, and femininity associated with interpersonal connection by sharing emotions with others.

Even if both men and women seeking IVF treatment often seem to be functioning well psychologically, infertility is still an existentially demanding situation. Infertile couples generally put quite a lot of energy into reacting to and coping with their infertility, and they need support. (Baram *et al.*, 1988; Möller and Fällström, 1991; Berg and Wilson, 1991; Collins *et al.*, 1992; Laffont and Edelman, 1994; Olivius *et al.*, 1994; Lalos, 1999; Wirtberg *et al.*, 2007). Because of the existential and specific problems related to infertility and its treatment, we find it appropriate to suggest professional counselling as an initial part of infertility treatments for all patients, in order to identify people at risk of developing severe emotional problems.

Peterson *et al.* (2012) suggests a stepwise process in psychosocial care and psychological help to be delivered to patients undergoing fertility treatments, where medical and health professionals deliver infertility counselling services and short-term crisis counselling. Medical doctors and the staff at fertility centers should deliver patient-centered care, while psychotherapists and psychologists should handle severe psychological problems.

Further perspective

In a systematic review and meta-analysis to estimate the rate of compliance with ART, Gameiro *et al.* (2013a) found that most patients were able to comply with three cycles of ART and 78 percent of patients underwent the cycles offered as a part of a typical ART program. They addressed the need of further research, focusing on why patients discontinued treatments.

Several studies show high dropout rates (Smeenk *et al.*, 2004; Olivius *et al.*, 2004; Brandes *et al.*, 2009), indicating a significant factor for discontinuing with infertility treatment to be the considerable physical and psychological burden associated with treatments. In a systematic review of why patients discontinue fertility treatment Gameiro *et al.* (2012) found the most frequent reasons for discontinuing treatment to be postponement of treatment, physical and psychological burdens, relational and personal problems, followed by clinical/organizational problems. Discontinuation of fertility treatments because of psychological burdens or problems at the clinical level must be an prioritized issue for clinics to deal with, both by offering the necessary support for patients to handle the physical and psychological strain of treatment and by organizing the care given at clinics in a more patient-centred way. Recent studies indicate that high quality services can influence patients' intentions to comply with treatment (Boivin *et al.*, 2011; 2012; Aarts *et al.*, 2012; Gameiro *et al.*, 2013b). Pedro *et al.*, (2013) found patient-centred care, including positive experiences regarding information received, respect from staff, competence and continuity in treatment, to be directly associated with higher intentions to comply with infertility treatment. On the other hand,

Huppelschoten *et al.* (2013c) did not find this relationship, although they measured patient experiences of patient-centred care with the same instrument (PCQ-infertility) as Pedro *et al.* (2013), and they concluded that patients' experiences of patient-centred fertility care were not related to drop out. More research, using validated fertility-specific instruments, is needed to investigate the relation between patients' experiences of quality of care and compliance with treatments.

Other factors that can impact on the decision to terminate fertility treatments have recently been investigated. Vassard *et al.* (2012) found aspects of social relations have an impact on the probability of deciding to terminate treatment before the treatment options are exhausted. For women, social support from family significantly decreased the probability of terminating treatment, and for men general support had a similar positive effect. Conflicts with partner or friends increased the probability of terminating treatment for women, while for men problematic communication with the partner had an impact on termination of treatment.

There seems to be a link between QoL and quality of care in both directions. Aarts *et al.* (2012) and Gameiro *et al.* (2013b) found patient-centeredness of fertility care and patients well-being to be related, indicating that improved patient-centred care can have an impact on quality of life and positive well-being. Mourad *et al.* (2010) found mental or general health status to be significant determinants for experiences of, and satisfaction with, fertility care in women. During recent years there has been a growing trend in science towards a more holistic approach to patient experiences of infertility

treatments. In the systematic review of why patients discontinue fertility treatment Gameiro *et al.* (2012) identified predictors of discontinuation, related to *treatment*, to the *clinic* and to the *patient*. They address the need for future studies attempting to explain treatment discontinuation to be theory led and longitudinal to allow causal inference to be made, and to include treatment, clinic and patient-related factors equally. Boivin *et al.* (2012) introduced the concept “*The Integrated Approach to Fertility Care*” which covers perspectives of treatment, clinical and patient factors that influence each other. The authors propose all three factors contribute to discontinuation by adding to the burden of fertility treatment. They propose different interventions to relieve the strain of treatment, such as provision of comprehensive educational material and tailored coping tools, screening to identify highly distressed patients, and improvements in the clinical environment and in medical interventions.

Huppelschoten *et al.* (2013d) found feedback from patients to professionals by means of patient-centred measurements, insufficient on its own to make improvements. The clinical staffs also have to develop insights and change behaviour to improve patient-centred care. The patients’ actual experiences are known to differ considerably from the professionals’ perceptions of their patients’ experiences (Sofaer and Firminger, 2005; Arts *et al.*, 2011a; van Empel *et al.*, 2011; den Breejen *et al.*, 2013). By interviewing gynaecologists, nurses and quality officers Huppelschoten *et al.* (2013d) found four steps necessary for professionals to increase their ability to translate feedback from patients into an optimal quality improvement strategy. The first step is *awareness* about

what the concept patient-centeredness really means – care through the patients’ eyes – and the practical meaning of the definition. The second step, *knowledge* includes actual provision of patient-centred care and recognition of difficulties in daily practice. The third step is *attitude*, which means to believe in improving the level of patient-centeredness. The fourth step, to change *behaviour*, involves the need of specific, concrete and clear feedback from patients, feedback that can easily be translated into improvement plans. Publishing the clinics’ levels of patient-centeredness was mentioned as a way of encouraging improvements, stimulating competition between clinics and hence increasing the medical staffs’ efforts to improve patient-centred care. A committed medical team was found to promote the process of improving patient-centred fertility care while the main obstacle to more patient-centred care was considered to be lack of time.

Further research to understand why patients discontinue treatments is important because besides the emotional suffering for the patients, discontinuation of treatments also reduces the success rate, which means that fewer couples reach their goal of becoming parents. Patients should be well-informed, have the opportunity to discuss values and worries about treatment and receive advice to decide about continuing treatment (Gameiro *et al.*, 2012). The rapid development of new treatment methods e.g. sperm and oocyte donation and PGD, may not only open up opportunities to conceive children. They may also mean new psychological and marital challenges, and even longer, stressful, treatment periods in these individuals’ lives. When is it time to say stop? The end of the treatment period seems more and more

unclear as the options expand. As fertility workers we also have to take responsibility for patients' needs for support in the decision to accept treatment failure, to terminate treatment and change focus towards other goals in life. Verhaak *et al.* (2007a) propose that the adjustment to unsuccessful treatments may involve changing from the coping strategy of behavioural control (seeking treatment) to the strategy of cognitive control (changing goals) and ask the question what the effects of the prospect of another treatment option would have on adaptation to fertility problems. In the review they address the need for further longitudinal research to study the adaptation process. Rita Alesi (2005) describes infertility and its treatment as an emotional roller coaster with every new treatment representing hope but also carrying with it the potential for continued failure. She summarises it this way (page 135): "The grieving process in IVF is often stagnated and chronic, and acceptance and resolution is not psychologically possible until closure is achieved, either by

becoming pregnant and giving birth, or ending infertility treatment and ceasing trying to conceive."

General summary of this thesis

This thesis gives an overview of the multi-dimensional aspects of infertility and treatment with respect to QoL and patient-centered quality of care and shows the development towards a more holistic approach when dealing with infertility and its treatments. The existential aspects are worth deeper illustration, investigation and analysis in order to be fully understood. The thesis also follows the development towards the use of validated instruments, to investigate the concepts of QoL and patient-centered quality of care, in a systematic way. This development makes it possible to achieve trustworthy results that can be compared between clinics over national borders and between different disciplines, and make quality improvements from the patient's perspective possible.

Conclusions from this thesis

- Infertile couples undergoing their first IVF treatment are generally well-adjusted and can cope with the strain of treatment. Most couples who failed to achieve a pregnancy after IVF and experienced the associated emotional pain were able to manage the attendant crisis in the short term.
- At the time of the first IVF/ICSI treatment cycle, a diagnosis of male infertility does not influence men's experience of infertility, view of life, relationship or psychological well-being differently from men in couples where the fertility problem is of female or unexplained origin. Men in this situation are generally well-adjusted before they start their first infertility treatment, regardless of which partner has the infertility diagnosis.
- We have developed an instrument from the patient's perspective, for both women and men, measuring the quality of care specific to IVF treatments. This instrument is both usable for making quality improvements and suitable for making national comparisons. The QPP-IVF is theory-based and has its roots in a patient perspective. The instrument has been psychometrically tested and validated.
- Women valued most aspects of care as significantly more important than their partners. Men and women evaluated however the importance of the different care factors in a similar pattern. The factors "Medical care" and "Information after treatment" were given the highest importance score by both men and women. Perceived reality for most factors and items was similar rated by men and women in the couples.

General Conclusion: The results of these studies support the idea of similar response patterns in men and women, both concerning quality of life and in the view of patient-centered quality of care in relation to IVF treatment.

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Papers I to IV

Appendix

Papers I and II

The Psychological General Well-Being Index

Describe how you feel and have been during the last week....

1. How have you generally felt?
2. Have you been bothered by illness or physical pain?
3. Have you felt depressed?
4. Have you had good control over your behaviour, your thoughts and feelings?
5. Have you felt nervous or anxious?
6. Have you felt energetic, high-spirited and lively?
7. Have you felt sad and downhearted?
8. Have you felt tense?
9. Have you felt happy and satisfied with life?
10. Have you felt healthy enough to do the things you want to or have to do?
11. Have you felt so sad, disheartened or without hope that you wondered about the meaning of everything?
12. Have you felt fresh and alert when waking up?
13. Have you been worried or anxious about your health?
14. Have you felt like you were going out of your mind or losing control over your feelings, thoughts and behaviour?
15. Have you felt your life was full of things that interest you?
16. Have you felt active and energetic or slow and out of sorts?
17. Have you felt anxious, upset or filled with anxiety?
18. Have you felt harmonious and self-confident?
19. Have you felt relaxed and calm or stressed, tense and easily upset?
20. Have you felt happy and unworried?
21. Have you felt tired and worn out?
22. Have you felt stressed, under pressure or that demands on you were too high?

Each item was ranked on a scale of 1 to 6. The higher the value, the better the well-being. The items are divided into six sub scales; *anxiety* (item 5,8,17,19,22) , *depressed mood* (item 3,7,11), *positive well-being* (item 1,6,9,15,20), *self-control* (item 4,14,18), *general health* (item 2,10,13) and *vitality* (item 12,16,21).

(Questionnaire 1)

The strength of the child-wish

1. How important is it to you to have children?
2. To what extent does your childlessness affect you emotionally?
3. How much do you think about your difficulty in having children?
4. To what extent does your childlessness affect your life?

Visual analogue scale 0-10 was used, where 0=not at all and 10=very much.

(Questionnaire 1)

The meaning of reproduction

Do you feel you must have children to be able to feel...

1. satisfied with yourself?
2. that life is meaningful?
3. that your goals in life are fulfilled?
4. like "a man among men?"
5. happy?
6. like a "whole person?"

Visual analogue scale 0-10 where 0=no, not at all and 10=yes, much.
(Questionnaire 1)

The difference between the ideal life and the real-life situation

Do you find a high level of agreement between how you wish your life was and how it actually is concerning...

1. work?
2. leisure time?
3. contact with friends and acquaintances?
4. contact with relatives?
5. relation in general with your partner?
6. your sex life?
7. your life in general?

Visual analogue scale 0-10 was used where 0=very good accord and 10=no accord.
(Questionnaire 1)

Optimism versus pessimism

1. What do you think will be the results of the treatment you are about to begin?
2. How do you describe yourself, as an optimist or a pessimist?

Visual analogue scale 0-10 where 10=absolutely optimistic and 0=absolutely pessimistic.
(Questionnaire 1)

The influence of the attitudes of family and friends toward your childlessness

1. How important do you think it is for your parents that you have children?
2. How much are you influenced by your parents' attitudes?
3. How much are you influenced by your parents-in-laws' attitudes?
4. How much are you influenced by other peoples' (relatives, friends) attitudes to your childlessness?

Visual analogue scale 0-10 where 0=not at all and 10=very much.
(Questionnaire 1)

The effects of infertility

Your childlessness is probably an issue of great significance in your life. You might feel it influences your general well-being in several ways or you might feel you can handle your life well in spite of your childlessness. To learn more about this issue we ask you to rank the extent to which you experience the following feelings on an average day:

1. Guilt
2. Success
3. Anger
4. Contentment
5. Frustration
6. Happiness
7. Isolation
8. Confidence
9. Anxiety
10. Satisfaction
11. Depression
12. Powerlessness
13. Competence
14. Control

Each item was ranked on a scale from 1 – 5. Low values indicate greater well-being. (Questionnaire 1, 2, 3)

Relationship with partner

1. Do you feel your childlessness has caused problems in your marriage?
2. Is talking to each other more difficult now than it was before infertility became an issue?

These items were ranked on a scale of 1-5 (1=not at all, 5=very much). (Questionnaire 1, 2, 3)

The effects of treatment on the respondent's relationship

How has the IVF treatment affected your relationship with your spouse?

1. For the better
2. For the worse
3. No difference

How much time have you and your spouse spent talking about the treatment?

1. No time
 2. A little time
 3. A great deal of time
1. Do you think you believe your spouse understood your feelings?
 2. Could he/she give you emotional support?

3. Do you think you understood your spouse's feelings?
 4. Could you give him/her emotional support?
- (Questionnaire 3)

The need of professional support

1. Have you ever had contact with a psychologist or other professional counsellor to talk about the strain of childlessness?
 2. If not, do you think such contact would have been valuable?
- (Questionnaire 3)

Openness about infertility and treatment

Who knows about your childlessness?

1. Parents
2. Siblings
3. Close friends
4. Other friends
5. Work colleagues

Who knows about your IVF treatment?

1. Parents
 2. Siblings
 3. Close friends
 4. Other friends
 5. Work colleagues
- (Questionnaire 3)

Attitude toward further treatment

1. Do you intend to undergo another treatment?
- (Questionnaire 3)

Paper III and IV Full text of all items in the final questionnaire
The female questionnaire

Dimension 1 Medical-technical competence

Medical care (single item)

I received the best possible medical care (examinations and treatments) as far as I can tell.

Pain Relief and Physical Care (2 items)

I received effective pain relief during oocyte aspiration

I received the best possible physical care during oocyte aspiration (as far as I can tell)

Waiting Time (2 items)

I received my first appointment at the clinic within an acceptable waiting time

I received this treatment within an acceptable waiting time

Dimension 2 Physical-technical conditions**Care room characteristics** (3 items)

I had access to a pleasant room while waiting for oocyte aspiration

I had access to a comfortable bed before and after oocyte aspiration

I had access to a pleasant treatment room during oocyte aspiration and embryo transfer

Dimension 3 Identity-oriented approach**Information during treatment** (3 items)

I received good information about how the treatment would take place

I received good information regarding the drugs I needed, so that I understood their effects, and how they were going to be administered

I received good information about results from examinations (for example ultrasound, hormone and sperm analyses)

Information after treatment (2 items)

I received good information regarding the fertilization and embryo development at the time of embryo transfer

I received good information regarding the time between embryo transfer and pregnancy test

Participation (2 items)

I had good opportunities to participate in the decisions that applied to my treatment

My care was determined by my own requests and needs rather than the staff's procedures

Responsibility/Continuity (4 items)

I received good information about which doctor was responsible for my treatment

I received good information about which midwife was responsible for my treatment

I met the same doctor at examinations and treatment during this treatment period

I met the same midwife at examinations and interviews during this treatment period

The Staff's respect/commitment/empathy (6 items)

The doctors were respectful towards me

The doctors showed commitment; "cared about me"

The doctors seemed to understand how I experienced my situation

The midwives/nurses/laboratory personnel were respectful towards me

The midwives/nurses/laboratory personnel showed commitment; "cared about me"

The midwives/nurses/laboratory personnel seemed to understand how I experienced my situation

Dimension 4 Socio-cultural atmosphere

Atmosphere and environment (3 items)

There was a pleasant atmosphere at the clinic

My partner was treated well

I had examinations and interviews in private without disturbance

Availability (New factor not included in the four dimensions – 2 items)

It was easy to get in contact with the clinic

It was easy to get an appointment at the clinic

Items not included in the factor analysis

I had good opportunities to see a psychologist if I needed*

I received good information about the reason why there was no embryo transfer*

I had good access to support after I received this information*

(*These three items were excluded from the statistical analyses because the majority answered the “not applicable” response alternative, but will still be present in the questionnaire because of their important content.)

Additional questions:

How would you rate your physical health now?

How would you rate your psychological well-being now?

Visiting the clinic – Did you receive your appointment in good time?

If no – How long did you usually have to wait?

Would you want to visit this clinic again (in case of future care needs)?

Did you receive embryo transfer (yes/no)? (This was followed by two sets of two questions, either, (1) “I received good information regarding the fertilization and embryo development at the time of embryo transfer” and “I received good information regarding the time between embryo transfer and pregnancy test,” or (2) “I received good information about the reason why there was no embryo transfer” and “I had good access to support after I received this information”).

Open-ended questions:

If answering “no” to the previous question – What is the reason that you would not like to visit this clinic again (for further care needs)?

I was especially satisfied with:

Suggestions for improvements:

Background questions:

Age

Country of birth

Education

The male questionnaire

The questionnaire for men consists of the same items as for women except for the two statements, “I had access to a comfortable bed before (and after) oocyte aspiration” and “I received effective pain relief during oocyte aspiration.” One additional item, “I had access to an undisturbed environment while delivering sperm sample” has been added to the male questionnaire.

When appropriate, the male questions are formed using, “We” and “My partner” instead of “I” (we had..., my partner received...).