

# Infertility and assisted reproduction in Denmark

## Epidemiology and psychosocial consequences

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### 1. INTRODUCTION

Clinically a couple is considered to be infertile after at least one year without contraception and without pregnancy (Weinberg and Wilcox 1998; Savitz et al. 2002). This thesis is about the epidemiological aspects of infertility; the conceptualizing and measurement of important psychosocial aspects of infertility; and a medical sociological analysis of the associations between these psychosocial variables among women and men in fertility treatment.

#### CHILDLESSNESS

There are many reasons why some people do not become parents. Some are infertile, some do not want children, children can be socially unacceptable and for others alternative life goals are more important. In previous time childlessness was more frequent than today. Among Danish women born 1907/08, 25% had never delivered a child (The Statistical Department 1962). In year 2000 14.0% of all 44-year old women in Denmark had not delivered a child. Further, 22.5% of all 44-year old men in Denmark was not registered as father to a child (Statistics Denmark 2005). These people are not necessarily living in a childless state. Some would have adopted children; some live with partners' children from a previous relationship or have in other ways made a life, which includes living together with children.

#### INFERTILITY AND CARE SEEKING – AN OLD STORY

There have always been couples who were unable to conceive. In Genesis, there is the story about Rachel and Jacob who were involuntary childless. Rachel said to Jacob: "Give me children, or else I die" (Genesis; 30,1). Rachel asked her maid to give her children with Jacob and the maid delivered two sons. This is, probably, one of the first written stories of motherhood surrogacy.

Historians have identified written statements from infertile women and professionals during the last 300 years showing that infertile women had suffered and that they have sought different kinds of treatment in order to become pregnant. The treatments in the 18th century included advice about seeking mutual sexual satisfaction, visits to mineral springs and medical herbs prescribed by midwives. During the 19th century, infertile women were advised to try different diets and to get more exercise and late in that century, fertility treatment included different surgical procedures to the uterus as well as donor insemination (Marsh and Ronner 1996).

Niels Steensen described "the women testes", the ovaries in 1668, and in 1677 Van Leeuwenhoek found spermatozoa when he studied semen in a microscope (Gonzales J, personal communication 2005).

In the 1920's the hormones regulating the menstrual cycle were identified and much more knowledge about it, conception and infertility was gained in the following years. However, during the post-World War II period infertility was still depicted as a product of psychoanalytic causes rooted in women's psychology (Epstein 2003). This author quotes a book about modern women published in 1947 describing how a mature woman without children was considered as "the psychological equivalent of a man without the male organ". When women sought effective fertility treatment, a psychoanalytic framework treated deficiencies lurking in the field of infertility. As society considered an infertile woman a failure, establishing her infertility within the context of her own repressed desires, had the consequence of women no longer being considered unwitting victims but culprits (Epstein 2003).

The ability to fertilize a human ovum outside the female body was first reported in 1944 (Marsch and Ronner 1996). The first baby following an in vitro fertilization was born in 1978 (Steptoe and Edwards 1978). For many years the only treatment of couples with severe male infertility was donor insemination. However, in 1992 the first baby was born after injecting a spermatozoa from a man with reduced sperm quality into an egg (Palermo et al. 1992).

Infertility and care seeking are therefore not new phenomena. What is new is that infertility and assisted reproduction have become issues for an intense public debate and that fertility treatment today has a high success rate, that is pregnancies, livebirths, and satisfied patients (paper IX). Based on the reports from all 20 fertility clinics in Denmark in 2001, Denmark is the European country with the highest number of assisted reproduction cycles compared to the population. In total, 3.9% of national births are children born after IVF (in vitro fertilization), ICSI (intracytoplasmic sperm injection), FER (frozen embryo replacement) or ED (egg donation) (Nyboe Andersen et al. 2005). When insemination treatment is included, it is estimated that around 6% of all children born in Denmark are a result of assisted reproductive technology (ART) (Nyboe Andersen A, personal communication 2005). The deliveries per transfer after IVF or ICSI are 25.0-25.8%, and inseminations result in 15.4-19.9% pregnancies per cycle among women < 40 years (Nyboe Andersen et al. 2005).

#### 1.1 THE EPIDEMIOLOGY OF INFERTILITY

The definition of infertility varies among clinicians, epidemiologists and demographers. Clinicians and epidemiologists use the concept infertility as meaning having difficulties to conceive, that is no conception after at least one year of attempting to achieve a pregnancy (Weinberg and Wilcox 1998; Savitz et al. 2002; Homburg 2005). In 1975 the World Health Organization (WHO) recommended more than 24 months of unprotected intercourse as the preferred definition (WHO 1975). Later WHO changed their infertility definition to a "lack of conception after at least 12 months of unprotected intercourse" (Rowe et al. 1993, p. 7).

Demographers define infertility, as the inability of a non-contracepting, sexually active woman to have a live birth, as collecting complete data about conceptions in population-based studies is difficult. In addition, demographic analyses are often based on secondary data, which contain complete birth histories, but often incomplete or no other information about adverse pregnancy outcomes (Larsen 2005). In many demographic studies, infertility has come to mean no live birth over a certain amount of time, irrespective of whether the couple wanted children or used birth control (Habbema et al. 2004; Homburg 2005).

In this thesis, the concept infertility is used in the clinical and epidemiological way as the non-achievement of a pregnancy after at least one year of attempting to become pregnant.

Primary infertility is the non-achievement of a first pregnancy. Secondary infertility is the non-achievement of a subsequent pregnancy. Further, involuntary childlessness is in this thesis called primary involuntary infecundity, and is defined as having no live birth

when wanting and attempting to have a child. Secondary involuntary infecundity is the non-achievement of a subsequent live birth. Most involuntarily infecund couples are infertile couples. However, couples with for example recurrent spontaneous abortions are possibly fertile (conception after less than one year of attempting a pregnancy) but as the pregnancies are spontaneously terminated before delivery these couples are involuntary infecund.

Until the mid-1980's few population-based studies from the industrialized countries concerning the prevalence of infertility, involuntary infecundity and medical care seeking were published (Rachootin and Olsen 1982; Poston and Kramer 1983; Noack 1984; Hull et al. 1985; Mosher 1985; Hirsch and Mosher 1987; Johnson et al. 1987; Marchbanks et al. 1989; Martin 1989; Page 1989; Sundby and Lund 1989).

In Denmark at that time, only one study had been carried out. Rachootin and Olsen (1981,1982) had in 1979 in a random, population-based study among 709 25-45 year old women researched the prevalence of infertility and medical care seeking. They reported that 16.1% were primary infertile and 16.6% were secondary infertile when the at least one year definition of attempting pregnancy was used. Further, 4.0% of the women were primary, involuntary infecund (Rachootin and Olsen 1982). Less than half of the women had sought medical advice (Rachootin and Olsen 1981).

The epidemiological knowledge about infertility in Denmark was sparse. In addition, fertility treatment had developed substantially during the 1980's. Therefore, we included items about infertility, primary involuntary infecundity and medical care seeking in a large population-based study, The Women and Health Survey. A study conducted in 1989 involving 3743 women age 15-44 years (Münster et al. 1992).

Infertility has previously been measured using different risk populations as the denominator in the infertility prevalence. Rachootin and Olsen (1982) used as the risk population women having attempted at least one conception (for primary infertility) and at least two conceptions (for secondary infertility). Other studies included the complete study population of 20-54 year old women (Marchbanks et al. 1989) or currently married participants exclusive of surgically sterile wives or husbands (Mosher 1985) irrespective of whether these married couples have tried to become parents or not.

In our population-based study the risk population (the denominator of the primary infertility prevalence) consisted of only those participants who had tried to have children up to the time of the survey. We measured both the current prevalence of primary infertility and the life-time prevalence (Kleinbaum et al. 1982) defined as the women who had ever experienced infertility up to the survey irrespective whether they were still infertile or not (paper II).

### **Reproductive outcome**

The overall outcome of fertility treatment is to be measured in a population of fertility patients. However, most of the studies about treatment outcome have been focused either on one single type of fertility treatment or on the outcome within a single diagnostic category (see overview in Collins and Van Steirteghem 2004).

When I in year 2000 launched the prospective cohort, The Infertility Cohort in the Copenhagen Multi-centre Psychosocial Infertility (COMPI) Research Programme, we included data of fertility treatment outcome as well as non-treatment related pregnancies and deliveries. Further, data about adoptions was included. The COMPI cohort included consecutively all new couples (n=2250 participants) entering one of four different public fertility clinics. Therefore, it included all the different diagnosis presented during the data collection period and all the different types of treatment offered during the two follow-up periods (one year and five year).

Collins and Van Steirteghem (2004) reported that during the last 50 years, 20 studies had reported the overall impact of fertility management on conception during a follow-up of one to eight years. The overall average live birth rate in the 11 studies from 1980 and up

to today was 30%. According to Collins and Van Steirteghem (2004) even the most recent reports did not include the results of IVF or ICSI treatments. A previous Danish study included the first 300 couples in IVF-treatment during 1991-1992 at a university hospital fertility clinic. The participants were followed until completion of treatments. In total 47.0% achieved at least one live born child, 31.3% did not achieve a delivery and 13.7% had, themselves, stopped treatment (Rex et al. 1998).

In the Women and Health Survey was included information about subsequent motherhood (deliveries and adoptions) among the infertile women in this study (paper II) as this was not investigated in previous population-based infertility studies.

### **1.2 PSYCHOSOCIAL ASPECTS OF INFERTILITY**

Infertility is a reproductive health problem that is related to a couple. Usually the health care system takes care of individuals having health problems, but with infertility the patient is the couple. The biological causes of infertility relate to either one or both partners or the infertility is unexplained, e.g. no medical diagnosis has been identified.

It is well-known that infertility for many couples causes a serious strain on their interpersonal relationships, as well as personal distress, reduced self-esteem and periods of existential crisis (Wirtberg 1992; Sundby 1994; Abbey et al. 1995; Schmidt 1996; Greil 1997; Tjørnhøj-Thomsen 1999, 2005). 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.

Up to the mid-1990's few longitudinal studies about the psychosocial consequences among couples in fertility treatment existed in the Scandinavian countries (Rosenkvist 1979; Lalos 1985; Möller 1985; Wirtberg 1992). Further, Sundby (1992) has conducted a follow-up study among former female fertility patients. The studies including both men and women all comprised less than 150 participants whereas Sundby's study (1992) included 250 women.

Therefore, I initiated a large prospective five-year cohort study with a main focus on the psychosocial aspects of infertility. It included: (i) fertility problem stress, (ii) marital benefit, (iii) partner communication, (iv) infertility-related communication strategies (ICS), (v) coping strategies, (vi) patients' attitudes to fertility treatment and (vii) patients' evaluation of treatment. See Table 1 for an overview of the psychosocial variables included in the thesis.

#### **(i) Fertility problem stress**

Fertility problem stress measured in three domains shown to be important in previous research: the personal domain, the marital domain and the social domain. We used items developed by Abbey et al. (1991a) as these items were related to all three domains. However, in qualitative interviews with infertile couples I recognised that the fertility problem stress especially among women was different in relation to one own family and to ones family-in-law (Schmidt 1996). In Danish infertile couples, nearly all women and men are actively employed. Therefore, managing the infertility in relation to colleagues is also an important aspect of fertility problem stress. Thus, questions about strain in relation to family-in-law and to colleagues were added in the COMPI questionnaires.

We have analysed whether fertility problem stress was associated with attitudes to and evaluation of treatment (paper VIII, IX). Also, whether fertility problem stress changed after an intervention study with The Communication and Stress Management Training Programme among couples in fertility treatment (paper VI).

#### **(ii) Marital benefit**

Previous qualitative studies among couples in fertility treatment have shown how infertility and treatment simultaneously be seen as a threat or a challenge for the couple. It can also be seen as a situation that can bring the partners closer together and strengthen the

**Table 1.** Overview of the psychosocial variables included in the epidemiological analyses.

The COMPI Fertility Problem Stress Scales	(i) Stress in the personal domain (ii) Stress in the marital domain (iii) Stress in the social domain
The COMPI Marital Benefit Measure	
Partner communication	
Infertility-related Communication Strategies (ICS)	(i) Secrecy (ii) Formal (iii) Open-minded
The COMPI Coping Strategy Scales	(i) Active-avoidance coping (ii) Active-confronting coping (iii) Passive-avoidance coping (iv) Meaning-based coping
Attitudes to treatment	(i) Medical care (ii) Patient-centred care (iii) Professional psychosocial services (iv) Intentions to use psychosocial services
Evaluation of treatment	(i) Medical care (ii) Patient-centred care

marriage (Greil et al. 1988; Schmidt 1996; Tjørnhøj-Thomsen 1999). The interview participants in these studies related that the infertility experience forced partners to talk about existential aspects of life and to talk about the emotional aspects of infertility experience. They also had to master a new terminology to talk about the different type of treatment used in ART to get a child. For half or most of the couples involved in these qualitative studies, the infertility experience had strengthened their marriage and had improved their partners' mutual connection. We have called this effect on marriage "marital benefit". It is defined as the perception that infertility has brought the partners' closer together and strengthened their relationship.

Other infertility studies have measured marital satisfaction (Abbey et al. 1995; Newton et al. 1999; Verhaak 2003). However, marital satisfaction is not identical with the concept marital benefit. Within health services research, satisfaction ratings are defined as a personal evaluation (Sitzia and Wood 1997), while we define marital benefit as an effect and not as an evaluation, a satisfaction rating of the marriage.

We have measured marital benefit in The Infertility Cohort and described how frequently it was, and analysed which communication and coping strategies were predictors of high marital benefit (paper VII). We have analysed how marital benefit was associated with attitudes to and evaluation of treatment (paper VIII, IX), and studied whether marital benefit changed after participation in The Communication and Stress Management Training Programme (paper VI).

### **(iii) Partner communication**

According to Abbey et al. (1995) "the marriage literature has a long tradition of examining elements of marital communication that distinguish distressed from nondistressed marriages. Nondistressed couples exhibit more mutual validation than do distressed couples" (p. 467). A recent study including couples in fertility treatment showed that when husbands were involved in trying to have a baby or wanted to talk with their wives about trying to have a baby, the quality of marital communication when discussing infertility was less negative (Pasch et al. 2002). We have measured difficulties in partner communication in The Infertility Cohort and analysed whether difficult partner communication was a predictor of high fertility problem stress (paper V) or of high marital benefit (paper VII). Further, we measured partner communication in more details in The Communication and Stress Management Training Programme among couples in fertility treatment and analysed changes in partner communication (paper VI).

### **(iv) Infertility-related Communication Strategies (ICS)**

A few previous studies had investigated whether infertile couples talked to people other than their partner about their situation. Abbey et al. (1991b) reported that more women than men had spoken with their friends and family about the fertility problem. Women described more benefits and costs to these interactions than men

did, while men described more reasons to be indifferent to the responses from other people than women did. Van Balen and Trimbos-Kemper (1994) showed among couples with long-term infertility that those 10% of men having the infertility as a secret reported lower well-being.

However, my previous qualitative interview study among infertile couples showed that it was important to investigate whether the couples talked to other people or not, and what they talked or did not talk about to others (Schmidt 1996). Infertility-related communication was in this study categorised into three strategies: an open-minded strategy including sharing both formal information and emotions related to infertility and treatment with other people; a formal strategy where only formal information was shared; and secrecy when the infertility experience was not shared with others.

Based on this result we developed detailed items about communication patterns in the questionnaire for The Infertility Cohort making it possible to describe communication patterns and to analyse whether the different communication strategies were predictors of a high level of fertility problem stress (paper V) or a high level of marital benefit (paper VII). Further, in The Communication and Stress Management Training Programme we investigated whether the participant changed their infertility-related communication strategies (paper VI).

### **(v) Coping strategies**

In the transactional coping model, coping is considered to be a process that starts with an event that is primarily appraised by the individual as either threatening, harmful or challenging (Lazarus and Folkman 1984). We suggested that infertility as a chronic stressor and non-event could be equally harmful as an event. If the problem is seen as being stressful, the person will try to manage it (problem-focused coping) and/or to regulate the distress (emotion-focused coping). Folkman (1997) has revised this model and added meaning-based coping, which includes positive reappraisal of the situation, goal-directed problem-focused coping, spiritual beliefs and practices, and the infusion of ordinary events with a positive meaning.

Most of the previous studies about coping with infertility have used standard scales for measuring coping, e.g. the Ways of Coping Questionnaire (WOCQ) (Folkman and Lazarus 1988; used in Dray et al. 1988; Abbey et al. 1991a; Litt et al. 1992; Stanton et al. 1992; Prattke and Gass-Sternas 1993; Lukse and Vacc 1999; Pook et al. 1999; Dhillon et al. 2000) or the COPE scale (used in Bar-Hava et al. 2001; Berghuis and Stanton 2002; Van den Akker 2005; Verhaak et al. 2005). A meta-analysis of gender differences in coping with infertility using the WOCQ showed that women used significantly more the strategies seeking social support, escape-avoidance, planful problem-solving and positive reappraisal (Jordan and Revenson 1999).

Lazarus and Folkman (1988) and Costa et al. (1996) have recommended that coping should be measured in a relation to a specific

stressor with an instrument developed specifically to measure coping with this stressor. Therefore, we have in The Infertility Cohort developed an infertility-related coping measure from three sources: the 66-item WOCQ (Folkman and Lazarus 1988), Folkman's (1997) later revision with the inclusion of meaning-based coping, and items developed from qualitative interviews with Danish infertile couples (Schmidt 1996) (paper IV).

Only a few of the infertility coping studies have been longitudinal. Most of the longitudinal studies are short-term follow-up studies with the first data collection prior to a treatment attempt and the second data collection one or two weeks after a pregnancy test (Hynes et al. 1992; Litt et al. 1992; Berghuis and Stanton 2002). One study included a third data collection six weeks later (Terry and Hynes 1998). Verhaak (2003; Verhaak et al. 2005) conducted a long-term coping study including three data collections: one before the first IVF/ICSI-treatment attempt, the second after the final cycle and the third six months later.

These longitudinal studies among couples or women in IVF-treatment (Hynes et al. 1992; Litt et al. 1992; Terry and Hynes 1998; Verhaak 2003; Verhaak et al. 2005) and among couples in donor insemination (Berghuis and Stanton 2002) have shown that problem-appraisal strategies were a predictor for better adjustment (Terry and Hynes 1998). Approach-oriented coping (including problem-focused coping, emotional processing, and expression) was related to lower distress (Berghuis and Stanton 2002). Avoidant or escape coping was a predictor of poor adjustment to infertility (Terry and Hynes 1998) and of increased distress after one treatment attempt (Litt et al. 1992; Berghuis and Stanton 2002). Verhaak et al. (2005) found no relationship between problem-focused, active coping and changes in anxiety or depression.

To increase our knowledge about coping strategies and its consequences we studied coping in a one-year follow-up and analysed if the different coping strategies were predictors of a high level of fertility problem stress (paper V) or of high marital benefit (paper VII). Further, we studied whether coping was associated with occupational social class (paper IV) because important elements of coping may be learned from one's membership and reference groups, in the same ways as other behaviours are learned and internalized (Pearlin 1989).

#### ***(vi) and (vii) Patients' attitudes to and evaluation of fertility treatment***

Despite a high number of couples using assisted reproduction, few studies had investigated what medical and psychosocial services infertile people expect from the fertility clinics and how they evaluate fertility treatment.

We separated past research in "expectation studies", i.e. those studies asking infertile patients about their motivations and expectations before they attend treatment, and "service-evaluation studies", where patients rated their evaluation either during or after treatment. We identified a single expectation study (Glover et al. 1999) which included 29 men attending a specialist male subfertility clinic. The most important motivation for seeking treatment was to increase their partner's chance of conceiving.

Prior to our data collection in The Infertility Cohort study we identified service-evaluation studies. These studies included couples in fertility treatment (Sabourin et al. 1991; Wirtberg 1992; Halman et al. 1993; Schmidt 1996), studies including women only (Sundby et al. 1994; Souter et al. 1998) and Glover et al.'s study (1999) including a second data collection among men after having attended infertility investigations. Both men and women were generally satisfied with the medical part of treatment offered (Sabourin et al. 1991; Halman et al. 1993; Schmidt 1996; Souter et al. 1998). The findings were mixed about the way emotional aspects of infertility and its treatment were addressed. Cross-sectional studies among former female patients showed that as many as 85% felt they had not been given emotional support or were dissatisfied with the support given

(Sundby et al. 1994; Souter et al. 1998). In a Canadian longitudinal study, only 19% of the women and 13% of the men were dissatisfied with the emotional support (Sabourin et al. 1991). In semi-structured interview studies, many women and men have expressed both satisfaction and dissatisfaction with attention to the emotional aspects in fertility clinics (Wirtberg 1992; Schmidt 1996).

Higher satisfaction ratings were associated with different medical and organisational aspects: less than 2 years of treatment and child birth (Sundby et al. 1994), treatment at a dedicated fertility clinic, treatment where the male partner attended on at least one occasion and where only one doctor was involved (Souter et al. 1998). In Glover et al.'s study (1999) satisfaction ratings were positive correlated with gaining a clearer understanding of their problem, having questions answered, discussing possible alternatives and help with decision-making. There was no correlation between distress and satisfaction ratings. Halman et al. (1993) analysed psychosocial and medical predictors of high satisfaction. Among men less use of escape coping and having more control were predictors of higher satisfaction ratings, whereas among women having more control and reduced number of treatments were predictors. Sabourin et al. (1991) reported how men and women who were more vulnerable from a social and personal standpoint tended to be less satisfied with the medical services after six months at the fertility clinic.

We have found no studies analysing associations between psychosocial variables and attitudes to fertility treatment, and only sparse knowledge about these variables and evaluation of treatment. Therefore, in this thesis I have focused on (i) fertility problem stress and marital benefit and its association at baseline in The Infertility Cohort with attitudes to treatment (paper VIII) and (ii) in the one-year follow-up of fertility problem stress and marital benefit as predictors of evaluation of medical and patient-centred care (paper IX).

#### ***In conclusion***

Previous studies about psychosocial aspects of infertility have only rarely been carried out in large, long-term prospective studies. Psychosocial predictors of patient satisfaction of fertility treatment have been but sparsely analysed. The reproductive outcome of a large population of consecutively included patients covering all fertility diagnosis and including all types of treatment has rarely been conducted. Population-based studies about infertility, involuntary infecundity, subsequent motherhood and treatment seeking were sparse. Further, important psychosocial variables, e.g. fertility problem stress and coping strategies have most often been measured with standardised questionnaires not specifically developed to measure these variables among people being infertile. The aim of this thesis is to reduce some of these gaps in scientific knowledge.

## **2. PURPOSE OF THE THESIS**

As stated in the Introduction section this thesis is about the epidemiological aspects of infertility, the conceptualizing and measuring of important psychosocial aspects of infertility. Further, a medical sociological analysis of the associations between these psychosocial variables among Danish women and men engaged in fertility treatment.

The thesis has three main purposes:

- (i) To review critically population-based prevalences of infertility, involuntary infecundity and medical care seeking in industrialised countries. Further, to examine these prevalences in a Danish population and to measure subsequent motherhood (e.g., current pregnancies, deliveries and adoptions) among women in former fertility treatment.
- (ii) To develop measures of the psychosocial consequences of infertility: fertility problem stress, marital benefit, partner

communication, infertility-related communication, coping strategies, attitudes to fertility treatment, and evaluation of care.

- (iii) To examine these phenomena among Danish women and men in fertility treatment. Further, to analyse the interrelations between these psychosocial measures.

### 3. MATERIALS AND METHODS

The basis of this thesis is data from four empirical studies:

- (i) The Women and Health Survey (Kvindesundhedsundersøgelsen), a cross-sectional population-based study among women 15-44 years old in Copenhagen County, 1989 (paper II).
- (ii) The Psychosocial Infertility Interview Study, a qualitative interview study among couples engaged in fertility treatment at The Fertility Clinic, Herlev University Hospital, 1992 (paper III).
- (iii) The Infertility Cohort, a longitudinal cohort study including consecutively, all couples beginning a new fertility treatment period at the Fertility Clinics at Brødstrup Hospital; Herlev University Hospital; Odense University Hospital; The Juliane Marie Centre, Rigshospitalet, University of Copenhagen; The Fertility Clinic Trianglen, 2000-2002 (paper IV-V, VII-IX).
- (iv) The Communication and Stress Management Training Programme, an intervention study among couples engaged in fertility treatment at The Fertility Clinic, The Juliane Marie Centre, Rigshospitalet, University of Copenhagen 2001-2003 (paper VI).  
Data from (iii) and (iv) are studies from The Copenhagen Multi-centre Psychosocial Infertility (COMPI) Research Programme (www.compipro.dk).

The author has launched The COMPI Research Programme (iii and iv), and is the Principal Investigator (PI). COMPI is a collaboration between an international, multidisciplinary research group and the

public Fertility Clinics at Brødstrup Hospital; Herlev University Hospital; Odense University Hospital; and The Juliane Marie Centre, Rigshospitalet, University of Copenhagen.

The author designed and conducted The Psychosocial Infertility Interview Study (ii). Gynaecologist Kirstine Münster was PI for the population-based study The Women and Health Survey (i). The methodology in this study was developed in collaboration by the PI, the author and Peter Helm.

Besides the eight papers based on the above-mentioned studies, a literature review (paper I) about the prevalences of infertility, involuntary infecundity and the care seeking of fertility treatment in population-based studies from industrialized countries is included.

The following sections 3.1-3.4 describes each data material in details (design and study population, procedures, data collection, participants and non-participants). The variables regarding the epidemiological studies are presented in section 3.5 followed by a section 3.6 presenting the analyses of the epidemiological data. The analyses of the qualitative data are reported when presenting this study (section 3.2). Table 2 shows an overview of the epidemiological study populations included in the thesis and the determinants and outcomes used in the analyses.

### STUDY POPULATIONS

#### 3.1 THE WOMEN AND HEALTH SURVEY

##### Design and study population

This cross-sectional study comprised a representative, population-based study about infertility, involuntary infecundity, medical care seeking, the menstrual cycle and menarche among women 15-44 years old in Copenhagen County. The collection of data took place in 1989 through a self-administered questionnaire.

##### Procedures

From a list of random numbers, a 2.75% sample was drawn of all the dates of birth of women born between January 1944 and December 1973 in Copenhagen County. This population (n=3743 women)

Table 2. Study populations, determinants, and outcomes in the epidemiological analyses.

Paper	Study population	Determinants	Outcomes
Paper II	The Women and Health Survey. Women 25-44 years n= 1907	Occupational social class	Seeking of fertility treatment
Paper IV	The Infertility Cohort. Study population at baseline n=1169 women, n=1081 men	Occupational social class	The COMPI Coping Strategy Scales
Paper V	The Infertility Cohort. Participants not having achieved pregnancy/delivery after ART during one year n= 441 women, n= 375 men	Partner communication Infertility-related Communication Strategies (ICS) The COMPI Coping Strategy Scales	The COMPI Fertility Problem Stress Scales
Paper VI	The Communication and Stress Management Training Programme. n= 32 women, n= 29 men	Intervention	Changes in: Partner communication Infertility-related Communication Strategies (ICS) The COMPI Coping Strategy Scales The COMPI Fertility Problem Stress Scales The COMPI Marital Benefit Measure
Paper VII	The Infertility Cohort. Participants not having achieved pregnancy/delivery after ART during one year n= 441 women, n= 375 men	Partner communication Infertility-related Communication Strategies (ICS) The COMPI Coping Strategy Scales	The COMPI Marital Benefit Measure
Paper VIII	The Infertility Cohort. Study population at baseline n=1169 women, n=1081 men	The COMPI Fertility Problem Stress Scales The COMPI Marital Benefit Measure	Attitudes to medical care Attitudes to patient-centred care Attitudes to professional psychosocial services Intentions to use psychosocial services
Paper IX	The Infertility Cohort. Study population at baseline and at one-year follow-up n=1025 women, n=909 men	The COMPI Fertility Problem Stress Scales The COMPI Marital Benefit Measure Occupational social class	Evaluation of medical care Evaluation of patient-centred care



received a questionnaire in 1989. Non-responders received up to two written reminders. The PI, gynaecologist Kirstine Münster, collected data.

#### Data collection

The participants completed a questionnaire about reproductive history, infertility, involuntary childlessness, medical care seeking for infertility, menstrual cycle, menarche, lifestyle, life events and socio-demographic data.

#### Participants

Sixty women were excluded from the study because they lived outside Denmark, could not be traced, or were mentally retarded. In total, 78% (n=2865) responded. The average age of having the first child was 26.1 years in 1988 (Statistical Yearbook 1990). Because of this, we restricted the analyses about infertility to the 25-44 year old women (response rate 76%, n=1907). See Table 3 for information about sociodemographic, reproductive and medical characteristics of the 25 to 44 year old study population.

#### Non-participants

Non-participants tended to be older than participants (p=0.093) and significantly more non-participants lived in the lower socio-economic municipalities (p< 0.010). Odds ratio for high occupational social class was 1.9 (95% CI 1.4-2.5) in participants compared to non-participants (Münster et al. 1992). A 27.3% of the non-participants were drawn at random. When possible, the women (n=92) were interviewed by a short, structured telephone interview about fertility treatment, menarche and the menstrual cycle. The infertility prevalence was 11.8% among participants and 6.2% among non-participants (OR=2.0, 95% CI 0.7-5.5) in the age group 25 to 44 years.

### 3.2 THE PSYCHOSOCIAL INFERTILITY INTERVIEW STUDY

#### Design and study population

This study included semi-structured interviews with 16 couples in fertility treatment at The Fertility Clinic, Herlev University Hospital in 1992. The author collected the interviews. The selection of participants was by purposeful sampling with maximum variation (Patton 1987).

**Table 3.** The Women and Health Survey. Sociodemographic and reproductive characteristics of the 25-44 year old participants.

	Women 25-34 years (n= 955) %	Women 35-44 years (n=952) %	p-value <sup>a</sup>
<b>Sociodemographic</b>			
Occupational social class			
High, I+II	18.7	26.7	< 0.001
Medium, III+IV	55.4	55.4	
Low, V	10.6	8.6	
Outside classification	15.3	9.3	
<b>Reproductive</b>			
Having achieved at least			
one pregnancy	78.0	93.0	< 0.001
Having achieved at least			
one delivery	66.7	89.4	< 0.001
Current pregnancy	6.5	0.6	< 0.001
Have not yet attempted to have			
a child	24.3	5.2	< 0.001
Lifetime prevalence of infertility <sup>b</sup>	28.9	23.9	0.024
Seeking of medical fertility			
treatment <sup>b</sup>	14.3	13.8	0.762

a) p-values calculated from the chi-square test based on the contingency tables.

b) The denominator in these percentages included only the population at risk, e.g. those women who had at some point in time attempted to have a child (n=719, age group 25-34 years; n= 877, age group 35-44 years).

#### Procedures

Five couples were selected for each of the most common treatment used: intrauterine insemination with donor semen (IUI-D), intrauterine insemination with partner's semen (IUI-H) and IVF. The couples were selected by each of the following five criteria: infertility period two to five years, not pregnant; infertility period more than five years, not pregnant; a couple with a second trimester pregnancy after ART; a couple with live-born child or children five months old conceived after ART; terminated treatment without a treatment-related pregnancy or delivery. Three couples from the waiting list for treatment with an infertility period of less than two years were selected. All participants were selected consecutively from the clinic's log book of treated couples and from the waiting list. The author (LS) or the consultant contacted the potential participants by phone and told them orally about the study. Afterwards the potential participant received written information about the study and contacted the author themselves if they wished to take part of the study.

#### Data collection

The interviewing of the couples took place separately one by one in their own homes using a semi-structured qualitative interview (Kvale 1981, 1996). The interview focused on the participants' reproductive history and how infertility and treatment were experienced as well as the psychosocial consequences of infertility and treatment.

#### Participants

In total, 23 couples were invited to participate in the study, and 69.6% (16 couples, n=32) responded positively. The female participants ranged in age from 27 to 34 years (mean 30.7), and the males from 27 to 44 years (mean 32.8). The couples had been married for a mean time of 8.8 years (range 3-18). Fourteen had a vocational training including more than two years of theoretical training.

#### Non-participants

Among the non-participants one couple was on the waiting list, one couple was in IUI-H treatment, three were in IUI-D, and two were in IVF-treatment.

#### Analyses

Interviews were transcribed verbatim and analysed by the sociological grounded theory method (Strauss and Corbin 1990, 1998). This is an inductive, systematical analysis where all parts of the text are coded and categorized. It includes a three-step analysis process: open coding is the process of breaking down, comparing, conceptualising, and categorizing data. Axial coding is the process of analysing connections between categories by using a specific paradigm model. Selective coding is the process of selecting the core category and systematically relating it to the other categories. The core category is the central phenomenon which best integrates the analytical story in the data.

### THE COPENHAGEN MULTI-CENTRE PSYCHOSOCIAL INFERTILITY (COMPI) RESEARCH PROGRAMME

#### 3.3 THE INFERTILITY COHORT

##### Design and study population

This study is an on-going prospective cohort study, which included consecutively all new couples about to begin fertility treatment at four public and one private clinic. Data were collected with a questionnaire at baseline immediately before the couple's first treatment attempt, a one-year follow-up and since January 2005 a five-year follow-up. Only data from the baseline (T1) and the one-year follow-up (T2) is included in this thesis. See Figure 1 for a flow diagram of the T1 and T2 study population.

##### Baseline data collection (T1)

Baseline data collection included consecutively all couples begin-

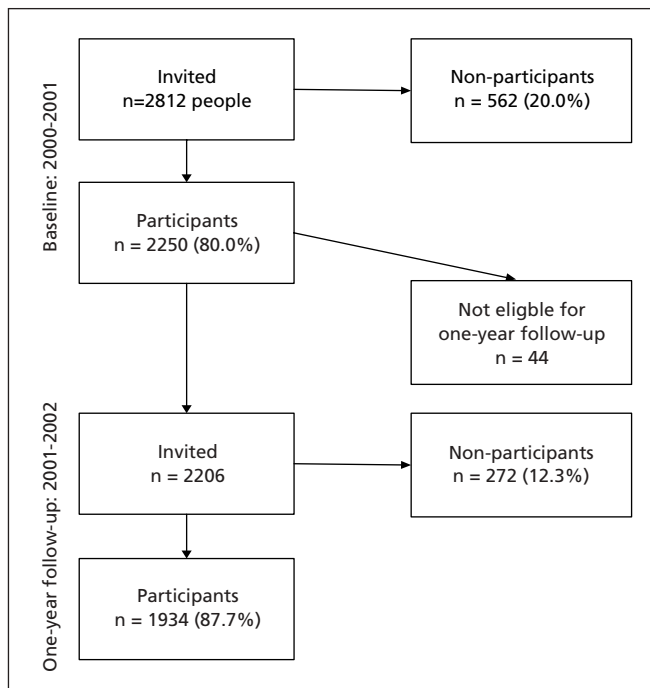


Figure 1. Flow diagram of the COMPI Infertility Cohort at baseline and at one-year follow-up.

ning a new period of fertility treatment at the public fertility clinics at Brødstrup Hospital, Herlev University Hospital, Odense University Hospital, and The Juliane Marie Centre, Rigshospitalet. Further, new couples from the private fertility clinic Trianglen were included. The data collection started January 2000 at all five clinics and continued to the Autumn 2000 at The Fertility Clinic Trianglen, to December 2000 at Rigshospitalet and to August 2001 at the remaining three clinics.

Table 4. The COMPI Infertility Cohort. Sociodemographic, medical and treatment characteristics of the baseline and the one-year follow-up population.

	Baseline Women (n=1169)	Men (n=1081)	p-value <sup>a</sup>	Follow-up Women (n=1025)	Men (n=909)	p-value <sup>a</sup>
<b>Sociodemographic</b>						
Age (years) . . . . .						
≤ 30 (%) . . . . .	25.8	15.0	< 0.001	26.1	15.5	<0.001
31-35 (%) . . . . .	56.0	50.6		49.3	41.9	
> 35 (%) . . . . .	18.1	34.4		24.7	42.6	
Occupational social class						
High, I+II (%) . . . . .	16.3	28.7	<0.001	16.3	27.8	<0.001
Medium, III + IV (%) . . . . .	60.3	47.5		59.5	46.9	
Low, V+VI (%) . . . . .	15.1	19.9		15.9	19.9	
Outside classification (%) . . . . .	8.3	3.9		8.2	4.4	
No former child with current partner (%) . . . . .	95.6	95.0	0.627	93.8	95.5	0.754
<b>Medical</b>						
Diagnosed female infertility (%) . . . . .	37.9	36.6	0.530	36.6	34.8	0.429
Diagnosed male infertility (%) . . . . .	39.5	41.4	0.356	40.0	41.1	0.579
Fertility treatment prior to inclusion in the baseline study (%) . . . . .	59.4	56.2	0.170	-	-	
<b>Treatment</b>						
No. of treatments at one-year follow-up, mean SD . . . . .	-	-		2.15 (1.38)	2.18 (1.42)	
IUI-H (%) . . . . .	-	-		17.9	20.6	0.122
IVF (%) . . . . .	-	-		66.2	68.0	0.369
ICSI (%) . . . . .	-	-		24.9	24.8	0.975
IUI-D, IVF-D (%) . . . . .	-	-		4.9	5.2	0.668
Others (%) . . . . .	-	-		7.7	6.1	0.157
Treatment-related pregnancy (%) . . . . .	-	-		62.6	63.4	0.637
Treatment-related delivery (%) . . . . .	-	-		32.4	33.4	0.676

a) p-values calculated from the chi-square test based on the contingency tables. IUI-H = intrauterine insemination with partner's semen; IVF = IVF with partner's semen; ICSI = intracytoplasmic sperm injection; IUI-D = intrauterine insemination with donor semen; IVF-D = IVF with donor semen.

### Procedures

All new couples entering one of the five clinics for the first time received a sealed envelope immediately before their first treatment attempt. It contained information about the study and a questionnaire, a form for declaration of non-participation in the study, and a stamped, pre-addressed return envelope for each spouse. The questionnaires were returned to the author (LS) who was not employed at any of the fertility clinics. The non-responders received up to two written reminders. The clinic staff was not aware of the patient's participation or non-participation in the study.

### Baseline questionnaire

The participants completed the COMPI questionnaire booklet which contained questions about reproductive history (women only), psychosocial aspects of infertility including fertility problem stress, marital benefit, communication about infertility and treatment with partner and with other people, coping strategies, sense of coherence, social relations, motivations and attitudes to treatment, health, well-being, and sociodemographic data.

### Pilot test and translation

The baseline questionnaire was pilot-tested among 122 infertile people; 54 men and 68 women. These participants were invited to comment on the questions, on the response categories, and on important themes that had not been addressed. The pilot-test showed good distributions of scores across the different response categories and few questions had to be reformulated. The author (LS) conducted eight individual telephone interviews about unclear items, missing response categories, and important themes omitted. Items originally in English were translated into Danish by two people independently and then translated back to English by two other people. In both cases, the translations were nearly identical.

### Participants

In total, 2812 fertility patients (1406 couples) received a question-

naire for each partner and 80.0% responded (n=2250). Slightly more women (83.1%, n=1169) than men (76.9%, n=1081) participated. In 1069 couples, both partners participated. In 100 couples, only the woman responded and in 12 couples, only the man responded. Response rates among the public clinics varied from 75.5 to 85.1% with the number of participants ranging from 417 to 724 from each clinic. The participation rate was lower in the private clinic (69.1%) and only 47 participants in the total sample were from that clinic. See **Table 4** for information about sociodemographic and medical characteristics of the baseline population. The couples had been married an average of 7.76 years (SD=3.71). Participants had been infertile for about four years (4.1 years (SD=2.3), 4.1 (SD=2.2), women, men, respectively), and most were about to start IVF-treatment (63.0% , 63.7%, respectively).

#### *Non-participants*

In total 20.0% (n=562) of the invited patients did not participate in the COMPI project. It was possible to obtain the age for 305 (54.2%) of these non-participants. When separated in three age groups ( $\leq 30$  years, 31-35 years,  $> 35$  years) the female non-participants were significantly older (23.0%, 44.8%, 32.2%) than the women who participated (25.9%, 56.0%, 18.1%, chi-square (2) = 18.72,  $p < 0.001$ ). The same was true for the men who did not participate (13.0%, 34.4%, 52.7%) and the men who participated (15.0%, 50.6%, 34.4%, chi-square(2)=16.59,  $p < 0.001$ ). We also have information about medical diagnosis, years of infertility, past fertility treatment, and current treatment as well as whether the couple had had children together in the past for 110 patients consecutively admitted to one clinic (68% of the non-participants at that clinic). Female non-participants differed significantly from female participants on a number of characteristics. Female non-participants were more likely to have tubal occlusions (43.2% vs. 27.0%, non-participants, participants, respectively, chi-square(1)=5.58,  $p=0.018$ ). More non-participants were about to begin ICSI (36.3% vs. 15.6%, chi-square(1)=13.37,  $p < 0.001$ ) and fewer about to begin IVF-treatment (45.5% vs. 64.5%, chi-square(1)=6.68,  $p=0.010$ ). Among the male non-participants there were significantly more men starting ICSI (28.8% vs. 14.6%, chi-square(1)=9.66,  $p=0.002$ ), and significantly fewer to begin IVF (53.0% vs. 64.5%, chi-square(1)=4.00,  $p=0.047$ ).

#### **One-year follow-up (T2)**

##### *Procedures*

All baseline participants, except 38 participants (19 couples) whose identity was not registered at baseline were sent a follow-up questionnaire, information about the study, and a stamped and pre-addressed envelope 12 month after baseline (January 2001 to August 2002). We could not trace the address for two men and two women, one man had died, and one woman suffered a severe brain injury following a road accident. The questionnaires were sent and returned to the author (LS).

##### *Follow-up questionnaire*

The participants completed the first follow-up COMPI questionnaire booklet, which contained questions about treatment and outcome in the past 12 months, psychosocial aspects of infertility including evaluation of treatment and drop-out of treatment, fertility problem stress, marital benefit, communication about infertility and treatment with partner and with other people. Further, coping strategies, sense of coherence, situation control, social relations, health, well-being, future plans for disclosure to the child and to other people about the treatment-related pregnancies and deliveries.

##### *Pilot test*

The follow-up questionnaire was pilot-tested among 31 infertile patients; 14 men and 17 women. A large part of the follow-up questionnaire was identical with the baseline questionnaire. The pilot-

test showed good distribution of scores across the different response categories, and no reformulation of questions was necessary.

#### *Participants*

In total, 2206 participants received the follow-up questionnaire and 87.7% (n=1934) responded (89.4%, n=1025 women; 85.8%, n=909 men) after two written reminders. In 135 couples, only the woman responded and in 20 couples, only the man responded. **Table 4** shows sociodemographic, medical and treatment characteristics of the follow-up study population. Among women 32.4% had delivered a baby after assisted reproduction. The average age of women was 32.8 years (SD 3.6) and of men 35.3 years (SD 5.0). The follow-up response rates among the clinics varied from 82.1 to 93.6% with the number of follow-up participants from the public clinics ranging from 350 to 613 and only 32 participants were from the private clinic.

#### *Non-participants*

A total of 12.3% (n=272) of the invited patients did not participate in the follow-up study. The non-participation was significantly higher among men than among women (men 150/1059= 14.2%; women 122/1147=10.6%, chi-square(1)=4.94,  $p= 0.026$ ). We compared the one-year follow-up participants and non-participants according to the baseline (T1) values of The COMPI Fertility Problem Stress Scales, the COMPI Marital Benefit Measure, the COMPI Coping Strategy Scales, partner communication and Infertility-related Communication Strategies (ICS). There were no significant differences between the one-year follow-up participants and non-participants neither among men nor women. **Table 5** presents percentage one-year follow-up non-participants by sociodemographic and medical background information.

### 3.4 THE COMMUNICATION AND STRESS MANAGEMENT TRAINING PROGRAMME

#### *Design*

An intervention with a training course for couples in fertility treatment was developed by the author and the two course teachers gynaecologist Kirstine Münster and gestalt therapist Michael Jungfalk. The intervention was evaluated prospectively by the participants with self-administered questionnaires and by a field study conducted by anthropologist Tine Tjørnhøj-Thomsen.

#### *The training course*

The intervention took place at the Fertility Clinic, The Juliane Marie Centre, Rigshospitalet, University of Copenhagen, 2001-2003. A male teacher trained in communication theory and skills and a female gynaecologist conducted the 18-hour course. The teachers received up-to-date scientific knowledge about the different psychosocial aspects of infertility by written information produced by three of the scientists in the COMPI programme (the author, Tine Tjørnhøj-Thomsen, Jacky Boivin).

Each course included in total five evening seminars and one weekend seminar. The courses followed a structured plan adapted to the specific needs of each group of participants:

- (i) psychological reactions to infertility and its treatment, general communication theories
- (ii) myths about infertility and how to manage them
- (iii) stress management; psychological defence strategies, generally and specifically in relation to infertility; coping strategies
- (iv) stress management, how emotions and defence strategies are connected to bodily experiences
- (v) infertility and the partner relationship
- (vi) decision-making in relation to ending unsuccessful treatment, adoption and, strategies for future life goals.

Each seminar included classroom education, group work, discus-



**Table 5.** The COMPI Infertility Cohort. Percentage of non-participants at one-year follow-up among women and men by sociodemographic and medical background factors.

	Women (n=122) %	p-value <sup>a</sup>	Men (n=150) %	p-value <sup>a</sup>
<b>Sociodemographic</b>				
Have child prior to treatment				
Yes .....	25.5	0.004	30.2	0.004
No .....	11.8		15.2	
Age (years)				
≤ 30 .....	8.6	0.009	14.6	0.675
31-35 .....	12.0		15.0	
> 35 .....	16.8		17.3	
Occupational social class				
High, I + II .....	11.2	0.078	15.1	0.911
Medium, III + IV .....	11.0		15.6	
Low, V + VI .....	15.5		16.7	
Outside classification .....	18.5		16.7	
Public clinics at university .....	14.0	0.002	17.7	0.001
Public clinic not at university .....	6.1		9.1	
<b>Medical</b>				
Duration of infertility				
< 2 years .....	29.7	0.024	20.2	0.002
≥ 2 years .....	15.0		11.8	
Diagnosed female infertility				
Yes .....	15.4	0.017	19.8	0.008
No .....	10.6		13.7	
Diagnosed male infertility				
Yes .....	11.1	0.265	16.4	0.861
No .....	13.3		15.8	
No. of treatment attempts prior to inclusion				
0-3 b) .....	13.6	0.046	16.6	0.288
≥ 4 b) .....	9.3		13.9	
Type of treatment at inclusion				
IVF/IUI-H .....	13.4	0.014	16.9	0.170
ICSI/IUI-D/IVF-D .....	6.3		11.2	
Others .....	15.4		14.8	

a) p-values calculated from the chi-square test based on the contingency tables.

b) Figures in paper IX, Table II, p. 2642 are unfortunately wrong. These are the correct figures.

IVF = IVF with partner's semen; IUI-H = intrauterine insemination with partner's semen;

ICSI = intracytoplasmic sperm injection; IUI-D = intrauterine insemination with donor semen;

IVF-D = IVF with donor semen.

sions among all participants and body exercises for focusing e.g., breathing exercises. Furthermore, seminars number ii-vi all started with a guided dialogue where each participant was encouraged to talk about their infertility and treatment experiences. These dialogues were guided by the teachers and related to the different topics being taught in the sessions.

#### *The intervention group*

All new couples (approx. 500) attending the Fertility Clinic during the period from January 2001 to January 2002 received information about the five training courses, and applicants were admitted consecutively by LS. In total, 46 couples (around 9%) applied for participation; nine couples withdrew their applications while on the course waiting list (e.g., because they had achieved a pregnancy after assisted reproduction). Finally, 37 couples (n=74) attended the course. The mean attendance rate was 4.81 (SD=1.49) sessions among men and 5.13 (SD=1.02) sessions among women out of six sessions.

#### *The non-intervention group*

Data from the intervention group was compared at baseline (T1) and one-year follow-up (T3) with a non-intervention group; The Infertility Cohort described above, 3.3.

#### *Evaluation*

All 74 participants received three questionnaires: immediately before the intervention (T1), immediately after the intervention

(around four months later; T2), and one year after the baseline collection (T3). The author (LS) who was not attending any of the courses collected all the questionnaires.

*The baseline questionnaire (T1)* was identical with the baseline questionnaire used for The Infertility Cohort study. Further, an open-ended question about motivations and reasons for wanting to participate in the training course was included.

*The first follow-up questionnaire (T2)* included the participants' evaluation of the intervention, assisted reproduction treatment the past four months, and identical items with the baseline and one-year follow-up questionnaire described above about fertility problem stress, marital benefit, communication, coping strategies, and sense of coherence.

*The second follow-up questionnaire (T3)* was identical with the one-year follow-up questionnaire used for The Infertility Cohort study. Further, open-ended questions about the impact of the training course in relation to the participant, to marital communication, to management of the infertility in relation to other people, and to the treatment process were included.

#### *Participants*

In total, 93.2% of the participants (n=32 women and 29 men) responded to the baseline questionnaire (T1); 85.1% (n=31 women and 28 men) responded to the first follow-up questionnaire (T2),

and 74.3% (n=30 women and 25 men) responded to the one-year follow-up questionnaire (T3). In total, 67.6% (n=50) responded to all three questionnaires, 82.5% (n=61) responded to questionnaire T1 and T2, and 70.3% (n=52) to questionnaire T1 and T3.

#### *Non-participants*

We have no information about those 6.8% of the intervention participants who did not respond to the baseline questionnaire.

### 3.5 VARIABLES

The following text describes the variables included in the epidemiological studies presented in paper II, IV-IX. All the psychosocial variables are based either completely or partly on the results from my qualitative PhD study (Schmidt 1996) some of which are also presented in paper III.

#### **Sociodemographic variables**

##### *Age*

The exact number of years were used in most of the data analyses in papers from the The COMPI Research Programme (paper IV-IX). In the remaining analyses, the participants were categorized in three age groups:  $\leq 30$ , 31-35, and  $> 35$  years. In paper II, data were either analysed in the age group from 25 to 44 years or separated into two groups (25-34; 35-44 years).

##### *Gender*

All analyses in papers IV-IX were done separately for women and for men. By performing the analyses separately, it was possible to look for similarities as well as differences between them.

##### *Occupational social class*

In papers II, IV-IX we used a standardised measure of occupational social class which included seven items about school education, vocational training, and occupation (Hansen 1984). Based on this measure, socio-economic position in the COMPI study (papers IV-IX) was categorised into a descending scale of occupational social class: from social class I (high) to social class V (low) (Hansen 1984) and social class VI which comprised individuals who received social welfare benefits. Participants who were impossible to classify according to this were categorized as Outside classification. Occupational social class was recoded into three levels: high (occupational social classes I+II including professionals, executives and medium level white collar employees), medium (occupational social classes III+IV including low level white collar employees and skilled workers) and low (occupational social classes V+VI including unskilled and semi-skilled workers and participants receiving social benefits). In paper II social class VI was not used and these participants were included in the social class V. In this paper we used the concept "social class" identically with the later introduced concept "occupational social class".

#### **Medical and reproductive variables**

##### *Infertility*

Infertility was measured in The Women and Health Survey by one item: "Have you ever tried to become pregnant for more than one year without achieving a pregnancy?" The response key was yes/no. The infertility prevalence was estimated as a cumulative prevalence. The numerator included all women who, up to the time of the survey, were or had ever been infertile. The denominator, the population at risk, included the study population excluding those participants who, up to the survey, had not attempted to have a child (paper II).

*Primary involuntary infecundity* was defined as those participants never having delivered a child although the woman had attempted to have one. We measured this by a combination of responses: "Have you ever tried to become pregnant for more than one year without

achieving a pregnancy?" Yes; "Have you until now got those children you wanted?" No; "Have you delivered a child?" No (Paper II).

*Medical care seeking* was measured by one item: "Have you or your husband/partner ever been examined or treated by a doctor or at a hospital for involuntary childlessness?" Response key was yes/no (Paper II).

##### *Fertility treatment*

We reported fertility treatment prior to inclusion in COMPI (paper IV-VIII). Further, we measured the different type of treatment the COMPI participants had tried during the one-year follow-up period (paper VI and IX). These treatments were: surgery (female or male), IUI-H, IUI-D, IVF, IVF with donor semen (IVF-D), ICSI, and ED with response key yes/no.

##### *Subsequent motherhood*

In papers V, VI and IX based on the one-year follow-up in the COMPI study (cohort and intervention participants) we measured whether the participants or their partners had become pregnant after fertility treatment during this one year period (yes/no), whether they were currently pregnant (yes/no), and whether they have got a child or children after ART (yes/no). In the thesis, only the data about treatment- and non-treatment related pregnancies and deliveries and about adoptions from the female participants is used. As most of the participants in COMPI are couples, they are reporting from identical pregnancies, deliveries and adoptions.

In paper II, the Woman and Health Survey, we measured whether those women who had sought medical fertility treatment subsequently became mothers. We asked whether the child was a result of a treatment-related pregnancy, a spontaneous conception, a change of partner, an adoption or unknown reason.

#### **Psychosocial variables**

These variables included partner communication; Infertility-related Communication Strategies, ICS; The COMPI Coping Strategy Scales; The COMPI Fertility Problem Stress Scales; The COMPI Marital Benefit Measure; attitudes to medical and patient-centred care and to professional psychosocial services as well as intentions to use psychosocial services; evaluation of medical and patient-centred care. These psycho-social variables were all developed either partly or completely from The Psychosocial Infertility Interview Study (Schmidt 1996, paper III). Table 1 shows a list of all the variables and Table 6 the distributions of these variables in The Infertility Cohort at baseline. Appendix A shows a list of items and response key for each of these psychosocial variables.

##### *Partner communication*

These items were based on results from The Psychosocial Infertility Interview Study (Schmidt 1996). Communication with a partner was measured in the The Infertility Cohort baseline questionnaire by one item: "Do you find it difficult to talk to your partner about your fertility problem?" The response key was: (1) yes, always, (2) yes, sometimes, (3) no, never; dichotomized into 1-2 vs. 3 (paper V, VII).

In paper VI (The Communication and Stress Management Training Programme) communication with a partner was measured by seven items related to the frequency of discussion about the childlessness, the reasons the couple was childless, medical examinations, the treatment, emotions related to infertility and to the treatment process, as well as future plans for having a child. The response key was (1) often, (2) sometimes, and (3) never.

##### *Infertility-related Communication Strategies, ICS*

In The Psychosocial Infertility Interview Study it was investigated how infertile people communicated about their infertility and treatment with others (paper III). The communication strategy appeared

**Table 6.** The COMPI Infertility Cohort. Baseline study population prevalences by partner communication, Infertility-related Communication Strategies (ICS), The COMPI Coping Strategy Scale; The COMPI Fertility Problem Stress Scales, The COMPI Marital Benefit Measure, attitudes to treatment and evaluation of treatment.

Variable	Women (n=1169)	Men (n=1081)	p-value <sup>a</sup>
<b>Difficult partner communication (%)</b> . . . . .	26.9	22.0	0.008
<b>Infertility-related Communication Strategies (ICS)</b>			
Secrecy (%) . . . . .	7.9	17.9	< 0.001
Formal (%) . . . . .	17.7	28.4	
Open-minded (%) . . . . .	74.4	53.7	
<b>The COMPI Coping Strategy Scales</b>			
<b>Active-avoidance coping</b>			
Range . . . . .	4-16	4-16	
Mean (SD) . . . . .	6.98 (2.27)	6.01 (1.98)	
Cronbach's alpha . . . . .	0.68	0.71	
Pct > 6 points . . . . .	50.2	29.2	< 0.001
<b>Active-confronting coping</b>			
Range . . . . .	7-26	7-26	
Mean (SD) . . . . .	15.67 (4.09)	13.42 (3.48)	
Cronbach's alpha . . . . .	0.76	0.74	
Pct > 16 points . . . . .	42.1	17.7	< 0.001
<b>Passive-avoidance coping</b>			
Range . . . . .	3-12	3-12	
Mean (SD) . . . . .	9.13 (1.97)	8.46 (2.15)	
Cronbach's alpha . . . . .	0.46	0.55	
Pct > 9 points . . . . .	44.4	29.7	< 0.001
<b>Meaning-based coping</b>			
Range . . . . .	5-20	5-20	
Mean (SD) . . . . .	11.20 (2.99)	10.47 (2.89)	
Cronbach's alpha . . . . .	0.59	0.53	
Pct > 11 points . . . . .	43.6	31.8	< 0.001
<b>The COMPI Fertility Problem Stress Scales</b>			
<b>Personal domain</b>			
Range . . . . .	0-20	0-20	
Mean (SD) . . . . .	8.26 (4.60)	5.34 (3.80)	
Cronbach's alpha . . . . .	0.81	0.78	
Pct > 8 points . . . . .	47.3	21.0	<0.001
<b>Marital domain</b>			
Range . . . . .	0-14	0-14	
Mean (SD) . . . . .	3.96 (3.19)	3.82 (3.14)	
Cronbach's alpha . . . . .	0.73	0.72	
Pct > 3 points . . . . .	49.9	49.1	0.110
<b>Social domain</b>			
Range . . . . .	0-12	0-12	
Mean (SD) . . . . .	2.24 (2.55)	1.45 (2.19)	
Cronbach's alpha . . . . .	0.79	0.84	
Pct > 3 points . . . . .	29.6	18.1	< 0.001
<b>The COMPI Marital Benefit Measure</b>			
Range . . . . .	0-8	0-8	
Mean (SD) . . . . .	5.79 (1.88)	5.36 (2.06)	
Pearson correlation coefficient . . . . .	0.83	0.84	
High marital benefit (%) . . . . .	25.9	21.1	0.007
<b>Attitudes to treatment</b>			
<b>Perceived importance of medical care</b>			
Explain test results (% important) . . . . .	98.3	98.5	0.663
Explain treatment options (% important) . . . . .	98.5	98.9	0.377
Written treatment information (% important) . . . . .	82.0	75.7	<0.001
Information about adoption (% important) . . . . .	25.0	24.1	0.610
<b>Perceived importance of patient-centred care</b>			
Show concern (% important) . . . . .	71.7	62.0	<0.001
Show understanding (% important) . . . . .	84.5	75.4	<0.001
Written information about psychosocial aspects of infertility (% important) . . . . .	56.0	44.9	<0.001
Contact information for infertility associations (% important) . . . . .	20.3	16.4	0.016
<b>Perceived importance of professional psychosocial services</b>			
Course about childlessness (% important) . . . . .	14.3	8.6	<0.001
Professionally led support group (% important) . . . . .	11.7	5.4	<0.001
Psychologist (% important) . . . . .	20.8	8.3	<0.001
Sex therapist (% important) . . . . .	10.7	6.6	<0.001

Table VI continues on the next page.

Table 6. Continued.

Variable	Women (n=1169)	Men (n=1081)	p-value <sup>a</sup>
<b>Intentions to use these services if available</b>			
Course about childlessness (% yes) . . . . .	13.9	8.9	<0.001
Professionally led support group (% yes) . . . . .	10.0	4.1	<0.001
Psychologist (% yes) . . . . .	18.7	7.5	<0.001
Sex therapist (% yes) . . . . .	8.9	5.7	0.004
<b>Evaluation of treatment</b>			
Evaluation of medical care			
Range . . . . .	7-35	7-35	
Mean (SD) . . . . .	29.16 (5.55)	29.26 (5.64)	
Cronbach's alpha . . . . .	0.91	0.91	
Pct > 32 point . . . . .	34.7	33.0	0.995
Evaluation of patient-centred care			
Range . . . . .	6-36	6-36	
Mean (SD) . . . . .	23.64 (5.53)	24.16 (5.43)	
Cronbach's alpha . . . . .	0.93	0.93	
Pct > 27 point . . . . .	29.5	31.1	0.157

a) p-values calculated from the chi-square test based on the contingency tables.

to be the core category in the selective coding process. The core category is the central phenomenon which best integrates the analytical story in the data (Strauss and Corbin 1990, 1998).

Three different communication strategies emerged: (i) a *secrecy strategy* when the infertility experience was not shared with others, (ii) a *formal strategy* when sharing only formal information, as e.g. date of treatment, number of eggs retrieved, or (iii) an *open-minded strategy* when both formal information and the feelings of the infertility experience were shared.

Based on this result we measured the participant's Infertility-related Communication Strategies (ICS) to other people in the COMPI study by the question: "Do you talk to other people about ..." followed by four items about factual issues related to childlessness and treatment, and two items about the emotions related to infertility and to the treatment process. The response key was (1) not to other people, (2) only to close other people, (3) to most people I know. The responses were categorised into four communication strategies: (i) *secrecy*, at least three out of four factual issues and at least one of two emotional issues are not discussed with others. (ii) *Formal*, at least three of four factual issues discussed with others and max. one of two emotional issues discussed only with intimates. (iii) *Open-minded*, at least three of four factual issues discussed with others and both emotional issues discussed with other close or distant social relationships. (iv) *Others*. No participants fell into the last category. The ICS is used in paper V and VII.

#### The COMPI Coping Strategy Scales

As recommended by Folkman and Lazarus (1988) and Costa et al. (1996), we developed a coping questionnaire specifically aimed at measuring coping strategies in relation to a specific stressor: infertility. This 29-item questionnaire was developed from three sources: (i) items were adapted from the 66-item Ways of Coping Questionnaire (WOCQ), a process-oriented measure of coping derived from Lazarus' and Folkman's transactional model of stress (Lazarus and Folkman 1984; Folkman and Lazarus 1988); (ii) Folkman's (1997) later revision of the coping model with the inclusion of the new concept, meaning-based coping; and (iii) items developed from the qualitative interview study (Schmidt 1996).

An item was selected from WOCQ if this specific way of coping was clearly revealed in the qualitative interview transcripts (Schmidt 1996). In total, 18 items were selected from WOCQ; and seven of these were re-formulated to focus on the specific stressor infertility. Further, we developed 11 items based on the results from the interview study. These 29 items covered a wide range of responses the participants may have engaged in when dealing with the fertility problem.

The items were categorised into four subscales based on their conceptual content: (i) *active-avoidance strategies* (e.g. avoid pregnant

women or children); (ii) *active-confronting strategies* (e.g. show feelings, ask others for advice); (iii) *passive-avoidance strategies* (e.g. hope for a miracle); and (iv) *meaning-based coping* (e.g. have grown as a person in a good way; find other goals in life). The response key was (1) not used, (2) used somewhat, (3) used quite a bit and (4) used a great deal. The subscales comprised items that were significantly intercorrelated. Ten items did not fit the scales, and we excluded them from the analyses. Only when the participants had answered at least half of the items in a subscale did we include their response for that subscale. A confirmatory factor analysis showed Goodness-of-fit-index (GFI)= 0.88 for the entire model. When subscales were removed from the model one at a time the GFI were > 0.91. The factor analyses were calculated in SAS, version 8.02, using proc calis and the macro polychor.sas (<http://ftp.sas.com/techsup/download/stat/polychor.html>).

In paper IV each subscale was dichotomized into high/low and in paper V and VII each subscale was trichotomized into high, medium and low. The cut-off points were chosen so that approximately one third of the respondents were categorised as high.

#### The COMPI Fertility Problem Stress Scales

Fertility related stress was measured using 14 items concerned with the strains related to infertility produced in the personal, social, and marital domain, as previous research has shown that infertility taps into these different arenas (Schmidt 1996; Greil 1997; Tjørnhøj-Thomsen 1999, 2005). Seven of these items were taken from The Fertility Problem Stress Inventory (Abbey et al. 1991a) as this instrument covers all three domains. The remaining seven items were developed from The Psychosocial Infertility Interview Study (Schmidt 1996).

The items were developed in relation to the three domains. Afterwards the items were factor analysed to produce a set of parsimonious factors, and strain in relation to the three different domains was confirmed.

The (i) *Marital stress subscale* (four items) assessed the extent to which infertility had produced strain on the marital and sexual relationships (e.g. "infertility has caused thoughts about divorce"). The (ii) *Social stress subscale* (four items) assessed the stress infertility had produced on social relations with family, friends and workmates. The (iii) *Personal stress subscale* (six items) tapped into the stress infertility had produced on the person's life and on mental and physical health. The response key for the subscales personal stress, social stress, and two items from marital stress was a four-point scale from (1) none at all to (4) a great deal. The response key for the remaining two items from marital stress was a five-point Likert response key from (1) strongly disagree to (5) strongly agree. Items from the different subscales were summed up to produce total scores. Higher scores indicated more personal, marital, and social

stress. The range, mean and Cronbach coefficients alpha differed depending on the subscale and on the population studied. See Table 6 for this information at baseline in The Infertility Cohort.

Fertility problem stress in all three domains was used in the analyses in paper V, VI, VIII and IX; in paper IV we included only the marital domain in the final analysis. In paper V, each fertility problem scale was dichotomized so approximately the most stressed third of the study population was defined as having a problem. In paper V, we used the means, in paper VI the median, and in papers VIII and IX, we used increase per unit of each scale.

#### *The COMPI Marital Benefit Measure*

We define marital benefit, as the perception that infertility has brought the partners closer together and strengthened their relationship. Therefore, marital benefit is a beneficial gain, a positive effect of infertility. The concept is different from marital satisfaction, as satisfaction is a personal evaluation (Sitzia and Wood 1997), a satisfaction rating of the marriage.

The items were developed from The Psychosocial Infertility Interview Study (Schmidt 1996). Two items measured marital benefit: Our childlessness has (i) brought us closer together, (ii) strengthen our relationship. The response category was a five-point Likert scale from (1) strongly disagree to (5) strongly agree. Higher scores indicated more marital benefits. In paper VII the measure was dichotomized into high (having responded "strongly agree" to both items) and low marital benefit. In papers VIII and IX the marital subscale was used as increase pr. unit, and in paper VI we used the median of marital benefit.

#### *Attitudes to medical and patient-centred care and to professional psychosocial services*

In total, the COMPI baseline questionnaire included 16 items about expectations and intentions to use services. The choice of these was made because they were identified as important in previous qualitative studies among Danish infertile couples (paper III; Schmidt 1996; Tjørnhøj-Thomsen 1999).

Eight items measured expectations about medical services with (i) four items measuring *attitudes to medical care* (e.g. explain test results) and (ii) four items measuring *attitudes to patient-centred care* (e.g. medical staff show understanding). (iii) Four items measured the *attitude to different professional psychosocial services* not available at the fertility clinics. The response key for these 12 items were (1) important, (2) less important, (3) not important.

In the analyses in paper VIII we dichotomized the responses in important vs. less important and not important. Further, we measured how likely the participants would be to use these professional psychosocial services if they were made available. The response key for intention to use a service was (1) yes, (2) maybe, (3) no, (4) don't know. In the analyses in paper VIII intention to use was dichotomized in yes vs. other ratings.

#### *Evaluation of medical and patient-centred care*

The COMPI one-year follow-up questionnaire included 13 evaluation items about the care received at the fertility clinic (paper IX). Eleven of these items were adapted from a European study about patients' priorities and evaluation of general practitioners (Grol et al. 1999; Mainz et al. 2000). Items were selected from a list of 23 items if the specific item had been identified in the transcripts from The Psychosocial Infertility Interview Study (Schmidt 1996). We modified the items to be specific to infertility, if necessary. The last two items (i.e., treatment plan individualised for the couple's special situation; explained what went wrong if treatment was unsuccessful) were added because they were identified as important in Schmidt (1996). The response key was (1) poor to (5) excellent and (6) don't know or irrelevant

The items were developed in relation to medical care and patient-centred (psychosocial) care as these aspects were identified as

important in the interview study (Schmidt 1996). All the 13 items covering evaluation of treatment were afterwards factor analysed. The analyses confirmed two factors: (i) *satisfaction with medical care*, seven items about medical procedures and examinations, medical information provided and explanations concerning treatment failures. (ii) *Satisfaction with patient-centred (psychosocial) care*, six items about how the staff took personal interest in the patient and responded to emotions related to the fertility problem. We dichotomized each of the two factors so approximately the most satisfied third of the participants were categorized as one and the rest as zero.

### 3.6 DATA ANALYSES

#### *Assessment of estimates*

Within epidemiology the criteria for evaluating estimated effects is a topic of discussion. Rothman and Greenland (1998) recommend that assessments are not be based on statistical significance alone. They state: "unfortunately, statistical hypothesis testing is a mode of analysis that offers less insight into epidemiologic data than alternative methods that emphasize estimation of interpretable measures" (p. 6). We followed this recommendation and based our results both on statistical significance and on assessment of estimates.

#### *Logistic regression analyses*

We assumed a multiplicative relationship between the variables in many of the analyses. Therefore, we have decided to use multivariate logistic regression analyses (paper IV-IX) rather than linear regression analyses. Further, the response categories to the psychosocial variables were not equidistant. Sumscales based on items with non-equidistant components do not meet criteria for a proper quantitative scale. Therefore, we preferred to use broad categories rather than the full scale, and we dichotomized or trichotomized each scale into high/low or high/medium/low. The threshold point was chosen in such a way that approximately one-third of the respondents were categorized as high. The choice of threshold points was confirmed by sensitivity analyses in order to make sure that the dichotomization or trichotomization did not hide important information about the studied statistical associations.

#### *Covariates and predictors*

Mainly based on previous studies we selected a list of covariates in relation to the specific association analysed. Covariates were included if they were associated with both the outcome measure and the determinant in the association studied (paper IV). Also mainly based on previous studies we selected lists of predictor variables. We treated the covariates and the predictor variables in two different ways in the analyses: (i) All covariates or predictor variables were included in the multivariate model at the same time (paper IV, VIII-IX). (ii) A final model where insignificant OR were eliminated with stepwise backwards elimination (paper IX). The analyses in paper IV and VIII were based on cross-sectional data. Cross-sectional data are not suitable for causal interpretations, e.g. for the distinction between predictor variables and outcomes. The use of the terms "predictor variable" and "outcome measure" in this thesis refer to analyses based on the hypotheses about which variables influence a certain "outcome".

#### *Associations*

We have analysed statistical associations in the cross-sectional analyses (paper II, IV, VIII). In the longitudinal analyses, we have analysed different variables as predictors at baseline for an outcome at follow-up (paper V, VII, IX).

#### *Missing*

Only very few responses on each item were missing in the questionnaires in COMPI and in The Women and Health Survey. When calculating percentages the number of missing was excluded from the



denominator. In the multivariate analyses missing responses were excluded.

A description of the epidemiological analyses relevant for this thesis follows.

#### *Paper II*

We calculated sociodemographic predictors for seeking medical fertility treatment. The Mantel-Haenszel test was used for testing for homogeneity in age-stratified analyses, as a number of variables were highly age-related.

#### *Paper IV*

The association between occupational social class and the four coping strategy scales was calculated by odds ratios. We included, among the variables which were hypothesized as influencing the association between occupational social class and coping, only those covariates showing a significant association with the outcome coping and the determinant occupational social class (age, the couple having a child together, years of cohabitation, years infertile, fertility problem stress in the marital domain, marital benefit, disruption of life). The age-adjusted crude odds ratios were calculated as well as the adjusted odds ratios where all covariates were included in the model at the same time.

#### *Paper V*

Comparisons of baseline distributions between the study population not having achieved a pregnancy or delivery after ART at the one-year follow-up and the comparison population who had achieved a delivery after ART were computed using chi-square analyses. Comparisons of fertility problem stress at T1 and T2 among the study population not having achieved a delivery or pregnancy were computed by mean, SD and Student's t-test for paired data. The associations between the communication and coping strategies used at T1 and fertility problem stress at T2 were calculated as odds ratios of high level of stress at the one-year follow-up. All odds ratios were adjusted for age and for the value at baseline of fertility problem stress.

#### *Paper VI*

We calculated odds ratios to estimate how the intervention participants changed their communication about infertility and treatment with their partner and with close family/friends/colleagues at T2 compared to T1. In the analysis of partner communication we examined whether participant's communication changed from "often" to the less frequent categories ("sometimes", "never") or vice versa. The same analyses were carried out in terms of communication with others except the responses were "do not talk" versus "do talk" to close family, close friends, and close colleagues. An OR > 1 indicated that proportionally more participants had changed their communication toward "talking" (or "talking often") at T2 compared to T1. An OR < 1 indicated that proportionally more participants had changed their communication toward "not talking" (or "not talking often") at T2 compared to T1. Because of the relatively small number of participants, most of the 95% confidence intervals were relatively broad. We interpreted OR ≥ 2 and OR ≤ 0.5 as an important change (Rothman and Greenland 1998). An OR ≥ 2 means that almost twice as many people had changed toward "talking" (or "talking often") compared to those who changed toward "not talking" (or "not talking often"). An OR ≤ 0.5 means that twice as many had changed toward "not talking often" compared to those who had changed toward "talking often". Comparisons of medians of the coping strategies reported pre- and post-intervention were tested by the non-parametric Wilcoxon signed rank test (Kirkwood and Sterne 2003). The reason being the differences in coping strategies post intervention (T2) compared to baseline (T1) were not normally distributed (these data are not shown in paper VI). Responses from the open-ended questions were categorized by the author (LS)

using an inductive, editing style (Miller and Crabtree 1999) and to increase validity a peer debriefing was conducted (Lincoln and Guba 1999).

#### *Paper VII*

Comparisons of baseline distributions between the study population not having achieved a pregnancy or delivery after ART at the one-year follow-up and the comparison population who had achieved a delivery after ART were computed using chi-square analyses. The association between marital benefit at T1 and T2 among the study population not having achieved a delivery or pregnancy after ART were computed by Pearson's correlation coefficient. The associations between the communication and coping strategies used at T1 and marital benefit at T2 were calculated as odds ratios of high level of marital benefit at the one-year follow-up. All odds ratios were adjusted for age and for the value at baseline of marital benefit.

#### *Paper VIII*

Psychosocial predictors of importance ratings and intentions to use professional services (yes vs. other ratings) were assessed using logistic regression. For each of the regression analyses the following covariates were used: age, years together, the couple having no child together, years infertile, former fertility treatment, diagnosed male infertility, diagnosed female infertility, clinic, fertility problem stress in the personal, marital and social domain, and marital benefit. All covariates were included in the model at the same time.

#### *Paper IX*

Predictors of satisfaction ratings (high vs. low) of medical and patient-centred care were estimated by multivariate logistic regression analyses. Each of these analyses included a list of predictor variables. The list was as follows: age, occupational social class, clinic, having no child together before baseline data collection, total number of fertility treatment attempts in the past year, diagnosed male infertility, diagnosed female infertility, a treatment-related pregnancy, a treatment-related delivery, fertility problem stress in the personal, marital and social domain, and marital benefit. We calculated (i) the age-adjusted crude OR for positive evaluation of medical care and patient-centred care, (ii) the adjusted OR where all predictors were included in the model at the same time, and (iii) the OR for the final model where insignificant OR were eliminated with stepwise backwards elimination.

## 4. RESULTS

The findings are described in detail in the papers. The main results are presented here with a short discussion. The discussion of materials and methods is in chapter 5.

### 4.1 DEFINITIONS AND ESTIMATES OF INFERTILITY, INVOLUNTARY INFECUNDITY AND THE SEEKING OF MEDICAL ADVICE IN INDUSTRIALIZED COUNTRIES

Paper I is a critical literature review of epidemiological studies on infertility, infecundity and medical care seeking in industrialized countries published 1970-1992. The review included data from 22 different surveys from Australia, Denmark, Finland, France, Norway, Sweden, UK, and USA.

#### *Definitions*

Most of the studies used the concept *infertility* for non-achievement of a pregnancy after attempts to achieve one over a certain period of time. This definition of infertility is in accordance with the clinical use of the word where infertility meaning difficulties to conceive, e.g. no conception after at least one year of trying to achieve a pregnancy (Weinberg and Wilcox 1998).

*Infertility* means that a pregnancy has not been achieved after at least one year or at least two years' attempting to become pregnant. The *current prevalence* is the present occurrence while *lifetime prevalence*

lence (Kleinbaum et al. 1982) is the cumulated prevalence up to the time of the survey whether infertility is still present or not. A real lifetime prevalence of infertility can only be estimated among post-menopausal women. *Primary infertility* is the non-achievement of a first pregnancy, and *secondary infertility* is the non-achievement of a subsequent pregnancy.

*Infecundity* means that the woman has not given birth. By *involuntary infecundity* we mean that a couple wants a child, are attempting to have one but have not been successful. *Primary involuntary infecundity* is the non-achievement of a first live birth, and *secondary involuntary infecundity* is the non-achievement of a subsequent live birth.

*Seeking of medical advice* means that a woman or couple had contacted a doctor because of infertility or involuntary infecundity, regardless of whether this contact resulted in further examinations and treatment.

### Estimates

*Infertility* was measured in different ways in the studies reviewed in paper I. The studies varied both in the definition of the numerator  $x$  (number of infertile) and the denominator  $n$  (the population at risk) of the infertility prevalence  $x/n$ .

The value of the *numerator* in the infertility ratio varied according to: (i) infertility period length (at least one year or at least two years); (ii) including only married or cohabiting infertile women; (iii) including all infertile women, only women who had consulted a physician or women having a fertility diagnosis; (iv) age group.

There was also no agreement on how to determine the *denominator*, i.e. the population at risk of a possible pregnancy. The studies used: (i) women who have attempted to have at least one or at least two children respectively; (ii) the entire (or almost entire) study population, regardless of whether the women have ever attempted to have children; (iii) married or cohabiting women sometimes excluding surgically sterilized women or partners; (iv) women who had currently given birth.

The studies reported lifetime prevalences of primary infertility of 13.3-16.0% when the infertility period used was at least one year and when the denominator included only women who have attempted to have a child. Similarly, the lifetime prevalences of secondary infertility was 17.0-17.4%. The lifetime prevalence when combining primary and/or secondary infertility was 24.2%. This combined infertility prevalence was measured in one study only (Greenhall and Vessey 1990).

Since the writing of paper I in 1994, more population-based studies about infertility have been conducted (Gunnel and Ewings 1994; Olsen et al. 1996; Sundby and Schei 1996; Buckett and Bentick 1997; Wulff et al. 1997; Chandra and Stephen 1998; Malin et al. 2001; Maconochie et al. 2004). When defining infertility as at least one year of attempting to conceive, a lifetime prevalence of infertility between 17.3% and 26.4% was reported in studies from UK (Gunnel and Ewings 1994; Buckett and Bentick 1997) and Sweden (Wulff et al. 1997). In contrast, a study from Norway reported a lifetime prevalence up to 10% (Sundby and Schei 1996).

Prevalence rates of infertility varied markedly in the same study population according to the definitions used. Marchbanks et al. (1989) and Larsen (2005) have shown how five different infertility definitions of the numerator used in the same study population resulted in prevalence rates varying from 6.1% to 32.6% (Marchbanks et al. 1989) and from 5.5% to 12.1% (Larsen 2005). Using the at least one year definition in defining a participant's infertility results in a higher infertility prevalence compared to using the at least two years' definition. The explanation is, that some women will become pregnant during their second year's attempt to conceive (Rachootin and Olsen 1982).

It is important in epidemiological and demographic studies both to define who is included as infertile in the numerator and who is included in the population at risk, the denominator. If the study

population comprised women in the post-fertile age groups, the use of different denominators will not contribute to significantly different infertility prevalences, as around 95% of all women have tried to have at least one child during their lifetime (Templeton et al. 1990; Sundby and Schei 1996).

However, if the study included women in the fertile age groups only, it is important to exclude those women who have not (yet) attempted to have a child from the denominator. An inclusion will result in lower, unreliable estimates of infertility. In most Western European countries the mean age at first birth is  $\geq 28$  years (Snick et al. 2005) indicating that a considerable part of women under 30 years have not tried to become mothers. In a recent population-based study from UK including nearly 18000 women younger than 55 years, 27% reported that they have never been pregnant and never attempted to conceive a child (Maconochie et al. 2004). Paper II illustrated how the lifetime infertility prevalence varied by the inclusion of two different risk populations as denominators (paper II, Table 1 p. 980).

*Involuntary infecundity*. The prevalence of primary, involuntary infecundity varied between 2.9% and 4.0% and secondary, involuntary infecundity varied between 3.5% and 5.9% when the prevalence was calculated with the denominator only including those women who had tried to have children. Population-based studies published later than paper I reported a primary prevalence of involuntary infecundity between 2.6% and 4.3% (Gunnel and Ewings 1994; Sundby and Schei 1996; Buckett and Bentick 1997; Maconochie et al. 2004).

*Seeking of medical advice*. Among 32-95% of primary infertile women and 22-79% of secondary infertile women had sought medical advice. In all reviewed studies in paper I primary infertile women sought medical advice more frequently than secondary infertile women. Population-based studies published later than paper I reported that 44.2-44.9% of primary and 33.9-48.4% of secondary infertile women had sought medical advice (Gunnel and Ewings 1994; Buckett and Bentick 1997). Wulff et al. (1997) found that 50% of ever infertile women had sought medical advice. A study including surveys from five European countries reported that among infertile couples who planned a pregnancy  $< 60\%$  sought medical fertility treatment except Denmark where 62.4% sought help (Olsen et al. 1996).

## 4.2 INFERTILITY, INVOLUNTARY INFECUNDITY, AND THE SEEKING OF FERTILITY TREATMENT IN COPENHAGEN COUNTY

Paper II presents results about infertility, primary involuntary infecundity, and the seeking of fertility treatment in a representative study population of women aged 25-44 years ( $n=1907$ ) living in Copenhagen County. The lifetime prevalence of at least one year infertility was 26.4% among those 1596 25-44 year old women who had tried to conceive; 4.1% were current primary infertile and 8.6% were primary involuntary infecund. There were no differences in lifetime prevalence of infertility according to occupational social class.

In total 224 women had sought fertility treatment, 26 of whom were not infertile (e.g., recurrent spontaneous abortions). Among the 418 infertile women 47.4% ( $n=198$ ) had sought fertility treatment. More than nine years of school education was a significant predictor of seeking treatment (OR=1.90, 95%CI 1.19-3.03). Further, high occupational social class and  $> 3$  years of vocational training were non-significant ( $p=0.06$ ) predictors of seeking fertility treatment.

There are contradictory results about the association of infertility with socio-economic position. Sundby and Schei (1996) reported from a Norwegian population-based study among 4034 women born 1950 to 1952 that significantly more infecund and infertile participants and their partners' had an education of more than 12

year compared to the fertile participants. In contrast Wulff et al. (1997) reported from a Swedish study among 1784 25-44 year old women that low educational level was significantly associated with a higher risk of being infertile compared to women of high educational level.

It is remarkable that we identified an association between shorter education and lower seeking of medical help. In Denmark, infertile couples have access to public fertility clinics where they do not have to pay for treatment themselves. The data in paper II was collected in 1989 before private fertility clinics with self-financed treatment were established in Denmark. Population-based studies from other countries with access to public treatment with no or low self-payment showed that around 50% had sought treatment (Gunnel and Ewings 1994; Bucket and Bentick 1997; Wulff et al. 1997). An identical association was reported in two studies between lower socio-economic position or low educational level, and a less likely seeking of medical care for fertility problems (Gunnel and Ewings 1994; Wulff et al. 1997). However, other studies reported no association between socio-economic position or education and medical help seeking (Rachootin and Olsen 1981; Buckett and Bentick 1997).

Population-based studies from Denmark about seeking of fertility treatment is based on data collected in the period from 1979-1993 (paper II; Rachootin and Olsen 1981; Olsen et al. 1996). It is reasonable to believe that fertility treatment seeking has increased since 1993. ART has improved, specialised public as well as private fertility clinics have been established, and waiting time to treatment has been reduced from more than one year to a few months for most treatments.

#### 4.3 SUBSEQUENT MOTHERHOOD

##### *Pregnancies and deliveries*

In The Infertility Cohort (paper IX) 62.6% (n=642) of the 1025 women reported a treatment-related pregnancy during the one-year follow-up. In total 248 women reported a current on-going pregnancy and 239 of these women reported how the conception was achieved; 97.0% (n=232) was pregnant after some kind of ART and 2.9% (n=7) had conceived spontaneously.

In total 32.4% (n=332) of the 1025 women reported at the one-year follow-up (paper IX) a treatment-related delivery during the past 12 months. We also asked about motherhood, e.g. a delivery or adoption during the one-year follow-up period. In total 317 women reported how their child or children delivered during the past 12 months was conceived. All conceptions were treatment-related. See Table 7 for details.

In the population-based study The Women and Health Survey (paper II) 54.9% (n=123) of those 224 women who had sought fertility treatment subsequently had a child. Among these women n=110 had delivered one or more children. Of these n=41 women reported that the successful pregnancy was treatment-related; 68 that the child was spontaneously conceived; 10 had a new partner and six stated that they were unable to report how the conception was achieved. Sixteen women reported more than one reason for

parenthood, mostly because the woman had delivered twice. Unfortunately, we do not have information about follow-up time after starting fertility treatment and the subsequent deliveries. However, we expect the average follow-up time to be more than the one year follow-up time in the COMPI Infertility Cohort, as we have included participants up to 44-years old in The Women and Health Survey.

The Women and Health Survey data was collected in 1989 and the COMPI data covered the years 2000-2002. The treatment of fertility patients in The Women and Health Survey took place before the establishing of specialized fertility clinics in Denmark and before there was access to high-technology treatment as IVF and ICSI. Therefore, the comparable proportion of treatment-related deliveries not withstanding, the different follow-up time in the two studies could be explained by the development of new reproductive technologies with higher treatment success rates. Recent treatment results from 2001 support this. The pregnancy rates per cycle for high-technology ART were 25.8% for IVF and 28.5% for ICSI compared with pregnancy rates of 15.4% for IUI-H and 19.9% for IUI-D (Nyboe Andersen et al. 2005).

Among couples on a waiting list for IVF the 12-months cumulative spontaneous pregnancy rates were 2.4% for couples with tubal fertility, 5.9% for unexplained fertility, and 6.6% for male infertility. The conclusion was that one cycle of IVF or ICSI was superior to 12 months of expectant management (Evers et al. 1998). Data from a large Danish public fertility clinic showed that during the years 1995-2004 1.4-4.9% of couples in fertility treatment experienced a spontaneous pregnancy (The Fertility Clinic, Rigshospitalet 1995-2004). In COMPI 0.7% (n=7) of the 1025 female participants achieved a spontaneous pregnancy during the one-year follow-up, which is lower than the percentages referred from the other studies.

##### *Adoptions*

In The Infertility Cohort 1.1% (n=11) had adopted a child during the one-year follow-up. In The Women and Health Survey (paper II) 5.8% (n=13) of the 224 women who had been in fertility treatment had subsequently adopted a child. Our expectancy is that more participants in The Infertility Cohort will adopt when the follow-up time is prolonged. Sundby et al. (1994) reported from a follow-up study among women in former fertility treatment that 31.3% of 262 female participants had adopted a child. Adoption was most frequent among women with a long investigation time and no biological child.

##### *In conclusion*

Epidemiological and demographic studies examining the prevalences of infertility differs in how they define the numerator (the infertile participants) and the denominator (the population at risk). Including only women who have attempted to have at least one child in the population at risk is important when calculating reliable estimates of the infertility prevalence. The reason being a notable proportion of women in the fertile ages have not attempted to become a

**Table 7.** The COMPI Infertility Cohort. Current pregnancies, deliveries and adoptions at one-year follow-up among women.

	Current pregnancies (n=239 reported how conception was achieved) n (%)	Deliveries during the last year (n=317 reported how conception was achieved) n (%)	Adoptions during the last year n
IUI-H . . . . .	16 (6.7)	41 (12.9)	11
IUI-D . . . . .	9 (3.8)	7 (2.2)	
IVF . . . . .	128 (53.6)	201 (63.4)	
IVF-D . . . . .	8 (3.3)	6 (1.9)	
ICSI . . . . .	54 (22.6)	57 (18.0)	
Other kind of treatment . . . . .	17 (7.1)	5 (1.6)	
Spontaneous pregnancy . . . . .	7 (2.9)	0 (0.0)	

IUI-H = intrauterine insemination with partner's semen; IUI-D = intrauterine insemination with donor semen; IVF = IVF with partner's semen; IVF-D = IVF with donor semen; ICSI = intracytoplasmic sperm injection.

mother. The lifetime prevalence of infertility was 26.4% and 5.8% in the age group 35 to 44 years were primary involuntary infertile. Even in a country with access to fertility treatment without self-payment lower education was a predictor of lower medical care seeking. After one-year follow-up in a cohort of participants starting a new period of ART treatment, almost a third had a treatment-related delivery and only 0.7% reported having achieved a spontaneous pregnancy.

#### 4.4. INFERTILITY-RELATED COMMUNICATION AND COPING

As stated previously an infertile couple faces important challenges. One is to learn how to manage the infertility in relation with one's partner and in other social relations, as well as managing infertility with oneself.

##### **Communication**

According to Lazarus and Folkman (1984), social skills refer to the ability to communicate and behave with others in ways that are socially appropriate and effective. Social skills seem to be an important coping resource. As mentioned, we have measured infertility-related communication with the partner and with other people. In the baseline study of The Infertility Cohort significantly more women than men reported having difficulties with partner communication (26.9%, 22.0%, respectively,  $p=0.008$ ; see Table 6).

Paper III reports how the infertility-related communication strategy (ICS) with other people than the partner appeared to be the core category in the grounded theory analyses in The Psychosocial Infertility Interview Study. The participants used, as described, one of three different strategies: (i) *secrecy*, when the infertility experience was not shared with others, (ii) *formal*, when only formal information was shared, and (iii) *open-minded* when both formal information and feelings of the infertility experience were shared with others. In The Infertility Cohort at baseline significantly more women than men used an open-minded strategy (74.4%, 53.7%, respectively,  $p<0.001$ ) and significantly more men than women used the secrecy strategy (17.9%, 7.9%, respectively,  $p<0.001$ ; see Table 6).

##### **Coping**

Infertility is for many infertile people chronically stressful. Chronic stressors develop slowly as continuous and problematic conditions in our social conditions or social roles (Wheaton 1999).

In the transactional coping model, coping is defined as the "constantly changing cognitive and behavioural efforts to manage specific external and/or internal demands that are appraised as taxing or exceeding the resources of the person" (Lazarus and Folkman 1984, p. 141). Coping is thus considered a process beginning with an event that is primarily appraised by the individual as threatening, harmful or challenging. We suggest that infertility, as a chronic stressor and non-event could be equally harmful as an event.

In The Infertility Cohort at baseline all four different coping strategies were used significantly more among women than men (Table 6).

##### **Coping and socio-economic position**

As mentioned, important elements of coping may be learned from one's membership and reference groups, in the same ways as other behaviours are learned (Pearlin 1989). However, few studies have focused on the relationship between socio-economic position and coping (Thoits 1995; Taylor and Seeman 1999) and none of these previous studies were related to coping with infertility. The studies showed that people from higher socio-economic position used more active problem-solving strategies (Westbrook 1979; Billings and Moos 1984; Ross and Mirowsky 1989; Grossi 1999) and less avoidant coping (Taylor and Seeman 1999; Christensen et al. 2006).

In paper IV, we measured how The Infertility Cohort at baseline coped with their infertility and analysed how coping strategies were

associated with occupational social class. Women from lower occupational social classes V+VI and men from lower social classes III+IV used significantly more active-confronting coping (e.g. let feelings out somehow; ask others for advice). Women from lower social classes V+VI used more meaning-based coping (e.g. grow as a person in a good way; think about the infertility problem in a positive light). Men and women from lower social classes III-VI used less active-avoidance coping (e.g. leave, when people are talking about pregnancies and children; turn to work or substitute activity to take the mind off things). Both men and women from lower social classes III-VI used significantly more passive-avoidance coping (e.g. hope a miracle will happen; feel that the only thing to do is to wait). Thus, the study supported Pearlin's (1989) theoretical considerations that important elements of coping may be learned from one's membership and reference groups.

Our results on passive-avoidance coping is in line with previous research (Carver, reported in Taylor and Seeman 1999; Christensen et al. 2006). But in contrast to the referred socio-economic position and coping studies we found that women and men from lower occupational social classes used more active-confronting coping and people from higher social classes I+II used significantly more active-avoidance coping. These differences in the associations between socio-economic position and coping strategies in different studies emphasizes that these patterns may be different depending on the stressor that is being coped with.

##### **Communication and coping as predictors of fertility problem stress**

In paper V based on The COMPI Infertility Cohort we analysed the infertility-related communication strategies (ICS), partner communication, and coping strategies as predictors of fertility problem stress among those participants who had not achieved a delivery or who were not pregnant at the one-year follow-up.

Among both men and women difficulties in partner communication predicted high fertility problem stress. This finding concurs with past research showing that the marital relationship is an important predictor of negative outcomes. Regardless of this being in symptom ratings of depression (Newton et al. 1999), marital life quality (Abbey et al. 1995) or the transition out of treatment (Daniluk 2001).

The Infertility-related Communication Strategies ICS was not a significant predictor of fertility problem stress. However, all associations among men and women indicated a higher risk of experiencing high fertility problem stress at follow-up when comparing the formal strategy with the open-minded strategy. Van Balen and Trimbos-Kemper (1994) reported that those 10% of long-term infertile men who kept infertility a secret reported a lower sense of well-being. The mean duration of infertility was 8.6 years in this Dutch study, whereas the mean duration of infertility in The Infertility Cohort was around four years at baseline (paper VIII). It is arguable that spending more years as infertile and still keeping it a secret would be more psychologically demanding than using a secrecy strategy during earlier years.

Among both men and women high use of active-avoidance coping (e.g., avoiding being with pregnant women or children; turning to work or substitute activity to take mind off things) predicted high fertility problem stress. We interpret high use of active-avoidance coping as a kind of defence strategy protecting the infertile participant from some of the emotional burdens of the infertility experience. Previous studies among fertility patients have reported that escapism and avoidance coping were associated with poor adaptation (Litt et al. 1992; Terry and Hynes 1998; Berghuis and Stanton 2002). However, these studies' measure of avoidant coping was overlapping with our passive-avoidance coping scale and we could identify no studies measuring active, avoidance strategies.

Among men, high use of active-confronting coping predicted low fertility problem stress in the marital domain. Other studies have measured coping overlapping with our active-confronting measure

and reported among men that emotional processing and expression were associated with decreased depressive symptoms (Berghuis and Stanton 2002).

Among women medium or high use of meaning-based coping predicted low fertility problem stress in the personal and marital domain. Other studies have measured coping overlapping with our meaning-based coping scale. Terry and Hynes (1998) reported in line with our result, that there was an association between problem-appraisal coping among women in failed IVF-treatment and better adjustment, whereas Litt et al. (1992) found no association between post-IVF distress and seeking meaning among women.

#### **Changes in communication and coping after intervention**

In paper VI, we presented changes in communication among couples in fertility treatment attending The Communication and Stress Management Training Programme. We estimated the bidirectional changes in communication, e.g. changes from talking often to talking less frequently and vice versa.

More intervention participants started to talking more often with their partner about infertility and its treatment after the intervention compared to the number who stopped to talk often. Most participants reported partner communication as improved ("increased openness", "deeper" and "more detailed" discussions) and with increased attention including "new perspectives" in the discussions.

Women and men changed occurrence, frequency, and content of their communication with others. More women started to talk with close family and friends than the number who stopped talking with them. In addition, more women stopped talking to close colleagues than the number who started talking with them. More men stopped talking with close family, close friends and colleagues than the number who started talking. However, more men had started talking with close family about the emotions related to infertility than the number who stopped talking. Many intervention participants reported an increased awareness about "what, how much and when" to discuss with others.

Learning how to manage infertility in relation to social relations is a well known challenge for infertile couples. Even so, we have not been able to identify any intervention studies, which have analysed changes in communication in detail. Stewart et al. (1992) reported a perception of improvement in six different areas: knowledge, depression, self-esteem, anxiety, communication skills and marital communication from professionally-led support groups for fertility patients. Over 50% of the participants rated themselves improved in all six areas, but "knowledge", "marital communication" and "communication skills" received the highest ratings.

We analysed coping strategies used before (T1) and after the intervention (T2) finding no significant changes among either women or men (data not shown). Few studies have examined coping strategies before and after interventions for infertile people. Lee (2003) reported from a randomised study no statistical differences in the level of psychosocial responses including coping strategies between women in IVF randomised to a nursing crisis intervention program and a control without intervention. Conversely, Stewart et al. (1992) reported that men and women after attending professionally-led support group significantly reduced their avoidance coping and increased their active coping. McQueeney et al. (1997) conducted a group therapy with emotion-focused and problem-focused therapy among women with fertility problems. Problem-focused training produced improvements in general distress and infertility-specific well-being at treatment termination. However, participants trained in emotion-focused therapy reported greater improvement at a one-month follow-up. The authors therefore argue for the efficacy of both emotion-directed and problem-focused interventions.

#### **4.5. MARITAL BENEFIT**

Paper VII showed that 25.9% of the women and 21.1% of the men reported high marital benefit at baseline in The Infertility Cohort.

Marital benefit was defined as infertility having strengthened the marriage and brought the partners closer together. Only few women (2.5% and 2.6%) and few men (5.1% and 5.4%) disagreed strongly.

#### **Communication and coping as predictors of marital benefit**

We analysed the Infertility-related Communication Strategies (ICS), partner communication and coping strategies as predictors of marital benefit among those participants who had not achieved a delivery or who were not pregnant at the one-year follow-up (paper VII).

No significant predictors were identified among women. Among men, medium use of active-confronting coping and use of meaning-based coping were significant predictors for high marital benefit. Further, among men having the infertility as a secret, having difficulties in partner communication, and using active-avoidance coping were significant predictors for low marital benefit. Our results about the secrecy communication strategy among men are in line with Van Balen and Trimbos-Kemper's study (1994). This study showed that long-term infertile men having the infertility as a secret reported lower well-being compared to the men who talked about their infertility.

Although we showed that infertility can have a positive effect on marriage, it is also well known that infertility can be a threat for the marriage. We have in the five-year follow-up but not in the one-year follow-up of the Infertility Cohort asked whether the participants have been divorced. Sundby et al. (1994) found in their follow-up study of 262 women in previous fertility treatment, that 3% (n=12) had discontinued the fertility treatment because of divorce.

#### **Changes in marital benefit after intervention**

In paper VI we analysed changes in marital benefit before (T1) and after (T2) the participation in The Communication and Stress Management Training Programme. Among women marital benefit increased significantly. Among men no changes occurred.

We have not been able to identify other intervention studies investigating a positive effect of infertility on the marriage as e.g. marital benefit, but other intervention studies have reported e.g. data about marital distress and marital satisfaction. In a review of psychosocial intervention studies in infertility Boivin (2003) reported that several studies using infertility counselling reported no effect from their intervention on partner or relationship satisfaction. However, two studies reported a significant decrease in marital distress (Tuschen-Caffier et al. 1999, after a sex therapy program; Domar et al. 2000, after a cognitive-behavioral and a support group intervention).

#### **4.6 FERTILITY PROBLEM STRESS**

Table 6 shows the prevalences of fertility problem stress in the personal, marital and social domain from The Infertility Cohort at baseline. Women reported significantly more fertility problem stress than men in the personal and social domain. Women and men reported a similar level of fertility problem stress in the marital domain.

#### **Changes in fertility problem stress after intervention**

Paper VI reported changes in fertility problem stress at follow-up (T2) compared to baseline (T1) in The Communication and Stress Management Training Programme. There were no significant differences in fertility problem stress among women or men in the personal, marital or social domain.

Boivin's (2003) review of 25 evaluations of psychosocial infertility interventions showed that previous intervention studies have shown a decrease in fertility problem stress and lowered levels of marital stress. A recent meta-analysis of 22 evaluations of psychotherapy infertility interventions showed that both group, individual and couple psychotherapy led to a decrease in feelings of anxiety and depression (de Liz and Strauss 2005). Possibly our intervention strengthened the marriage through more frequent and deeper discussions between partners about important aspects of infertility. It



is also possible this did not reduce substantially the stressful nature of the infertility experience. It is also possible that actively making changes in communication frequency and content with close intimates is a stressful experience.

#### **Fertility problem stress, marital benefit and attitudes to fertility treatment**

Paper VIII reported the associations of fertility problem stress and marital benefit with attitudes to fertility treatment. Attitudes were measured as importance ratings in relation to: (i) *medical care* (e.g. explain treatment options and test results), (ii) *patient-centred care* (e.g. medical staff show understanding), (iii) *professional psychosocial services* (e.g. support groups, consultation with a psychologist), and (iv) *intentions to use those services* if they have been available. The professional psychosocial services were not available in the period when the baseline data were collected. In general women and men had similar perceived importance ratings of medical care. Significantly more women perceived patient-centred care and professional psychosocial services as important (Table 6).

**Fertility problem stress.** Among women fertility problem stress (in the personal and marital domain) were significantly associated with higher importance ratings for patient-centred care, higher importance ratings of professional psychosocial services and with high intention to use these services if they had existed. Among men we identified the identical significant associations. Further, among men fertility problem stress in the marital domain was associated with higher importance ratings for information and discussions about adoption with medical staff.

**Marital benefit** was significantly associated with higher importance ratings for patient-centred care and higher intentions to use professional psychosocial services among both men and women. Further, among women marital benefit was associated with higher importance ratings of most of the different proposed professional psychosocial services, while marital benefit among men was only associated with higher importance ratings of support groups.

To our knowledge, this is the first expectation study that has analysed the associations with psychosocial variables and attitudes to fertility treatment. The results indicated clearly that those participants who experienced high fertility problem stress also significantly rated patient-centred care and professional psychosocial services as being of higher importance. It seems though that patients who need more care were aware of this.

Also the men and women who reported marital benefit, e.g. those who recognised a positive effect of their infertility experience, had higher importance ratings on patient-centred care and psychosocial services. We propose the interpretation that activities involved in patient-centred care and many psychosocial services are consistent with this type of coping (experiencing marital benefit). This is because patient-centred care and psychosocial services involve sharing thoughts, discussion of feelings and of the infertility experiences' impact on life.

#### **Fertility problem stress and marital benefit as predictors of evaluation of fertility treatment**

Paper IX reported patient evaluation of: (i) *medical care* and (ii) *patient-centred care*. Both men and women had high ratings on care. It seemed that satisfaction with the patient-centred care was higher than in earlier studies from other countries.

We reported longitudinal analyses of fertility problem stress and marital benefit at baseline in The Infertility Cohort as predictors of the evaluation of fertility treatment.

**Fertility problem stress** in the marital domain was a significant predictor of lower satisfaction ratings of both medical and patient-centred care among women. Sabourin et al. (1991) found lower satisfaction ratings among both the more psychologically vulnerable men and women. Sabourin et al.'s concept "vulnerability" is a

broader concept than fertility problem stress and included variables concerning stress experience, psychiatric symptoms, social network, and satisfaction with marriage. It is therefore not possible to conclude whether the different results are real differences or whether they reflect different measurements. Corresponding to our result for men, Glover et al. (1999) reported no correlation between distress and satisfaction ratings among 29 men attending a specialist male subfertility clinic.

**Marital benefit** was a significant predictor of high satisfaction with medical and patient-centred care among both men and women. Sabourin et al. (1991) has as mentioned above included "satisfaction with marriage" in the complex "vulnerability" concept. We have not been able to identify other studies analysing marital satisfaction or other related concepts and satisfaction with fertility treatment.

#### **In conclusion**

All the medical sociological analyses showed the variables of psychosocial consequences of infertility and treatment to be interwoven with each other's in a complex pattern, a pattern that both differed and was similar when comparing women and men. It is a challenge to manage infertility in relation to other people, and the infertility-related communication strategy (secrecy, formal, open-minded) identified in the qualitative interviews was later confirmed in the COMPI Infertility Cohort. Using the formal strategy indicated a risk of high fertility problem stress. The coping strategies studied showed significant occupational social class differences and active-avoidance coping was a significant predictor of high fertility problem stress. A positive effect of infertility on the marriage, marital benefit, was common. Men using the secrecy communication had increased risk of low marital benefit. Difficult partner communication was a significant predictor of high fertility problem stress and among men of low marital benefit. The intervention study showed that it was possible for the participants to change their communication with their partner and other intimates and that participants achieved an increased awareness of "what, how much and when" to discuss with others. High fertility problem stress and high marital benefit were associated with high importance ratings of patient-centred care and intentions to use professional psychosocial services. Among women, high fertility problem stress was a predictor of lower satisfaction ratings with fertility treatment. High marital benefit was a predictor of high satisfaction ratings with medical and patient-centred care.

## **5. DISCUSSION OF MATERIALS AND METHODS**

### **5.1 STUDY POPULATIONS AND DESIGN**

**The Women and Health Survey** was a representative population-based study with a high response rate (78%). Significantly more non-participants were from lower socio-economic municipalities, and there was a non-significant tendency for the people not participating to be older than those participating. Based on telephone interviews with some non-participants the prevalence of infertility was shown to be insignificantly lower among non-participants. As there was no significant difference between the prevalence of infertility among participants compared to non-participants, it is not likely that this selection bias has resulted in an overestimation of the infertility prevalence. Further, as infertility in this study was not associated with occupational social class it is not likely that this bias has invalidated the analyses. The main limitation of the study is the exclusion of women not reading Danish, as data was personally responses to a questionnaire written in Danish.

This cross-sectional study provided estimates of prevalences of infertility, involuntary infecundity and seeking of fertility treatment and the study was appropriate for the results presented. It was appropriate to demonstrate two different lifetime prevalences of infertility when the whole study population was included as the risk population in the denominator compared to including only those women who had tried to have a child. When estimating prevalences

of infertility and infecundity the fact that the study was population-based and not based on a population of patients in fertility treatment (as e.g. Hull et al. 1985) was an advantage, as only some of infertile couples seek treatment. The study could have been improved by measuring the participants' reproductive history in more detail, e.g. estimate prevalences of secondary infertility and secondary involuntary infecundity. Around 12% of the 25-44 year old participants were outside the occupational social classification. Most of the unclassified participants were still under education indicating that a proportion of these participants were attending advanced education. It would have strengthened the analyses if we had been able to include these participants in the social class classification.

**The COMPI Infertility Cohort** is an on-going prospective, cohort study with high response rates both at baseline (80.0%) and at the one-year follow-up (87.7%). One of the limitations of the study is the exclusion of participants from other ethnic groups. As the experience of kinship, family and childlessness is different in different cultural settings (Gerrits 1997; Sundby 1997; Orji et al. 2002; Inhorn 2004), we expect that our analyses of the psychosocial consequences of infertility and treatment could not be generalised to other ethnic groups.

Another limitation is that the cohort only included people who had sought fertility treatment in the public health-care system. We have no knowledge about how women and men who do not seek public treatment experience and manage their infertility. Further, as I did not succeed in including fertility patients treated at private clinics we were not able to analyse the psychosocial aspects of infertility comparing participants with and without self-financed treatment.

It was possible to analyse in detail non-participants at baseline and at the follow-up. The non-participants at baseline were significantly older. This could have underestimated the results about attitudes to treatment, as increasing age was significantly associated with lower importance ratings for adoption information and some aspects of patient-centred care as well as lower importance ratings for psychosocial services (paper VIII). In addition, more non-participants were about to begin ICSI treatment, but infertility diagnosis (male or female) was not associated with importance ratings of fertility treatment (Paper VIII). However, male infertility was associated with lower satisfaction ratings of medical care among women (paper IX) and the selection bias with inclusion of fewer couples starting ICSI treatment probably resulted in underestimating this association.

Having a child prior to ART could have influenced fertility problem stress, marital benefit, coping and communication strategies. It probably would have been an advantage to analyse predictors of fertility problem stress and marital benefit with the exclusion of those few couples (around 4%) who had a child together prior to treatment (paper V, VII). We also compared the values at baseline of the psychosocial variables and we identified no significant differences when comparing the one-year follow-up participants with the non-participants. Therefore, there was no selection bias regarding the analysed psychosocial variables in the thesis.

The four public clinics involved in this cohort study conducted during the years 2000-2001, when data collection was began, 62.8% of all IVF, ICSI, FER and ED donation cycles conducted at public fertility clinics in Denmark. Therefore we assess the results based on the COMPI Infertility Cohort to cover public fertility treatment in Denmark acceptably.

When we analysed for predictors of evaluation of treatment (paper IX) and for predictors of high fertility problem stress and high marital benefit (paper V, VII) we took advantage of the longitudinal design. When analysing prevalences and associations of attitudes to treatment (paper VIII) and of coping strategies (paper IV) we made use of the baseline data, the cross-sectional part.

**The Communication and Stress Management Training Programme** included a three-wave prospective data collection with high response rates and with measurements before and two times after the intervention. These data were compared at baseline and at the one-year follow-up with data from the COMPI Infertility Cohort where no intervention participants were included. The data collection in the COMPI cohort ended at the Fertility Clinic, Rigshospitalet before the intervention was initiated.

The design of the intervention study was discussed with a specialist in clinical epidemiology before conducting the study. Based on the discussion we decided to use a non-randomized design instead of a randomized controlled trial (RCT). There were three main reasons for this decision. (i) RCT's are used when there is doubt whether treatment A is better than treatment B. Based on previous research we were convinced that different psychosocial interventions for infertile people seeking these interventions were of benefit compared to control groups with routine care only (reviews in Boivin 2003; de Liz and Strauss 2005). (ii) For ethical reasons we did not find it appropriate to randomise fertility patients to psychosocial intervention or a control group. We expected from the baseline data in the COMPI cohort that a training course would appeal to only a small percentage of couples. Those having intentions to attend such an intervention were those who had higher fertility problem stress (paper VIII) and therefore needed a professional psychosocial service. As we were unable to refer the couples in the control group to a psychosocial service at the fertility clinic after having finished an RCT, we found it unethical to offer the training programme for only half of those who assessed that they were in need of it. (iii) We also discussed whether it would be possible to collect data from a control group attending routine care only. We assessed that probably only a minor part of the control group wished to answer three detailed questionnaires without receiving the psychosocial service they had desired. If the control group response rates were low we would have been unable to compare responses from participants and controls. Thus, we decided to use only self-selection to the intervention and compare the intervention group with a large non-intervention group having received routine care at clinics with no offer of specialised psychosocial services. When comparing the intervention group with the non-intervention group at baseline no differences regarding fertility problem stress, marital benefit, infertility diagnosis or age were shown. However, the participants in the intervention group were significantly more likely to have a high occupational social class and had received more fertility treatment attempts at the time of study entry than did the non-intervention COMPI Infertility Cohort (paper VI).

It appeared to be appropriate to analyse the bidirectional changes in communication because it allowed us to show the complex pattern of changes. Collecting both quantitative data with closed response categories and qualitative data from open-ended questions was an advantage because this combination of data made it possible to get a deeper understanding of the participants' changes in communication.

**The Psychosocial Infertility Interview Study** was a large qualitative study with a high response rate. One limitation was that couples from other ethnic groups were not included. It was possible only to collect sparse medical knowledge about the non-participants. It was difficult to include couples in IUI-D treatment and thus important aspects of male infertility could have been investigated in more detail.

Peers listening to and commenting pilot interviews improved the authors' skills as interviewer. All interviews were transcribed verbatim in full length, and the author compared the transcription with the tape and corrected errors. The grounded theory method used for analyses was a systematic method to analyse nearly all the data material.

## Gender

Infertility and its treatment is a different experience for women and men (Greil 1997). We did all analyses separately for women and men (paper III-IX). By doing this we were able to identify gender differences and similarities in the level of the psychosocial variables studied as well as in the associations studied.

## Identical study objects – multiple methods

Studying infertility and assisted reproduction for many years in a multidisciplinary research group has been satisfying, as has using different methods (epidemiological, qualitative and evaluation of an intervention). By combining different methods, it has been possible to get a deeper insight in the complex psychosocial aspects of infertility and its treatment. Developing the intervention was to some extent guided by information from the qualitative interviews, as these interviews contained information about what couples in fertility treatment found stressful and difficult to manage in their daily life as infertile people. The COMPI data collections have also been developed after discussions with the fertility clinic staff in order to improve clinical relevance of the problems studied.

## 5.2 VALIDITY

### Self-reported data

The use of self-reported data introduced two main validity issues: (i) Unwillingness to respond and (ii) reduced response ability.

Ad (i). The participants were in the interviews as well as in the questionnaires asked about private and perhaps confidential aspects of infertility and its treatment. Possibly some participants chose to present themselves in a more positive way. That is as experiencing less fertility problem stress, and using more coping and communication strategies that they assessed as a positive way of managing the infertility. It is, however, my sincere conviction that this was not the case. The qualitative interviews gave a deep insight into the thoughts and emotions of infertile couples, and I have no reason to believe that self-reported data gave a wrong picture of the couples' situation.

Ad (ii). The participants were asked in detail through lengthy questionnaires about complicated and probably difficult psychosocial aspects of infertility and ART. It is possible that some participants were not fully aware of their own assessment of their situation when they answered the questionnaires. In addition, it could be that some participants were exhausted by responding to up to 30 pages of questions and they may have answered the last questions less carefully. It was therefore reassuring to experience a high response rate in all data collections because a high response rate suggests that the participants were not exhausted by responding to the questionnaires.

Furthermore, it is not easy to imagine any other method than self-reports in the study of the psychosocial aspects of infertility and ART. During the years, I have read thousands of the questionnaires inclusive the written comments provided by many of the participants. Based on that and on the collection of the semi-structured interviews I am convinced that self-reported data about these topics is a valid and useful resource to gain insight in these topics. However, it is a condition that the epidemiological measurements are developed and tested carefully to assure their appropriateness to measure the concepts studied. One example is that the identification of three different infertility-related communication strategies in the qualitative interviews (paper III) were confirmed in the epidemiological study (paper V, VII).

### Self-reported reproductive data

Previous studies have shown that self-reported information is considered reliable and valid for several reproductive issues such as time to pregnancy, infertility, birth weight and gestational age for recall periods of up to twenty years or more (Joffe 1989a,b; Baird et al. 1991; Zielhuis et al. 1992; Dick et al. 2003). We therefore believe that our reproductive measures are valid. For ethical reasons we were not

allowed to compare the self-reported data with data from the medical records at the fertility clinics.

## Psychosocial measurements

The psychosocial measurements were developed carefully. These were all based either exclusively or partly on results from detailed qualitative interviews with couples in fertility treatment. This method triangulation (Patton 1987) assured that both the items and the response categories were appropriate and relevant for the participants. Further, questionnaires in the COMPI studies were pilot-tested and some of the test-persons were later telephone interviewed in detail about items and response categories in the questionnaire. We believe that the development of psychosocial measures specifically in relation to infertility increased the validity of these measures.

Most of the psychosocial scales were reliable and had acceptable psychometric values of e.g., Cronbach's alpha above 0.70. Only the passive-avoidance coping scale including three items had among women a Cronbach's alpha below 0.50 (Table 6). Although carefully developed, the psychosocial variables still need to be tested in other populations of fertility patients. We identified several clear and understandable patterns of how the psychosocial variables were inter-related and how they were related with treatment outcome. Therefore, we assess that our measurements of communication, coping strategies, marital benefit, fertility problem stress and attitudes to and evaluation of treatment were valid.

## Residual confounding

We have included several relevant covariates in the different psychosocial analyses, but it is not possible to include all factors that could have been relevant. The risk of a very important but not yet detected covariate being omitted is always present in analytical research.

## Qualitative data

To increase validity of the analyses in The Psychosocial Infertility Interview Study the analyses was discussed with peers and the first six interviews were coded separately and afterwards discussed in detail by the author and one peer. To increase the validity of the analyses of the open-ended questions in The Communication and Stress Management Training Programme the categorization was discussed with two peers qualified in qualitative research methods and not involved in the study.

## 6. ETHICAL CONSIDERATIONS

The Women and Health Survey (paper II) and The Psychosocial Infertility Interview Study (paper III) were both approved by the local Scientific Ethical Committees of the regions involved (Copenhagen County; Copenhagen and Frederiksberg Municipalities). The COMPI Infertility Cohort (paper IV-V, VII-IX) and The Communication and Stress Management Training Programme (paper VI) both followed the usual ethical rules for medical scientific studies (Declaration of Helsinki), but as the legislation regarding biomedical science has changed, questionnaire studies are no longer included as biomedical science. Notwithstanding, both studies were assessed by the Scientific Ethical Committee of Copenhagen and Frederiksberg Municipalities who had no objections. All studies were approved by the Danish Data Protection Agency.

In all studies people participated voluntarily. In the Women and Health Study, the women could choose not to respond. In The COMPI Infertility Cohort Study, it was possible to not respond or simply to tick a declaration of not wanting to participate. In The Psychosocial Infertility Interview Study, couples were contacted by telephone for acceptance to receive written information about the study. The couples should then themselves contact the researcher if they wished to participate. In The Communication and Stress Management Training Programme, all new couples at the fertility clinic were informed at meetings and in writing about the training pro-

gramme and how it would be evaluated. Participation in the training programme was not dependent on responding to the questionnaires. In none of the studies including fertility patients, was the clinic staff told which patients that did and did not participate in the studies.

In all studies, contact information about the principal investigator was given to the people contacted for participation. All approaches from participants and potential participants whether telephone calls, letters, and e-mails were answered by the principal investigator (Kirstine Münster, The Women and Health Survey) and the author for the rest of the studies.

It was considered as a heavier strain to participate in the qualitative interviews than to answer a questionnaire. During The Psychosocial Infertility Interview Study, I made sure, where necessary, that the participants were feeling well during and after the interview. Further, if necessary, I made certain the participant had someone to talk to afterwards. On one occasion I did afterwards contact the fertility clinic and inform about the couple's stressful situation after first having got permission from the couple interviewed. On another occasion, I contacted the couple afterwards by letter to ensure that everything was all right.

## 7. CONCLUSIONS

The thesis focused on reproductive epidemiology of infertility, on how to develop and measure psychosocial aspects of infertility and treatment. It also focused on medical sociological analyses of how these psychosocial variables were connected in a cohort of women and men in assisted reproduction in the public health-care system in Denmark. Several important findings were reported:

### *Reproductive epidemiology*

- It was complicated to measure prevalences of infertility, involuntary infecundity (involuntary childlessness) and the seeking of fertility treatment in population-based studies. Measurement of these prevalences can be done in several different ways. Therefore, it is important that the prevalences in each study be defined in detail. It is necessary to define who was included as the infertile person, who was involuntary infecund or a fertility patient (the numerator). Further, who was included in the population at risk of pregnancy or delivery (the denominator) in order to make comparisons across the epidemiological studies possible.
- It was important to measure prevalences of infertility and involuntary infecundity only among women who had attempted to have a child since many women in the fertile age groups had not attempted to become pregnant.
- Infertility was a common experience. In our population-based study the lifetime prevalence of infertility among 25-44 year old women who had attempted to have a child was 26.4%. However, only 5.8% of the 35-44 year old women was primarily involuntarily infecund (involuntarily childless).
- Infertility was not associated with occupational social class. Nevertheless, even in Denmark, with free access to fertility treatment in a public health-care system, lower occupational social class and shorter duration of school education were predictors of lower seeking of fertility treatment.
- In our population-based study in 1989 nearly half (n=224) of the infertile women had sought fertility treatment. Among these women 49.1% (n=110) subsequently delivered at least one child. In total 41 of the deliveries was reported as a pregnancy following successful fertility treatment. Among the women in former fertility treatment 5.8% (n=13) had adopted a child subsequently.
- In our prospective cohort study of new couples in assisted reproduction 2000-2002 62.6% (n=642) of the women reported a treatment-related pregnancy and 32.4% (n=332) reported a delivery after ART at the one-year follow-up. In total 1.1% (n=11) had adopted a child during the one-year follow-up period.

### *Psychosocial concepts and measurements*

- It was possible to measure the psychosocial aspects of infertility and assisted reproduction. It was important that these measurements were based on thorough conceptualization of the central phenomena followed by a thorough development of a questionnaire. The measurements had to be tested in pilot studies before use in large-scale studies.
- It was a strength to develop the measuring of these psychosocial variables in relation to the specific stressors studied: infertility and assisted reproduction. By conducting semi-structured interviews before developing the epidemiologic measurements, it was reassured that these psychosocial measurements included both relevant items and relevant response categories to the participating fertility patients.

### *Medical sociological analyses*

- The psychosocial variables were interwoven in a complex pattern.
- A notable proportion of both female and male participants starting a new period of fertility treatment experienced a high level of fertility problem stress. A minor but still substantial proportion of both women and men used communication and coping strategies that were predictors of high fertility problem stress. It seems to be possible to change communication strategies through intervention.
- Fertility treatment in the public health-care system in Denmark has high success rates, e.g. high rates of pregnancies, deliveries and patients satisfied with the medical and patient-centred care. Satisfaction with the patient-centred care was high and higher than in earlier studies from other countries.
- Fertility patients were aware of their expectations to care and more than three quarters of the participating men and women rated the medical care (e.g. written treatment information) and patient-centred care (e.g. that the staff shows concern and understanding) as important. Around 11% of the women and 7% of the men rated professional psychosocial services (e.g. a course, support group, psychologist consultation) as important. These professional services were not available at the fertility clinics when the data were collected.
- Fertility problem stress in the personal and marital domain were common and significantly associated with higher importance ratings for patient-centred care, for psychosocial services and for intentions to use these services among women and men.
- Fertility problem stress in the marital domain was a significant predictor of lower satisfaction ratings for medical and patient-centred care among women.
- Difficulties in partner communication and use of an active-avoidance coping strategy (e.g., avoiding being with children or pregnant women, turning to work or substitute activity to take mind off things) were significant predictors of high fertility problem stress among men and women not having achieved an ART-pregnancy at the one-year follow-up.
- Use of a formal infertility-related communication strategy, e.g. not talking to other people about the emotional aspects of infertility and treatment, indicated a higher risk of experiencing high fertility problem stress.
- Among men, the use of active-confronting coping (e.g. letting feelings out, accepting sympathy and understanding, asking for advice) was a significant predictor of low fertility problem stress in the marital domain.
- It was possible to change fertility patients' partner communication and infertility-related communication strategies after attending a training programme. Partner communication was reported as improved with increased openness and with inclusion of new perspectives in the discussions. Women and men changed occurrence, frequency and content of their communication with others. Many reported an increased awareness about what, how much and when to discuss with others.

- Marital benefit was defined as the infertility both has strengthened the marriage and bringing the partners closer together. Around a quarter of the women and a fifth of the men reported high marital benefit when starting fertility treatment.
- It was important not only to measure the strain related to infertility and ART but also a positive effect as marital benefit. This effect of infertility was among women and men significantly associated with higher importance ratings of patient-centred care and with high satisfaction ratings of medical care and patient-centred care.
- Among men, having the infertility as a secret, difficulties in partner communication and using active-avoidance coping were significant predictors of low marital benefit.
- Among women marital benefit increased significantly after participating in the training programme.
- Significant patterns of associations between occupational social class and coping strategies were identified. There were no gender differences in these associations. Unexpectedly, women and men from lower occupational social classes (V+VI and III+IV respectively) used more active-confronting coping (e.g. letting feelings out, accepting sympathy and understanding, asking for advice) than participants from higher social classes. Also unexpectedly women and men from higher social classes I+II used more active-avoidance coping (e.g. avoiding being with children or pregnant women, turning to work or substitute activity to take mind off things) than participants from lower social classes.
- There were significant gender differences in several psychosocial phenomena: Women reported higher fertility problem stress in the personal and social domain, higher use of the four different coping strategies, higher marital benefit and a higher use of the open-minded communication strategy than men did.
- There were gender differences for most of the associations between the psychosocial variables studied.
- The analyses showed the psychosocial variables were often more significant predictors than the medical variables. This stresses the importance of fertility clinic staff to be aware of the medical aspects as well as the psychosocial aspects of assisted reproduction.

## 8. PERSPECTIVES FOR FUTURE RESEARCH

It is important to continue the prospective COMPI Infertility Cohort study and from January 2005 we have initiated a five-year data collection among all participants included in the baseline study. This second follow-up focuses on reproductive outcome (pregnancies, deliveries) after treatment and non-treatment, adoptions, side effects of treatment, reasons for dropping out of treatment. For those who still have not delivered through the last five year we repeat the psychosocial measurements (communication, coping, fertility problem stress, marital benefit, attitudes to professional psychosocial services). For those who had become parents we collect data about secrecy or disclosure regarding fertility treatment and outcome.

We plan to link the female participants in The COMPI Infertility Cohort with the National Medical Birth Registry and the Danish IVF Registry in order to analyse reproductive outcome. The reproductive outcome data will be combined with data for costs of fertility treatment in order to conduct a cost-effectiveness analyses of ART. Further, we have planned a link to the Danish National Psychiatric Central Registry in order to study psychiatric admissions before and after ART.

Analyses of the one-year follow-up data indicated that high fertility problem stress was a predictor of a lower chance of achieving pregnancy after ART (Boivin and Schmidt 2005). However, other factors as smoking, alcohol and body mass index not included in these analyses could be confounders for the association studied. Therefore, and because we are also interested in studying the association between self-reported fertility problem stress and egg and semen quality, we are now applying the Ethical Committee for per-

mission to combine data from the COMPI Infertility Cohort with information from medical records.

Our psychosocial measurements still need to be tested in other populations of fertility patients. Some researchers and clinicians from the Netherlands, Greece, Turkey and Utah are now involved in using some of the COMPI psychosocial measurements in different local studies.

In this thesis, we have focused all analyses separately on women and men. As infertility and its treatment is a couple experience it would be of interest to analyse further the COMPI data with the couple as the unit and not the individual. This could allow analyses of couples where both report high or low fertility problem stress and couples where one is highly stressed and the other partner experiences low stress.

We showed that an 18-hours training programme had effects on communication among male and female participants as well as on marital benefit among female participants. However, the Danish health-care system employ few psychologists, and we have no counsellors or mental health workers as many other countries have in their health-care systems. With only a few persons in the health-care system trained professionally in psychosocial care, it would be good to develop and evaluate other interventions in order to meet the need of the most stressed couples in fertility treatment.

We examined the infertility-related communication in detail and showed that measurement of the contents of communication with other people was also important. Further, during an intervention with couples in fertility treatment we were reassured that learning to manage the communication with others was an important topic for the participants. It could be suggested that communication with others is also important for persons with other chronic as well as life-threatening diseases. Usually psychosocial studies among cancer patients measure only whether the patient talk to other people or not. Based on our research it would be interesting in future studies to measure communication in more details.

We developed a coping measure specifically aimed at measuring coping strategies with infertility partly based on previous detailed knowledge about how fertility patients cope. It could be interesting to use specifically developed coping measures in relation to other stressors, because the use of standard coping measurements instrument bear the risk of measuring coping strategies not relevant to the stressor studied.

## 9. CLINICAL IMPLICATIONS

The analyses in this thesis showed that people attending public fertility treatment in Denmark are highly satisfied with both the medical and patient-centred care. However, a minor proportion of the patients are highly stressed and these patients expressed a need for professional psychosocial services usually not available at fertility clinics in Denmark. It is important to take more care of these patients in order to increase their well-being.

Fertility patients having difficulties in partner communication and using active-avoidance coping (e.g. avoiding pregnant women and children; turning to work or substitute activity to take mind off things) had an increased risk of experiencing high fertility problem stress. I recommend that clinicians be aware of patients having problems in partner communication and with a high use of active-avoidance coping. These couples are probably in need of extra psychosocial support in order to reduce their fertility problem stress.

A substantial minority of the participants studied experienced high marital benefit; e.g., that the infertility has brought the couples closer together and strengthened their relationship. Among men having infertility as a secret and using active-avoidance coping were significant predictors of low marital benefit. I recommend that clinicians be aware of this and tell the couples, particularly the men, that talking with other people about their infertility and treatment experience is probably a good way to strengthen their partner relationship. In addition, the information to the fertility couples that men



using active-confronting coping (e.g., letting feelings out, seeking support and advice) experience lower fertility problem stress is important. Further, I recommend clinicians to inform the fertility couples that communicating with other people about the infertility and its treatment is a good advice. Further, some of these talks should include both formal and emotional aspects. It seems important also to stress that communication with others should be based on an active decision-making where the infertile person decides when to talk, with whom to talk and what to talk about.

During the intervention study, with a training programme for couples in fertility treatment, we showed how a larger proportion of the intervention participants started to seek information about adoption earlier compared to a non-intervention group. It seems important to introduce effectively, discussions of adoption and other alternatives to ART earlier in the treatment process thereby potentially reducing the proportion of couples who continue unsuccessful ART for far too long. Earlier discussions and information-seeking about adoption would also prevent couples from being ineligible for adoption because they were not able to meet the adoption criteria for age and length of marriage.

## SUMMARY

Clinically a couple is considered to be infertile after at least one year without contraception and without pregnancy. There was scant knowledge about the prevalences of infertility, involuntary childlessness and the seeking of fertility treatment and only few longitudinal studies about the psychosocial consequences of infertility and its treatment. This thesis is about the epidemiological aspects of infertility; the conceptualization and measurement of important psychosocial aspects of infertility; and a medical sociological analysis of the associations between these psychosocial variables among Danish women and men in fertility treatment. The thesis is based on nine papers.

The three main purposes were: (i) to review critically, population-based studies of infertility and medical care seeking in industrialised countries. Further, to examine these prevalences and subsequent motherhood among women in former assisted reproduction in a Danish population. (ii) To develop measures of psychosocial consequences of infertility: fertility problem stress, marital benefit, communication, coping strategies, attitudes to and evaluation of fertility treatment. (iii) To examine these phenomena and to analyse their interrelations among Danish women and men in fertility treatment.

The thesis is based on four empirical studies: (i) The Women and Health Survey, a cross-sectional population-based study among 15-44 year old women (n=1907, 25-44 year old) in Copenhagen County, 1989. (ii) The Psychosocial Infertility Interview Study, a qualitative interview study among 16 couples (n=32 participants) in fertility treatment at The Fertility Clinic, Herlev University Hospital, 1992. (iii) The Infertility Cohort, a longitudinal cohort study consecutively including all couples (n=2250 participants) beginning a new fertility treatment period at one of four public (Brødstrup, Herlev, Odense, Rigshospitalet) and one private fertility clinic (Trianglen), 2000-2002. (iv) The Communication and Stress Management Training Programme, an intervention study among couples (n=74 participants) in fertility treatment at The Fertility Clinic, The Juliane Marie Centre, Rigshospitalet, 2001-2003. Included is also a literature review of population-based infertility studies from industrialised countries. Data from (iii) and (iv) are studies from The Copenhagen Multi-centre Psychosocial Infertility (COMPI) Research Programme ([www.compipro.dk](http://www.compipro.dk)).

Epidemiological and demographic studies investigating the prevalences of infertility differed in how they defined the numerator (the infertile participants) and the denominator (the population at risk). It was important to calculate reliable estimates of the infertility prevalence by including only women who had tried to have at least one child in the population at risk, as a notable proportion of women in the fertile ages had not (yet) attempted to become a mother. The lifetime prevalence of infertility in the representative

population-based study was 26.4%. In the age group 35 to 44 years 5.8% were primarily involuntarily infecund (involuntarily childless). Even in a country with access to fertility treatment in a public health-care system without self-payment lower education was a predictor of lower treatment seeking. In the cohort study (2000-2002) of couples starting a new period of assisted reproduction treatment 62.6% reported a treatment-related pregnancy at the one-year follow-up. In total 32.4% reported a treatment-related delivery. In total 24.2% reported a current continuing pregnancy and spontaneous pregnancies accounted for 2.7% of these.

We developed measures of fertility problem stress, marital benefit (that infertility has brought the partners closer together and strengthened their marriage), partner communication, infertility-related communication, coping strategies, attitudes to fertility treatment and evaluation of care.

The medical sociological analyses showed that the variables of psychosocial consequences of infertility and treatment are interwoven with each others in a complex pattern, a pattern that both differed and was similar when comparing women and men. The infertility-related communication strategy (secrecy, formal, open-minded) identified in the qualitative interviews was later confirmed in the COMPI Infertility Cohort. Using the formal strategy and not talking about the emotional aspects of infertility and its treatment suggested high fertility problem stress. The coping strategies studied showed significant social differences and active-avoidance coping was a significant predictor of high fertility problem stress. A positive effect of infertility on the marriage, marital benefit was common. Men using the secrecy communication strategy had increased risk of low marital benefit. Difficult partner communication was a significant predictor of high fertility problem stress and among men, of low marital benefit. The intervention study showed that it was possible for the participants to change their communication with partner and other people close to them and that participants achieved an increased awareness of what, how much and when to discuss with others. High fertility problem stress and high marital benefit were associated with high importance ratings of patient-centred care and intentions to use professional psychosocial services. Among women, high fertility problem stress was a predictor of lower satisfaction ratings with fertility treatment. High marital benefit was a predictor of high satisfaction ratings of both medical and patient-centred care.

In conclusion, infertility is a common experience among couples attempting to become parents. Assisted reproduction in the public health-care system in Denmark has high success rates, i.e. pregnancies, deliveries and high patient satisfaction. A large minority of people in fertility treatment experience high fertility problem stress, and some use communication and coping strategies that predicts high stress. Developing and evaluating different psychosocial interventions are necessary to offer the psychosocial support needed for this minority of fertility patients.

## ABBREVIATIONS AND DEFINITIONS

ART	Assisted reproductive technology. Includes in this thesis all kinds of assisted reproduction.
CI	Confidence interval
COMPI	The Copenhagen Multi-centre Psychosocial Infertility Research Programme
ED	Egg donation
FER	Frozen embryo transfer
ICS	Infertility-related Communication Strategies
ICSI	Intracytoplasmic sperm injection
IUI-D	Intrauterine insemination with donor semen
IUI-H	Intrauterine insemination with partner's semen
IVF	In vitro fertilization
IVF-D	In vitro fertilization with donor semen
OR	Odds ratio
RCT	Randomized controlled trial
SD	Standard deviation

## THE THESIS IS BASED ON THE FOLLOWING PUBLICATIONS:

- I. Schmidt L, Münster K (1995) Infertility, involuntary infecundity, and the seeking of medical advice in industrialized countries 1970-1992: a review of concepts, measurements and results. *Hum Reprod* 10, 1407-1418. Copyright European Society of Human Reproduction and Embryology. Reproduced by permission of Oxford University Press/Human Reproduction.
- II. Schmidt L, Münster K, Helm P (1995) Infertility and the seeking of infertility treatment in a representative study population. *Br J Obstet Gynaecol* 102, 978-984. Reproduced by permission of Blackwell Publishing.
- III. Schmidt L (1998) Infertile couples' assessment of infertility treatment. *Acta Obstet Gynecol Scand* 77, 649-653. Reproduced by permission of Chief Editor Per Olof Janson.
- IV. Schmidt L, Christensen U, Holstein BE (2005) The social epidemiology of coping with infertility. *Hum Reprod* 20, 1044-1052. Copyright European Society of Human Reproduction and Embryology. Reproduced by permission of Oxford University Press/Human Reproduction.
- V. Schmidt L, Holstein BE, Christensen U, Boivin J (2005) Communication and coping as predictors of fertility problem stress: cohort study of 816 participants who did not achieve a delivery after 12 months of fertility treatment. *Hum Reprod* 20, 3248-3256. Copyright European Society of Human Reproduction and Embryology. Reproduced by permission of Oxford University Press/Human Reproduction.
- VI. Schmidt L, Tjørnhøj-Thomsen T, Boivin J, Nyboe Andersen A (2005) Evaluation of a communication and stress management training programme for infertile couples. *Patient Educ Couns* 59, 252-262. Copyright (2005) with permission from Elsevier.
- VII. Schmidt L, Holstein BE, Christensen U, Boivin J (2005) Does infertility cause marital benefit? An epidemiological study of 2250 women and men in fertility treatment. *Patient Educ Couns* 59, 244-251. Copyright (2005) with permission from Elsevier.
- VIII. Schmidt L, Holstein BE, Boivin J, Sångren H, Tjørnhøj-Thomsen T, Blaabjerg J, Hald F, Nyboe Andersen A, Rasmussen PE (2003) Patients' attitudes to medical and psychosocial aspects of care in fertility clinics: findings from the Copenhagen Multi-centre Psychosocial Infertility (COMPI) Research Programme. *Hum Reprod* 18, 628-637. Copyright European Society of Human Reproduction and Embryology. Reproduced by permission of Oxford University Press/Human Reproduction.
- IX. Schmidt L, Holstein BE, Boivin J, Tjørnhøj-Thomsen T, Blaabjerg J, Hald F, Rasmussen PE, Nyboe Andersen A (2003) High ratings of satisfaction with fertility treatment are common: findings from the Copenhagen Multi-centre Psychosocial (COMPI) Research Programme. *Hum Reprod* 18, 2638-2646. Copyright European Society of Human Reproduction and Embryology. Reproduced by permission of Oxford University Press/Human Reproduction.

The papers are referred to in the text by their Roman numeral in parenthesis.

Paper III is based in results from my previous PhD-thesis (Schmidt 1996), but was not a part of the PhD-thesis. The papers I-II and IV-IX or results presented in these papers have not previously been assessed for an academic degree.

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## APPENDIX A

### LIST OF ITEMS OF THE PSYCHOSOCIAL VARIABLES INCLUDED IN THE ANALYSES

#### **Partner communication**

In The COMPI Infertility Cohort at baseline:

Do you find it difficult to talk to your husband/partner about your fertility problem?

Response key: (1) yes, always, (2) yes, sometimes, (3) no, never

In The Communication and Stress Management Training Programme:

Do you talk to your partner about ...

1. that you are not able to have children?
2. the reason why you are childless?
3. your tests?
4. what kind of treatments you are trying?
5. your emotional feelings as childless?
6. how tests and treatments affect you emotionally?
7. what you will do in the future to have a baby?

Response key: (1) often, (2) sometimes, (3) never

#### **Infertility-related Communication Strategies (ICS)**

Do you talk to other people about ...

1. that you are not able to have children?
2. the reason why you are childless?
3. your tests and examinations?
4. what kind of treatment you are trying?
5. your emotional feelings as childless?
6. how tests and treatments affect you emotionally?

Response key: (1) not to other people, (2) only to close other people, (3) to most people I know

#### **The COMPI Coping Strategy Scales**

People cope with their fertility problem in different ways.

How do you cope?

I ...

##### *Active-avoidance Coping Scale*

1. avoid being with pregnant women or children
2. leave, when people are talking about pregnancies and children
3. try to keep my feelings to myself
4. turn to work or substitute activity to take my mind off things

##### *Active-confronting Coping Scale*

1. let my feelings out somehow
2. accept sympathy and understanding from someone
3. ask other childless people for advice
4. ask a relative or friend for advice
5. read or watch television about childlessness
6. talk to someone about my emotions as childless
7. talk to someone about how tests and treatments affect me emotionally

##### *Passive-avoidance Coping Scale*

1. hope a miracle will happen
2. feel that the only thing I can do is to wait
3. have fantasies and wishes

##### *Meaning-based Coping Scale*

1. have grown as a person in a good way
2. think about the infertility in a positive light
3. find my marriage/partnership even more valuable now
4. find other life goals
5. believe there is a meaning in our difficulties in having children

Response key: (1) not used, (2) used somewhat, (3) used quite a bit, (4) used a great deal

### **The COMPI Fertility Problem Stress Scales**

#### *Personal domain*

1. My life has been disrupted because of this fertility problem
2. It is very stressful for me to deal with this fertility problem

How much stress has your fertility problem placed on the following

...

1. your relationship with people with children?
2. your relationship to pregnant women?
3. your physical health?
4. your mental health?

#### *Marital domain*

What consequences has your childlessness for your marriage?

The childlessness has ...

1. caused crisis in our relationship
2. caused thoughts about divorce

How much stress has your fertility problem placed on the following

...

1. your marriage?
2. your sex life?

#### *Social domain*

How much stress has your fertility problem placed on the following

...

1. your relationships with your family?
2. your relationships with your family-in-law?
3. your relationships with friends?
4. your relationships with workmates?

Response key for items 1-2 on personal domain and for items 1-2 on marital domain: (1) strongly disagree, (2) somewhat disagree, (3) neither agree nor disagree, (4) somewhat agree, (5) strongly agree. Response key for remaining items: (1) none at all, (2) a little, (3) some, (4) a great deal.

### **The COMPI Marital Benefit Measure**

The childlessness has ...

1. brought us closer together
2. has strengthened our relationship

Response key: (1) strongly disagree, (2) somewhat disagree, (3) neither agree nor disagree, (4) somewhat agree, (5) strongly agree.

### **Attitudes to treatment**

I wish the staff at the fertility clinic ...

#### *Medical care*

1. tells the results of the tests
2. inform us about the different treatment options relevant for us
3. inform us about the possibilities of adoption
4. gives us written information about our treatment

#### *Patient-centred care*

1. asks us about our emotional feelings
2. shows us understanding
3. gives a pamphlet about the emotional consequences of childlessness
4. refers to associations for childless people

#### *Professional psychosocial services*

I wish there was a possibility to ...

1. participate in a course about childlessness

2. to participate in a support group
3. to talk to a psychologist
4. to talk to a sex therapist

Response key: (1) important, (2) less important, (3) not important.

#### *Intentions to use psychosocial services*

If these services existed, I would like to ...

1. participate in a course about childlessness
2. to participate in a support group
3. to talk to a psychologist
4. to talk to a sex therapist

Response key: (1) yes, (2) maybe, (3) no, (4) don't know

### **Evaluation of treatment**

How do you assess the staff at the fertility clinic after having started treatment 12 months ago

#### *Medical care*

1. to be thorough and careful
2. to examine you
3. to explain the purpose of tests and treatments in detail
4. to tell you all you want to know about infertility and treatment
5. to inform you of what you could expect from the fertility clinic
6. to make an individualised treatment plan for your situation
7. to explain what went wrong if treatment was unsuccessful

#### *Patient-centred care*

1. to make you feel you had enough time during consultation
2. to take a personal interest in you as a person
3. to make you feel free to talk about your problems
4. to involve you in decision-making
5. to listen to you
6. to take care of the emotional problems of our fertility problem and treatment

Response key: (1) poor to (5) excellent, (6) do not know/not relevant