

“It is better to have tried, no matter what”

Psychological perspectives on pre-implantation genetic
diagnosis (PGD)

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diagnosis (PGD)

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Till Julia, Olivia och Ester

*Ett barn ska jag ha när jag blir stor, med smala ben och mjuka skor,
små vassa tänder och skära händer, mage som en sockertopp
och ljusbrunt hår precis rakt opp.
Och om mitt barn får ont i magen några gånger
ska jag sjunga för det jättefina sånger
och jag ska byta blöjor på mitt barn
och sätta på små kläder
och världens minsta gummistövlar ifall det blir dåligt väder*

*Men, ska jag säga: akta dig för eld och djupa vatten.
Spring aldrig aldrig bort från mig i den svarta natten.*

Jojje Wadenius

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Abstract

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"It is better to have tried, no matter what." Psychological perspectives on pre-implantation genetic diagnosis (PGD)

Department of Psychology, University of Gothenburg, Sweden.

Couples with the risk of transmitting a genetic disease face different diagnostic options when they wish to become parents. Pre-implantation genetic diagnosis (PGD) combines in vitro fertilization (IVF) with biopsy of the embryo. With PGD the couple can start a pregnancy knowing that the child will not be affected by the particular disease. PGD is however a difficult way to become a parent and little is known about the psychological challenges for men and women who undergo PGD. The overall aim of this thesis was to increase the understanding of psychological perspectives and to explore factors related to psychological health and relationship satisfaction, in men and women during the PGD process.

The thesis consists of four studies, all based on data from the same group of men ($n=17$) and women ($n=19$) undergoing PGD. Interview data and self-report measures were collected at the start of PGD treatment and three years later. Study I and IV are based on interviews with men and women when they applied for PGD, and three years later. Study II and III are based on self-report questionnaires from the same group at inclusion and three years later. The second study also includes a contrast group of men ($n=23$) and women ($n=24$) applying for first time IVF.

The aim of **Study I** was to investigate the psychological aspects of men's and women's decisions to undergo PGD, the influence of the healthcare system and ethical considerations. The aim of **Study II** was to investigate the presence of symptoms of depression and anxiety in men and women who made the choice to undergo PGD and to study the relationship between levels of depression and anxiety and six theoretically derived risk factors. In **Study III** the aim was to study the quality of the marital relationship in couples undergoing PGD at the start of PGD treatment and at follow-up three years later. In **Study IV** the aim was to investigate long-term psychological experiences of PGD on men and women.

In **Study I** the men and women were interviewed individually. The interviews followed a semi-structured guide. The material was analysed inductively using thematic analysis and resulted in a model where *Choosing* was seen as a master theme, affecting three underlying sub-themes 1) Choosing in relation to myself, 2) Choosing in relation to the child, 3) Choosing in relation society. On the next level, there were nine underlying categories. Men and women had similar reflections about the decision. In **Study II** a comparison was made between the PGD group and a group of men and women planning for their first IVF. The Hospital Anxiety and Depression Scale (HADS) was used to measure anxiety and depression. The main findings from **Study II** were that women planning for PGD did not differ significantly from women planning for IVF in symptoms of anxiety or depression. Men planning for PGD reported significantly more symptoms of anxiety than men planning for IVF ($p < 0.03$) and had lower SoC ($p < 0.05$). Of the analysed risk factors, reproductive history and SoC gave unique significant contributions and explained 64% of the variance in levels of depression among women in the PGD group. Having an affected child and lower socioeconomic risk gave unique significant contributions and explained 56% of the variance in anxiety among men in the PGD group. In **Study III** the participants answered questionnaires about satisfaction with the quality of the marital relationship (Dyadic Adjustment Scale), anxiety and depression (HADS) and perceived parental stress (Parental Stress Questionnaire) before PGD treatment, and three years later. Women who underwent PGD rated the quality of their marital relationship similarly to that of first time parents and IVF couples, whereas men rated the marital quality somewhat lower than the contrast groups. Satisfaction with marital quality was stable over the three-year period and men were less satisfied than women on both occasions. At both time-points there was a significant correlation between marital satisfaction and perceived parental stress in men (-0.83 and -0.70 , $p < 0.05$). For women, anxiety (-0.52 , $p < 0.05$) and depression (-0.61 , $p < 0.01$)

correlated significantly with lower satisfaction with the quality of the relationship at follow-up. **Study IV** focused on men and women's psychological experiences of PGD three years later. Men and women were interviewed individually and data was analysed thematically. *It is better to have tried* was identified as a master theme, with three underlying sub-themes: *Practical experience of PGD*, *Psychological experience of PGD* and *Goals of PGD*. The results showed that men and women were still psychologically affected by their experiences three years later. The men and women in the study expressed the view that their relationship had been affected, both positively and negatively, and some reported that they still had feelings of anxiety and depression.

Both men and women were engaged in the decision-making process leading to PGD and they were still affected three years later. Men and women having the experience of miscarriages and termination before PGD, and/or having a child affected by the genetic disease, might be at increased risk of developing psychological symptoms. Men are equally, or even more, affected by the situation than their female partners, with consequences for their satisfaction with marital quality. Results from the four studies underline that men and women who apply for PGD constitute a heterogeneous group and the need for counselling can arise at different times and in relation to different areas, regardless of the outcome of the PGD.

Keywords: *Pre-implantation Genetic Diagnosis (PGD), Decision-making, Men and Women, Risk Factors, Depression, Anxiety, Marital Relationship, Counselling.*

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Populärvetenskaplig svensk sammanfattning

Att stå inför önskan om föräldraskap är en av de stora livsövergångarna för oss som människor. För kvinnor och män som vet att de är bärare av ärftliga sjukdomar innehåller denna livsfas ytterligare ställningstaganden. Vill de använda sig av fosterdiagnostik för att veta om det kommande barnet får den ärftliga sjukdomen? I så fall vilket av de olika diagnostiska val som sjukvården erbjuder skall de välja? För de par som har möjlighet att bli spontant gravida finns alternativet med fosterdiagnostik och vid ett besked om att fostret bär den ärftliga sjukdomen att ta ställning till ett avbrytande. Vid vissa genetiska tillstånd är det svårt att uppnå graviditet medan andra upplevt upprepade missfall. I dessa fall har paret inte bara den genetiska sjukdomen att förhålla sig till utan är också infertila. Sedan 1990-talet finns alternativet preimplantatorisk genetisk diagnostik (PGD) för par med allvarlig genetisk sjukdom. Metoden förutsätter så kallad provrörsbefruktning som också kallas in vitro fertilisering (IVF), d.v.s. befruktning utanför kroppen. PGD innebär att efter befruktning tas en cell ut från det befruktade ägget (embryot), och undersöks med en genetisk analys som gör att man kan identifiera embryon som bär på sjukdomsanlaget. Därefter sätts enbart de embryon som inte är anlagsbärande av den aktuella genetiska sjukdomen tillbaka in i kvinnan och kan ge upphov till ett barn utan sjukdomen. Till en början var PGD endast tillåtet för ett mycket litet antal sjukdomar i Sverige men sedan lagen om Genetisk integritet kom år 2006 har antalet sjukdomar där PGD tillåts blivit betydligt fler. Sjukdomar där PGD kan vara aktuella är exempelvis Duchennes muskeldystrofi, Cystisk fibros, Huntingtons sjukdom och Fragil X. Bland patienter som genomgår PGD finns också par som är bärare av kromosomala fel t.ex. balanserade translokationer vilket är en genetisk avvikelse som sällan märks i det egna livet men som kan resultera i upprepade missfall och en risk att få barn med funktionsnedsättningar. Det finns också andra sätt att hantera kunskapen om att bära på ett sjukdomsanlag. Man kan välja att bli förälder genom adoption eller IVF-behandling med donerade ägg eller spermier. Man kan också välja att bli förälder men avstå från diagnostik och föda sitt barn utan vetskap om huruvida det kommer vara drabbad av den ärftliga sjukdomen. För en del par upplevs dessa frågeställningar och val så komplicerade att de avstår föräldraskap.

Ett område som inte studerats så mycket är de psykologiska aspekterna av att välja PGD. Hur upplever dessa kvinnor och män PGD-processen? I fyra studier undersöktes 19 kvinnor och 17 mäns upplevelse av att ta beslutet om att söka för att genomgå PGD, vilka riskfaktorer som kan finnas för symptom på ångest och depression då man söker för PGD, hur tillfredsställelsen med parrelation är när man söker för PGD och tre år senare samt hur beskriver de sin upplevelse av PGD 3 år efter att de påbörjade processen. De 17 paren och 2 kvinnorna som ingick i studien rekryterades under 2010-11 på Reproduktionsmedicin, Sahlgrenska Universitetssjukhuset. Under denna period var totalt 22 par aktuella för PGD. De som avböjde medverkan angav tidsbrist eller att situationen var för svår för att prata om. Av de par som medverkade hade ungefär hälften ärftliga sjukdomar såsom Dystrofia Myotonica eller Fragil X och den andra hälften hade translokationer. Paren hade i snitt levt 10 år i aktuell relation och kvinnornas

medelålder var 31 år och männens 35. Tolv av paren hade drabbats av ett eller flera missfall och/eller avbrytande av önskade graviditeter innan behandling. Fem av familjerna levde eller hade levt med ett barn med den aktuella sjukdomen. Efter tre år hade 6 kvinnor fött barn efter PGD (7 barn, ett tvillingpar). Tre par hade blivit föräldrar efter att först misslyckats med PGD men därefter blivit spontant gravida, genomgått fosterdiagnostik och fött barn utan den aktuella sjukdomen. Ett par hade blivit föräldrar efter donationsbehandling. Två par blev gravida innan de hann påbörja PGD, där föddes ett friskt barn och ett barn med den genetiska sjukdomen. Sex par och en kvinna var fortfarande barnlösa efter tre år.

I **studie I** var syftet att undersöka hur paren kommit fram till beslutet att genomgå PGD. Kvinnor och män intervjuades var för sig. Intervjuerna spelades in och skrevs sen ut ordagrant. Intervjuerna analyserades i syfte att finna och systematisera gemensamma teman. Analysen visar att situationen inför PGD präglas av "Valet" och att detta val relateras till "Relation till sig själv", till "Barnet" och till "Samhället i övrigt". Deltagarna uppfattar valet av PGD både som en möjlighet och en belastning. Både de som har och inte har barn vill genomgå PGD med önskan att få ett friskt barn, men också för att skydda det/de barn som redan finns eller att undvika lidande hos eventuella framtida barn. Kvinnorna och männen relaterar också sitt beslut till att andra individer och samhället kan påverkas om de med PGD "väljer bort" människor med risk för sjukdomar och funktionshinder. De sätter också sitt beslut i relation till samhällets kostnader för PGD och risken att deras behov av diagnostik tar resurser från andra delar av sjukvården. Inga skillnader fanns mellan hur män och kvinnor resonerade kring valet. Både män och kvinnor beskrev det som en process där de rörde sig fram och tillbaka i sitt beslut.

I **studie II** undersöks förekomst av symptom på ångest och depression hos kvinnor och män som planerar PGD och en modell för vilka riskfaktorer som påverkar dessa symptom testades. Kvinnor och män hade i enkäter skattat symptom på ångest och depression. Först jämfördes PGD gruppen med en grupp kvinnor och män som endast gör IVF och där visade det sig att kvinnorna i de båda grupperna inte skiljde sig åt vad gällde symptom på ångest och depression. Vad gäller männen så rapporterade de män som planerade PGD mer symptom på ångest. Det är dock viktigt att komma ihåg att både kvinnorna och männen i PGD-gruppen på gruppnivå, gällande symptom på ångest och depression, var relativt lika svenska normgrupper. I studien testades därefter om ett antal riskfaktorer hade samband med symptom på ångest och depression i PGD-gruppen. De testade riskfaktorerna var: att ha erfarenhet av missfall eller avbrytande av graviditet, att vara förälder till ett sjukt barn, att själv vara sjuk eller bärare av det genetiska anlaget, att ha låg känsla av sammanhang (KASAM), att ha låg utbildning och att vara invandrad till Sverige i första eller andra generation och att ha allmänt nedsatt hälsa. Det visade sig att för kvinnor var erfarenhet av missfall eller avbrytande av graviditet samt låg känsla av sammanhang relaterat till fler symptom på depression. Bland män hade erfarenhet av sjukt barn ett samband med ångest. Tvärt emot vad som var förväntat visade det sig att högre utbildning och svensk härkomst var relaterat till högre symptom på ångest. Andra faktorer än de testade kan också ha betydelse och en del av de riskfaktorer som här inte gav utslag skulle kunna ha ett samband med ångest och depression om det hade varit en större studiegrupp.

I **studie III** var syftet att undersöka om män och kvinnor som sökte för PGD var nöjda med kvaliteten på sin parrelation och jämföra den med förstagångsföräldrar och par som planerade för IVF utan PGD. Syftet var också att se om det skedde några förändringar under PGD-processen i tillfredsställelse med relationen och om denna tillfredsställelse var relaterad till ångest, depression och/eller upplevd föräldrastress. För att mäta tillfredsställelse med relation och symptom på ångest, depression och föräldrastress fyllde männen och kvinnorna i enkäter både vid starten av PGD och tre år senare. För att jämföra med förstagångsföräldrar och par som genomgick IVF utan PGD användes resultat från två andra studier. Det visade sig att kvinnorna som planerade för PGD och när de följdes upp tre år senare var ungefär lika nöjda med kvaliteten på sin relation som de kvinnor som fått sitt första barn eller som de kvinnor som genomgick IVF. Männen i PGD gruppen skattade kvalitén på sin relation lägre jämfört med männen i de två andra grupperna. Männen i PGD gruppen var också mindre nöjda än kvinnorna i PGD gruppen och detta gällde både när de ansökte om PGD och tre år senare. Det fanns ett samband med att vara mindre nöjd med parrelationen och upplevd föräldrastress hos männen både vid start och efter tre år. För kvinnor fanns ett samband mellan att vara mindre nöjd med relationen och ökad förekomst av symptom på depression och ångest efter tre år.

I **studie IV** var syftet att beskriva män och kvinnors upplevelse av PGD tre år efter ansökan om behandlingen. Kvinnor och män intervjuades var för sig. Intervjuerna analyserades på samma sätt som i studie I. Det övergripande temat var *Det är bättre att ha försökt* och det hade tre underliggande teman: *Praktisk erfarenhet av PGD*, *Psykologisk erfarenhet av PGD* och *Målen med PGD*. Kvinnorna och männen var tre år efter PGD-starten fortsatt påverkade av erfarenheten av PGD både i positiv och negativ bemärkelse. Behandlingen upplevdes som hoppfull men den hade i vissa fall bidragit till att de väntade för länge med att påbörja andra möjliga alternativ till föräldraskap såsom adoption. Att genomgå IVF upplevdes som påfrestande både medicinskt och i vardagen. Relationen beskrivs både som stärkt och belastad och känslor av oro och nedstämdhet kan fanns kvar hos en del. Målet med PGD uttrycktes som att sätta stopp för den genetiska sjukdomen både för deltagarna själva men också att kommande barn skulle slippa vara i den situation de själva befunnit sig i.

Par som söker för PGD är en grupp med olika upplevelser av sjukdom och förluster, vissa är barnlösa vid ansökan andra har barn sen innan. Tre år efter starten är gruppen än mer olika i sina erfarenheter då vissa blivit föräldrar och andra inte. En del har försämrats i sin genetiska sjukdom medan andra bara bär anlaget och därför inte är märkta av sjukdomen själva. För vården ger aktuella studier kunskap om att stöd som erbjuds när man ansöker om PGD bör riktas till båda i paret, inte bara kvinnorna. När samtal förs kring beslutet om PGD bör tankar och känslor om beslutet i relation till sig själv, barnet och samhället i övrigt uppmärksammas. Både kvinnors och mäns psykiska situation behöver uppmärksammas och extra uppmärksamhet bör ges åt de som har sjuka barn eller erfarenhet av missfall och/eller avbrytande av graviditet eller låg känsla av sammanhang. Män visade sig vara mindre nöjda med parrelationen än kvinnor både när de sökte PGD och så också tre år senare. Alla 17 par som deltog i studien var kvar i samma relation tre år senare. En av de kvinnor som deltog själv separerade och fortsatte genomgå PGD med en ny partner. Erfarenheterna av PGD tre år senare var att det var bra att ha

försökt att påverka sin situation oavsett utgången. Parrelationen upplevdes både som stärkt och belastad och en del känslor av nedstämdhet kvarstod. För vården är det av vikt att uppmärksamma att många som söker PGD är aktuella för behandling under lång tid och att de kan behöva stöd i olika situationer och vid olika tidpunkter under PGD-processen.

För samhället i stort och för debatten kring etik vid fosterdiagnostik är kunskapen från studierna värdefull då det visade sig att dessa par har en hög grad av omvärldsorientering i sina beslut och sina erfarenheter av PGD.

List of papers

This thesis is based on the following four studies, which will be referred to by their Roman numerals:

- I. Järholm, S., Broberg, M. & Thurin-Kjellberg, A. (2014) The choice of Pre-implantation Genetic Diagnosis (PGD), a qualitative study among men and women. *Journal of Reproductive and Infant Psychology*, 32 (1), 57-69.
- II. Järholm, S., Broberg, M. & Thurin-Kjellberg, A. (2016) Risk factors for depression and anxiety among men and women planning for pre-implantation genetic diagnosis. *Journal of Reproductive and Infant Psychology*, 34 (3), 282-292.
- III. Järholm, S., Thurin-Kjellberg, A. & Broberg, M. (2017) Is pre-implantation genetic diagnosis (PGD) more of a strain regarding satisfaction with marital quality for male or female partners? A three year follow-up study. *Journal of Psychosomatic Obstetrics and Gynecology*, in press 10 April 2017.
- IV. Järholm, S., Thurin-Kjellberg, A. & Broberg, M. (2017) Experiences of pre-implantation genetic diagnosis (PGD) in Sweden: a three year follow-up of men and women. *Journal of Genetic Counseling*, published first online 12 February 2017.

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Abbreviations

ART	Assisted reproductive technique
DAS	Dyadic adjustment scale
ET	Embryo transfer
FUB	Förbundet för barn, unga och vuxna med utvecklingsstörning
GRR	Generalized resistance resources
HADS	Hospital anxiety and depression scale
HADS-A	Hospital anxiety and depression scale, anxiety items
HADS-D	Hospital anxiety and depression scale, depression items
ICSI	Intracytoplasmic sperm injection
IVF	In vitro fertilization
PGD	Pre-implantation genetic diagnosis
PGS	Pre-implantation genetic screening
PND	Prenatal diagnosis
SoC	Sense of coherence
SPSQ	Swedish version of parental stress questionnaire

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Introduction

It is better to have tried, no matter what - Psychological perspectives on pre-implantation genetic diagnosis (PGD)

“What’s bothering me about PGD is that it feels like, “Oh, there is something that we could do” that maybe will prevent difficult decisions later on... but at the same time, it’s very..., well you are selecting an egg. You are choosing who is going to ... have the chance to exist and who isn’t. I thought this was very strange in the beginning.”

Female (couple16)

When you know that you have an increased risk of transmitting a genetic disease to your offspring the wish to become a parent puts you in a challenging position. Nowadays there is the opportunity to choose between different kinds of prenatal diagnosis (PND). One diagnostic option is pre-implantation genetic diagnosis (PGD). PGD is a combination of in vitro fertilization (IVF) and genetic analysis of the embryo before implantation. There is also the choice to refrain from prenatal diagnosis and decide to try to become a parent, regardless of whether the child inherits the disease or not. Other ways to fulfil one’s wish for a child is to become a parent through adoption, IVF treatment with donated eggs or sperm, or to foster a child. Some couples may find making choices too hard to handle and give up the wish for a child all together. At the same time that they wish to become parents, couples often also need to deal with the disease, in one way or the other, in their own lives. The man, the woman or both, can be carriers or be directly affected by the genetic disease. They may also have a parent, brothers or sisters or other relatives with the genetic disease. Sometimes they seek to undergo prenatal diagnosis when they have already given birth to an affected child. In some cases the couple has lost one or several children and/or has terminated desired pregnancies due to the genetic disorder. Others may have experienced several miscarriages or be involuntarily childless (ESHRE, 2012).

The journey to PGD starts with a longing for a child. PGD is not the goal, it is just the means to the end - to have a child unaffected by the known disease. Rotkirch (2007) describes the wish for children in her study of Finnish women as “baby fever” that can be understood both as a need experienced by a nurturing type of personality, but also as a sudden longing due to age or hormonal changes. Rotkirch

also uses the description “acute longing” when the wish for a child is faced with obstacles. This description may be helpful in understanding the driving forces in couples applying for PGD. Foster (2000) proposes a biosocial model for understanding fertility motivation among women, including dimensions of hormonal, environmental, and normative pressures as well as genetic predisposition. All are considered important explanations of why we want children. These dimensions are modified by a number of factors including: a relationship with a liked-minded partner, perceived benefits and cost, financial circumstances, and impact on career and age. There have been fewer studies of men’s fertility motivation and the question is more often addressed as “fatherhood.” Parenthood was found to be viewed as an important part of life both by fathers and non-fathers (Tichenor, McQuillan, Greil, Contreras, & Shreffler, 2011). The ways we have tried to understand humans’ desire to reproduce have shifted during history from being a normal expectation of a heterosexual couple to include today’s medical and legal options, which provide people within different relational and individual contexts with the opportunity to become a genetic parent. A full understanding of the complex and existential question of reproductive motives may not be possible since we all find ourselves in the same discourse and are all a part of this dialogue, as discussed by Möller (2004).

The present thesis is based on four studies focusing on the choice to undergo PGD, risk factors for anxiety and depression when planning for PGD, how satisfaction with marital quality is experienced when applying for PGD treatment and after and also men and women’s long-term psychological experience of PGD three years later.

Aim

The overall aim of this thesis is to increase the understanding of psychological perspectives and to explore factors related to psychological health and relationship satisfaction, in men and women during the PGD process.

Pre-implantation genetic diagnosis (PGD)

The use of PGD in Sweden is regulated in the law on genetic integrity (SFS 2006:351). It states that PGD may only be used if the man or the woman carries genes for a severe monogenic or chromosomal disease, which means a high risk of having a child with a genetic disease or injury. PGD is not allowed for the purpose of choosing traits in a child, and shall focus only on blocking the inheritance of a specific, predefined disease or injury. Before 2006 the legislation in Sweden was even more restricted and PGD was only allowed for diseases causing death during childhood. PGD is a method that gives the couple the opportunity to start a pregnancy knowing that the risk that the fetus will be affected by the known genetic disease is almost totally absent. PGD is most commonly used when potential parents want to use their own gametes. Therefore, PGD is a method that is mostly used by men and women who are living in a heterosexual relationship, who both wish for a child and both want a genetic link to that child. The other scenario when PGD can be used, is more rare. It is when a lesbian couple, or a single woman, wish for a child and where a dominant disease is present in the woman who plans to become pregnant.

The technique

PGD is a challenging way to achieve pregnancy. The couple must first undergo IVF treatment with intracytoplasmic sperm injection (ICSI) and then wait for the genetic analysis, performed on a cell from the embryo, as seen in Figure 1, to see if there is at least one embryo without the known disease and whether this embryo is of the quality that makes it possible to transfer it into the uterus of the woman.



Figure 1. Embryo at day 3, cell is levied for biopsy.

After the embryo transfer (ET) a waiting period of two weeks starts before it is known if implantation has occurred and whether a pregnancy has begun. The process of PGD treatment can be seen in Figure 2.

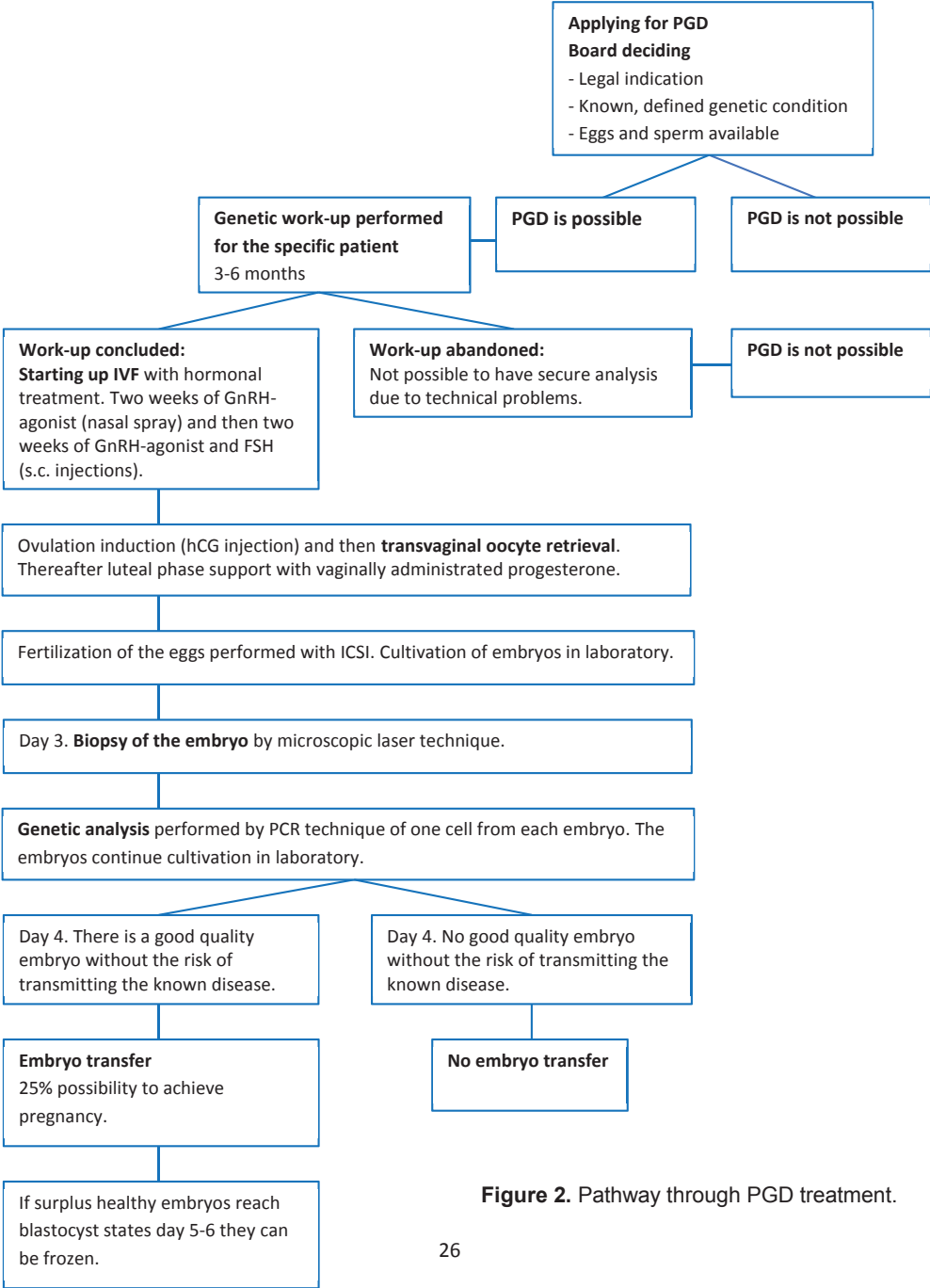


Figure 2. Pathway through PGD treatment.

In a study of outcome after PGD (also including pre-implantation genetic screening) including 1498 couples, it was found that 29% of the couples who underwent a maximum 6 PGD cycles, became parents after PGD treatment (Verpoest et al., 2009).

The success rate differs, and the types of genetic conditions and the age of the woman at the time of PGD are the most significant predictors of success. If pregnancy is achieved the couple face the same worries and decisions as every other pregnant couple, for example the question about other prenatal diagnosis options or screening for Down syndrome and other chromosomal aberrations. PGD was first used in humans in 1990 and since then approximately 10,000 children in the world have been born after PGD (Simpson, 2010). Cystic fibrosis, dystrophia myotonica, Huntington disease and Fragile X are examples of diseases where PGD is allowed in Sweden. To choose PGD for late onset diseases such as inherited cancer is more uncommon, the exception being Huntington disease (Harper et al., 2012). More common is the use of PGD for diseases which manifest themselves during childhood such as congenital metabolic defects. PGD can also be used for chromosomal disorders including the rearrangement of genetic material (translocations or inversion) that may lead to repeated miscarriages (Simpson, 2010).

International legislation regarding PGD varies from country to country, from it being totally forbidden to allowing screening for couples without inherited diseases. In Sweden, the genetic analysis of the embryo is limited to the known genetic disease of the couple, and no screening for other genetic diseases can be performed. In Sweden research into PGD started in the 1990's and in 1997 the first child was born after PGD. PGD now forms part of clinical praxis at Karolinska University Hospital in Stockholm and Sahlgrenska University Hospital in Gothenburg. Each county in Sweden decides which kind of treatments it will offer and for this reason there are regional differences in the provision of PGD. When offered, PGD is covered by national health insurance. Pre-implantation genetic screening (PGS) is not allowed in Sweden except for research purposes. However, in many other countries PGS is allowed. Even though the medical technique is the same for these two groups, the situations differ since individuals in the latter group do not have a genetic condition. Some previous psychological studies have methodological flaws (Karatas et al., 2011) such as combining groups of individuals undergoing PGD with individuals undergoing PGS.

Historical perspective on prenatal testing

Today's opportunities to choose prenatal testing, such as PGD, are the result of social and medical development during the last decade. During the 20th century Sweden implemented reforms to improve maternal and infant health and provide good conditions for the coming child and their mothers/parents. The reforms included socioeconomic benefits (for example child allowance, child care and paid parental leave) and medical interventions (for example maternity care and health care centers). The era of social engineering in the 1930s also contributed to a way of viewing pregnancy and childbirth as a rational decision-making process where increased education, the women's movement, sex education and popular scientific ideas were some of the changes (Porter, 1999). This combination of progressive reforms, medical advances and new thinking paved the way for the acceptance of prenatal testing by many western countries today.

During the 20th century there was a growing awareness of the possible genetic risk of a child inheriting unwanted traits or diseases from their parents. Unfortunately the increased knowledge of genetics coincided with reactionary political ideas and fears of "pollution" of the gene pool, and in Sweden a law was passed to allow the sterilization of persons with intellectual disabilities, psychiatric illnesses or people from different ethnic groups including Roma. In Sweden, the sterilization law existed from 1934 to 1975. In 1941 the law was altered and the compulsory element was more clearly defined. Approximately 90% of those who were sterilized between 1925 and 75 were women. The sterilization could be carried out on different grounds - for racial, social or medical reasons. The underlying rationale in all three cases was to prevent unsuitable genes or behaviors from being passed forward to the next generation. Even though most women and men signed a consent form before surgery, in reality this was a decision made by society and by the physician (SOU1999:2). Since the history of eugenics is associated with sterilization, Nazism and abuse during World War II, the link between it and today's genetic options makes it a difficult subject to discuss. Koch (2004) focused on the complex relationship in Scandinavia between ideas of genetic purity (eugenics) and modern genetic options. Historically, the eugenics argument took various forms at different times; it was part of the women's movement, part of socialist thought as well as part of the liberation of reproductive rights.

Another idea from eugenics was using sperm donation in order to enhance wanted traits. Brewer in the 1940s was, in the Eugenics Review, the first to call the

large number of insemination treatments with sperm from specially selected donors, 'Euteleogenesis', "Assuming then, that a rather superior woman is artificially fertilized with the gametes of a superlatively excellent man, it might be expected that the resulting offspring would exhibit characteristics of a decidedly desirable kind. Thus, in meeting the problem of sterility, we may progress towards the central objectives of positive eugenics." (McMillan, 2007). From this perspective, donation was seen more as a positive intervention to improving genetic stock, rather than a solution to avoiding diseases or a treatment to compensate for male sterility. Questions of morality, religion, sexuality and aspects of parenthood were also raised in this debate. For example, should parenthood be driven by individual choice and love, or should the focus be on society's need to ensure the creation of the best possible new human (McMillan, 2007)?

The growth of prenatal testing was also a consequence of technological advances in radiology, sonography, and cell culture techniques. The first attempt at prenatal diagnosis started with the discovery of the X-ray. In 1916, Case tested X-ray on a pregnant woman. At this time no legal method of abortion was available and the aim of the diagnosis was to prepare for delivery and minimize the risk to the woman during delivery (Resta, 2001). Prenatal diagnosis of fetal abnormality with the option to terminate an affected fetus developed after knowledge about the human chromosomal structure and the possibility to test for abnormalities, increased during the 20th century. Therapeutic abortion following amniocentesis was first reported in 1960. PND was also associated with the legalization of abortion that took place in many western countries during the late 60s (Statham, 2002). This kind of healthcare is still available today, mostly in western industrial societies where it reflects improvements in welfare combined with regulated and well-educated state governments (Porter, 1999). Another part in understanding today's views on prenatal testing is the acceptance and availability of contraceptives during the last 50 years. This has strengthened the belief that one can get the kind of children one wants. PGD is a recent tool in the prenatal diagnostic toolbox but needs to be understood and reflected upon in its historical context. The science of genetics has a dark history with disturbing rationales for controlling the genetic make-up of children that are "allowed" to be born. We are likely to see new prenatal diagnostic alternatives evolving and, taking into account mistakes made in the past, researchers, practitioners and the public have to ask critical questions and reflect on the ethical and societal consequences of new medical procedures.

Today men and women who know that they are at risk of transmitting a genetic disease have the choice of PGD and it is mostly seen as a choice for the individuals involved. Medical techniques are found in the front line of a changing society, where the focus is on improvement. The mind sometimes finds it hard to keep up with the complexity of new developments. This is summarized by Koch (2004) as “Present and past uses of genetic knowledge are neither opposites or identical but linked together in a complex relationship of similarities and differences.” (p 329).

Ethical perspectives on PGD

Ethical concerns have been raised that PGD might contribute to the selection of fetuses on other grounds than intended, for example the fetus’ sex or other traits. Issues to do with genetic testing are regulated by law and give both the couple and the health care authorities support in their decisions. Both users and non-users of PGD are often found to favor PGD over traditional PND such as chorion-villi-biopsy or amniocentesis, with the possible risk of having to undergo termination of pregnancy (Alsulaiman & Hewison, 2006; Chamayou et al., 1998; Lavery et al., 2002; Quinn et al., 2010; Snowdon & Green, 1997; van Rij et al., 2011). PND and termination due to the fetus being affected is allowed in most western countries but gives rise to ethical dilemmas. For example: should a pregnancy with a fetus having Down syndrome be terminated or not? Although termination in early pregnancy without performing any genetic tests is allowed, for practical, financial or emotional reasons (or no given reason in most western societies), sex selection or other trait-selection using traditional PND or PGD, is not widely accepted in the West. (Klipstein, 2005). The ethical concerns regarding PGD often focus on the fact that PGD is an “easier”, more tolerable kind of PND, which does not burden the couple with the decision to terminate a pregnancy and therefore there may be a higher risk that it is used more recklessly, which may be a slippery ethical slope (Munthe, 1999). Representatives of the disabilities movement are often heard in these discussions. An example is a debate article from 2014 published in Aftonbladet (2014-10-03) “Vi måste prata om fosterdiagnostiken”. (“We need to talk about pre-natal diagnostics.”) Thomas Jansson & Maria Hård af Segerstad-Lindhoff were representatives of the Down syndrome patients’ organization and FUB (the Swedish organization for children, young people and adults with intellectual disability). The debate was that the improvement and availability of prenatal testing put persons with disabilities in an even more exposed position. They describe it as “painful to their members to be described as not-wanted, expensive and ill”. Men and women applying for PGD often

find themselves on both sides of this discussion. The disease may be present in their own lives, as they may be sick themselves or have a child with the disease, but at the same time they wish to prevent future children from being born with the disease.

The main reason for undergoing PGD reported in previous studies, was a wish to avoid miscarriage and termination and also to avoid giving birth to children with the disease (Karatas et al., 2010). To offer genetic testing, during or before pregnancy, raises ethical questions both for individuals, healthcare workers, and society. To make an exact definition and exhaustive list of which diseases that should be considered “a severe disease”, the intention of the law regulating PGD, will probably not be possible. In Sweden, a multidisciplinary team of health workers decides if PGD is allowed for a specific disease or genetic condition, and if uncertainties arise the case can be discussed with the National Board of Health and Welfare. The same disease can manifest itself in different ways and first-hand experience of a genetic condition in your own or your family’s life is what defines the situation and severity of the disease (Clancy, 2010; Wertz & Knoppers, 2002). Individuals affected by the disease often have a positive view of the idea of genetic testing. In spite of that, only a minority actually choose to undergo PGD (Clancy, 2010). For example Kelly (2009) found in a qualitative study among mothers in the US who already had a child with a genetic condition that a majority of those chose to refrain from testing during future pregnancies. Kelly highlights the contradiction between the rational decision to offer testing to families at risk, and the emotional reactions to this real-life situation.

Making the decision to apply for PGD

All decisions contain several dimensions: practical (What shall I do?), philosophical (What do I think about it?) and psychological (How does it make me feel?). Decision making is also a process in which both intuitive and deliberative systems are present. When making complex decisions such as deciding on which prenatal diagnostic alternative to use, results by Mikels, Maglio, Reed, and Kaplowitz (2011) suggest that affective decisions, that focus on how the decision makes me feel, may be more effective than deliberative strategies, that focus on cognitive aspects of the decision. Choosing a prenatal diagnostic alternative is further complicated by being a joint decision, a choice that the man and the woman share. On one hand, for certain types of decisions, couples are more able to handle and use facts in a correct way. On the other hand this kind of research on decision-making is often carried out on the basis

of rational choices with a more simple “right” or “wrong” decision, that may not be applicable in prenatal testing (Allwood & Granhag, 1996). Abdellaoui, l’Haridon and Paraschiv (2013) investigated attitudes to risk in individuals and couples found that couples’ attitudes are a mix of the individuals’ attitudes with the women being more influential, at least at low probability levels. They conclude that couples are less risk-averse than individuals at high probability levels, and also less risk-seeking at low probability levels. For this reason, joint decisions should be more “correct,” taking external circumstances into account.

Since the decision to undergo PGD is made before pregnancy, men and women are in a more equal position to influence the choice than with traditional PND (Zeiler, 2007). Maddi and Wong (2012) discussed the complexity of choosing an unknown future, like the situation when couples choosing PGD enter into a demanding procedure not knowing if it will result in a child or not. Maddi views the possibility of making a choice as a way to avoid stagnation, in other words, even when the choice turns out to be a failure the alternative of “not having tried” seems even worse. Choice is also a central part of ethical reasoning since it is about thoughts and actions and what makes one decision more acceptable than another. The process of making a choice can be understood from many angles and at many levels within and between individuals. What makes one decision more acceptable than another also has to do with cultural values. The attribution of the morality of a choice or action is often regarded as an objective, rational process, but research has shown that in daily life this most often occurs after the choice has already been made and is more about justification of the decision (Bloom, 2012). For example the statement that you have chosen PGD to prevent a child from suffering seems rational and objective but this explanation is most likely to occur after the decision has been made. If this was a totally rational process the prevention of suffering should be compared with not being born at all.

In a review on decision making in PGD, Hershberger and Pierce (2010) found three dimensions that influence the decision to consider PGD. These were: cognitive appraisals including risk, cost and time; emotional responses such as pain and joy; moral judgments such as social significance and disease prevention. Hershberger et al. (2012) found that the decision to undergo PGD was a dynamic process occurring over time with a series of choices, where the persons involved moved back and forth in four different dimensions called identify, contemplate, resolve and engage. The participants in the Hershberger study as well as in the present study had all reached the engage dimension when they applied for PGD, but

they were still able to re-visit and reflect on the other dimensions. The phases proposed by Hershberger et al. (2012) before engaging in PGD is shown in Figure 3.

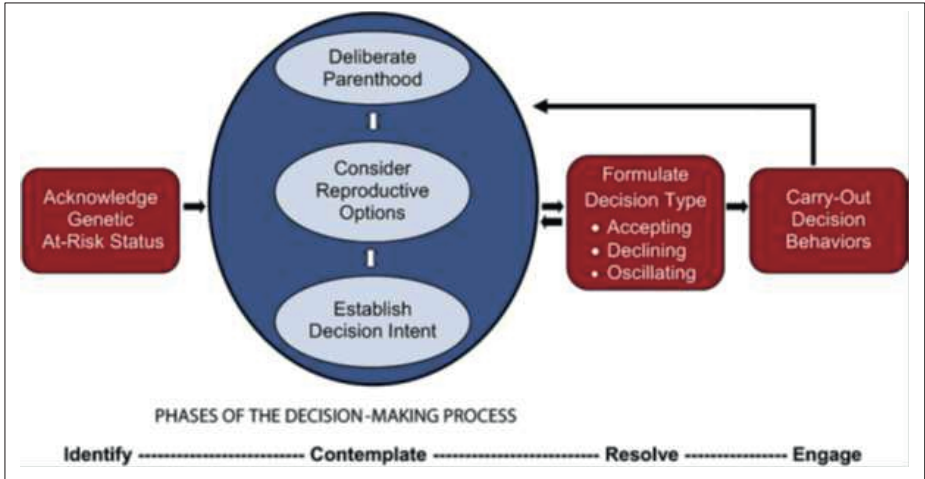


Figure 3. Genetically at-risk couples’ decision-making process relating to PGD. With permission from Hershberger et al. (2012).

When health care workers meet men and women applying for PGD they are meeting a heterogeneous group with a diversity of experiences. Some experiences are shared by all. For example; they have all been faced with a complex choice, when they want to become parents, and have reached a decision to carry out this choice. Some have made this choice due to the experience of living with an affected child and/or loss of a child, or have the disease themselves. For others, infertility and/or a history of miscarriages and sometimes terminations of wanted pregnancies led them to PGD. Others have never yet dared to try to become pregnant and start their journey to parenthood with PGD as their first choice.

Psychological perspectives of PGD

Men and women applying for PGD are a heterogeneous group due to the differences in experiences which have led up to the choice of PGD. They all share a proximity to a disease or genetic condition, which influences their path to becoming parents. It would be psychologically interesting to delineate preexisting life conditions that may explain within-group-differences in distress and mental health symptoms in men and women seeking PGD. It would also be of interest to look at different psychological reactions that can be understood as an effect of PGD treatment. Increased knowledge

about psychological strain experienced at different times during the PGD process could be a guide to when, why and to whom counselling should be offered. Psychological symptoms, for example anxiety and/or depression in times of stress, are expected and can be seen as a normal psychological response to severe life circumstances. But how can we understand why some individuals experience considerable stress and related psychological symptoms while others do not, and can it be predicted who will be in need of increased psychological support and intervention before, during and/or after the PGD process?

Several studies have investigated psychological distress when planning and undergoing ordinary IVF (without PGD). The results are mostly based on women's experiences and show that despite increased stress during treatment they seem to adjust fairly well to the treatment. When comparing men with women, the women report more symptoms of anxiety and depression (El Kissi et al., 2013; Wichman, Ehlers, Wichman, Weaver, & Coddington, 2011). Both men and women who managed to go through with the offered IVF treatments, were well-adjusted at the end of the treatment, regardless of the outcome (Sydsjö, Ekholm, Wadsby, Kjellberg, & Sydsjö, 2005; Sydsjö, Wadsby, Sydsjö, & Selling, 2008). The knowledge attained in studies from IVF couples may apply also to men and women undergoing PGD, since it requires the IVF technique. There are both similarities and differences in experiences of undergoing PGD, and undergoing IVF simply. Only some couples applying for PGD have the experience of infertility that all couples applying for IVF share. Karatas et al. (2010) conducted a review of studies on the psychological aspects of PGD and found that the question had often been explored by "non-users". In studies of hypothetical situations people often saw PGD as a positive option. However, studies carried out on couples with actual experience of PGD reported it as stressful. Karatas et al. (2011) saw that symptoms of depression and anxiety in women undergoing PGD were slightly higher than normal and increased during treatment, but after the treatment the depression and anxiety symptoms returned to baseline.

Although some people in the study experienced similar, severe life-events prior to PGD they did not all react to treatment in the same way. How can we understand why some individuals do well when applying for and undergoing PGD while others react with distress?

Risk factors for psychological distress and PGD

When applying for PGD, men and women often say they are at the right place within the health care system and express a sense of hope: “Finally we will get help.” The process of PGD therefore often starts with an optimistic, positive outlook and a view of a way to achieve parenthood while eliminating the risk of the sort of distress that at least some of them have experienced. At the same time uncertainty and stress is often expressed: “Is this the method for us?” and “Will we be able to manage the strain of the IVF treatment?” Risk factors for distress are often associated with the IVF treatment and involve emotional or practical strains. After the treatment there is also the risk of still being involuntarily childless and facing other difficult options or choices, including more prenatal testing or the decision not to have a child. Some risk factors both before, during and after PGD are more specific and pronounced, such as personal experiences of genetic conditions, severe illness of other children or a troublesome reproductive history. Other experiences are shared with the general population, such as worries about domestic finance, general problems with health and the stress that the transition to parenthood can evoke.

Living with a genetic disease

“Well my husband found out about it (PGD) at a meeting. And at first when he told me I felt like, am I not good enough because of my disease. That was kind of a first reaction just because he thought that it was a great alternative, we don’t have to get sick children ... but then when I got the time to think about it I felt that it was pretty good.”

Female (couple 14)

There is an increased risk of depression and/or anxiety among individuals living with a chronic disease (Bayat et al., 2011). Individuals with knowledge of a risk of transmitting their own or their partner’s disease have, among other parent-related questions, to decide if they will, or will not, give birth to a child with the disease. A pregnancy may provoke an existential crisis among individuals with a risk of transmitting a genetic disease with questions such as “Am I ready to find out about my own condition?” or “Am I able to care for my child when/if I or the child develops

a disability” (de Die-Smulders, de Wert, Liebaers, Tibben, & Evers-Kiebooms, 2013).

The kind of genetic conditions that PGD are allowed for in Sweden are all associated with impairment of different kinds and degrees. For example, myotonic dystrophy affects not only the skeletal muscle but also other organs, including the heart, gastrointestinal organs, endocrine organs, lungs, peripheral nerve, brain, skin, eyes, and bone. This multi-organ involvement is associated with slowly progressive muscle weakness and disrupted social participation. Myotonic dystrophy can be a fatal condition if congenital, when a child has a mother with the condition. Another condition is Fragile X which involves varied degrees of intellectual and/or developmental disabilities in all boys and some girls. LCHAD is a severe metabolic condition that can be lethal during childhood and affect the liver and heart and result in muscle weakness. Even with treatment the condition is progressive and like the other examples above the strain on everyday life is extensive (socialstyrelsen.se/ovanligadiagnoser).

Parents of children with chronic illnesses report more care-related stress compared to other parents and living with a child with a chronic illness may threaten parental integrity and identity (Cashin, Small, & Solberg, 2008; Ingerski, Shaw, Gray, & Janicke, 2010; Sawyer, Antoniou, Toogood, Rice, & Baghurst, 2000; Young, Dixon-Woods, Findlay, & Heney, 2002). However studies have also found that parents, despite the strain associated with chronic illness, tend to see their child’s uniqueness and they become appreciative of things that really matter like personal growth, and they gain clarity about life’s meaning, and discover inner strength they never thought they possessed (Kratz, Uding, Trahms, Villareale, & Kieckhefer, 2009; Samson et al., 2009). However, parents are forced to come to terms with their children’s pain or distress due to the chronic illness and the sadness of knowing that the child has an uncertain and/or limited future (Gibson, Zitzelsberger, & McKeever, 2009; Moola, 2012).

To live with a genetic disease often means a complicated reproductive history starting long before the choice of PGD. One common experience is miscarriage and/or termination before choosing PGD. This experience affects the woman physically, but may also be emotionally distressing for both men and women. PGD is a diagnostic option for parenthood where the man and the woman can be considered equal in the decision-making process since the embryo at this stage is not a part of the woman’s body (Zeiler, 2007). In other aspects however, there are gender

differences also in PGD since the process requires IVF, which affects the female body. Couples applying for PGD often have the experience of miscarriage, prenatal diagnosis such as amniocentesis, or termination of desired pregnancies. These kinds of experiences may cause psychological stress and affect life in the short perspective, but in the longer perspective the majority of people seem to adapt well to the experiences (Korenromp, 2009; Lok & Neugebauer, 2007).

Anxiety and depression

Depression is the most frequent psychiatric diagnosis for individuals experiencing psychological distress in high-income countries (Lopez, Mathers, Ezzati, Jamison, & Murray, 2006). The conditions of depression and anxiety contain a broad spectrum of suffering, from individuals being mildly affected in their everyday life to severe conditions requiring hospitalization. To react with anxiety or depression is an expected and common reaction when faced with severe life events. Expected life changes, such as parenthood, bereavements or sickness, increase the risk of depression and anxiety in the population (Bayat et al., 2011; McKenzie & Carter, 2013). Some individuals are more vulnerable and experience chronic symptoms. Angst, Gamma, and Endrass (2003) showed that persons with frequent “ups and downs” of mood have an elevated risk of depression as well as those who have a family history of depression. But differences in vulnerability to depression and anxiety can also be explained by differences in perceived social support and coping strategies (Roohafza et al., 2014) and/or level of sense of coherence (Lindström & Eriksson, 2005).

In a recent study in the Swedish general population, it was found that the point prevalence of depression was 5.2%, and for generalized anxiety disorder, 8.8% (Johansson, Carlbring, Heedman, Paxling, & Andersson, 2013). Furthermore, the comorbidity between depression and anxiety was high (28.2%). Van de Velde, Bracke, and Levecque (2010) studied gender differences regarding depression in 25 countries in Europe and found that in almost all countries (except Ireland, Finland and Slovakia) women report significantly higher levels of depression than men. Similar gender differences are reported for anxiety in a review study by McLean and Anderson (2009), who also point out that there are gender-specific risk factors where women are more distressed by potential threat and feelings of uncontrollability than men. A combination of life stress such as adverse life-events, chronic stress exposure, poor social support, and limited social networks coupled with limited

psychosocial resources is associated with adverse psychological, physical and quality of life outcomes (Stephens & Marmot, 2003). Furthermore, an individual's social and/or economic situation has also been found to be related to well-being. A study performed by the Swedish National Survey of Public Health found that good standards of living and high social capital are associated with higher degrees of psychological well-being (Ahnquist, Wamala, & Lindstrom, 2012).

Resistance factors when facing severe life events

Different theoretical perspectives within psychology try to answer the question of why some individuals adapt better to stress or challenges in life than others. Common for these theoretical perspectives is the wish to explain individual variation in reaction to, and adaptation to, adversity. Some of the theoretical concepts that can be relevant are resilience, sense of coherence, hardiness, purpose in life and self-transcendence. Lundman et al. (2010) investigated what these concepts had in common and found that they are all different ways to understand inner strength. Lundman et al. (2010) hypothesizes that inner strength is an interaction of four dimensions; connectedness, firmness, flexibility and creativity. Aujoulat, Marcolongo, Bonadiman, and Deccache (2008) describe the core of resistance theory as a protective process where a person is able to both “hold on” and “let go” in relation to thoughts and strategies, when faced with a severe life event such as the need to undergo PGD.

In this thesis, sense of coherence (SoC), coping and resilience are used as theoretical concepts for understanding individual differences in psychological distress. SoC is a theory developed by Antonovsky (1987). He proposed SoC as a global orientation, determining the extent to which an individual feels that he/she possesses resources to handle difficult situations and experience these as challenges worthy of investing energy in. In contrast individuals with weaker SoC might experience the same situation as a threat, exceeding their resources and making them more prone to experience stress, and stress-related symptoms such as depression or anxiety. Coping has to do with the strategies individuals use to manage stressful situations in everyday life. Coping strategies can be both adaptive and maladaptive for the individual’s long-term adaption. Resilience theory focuses on the development of health in spite of risk exposure; how can some individuals overcome adversity and sometimes even turn their experiences into strengths? Although the PGD group is heterogeneous it is reasonable to assume that they have experienced more severe life events than most people of similar age. The concepts of SoC, coping strategies and resilience are theoretically related and can complement each other in understanding strengths and vulnerability in individuals undergoing PGD. SoC can be seen as a resistance factor among others, while coping strategies serve the purpose of handling stress when facing life events such as PGD, and resilience theory offers a broader understanding of how resistance and risk factors co-exist and interact.

Sense of Coherence

SoC is commonly used in medicine and has been shown to be related both to how individuals cope with their illness in terms of psychological symptoms and also to physical health outcomes and recovery in, for example, cancer and rheumatism (Goulia et al., 2015; Sales, Carvalho, McIntyre, Pavlidis, & Hyphantis, 2014). Antonovsky (1987) defined SoC as “a global orientation that expresses the extent to which one has a pervasive, enduring though dynamic feeling of confidence that (1) the stimuli, deriving from one’s internal and external environments in the course of living are structured, predictable and explicable; (2) the resources are available to meet the demands posed by these stimuli; and (3) these demands are challenges, worthy of investment and engagement” (p 19).

SoC comprises:

(1) A cognitive component labeled *comprehensibility*, representing the extent of the belief that the problem faced is clear. The fact that many couples undergoing PGD have had many previous contacts with healthcare puts them in a position where they have received information at different phases, where the quality of the information has varied and couples may have been in different states of mind. Karatas et al. (2010) found that women facing PGD had information needs that were not catered for and felt that they had a lack of knowledge about the PGD treatment. This dimension affects the second central concept of SoC namely, manageability.

(2) The component labelled *manageability*, represents the belief that the necessary resources to cope successfully with the challenges are available. Franklin and Roberts (2006) found that when men and women came to the clinic where PGD was performed it was with relief and the feeling that the situation was possible to handle together. Even though the outcome was still uncertain, they felt it was manageable. Couples who are about to start PGD can be seen as moving from a situation of obstacles towards a more manageable situation, where the treatment can be perceived as full of hope and promise (Hershberger & Pierce, 2010).

(3) The third motivational component is labelled *meaningfulness* and represents the extent to which a person participates in the process of shaping his or her own destiny and daily experience (Antonovsky, 1987). The couples applying for PGD find themselves in a position where they are trying to put life back to a previous, hopeful phase. To use the concept of Aujoulat et al. (2008), they were “holding on” to their wish for pregnancy with a genetic child of both the man and the woman. But they

have already “let go” of the original plan, based on the realization that this was no longer a decision within their own control.

Volanen, Lahelma, Silventoinen, and Suominen (2004) investigated factors both in the past and the present that were related to SoC. They suggest a framework of understanding SoC as laid out in Figure 4.

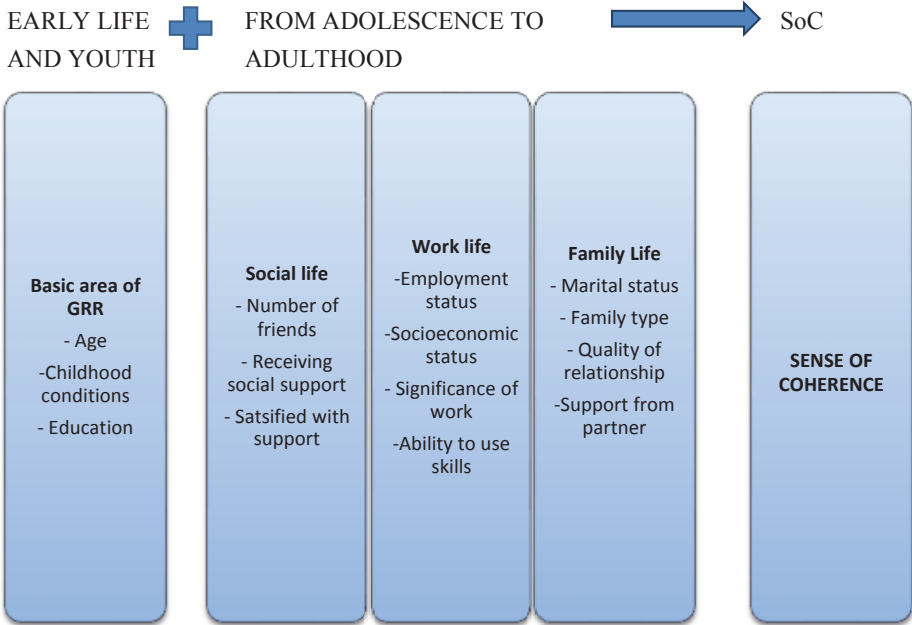


Figure 4. Framework of four general areas of GRR (generalized resistance resources) assumed to contribute to SoC.

Volanen et al. (2004) study showed that of all variables the quality of one’s marital relationship showed the strongest correlation with SoC for both sexes. Being in an unsatisfactory relationship or not receiving support from the partner was strongly related to low SoC. In couples facing PGD it could be hypothesized that the relationship is at a level which is good enough to allow partners to formulate a joint wish to become parents. However due to the burden of PGD a shortage of support can occur. It is also important to bear in mind that the men and women undergoing PGD are not spared strains from other domains of life such as unemployment, and experiences from childhood or from work.

Several studies also discuss whether SoC should be seen as a relatively stable dimension of personality or a dimension that increases or decreases in relation to supportive or stressful life events (Schnyder, Büchi, Sensky, & Klaghofer, 2000; Snekkevik, Anke, Stanghelle, & Fugl-Meyer, 2003; Volanen et al., 2004; Volanen, Lahelma, Koskenvuo, & Silventoinen, 2007). Antonovsky (1987, 1993) first proposed that SoC should be seen as relatively stable after the age of 30 and that GRR could be seen as protective factors especially among the group with high SoC. More recent studies (Antonovsky, 1991; Hakanen, Feldt, & Leskinen, 2007) have shown that low SoC is less stable during adulthood. Others have found that low SoC is more strongly associated with health variables than high SoC. The same study showed an overlap between SoC and levels of depression and anxiety leading to a discussion of the validity of the SOC concept (Kontinen, Haukkala, & Uutela, 2008).

Coping strategies

To choose and to go through with PGD probably favors individuals with psychological strengths. One way to understand psychological strength and vulnerability is to look at ways of coping. Lazarus and Folkman (1984) formulated coping as “constantly changing cognitive and behavioral efforts to manage specific external and/or internal demands that are appraised as taxing or exceeding the resources of the person” (p 141). Coping is a way to understand the process of trying to manage psychological stress in everyday life and, according to Lazarus and Folkman, should not be viewed as a fixed trait. Yet other theoretical approaches, such as McCrae (1989), view coping as a relatively stable trait through life.

Coping is generally divided into categories of coping skills. One way to sort coping skills is into cognitive or behavioral strategies and these can be approach or avoidant-oriented as seen in Figure 5 (Billings & Moos, 1981).

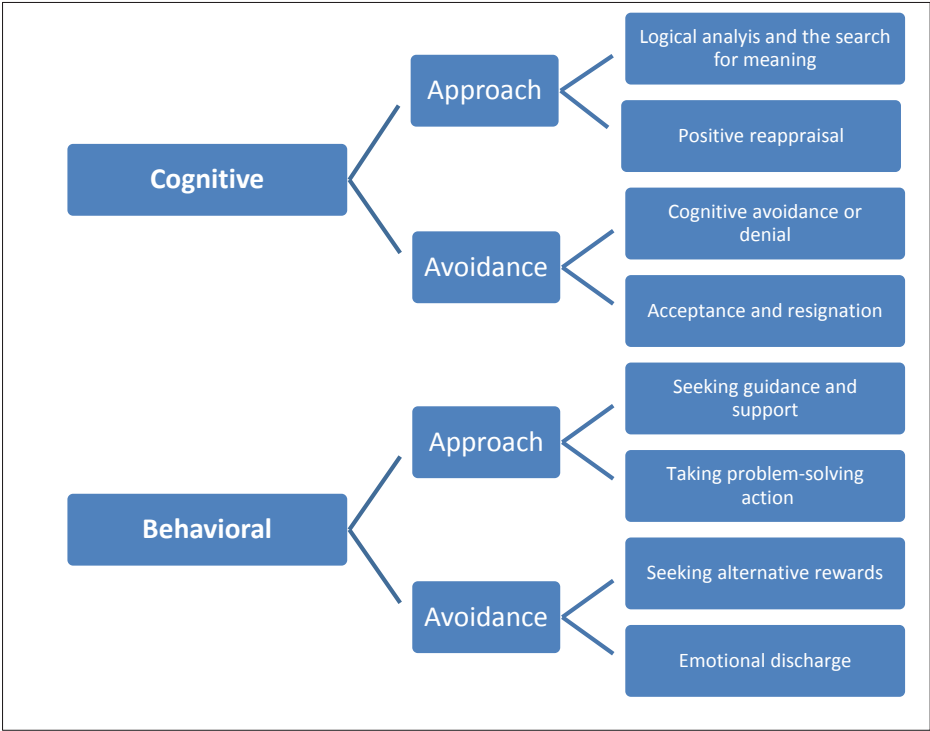


Figure 5. Cognitive and behavioral coping according to Billings and Moos.

When applying for PGD both behavioral and cognitive approach oriented skills are used, such as logical analysis and problem-solving action. As the PGD process evolves, in addition to the approach strategies, avoidance related strategies such as acceptance and resignation may be useful for dealing with unsuccessful treatments.

Another common way to describe coping strategies is to divide them into emotion-focused or problem-focused. Examples of emotion-focused strategies are seeking social support or ruminate. Examples of problem-focused strategies are seeking information or actively trying to change the situation. In addition, dysfunctional strategies, for example drinking, are often added as a third category. A third way is to sort coping into passive or active strategies (Carver, Scheier, &

Weintraub, 1989). The use of emotion-focused strategies is more common among women while men more often use instrumental problem solving strategies (Matud, 2004; Wilson, Pritchard, & Revalee, 2005). There are also studies indicating that women tend to use a greater variety of coping behaviors or skills than men (Tamres, Janicki, & Helgeson, 2002). However, the gender differences may change or disappear as they may parallel social gender differences that can transform and coping is context-dependent. Regardless of differences in the theoretical structure of the coping concept it has been found that approach-oriented or active coping is associated with less distress and more well-being among persons with chronic illness and disability (Penley, Tomaka, & Wiebe, 2002; Wilson et al., 2005).

SoC has been studied in relation to coping. Pallant and Lae (2002) found that individuals with a high sense of coherence were more likely to adopt active, problem-focused coping, and a higher SoC was also related to a more flexible use of coping strategies. Gooding, Organista, Burack, and Biesecker (2006) hypothesized that people facing genetic testing best managed this situation if they were able to shift between emotion-focused coping and problem-focused coping, the former to be used in situations judged to be uncontrollable and the latter if the stressor is judged to be controllable and amenable to change. This flexibility in coping styles depending on the situation has been called “goodness of fit hypothesis” (Zakowski, Hall, Klein, & Baum, 2001). Coping strategies have also been studied in the IVF group and it has been found that women who practice avoidant coping strategies experience the treatment situation as more stressful and less manageable than women with a more problem-focused coping style (Gourounti et al., 2012). Individuals with active problem-focused coping strategies are probably more likely to choose PGD and go through with it, than individuals who use more passive coping styles. It seems reasonable to expect that individuals with high SoC are more likely to practice “goodness of fit” between problem-focused coping and emotional-focused coping in different steps of PGD treatment and therefore are more able to handle the stress.

Resilience

Rutter (1987) published the framework of the resilience theory. He states that resilience is a way to understand how people adapt to adversity. Key components in this theory are risk and protective factors and a focus on strengths rather than deficits. Resilience is not something that lies primarily within the person but is a transactional process between the person experiencing adversity and risk, and his or her internal

and external protective factors. For example, a person applying for PGD that has recently been diagnosed with a genetic disease can show positive adaptation despite this adversity, in other words, resilience. The person in this example will probably also have some protective factors available such as flexible coping strategies, stable relationship with partner, good social support from family or work, or being helped by an empathic doctor. Fergus and Zimmerman (2005) constructed a model of resilience, Figure 6, (adapted from Tiet, 2002) that can be used to describe possible risk and protective factors for an individual facing PGD. The person in the example above can be considered as resilient (B), according to the model. Another person in the same situation but with a low SoC, poor relationships, lack of support and a poor financial situation could be at greater risk of experiencing the situation as overwhelming, leading to poor adaptation (D) showing distress and not being able to cope with everyday life during PGD.

	Low risk	High risk
Positive outcome	A (normative development)	B (resilience theory)
Negative outcome	C (inadequate risk assessment)	D (risk models)

Figure 6. Model of resilience, positive adaptation to high risk.

From one perspective, men and women facing PGD may be considered as being at risk of distress since they are preparing themselves for a medical procedure with a desired outcome, a child, although they have no guarantee that they will actually become parents. For some who are applying for PGD the method can be seen as a relief after several miscarriages and terminations and PGD brings the hope of not having to repeat the experience. According to resilience theory the psychological outcome will be positive regardless of whether there is a child or not, if the individual finds a way to cope with the situation. The possibility of coping with severe life events will depend on both internal factors, such as SoC, and coping strategies and external factors, such as the socioeconomic situation and social support. In resilience theory, the probability of a positive or negative outcome can be understood in the light of the person’s accumulated experience of risk and protective/resilience factors. PGD can be seen as a potential stressor/challenge which it is possible to cope with (resilience), or as an adverse event which together with other accumulated risk factors exceeds what the individual is able to adjust to. As resilience incorporates social and environmental influences it means in the case of PGD that it is possible

both for healthcare workers to improve resilience if they offer good support (which acts as a protective factor), but also to constitute a risk factor if they add to the patient's stress by not being supportive and thereby contributing to a negative psychological outcome.

Emotional partnership

Why do many men and women want to be a part of an emotional partnership and have children? The answer to the first part of the question is that being a part of an emotional partnership, regardless of whether the civil status is marriage or cohabitation (from now on in this text, all emotional partnerships regardless of civil status, are called marital relationships) is associated with better mental health and reduced stress. This applies particularly to men but is also true for women. Good-quality relationships, as compared to remaining single, bestow mental health benefits for both men and women. Mental health for men is similar if they are in a poor relationship or single, while women's mental health is better when they are single than when they are in a poor relationship (Leach, Butterworth, Olesen, & Mackinnon, 2013; Muhammad & Gagnon, 2010). The answer to the second question is more complex. Parenthood increases stress for both men and women (Widarsson et al., 2013) and the quality of the marital relationship does not seem to be negatively affected by infertility and childlessness (Sydsjö et al., 2005). The impact of parenthood on marital quality is hard to study since the impact of a child's arrival is affected by several dimensions such as the age of parents, length of relationship and whether the pregnancy was planned or unplanned. Or as Cowan and Cowan (1995) stated, "a baby's arrival is unlikely to destroy very well-functioning marriages or generate closer, more satisfying relationships between already troubled partners" (p 415).

Affected by infertility

Some couples undergoing PGD have infertility problems as a consequence of the genetic condition, but far from all couples undergoing PGD are infertile. But PGD treatment involves IVF regardless of whether or not there are infertility problems. The extensive research into marital relationship in couples undergoing infertility treatment is multifaceted and shows that infertility can be a strain (Greil, Slauson-Blevins, & McQuillan, 2010; Herrmann et al., 2011) but the relationship between partners can also be strengthened by the experience (Reporaki et al., 2007; Schmidt, Holstein, Christensen, & Boivin, 2005; Sydsjö et al., 2005). Coping patterns, perceived social support and infertility treatment all play central roles in the adaptation to, and experience of, infertility and its effect on the quality of marital

relationships (Benyamini, Gozlan, & Kokia, 2009; Martins, Peterson, Almeida, Mesquita-Guimarães, & Costa, 2014; Peterson, Pirritano, Block, & Schmidt, 2011; Van Den Broeck, D'Hooghe, Enzlin, & Demyttenaere, 2010). Resilience and the ability to cope together as a couple are protective factors in preserving marital satisfaction in the face of infertility (Herrmann et al., 2011; Ridenour, Yorgason, & Peterson, 2009). However, Gameiro, Nazaré, Fonseca, Moura-Ramos, and Canavarro (2011) found that the shared experience of infertility could not protect the couple from the challenges of parenthood once they had succeeded in becoming parents.

Influenced by parenthood

The transition to parenthood is a vulnerable period in terms of psychological well-being (McKenzie & Carter, 2013). Giallo et al. (2013) investigated stress among Australian fathers and found that approximately 10% of first time fathers experienced elevated psychological stress. The elevated stress was related both to internal factors such as low parental self-efficacy but also to external factors such as trouble at work or poor quality relationships. A Swedish study found that depression among first time fathers was related to low educational level, low income, poor partner relationship quality and financial worry (Bergstrom, 2013). There was also an increased risk of depressive symptoms if the man was below 29 years of age. Leight, Fitelson, Weston, and Wisner (2010) found, in a review of childbirth and mental disorders among women, that there is an elevated risk of developing several mental conditions during pregnancy and the strongest predictor of mental illness during the perinatal period is a history of previous psychiatric illness, particularly affective illness. A large-scale epidemiological study on Spanish women noted that the prevalence of all non-psychotic postpartum psychiatric disorders at six weeks postpartum was 18.1%, and mood disorders comprised the majority (9.8%), followed by adjustment disorder (4.3%) and anxiety disorders (4%) (Navarro et al., 2008).

The influence of parenthood on satisfaction with the quality of the marital relationship is affected by the presence of protective and risk factors. Knowing each other for a long time before parenthood, good financial resources, high levels of education and good health are all protective factors while lack of consensus regarding child upbringing or division of household labor increases the risk of relationship termination (Loft, 2011). Lawrence, Rothman, Cobb, Rothman, and Bradbury (2008) found that parenthood hastens marital decline even for those couples who have

chosen to have children, but planning for pregnancy seems to protect couples from this decline. The general protective factors such as long-term relationship and having extremely well planned pregnancies would favor levels of marital satisfaction during the transition to parenthood in couples undergoing PGD.

Beukers et al. (2012) compared Dutch couples who achieved parenthood after IVF/ICSI with and without PGS and found that there were no differences between these two groups with regard to psychological distress and parenthood. Several assumed predictors such as maternal age or time to pregnancy were not associated with parental distress. Child behavior problems were found to be associated with stress and were found to decrease over time. In a review Hammarberg, Fisher, and Wynter (2008) report that women who became parents after IVF expressed more anxiety and worries during pregnancy than women who had become spontaneously pregnant. But nevertheless, marital satisfaction and parent-infant relationships in assisted reproduction technique (ART) groups are similar or better compared to the general population. A large population-based study in Denmark found a lower risk of psychiatric illness for men and women who had become parents after IVF than for parents who had become spontaneously pregnant (Sejbaek, Hageman, Pinborg, Hougaard, & Schmidt, 2013). Despite some in the PGD group having the risk factors associated with being a parent of a child with a severe disease, it is reasonable to conclude that the group who were already parents before the start of PGD, or who became parents after PGD, should not on a group level be viewed as more troubled by parenthood than the general population.

In conclusion, when facing PGD men and women are in a phase where they have made a decision to change their life situation, hopefully to become parents, and at the same time they approach a period with increased risk of psychological strain and uncertainty. They all come to the health care system prepared for extensive medical treatment and they are all individuals with risk and protective factors in their lives. When applying for PGD the group is heterogeneous in regard to their previous experiences and perhaps even more heterogeneous after their experiences of undergoing PGD. The procedure affects them differently and for some it will result in a child. The overall aim of this thesis is to increase the understanding of psychological perspectives and to explore factors related to psychological health and relationship satisfaction, in men and women during the PGD process.

Summary of studies

All four studies are based on data from the same group of men and women undergoing PGD. Both interview data and self-report measurements were collected at two time points, at the start of PDG and three years later. The first study in the thesis is based on interviews with men and women applying for PGD. The second and third studies are based on self-report questionnaires from inclusion and three years later. The second study also includes a group of men and women applying for first time IVF. The forth study is based on interviews three years later.

Specific aims

The aim of *Study I* was to investigate the psychological aspects of men's and women's decisions to undergo PGD, the influence of the healthcare system and ethical considerations.

The first aim of *Study II* was to compare symptoms of depression and anxiety in men and women who made the choice to undergo PGD, with men and women who were planning their first IVF. The second aim was to understand individual differences in depression and anxiety within the PGD group by investigating if six theoretically proposed risk factors could explain variation in self-reported symptoms of anxiety and depression in men and women planning to undergo PGD. The factors were: (1) reproductive history, (2) having a child/children with the genetic disease, (3) being affected by or being the carrier of the genetic disease oneself, (4) self-reported SoC, (5) socioeconomic factors, and (6) problems with health.

In *Study III* the aim was to study the quality of the marital relationship in couples undergoing PGD. Research questions were: (1) Is the satisfaction with the quality of the marital relationship in men and women applying for PGD similar to that of first-time parents and couples undergoing IVF without PGD? (2) Does satisfaction with the quality of the marital relationship change between the start of PGD and the follow-up three years later? (3) Is there a correlation between satisfaction with the quality of marital relationships in men and women undergoing PGD and levels of anxiety, depression and parental stress?

In *Study IV* the aim was to investigate long-term psychological experiences of PGD in men and women, for example how their relationship have been affected and how they coped with parenthood or childlessness three years later.

Methods

Data used in the thesis comes from couples referred for PGD to Reproductive Medicine, Sahlgrenska University Hospital from January 2010 to June 2011. The participants were recruited by their gynaecologist at their first visit. The IVF couples participating in *Study II* were recruited in 2011 at the same clinic and by the same procedure. The study was approved by the Ethical Review Board in Gothenburg, (2009-06-15, Dnr: 300-09).

The research group that carried out the project consisted of a professor in psychology at the University of Gothenburg, an associate professor in medicine at Sahlgrenska Academy and a psychologist at Reproductive Medicine and PhD student in psychology at the University at Gothenburg.

Participants

In 2010 and 2011, twenty-two PGD couples were eligible to join the study and of these 17 couples (both men and women) and two women agreed to participate ($n=36$). Participants in the PGD group had opted for PGD but had not yet started the programme. In the PGD group the only inclusion criterion was planning for PGD; no exclusion criteria were stated. Non-participants gave emotional or practical reasons for declining. Ten of the couples carried genes for monogenetic diseases, and nine couples had chromosomal disorders. Seven of the couples lived in rural areas and twelve in urban areas. Four women and three men were first or second generation immigrants. Six women and seven men (one man had a child from a previous relationship) were parents at the start of PGD. In addition, one couple and one woman who participated on her own had the experience of previously losing their first child due to the genetic condition. The PGD participants' reproductive histories at inclusion are presented in Table 1.

Table 1. Reproductive history at inclusion.

Couple	Age M/F	Genetic condition	Miscarriages/ Terminations*	Disease
1	34/30	F-c M-c		Krabbes disease
2	29/35	F-c	7/-	Translocation
3	/30	F-c	3/-	Chromosomal inversion
4	32/29	F-s		Myotonic dystrophy
5	38/35	F-c		Translocation
6	36/36	F-s	-/1	Myotonic dystrophy
7	27/23	F-s	-/1	Myotonic dystrophy
8	30/28	F-c		Fragile X
9	/30	F-c M-c	-/4	Metabolic disease
10	46/37	F-c	3/-	Translocation
11	39/35	M-c	1/2	Translocation
12	39/34	M-c	4/-	Translocation
13	30/35	M-c	1/-	Translocation
14	36/25	F-s		APC cancer
15	36/38	F-c	1/2	Translocation
16	32/28	F-c M-c	3/-	Metabolic disease
17	32/32	F-s		Myotonic dystrophy
18	36/30	M-c	4/-	Translocation
19	28/26	M-s		APC cancer

Note: M, male; F, female; c, carrier; s, sick; *numbers of terminations due to the known genetic condition.

The number of participants in the IVF group (used in Study II) was chosen to match the number of participants in the PGD group. The participants in the IVF group were planning for their first IVF cycle. In the IVF group 24 out of 39 women and 23 out of 39 men agreed to participate. Among the 39 IVF couples, four couples were excluded for medical reasons (planning for donation instead, or requiring surgery prior to IVF) or insufficient knowledge of Swedish to complete the questionnaires. Eleven couples did not return the survey, although a reminder letter was sent. Participants' characteristics at inclusion are presented in Table 2. Compared to the IVF group the PGD group had a higher level of education and their marital relationships were longer when the treatment was planned. No significant differences were found regarding age or occupation.

Table 2. Participants' characteristics (PGD and IVF patients).

Variable	PGD		IVF	
	Female (n=19)	Male (n=17)	Female (n=24)	Male (n=23)
Age				
Mean (SD)	31.3 (4.1)	34.8 (4.9)	32.2 (3.7)	35.1 (3.6)
Median (min; max)	30 (23; 37)	36 (27; 46)	33 (24; 38)	35 (28; 41)
Years in relationship				
Mean (SD)	9.58 (4.36)*	9.88 (4.36)*	6.33 (3.97)*	6.48 (4.00)*
Highest level of education				
Primary school	0	0	1 (4.2%)	0
Secondary school	4 (21.1%)	5 (29.4%)	11 (45.8%)	17 (73.9%)
University	15 (78.9%)	12 (70.6%)**	12 (50.0%)	6 (26.1%)**
Employed/self-employed				
	16 (84.2%)	17 (100%)	20 (83.3%)	20 (87.0%)
Student				
	0	0	3 (12.5%)	1 (4.3%)
Unemployed				
	1 (5.3%)	0	1 (4.2%)	2 (8.7%)
Parental or sick leave				
	2 (10.5%)	0	0	0
Parent at T1				
	6 (31.6%)	7 (41.1%***)		
Parent at T2				
	12 (63.2%)	11 (64.7%)		

* $P < 0.017$ significant difference regarding length of relationship.

** $P < 0.009$ significant difference regarding education between men.

***One man had a child from a previous relationship.

After three years all participants in the PGD group had tried to achieve pregnancy. The outcomes are shown in Figure 7.

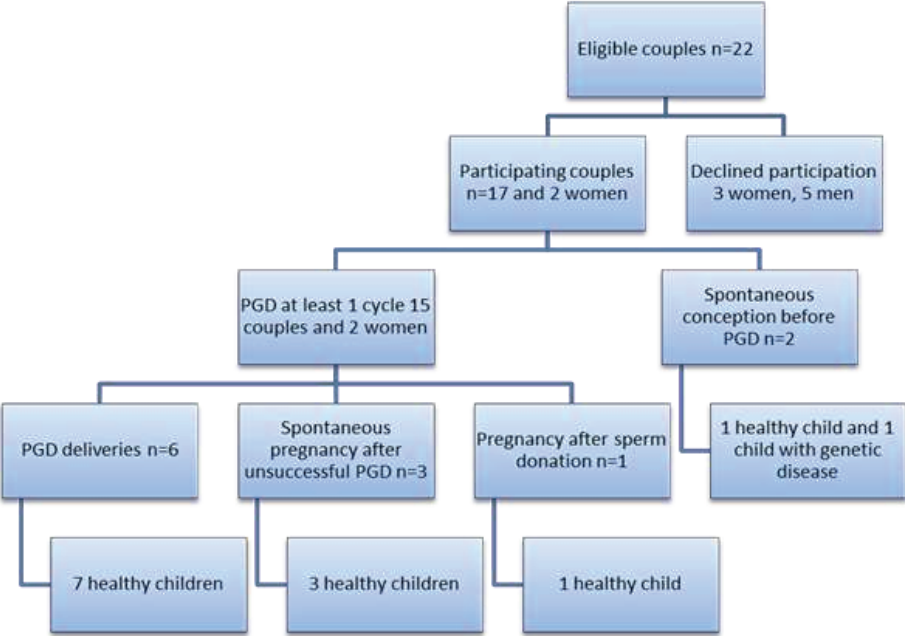


Figure 7. Pregnancy results three years after applying for PGD.

Fifteen of the couples and both of the two women had undergone at least one PGD cycle, and seven children (five singletons, one set of twins) were born after PGD. The two couples who had not undergone PGD achieved spontaneous pregnancies before starting PGD treatment, resulting in one healthy child and one child with the known genetic disease. In addition, three children were conceived spontaneously during the three years by couples who had gone through unsuccessful PGD treatments, and their children were born without the known genetic disease. One child was born after sperm donation. Four couples were still undergoing PGD treatment after three years, three of them making new attempts to try to achieve a sibling for a child born after previous successful PGD treatment. One of the two women who participated in the study without the participation of a partner was divorced from her first husband and at follow-up she was undergoing PGD with her new partner. Six couples and one woman were still childless three years later.

Procedures

Data was collected on two occasions; at inclusion (interview PGD and questionnaires PGD/IVF) and three years later (interview PGD and questionnaires PGD).

Both the PGD group and the IVF group (*Study II*) were recruited by their gynaecologist at their first visit when planning for treatment. The question of participation was asked personally and the men and women were encouraged to make the decision about participation regardless of their partner's decision. The men and women were recruited consecutively during 2010 and 2011. All couples (22) applying for PGD during this period were asked to participate. If the man and/or woman in a PGD couple consented to participate they were contacted and booked for an interview and at the interview they got the questionnaires, and filled them out at the time of the interview or returned them in a pre-paid envelope. The follow-up was carried out at three years from inclusion in 2013 and 2014. First the men and women in the PGD group were contacted by letter and informed that the three-year follow-up was coming up. Thereafter they were contacted by phone and asked if they were willing to participate. All 19 women and 17 men agreed to take part in the follow-up interview and also to fill out questionnaires. Both at inclusion and three years later about half of the participants came to the hospital for the interview. About half preferred to be interviewed in their home mainly because of the need to take care of children or because they lived a long way from the hospital. The interviews were performed individually. The lengths of the first interviews were for women between 18 and 60 minutes and for men between 13 and 54 minutes. The lengths of the follow-up interviews were for women between 19 and 53 minutes and for men between 13

and 45 minutes. The follow-up interviews were in general a bit shorter since the background questions were already answered on the first occasion. Two interviews (one man, one woman) were less than 30 minutes at the first time and were also less than 30 minutes at follow-up. This was mainly associated with personal factors; those who spoke most sketchily did this both times regardless of experiences of PGD. The interviews were all recorded and then transcribed verbatim.

If the man and/or woman from an IVF couple agreed to participate they were given a booklet of questionnaires at the clinic and could chose to fill them out there or send them back by post in a pre-paid envelope.

Instruments

Interviews

In *Study I* and *IV* a semi-structured interview guide was used. The guide was constructed from clinical knowledge and previous research. For *Study I*, the guide contained four themes: (a) psychological aspects, (b) how the PGD decision had been made, (c) how and where they obtained the information about PGD, (d) and ethical considerations. Examples of questions from the first interview were: Do you already have children? Are they diagnosed with the genetic disease? Sick? Diseased? Do you/your partner carry/have this disease/gene; do you have any thoughts about this? How does your wish for children affect you emotionally? Through your life, what feelings and thoughts have you had about the possibility of becoming a parent? How have you and your partner reasoned about different options (prenatal testing)? Are there aspects where you disagree? Which dis/advantage do you see to the option you have chosen now? Have you taken into account ethical considerations when making your decision?

The semi-structured interview guide used at follow-up, *Study IV*, was derived from the guide used in *Study I* and contained the following themes: (a) psychological aspects (b) experiences of the decision-making process regarding their wish for children, (c) experiences of PGD and (d) ethical and religious considerations. Examples of questions are: Do you think that your marital relationship has been affected by the PGD-treatment? If yes, in what way? How do you perceive your psychological health? How do you feel about the choice of PGD when you look back at it today? If you think about the knowledge you have today, what would your advice be to someone who is just about to start PGD? Have you considered other options for parenthood (adoption or donation)?

On both occasions the interviews started with a broad question about whether they could start by describing what they were planning for (first time) and what they had been going through (follow-up). In addition, they were encouraged to describe their day-to-day lives. Thereafter the interview was deepened and the participants were encouraged to respond freely about the areas/questions introduced by the researcher. The goal of the interview was to create a climate which was able to support an organised conversation and to avoid question-answer collaboration. For example, when participants asked “Is this the kind of answer I was supposed to give?” they were told “We are interested of **your experience** and there is no right or wrong answer.”

Questionnaires

In *Study II* the Hospital Anxiety and Depression Scale (HADS), a self-report questionnaire by Zigmond and Snaith (1983), was used to measure anxiety and depression. HADS includes 14 items, seven measuring anxiety and seven depression. Each item is rated on a four-point Likert scale. In a systematic review of a large number of studies by Bjelland, Dahl, Haug, and Neckelmann (2002) a cut-off point of 8/21 for anxiety and depression was identified. For anxiety (HADS-A) this gave a specificity of 0.78 and a sensitivity of 0.9. For depression (HADS-D) this gave a specificity of 0.79 and a sensitivity of 0.83. Cronbach’s alpha in the present study was 0.76 for HADS-A and 0.84 for HADS-D.

The Swedish version of the short sense of coherence SoC scale (13 items) was used to measure individuals’ sense of coherence. Items are rated on a seven-point Likert scale (Antonovsky, 1993). Although the scale consists of the three concepts of SoC, *comprehensibility*, *manageability* and *meaningfulness*, it is commonly used as a total scale comprising the total concept of SoC. In the present study, total score is used. The SoC 13 has been shown to have good psychometric properties in previous studies, test-retest reliability R (0.52–0.97) and excellent internal consistency, Cronbach’s alpha (0.74–0.91) (Antonovsky, 1993; Schnyder et al., 2000). Cronbach’s alpha in the present study was 0.87.

In addition, participants completed a background questionnaire with eleven questions on their socioeconomic situation, reproductive history, if they were affected by or carrier of the genetic disease, and questions on problems with health. The background questions and SOC was grouped into six risk factors or predictors for use in a regression model.

In *Study III* the Swedish version of the Dyadic Adjustment Scale (DAS) was used to measure satisfaction with the quality of the relationship (Hansson, 1994). The questionnaire includes 32 items divided into four sub-scales: Dyadic Consensus (13 items; the degree to which the couples agree in matters of importance to the relationship), Dyadic Satisfaction (10 items; the degree to which the couple is satisfied with their relationship), Dyadic Cohesion (5 items; the degree of closeness and shared activities experienced by the couple) and Affectional Expression (4 items; the degree of demonstrations of affection and sexual relationships). The items are either Likert-type (0-5) or dichotomous (yes/no) with a maximum score of 151 (higher scores indicate higher satisfaction with quality of the relationship) with a Cronbach alpha .96. (Graham B. Spanier, 1976). Cronbach alpha for the present study was for DAS total at inclusion (women .85, men .90) and for the sub-scales Cohesion (women .62, men .74) Consensus (women .70, men .91) Satisfaction (women .89, men .82) and Affectional expression (women .56, men .54).

HADS (described previous at *Study II*) was used to measure depression and anxiety. At inclusion, Cronbach alpha in the present study was for HADS-A women .84, and for men .69. For HADS-D women it was .91, and for men .84.

Parental stress was measured by the Swedish version of parental stress questionnaire (SPSQ) (Östberg, Hagekull, & Wettergren, 1997). It is composed of 34 items assessed on a five point Likert scale, ranging from “do not agree at all” to “strongly agree”. Cronbach alpha in previous studies on Swedish mothers and parents was 0.88-0.90 (Hildingsson & Thomas, 2014). At inclusion, Cronbach alpha in the present study was for women .93, and for men .93.

Analyses

The interview material in *Studies I* and *IV* was analyzed inductively using thematic analysis according to Braun and Clarke (2006). This method was chosen because the approach was explorative and aimed to increase knowledge about individual experiences of decision-making concerning PGD, and experience of PGD three years later. ATLAS.ti was used to facilitate the qualitative data analysis. For *Study I* initial codes were created and these were organized into six broad themes: diagnostic in relation to the child, ethical considerations, genetic heritage, society sets the limit for what is possible, existential thoughts and religious considerations. In the next stage of the analysis, the six themes were restructured. Thereafter, the research group agreed upon a final understanding of the themes and subcategories and reviewed them to ensure that the themes and sub-themes covered the research question,

Choosing was seen as a master theme, affecting the three underlying sub-themes, which were labelled as follows: *In relation to myself*, *In relation to the child* and *In relation to the society* with nine underlying categories. In *Study IV* initial codes were created and organized into these three broad themes: 1) the experience of PGD, 2) goals, 3) strains and gains, with a total of 19 underlying categories. In the next stage of the analysis, the three themes were restructured into four main themes: 1) the practical experience of PGD, 2) the emotional experience of PGD, 3) psychological aspects and 4) goals, which in total made 17 subcategories. Thereafter, the first and third author worked together with the model and the authors agreed on a final understanding of the themes and subcategories. *It is better to have tried* was identified as a master theme, affecting the three underlying sub-themes, which were labelled as follows: *Practical experience of PGD*, *Psychological experience of PGD* and *Goals of PGD* with eleven underlying categories.

In *Study II* the aim was to study predictors for anxiety and depression in the PGD group. Hierarchical regressions with the six predictors were performed separately for men and women in the PGD group. Previous research has shown that predictors for depression and anxiety may differ for men and women (Leach et al., 2013). The six risk factors were:

- *Reproductive history*. This index includes miscarriage (1–2=1, 3 or more=2), and termination (1 or 2=1, 3 or more=2), with a total range of 0–4.
- *Having a child /children with the genetic disease*. Alive or deceased (no=0, yes=1).
- *Being affected by or being the carrier of the genetic disease oneself*. (no=0, yes=1)
- *Socioeconomic factors*. This index includes education, occupation and immigrant status. A sum of the scores for highest education (0=university, secondary=1 and primary=2), present occupation (student or employed=0, unemployed or sick leave=1) and immigrant status (Swedish descent=0, first or second generation immigrant=1) was calculated with a total range of 0–4.
- *Problems with health*. This index is a sum of worry about one's health (no=0, yes=1), other problems with health (no=0, yes=1) and current contact with the healthcare service for medical reasons other than reproductive care (no=0, yes=1), with a total range of 0–3.
- *Self-reported SoC*. The Swedish version of the short SoC scale (13 items) was used to measure sense of coherence.

For comparison of symptoms of depression and anxiety between the two groups (IVF and PGD) three tests were used: Fisher's non-parametric permutation test was used for continuous variables, the Mantel–Haenszel chi-square test for ordered categorical variables and Fisher's exact test for dichotomous variables. For comparisons of women and men within couples, Fisher's non-parametric permutation test for paired observations was used. Effect sizes, reported as Cohen's *d* (Cohen, 1988), were calculated for tests of group differences. Correlations were described using Pearson correlation coefficient and *P*-values were analyzed using Pitman's non-parametric permutation test. Regarding measurements of HADS depression and HADS anxiety, in all analyses of women and men together, mixed models were used to allow for adjustment for intra-couple correlation. In order to identify independent factors related to HADS depression and HADS anxiety in the PGD group all variables with a correlation to any of the dependent variables with a univariable *p*-value <0.2 were entered into a stepwise linear regression model. The choice of <0.2 was made because there were few variables with a significance of <0.05 and a predictor can be shown as significant if there are other variables already in the model. Only the predictors with an adjusted *P*-value <0.05 were included in the final stepwise hierarchical regression model. The selected final model was then reanalyzed with mixed models to allow for adjustment of intra-couple correlation (Good, 2000). All significance tests were two-sided and conducted at 5% significance level.

In *Study III* the aim was to see if satisfaction with the quality of the marital relationship changed from the start of PGD to the follow-up three years later. Men's and women's results at DAS at inclusion and three years later were compared using a paired t-test. The paired test was used since the individual scores for the man and the woman within in the same couple are dependent. Only data from the 17 men and women participating as couples was included in the DAS results.

When comparing means with reference populations, to see if the satisfaction with the quality of the marital relationship in men and women applying for PGD was similar to that of first time parents and couples undergoing IVF without PGD, a two-sample t-test (using mean and SD) was used. This can be found on the website of <http://www.evanmiller.org/ab-testing/t-test.html>. Missing values on DAS were replaced by the individual mean on the sub-scale. Effect sizes, reported as Cohen's *d* (Cohen, 1988), were calculated for tests on group differences. To investigate if satisfaction with the quality of marital relationships in men and women undergoing PGD was related to anxiety, depression and parental stress, correlations were

reported using Pearson correlation coefficient. All significance tests were two-sided and conducted at 5% significance level.

Main findings

In the overview of the results from *Studies I* and *IV* the main themes are presented in Table 3 and in Table 9 along with one quotation for each theme to highlight their essence. For Study II and III the main findings are presented in text and in Tables 4 to 8.

The overall master theme in *Study I* was labeled *Choosing* and affected all underlying themes. The participants were all in a position where they had reached what Hershberger et al. (2012) calls the “engage dimension” but still were able to revisit and reflect on the other dimensions.

Table 3. The data analysis; master theme, main themes and underlying categories.

Choosing
1. In relation to myself
1.1 Choice as a possibility
1.2 Choice as a burden
1.3 Avoiding the choice
1.4 To deselect oneself
2. In relation to the child
2.1 Protect the unborn child
2.2 Protect the born child
2.3 Choose the healthy child
3. In relation to the society
3.1 The effects on others
3.2 My needs have a price

The perspective of attribution of morality to a choice involves philosophy and psychology. Choice is often regarded as an objective, rational process, but as research has shown, in daily life this attribution often occurs after the choice has been made and can be understood more as a justification of the decision (Bloom, 2012). The aspects of choosing are present in all three main themes.

“It’s a bit like to be chosen or not, well ... had I been as welcome as I am even with a disease, a bit like that I think, and at the same time PGD is a choice that takes away the choice from the child later on, to avoid being in the same situation as we are right now... So I reckon you have to think back and forwards in both directions.”

Female (couple 14)

Three main themes were formed, the first was *Choosing in relation to myself*. Both the men and women in the study related the decision of PGD to how they handled and processed the choice and how they were affected by it. They also related the decision to their partner, but when this occurred it was mainly expressed as a concern for the partner.

“At the same time I blamed myself so much... and when you find out it is genetic, well I thought I couldn’t prevent it but at the same time... it was me and my husband’s sick genes that has made our child suffer.”

Female (couple 9)

The second theme was *Choosing in relation to the child* and the focus was on the child. Both men and women reflected on their decision in relation to the born and unborn child, the healthy and sick child, a child who had died, or the imagined child they were hoping to have.

“So you can reckon, what would your child think when they get to know that they weren’t conceived naturally... but on the other hand they will be able to see that they did not just happen, they were something that you really wanted.”

Female (couple 4)

The final theme was *Choosing in relation to the society*. People who need society’s support to become parents are sometimes portrayed as mainly focusing on their own needs and being unable to see the consequences for the rest of the society. However, it became clear that both men and women who were planning for PGD reflected on consequences for society.

“I can think a bit about the fact... that this part of the healthcare has worked very well for us but at the same time it’s a really expensive treatment and... well... like an ethical consideration... where shall we put resources in society... I think about this sometimes.”

Male (couple 15)

These themes were present among most men and women despite them having made the decision about PGD at different stages of their reproductive history. The participants seemed to see the offer of PGD as both a possibility and a burden; the outcome could be joyful (if they had a child without the genetic disease) or distressing (if the treatment was unsuccessful) or a mix of both. They moved back and forwards regarding their decision. Men and women reflected in similar ways according to the themes, cognitive attributions and emotional depth. The participants who themselves were affected or carried the disease asked questions about their own lives: “What life is good enough to be worth living?” “If I say no to having a child with the same disease as myself, is it the same as saying my life is not worth living?” The same ambivalence was found when a person had a living child with the disease, but this related more to reasoning about what the best choice was for present or future children than to the burden of the disease.

For *Study II* the descriptive data on the PGD and IVF groups regarding reported symptoms of depression (HADS-D), anxiety (HADS-A), and sense of coherence (SoC) are presented in Table 4.

Table 4. Comparison of HADS depression (HADS-D), HADS anxiety (HADS-A) and Sense of Coherence (SoC) in PGD and IVF patients by gender.

Variable	PGD		IVF	
	Female (n=19) Mean (SD)	Male (n=17) Mean (SD)	Female (n=24) Mean (SD)	Male (n=23) Mean (SD)
Depression (HADS-D)	4.16 (3.98)	4.29 (3.60)	3.17 (2.78)	2.65 (2.37)
HADS-D > 8	n=5 (26.3%)	n=2 (11.8%)	n=3 (12.5%)	n=2 (8.7%)
Anxiety (HADS-A)	6.21 (3.98)	6.42 (3.04)*	7.08 (3.16)**	4.35 (2.71)*,**
HADS-A > 8	n=7 (36.8%)	n=7 (41.2%)	n=10 (41.7%)	n=4 (17.4%)
Sense of Coherence (SoC)	n=18 64.2 (10.7)	n=17 64.2 (11.6)***	n=23 65.7 (11.8)	n=23 70.3 (7.5)***

*Significant difference between men in PGD and IVF group, $P=0.03$.

**Significant difference between men and women in the IVF group, $P=0.001$.

***Significant difference between men in PGD and IVF group, $P=0.05$.

Hospital Anxiety and Depression scale- Depression (HADS-D).

Hospital Anxiety and Depression scale- Anxiety (HADS-A).

The comparison of symptoms of depression and anxiety in men and women who had made the choice to undergo PGD, and men and women who were planning for IVF, (see Table 4) showed that men in the PGD group reported significantly more symptoms of anxiety and lower SoC than men in the IVF group ($P=0.03$, $d=0.72$; $P=0.05$, $d=0.62$). For depression no significant difference between men in the PGD and IVF groups was found but the effect size ($d=0.54$) indicated that the difference could be clinically relevant and might become significant with a larger sample.

With regard to the second aim of the study, to understand individual differences in depression and anxiety levels by investigating six risk factors, univariate predictors of HADS-A and HADS-D in the PGD group were tested with Spearman's correlations.

Table 5. Risk factors for HADS Depression (HADS-D) and HADS Anxiety (HADS-A), in total and by gender (PGD patients).

		HADS-D Total (Depression)	HADS-A Total (Anxiety)	HADS-D Female	HADS-A Female	HADS-D Male	HADS-A Male
Sum SoC	<i>r</i>	-0.59	-0.42	-0.73	-0.39	-0.46	-0.45
	<i>p</i>	0.0008	0.03	0.002*	0.11*	0.08*	0.07*
Problems with health	<i>r</i>	0.23	0.35	0.34	0.51	0.01	0.13
	<i>p</i>	0.09	0.01	0.18*	0.03*	0.71	0.66
Socioeconomic factors	<i>r</i>	-0.08	-0.16	0.14	0.18	-0.29	-0.51
	<i>p</i>	0.91	0.43	0.58	0.48	0.25	0.04*
Reproductive history	<i>r</i>	0.50	0.23	0.68	0.39	0.25	-0.04
	<i>p</i>	0.06	0.27	0.003*	0.11*	0.38	0.91
Child with genetic disease Yes, <i>n</i> =9	Mean (SD)	4.22 (3.31)	7.33 (3.77)	4.60 (4.16)	5.80 (4.44)	3.75 (2.36)	9.25 (1.71)
Child with genetic disease No, <i>n</i> =27	Mean (SD)	4.22 (3.95)	5.96 (3.12)	4.00 (4.06)	6.36 (3.41)	4.46 (3.97)	5.54 (2.85)
	<i>P</i>	0.18	0.51	0.80	0.83	0.85	0.03*
Genetic disease or carrier Yes, <i>n</i> =21	Mean (SD)	4.48 (3.28)	6.81 (3.04)	4.64 (3.78)	6.45 (3.39)	4.30 (2.83)	7.20 (2.74)
Genetic disease or carrier No, <i>n</i> =15	Mean (SD)	3.87 (4.42)	5.60 (3.60)	3.50 (4.41)	5.88 (4.05)	4.29 (4.75)	5.29 (3.30)
	<i>P</i>	0.85	0.35	0.59	0.78	0.96	0.24

*All variables with $P < 0.2$ were entered in the regression model for men and women separately. Hospital Anxiety and Depression scale- Depression (HADS-D). Hospital Anxiety and Depression scale- Anxiety (HADS-A). Sense of Coherence (SoC).

All factors with a correlation with a significance value of $P < 0.2$ were included in a regression model. SoC ($P=0.0006$) and reproductive history ($P=0.04$) were found to be significant independent predictors of symptoms of depression in women. Socioeconomic factors ($P=0.01$) and having a child with the genetic disease ($P=0.03$) were significant independent predictors for anxiety in men as shown in Table 6. Surprisingly, the socioeconomic factors hypothesized to increase risk showed a reverse correlation. None of the tested risk factors were individually significant in predicting anxiety in women or depression in men. However, there was a tendency for lower SoC levels to be associated with depression ($P=0.06$ HADS-D) and anxiety among men ($P=0.05$ HADS-A). The full regression models explained 64% of the variance in depression among women and 56% of the variance in anxiety among men as shown in Table 6.

Table 6. Results of stepwise hierarchical regression of depression and anxiety, analysis by gender.

	Adjusted beta (SE)	Adjusted P-value	R ² change
Women HADS-D			
SoC	-0.20 (0.06)	0.0006	
Reproductive history	1.15 (0.52)	0.04	0.64
Problems with health	The variable did not meet the 0.0500 significance level for entry into the model.		
Men HADS-D			
No variables met the 0.0500 significance level to be included in stepwise model.			
Women HADS-A			
No variables met the 0.0500 significance level to be included in stepwise model.			
Men HADS-A			
Child with genetic disease	-3.80 (1.24)	0.03	
Socioeconomic factors	-1.52 (0.52)	0.01	0.55
SoC	The variable did not meet the 0.0500 significance level for entry into the model.		

Hospital Anxiety and Depression scale- Depression (HADS-D).

Hospital Anxiety and Depression scale- Anxiety (HADS-A).

Sense of Coherence (SoC).

For *Study III* descriptive data are shown in Table 7. Women were significantly more satisfied with the quality of the marital relationship than men, both at inclusion ($t(16)=3.54$, P 0.003, d 0.81) and at the three year follow-up ($t(16)=2.24$, P 0.04, d 0.51). The level of satisfaction was the same at inclusion as it was three years later for both men and women.

Table 7. Full scale and sub-scales for marital satisfaction (DAS), anxiety (HADS-A), depression (HADS-D), and parental stress (SPSQ). Mean, standard deviations and range at inclusion (T1) and three years later (T2) comparison by gender.

	T1			* <i>P</i> -value	T2			<i>P</i> -value
	Mean	SD	Range		Mean	SD	Range	
DAS Total (n=17)								
Women	121.27	9.87	103-142		120.14	15.14	93-147	
Men	111.89	13.05	87-134	0.003	111.78	17.55	83-144	0.04
Cohesion								
Women	17.71	2.8	10-23		17.63	3.61	10-22	
Men	17.24	3.33	9-21	n.s	16.29	3.67	10-22	n.s
Consensus								
Women	51.12	4.79	45-63		50.91	7.36	39-65	
Men	46.24	6.16	36-58	0.001	47.37	7.09	36-63	0.02
Satisfaction								
Women	42.68	4.95	30-48		42.49	5.33	32-49	
Men	40.47	4.74	30-49	n.s	39.84	6.23	28-49	n.s
Affectional Expression								
Women	9.76	1.52	6-12		9.12	2.71	2-12	
Men	7.94	1.6	5-10	0.002	8.28	2	5-12	n.s
HADS-A								
Women (n=19)	6.21	3.58	0-12		5.53	3.12	1-10	
Men (n=17)	6.41	3.04	0-11	n.s	5.59	3.22	0-12	n.s
HADS-D								
Women (n=19)	4.16	3.98	0-12		3.58	3.13	0-10	
Men (n=17)	4.29	3.60	0-14	n.s	3.23	3.09	0-12	n.s
SPSQ								
Women	2.30	0.68	1.38-3.03		2.37	0.48	1.56-3.00	
(T1 n=6; T2 n=12)								
Men	2.28	0.55	1.26-2.82	n.s	2.34	0.53	1.29-3.15	n.s
(T1 n=7; T2 n=11)								

Satisfaction with relationship was measured with Dyadic Adjustment Scale (DAS). Anxiety and depression was measured with HADS questionnaire. Parental stress was measured with SPSQ. Only those who were parents at T1 or T2 filled out this form.

**P*-value difference between men and women, (n.s *P* > 0.05).

There were significant differences between men and women on the sub-scales Dyadic Consensus ($t(16)=4.20, P 0.001, d 0.88$) and Affectional expression ($t(16)=3.81, P 0.002, d 1.17$) at inclusion. However, three years later only the sub-scale Dyadic Consensus showed differences ($t(16)=2.69, P 0.02, d 0.49$). Effect size is large both at inclusion and three years later.

Women and men in the PGD group was compared with a sample of Swedish first-time parents (Moller, Hwang, & Wickberg, 2008). No significant difference in satisfaction with marital quality was found in women, either when applying for PGD or three years later. However, men applying for PGD and three years later reported significantly lower satisfaction with marital quality than did the first-time fathers ($P < 0.05$). The pattern was the same when comparing the men and women at the start of PGD treatment with a sample of men and women prior to IVF (Peterson, Newton, Rosen, & Skaggs, 2006) men in the PGD group reported lower satisfaction with marital quality than men in the IVF group ($P < 0.05$).

At inclusion, three out of seventeen men reported marital quality below 100 (which has previously been suggested as a cut-off to determine couples at risk of break-up). Three years later the same three men, plus one more man and three women, also scored below 100. One of the women was part of a couple with one of the men scoring below 100. The other three men and the two women all had a partner who scored above 100. If using the continuum 92-107 suggested by Graham, Liu, and Jeziorski (2006) no woman scored below 92 either at inclusion or at the three-year follow-up. If 107 is used as cut-off one more woman scored below cut-off (i.e. one at inclusion, four at follow-up). If using the cut-off of 92 two men were below the score both at inclusion and after year three, and if using 107 as cut-off six men were below both times. Four men were below cut-off at both times while two cases shifted. Five out of seven participants who scored below 100 had not become parents after three years.

Correlations between marital quality and anxiety, depression and/or perceived parental stress, are presented in Table 8. When it came to women, no significant correlations were detected at inclusion, but three years later both anxiety ($-.52, P < 0.05$) and depression ($-.61, P < 0.01$) correlated significantly with lower satisfaction with the quality of the relationship. No significant correlations were found for men at any time point regarding anxiety and depression and satisfaction with marital quality. Perceived parental stress, both at inclusion and three years later,

correlated negatively with marital quality for men (-.83 and -.70, $P < 0.05$), but not for women.

Table 8. Bivariate correlations between couple's quality of relationship (DAS) and self-reported symptoms of anxiety, depression and parental stress. At inclusion (T1) and three years later (T2).

	DAS		T1		DAS		T2	
	Women		Men		Women		Men	
	<i>r</i>	<i>r</i>	<i>r</i>	<i>r</i>	<i>r</i>	<i>r</i>	<i>r</i>	<i>r</i>
Anxiety	-.23	-.14	-.52*	-.31	-.52*	-.31	-.52*	-.31
Depression	-.27	-.18	-.61**	-.30	-.61**	-.30	-.61**	-.30
Parental stress	-.66	-.83*	-.53	-.70*	-.53	-.70*	-.53	-.70*

Anxiety and depression are measured with HADS questionnaire.

Parental stress is measured with SPSQ.

*Correlation is significant at the 0.05 level (2-tailed).

**Correlation is significant at the 0.01 level (2-tailed).

In *Study IV It is better to have tried* was identified as a master theme, affecting the three underlying main themes which had together 11 underlying categories as presented in Table 9.

Table 9. The data analysis; master theme, main themes and underlying categories.

It is better to have tried, no matter what	
1. Practical experience of PGD	1.1 Opportunities 1.2 Difficulties 1.3 Relationship with healthcare service
2. Psychological experience of PGD	2.1 Development 2.2 Deterioration 2.3 Never give up 2.4 Marital relationship 2.5 Childlessness 2.6 Ethical considerations
3. Goals of PGD	3.1 Parenthood 3.2 To be like everyone else

Although all participants had decided on PGD, not all went through with it. Two couples achieved pregnancy spontaneously before starting PGD and only six (out of 19) women gave birth to a child after PGD. However, all had been involved in PGD and had the feeling of having gone through with PGD. Three years later they still struggled with the same questions as when they started: practical (What shall I do?) philosophical (What do I think about it?) and psychological (How does it make me feel?) but the first one had changed to “What have I done?” The answer to that question was “I have tried” and that affected the underlying themes and was important in the participants’ psychological understanding of the experience of PGD, regardless of the actual process and outcome.

“If there is the opportunity, there is no reason not to go through with it... I can hardly see that you would regret it... But I reckon that that’s sort of my attitude - that you seldom regret something that you do, more likely the things that you don’t do.”

Male (couple 19)

In the theme labelled *Practical experience of PGD*, both men and women addressed the practical pros and cons associated with PGD, such as the possibilities of avoiding termination, or difficulties in planning everyday life during treatment and having to take medication. They were also able to address the fact that the practical aspects of PGD are a mix of possibilities and strains and this causes ambivalence.

“PGD felt like a fantastic way out of everything... and yet it was a much tougher process than I could imagine and what I was informed about...”

Female (couple 19)

In the theme *Psychological experience of PGD* the experience of PGD was described as a mix of emotions, and that both psychological development and deterioration occurred. A central perspective three years after initiating PGD was that they had to cope with the fact that they had “chosen” PGD and “had to” keep on doing it even when it was experienced as painful.

“It is a rollercoaster. Sometimes I feel awful and sometimes I feel pretty good, but the rollercoaster has been less extreme lately. There are not so many peaks and the worst valleys are gone, but it is more, like ... it has levelled out. In both good and bad ways. This protects you a bit but of course you would like to keep the peaks.”

Female (couple 13)

In the last theme, *Goals of PGD*, the goal of PGD - to put a stop to the known disease - was described in the same way regardless of whether the couple had achieved parenthood or not through PGD. The men and women who were childless three years later still expressed commitment to the goals.

“To get a chance to have a child without this gene, and with proof that this is most likely - that the child will not have this gene- that felt really good.”

Female (couple 19)

The goal of PGD was also related to the future and the hope that the child as an adult would not have to face the strain of decision-making regarding prenatal testing.

"It was the best decision we have ever made, I think. Now we know. Our child is healthy... and if he wants to have children he doesn't have to think about this. We have put a stop to the disease..."

Male (couple 8)

The findings conceptualize common themes within the group, despite the different experiences, and give an in-depth understanding of this situation.

Discussion

The overall aim of this thesis was to increase the understanding of psychological perspectives during the PGD process and factors related to psychological health and relationship satisfaction in men and women during the PGD process. The present thesis also explores the idea that PGD will affect individuals differently due to the presence of risk and protective factors. To undergo a prenatal diagnosis such as PGD raises questions about one's own life. "What would have happened to me if this had been a possible choice for my parents?" "What sort of life is good enough to be worth living, and if I say no to having a child with the same disease as myself, is it the same as saying my life is not worth living?" Of course, there are no given answers to these kinds of questions, but the existential dimension is obvious in this situation. Afterwards there are also the questions of "What have I done?" and "Was it worth it?"

Study I. The choice of PGD

Applying for PGD, means you are applying for a method where it is hard to fully estimate what possibilities and risks it brings and also to know how it will affect you on an individual level. It is also a choice made from a position where your options are diminished. In Study I the men and women talked about their choice as the next step on a journey from hoping to achieve pregnancy naturally, to an unknown future. It was also clear that men and women had difficulties understanding the possibilities and limitations of PGD as a method. For example, they expressed the belief that the method would give them a healthy child, not only a child without the risk of a specific genetic disease. Hershberger et al. (2012) has shown the choice of PGD is not made easily or only once. The results in Study I are consistent with Hershberger's findings and provide a more in-depth understanding of the motives behind the choice of PGD. Both men and women put the decision in relation to themselves as well as in relation to a present or future child. The choice was made in a positive way "it's good to have a choice" and in a way seen as avoiding future burdens, "it's not right to give birth to such a sick child". Both men and women included a broader perspective when they reasoned about their choice. They saw their choice in relation to society and focused on how other individuals and society might be affected by their choice of PGD. This could be seen to be a contradiction to the ethical concerns raised that PGD

could entail the risk of putting society on a slippery slope towards selecting certain types of humans. (Munthe, 1999). No gender differences were found, the men and women seemed equally engaged in the decision-making process.

Study II. Resistance and risk when applying for PGD

Despite the risk of experiencing stress, previous studies have shown that on a group level both men and women applying for IVF or PGD are emotionally stable and well-adjusted (El Kissi et al., 2013; Karatas et al., 2010; Wichman et al., 2011). This was also what was found in Study II, where both men and women in the IVF and PGD groups reported levels of anxiety, depression and SoC comparable to the general population. However, both healthcare and the wider community will gain if they bear in mind that men and women undergoing PGD are a heterogeneous group, and are affected by risk and resistance factors, both in their present and from their past. Couples who undergo PGD share experiences with couples who undergo IVF. They share the experience of having to prepare for the IVF treatment, but their situations in life when entering the clinic can vary greatly. In our study, the most obvious difference was that not all couples undergoing PGD were infertile. Some had already conceived spontaneously and had the experience of parenthood. Despite the different life situations in the PGD and in the IVF groups the women in Study II showed similar levels of anxiety and/or depression. Preparing for the treatment is a major factor for women at this point and it is a situation that affects women and men differently. Men facing IVF treatment did report lower anxiety scores compared to men facing PGD indicating that PGD men may be more emotional affected by facing the treatment.

The factor *General health risk* was not a significant predictor of symptoms of anxiety and/or depression in Study II, although a previous study found evidence that worries or problems with health in general are related to impaired quality of life (Bayat et al., 2011). The unexpected result could have several explanations. One is that the study relies on self-reported data which may lead to underreporting, and the other is not knowing what general health risks are, as explanations were not sufficiently explicit.

Low *SoC* was found to be a predictor of depression among women, which is consistent with previous research (Lindström & Eriksson, 2005). However, no significant relation between *SoC* and depression was found for men. This failure to

establish a link between SoC and depression in men could be due to the size of the sample and that other factors are even more significant for men's risk of psychological distress, such as having a sick child. Compared to men in the IVF group, men undergoing PGD reported more symptoms of anxiety and lower SoC. The low SoC in men undergoing PGD could be understood in line with previous research; that SoC was reduced due to the presence of depressive symptoms and could increase over time if the life situation and the depressive symptoms changed (Hakanen et al., 2007; Konttinen et al., 2008).

Living with chronic illness, as genetic diseases, has in previous studies been related to anxiety and depression (Bayat et al., 2011; Timman, Tibben, & Wintzen, 2010). However, the factor *genetic disease* was not significantly associated to anxiety and/or depression in Study II. This may be a result of the small sample size, or of both the carrier and the partner feeling, "we are in this together". Previous research show (Korenromp, 2009; Lok & Neugebauer, 2007) that most individuals adjust to the experience of miscarriages and/or termination over time. For men and women undergoing PGD the negative experience was often recent, and feelings were reactivated when trying to achieve pregnancy again. The *reproductive history* (miscarriages and terminations) made a significant contribution to understanding women's risk of symptoms of depression.

Having *a child with the genetic disease* had a significant association with the risk of anxiety among men in the PGD group. In several studies parents of children with chronic illnesses report more stress, and living with a child with a chronic illness may threaten parental integrity and identity, compared to other parents (Cashin et al., 2008; Ingerski et al., 2010; Sawyer et al., 2000; Young et al., 2002). However, studies have also found that parents tend to see their child's uniqueness, and gain appreciation for things that really matter, which may lead to personal growth (Kratz et al., 2009; Samson et al., 2009). This duality can be used to understand the presence of this risk factor among the fathers and the absence of the factor among the mothers in our study.

In Study II *socioeconomic risk* had a significant effect, and for men only there was, surprisingly, a reverse relation to anxiety. This could be interpreted as of you are well-educated and being used to be able to affect your life can cause even more strain when you are in an unchangeable situation. It is interesting to study the Swedish population applying for PGD since the treatment is covered by national health insurance and the group is not biased as it is not financially better-off, as it

may be in many other countries. On the other hand, finding and go through with such a difficult treatment probably favor individuals with strengths regardless of financially situation.

Study III. PGD and satisfaction with marital quality

To be able to apply for and go through with PGD the man and woman need to be engaged in the decision and process together. The couple had often experienced difficulties together, previous to PGD. Men were less satisfied than women with the quality of the relationship both at inclusion and three years later. The effect size was large, suggesting that the difference might be clinically relevant. This finding is inconsistent with previous findings in a group of first time parents (Moller et al., 2008) and a study of men and women undergoing IVF (Peterson et al., 2006), where men and women usually rate the quality of their relationship similarly (Moller et al., 2008; Peterson et al., 2006). However, women who undergo PGD rate the quality of their marital relationships similarly to first-time mothers or women preparing for IVF, while men undergoing PGD as a group experience lower relationship quality than men in the other two groups.

In men, a significant correlation between perceived levels of parental stress and satisfaction with marital quality was found both at inclusion and follow-up. Previous findings on parental stress are contradictory. Muhammad and Gagnon (2010) found in a large Canadian study that motherhood did not seem to affect perceived stress if you were married but fatherhood increased perceived stress regardless of marital status. Other studies have found that mothers in general experienced higher levels of stress than fathers (Widarsson et al., 2013). Both at inclusion and three years later, men and women differed significantly on the Dyadic Consensus sub-scale (the degree to which the couple agree or disagree on a number of issues in everyday life). This sub-scale includes areas in a relationship that are usually changed by parenthood. However, being a parent or not was not related to rating of Dyadic consensus

Since sample size was small the difference between men and women here has to be interpreted with caution. But one possible interpretation of the finding could be that women and men are stressed by different circumstances. Women may find partnership confers a form of protection when fighting infertility (Schmidt et al., 2005) while men are burdened by factors associated with parenthood (McKenzie &

Carter, 2013). However, this association is multifaceted, since men with the lowest marital satisfaction in the study were not fathers. For women, there was a significant correlation between depression and anxiety and marital quality three years later, but not for men. This is consistent with previous findings that women's mental health is more strongly associated with the quality of the marital relationship (Leach et al., 2013).

Study IV. Experiences of PGD, three years later

The group was heterogeneous when applying for PGD and even more heterogeneous in their reproductive experiences three years later. Three years after applying, all men and women in the present study reported that they had tried to achieve pregnancy and seventeen out of nineteen women had undergone at least one PGD cycle. Four were still in contact with healthcare services regarding their wish for a child and only six women had given birth after PGD. The strength of the present study is that it conceptualizes common themes despite the different experiences of the group, and gives an in-depth understanding of their situations.

The master theme *It is better to have tried, no matter what*, can be seen as an active, problem-focused, coping strategy. Previous studies have shown that active coping is associated with strength and the ability of men and women to handle the stress of IVF treatment (Gourounti et al., 2012; Peterson et al., 2006). The advantages associated with an active coping strategy are consistent with previous work about coping and IVF treatment; those with active coping strategies better manage the situation. An active coping strategy could be a trait that is needed for people to find, and go through with, PGD. It is also allied with the sub-theme *Never give up* where participants described the negative side of this strategy, when it put other options on hold, prolonged the process of adjustment to childlessness, and put the focus on the demanding process of shifting between different coping strategies.

Men and women seem to be affected differently by *Childlessness*, and their perceptions of the *Marital relationship* also seem to differ. Women in the study described more distress from being childless than the men did. This is consistent with previous work (Huppelschoten et al., 2013; Preedy & Watson, 2010). Regardless of whether the women participating were childless or were receiving treatment to conceive a sibling, they both experienced strain when exposed to other couple's pregnancies. Feelings of tension when faced with other couple's pregnancies are not

only linked to childlessness but could be related to marital satisfaction or feelings of depression. In the *Marital relationship* sub-theme both men and women stated that they had been affected by PGD in different ways. The women described more stress relating to the IVF procedure, and the men more stress relating to feelings of exclusion. It is well-known that stress levels in women facing IVF treatment are elevated, while men tend to be less affected (El Kissi et al., 2013; Wichman et al., 2011). For men and women undergoing PGD the situation resembles ordinary IVF treatment but also differs from it. The PGD couples may be more equally affected by the burden of disease and/or have a more troubled reproductive history, which could contribute to the common theme found in both men and women in the PGD group. The broad diversity of experiences among these men and women is interesting in its full complexity and cannot be reduced to generalized statements of “always” or “never”. Of course, it is to be expected that the experience three years later will be affected both by PGD and other circumstances.

General discussion

The present study is consistent with previous research but contributes with a more in-depth understanding of the choice of PGD and how men and women are affected by specific risk factors, such as having a sick child or a complicated reproductive history. The study also adds to knowledge about marital satisfaction, both when applying for and after receiving treatment, and how life is affected over time by experiences connected with PGD. Apart from specific risk and protective factors individuals are also affected by general and nonspecific factors such as previous life experiences, social support and socioeconomic situation. Although the present study does not cover the full range of previous experiences or contextual factors we did include the socioeconomic situation. Education has generally been shown to be a protective factor (Volanen et al., 2004), but for men in the present study results pointed in the opposite direction. There could be several possible explanations, for example in this small sample some of the most well-educated men lived with women who were most significantly affected by the genetic disease, leading to great strain in these families. Another possible explanation could be that education may not be a protective factor when you have to engage in healthcare with an uncertain outcome. To engage in knowledge acquisition when facing a highly technical treatment such as PGD, may lead to increased anxiety since almost any answer simply leads to new questions, resulting in feelings of reduced control. This also highlights the fact that when trying to understand risk and resilience, with a model like Fergus and

Zimmerman (2005), it is important to understand risk and promotive factors from the individual's perspective. The men and women in the PGD group are all in a position where they opted for PGD, whereas previous research was often conducted in a hypothetical setting and sometimes among individuals not carrying the genetic disease themselves (Alsulaiman & Hewison, 2006; Chamayou et al., 1998). When favoring PGD in a hypothetical setting, as in previous studies, it seems a more easy and uncomplicated choice, compared with being faced with it in your own life.

As stated in Study I, PGD is not an easy choice and it is not a decision taken once; it seems more like a process where the individual goes back and forth between contemplation, resolving and engaging, which is consistent with the Hersherberger et al. (2012) model. Participants seem to experience the choice both as a possibility and a burden. Even more important in the present studies is the presence of both men's and women's experiences. To be two persons in a decision-making process seems to add both pros and cons and both men and women are at risk for distress. Previous research has shown that when making a decision, a couple seems to have a better chance of making a wiser one than an individual (Abdellaoui et al., 2013; Allwood & Granhag, 1996). Although PGD is considered one of the most gender-equal prenatal diagnostic options in decision-making, and men and women showed the same pattern in how they understood the choice, women are the ones who have to undergo the treatment, and therefore probably have a greater input on which choice to make.

Other aspects of the relationship will also affect the ability to make the choice and general well-being. If a relationship is satisfying it is a protective factor and associated with higher SoC and flexible coping strategies. On the other hand, a troubled relationship has been found to be associated with a risk of low SoC (Volanen et al., 2004). Satisfaction with marital quality was lower for men than women both at start and three years later. The men in the PGD group were also less satisfied than first time parents and men undergoing IVF without PGD. In Study III, less satisfaction was found to be associated with parental stress at both inclusion and three years later. This pattern was not shown among the women. SoC was not tested but may have contributed to understanding. All the couples stayed in their relationships during the three years. One of the two women that participated without their partners got divorced. Although the men were less satisfied they stayed in the relationship. This could be interpreted as being consistent with previous knowledge (Leach et al., 2013) that men's mental health is better off if they are in a relationship regardless of

the quality. No correlation with depression, anxiety and dissatisfaction was shown among men.

The persons who can be offered PGD in Sweden are affected by more severe conditions, since PGS is not allowed in Sweden. PGS is allowed in many other countries and the patients undergo the same technique, PGD, but do not have a known genetic condition. The PGS group of patients is often included in studies of psychological aspects of PGD. This fact may lead to an underestimation of the distress, in international studies, since a large proportion of the study participants do not have an experience of a genetic condition. But the Swedish group probably also has a bias; to consider PGD as an alternative, offered only at two clinics in Sweden, and to decide to go through with it, could favor individuals with psychological strengths such as high SoC or few general psychosocial risks. In the interviews participants often described the struggle to find their way to PGD and their surprise when realizing that professionals in health care did not know of this alternative. This delayed their starting PGD.

The goal of PGD is of course to become a parent of a child without the genetic disease. Before the start of the PGD treatment this seems like the perfect solution. But it is a demanding treatment in combination with what has been a demanding situation before treatment commenced, and therefore PGD is probably most well-suited for self-selected couples with psychological strengths. The men and women in Study IV described both practical and emotional strain continuing for years, and the experience of PGD kept affecting them in both positive and negative ways. It became clear that the goal was not just to have a child; it was also to put an end to the disease and to prevent the child from being in the same situation as themselves in the future. Having a healthy child was also a way the parents could become like everyone else.

Ethical considerations

The study (I-IV) was not accepted by the Regional Ethics Board at the first application. The Board pointed out the vulnerability of participants in the group who had already lost a child and that they were at risk of distress when being asked our questions. After clarifying the plan for support for the participants the study was approved. Both those who accepted or declined the invitation to participate had the possibility of support from a psychologist. Furthermore, the interviews were carried

out by an experienced clinical psychologist working with these patients on a daily basis. Thus, support was offered when needed, and there was the possibility, if a participant should experience distress during the interviews, to stop. Even if there were initial concerns about increased distress among the participants they expressed satisfaction with the fact that their experiences were requested, even when it was hard to talk about. Also, three years later the participants, often those most burdened by their experiences, described satisfaction with the fact that what they had to say was of interest even when the outcome was unsuccessful. In public discussions, people who need society's support to become parents are sometimes portrayed as mainly focusing on their own needs and as unable to see the consequences for the rest of the society. Both men and women who were planning for PGD reflected on consequences for society from medical, psychological and ethical perspectives.

Methodological considerations

When choosing methods and analytical tools several perspectives needed to be addressed. In this thesis both self-report questionnaires and in depth-interviews were used in order to capture well-known types of strain and individual experiences. The advantage of the qualitative research approach is that it can capture an understanding of individuals' experiences, the limitation is that the external validity and generalizability are limited (Ring, Gross, & McColl, 2010). The semi-structured interview guide and the inductive qualitative approach that were used in Study I and in Study IV made it possible to gain knowledge about the patients' own reasoning about decision-making and PGD, and their subsequent experiences, something that has not previously been studied. The number of qualitative interviews was large (36) and during the analysis it seemed as though saturation was achieved with a fewer number of interviews. It might have been better to include fewer participants, and spend the time on doing repeated interviews instead. With repeated interviews it could have been possible to capture more of the process involved in the decision and treatment. Also, it might have been beneficial to interview some of the participants individually and some as couples. This would have contributed to the understanding of the interaction within the couple during the decision-making process and their experiences of PGD.

It could be considered a limitation that all the participants were recruited from the same clinic and followed by a researcher that was also a part of the PGD team, as a clinical psychologist. This might have affected the answers and

understanding in several ways. One could be that the participant might have avoided bringing up thoughts that they thought could affect their upcoming treatment, for example feelings of uncertainty or severe impairment in health. On the other hand the feeling of confidence by being in a known environment could have contributed to the high participation rate. Individuals in an unknown setting may have refrained from talking about their experiences due to uncertainty or the burden of several contacts. The feeling of being a part of both the clinic and the research carried out contributed to the participants' loyalty and willingness to participate at follow-up after three years, without any drop-outs. At follow-up the majority were no longer patients at the clinic.

The most obvious limitation in Study II and Study III is the small sample size. We had 22 couples who were eligible for the study, during the one and a half years of inclusion, and we had a high participation rate. In this project, there was no practical incentive to involve the other possible clinic in Sweden, Karolinska University Hospital. Pros and cons for a prolonged inclusion time were discussed. Power and sample size analyses were carried out after Study II. To be able to find significant differences at 80% power between the men and women in the IVF and PGD groups, 32 men and 220 women was needed in the PGD group. It would have taken almost 15 years to collect a large enough group of women and about three years for the men, given the same high participation rate as in the present study, and this was not considered feasible. Although a larger sample would have been desirable we decided to divide the group into men and women when conducting the regression analyses in Study II for identifying risk and protective factors. There were two main reasons for this choice. Firstly, previous research points to different predictors for depression and anxiety in men and women and we wanted to be able to detect that. Secondly there was dependency within the couple which made it statistically challenging. Effect sizes for anxiety and depression were calculated and found to be medium to large for the men but small for the women.

Trying to gain knowledge about mental health and satisfaction levels with the quality of marital relationship is difficult. There is always a "social desirability" risk. This risk could be present in this study group as the study is carried out by clinicians working in the clinic where the participants were patients. However, mixed feelings and strains were expressed by the participants during the interviews. The combination of interviews and questionnaires (triangulation) also provided the participants with the opportunity to more privately express their thoughts and feelings. The methodical advantage of using standardized questionnaires is that it is

possible to compare this small group both with norm populations and other groups of patients facing equal and/or similar experiences. The questionnaires chosen are commonly used and have previously shown both good validity and reliability.

The choice of HADS in Study II and III and Antonovsky's 13-item SoC in Study II scale can be also discussed. HADS is used to detect symptoms of anxiety and depression in non-psychiatric populations but has been criticized for underreporting the presence of depression (Cameron, Crawford, Lawton, & Reid, 2008). The validity of SoC is well tested. The use of the SoC concept is more questioned, should SoC really be viewed as a stable trait, or should SoC be considered diminished due to the distressful situation as proposed in other studies (Schnyder et al., 2000; Snekkevik et al., 2003; Volanen et al., 2004; Volanen et al., 2007)? A questionnaire regarding coping styles might have revealed another interpretation of the results. Detecting a flexible coping pattern may be a better way of understanding which individuals and couples are at risk of experiencing strain when facing PGD.

The proposed risk factors might have shown significances with a larger sample. Also the chosen risk factors should be viewed with caution. For example the reverse significance of socioeconomic status may be explained by the fact that a few well-educated men in this group lived with the women most impaired by their genetic disease. The risk factor, genetic disease, would probably contribute to better understanding if there had been possibilities to divide this risk factor into several categories. It would have been more accurate if the participants had been divided into sub-groups due to how they were affected by the genetic condition in everyday life. Other non-tested risk factors could also have given a better understanding of the presence of anxiety or depression, for example satisfaction with the relationship or income.

In Study III satisfaction with marital quality was measured by DAS. This is one of the most commonly used tests to measure marital satisfaction (Graham et al., 2006). However the sub-scales are more questioned. The original cut-off at 100 for distressed couples at risk of divorce determined by Graham B. Spanier (1976) was later stated as arbitrary (Graham B Spanier, 1989). Other studies (Graham et al., 2006) found a cut-off score between 92 and 107 differentiated distressed and non-distressed couples. Later South, Krueger, and Iacono (2009) investigated the sub-scales of DAS and found that they could be used to find true gender differences, which means that differences among men and women arise from actual differences

in relationship adjustment, not that the scale measures different concepts in the two groups. Although DAS has some shortcomings it was found to be the most useful questionnaire, not least because of extensive prior use and therefore being able to compare the PGD group with other similar groups. The choice of depression, anxiety and parental stress as factors tested to correlate negatively with marital satisfaction has large support in previous work. A more salutogenetic way to carry out the study would have been to test whether supportive factors such as satisfaction at work or support from peers affected satisfaction with marital quality positively. High SoC and/or flexible coping strategies were also shown in previous studies to be protective of marital satisfaction and could have been used instead of the chosen risk factors.

A strength in all the studies is the high participation rates among the eligible men and women and that the studies only included persons who were affected by the issues raised by PGD in their own lives.

Future research

It would be of interest to follow the men and women applying for PGD over time to further study if risk factors for anxiety and/or depression stay the same or if other factors, such as treatment success, contribute to better understanding. It would also be of interest to study SoC over time and see if it still could be used as a predictor since low SoC has been shown to be changeable (Hakanen et al., 2007). Three years were not enough to capture all participants' experiences after PGD, as some were still in treatment at that point. Therefore a longer time to follow-up will be of interest. Then it would also have been possible to gain knowledge about the one third of the study population who at year three still had not become parents, and learn more about their mental well-being and choices. To increase understanding of which strains and protective factors affect marital satisfaction a couple-based study approach would also be of relevance. To compare men and women with genetic conditions who chose other options than PGD, such as other forms of prenatal diagnosis, or who refrained from testing, would also be most interesting. This would add knowledge to what should be regarded as an effect of treatment and what is due to the life situation in general.

Clinical implications

Taken together the results of the four studies in the present thesis it was showed that going through the process of PGD affects both men and women over a long period of time. When counselling is offered, a strong clinical implication is that it should be provided not only to the women but also to the men. The decision to undergo PGD is not a decision taken only once or a simple solution; it should be seen more as a part of a greater existential question, namely the wish for parenthood. In clinical practice one initial counselling session, offered to both men and women, would be a good standard of care for couples applying for PGD. To determine who is in need of more counselling is a much more complex question. SoC was found to be a predictor for depression among women, clinicians could use the HADS form to screen for those who may be at risk of poor psychological health and the use of the SoC form could give a broader understanding of the way the individual perceives their situation. Special attention should be paid to those who have had a previous experience of termination, miscarriage or a dead or living child with the disease as it was found to be associated with anxiety and/or depression. Overall, most of the men and women planning for PGD were well adjusted, with HADS scores in the normal range although many of them had experienced severe events before applying for PGD.

The PGD group was heterogeneous when it started and even more so during and after the process of PGD. Men's and women's experiences three years after inclusion show that the relationship and the participants' well-being were affected by the experiences, in both positive and negative ways. The results from this thesis show that focus and time for support are as important to consider as questions of to whom and why to offer support. Since this is a heterogeneous group of men and women with a complex mix of risk and protective factors the question of support should be addressed more than once at different stages. Support should also be offered to those who become parents. There may be aspects that could be viewed as the responsibility of the reproductive clinic which is not over once a child is conceived. The need for support during the transition to parenthood may be related to patients' experiences of PGD, or the factors that led to PGD, and may be best handled in collaboration between the reproductive health clinic and maternity and well-baby clinics.

To conclude, the complexity of this field and part of life, for the men and women in the study as well as for the clinicians and society is well stated by Shakespeare (2011) “It is tempting also to see prenatal intervention as either wonderfully progressive and health-improving, or nightmarishly evil and destructive. The truth is far less extreme and more complex.” (p 43).

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