

# A novel intervention for medical waiting periods in IVF and early pregnancy

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# A novel intervention for medical waiting periods in IVF and early pregnancy

Een nieuwe interventie voor medische wachtperiodes in IVF  
en vroege zwangerschap  
(met een samenvatting in het Nederlands)

PROEFSCHRIFT

ter verkrijging van de graad van doctor aan de Universiteit Utrecht op gezag van  
de rector magnificus, prof. dr. G.J. van der Zwaan, ingevolge het besluit van het  
college voor promoties in het openbaar te verdedigen op donderdag 30 september  
2014 des ochtends te 10.30 uur

door

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# Chapter 1

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## *General introduction*

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## Introduction

These following quotes are from women that participated in the research projects of this thesis and illustrate the different emotions women experience during waiting periods.

I don't want to live without being a mother.....It might go wrong with the implantation like that miscarriage at 8 weeks.....I try to prepare myself for a childless life because I am afraid that ICSI might not succeed.....Frustration, I heard on the news that oocytes can be frozen, why not when I was thirty.....I feel bad because I have no control over this situation and I can't rely on my body.

### *Women talking about the waiting period after embryo transfer*

I'm anxious because the last time the baby died in the 8th week, and we found out in the 10th week, I am now in the 8th week.....In de beginning I thought please let it be a miscarriage right away, than at least I know it.....The contact that I make with the embryo is mainly through the ultrasounds, not with my belly but with the screen and a beating pixel. I look at a pixel of a little heart, but not with the idea that it is a little person..... Somehow you have to keep on living so we use humour like we have a rice grain with a little heart.

### *Pregnant women with a miscarriage history talking about the waiting period*

In healthcare there are many different waiting periods that oblige patients to wait for results that are potentially threatening to their well-being (e.g., biopsy results, pregnancy test results after fertility treatment, genetic screening outcomes) (Lancastle & Boivin, 2008; Boivin & Lancastle, 2010). These waiting periods often cause high levels of anticipatory anxiety and uncertainty because the outcomes of the waiting periods are often unpredictable, uncontrollable and difficult to cope with (Boivin & Lancastle, 2010). Patients in medical waiting periods cannot alter the situation but theory predicts that coping strategies should be directed at regulating the negative anticipatory emotions associated with waiting (e.g., feeling nervous, tense, worried, anxious) (Folkman & Lazarus, 1988).

This thesis focuses on two different waiting periods namely the waiting period in fertility treatment and the waiting period in early pregnancy after having experienced miscarriages. A very stressful waiting period in a fertility treatment, such as In Vitro Fertilization (IVF) or IntraCyttoplasmic Sperm Injection (ICSI), is the two weeks



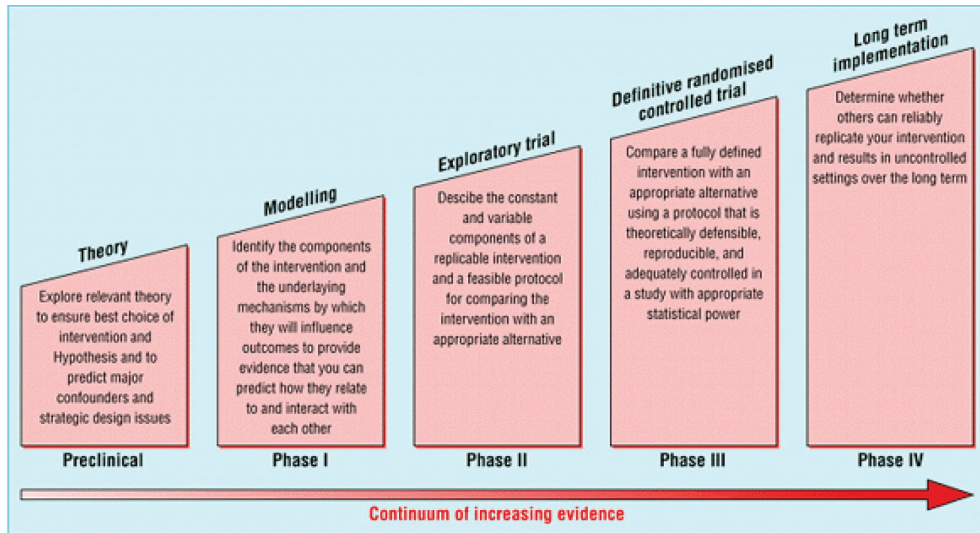
patients have to wait before they learn the outcome of their treatment (Merari et al., 1992; Boivin & Takefman, 1995; Eugster & Vingerhoets, 1999; Yong et al., 2000; Lancaster & Boivin, 2008; Verhaak et al., 2007). A cycle of an IVF/ICSI treatment requires 9 to 12 days of self-injection with drugs to stimulate the production of oocytes (eggs), retrieval of oocytes via trans-vaginal ultrasonography, fertilization of oocytes in the laboratory with partner or donor sperm, and transfer of the resulting embryo to the uterus. After the embryo transfer (ET) couples wait two weeks to find out whether implantation and a pregnancy have occurred. Women experience this waiting period after ET as very stressful, symptoms of anxiety and depression have been shown to increase between undergoing the transfer procedure and learning the outcome of treatment (Eugster & Vingerhoets, 1999; Yong et al., 2000; Lancaster & Boivin, 2008; Boivin & Lancaster, 2010).

Another group that faces difficult waiting periods are pregnant women with a history of miscarriage(s). These women have to deal with three different waiting periods: first the period of the actual loss until the woman tries to conceive again (miscarriage period), second the period between renewed attempts to conceive and conception (conception period), and third the period between conception and confirmation that the pregnancy is on-going (pregnancy period). Women not only experience stress during the miscarriage period but also in a subsequent pregnancy. Women with a miscarriage history have higher anxiety levels in a subsequent pregnancy than women with no previous miscarriages (Geller et al., 2004; Tsartsara & Johnson, 2006; Gong et al., 2013).

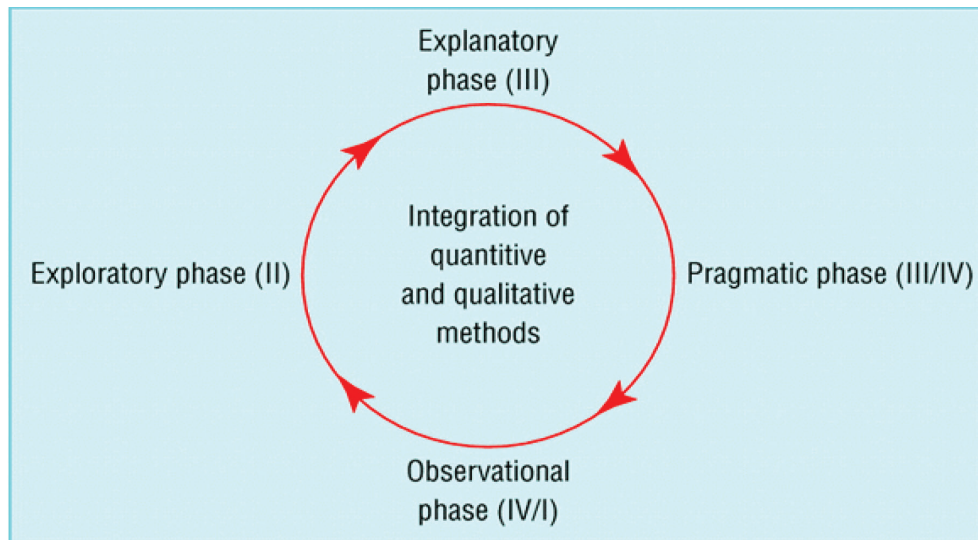
### **The Positive Reappraisal Coping Intervention (PRCI)**

Several psychosocial interventions are available to support women with infertility (Boivin 2003; Hammerli et al., 2009) or in a subsequent pregnancy (Nikcevic et al., 2007; Swanson et al., 2009) but these interventions do not focus specifically on waiting periods. Furthermore women do not always have access to these interventions and some are very time consuming. The Positive Reappraisal Coping Intervention (PRCI) was designed to address unmet coping needs specific to medical waiting periods such as waiting for fertility treatment results. The PRCI is self-administered and contains ten statements designed to promote positive reappraisal coping and an explanatory leaflet describing this method of coping. The PRCI was developed according to the Medical Research Council framework for developing complex interventions (figure 1) (Campbell et al., 2000; Craig et al., 2008). An advantage

of the framework is that it helps researchers to clearly define where they are in the developing process. Furthermore the iterative phased approach that connects qualitative and quantitative methods (figure 2) should lead to improved study design, execution, and generalisability of results.

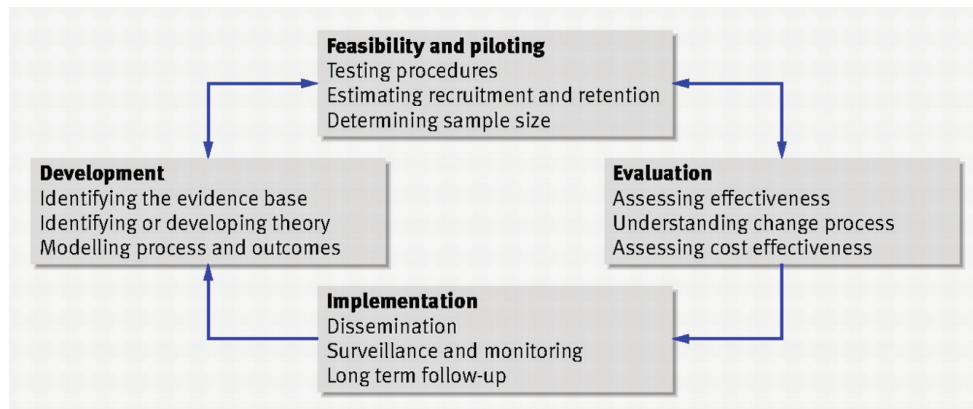


**Figure 1.** The MRC framework for the evaluation of complex interventions.



**Figure 2.** Iterative view of development of randomised controlled trials of complex interventions.

The MRC-framework was revised and updated in 2008 (Craig et al., 2008). This revised model for developing and evaluating a complex intervention consists of several phases, but does not necessarily need to follow a linear sequence (see figure 3).

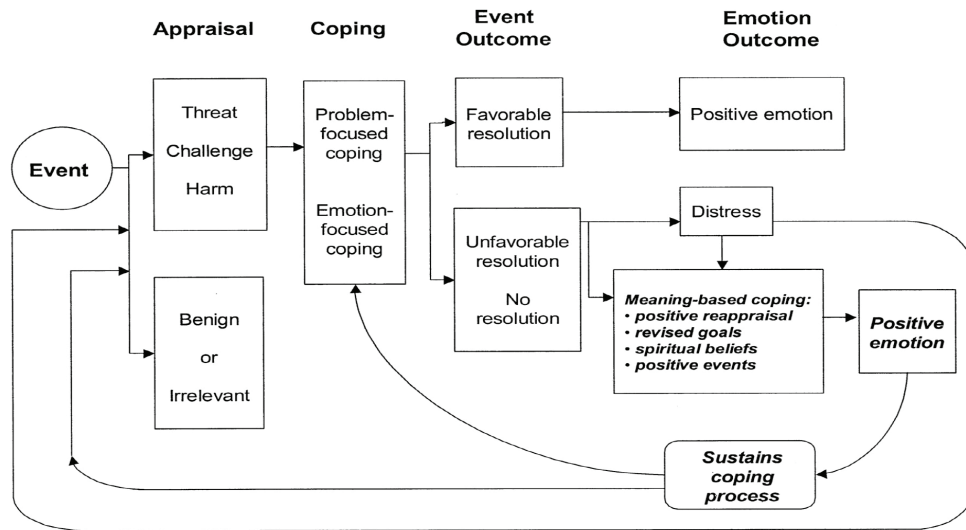


**Figure 3.** Revised MRC framework for the evaluation of complex interventions.

The development of the PRCI has been described in detail elsewhere (Lancastle, 2006). The PRCI is conceptualised from the cognitive model of stress and coping (figure 4) (Lazarus & Folkman, 1984; Folkman, 1997; Folkman, 2011) and based on the positive mood induction procedures (Velten, 1968).

The first pilot study generated the potential pool of statements for the PRCI card (Lancastle 2006). Seventeen items with face validity as intervention items were selected from the COPE questionnaire, the problem-appraisal coping scale and Ways of Coping questionnaire. Two items: “try to do something meaningful” and “try to do something that makes me feel good” were adapted from a qualitative interview schedule designed to investigate the experience of positive meaningful events (Folkman & Moskowitz, 2000). Seven further statements, each of which represented an alternative way of coping with stressful situations, were then added. A second pilot study was conducted to further model the intervention (Lancastle, 2006). This study investigated the effect of the PRCI on psychological wellbeing of medical students while they were waiting for seven days to sit important exams. Students who received the PRCI read the card as instructed (twice per day on average), felt more optimistic about their exam results in the last three days before the exam and reported marginally fewer physical stress reactions (e.g., racing heart,

sweaty palms) compared to a control group. The acceptability and feasibility of the PRCI was explored in a RCT of 55 women undergoing IVF (Lancastle & Boivin, 2008). Results showed that compared to the control group that used positive mood items, the PRCI group rated the intervention as more helpful and suitable for the IVF/ ICSI situation, more able to help women feel positive, as well as better in sustaining coping during the waiting period.



**Figure 4.** Revised model of Folkman's original Lazarus and Folkman stress and coping paradigm.

## Quantitative versus qualitative approach

Quantitative research has its roots in the positivism and qualitative in constructivism (Boeije, 2009; Holloway & Wheeler, 2010; Creswell, 2013). Positivism is a direction which aims to find general laws and regularities based on observation and experiments parallel to the methods of the natural sciences (Holloway & Wheeler, 2010). Constructivism is a direction based on the assumption that human beings construct their social reality and that the social world cannot exist independently of human beings (Holloway & Wheeler, 2010). Although quantitative research is the traditional and still the dominant approach, qualitative research is becoming increasingly accepted as a rigorous and valid discipline (Boeije, 2009; Holloway & Wheeler, 2010). There is however still a debate going on as to whether researchers

should use these two methods, based on different paradigms. Although some scientists believe quantitative and qualitative research should be used pragmatically and others that they are incompatible, a third paradigm has developed namely mixed methods (Boeije, 2009; Holloway & Wheeler, 2010). Mixed methods can be defined as research in which the investigator collects and analyses data, integrates the findings and draws inferences using both qualitative and quantitative methods in a single study or program (Boeije, 2009). Mixed methods research has its roots in pragmatism. Pragmatism sees the world as a reality of diverse experiences, theory and practice are not only related, but theory is an abstraction from reality (Holloway & Wheeler, 2010).

In this thesis, work using both quantitative and qualitative methods is presented. Adoption of this approach is supported by specific recommendations within the MRC framework (Campbell et al., 2000; Craig et al., 2008). A mixture of qualitative and quantitative methods can be used, for example, to understand barriers or to show how the intervention works and to find potential barriers to change in trials that seek to alter patient or professional behaviour (Campbell et al., 2000).

## **Aims and outlines of this thesis**

The general aim of the work presented in this thesis was to investigate the use of the PRCI for waiting periods within two populations. The first context explored, which is described in Part One of this thesis, the waiting period following an IVF/ICSI treatment. The second context is PRCI use during the waiting period faced by newly pregnant women with a past history of miscarriage, as described in Part Two of this thesis.

### **The specific aims of this thesis were:**

#### *Part one: waiting period in fertility treatment*

- To describe a study protocol to investigate the effect of the PRCI on psychological well-being of women waiting for the results of an IVF/ICSI treatment (Chapter 2).
- To investigate the effect of the PRCI on anxiety, depression and daily treatment reactions in women awaiting the outcome of an IVF/ICSI cycle (Chapter 3).
- To assess the effectiveness of the PRCI on anxiety and depression for women waiting for the results of a fertility treatment after adding a fourth non-randomised group (Chapter 4).

- To report the effect of PRCI on coping strategies in women awaiting the outcome of an IVF cycle (Chapter 5).

*Part two: waiting period for pregnant women with a history of miscarriage(s)*

- To explore how women with single or recurrent miscarriages cope during the waiting periods after miscarriage, waiting for pregnancy or waiting for pregnancy confirmation, and to learn their perception of the PRCI designed for these waiting periods (Chapter 6).
- To gain insight into emotions and coping strategies employed during the period of miscarriage, conception and pregnancy (Chapter 7).
- To examine whether the PRCI and Daily Record Keeping chart, developed for use in assisted conception treatment, are also appropriate for use in pregnant women with a history of miscarriage(s) (Chapter 8).

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# Chapter 2

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*The PRCI study: design of a randomized clinical trial to evaluate a coping intervention for medical waiting periods used by women undergoing a fertility treatment*

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*Published in BMC Women's Health: 2013: 13: 35.*

## Abstract

**Background:** Many medical situations necessitate a stressful period of waiting for potentially threatening test results. The medical waiting period is often associated with negative anticipatory anxiety and rumination about the outcome of treatment. Few evidence-based self-help coping interventions are available to assist individuals manage these periods. Theory and research suggest that positive reappraisal coping strategies may be particularly useful for this type of unpredictable and uncontrollable stressful context. The objective of this study is to investigate the effects of a Positive Reappraisal Coping Intervention (PRCI) on psychological well-being of women waiting for the outcome of their fertility treatment cycle.

**Methods/design:** In a three-armed randomized controlled trial, the effectiveness of the PRCI will be tested. Consecutive patients undergoing in vitro fertilisation in a Dutch university hospital and meeting selection criteria will be invited to participate. Those who agree will be randomized to one of three experimental groups (N=372). The PRCI Intervention group will receive the intervention that comprises an explanatory leaflet and the 10 statements designed to promote positive reappraisal coping, to be read at least once in the morning, once in the evening. To capture the general impact of PRCI on psychological wellbeing, patients will complete questionnaires before the waiting period (pre-intervention), on day ten of the 14-day waiting period (intervention) and six weeks after the start of the waiting period (post-intervention). To capture the specific effects of the PRCI during the waiting period, patients will also be asked to monitor daily their emotions and reactions during the 14-day waiting period. The primary outcome is general anxiety, measured by the Hospital Anxiety and Depression Scale. Secondary outcomes are positive and negative emotions during the waiting period, depression, quality of life, coping and treatment outcome. During recruitment for the RCT it was decided to add a fourth non-randomized group, a PRCI-comparison group that received the PRCI and completed the questionnaires but did not complete daily monitoring.

**Discussion:** Positive reappraisal is one of the few ways of coping that has been shown to be associated with increased wellbeing during unpredictable and uncontrollable situations like medical waiting periods. A simple evidence based self-help intervention could facilitate coping during this common medical situation. This RCT study will evaluate the value of a self-help coping intervention designed for medical waiting periods in women undergoing fertility treatment.

**Trial registration:** The study is registered at the Clinical Trials.gov (NCT01701011).

**Keyword:** Coping-intervention, Anxiety, Medical waiting period, Fertility, Randomized Clinical Trial.

2

## Background

The diagnosis and treatment of various medical conditions requires patients to wait for results that are potentially threatening to their well-being (e.g., breast biopsy results, pregnancy test results after fertility treatment, genetic screening outcomes) [1]. The outcomes of these tests are often unpredictable and often cause high levels of anticipatory anxiety and uncertainty [2] that are difficult to cope with. As the outcome of the medical tests or procedures for which patients are waiting cannot be changed or controlled, there is little point for the patient in trying to alter the situation. Instead, coping efforts should be directed at regulating the negative anticipatory emotions associated with waiting (e.g., feeling nervous, tense, worried, anxious) [3]. Despite the pervasiveness of medical waiting periods, few studies have investigated coping interventions to manage this stressful medical context [4].

Meaning-based coping strategies have been observed to be effective in contexts that involve a sustained period of unpredictability and uncertainty. Tedlie Moskowitz et al. [5] and Folkman and Moskowitz [6] observed that even in very stressful and uncertain situation such as caring for a terminally ill partner participants reported experiencing positive feelings. One type of coping strategy associated with these positive psychological states was positive reappraisal coping, which helped the person to redefine the situation in a more positive way, allowing them to derive some benefit from the negative experience. Folkman [3] proposed that these positive emotions had an important role in motivating people to continue in their efforts to cope in these ongoing stressful situations.

Fertility treatment is an example of a medical context that requires patients to wait for several weeks for the outcome of their treatment. The use of Assisted Reproductive Techniques (ART) (e.g., In Vitro Fertilization (IVF) and IntraCytoplasmic Sperm Injection (ICSI)) continues to increase and worldwide the total number of babies born through IVF is now exceeds 5 million [7].

A cycle of in vitro fertilisation typically requires nine to 12 days of self-injection with potent fertility drugs to stimulate the production of oocytes (eggs), retrieval of oocytes via trans-vaginal ultrasonography, fertilisation of oocytes in the laboratory with partner or donor sperm, and transfer of the resulting embryo to the uterus. Couples then wait two weeks to find out whether implantation and a pregnancy have occurred. Women often report that IVF/ICSI is an emotional and physical burden that can cause anxiety and stress [8,9]. The aspects most frequently reported as stressful are the fourteen-day waiting period between embryo transfer and the pregnancy test, and being informed that the treatment was unsuccessful [8-12]. Symptoms of

anxiety and depression have been shown to increase during the waiting period after ET [1,2,10,11]. The lack of control the patient has to influence outcome during this period has also been shown to contribute to the increase in distress [2].

Despite the emotional stress reported during fertility treatment, many women do not seek professional support [13,14]. The stated reasons for this are often practical, such as the costs of counselling, distance to the appointment or being unsure how to arrange an appointment [13]. Nevertheless, women still worry about the impact of stress on the outcome of treatment and available meta-analyses are inconclusive on such effects [15,16]. A meta-analysis of 31 prospective studies found a small but significant association between stress, distress and reduced pregnancy chances [15]. Another meta-analysis of 14 prospective studies found no significant effect of emotional distress on the chance of becoming pregnant [16]. Several psychosocial interventions designed to support women with infertility have been described [17,18]. However, these are mostly aimed at providing general support throughout the entire fertility treatment and not at a specific point in the treatment, such as the waiting period. The impact of psychosocial interventions on anxiety, depression, coping and treatment outcome is inconsistent across reviews. One review of 25 studies concluded that psychosocial interventions reduced negative affect such as anxiety and infertility-specific distress but had no effect on pregnancy rates [17]. A subsequent meta-analysis of 22 studies concluded that psychotherapy was effective in reducing anxiety delivered in individual and group format [19]. The pregnancy rate with assisted reproductive techniques (ART) was similar in individual and group therapy however there was a difference in pregnancy rates between psychotherapy (45%) and the control group (14%) [19]. A final meta-analysis of 21 controlled studies showed that psychosocial interventions did not impact any form of psychological distress but the meta-analysis for pregnancy rate was significant with sub-group analysis showing increased pregnancy rate but only in patients undergoing non-ART treatments [18]. Inconsistent results could be due to interventions being too general. Indeed, Boivin [17] found that interventions with a strong educational and skills component that focused on specific targets (e.g., coping training, sex during fertile period) were more effective than those focused primarily on emotional expression and support.

The Positive Reappraisal Coping Intervention (PRCI) was designed to address unmet coping needs during medical waiting periods such as waiting for fertility treatment results. During the stressful waiting period after ET, women do not normally attend a clinic for tests or procedures and therefore lose the opportunities they had to receive informal support from the medical staff, clinic or other patients

undergoing treatment at the same time [1]. Individual counselling of women during the waiting period is often not possible for hospitals because of the time investment and costs [13]. The PRCI is self-administered and comprises an explanatory leaflet describing this method of coping and ten statements designed to promote positive reappraisal coping. PRCI was conceptualised from the cognitive model of stress and coping [20,21] and developed according to the Medical Research Council framework for developing complex interventions [1]. Lancaster and Boivin [1] investigated the acceptability and feasibility of the intervention in a RCT of 55 women who used PRCI during the waiting period of an IVF/ICSI cycle versus a control group reading ten control positive statements. Results showed that the PRCI group rated the intervention as more helpful and suitable for the IVF/ICSI situation, more able to help women feel positive as well as better in sustaining positive reappraisal coping strategies during the waiting period. A feasibility study in the Netherlands showed that it is possible to recruit the amount of women necessary for the RCT in two years. Furthermore, the majority of the 27 women included in the study found the PRCI was suitable and feasible (unpublished data, Ockhuijsen). These results suggest that PRCI could be useful for medical waiting periods. However, its effectiveness on general or treatment-specific anxiety has not yet been systematically evaluated in a randomized controlled trial.

## **Methods/design**

The PRCI will be evaluated in a three-arm Randomized Controlled Trial (RCT). Participants will be randomized to an intervention, monitoring control group or routine care. To capture the general impact of the PRCI all three groups will complete questionnaires at three time points: just before the waiting period (Time 1: pre-intervention), on Day 10 of the 14-day waiting period (Time 2: intervention) and 6 weeks after the start of the waiting period (Time 3: post-intervention). See Table 1. Mobile phone text reminders will be sent to patients about completing the Time 1 and Time 3 questionnaires (if necessary) and all patients will receive a reminder just prior to the Time 2 assessment on the ninth day of the waiting period.

**Table 1.** Measurement timetable according to group.

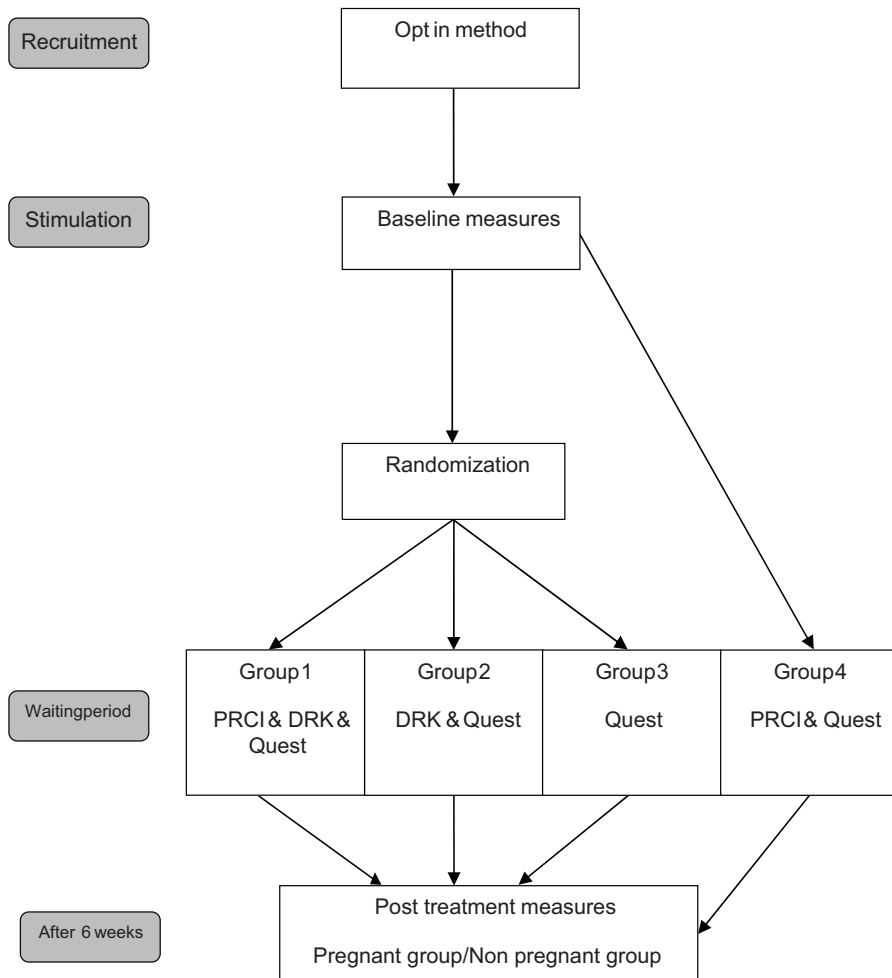
Measurements	T1 hCG to Embryo transfer	T2 Day 10 waiting period	T3 Six weeks after Embryo transfer
BIF	1,2,3,4	-----	-----
HADS	1,2,3,4	1,2,3,4	1,2,3,4
FertiQol	1,2,3,4	1,2,3,4 (Treatment only)	1,2,3,4 (non-pregnant group only)
WCQ	1,2,3,4	1,2,3,4	1,2,3,4
DRK one day	1,2,3,4	3,4	-----
IEF	-----	1,4	-----
DRK daily	-----	1,2	-----
Medical chart review	-----	-----	1,2,3,4

Note. Numbers refer to group: 1=PRCI Intervention, 2=Monitoring Control, 3=Routine Care and 4= PRCI-comparison (non-randomized). BIF=Background Information Form, HADS=Hospital Anxiety and Depression Scale, FertiQol= The Fertility Quality of Life, WCQ= Ways of Coping Questionnaire, DRK= Daily Record Keeping, IEF= Intervention evaluation form.

To capture the specific impacts of PRCI on the waiting period the intervention group will rate daily their emotions and reactions during the 14-day waiting period. Daily monitoring has previously been shown to be an efficient and sensitive way of evaluating emotional reactions during fertility treatment [2,9] and to be sensitive to intervention effects during ART [22]. One potential drawback of this method of assessment is that it may impact on the reporting of emotions itself. For example, habituation or sensitisation to monitoring per se may decrease or increase reporting of anxiety compared to groups that do not monitor [23]. Due to this potential reactivity the monitoring control group will also monitor emotions and reactions daily during the waiting period. The routine care control group will not receive the intervention or monitor reactions.

During recruitment for the RCT it was decided to add a fourth non-randomized group. The decision to add this group was based on preliminary results of ongoing qualitative research with the PRCI and daily monitoring among women who had experienced miscarriages (unpublished data, Ockhuijsen). The women in the miscarriage study reported that the daily monitoring had an effect on their emotions in that it helped them take account of the impact of miscarriages on their emotional lives. If daily monitoring was itself an intervention then it could attenuate, heightened or obscure effects of the PRCI intervention in unknown ways. Therefore it was

decided to add a PRCI-comparison group that received the PRCI and completed the questionnaires but did not complete daily monitoring.



**Figure 1.** Flow chart PRCI Study.

### Participants/recruitment

The RCT will be conducted over a two-year period in a fertility clinic at a University hospital in the Netherlands. See Figure 1 for the flow chart of the study. The opt-in method will be used to recruit participants. In this method participants are sent an invitation to the trial and themselves contact the team to take part. The inclusion criteria will be all women undergoing a stimulated or cryopreserved IVF/ICSI



treatment. The exclusion criteria will be women not speaking the Dutch language. All women meeting these criteria and starting a treatment will be sent a letter with general information about the study. Doctors and nurses working in the fertility clinic will remind women of the letter and the study. Patients who are interested in the study will return a reply form or e-mail indicating their interest and a researcher will contact them to give more information about the study and answer any questions. Those who decide to participate will be sent a written information sheet and a consent form to return in a pre-addressed stamped envelope. During their first visit to the hospital, more information will be given about the logistics of the study, as needed, but all patients will be given the same information according to a written protocol.

The fourth group will be recruited as for the RCT. The fourth group will receive the same information as the participants from the RCT. Although this group will not be randomized, participants will be told that randomization will take place. Participants will be fully debriefed about the need for this deception at the end of the study.

The Ethical committee of the University of Utrecht provided ethical review and approval for this study, including the addition of the fourth non-randomized group (protocol number 10-174/K).

### **Sample size**

The sample size calculation for the three-arm RCT is based on the following parameters. To test the difference on anxiety between three groups using a mixed factorial ANOVA, power of 95%,  $\alpha=0.05$  and a medium effect size a total of 297 subjects was required (99 patients per group) [24,25]. However, taking into account a 20% attrition rate at least 124 women will be recruited in each group. Effect size and attrition were derived from Lancaster and Boivin [1]. The addition of the fourth group only slightly modified sample size and 110 participants were recruited to the fourth group.

### **Randomization**

Stratified randomization of the 372 women into one of the three groups will be performed by using a computer-generated table of random numbers. The type of treatment (stimulated or cryopreserved IVF/ICSI) will stratify the population because emotions and expectations relative to a stimulated IVF/ICSI may differ from a cryo-preserved treatment [26,27]. Randomization will take place after the first assessment (Time 1 pre-intervention) between follicle aspiration and embryo transfer. An independent research nurse will be responsible for the randomization. Double blinding will take place for participants and clinic staff. Participants will not be

told what intervention is being evaluated. The researcher will have no contact with participants after randomization. All women will receive written information about group assignment on the day of the embryo transfer. They will receive instructions for the waiting period in an opaque sealed envelope after the embryo transfer. The clinical staff that performs the embryo transfer will be blinded for the content of the envelope. After the embryo transfer, there will be no further contact between the clinical staff, other patients, or the researcher during the 14-day waiting period.

### **Intervention and control groups**

Patients will be randomly assigned to one of the three groups: PRCI Intervention, Routine Care Control and Monitoring Control. In addition data will be collected for the PRCI-comparison group.

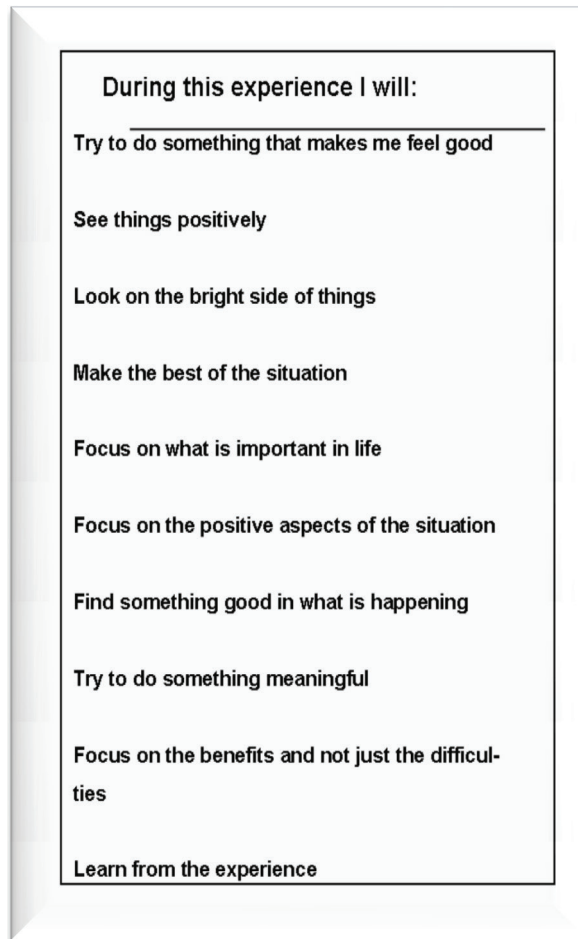
The PRCI Intervention and PRCI-comparison groups will receive the PRCI. The PRCI is a small card that contains ten positive reappraisal statements and a leaflet with a detailed explanation about this coping approach. See Figure 2 for the PRCI card. Women will be instructed to read the PRCI at least twice a day, once in the morning and once in the evening as well as at any time they feel the need, and to think about how each statement applies to them personally. The other groups will not receive the PRCI. The Monitoring Control group will complete daily monitoring and questionnaires, whereas the Routine Care Control and PRCI-comparison groups will only complete questionnaires.

### **Objective**

The aim of this study is to investigate the effect of the PRCI on psychological well-being of women waiting for the results of an IVF/ICST treatment. The primary outcome is level of general anxiety measured before the waiting period (pre-intervention), on day ten of the 14-day waiting period (intervention) and six weeks after the start of the waiting period (post-intervention). Secondary outcomes are positive and negative treatment emotions during the waiting period, depression, coping style, quality of life and treatment outcome.

### **Hypotheses**

The PRCI increases the use of positive reappraisal coping strategies and reduces symptoms of general anxiety and depression, improves quality of life across assessment as well as increases positive and decreases negative emotions during the fourteen days of the waiting period in patients undergoing an IVF/ICSI treatment.



**Figure 2.** PRCI intervention. © 2008 by Cardiff University. All rights reserved. No part of this document may be reproduced or transmitted in any form or by any means, electronic, mechanical, photocopying, recording, or otherwise, without prior written permission of authors.

### **Study measures**

Data will be obtained with self-reported questionnaires, daily monitoring and from the treatment medical records. Table 1 shows the assessment timetable. Questionnaires will be completed prior to, during and after the intervention whereas monitoring will be daily during the two-week waiting period.

The following self-report measures will be used:

The Background Information Form (BIF) is a 16-item questionnaire to measure demographic (e.g., age, educational status), medical (e.g., previous illness) and gynaecological (e.g., infertility diagnosis, previous infertility treatment) characteristics as well as treatment expectations (e.g., chances of conceiving, perceived control over the outcome).

The Hospital Anxiety and Depression Scale (HADS) will be used to measure general anxiety and depression. The HADS consists of 14 items (7 items for each subscale) that are rated on a 4-point Likert scale. The total score is the sum of the 14 items, and for each subscale the score is the sum of the respective seven items (ranging from 0–21). Scores on each scale can be interpreted in ranges: normal (0–7), mild (8–10), moderate (11–14) and severe (15–21). The Dutch version of the HADS has been shown to be a valid and reliable instrument [28].

The Fertility Quality of Life (FertiQoL) scale will be used to measure the impact of infertility and its treatment. FertiQoL consist of 36 items that assess core (24 items) and treatment related quality of life (10 items) and overall life and physical health (2 items). Items are rated on a 5-point response scale. Cronbach reliability coefficients for the Core and Treatment FertiQoL were 0.92 and 0.81, respectively [29]. The convergent validity of the Dutch version of the FertiQoL has been investigated and shows similar reliability [30]. Items are summed and scaled, with a range of 0 to 100. Higher scores indicate better quality of life.

The Ways of Coping Questionnaire (WCQ) will be used to measure use of coping strategies. The WCQ is based on the cognitive stress and coping model of Lazarus and Folkman [31,32]. The instrument is designed to measure situation-specific coping. The 41 items of the Dutch version are rated on a 4-point response scale that, when summed, yields 6 subscales. Taking responsibility (6 items), problem solving (8 items), social support (6 items), wishful thinking (8 items), avoidance (7 items), positive reappraisal (6 items). The Cronbach alpha coefficients reported for the six subscales ranges from 0.65 to 0.80. To measure the concurrent validity the WCQ has been compared with the seven scales of the Utrecht Coping List with good correspondence between these [33].

The Intervention evaluation form (IEF) is a 24-item questionnaire developed to assess intervention feasibility, acceptability and effects, which was used to assess PRCI in previous research [1]. It measures the following aspects of the intervention: practicality (6 items), acceptability (4 items), endorsement (4 items), perceived psychological effects (8 items) and perceived duration of intervention effects (2 items).

The Daily Record Keeping (DRK) sheet will be used daily to rate reactions to the 14-day waiting period (PRCI Intervention and Monitoring Control groups only). The DRK comprises 46 possible reactions to the IVF waiting period, including 20 emotions, optimism and pessimism about pregnancy, 12 physical symptoms, five appraisals, and seven coping strategies. The emotional subscale is based on the theory of Lazarus and Folkman [20] and contains affective reactions that are averaged to produce anxiety (i.e., tense, nervous, worried), depression (i.e., anger, frustrated, sad) and positive affect (i.e., happy, content, fulfilled). The five coping strategies are measured with Stone and Neale's [34] daily coping measure namely strategies of distraction, positive redefinition, problem-focused, seeking emotional support and acceptance. The twelve physical symptoms list two common side effects of medication (i.e., abdominal discomfort, spotting), two symptoms related to treatment success/failure (e.g., breast tenderness, menstrual cramps) and the remaining eight symptoms originate from the physical stress reactions (e.g., racing heart, muscle tension) of the Pennebaker Inventory of Limbic Languidness (PILL) [1]. Subscale scores were created (where relevant) by averaging across subscale items and higher scores indicate more of the attribute (e.g., more tension, breast tenderness, distraction). Participants will be instructed to complete the DRK at the end of the day, and for the PRCI intervention group at least one hour after reading the PRCI card to limit the chance of DRK ratings being artificially and transiently influenced by completing the DRK.

The DRK has been shown to be acceptable for monitoring during protracted periods of treatment with 15% attrition during 75 days of monitoring and 9% over a period of 30 days [9]. The reported Cronbach alpha ranges from 0.70 – 0.82 for subscales [2]. The DRK was translated and used in a Dutch study [22] that showed good correspondence between the original and Dutch version, and acceptable convergent and discriminant validity with other measures of anxiety and depression. The DRK was also tested in a feasibility study in a population from the recruitment clinic in the Netherlands showing acceptability and feasibility (unpublished data, Ockhuijsen).

A medical chart review at the end of treatment will be used to obtain treatment data and will include the total number of past IVF/ICSI stimulated and cryopreserved cycles, past intra-uterine insemination cycles, previous conceptions/births, infertility diagnosis, smoking status, alcohol use, and body mass index. Data about the current treatment will include: type of treatment and protocol, date of first and subsequent treatment attempt, treatment cancellation (yes/no) and reason for cancellation, number of oocytes retrieved, total number of embryos created, transferred and

cryopreserved, treatment outcome (positive pregnancy test, clinical pregnancy, live birth), physician recommendation for next cycle and patient compliance with physician recommendation”.

### **Statistical analysis**

IBM SPSS Statistics will be used to perform the statistical analysis. Equivalence of baseline measures between groups will be examined by one-way analyses of variance (ANOVA) for normally distributed variables on interval or ratio level, chi-square for normally distributed variables on nominal level and Kruskal Wallis *H* test for normally distributed variables on ordinal level. If study variables are not normally distributed then data will be transformed to normalise (e.g., square root, log, etc. as is required). If the groups are not comparable on demographics, medical history or gynaecological variables, those variables will be employed as covariates in subsequent analyses. To examine the differences between groups over time a repeated measure mixed factorial ANOVA design will be used for variables on interval or ratio level. To compare the fourth group with the three separate groups also an ANOVA design will be used. Intention to treat and multi-level modelling will be used to analyse the data to take account of attrition.

### **Discussion**

Waiting for a potentially threatening medical test result in a period where there is no control in the outcome is very stressful and can bring about feelings of tension, nervousness and worry. The Positive Reappraisal Coping Intervention (PRCI) investigated in this RCT was specifically designed to help people cope with these medical waiting periods. Positive reappraisal coping is a set of strategies in which the significance of the event is reinterpreted in a more positive way [6]. In the present study, we will evaluate the effectiveness of the PRCI on psychological wellbeing of woman waiting for the results of an IVF/ICSI treatment cycle. Although the effectiveness of the PRCI has not yet been investigated, the coping literature shows that positive reappraisal strategies are one of the few ways of coping that are associated with increased positive affect and sustained ability to cope in unpredictable and uncontrollable stressor situations [6]. The results of this study could therefore be important because there is a lack of inexpensive self-help evidence based coping-interventions that could be used during the common medical waiting period.

This study has several strengths. This RCT was developed based on the results of several previous studies. The framework for developing complex interventions was used to design the PRCI and provide evidence of feasibility and acceptability in the studied population [35,36]. The MRC framework guides development to be theory based to create active components that can be delivered effectively during the RCT. Also the development and validation of the assessment tools was based on previous research showing good psychometric properties in Dutch translations for the key measures [9,35]. We chose a three-armed RCT to ensure balance between the determination of the general impacts of PRCI measured by questionnaires and its more specific impacts on the waiting period measured by monitoring. The Monitoring Control group of women who only monitor will allow us to disentangle effects due to PRCI and those due to monitoring per se on emotions and reactions during the waiting period. The RCT procedures match those of high quality trials with randomization and allocation concealment, blinding of patients and clinical staff [37].

The decision to add the PRCI-comparison group after the RCT has the disadvantage that this group will not be randomized. However, the group will allow us to estimate PRCI effects independent of daily monitoring, in case monitoring has an unexpected intervention effect that interacts with PRCI effects. Our RCT procedures use written protocols and blinding which should minimise the chance of systematic bias even in this non-randomized group with respect to attributes that may affect the dependent variables. The expected sample size will provide adequate power for detection of effects, determined from previous studies using the PRCI tool.

A limitation of this study is the method used for recruiting the participants. The opt-in method was employed to recruit on the advice of the Ethics Committee. In this method participants are sent an invitation to the trial and themselves contact the team to take part, which differs from the more conventional opt-out approach where all patients are contacted about the trial unless they have contacted the team to indicate that they do not wish to be approached. Although the opt-out method improves recruitment, the ethical committee often does not approve this method because repeated contact is too burdensome for participants [38,39]. In the study of Junghans et al. [38] there was a difference in risk factors between the two methods. Patients in the opt-in arm had fewer risk factors (44%) compared to patients in the opt-out arm (60%) ( $P = 0.053$ ).

Another limitation could be the participation of only one hospital. We choose to recruit in only one hospital because this university hospital attracts patients from all over the country. However, as there is collaboration with other clinics nationwide

inferences about the generalizability of findings can be determined via comparison of patient characteristics collected as part of wider collaborations.



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# Chapter 3

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*The impact of a self-administered coping intervention on emotional well-being in women awaiting the outcome of IVF treatment: a randomized controlled trial*

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## Abstract

**Study question:** What is the effect of the positive reappraisal coping intervention (PRCI) on anxiety in women awaiting the outcome of an IVF/ICSI cycle?

**Summary answer:** Women reported significantly more anxiety during the waiting period than before treatment, but the use of the PRCI did not significantly reduce anxiety during the waiting period.

**What is known already:** Waiting for the outcome of IVF/ICSI treatment after embryo transfer is one of the most stressful periods of fertility treatments. At present, no evidence-based coping interventions are available to assist women though this waiting period. The PRCI has been designed to address this unmet need by promoting positive reappraisal coping.

**Study design, size, duration:** A three-armed randomized controlled trial (RCT) was designed to evaluate the PRCI in women undergoing IVF/ICSI. Data were collected between October 2010 and June 2012. A total of 377 participants were randomized to receive either the PRCI and emotional monitoring, emotional monitoring only, or routine care. Only the PRCI-monitoring group received the coping intervention, comprising an explanatory leaflet and ten statements to be read at least once in the morning and once in the evening.

**Participant, materials, setting, methods:** To capture the general impact of the PRCI, all three groups completed questionnaires at three time points: just before the waiting period (time 1: stimulation phase), on Day 10 of the 14-day waiting period (time 2: waiting period) and 6 weeks after the start of the waiting period (time 3: 6-week follow-up). In addition, to capture the specific impacts of the PRCI on the days of the waiting period, the PRCI-monitoring group and the monitoring-control group also rated daily, for the 14-day waiting period, their emotions and reactions.

**Main results and the role of chance:** Of the women who agreed to participate and who met eligibility criteria, 377 were randomized. All study participants reported significantly more anxiety and depression during the waiting period than before treatment ( $P < 0.001$ ). The mean difference in anxiety between time 1 versus time 2 was 1.465 (95% CI 1.098–1.832). The mean difference in depression between time 1 versus time 2 was 0.514 (95% CI 0.215–0.813). Use of the PRCI did not significantly reduce anxiety or depression, or daily negative emotions during the waiting period. However, patients randomized to the PRCI reported significantly more positive emotions during the waiting period ( $P < 0.001$ ) than the monitoring-control group, and reported the intervention to be easy to use, and as having a

positive psychological effect. No significant differences were found between the groups in treatment outcome.

**Limitations, reasons for caution:** The lack of difference observed in the present study for anxiety levels between the PRCI and the monitoring-control group could have been due to the effects of monitoring itself or its ability to attenuate or obscure the effects of the PRCI intervention in unknown ways. A randomized group of women who used only the PRCI without daily monitoring would provide more insight.

**Wider implications of the findings:** The PRCI was shown to help women reinterpret the demands of the waiting period in a more positive way. These results are consistent with previous studies showing that positive reappraisal coping is a useful strategy for unpredictable and uncontrollable situations represented by a medical waiting period. This simple low cost self-help coping intervention increases positive affect during the waiting period in an IVF/ICSI treatment.

**Study funding/competent interest(s):** The Women and Baby Division of the University Medical Centre Utrecht funded the study. The authors have no conflicting interest(s).

**Trial registration number:** The study is registered at the Clinical Trials.gov (NCT01701011).

**Key words:** coping intervention, medical waiting period, randomized controlled trial, anxiety, positive emotions.

## Introduction

In health-care, patients often have to deal with different waiting periods that could be stressful because the outcome of that period cannot be predicted or controlled, and is often difficult to manage (Lancastle and Boivin, 2008; Boivin and Lancastle, 2010). Theory shows that patients who are waiting for the results of medical treatments or examinations should use meaning-based coping strategies to deal with negative anticipatory emotions (Folkman and Lazarus, 1988). Although medical waiting periods are stressful, research on coping interventions to deal with waiting periods is limited (Phelps et al., 2012).

Meaning-based coping strategies can be helpful in situations that involve a prolonged period of unpredictability and uncertainty. Tedlie Moskowitz et al. (1996) and Folkman and Moskowitz (2000) observed that the use of the coping strategy, positive reappraisal, by carers of partners in the final stage of AIDS, led to positive emotions. People who use this strategy try to reinterpret the meaning of the situation so that they can obtain some benefit. Folkman and Lazarus (1988) suggested that the effect of positive emotions is to stimulate people to go on in their efforts to deal with these enduring stressful situations.

Woman undergoing fertility treatment, cope with an unpredictable and uncontrollable waiting period when they wait to find out whether or not treatment is successful. In a cross-sectional study among 242 women undergoing fertility treatment, ten significant difficulties were identified such as: monthly anticipation of treatment results (40%), lack of spontaneity in sexual relationship (30%), uncertainty regarding the future (29%), not being able to solve the problem myself (17%) (Benyamini et al., 2005). Research shows that the most stressful parts of a fertility treatment cycle are the waiting period after embryo transfer (ET), doing a pregnancy test and finding out the treatment was unsuccessful (Merari et al., 1992; Boivin and Takefman, 1995; Eugster and Vingerhoets, 1999; Yong et al., 2000; Verhaak et al., 2010). Although women have increased anxiety and depressive symptoms during the waiting period after embryo transfer (Eugster and Vingerhoets, 1999; Yong et al., 2000; Lancastle and Boivin, 2008; Boivin and Lancastle, 2010), they often do not look for psychological support (Boivin et al., 1999; Van Dongen et al., 2012). Arguments for not searching for professional support are the perceived difficulty of scheduling sessions, not knowing who to contact, and potential cost of sessions (Boivin et al., 1999). There is lack of action despite the fact that women often wonder whether stress influences the outcome of their fertility treatment. Meta-analyses make conflicting conclusions about the role of stress, with a lack of effect on single cycles (Boivin et al., 2011) but



possible effects on multiple cycles of treatment (Matthiesen et al., 2011). Narrative and meta-analytic reviews about the impact of psychosocial interventions on anxiety, depression and treatment outcome are also inconsistent (Boivin, 2003; Hammerli et al., 2009). Inconsistency in these reviews could be due to the fact that psychosocial interventions are generally aimed at the entire fertility treatment and not at a specific stage like the waiting period after embryo transfer. A review found that psychosocial interventions in infertility which emphasized education and skills training focussing on specific targets were more effective than more general interventions which emphasized emotional expression and support (Boivin, 2003).

The positive reappraisal coping intervention (PRCI) is designed for medical waiting periods such as waiting for the outcome of a fertility treatment. The PRCI consists of a card with ten statements and an information leaflet about the coping strategy which was designed to stimulate the use of positive reappraisal coping. The development of the PRCI was in keeping with the Medical Research Council framework for development of complex interventions: it used theory, integrated empirically validated determinants of behaviour, tested the acceptability and feasibility of the intervention and estimated the effect size for future randomized controlled trials on effectiveness (Campbell et al., 2000; Craig et al., 2008). The development of the PRCI is described in detail elsewhere (Lancastle, 2006; Lancastle and Boivin, 2008) but is briefly summarized here. Our goal was to develop a coping intervention that was theoretically derived, simple enough for untrained patients to use by themselves (whenever needed), sufficiently inexpensive to be made freely available, and generic so it could be adapted for other health contexts.

From these considerations, the PRCI was conceptualized using the cognitive model of stress and coping (Lazarus and Folkman, 1984; Folkman, 1997, 2011) and the Velten positive mood induction (PMI) procedures (Velten, 1968). The first pilot study generated the potential pool of statements for the PRCI card. Seventeen items with face validity as intervention items were selected from three existing coping scales (COPE questionnaire, problem-appraisal coping scale and ways of coping questionnaire). Two further items ('try to do something meaningful' and 'try to do something that makes me feel good') were adapted from a qualitative interview schedule designed to investigate the experience of positive meaningful events (Folkman and Moskowitz, 2000). Seven filler items were also added, each of which represented an alternative way of coping with stressful situations. In the first pilot study of the PRCI, 36 patients waiting for assessment or treatment in the Accident and Emergency department were provided with a hypothetical scenario of a patient waiting for important medical test results and asked to imagine themselves in this

situation and to rate (for all 26 selected reappraisal and filler coping strategies) whether they would use the strategy, and find it helpful, and whether it would be capable of making them feel more positive during this experience of waiting for important medical test results. The analysis showed discriminant validity with the capacity of positive reappraisal items to make the patient feel more positive in this situation rated higher than for filler items (i.e. other coping strategies) [ $t(35) = 2.13, P < 0.05$ ]. As expected from theory, the perceived helpfulness of the positive reappraisal items for this (unpredictable, uncontrollable) medical waiting period was significantly higher than for the filler items (i.e. other coping strategies). There was no gender difference in response to any items (all  $P$ s  $> 0.05$ ) and internal reliability amongst all positive reappraisal items was high (Cronbach alpha 0.89 for beneficial ratings). Given these results, the final selection of the ten PRCI statements was based on optimizing the percentage of patients endorsing use of the item and their correlation with other items, perceived helpfulness and potential for improved positive mood ratings. A second pilot study was conducted to further model the intervention. In this study, the psychological well-being of medical students who used the PRCI ( $n = 19$ ) while they were waiting for seven days to sit important exams was compared with a control group ( $n = 20$ ) who did not receive the intervention. Students who received the PRCI read the card as instructed (twice per day on average), felt more optimistic about their exam results in the last 3 days before the exam and reported marginally fewer physical stress reactions (e.g., racing heart, sweaty palms). The acceptability and feasibility of the PRCI was explored in a RCT of 82 women undergoing IVF who were randomly assigned to PRCI, a PMI control group ('I feel good') or a daily monitoring control group. The RCT was additionally designed to estimate effect sizes for PRCI effects on coping, appraisals and other psychological factors related to the cognitive model of stress and coping (Lancastle, 2006). Women using the PRCI were found to appraise the waiting period as significantly more controllable [ $F(2, 79) = 3.10, P < 0.05$ ] and reported significantly more challenge appraisals [ $F(2, 79) = 2.58, P < 0.05$ ] than the PMI group (Lancastle, 2006).

A feasibility study carried out in the Netherlands for the present study showed that 12/19 women (63%) undergoing IVF found that the PRCI was suitable for this context and 17/19 (89.5%) rated the PRCI as quick and easy (unpublished data).

These feasibility results suggested that the PRCI could be useful for medical waiting periods and that there would be sufficient interest among patients to make feasible a full RCT within the 2 years available to do a trial. The aim of the present study was to investigate the effect of the PRCI on emotional well-being in women awaiting the outcome of an IVF/ICSI cycle. The primary outcome was general anxiety. Secondary

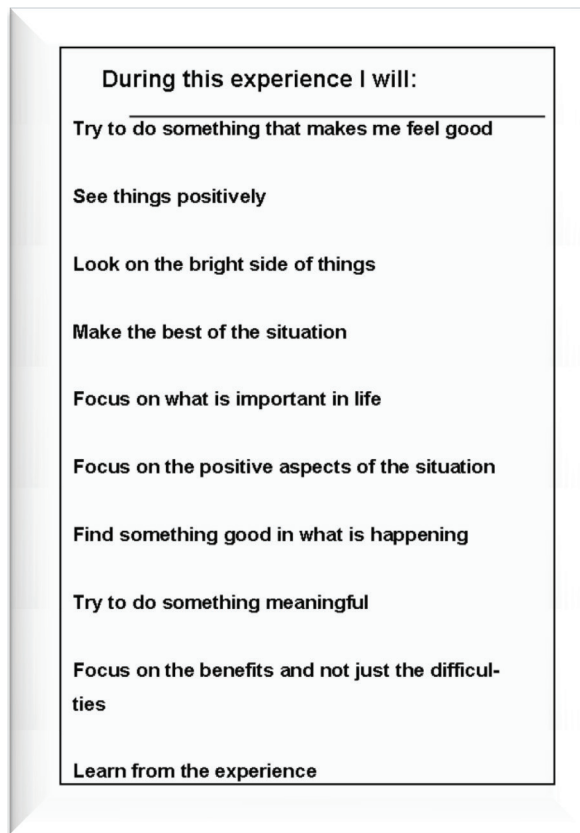
outcomes were general depression, treatment-specific positive and negative emotions, evaluation of the intervention and treatment outcome. It was hypothesized that the PRCI would reduce general and treatment-specific negative emotions in infertile women waiting for the outcome of their fertility treatment compared with control conditions.

## Materials and methods

### Trial design

The PRCI was evaluated in a three-arm Randomized Controlled Trial (RCT). Participants were randomized to a PRCI-monitoring group or to one of two control groups: monitoring-control or routine care control group. To capture the general impact of the PRCI, all three groups completed anxiety and depression questionnaires at three time points: just before the waiting period (Time 1: pre-intervention), on Day 10 of the 14-day waiting period (Time 2: waiting period intervention) and 6 weeks after the start of the waiting period (Time 3: post-intervention). Mobile phone text reminders were sent to patients regarding completing the Time 1 and Time 3 questionnaires (if necessary) and all patients received a reminder just prior to the Time 2 assessment on the ninth day of the waiting period.

To capture the specific impacts of PRCI on the days of the waiting period, the PRCI-monitoring and the monitoring-control group also rated daily, for the 14-day waiting period, their treatment specific emotions and reactions. Daily monitoring has previously been shown to be an efficient and sensitive way of evaluating emotional reactions during fertility treatment, including the waiting period (Boivin and Takefman, 1995; Boivin and Lancaster, 2010) and to be sensitive to intervention effects during Assisted Reproductive Technologies (ART) (de Klerk et al., 2005). One potential drawback of this method of assessment is that it may impact on the reporting of emotions itself. For example, habituation or sensitization to monitoring per se may decrease or increase reporting of anxiety compared with groups that do not monitor (Cohen et al., 1995). Due to this potential reactivity the monitoring-control group also monitored emotions and reactions daily during the waiting period. The routine care control group did not receive the intervention and did not monitor daily their reactions, but completed questionnaires as per the other groups.



**Figure 1.** Coping statements included in the PRCI intervention (contact author JB for complete intervention, including explanatory leaflet and permissions for use). © 2008 by Cardiff University. All rights reserved. No part of this document may be reproduced or transmitted in any form or by any means. Electronic, mechanical, photocopying, recording, or otherwise, without prior written permission of authors (Lancastle, 2006; Lancastle and Boivin, 2008).

## **Participants**

The RCT was conducted over a period of twenty months in a fertility clinic at a university hospital in the Netherlands. The sample size calculation for the three-arm RCT was based on the following parameters. To test the difference in psychological wellbeing between three groups with a power of 95%,  $\alpha = 0.05$  and a medium effect size ( $f = 0.25$ ), a total of 297 participants were required (99 patients per group) (Polit and Hungler, 1999; Polit and Beck, 2008). Taking into account a 20% attrition rate at least 124 women had to be recruited in each group. Effect size and attrition were derived from Lancastle and Boivin (2008). The inclusion criteria were woman

undergoing a stimulated or cryopreserved IVF/ICSI treatment cycle. Women not speaking the Dutch language were excluded.

### **Intervention and control group**

The PRCI-monitoring group received the PRCI. The PRCI is a small card that contains ten positive reappraisal statements and a leaflet with a detailed explanation about this coping approach. See Figure 1 for the PRCI card (contact author JB for complete intervention, including PRCI leaflet). Permission was obtained from Cardiff University to reproduce the PRCI card. The leaflet instructed women to read the PRCI at least twice a day, once in the morning and once in the evening as well as at any other time they felt the need, and to think about how each statement applied to them personally. The other groups did not receive the PRCI.

### **Materials**

Data were obtained with self-reported questionnaires, daily monitoring and from the medical records. The following self-report measures were used:

The Background Information Form (BIF) is a 16-item self-report questionnaire designed to obtain demographic (e.g., age, educational status), medical (e.g., previous illness) and gynaecological (e.g., infertility diagnosis, previous infertility treatment) characteristics. This form was completed by all groups pre-intervention (Time 1).

The Hospital Anxiety and Depression Scale (HADS) was used to measure general anxiety and depression (Zigmond and Snaith, 1983). The HADS consists of 14 items (7 items for each subscale) that are rated on a 4-point Likert scale. The total score is the sum of the 14 items, and for each subscale the score is the sum of the respective seven items (ranging from 0 to 21). Scores on each scale can be interpreted in ranges: normal (0 - 7), mild (8 - 10), moderate (11 - 14) and severe (15 - 21) anxiety and depression. The Dutch version of the HADS has been shown to be a valid and reliable instrument, including in the IVF/ICSI context (de Klerk et al., 2005). All groups completed the HADS at Time 1, Time 2 and Time 3.

The Daily Record Keeping (DRK) form was used to rate positive and negative emotions daily during the 14-day waiting period (PRCI-monitoring and monitoring-control groups only) (Boivin and Takefman, 1995). The DRK was developed for use in fertility treatment and comprises 46 possible reactions to the IVF waiting period, including the 20 positive and negative emotions used in the present analysis. Women endorsed each of the reactions provided on the DRK (e.g., happy, sad, anxious) according to whether, and to what extent, they had felt that way in the

previous 24 hours. Emotions were rated on a scale from 0 to 3, with higher scores representing more emotion. These ratings were summed to compute positive and negative emotion subscales that Folkman and Lazarus (1985) proposed to be the emotional counterparts of particular appraisals of a situation. Negative emotions comprised threat (e.g., tense, worried) or harm emotions (e.g., sad, discouraged) whereas positive emotions referred to challenge (e.g., hopeful, positive) or benefit emotions (e.g., content, happy) (Folkman and Lazarus, 1985).

The DRK has been used in numerous treatment studies with the Cronbach alpha for the emotional subscale in the range of 0.76 to 0.82 for subscales (Boivin, 1997). The DRK item on vaginal bleeding (i.e., spotting) was also used and was rated in the same way. This item referred to light bleeding or spotting which occurs during the waiting period in approximately 30% of patients (De Sutter et al., 2006). Vaginal bleeding is not consistently associated with pregnancy outcome (De Sutter et al., 2006) but may nevertheless affect daily emotional reactions due to patient perceptions of the meaning of this symptom. The DRK was translated and used in a Dutch study that showed good correspondence between the original and Dutch version, and acceptable convergent and discriminant validity with other measures of anxiety and depression (de Klerk et al., 2005). Participants were instructed to complete the DRK at the end of the day and for the PRCI-monitoring group at least one hour after reading the PRCI card to limit the chance of DRK ratings being artificially and transiently influenced by completing the DRK. The PRCI-monitoring and the monitoring-control groups completed the DRK daily during the two-week waiting period from the day of embryo transfer until the day before the pregnancy test. Women also noted on the DRK the number of times per day they read the PRCI. The Intervention evaluation form (IEF), a 23-item questionnaire developed to assess perceptions of intervention, was used to assess PRCI in previous research (Lancastle and Boivin, 2008). It measures the following aspects of the intervention: practicality (6 items), acceptability (4 items), endorsement and feasibility (4 items), perceived psychological effects (7 items) and perceived duration of intervention effects (2 items). The response scale varies by item. The PRCI-monitoring group completed the IEF at Time 2.

A medical chart review at the end of treatment was used to obtain data about treatment outcome: clinical pregnancy and clinical pregnancy with fetal heartbeat. Clinical pregnancy is a pregnancy diagnosed by ultrasonography of one or more gestational sacs or definitive clinical signs of pregnancy (Zegers-Hochschild et al., 2009). Clinical pregnancy with fetal heartbeat is a pregnancy diagnosed by ultrasonography or clinical documentation of at least one fetal with heart beat

(Zegers-Hochschild et al., 2009). The medical chart of all groups was examined at 6-weeks follow-up.

### **Procedure**

The ethical committee of the University of Utrecht provided ethical review and approval for this study. The opt-in method was used to recruit participants as per requirements of the Ethics Committee. Participants were sent an invitation to the trial and if interested asked to contact the research team using the reply form or email address provided. A researcher contacted patients interested in the study to give more information about the study and answer any questions. Those who decided to participate were sent a written information sheet and a consent form to return in a pre-addressed stamped envelope. During their first visit to the hospital, more information was given about the logistics of the study, as needed, but all patients were given the same information according to a written protocol.

A computer-generated table of random numbers was used to achieve the stratified randomization of the 372 women who met the eligibility criteria. The type of treatment (stimulated or with use of own cryopreserved embryos from a previous cycle) stratified the population because emotions and expectations relative to a stimulated IVF/ICSI may differ from a cryo-preserved treatment (Svanberg et al., 2001; Provoost et al., 2010). Randomization took place after the first assessment (Time 1: pre-intervention) between follicle aspiration and embryo transfer. An independent researcher was responsible for the randomization. Participants were not told what intervention was being evaluated, whether it was the intervention card or monitoring form or psychological questionnaires. The independent researcher had no contact with participants after randomization. All women received written information about group assignment on the day of the embryo transfer. They received instructions for the waiting period in an opaque sealed envelope after the embryo transfer. The clinical staff that performed the embryo transfer was blinded to the content of the envelope. After the embryo transfer, there was no further contact between the clinical staff, other patients, or the researcher during the 14-day waiting period. An independent research assistant verified random data input for accuracy of the database.

### **Statistical methods**

IBM SPSS Statistics 20 was used to perform the statistical analysis. Descriptive statistics for means and standard deviations were used to describe baseline variables and outcome of the intervention evaluation. Equivalence of baseline measures

between groups was examined by one-way analyses of variance (ANOVA) for normally distributed variables on interval or ratio level and chi-square for variables on nominal level. If the groups were not comparable on demographics, medical history, or gynaecological variables, those variables were employed as covariates or factors in subsequent analyses. The onset of menstrual bleeding during the waiting period could differ between women and therefore vaginal bleeding (i.e., spotting) was used as a covariate in analyses. A mixed model for repeated measures was used to examine the differences between the three groups over time for the primary outcome anxiety and secondary outcomes depression and treatment-specific positive and negative emotions. All models were estimated by the method of restricted maximum likelihood (REML) and the compound symmetry covariance structure was chosen for the repeated measures. For the DRK analysis, with 14 repeated measures, we used time as a continuous variable with a linear contrast. The parameter of the convergence criteria was set at 0.000001(absolute). Results for this outcome will be presented as slope over time and differences in slope between groups when a group by time interaction is analysed. The analysis was performed according to intention to treat. The main effect of time indicated change over time (regardless of group), the main effect of group indicated overall differences between groups (regardless of time) and the group by time interaction indicated differences between groups at each time point. One sample t-tests were used to test whether evaluations of the intervention within the PRCI-monitoring group were significantly different from the 'no effect' rating.

## Results

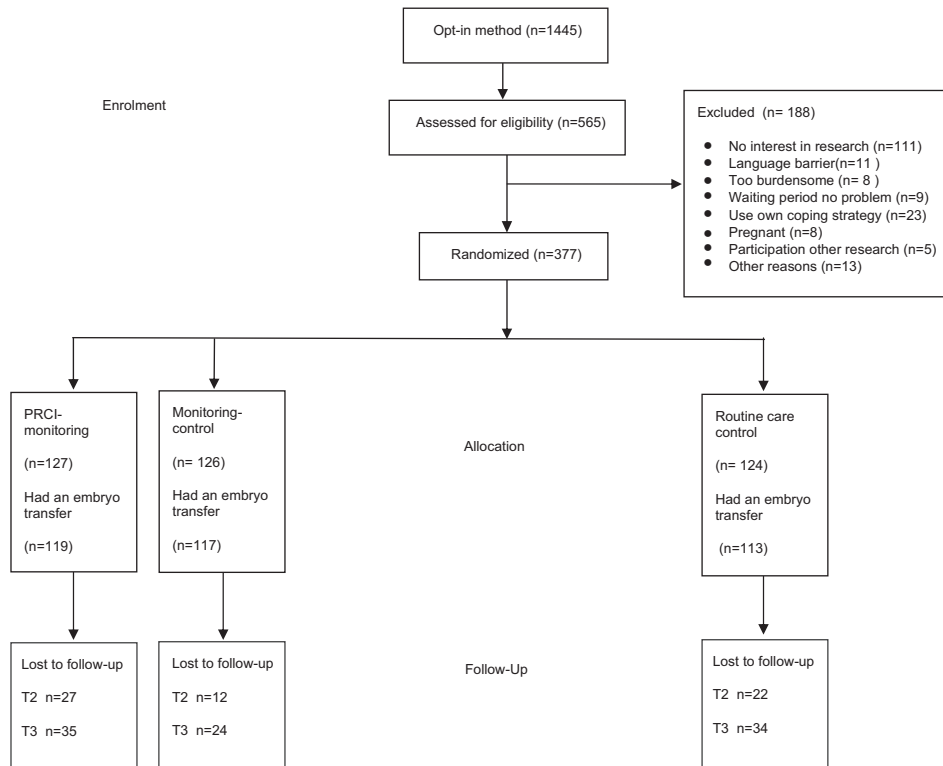
### Recruitment, participant flow and baseline data

Figure 2 shows the study flow chart. In the 20 months of recruitment, between October 2010 and June 2012, 1445 letters were sent to women with an invitation to the trial.

Of the 565 women who replied via a letter or email, 188 (33%) were not eligible. See Figure 2 for the main reasons of non-eligibility. The remaining 377 women were randomized and the 349 who had an embryo to transfer (n = 119 PRCI-monitoring, n = 117 monitoring-control, n = 113 routine care control) received an opaque sealed envelope after transfer with detailed instructions of the study procedures during the waiting period. The number of questionnaires returned at Time 2 was 79% (n = 100) in PRCI-monitoring, 90% (n = 114) in monitoring-control and 82% (n = 102) in routine



care control. The number of questionnaires returned at Time 3 was 72% (n = 92) in PRCI-monitoring, 81% (n=102) in monitoring- control and 73% (n=90) in routine care control group. Baseline characteristics of the participants are shown in Table I.



**Figure 2.** Flow chart for the three randomized groups.

The three randomized groups were similar on these baseline characteristics except previous use of counselling for infertility, which was more frequent ( $p = 0.009$ ) in the PRCI-monitoring (21.4%) and monitoring-control groups (27%) than in the routine care control group (11.3%). This variable was used as a covariate in subsequent analyses. Participants were also similar on highest education achieved, duration of fertility treatment, child with current partner, child with previous partner, other medical problems, previous experience of miscarriage, abortion, ectopic pregnancy, stillbirth and perinatal death.

**Table I.** Baseline characteristics of the three randomized groups.

<b>Baseline characteristics</b>	<b>PRCI- monitoring n=127</b>	<b>Monitoring- control n=126</b>	<b>Routine care control n=124</b>
Mean age, Y (SD)	34.9 (4.7)	34.6 (4.7)	34.8 (5.0)
Years living with partner	8.3 (4.3)	8.4 (4.1)	8.3 (4.2)
University education n (%)	26 (20.6)	30 (24.4)	36 (29.3)
Duration of infertility, Y (SD)	3.4 (2.2)	3.1 (2.2)	3.1 (2.3)
Primary infertility diagnosis n (%)			
Unexplained	49 (38.6)	31 (25)	34 (27.6)
Male	34 (26.8)	44 (35.5)	40 (32.5)
Female	28 (22)	24 (19.4)	26 (21.2)
Mixed	3 (2.4)	6 (4.8)	5 (4.1)
Other	13 (10.2)	19 (15.3)	18 (14.6)
Live birth n (%)	32 (25.2)	35 (27.8)	34 (27.4)
Previous treatments m (SD)			
Insemination cycles	2.5 (3.3)	2.1 (3.0)	1.7 (2.8)
IVF cycles	0.9 (1.3)	0.6 (0.9)	0.6 (1.0)
ICSI cycles	0.3 (0.9)	0.4 (0.8)	0.5 (1.2)
PGD cycles	0.05 (0.3)	0.06 (0.2)	0.01 (0.1)
Cryo cycles	0.5 (1.2)	0.5 (1.3)	0.4 (1.0)
Other treatments	0.3 (1.8)	0.4 (1.7)	0.2 (1.3)
Previous treatments successful n (%)			
Insemination	8 (6.3)	7 (5.7)	2 (1.6)
IVF	15 (11.8)	15 (12.1)	17 (13.8)
ICSI	8 (6.3)	8 (6.5)	9 (7.3)
Cryo	9 (6.9)	10 (8.1)	9 (7.2)
Treatment per group n (%)			
IVF	56 (44.1)	44 (34.9)	46 (36.3)
ICSI	28 (22.0)	38 (30.2)	35 (28.2)
Cryo natural cycle	24 (18.9)	23 (18.3)	22 (17.7)
PGD	7 (5.5)	12 (9.5)	12 (9.7)
ED	6 (4.7)	4 (3.2)	4 (3.2)
Cryo artificial cycle	6 (4.7)	5 (4)	6 (4.8)
Previous counselling for infertility n (%)	27 (21.4)	33 (27)	14 (11.3)

Values are number (percentage) of participants unless stated otherwise.

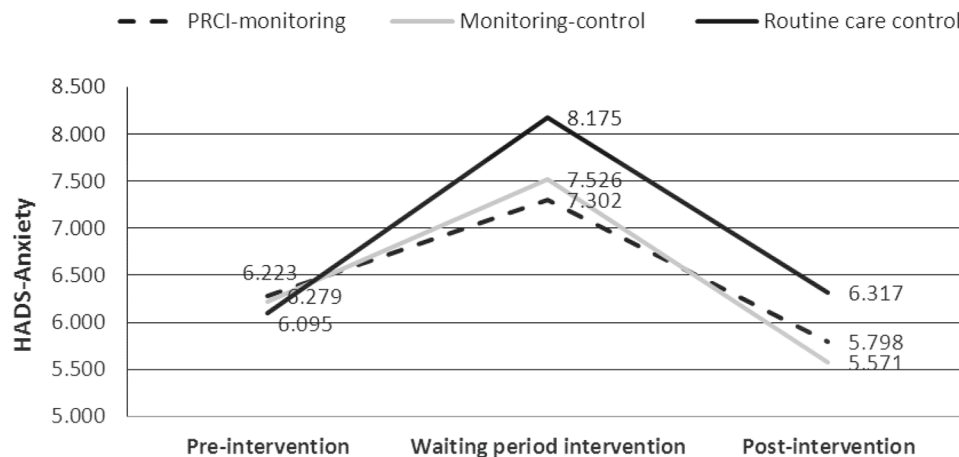
Note: Y=Years, m=mean, SD=standard deviation, n=number, IVF= In Vitro Fertilization, ICSI=Intra Cytoplasmic Sperm Injection, PGD= Pre-implantation Genetic Diagnosis, ED=Egg Donation.

## Outcomes

All women used the PRCI. Women read the PRCI on average twice a day with a mean of 1.97 (*SD*: 0.63) and a range from 0.29 to 4.50. The percentage of women who read PRCI between 1 and twice per day was 47.5%. The percentage of women who read PRCI twice or more a day was 52.5%.

## General anxiety

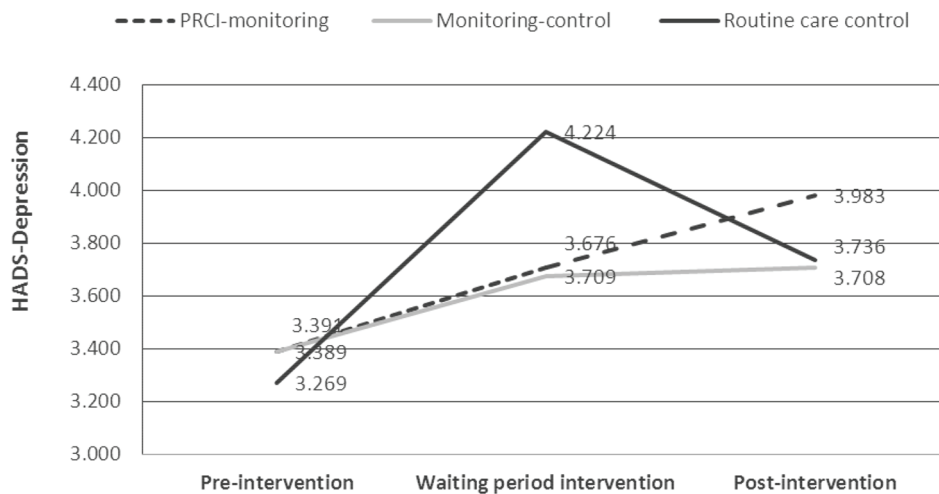
The final model had a random intercept for subject and fixed effects for groups and time with adjustment for the baseline variable previous counselling for infertility and baseline anxiety. For the models for Anxiety and Depression, respectively 4.9 and 4.2% of the studentised residuals were outside the -2 to +2 range. Further, the maximum Restricted Likelihood Distance (ranged 1.0 and 1.3) and the covratio (0.80 to 1.10 and 0.70 to 1.10 for Anxiety and Depression respectively), all indicated no influential observations. The results for HADS-A anxiety indicate a significant main effect of time [ $F(2, 670) = 47.37, p = 0.000$ ], but no significant main effect for group [ $F(2, 373) = 2.09, p = 0.125$ ] or group by time interaction [ $F(4, 670) = 1.79, p = 0.129$ ]. The contrast for the significant main effect of time revealed that for all groups the anxiety level was significantly higher during Time 2 (waiting period intervention), than Time 1 (pre-intervention) or Time 3 (post-intervention) (see Fig. 3). The mean difference between time 1 versus time 2 was: 1.465 (95%CI, 1.098 to 1.832). The mean difference between time 2 versus time 3 was: -1.783 (95% CI, -2.175 to -1.392).



**Figure 3.** Means for each group on HADS-Anxiety across the three assessment times.

## General depression

The final model had a random intercept for subject and fixed effects for groups and time with the adjustment for the baseline variables previous counselling for infertility and baseline depression. The results for HADS-D depression indicate a significant effect of time [ $F(2, 673) = 7.04, p = 0.001$ ] but no significant main effect for group [ $F(2, 379) = 0.32, p = 0.728$ ] or group by time interaction [ $F(4, 673) = 1.38, p = 0.241$ ]. Contrasts for the significant main effect of time revealed that the depression score was significantly lower at Time 1 (pre-intervention), compared with Time 2 (waiting period intervention) and Time 3 (post-intervention) (see Fig. 4). The mean difference between time 1 versus time 2 was 0.514 (95% CI, 0.215 to 0.813). The mean difference between time 1 versus time 3 was 0.457 (95% CI, 0.148 to 0.766).



**Figure 4.** Means for each group on HADS-Depression across the three assessment times.

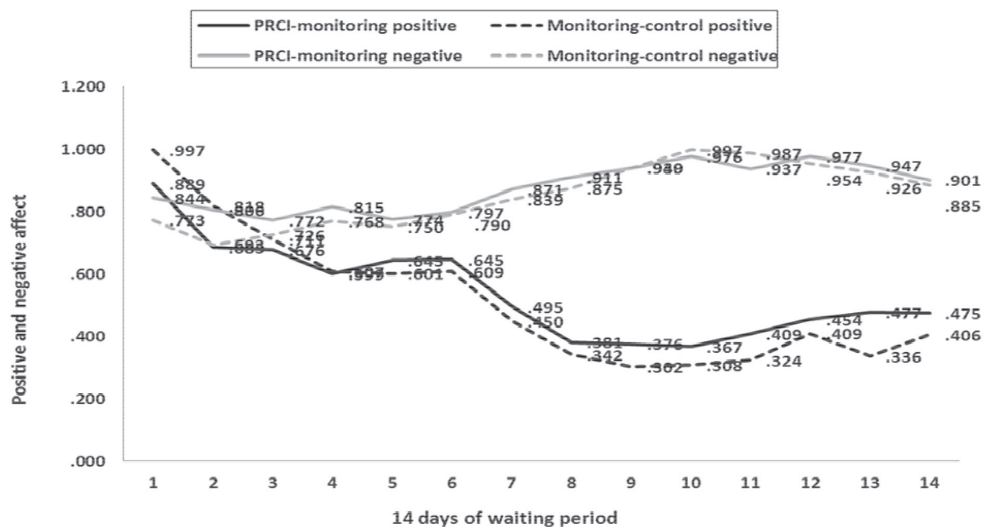
## Treatment-specific negative and positive emotions

The final model for the daily monitoring data had a random effect for subjects and fixed effects for groups and time with adjustment for vaginal bleeding (spotting). Influential observations for the final models were identified through the distribution of studentised conditional residuals. Only 4.2% of these residuals were outside the -2 to +2 range both in the models for both positive and negative affect. Further, the maximum Restricted Likelihood Distance (1.25 and 1.7) and the covratio (0.90 to

1.15 and 0.85 to 1.10 for positive and negative affect respectively), all indicated no influential observations.

Results for the DRK positive emotions indicated a significant main effect of time [ $F(1, 2669) = 322.06, p = 0.000$ ] and a significant group by time interaction [ $F(1, 2652) = 16.15, p = 0.000$ ] with a non-significant group main effect [ $F(1, 285) = 1.44, p = 0.231$ ]. The significant main effect of time showed that the overall slope of positive emotions per day was  $-0.041$  (95% CI,  $-0.046$  to  $-0.037$ ) and the significant group by time interaction showed that the slope of positive emotions per day in the PRCI-monitoring group was higher (0.016, 95% CI, 0.008 to 0.024) than in monitoring-control group.

Results for the DRK negative emotions for the two groups indicated a significant main effect of time [ $F(1, 2672) = 73.93, p = 0.000$ ] but no significant main effect of group ( $F(1, 292) = 1.17, p = 0.281$ ) or group by time interaction [ $F(1, 2655) = 3.38, p = 0.066$ ]. The significant time effect showed the slope of negative emotions per day was 0.018 (95% CI, 0.014 to 0.022). See Fig. 5.



**Figure 5.** Means for the PRCI-monitoring group and monitoring-control group on positive and negative emotions during the 14 days of the waiting period.

### Intervention evaluation

Women perceived that the stress of waiting would have been significantly higher without PRCI: mean (SD): 7.04 (2.27), then with PRCI, 6.27 (2.05), PRCI [ $t(101) = -7.20, p = 0.000$ ]. Other aspects of the acceptability, feasibility and perceived

helpfulness and benefits of PRCI were all significantly different from the 'no effect' point on the item response scale (all  $P$ s < 0.001). The effect of reading the PRCI was rated as lasting  $\leq$  20 minutes by 64.4%, mean (SD): 1.62 (1.02), which on average women perceived as long enough, 3.04 (1.41). PRCI was rated as helpful, 3.54 (1.26) and women would use it again, 3.73 (1.56), recommend it to friends, 4.01 (1.34) or recommend it for other medical waiting periods (e.g., genetic testing), 3.66 (1.22). Furthermore the psychological effect of the PRCI was perceived to be in helping to see things more positively, mean (SD): 4.78 (0.93), feeling more positive, 3.40 (1.34), and sustaining coping, 3.05 (1.45). PRCI was less perceived to be a distraction, 2.89 (1.60), and helping in making future plans, 2.36 (1.47).

Practicality was good. PRCI was rated as suitable, mean (SD): 3.97 (1.25), for the waiting period, quick, 4.61 (1.18), and easy, 4.81 (1.07), to use. PRCI fitted in with the daily routine, 4.55 (1.19), and was not perceived to be a hassle to read, 1.89 (1.23). Women could memorise statements, mean (SD): 3.73 (1.31), but thought it was difficult to remember to read the card, 3.08 (1.61).

### Treatment outcome

No significant differences were found between groups on clinical pregnancy ( $p = 0.83$ ) and clinical pregnancy with heartbeat ( $p = 0.76$ ) (see Table II).

**Table II.** Treatment outcome for the randomized groups.

<b><math>\chi^2</math> Tests</b>	<b>PRCI-monitoring</b>	<b>Monitoring-control</b>	<b>Routine care control</b>	<b>P-value</b>
Clinical pregnancy	24.4%	26.5%	23.0%	0.83
Clinical pregnancy with heartbeat	24.4%	22.2%	20.4%	0.76

### Discussion

Waiting for the outcome of an IVF/ICSI treatment cycle was stressful with anxiety and depression levels during the waiting period significantly higher than before treatment. Women who used the PRCI intervention during the waiting period of IVF/ICSI reported significantly more positive affect but not significantly less anxiety, depression or negative treatment-specific emotions. Nevertheless, women evaluated the PRCI as acceptable, practical and they perceived a psychological benefit to its use. PRCI had no effect on treatment outcome. Overall, the pattern of results suggests that the main impact of PRCI was to make the stress of the

waiting period seem more tolerable rather than in taking away the negative emotions waiting produces. This simple low cost self-help coping intervention can be offered to women to increase positive affect during the waiting period of fertility treatment. Waiting for the outcome of treatment was perceived to be stressful and was associated with an increase in general anxiety and depression and negative emotions specific to treatment. These results are consistent with those of numerous studies on ART (Boivin and Takefman, 1995; Boivin and Takefman, 1996; Yong et al., 2000) that show that women appraise the waiting period as a potential threat and as causing related anticipatory negative emotions (e.g., feelings of worry, tension, nervousness). According to cognitive stress theory, the factors that make waiting periods stressful are the unpredictability and uncontrollability of the outcome (Lazarus and Folkman, 1984). Rumination about the outcome arrests the coping process because coping strategies would differ depending on whether one outcome (pregnant) or the other outcome (not pregnant) was most likely (Lancastle and Boivin, 2008). These results reinforce the need for effective coping interventions that help women manage the strains of medical waiting periods, such as waiting for the pregnancy test in IVF. PRCI produced the effects for which it was designed, namely to help women reinterpret the demands of the waiting period in a more positive way. Women who used PRCI reported significantly more positive emotions (e.g., encouraged, content, confident) during the waiting period than did women assigned to the control group. In addition, patients perceived PRCI to have benefit in helping to manage the stress of fertility treatment, even though PRCI use was not associated with a significant reduction in negative emotional reactions (general or treatment-specific). The generation of challenge emotions (encouraged, confident) is in line with original development data that showed that women using PRCI made more challenge appraisals and perceived the waiting period as more controllable than women using a control intervention (Lancastle, 2006). We have collected further data (to be reported separately) on the effects of PRCI that shows that PRCI is associated with a greater use of positive reappraisal coping compared with the control group. Our results support other research showing that positive reappraisal coping is a useful strategy for unpredictable and uncontrollable situations like the medical waiting period (Boivin and Lancastle, 2010). Fredrickson (1998) proposes that positive affect can undo the after-effects of negative emotions. Positive affect may restore autonomic inertness following negative emotional arousal (Fredrickson, 1998). According to Folkman (2011) positive reappraisal and the positive emotions it produces, can allow “psychological respite” during the waiting period, which helps sustain coping during stressful situations. It should be noted too that the PRCI

items although originally culled from positive reappraisal measures such as the ways of coping and COPE questionnaire may also tap into other related forms of meaning-based coping (e.g., benefit-finding). Future research needs to consider the extent to which cognitive efforts to redefine the situation and/or derive benefit act synergistically or independently to generate psychological benefits in uncontrollable and unpredictable situations like the waiting period.

We expected that the beneficial effects of PRCI (i.e., generation of positive emotions, perceptions of helpfulness) would reduce the burden of waiting. However, women using PRCI did not report lower day-to-day negative emotions during the waiting period (anxiety, tension, nervousness), or lower general anxiety and depression during and after treatment. Why the intervention only had an effect on positive affect is unclear but there could be a few explanations. There is still an on-going debate about the importance of positive and negative affect, and how they relate to each other (Folkman and Moskowitz, 2000; Folkman 2011). The results of the present study indicate that feeling positive does not necessarily mean one feels less negative. Cognitive reappraisal may play a more definite role in the ability to regulate positive emotions whereas other types of coping (e.g., distraction, acceptance) may be more central in the regulation of negative affect and symptoms of anxiety and depression (Andreotti et al., 2013). The results suggest that interventions may need to comprise multiple modes of coping beside positive reappraisal to help women deal with anxiety and depression during treatment.

Research has demonstrated that positive affect is associated with better physical health and lower risk of mortality, independent of negative affect (Folkman and Moskowitz, 2000; Folkman, 2011). However, in the present study the use of PRCI was not associated with any advantage for treatment outcome. This result is consistent with another study that showed that positive affect was not related to pregnancy rates in fertility treatment (de Klerk et al., 2008) but inconsistent with a study that found that enhanced positive affect was associated with lower probability of failed treatment in IVF (Klonoff-Cohen et al., 2001). Our study differs from the prospective study of Klonoff-Cohen et al. (2001) in the eligibility criteria and the questionnaires and time points used for measuring positive affect. Past reviews and meta-analytic studies on the impact of psychosocial interventions on treatment outcome are inconsistent (Boivin, 2003; de Liz and Strauss, 2005; Hammerli et al., 2009). Further our sample size calculation was not based on effect sizes for treatment outcome and therefore may be underpowered for this outcome.

The results need to be considered in light of the strengths and limitations which should also be considered for future evaluations of the PRCI tool. Feasibility



studies had previously been carried out to determine key uncertainties like attrition, recruitment, effect size, acceptability and compliance of the intervention in the present (Lancastle, 2006; Lancastle and Boivin, 2008). Attrition was 20% (at Time 2), similar to that observed in previous studies (Lancastle and Boivin, 2008) but was about 30% at Time 3. The use of mixed or multilevel modelling (MLM) allowed analysis of partial response whilst maintaining power (Hoffman and Rovine, 2007). However, maximum likelihood estimation has been shown to provide unbiased and efficient estimates only when the data are missing at random (Hoffman and Rovine, 2007). We contend this to be the case but it is possible that attrition was due to some unknown systematic cause. An important aspect of intervention evaluation is to ensure that the intervention is delivered consistently across participants and this is often achieved by manualising the intervention (e.g., manual for lifestyle intervention in infertility, see Ockhuijsen et al., 2012). As a self-administered tool the PRCI comes with a two-page leaflet that describes the rationale for the intervention, including the recommendation that it should be read PRCI twice daily. On average women complied with this recommendation (mean number of times read daily 1.97) but a proportion of women used it less frequently. Lower frequency could reflect that women became less interested in using the tool which could impact on PRCI effects. The PRCI was designed to help women reinterpret the demands of the waiting period in a more positive way and we used the DRK, a measure of treatment specific reactions, to capture the daily effects of PRCI during the waiting period. However, because daily monitoring itself may have an impact on the reporting of emotions (Cohen et al., 1995) we added a monitoring-control group to disentangle between this methodological artefact and genuine effects of PRCI. We considered this control as a strength of the RCT though this may not be the case. In a parallel study, interviews among women with miscarriage showed that the use of the DRK was affecting emotions, as if the DRK itself was an intervention (unpublished data). If daily monitoring is perceived to be an intervention then the lack of difference observed in the present study between the PRCI and the monitoring-control group could have been due to active effects of monitoring or the possibility that active effects attenuated or obscured effects of the PRCI intervention in unknown ways. Further, the PRCI benefits may be due to an interaction between PRCI and monitoring. The use of a monitoring-control could thus be a weakness of the study because assessment and intervention were confounded. A randomized group of women that used only the PRCI without daily monitoring would provide more insight. We collected such data ( $n = 110$ ) and it would seem that daily monitoring attenuates

the effects of PRCI on anxiety and the pregnancy rate. However, only a randomized trial could definitely identify the benefits of PRCI when it is administered on its own. Another methodological limitation worth considering is the use of the opt-in method to recruit participants. In this method patients indicate a willingness to be included the study (opt-in) instead of the more conventional approach where all patients are enrolled in the trial unless they have indicated a willingness to be excluded (opt-out). Although the opt-out method produces a larger pool of eligible participants at recruitment, ethical committees often do not approve of this method, as was the case in the present RCT, because it requires repeated contact which may be burdensome for participants (Junghans et al., 2005; Treweek et al., 2010). In a RCT designed to evaluate the effects of the opt-in compared with opt-out recruitment strategies, patients in the opt-in arm were healthier on clinical indicators (e.g., fewer risk factors, symptoms of disease etc) than patients in the opt-out arm, presumably because they could better manage the demands of the study (Junghans et al., 2005; Treweek et al., 2010). In the present study, it is likely that mainly women who were interested in psychological interventions opted-in to participate. Indeed, the overall percentage of past users (19.7%) of infertility counselling in the present sample was higher than previously reported in a British sample (8.5%) (Boivin et al., 1999). It could be that previous use of more in-depth psychological interventions had an impact on study results. Although numbers were too few in the present study to examine this issue fully it warrants consideration in future trials using the opt-in method. Overall readers should consider these limitations as they may affect generalizability.

Although PRCI was not associated with benefit on the psychological questionnaires it was on the IEF. Positive evaluations on the intervention form could be due to demand characteristics. However, patient and researcher were not connected in any way, and the medical staff did not have access to any study responses, which makes this possibility unlikely. A discrepancy between outcome measures and intervention evaluations has been reported in previous research (Emery et al., 2003; Bird et al., 2011). In a qualitative study, 15 trial participants and five staff members were interviewed at the end of a trial evaluating a rehabilitation programme that had previously been highly rated by patients (Emery et al., 2003; Bird et al., 2011). Although no scientific evidence was found for the efficacy of the rehabilitation programme, participants and staff members continued to have strong views about the benefit of the intervention. During the interview one of the staff members suggested that *“the trial had killed the intervention”*. Their perspective was that because the pilot phase had in their opinion been a success, then the process of the RCT must have affected the intervention in such a way as to take away from its benefits. This too

may have been an issue for the PRCI trial with, as noted, the addition of monitoring potentially impacting PRCI effects. Bird et al. (2011) recommended that the views and experiences of staff and participants be taken before and after conducting the RCT to evaluate the impact of investigative process on perceptions and we concur with this recommendation. Future research on PRCI could also identify for whom the intervention works best and whether the PRCI could be made more or less effective with change to the item list.

The pattern of results, theoretical, empirical and methodological considerations, all point to the main impact of PRCI as being to make the stress of the waiting period more tolerable than in taking away the negative emotions waiting produces. If PRCI was expensive or difficult to administer one might consider the costs and modest (mainly perceived) benefits of PRCI to argue against a recommendation for the waiting period. However, PRCI is self-administered, comprises a sheet of A4, and can be implemented at a time when patients are not in contact with the medical team or other patients for more interpersonal forms of support. As such we contend that the positive emotions and sense of being helped that PRCI generates are sufficient for it to be offered singly or in combination with other interventions to help women manage the demands of the ART waiting period. Future research should investigate whether PRCI helps to make other medical waiting periods more tolerable.

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# Chapter 4

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*Clarifying the benefits of the Positive Reappraisal Coping  
Intervention for women waiting for the outcome of IVF*

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*Under review*

## Abstract

**Study Question:** Does the use of a Positive Reappraisal Coping Intervention (PRCI) alone following IVF embryo transfer influence anxiety, depression and treatment outcome when compared to its use combined with monitoring emotions, monitoring emotions alone or no intervention?

**Summary answer:** Woman using the PRCI alone had significantly lower anxiety levels at day 10 of the waiting period and six weeks after the start of the waiting period but also a significantly higher clinical pregnancy rate compared to the other three groups.

**What is known already:** The waiting period which follows embryo transfer after IVF/ICSI is very stressful. The use of the PRCI together with a daily monitoring form increases positive emotions but appears not to reduce anxiety. The impact of using the PRCI alone without daily recording of emotions may be more beneficial.

**Study design, size, duration:** Following completion of recruitment to a recently published three-arm Randomized Controlled Trial (RCT) of the use of the PRCI in the post embryo transfer waiting period, a further one hundred and ten participants were recruited to study the impact of the PRCI in clinical practice without concurrent emotional monitoring. Data collection took place between May 2012 and December 2012. Outcomes were compared with those generated by a RCT of the PRCI with daily emotional monitoring, daily emotional monitoring only, or routine care.

**Participant, materials, setting, methods:** To capture the impact of the PRCI on this further group, questionnaires were completed at three time points: just before the waiting period (Time 1: pre-intervention), on day 10 of the 14-day waiting period (Time 2: waiting period intervention) and 6 weeks after the start of the waiting period (Time 3: post intervention). Data generated were compared with the data from the RCT. To compare the impact over time on anxiety and depression, a repeated multilevel linear model (MLM) design was used.

**Main results and the role of chance:** Ninety-eight of the 110 women who were recruited received the PRCI intervention without daily monitoring (PRCI-comparison group). After correcting for known confounding factors, women in the PRCI-comparison group had a significantly lower anxiety at Time 2 and Time 3 but not significantly lower depression levels. Women in the PRCI-comparison group had a significantly higher clinical pregnancy rate (39.8%,  $p=0.033$ ) but there were no significant differences in clinical pregnancies with foetal heartbeat ( $p=0.10$ ).

**Limitations, reasons for caution:** A limitation of this study is that the additional study group was not randomized to the intervention, and may therefore be subject to selection bias.

**Wider implications of the findings:** This simple low cost self-help coping intervention can be offered to women during the waiting period in an IVF/ICSI treatment. A further RCT comparing PRCI only to a non-intervention group is necessary to confirm these findings.

**Study funding/competent interest(s):** The Women and Baby Division of the University Medical Centre Utrecht funded the study. The authors have no conflicting interest(s).

**Key Words:** Coping-intervention, Medical waiting period, Anxiety, depression.

## Introduction

Women experience an In Vitro Fertilization (IVF) or Intra Cytoplasmic Sperm Injection (ICSI) treatment as an emotional and physical burden (Boivin & Takefman, 1995; Merari et al., 1992). The most stressful aspects of an IVF or ICSI treatment are unsuccessful treatment, oocyte retrieval, the fourteen days of waiting for the result of the treatment and having a pregnancy test (Merari et al., 1992; Boivin & Takefman, 1995; Eugster & Vingerhoets, 1999; Yong et al., 2000). Waiting periods cause high levels of anticipatory anxiety and uncertainty that are difficult to cope with (Boivin & Lancaster, 2010). Theory and research suggest that positive reappraisal coping strategies may be particularly useful for this type of unpredictable and uncontrollable stressful context (Tedlie Moskowitz et al., 1996; Folkman & Moskowitz, 2000). Positive reappraisal involves redefining the situation in a more positive way, which allows people to derive some benefit from their stressful experience (Lazarus & Folkman, 1984; Folkman, 2011).

The Positive Reappraisal Coping Intervention (PRCI) is designed to be an intervention for medical waiting periods (Lancaster, 2006; Lancaster & Boivin, 2008). The PRCI is self-administered and comprises an explanatory leaflet with a detailed explanation about positive reappraisal, as well as ten statements designed to promote this method of coping. The PRCI was conceptualised from the cognitive model of stress and coping of Lazarus & Folkman (1984) and developed according to the Medical Research Council framework for developing complex interventions (Campbell et al., 2000; Craig et al., 2008). It has been shown to be acceptable and feasible for women facing stressful waiting periods and was perceived to be more helpful and sustaining for the coping process than a control intervention with positive mood statements (Lancaster & Boivin, 2008).

Our research group previously examined the effectiveness of the PRCI in a three-armed Randomized Controlled Trial (RCT) (Ockhuijsen et al., 2014). Participants randomized to a PRCI-monitoring group received the PRCI tool and monitored their emotional reactions using a daily record keeping chart. Participants randomized to the two control groups either underwent a monitoring only or no intervention/monitoring. All groups completed anxiety and depression questionnaires prior to the waiting period, on day 10 of the waiting period and six weeks after the start of the waiting period. The results of this study showed that women read the card twice a day (as instructed), and that the PRCI was effective in increasing positive emotions compared to the control groups. Further, women perceived the PRCI card as helpful, useful and as sustaining the coping process during the waiting

period. However, the PRCI had no effect on anxiety or depression levels of women waiting for the outcome of their fertility treatment cycle (Ockhuijsen et al., 2014). One methodological weakness of the study was the lack of a PRCI intervention only group, which prevented the differentiation of the effect of the intervention from that of the concurrent daily monitoring, which may itself have modulated any therapeutic effect. This weakness was recognized early in the trial as a result of preliminary results from a parallel ongoing qualitative study that showed that daily emotional monitoring was perceived to have had an effect on the emotions of newly pregnant women with a history of miscarriage, as if emotional monitoring was itself an intervention. If daily emotional monitoring was perceived to be an intervention then it could attenuate, heightened or obscure effects of the PRCI intervention in our three-arm RCT in unknown ways. In light of these qualitative findings, the aim of this study was to investigate a PRCI-comparison group that received the PRCI but did not complete daily monitoring. This group was not randomized but recruited after the recruitment for the RCT to avoid undermining the design of the original trial.

The objective of the present report is to present the effects of the no-monitoring PRCI-comparison group on anxiety and depression levels of women waiting for the outcome of their fertility treatment cycle as well as on the outcome of treatment, relative to the outcomes in the three groups which participated in the RCT (PRCI-monitoring, monitoring-control, routine care).

## Materials and methods

Information about the methodology for the three-arm RCT, which was carried out according to standard RCT methodology is published elsewhere (Ockhuijsen et al., 2013). Data were collected for the RCT between October 2010 and June 2012. Data collection for the (non-randomized) PRCI-comparison group was between May 2012 and December 2012. Participants for the fourth non-randomized arm were recruited in the same way and given the same information as the other groups but were only ever assigned to receive the PRCI with no concurrent monitoring. Once recruited, the researcher had no contact with participants during the study period.

The materials used are described in detail (Ockhuijsen et al., 2013). Briefly, participants completed the Hospital Anxiety and Depression Scale (HADS) to measure general anxiety and depression (Zigmond & Snaith, 1983) just before the waiting period (Time 1: pre intervention), on day 10 of the 14-day waiting period (Time 2: waiting period intervention) and 6 weeks after the start of the waiting

period (Time 3: post intervention). The HADS consists of 14 items (7 items for each subscale) that are rated on a 4-point Likert scale. Total scores on each scale can be interpreted in ranges: normal (0-7), mild (8-10), moderate (11-14) and severe (15-21) anxiety and depression. A medical chart review at the end of treatment was used to ascertain whether treatment had led to a clinical pregnancy and clinical pregnancy with fetal heartbeat.

The sample size power calculation for the addition of this fourth study group assumed a test of the difference on psychological wellbeing between three groups with a power of 95%,  $\alpha=0.05$  and a medium effect size ( $f=.25$ ) yielding a minimum sample size of 110 participants to be recruited to the non-randomized PRCI group. Effect size and attrition were derived from Lancaster & Boivin (2008).

### **Statistical methods**

IBM SPSS Statistics 20 was used to perform the statistical analysis. Equivalence of baseline measures between groups was examined by one-way analyses of variance (ANOVA) for normally distributed variables (interval or ratio level) and chi-square for normally distributed variables on nominal level. If the groups were not comparable on demographics, medical history, or gynaecological variables, those variables were employed as covariates or factors in subsequent analyses. To examine the difference between the four groups over time for anxiety and depression, a repeated multilevel linear model (MLM) design was used. To examine the difference in treatment outcome between the four groups chi-square was used and the effect size was measured by Cramer's V with values between 0 and 1 (Field, 2012). An 'intention to treat' analysis was employed to take account of attrition.

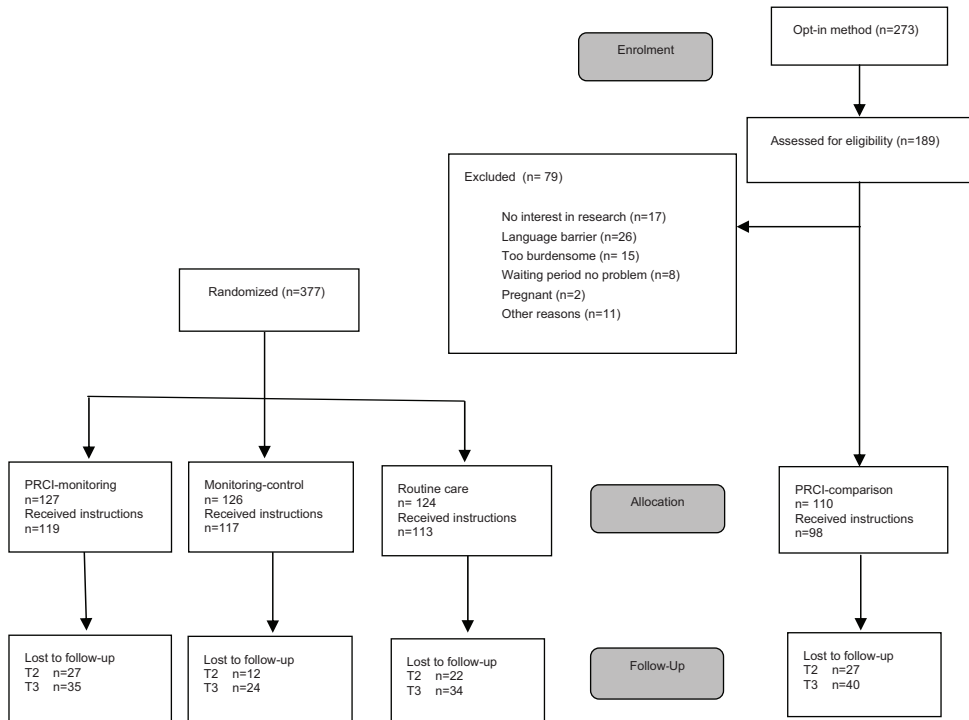
### **Ethical approval**

The Ethical committee of the University of Utrecht provided ethical review and approval for the study of a fourth, PRCI-comparison group.

## **Results**

Two hundred seventy three consecutive patients were invited to consider participation in the PRCI-comparison group. Seventy nine (42%) of the 189 women who responded were not eligible. The remaining 110 of the women were entered into study group and 98 women received an opaque sealed envelope after the embryo transfer with the instructions for the waiting period. Twelve women had no embryo

transfer because of a cancellation of treatment. The number of questionnaires returned at Time 2 was 75% (n=83) and at Time 3 was 64% (n=70). A flow chart of the study is shown in Figure 1.



**Figure 1.** Flow Diagram of the four groups.

Significant differences were found in three baseline characteristics. The PRCI-comparison group had more children with current partner ( $p = 0.01$ ), had more previous successful ICSI treatments ( $p = 0.012$ ) and the routine care group had less previous counselling for infertility ( $p = 0.022$ ) than the other groups. These variables were employed as covariates/control factors in subsequent analyses. Baseline characteristics of the participants are shown in Table I.

**Table I.** Baseline characteristics of the four groups. Values are number (percentage) of participants unless stated otherwise.

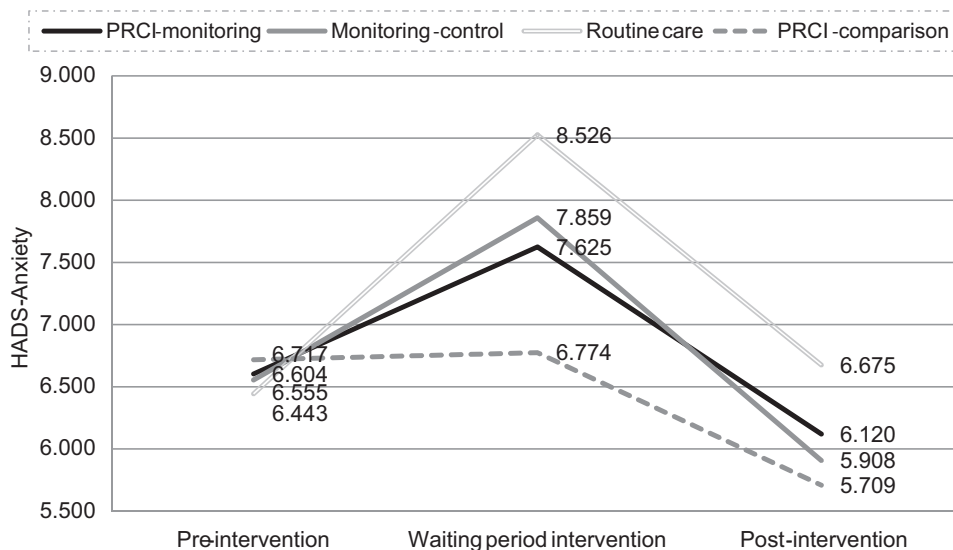
<b>Baseline characteristics</b>	<b>PRCI- monitoring n=127</b>	<b>Monitoring- control n=126</b>	<b>Routine care n=124</b>	<b>PRCI- comparison n=110</b>
Mean age, y (SD)	34.9 (4.7)	34.6 (4.7)	34.8 (5.0)	34.5 (4.8)
Years with partner	8.3 (4.3)	8.4 (4.1)	8.3 (4.2)	9.0 (4.9)
University education n (%)	26 (20.6)	30 (24.4)	36 (29.3)	26 (25.7)
Duration of infertility, Y (SD)	3.4 (2.2)	3.1 (2.2)	3.1 (2.3)	2.9 (2.2)
Duration of fertility treatment, Y (SD)	2.0 (1.7)	1.9 (1.6)	2.0 (1.9)	1.8 (2.0)
Child with current partner n (%)	28 (22)	44 (35.3)	35 (28.5)	43 (42.6)
Primary infertility diagnosis n (%)				
Unexplained	49 (38.6)	31 (25)	34 (27.6)	35 (34.7)
Live birth n (%)	32 (25.2)	35 (27.8)	34 (27.4)	37 (33.6)
Previous treatments m (SD)				
Insemination cycles	2.5 (3.3)	2.1 (3.0)	1.7 (2.8)	2.2 (2.9)
IVF cycles	0.9 (1.3)	0.6 (0.9)	0.6 (1.0)	0.5 (1.2)
ICSI cycles	0.3 (0.9)	0.4 (0.8)	0.5 (1.2)	0.2 (0.6)
PGD cycles	0.05 (0.3)	0.06 (0.2)	0.01 (0.1)	0.04 (0.2)
Cryo cycles	0.5 (1.2)	0.5 (1.3)	0.4 (1.0)	0.3 (0.9)
Other treatments	0.3 (1.8)	0.4 (1.7)	0.2 (1.3)	0.02 (0.2)
Previous treatments successful n (%)				
Insemination	8 (6.3)	7 (5.7)	2 (1.6)	8 (7.9)
IVF cycles	15 (11.8)	15 (12.1)	17 (13.8)	14 (13.9)
ICSI cycles	8 (6.3)	8 (6.5)	9 (7.3)	9 (7.9)
PGD cycles	0 (0)	1 (0.8)	0 (0)	1 (1.0)
Cryo cycles	9 (6.9)	10 (8.1)	9 (7.2)	4 (4.0)
Other treatments	0 (0)	0 (0)	1 (0.8)	0 (0)
Treatment per group n (%)				
IVF	56 (44.1)	44 (34.9)	46 (36.3)	57 (51.8)
ICSI	28 (22.0)	38 (30.2)	35 (28.2)	21 (19.1)
Cryo natural cycle	24 (18.9)	23 (18.3)	22 (17.7)	8 (7.3)
PGD	7 (5.5)	12 (9.5)	12 (9.7)	16 (14.5)
ED	6 (4.7)	4 (3.2)	4 (3.2)	5 (4.5)
Cryo artificial cycle	6 (4.7)	5 (4)	6 (4.8)	3 (2.7)
Previous counselling for infertility n (%)	27 (21.4)	33 (27)	14 (11.3)	19 (18.8)

Note: Y=Years, SD=standard deviation, n=number, m=mean, IVF= In Vitro Fertilization, ICSI=Intra Cytoplasmic Sperm Injection, PGD= Pre-implantation Genetic Diagnosis, ED=Egg Donation.



### General anxiety

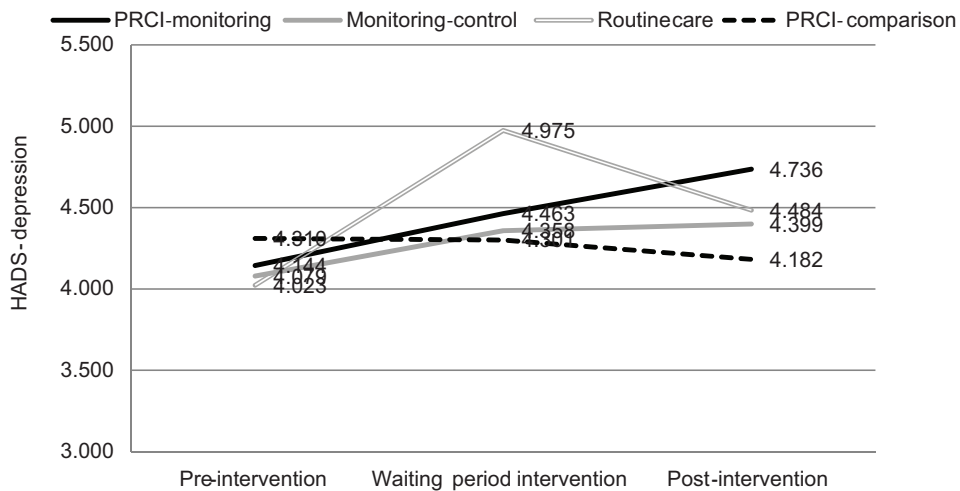
The results describing impact on anxiety are shown in Figure 2. The results indicate a significant main effect of group ( $F(3, 476) = 3.45, p = 0.017$ ) and time ( $F(2, 850) = 43.15, p = 0.000$ ) and group by time interaction ( $F(6, 849) = 3.24, p = 0.004$ ). The contrast for the significant main effect of group revealed that the anxiety level of the PRCI-comparison group was significantly lower compared to the routine care group. The mean difference between the PRCI-comparison group and the routine care group was  $-0.704$  (95%CI,  $-1.166$  to  $-0.243$ ) showing that the PRCI-comparison group reported less anxiety than the other groups. The contrast for the significant main effect of time revealed that for all groups the anxiety level was significantly higher during Time 2 (waiting period intervention), than Time 1 (pre-intervention) or Time 3 (post-intervention). Anxiety level was also significantly higher at Time 1 than at Time 3 (see Figure 1). The contrasts for the significant group by time interaction revealed that at Time 2 (day 10 of the waiting period) the PRCI-comparison group had a significantly lower anxiety score than the PRCI-monitoring group, the monitoring-control group and the routine care group. Further the PRCI-monitoring group had a significantly lower anxiety score than the routine care group. At Time 3 the monitoring-control and the PRCI-comparison group had a significantly lower anxiety score than the routine care group.



**Figure 2.** Means for each group on HADS-Anxiety across the three assessment times with the solid lines showing the randomized groups and the dashed line showing the non-randomized PRCI-comparison group.

### General depression

The results regarding impact on depression (see Figure 3) indicate a significant main effect of time ( $F(2,853) = 4.22, p = 0.015$ ) but no significant main effect for group or group by time interaction. Contrasts for the significant main effect of time revealed that the depression score at Time 1 (pre-intervention) was significantly lower compared to Time 2 (waiting period intervention) and Time 3 (post-intervention).



**Figure 3.** Means for each group on HADS-Depression across the three assessment times with the solid lines showing the randomized groups and the dashed line showing the non-randomized PRCI-comparison group.

### Treatment outcome

Significant differences were found between the four groups for treatment outcome. The PRCI-comparison group had a significantly higher clinical pregnancy rate (39.8%,  $p = 0.033$ ) compared to the PRCI-monitoring (24.4%), monitoring-control (26.5%) and routine care (23%) groups. Effect size for the clinical pregnancies was small (Cramer's  $V = 0.141$ ). There were no significant differences in clinical pregnancies with foetal heartbeat ( $p = 0.10$ ). (See Table II.)

**Table II.** Treatment outcome for the four groups.

$\chi^2$ Tests	PRCI-monitoring	Monitoring-control	Routine care	PRCI-comparison	p-value	Cramer's V
Clinical pregnancy	24.4%	26.5%	23.0%	39.8%	0.03	0.141
Clinical pregnancy with heartbeat	24.4%	22.2%	20.4%	34.4%	0.10	0.119

## Discussion

The PRCI coping intervention is an effective tool to alleviate anxiety during the waiting and post-treatment period in IVF and may be most effective when not combined with daily monitoring of emotional reactions. The addition of the presented PRCI-comparison group indicates that daily monitoring of emotions could attenuate the effects of the PRCI intervention. When used on its own the PRCI was associated with reduced anxiety during the waiting period and a higher clinical pregnancy rate compared to the routine care and monitoring-groups. However, when the PRCI was combined with daily monitoring of emotions these effects were attenuated. It should be noted too that daily monitoring of emotions was also associated with reductions of anxiety compared to the routine care group suggesting an unintended beneficial consequence of our assessment procedure. These results show that it is possible to reduce anxiety (tension, worry) during the two week waiting period using simple interventions (coping, emotional monitoring).

A limitation of this study is that we were unable to randomize this fourth group. A non-randomized group is a threat for internal validity due to selection bias and history (Dimitrov & Rumrill, 2003). Posttest differences could be due to characteristic differences between groups. In our study we used two methods to minimize selection bias. The first method is the comparison of baseline differences between the randomized and non-randomized groups. We found three baseline differences: counseling for infertility, child with current partner and success of pervious ICSI treatments. These baseline differences were used in MLM analysis. MLM analysis is an alternative to ANCOVA where dependent variables scores are adjusted for covariates (individual differences) prior to testing treatment differences (Tabachnick and Fidell, 2007). The second method we used is that we treated the non-randomized control group the same as if it has been one of the randomized groups in all our recruitment and testing procedures. Women in the non-randomized group were told that they would be randomized. All participants received the same information according to a written protocol. History can also influence post-test differences. Outside events for instance in the clinic, may affect participants responses. We recruited the fourth group in seven months immediately after recruiting participants for the RCT.

We found that the PRCI had an effect on anxiety but not on depression levels. The de-coupling of effects is likely to be due to the inherent demands of the waiting and post-treatment period in IVF. Waiting in IVF has been shown to be associated with anticipatory emotions (feeling nervous, worried) elicited by the threat of negative

treatment results whereas after the pregnancy test the outcome is known and emotions elicited are in response to the actual outcome (feeling sad, disappointed or happy and content) (Boivin & Lancaster, 2010). According to Lazarus & Folkman (1984) a perception of threat is at the root of anxiety and depression but anxiety is future orientated and predictive of threat whereas depressive symptoms are tied to perceived or actual outcomes of imminent events. The PRCI was developed specially for the waiting period and positive reappraisal involves efforts to focus on positive aspects of uncontrollable, unpredictable situations, regardless of the eventual outcome. As such the PRCI may not be optimized to reduce depression. Whilst our results showed that the PRCI (and the daily emotional monitoring) affected anticipatory emotions only, it may also be possible to affect outcome emotions if the PRCI were administered in a different way, for example, used for longer period after treatment outcome is known.

Much research has been done on the effect of psychosocial interventions on well-being during an IVF/ICSI treatment with variable impacts reported. Study design, time measurements and interventions are not comparable with our study because other interventions tend to focus on overall emotional needs rather than those specific to the waiting stage of treatment. In a meta-analysis, the effect of psychological interventions on anxiety and/or depression during IVF/ICSI treatment was measured in 12 randomized and non-randomized trials (Hammerli et al., 2009). Psychological interventions had no significant effect on anxiety and depression level. In another meta-analysis psychotherapy led to a decrease of anxiety however a reduction of depressive symptoms was greater after 6 months upon termination of psychotherapy (de Liz & Strauss, 2005). It may be that lack of attention to the specific stage of treatment could explain these variable results.

In this study women of the PRCI-comparison group had a significantly higher biochemical pregnancy rate but no significant difference in ongoing clinical pregnancy rate (with fetal heartbeat) compared to the other three groups. This may simply reflect the reduced sample size at the time of the scan. Effect size for pregnancy rate was small (Cramer's  $V=0.141$ ). A similar pattern between significant biochemical and non-significant ongoing clinical pregnancy rate was reported in a meta-analysis of stress associations with IVF treatment outcome (Boivin et al., 2011). It should be noted however that the sample size power calculation was not based on effect sizes for treatment outcome and the study may thus be underpowered for later stages of pregnancy outcome. A replication randomized control trial is warranted to confirm the PRCI effects on anxiety and pregnancy.

In this study the PRCI intervention had a significant effect on anxiety and clinical pregnancy for women waiting for the results of an IVF/ICSI treatment. This simple low cost self-help coping intervention can be offered to women during the waiting period in an IVF/ICSI treatment. Another RCT has to be performed with the PRCI-comparison group as a randomized group to strengthen our conclusions and to investigate the potential beneficial effects of daily monitoring of emotional reactions during the waiting period.

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# Chapter 5

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*A Self-help Positive Reappraisal Coping Intervention for Women during Fertility Treatment: a Randomized Controlled Trial*

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*Manuscript in preparation*

## Abstract

**Objective:** The aim of this study was to test the Positive Reappraisal Coping Intervention (PRCI) in terms of its effect on appraisal and coping in women awaiting the outcome of assisted reproductive techniques (ART).

**Method:** Patients using ART were invited to participate and randomized to one of three experimental groups. The PRCI-monitoring (PRCI-M) group used the intervention at least twice a day. Coping and appraisal were measured with a Daily Record Keeping (DRK) form and the Way of Coping Questionnaire (WCQ). Multilevel modeling was used to assess group, time and group by time effects during the 14 days of the waiting period and at follow-up six weeks later.

**Results:** Three hundred seventy-seven women were randomized. Significant time effects showed increasing appraisals of threat, uncontrollability and inability to cope as the day of the pregnancy approached combined with decreasing coping effort. The PRCI-M group showed more challenge appraisals and a slower rate of decrease in these appraisals and coping (positive reappraisal, acceptance, relaxing) compared to the two control groups (Monitoring-control, Routine care control).

**Conclusion:** PRCI produced the effects for which it was designed as it helped sustain a more positive outlook on the waiting period (i.e., positive reappraisal coping, challenge appraisals) when waiting for potentially threatening medical test results.

**Trial registration number:** The study is registered at the Clinical Trials.gov (NCT01701011).

**Key words:** Self-help coping intervention, Medical waiting period, Randomized controlled trial, Infertility, Positive reappraisal coping.

## Introduction

The medical waiting period refers to the time interval during which patients wait for medical test results that may threaten their wellbeing (e.g., biopsy results, pregnancy test results after fertility treatment, genetic screening) (Boivin & Lancaster, 2010). Particular characteristics of any experience can amplify the extent to which an individual appraises that experience as stressful (Lazarus & Folkman, 1984). In the case of medical waiting periods, the results of medical tests mean a great deal to the patient, but there may be nothing he or she can do to change or control the outcome. There may also be insufficient information for the patient to determine whether the outcome will be positive or negative. This combination of meaningfulness, uncertainty and lack of control can make it difficult to engage in anticipatory coping (Lazarus & Folkman, 1984) during medical waiting periods and distress is a likely consequence (Boivin & Lancaster, 2010). Lancaster & Boivin (2008) developed the self-help Positive Reappraisal Coping Intervention (PRCI) to encourage positive reappraisal coping during medical waiting periods. The present study examined the impact of this intervention on coping and appraisal during the two-week waiting period during fertility treatment.

5

### **Medical waiting periods, imminence and anticipatory anxiety**

Waiting for pregnancy test results following fertility treatments with assisted reproductive techniques (ART) is stressful (Boivin & Takefman, 1996). ART typically requires an active phase of drug stimulation followed by the transfer of an embryo to the uterus and a two week waiting period to find out whether the woman is pregnant. Women report significantly more emotional distress during the two-week waiting period in fertility treatment than in a comparable waiting period in a no-treatment menstrual cycle (Boivin & Takefman, 1996). Daily monitoring of emotions shows the effect of imminence with a significant linear increase in feeling tense, nervous and worried as the day of the pregnancy test approaches and a sharp drop thereafter (Boivin & Lancaster, 2010). Similar effects have been reported in women waiting for the outcome of genetic screening (Phelps, Bennett, Hood, Brain, & Murray, 2013) or breast disease diagnosis (Poole et al., 1999).

### **Coping with waiting as a specific target of intervention**

Pragmatically, the nature of the medical waiting period in ART and other health contexts calls for interventions that have particular characteristics (Lancaster & Boivin, 2008). Interventions should be self-administered and fully accessible

because patients tend to wait at home and may need support at any time. Missed workdays due to medical appointments can already be considerable (Bouwman et al., 2008) making further in-clinic appointments for support impractical. The high turnover of patients in clinics can also make such interventions unfeasible in many health contexts. For example, American ART clinics carry out 165.172 ART cycles per year (SART, 2014) making it difficult for staff to schedule weekly interventions with all patients entering the waiting period that week. Typical medical waiting periods are brief, usually two to six weeks whereas many support interventions require six to 12 weeks to deliver (Boivin, 2003). Finally, uptake of support groups can be low because people can prefer to rely on their own resources (Boivin, Scanlan, & Walker, 1999). In line with such preferences online interventions have been shown to have benefits in some subgroups (Cousineau et al., 2008) and supportive telephone calls during the medical waiting period can be perceived as helpful even though they do not necessarily decrease perceived stress (Skiadas et al., 2011). Such modes of intervention delivery, however, introduce significant development and/or staff costs whilst not necessarily producing strong benefits, as noted. The most demanding characteristic of waiting however is the unpredictable and uncontrollable nature of the pregnancy test. The controllability of a situation is a central premise affecting the most appropriate choice of coping strategy, according to the goodness-of-fit hypothesis, but evidence supporting this proposal is mixed. A meta-analysis showed that controllability moderated the effect of some strategies (e.g., wishful thinking, distancing) but not others (e.g., problem solving, positive reappraisal) (Penley, Tomaka, & Wiebe, 2002). However, in an infertile population positive reappraisal coping was associated with better adjustment in the low control context of failed treatment (Berghuis & Stanton, 2002; Terry & Hynes, 1998). Together, such issues suggest the need for inexpensive, self-administered coping interventions for medical waiting periods focusing on strategies that could help in this uncontrollable and unpredictable context.

The Positive Reappraisal Coping Intervention (PRCI) (Lancastle, 2006; Lancastle & Boivin, 2008) was developed for medical waiting periods and was conceptualized from the cognitive model of stress and coping (Folkman, 1997; Lazarus & Folkman, 1984) and Velten positive mood induction procedures (Jennings, McGinnis, Lovejoy, & Stirling, 2000). The PRCI presents ten statements that encourage positive reappraisal coping and a leaflet that describes the challenges of the waiting period, the nature of positive reappraisal coping and instructions to use of the intervention (See for detailed information Ockhuijsen, van den Hoogen, Macklon, & Boivin, 2013). Patients read the ten statements at least twice a day during the waiting period.

The statements refer to efforts to reinterpret the situation (as it stands) in a more positive light by focusing on positive aspects or its potential for positive benefits (Park & Folkman, 1997). Initial development and validation of the PRCI was carried out in multiple studies among patients waiting for assessment or treatment in an Accident and Emergency department and medical students sitting important exams (Lancastle, 2006). The acceptability, feasibility and differentiation of PRCI from standard positive mood induction (PMI) effects were examined in an exploratory RCT with women awaiting the pregnancy test result after ART. The intervention group received the ten PRCI statements and a control group received ten standard positive mood induction (PMI) statements (“I feel good”) selected from Velten mood procedures (Jennings et al., 2000). Compared to the PMI group the PRCI group rated the card as significantly more helpful and suitable for the IVF waiting period, as helping to feel less stressed and more positive, and rated it significantly higher in helping to sustain coping efforts during the waiting period (Lancastle & Boivin, 2008). Women also rated daily their emotions, appraisal and use of coping strategies during the waiting period. The PRCI did not have significant effects on emotions but did have positive effects on control and challenge appraisals and coping effort (positive reappraisal, emotional expression, distraction), suggesting it influenced the coping process during the waiting period (Lancastle, 2006). The small group sample sizes in this preliminary work made it difficult to attribute effects only to PRCI.

### **Families of coping and primary reappraisal in the waiting period**

Coping interventions such as the PRCI focus on changing specific coping strategies but may have other impacts that benefit the patient. The Hierarchical Model of Adaptive Processes and Families of Coping (Skinner & Zimmer-Gembeck, 2007) proposes that ways of coping are best classified according to the specific adaptive processes and families of coping to which their function best relates. Skinner’s organizational structure emphasizes functional similarity within families and functional differentiation between families and adaptive processes. Functional similarity (or differentiation) has implications for coping interventions. Teaching one coping strategy (positive reappraisal) implies teaching about its functional goal (i.e., accommodation). Spillover of functionally similar ways of coping in the same family (e.g., acceptance, distraction) may occur, with relatively little stimulation amongst other families of coping.

Conversely, teaching about a single coping strategy could also increase coping efforts in all families of coping because it draws attention to the need for effortful coping. Support for such a proposal comes from a prospective study, in which McQueeney,

Stanton, & Sigmon (1997) investigated the effectiveness of a six-month program that trained women to use problem-focused or emotion-focused coping on emotional adjustment and parenthood status. The two groups both engaged in significantly more problem-focused coping than the no-treatment control group, and did not differ in emotion-focused coping, controlling for baseline coping. It is possible, however, that benefits in the emotion-focused group were due to an unintended increase in information-seeking skills rather than solely to increases in emotion-focused coping. Crossover effects are difficult to gauge from existing literature because interventions typically teach a variety of strategies of the same type (McQueeney et al., 1997) or teach one coping strategy but do not measure impacts on other strategies (Phelps et al., 2013).

Another way in which coping interventions could achieve benefits is via their influence on subsequent reappraisals of the situation. According to Lazarus & Folkman (1984) most events that require coping will be repeatedly reappraised as the event unfolds due to changes in the actual demands of the situation or changes in the coping context (availability, effectiveness) (Eschleman, Alarcon, Lyons, Stokes, & Schneider, 2012). For example, in the case of ART physical signs like vaginal bleeding occur during the waiting period. Although vaginal bleeding is not consistently associated with pregnancy outcome (De Sutter et al., 2006), women interpret it as a sign of imminent treatment failure, which could increase threat or harm appraisals. Positive and negative appraisals and their associated emotions may co-exist in ambiguous situations like waiting periods (Folkman & Lazarus, 1985). The PRCI should increase vigilance for positive aspects of the situation and this positive focus would be expected to generate appraisals reflecting the potential for benefit (i.e., challenge appraisals) even when other negative events co-occur.

### **Daily monitoring of coping and the waiting period**

When assessing the use of coping strategies a number of complexities arise. Asking people what they 'generally do' requires the assimilation and synthesis of many specific acts or set of acts (Stone & Neale, 1984). A discrepancy between coping reported at the time and coping after the event has been found in numerous studies (e.g., Tennen, Affleck, Armeli, & Carney, 2000), as has discrepancy between daily and recalled emotional distress in the ART waiting period (Boivin & Takefman, 1995). This may be due to an active re-conceptualization of experience based on outcomes, new experiences and changing attitudes or beliefs (Ross, 1989). Proponents of daily monitoring methodology (Stone & Neale, 1984) argue that daily monitoring is a more accurate way of assessing coping responses because it captures the dynamic

nature of events. Indeed, daily assessments during fertility treatment showed that women used multiple strategies to manage the waiting period and that change in the use of strategies were seen at different stages (e.g., waiting, outcome) of the ART experience (Boivin & Lancaster, 2010).

One drawback of daily monitoring is that it may impact on reporting itself. For example, habituation or sensitization to monitoring may alter the reporting of variables (Tennen et al., 2000). Differences between aggregated and daily reports may therefore reflect the impact of monitoring itself (i.e., be a methodological artifact) rather than reflecting the changes brought about by changes in the demands of the situation, including any effects of an intervention. Evaluations of coping interventions should therefore, include daily monitoring but also have a no-monitoring control group to evaluate the impact of monitoring itself.

### **Coping during the waiting period and fertility outcomes**

Coping influences biological outcomes in fertility treatment although the evidence is equivocal. A meta-analysis also shows inconsistent associations between coping and other physical outcomes (Penley et al., 2002). A measure of greater negative affectivity that included escapist coping (i.e., pessimism, trait anxiety, escape coping) predicted poorer ovarian response during the stimulation phase of IVF treatment (Lancaster & Boivin, 2005). Similarly, in another study it was found that women who started ART treatment with more positive appraisals of ART (less threat, more optimistic about outcome) or who used relatively more approach than avoidance strategies had a significantly higher biochemical pregnancy rate than those with other coping combinations (Kirchner et al., 2011). Expressive coping used during the waiting period was associated with a lower pregnancy rate during ART (Panagopoulou et al., 2006). Variable results could be due to goodness of fit between coping and specific tasks of treatment that require different forms of coping. For example, at the start of treatment, approach strategies could ensure that drug stimulation schedules are strictly adhered to for an optimal chance of pregnancy whereas escapist coping could interfere with success of stimulation, as suggested by results. During the waiting period accommodative coping strategies, such as those promoted in PRCI are more adaptive to the less controllable aspects of treatment. The secondary aim of the present study was to establish the effect of the PRCI on pregnancy rates during IVF.



## The Present Study

The aims of the present study were to examine whether the PRCI would increase the use of positive reappraisal coping, and related accommodative coping strategies in women awaiting the outcome of an ART cycle RCT. Women were randomized to the PRCI-monitoring (PRCI-M) group or one of two control groups: Monitoring-control (MC) or Routine care control (RCC) group. The PRCI-M group rated their appraisals and coping daily for the 14 days of the waiting period. To establish whether daily monitoring had intervention effects, the MC group also rated daily appraisals and coping but did not use the PRCI. To capture the global and longer term impact of the PRCI women in all groups completed the Ways of Coping Questionnaires (WCQ) just before the waiting period (Time 1: pre-intervention), on day 10 of the 14-day waiting period (Time 2: waiting period intervention) and 6 weeks after the start of the waiting period (Time 3: post-intervention). The RCC group completed the WCQ assessments but did not undertake daily monitoring or use the PRCI. It was expected that women in the PRCI-M group would report significantly more positive reappraisal coping and more challenge appraisals during the waiting period than those in the control groups. Encouraging positive reappraisal was expected to have cross over effects with other coping strategies (distraction, acceptance) from the same coping family (accommodative coping) but not to strategies from other families. Further it was expected that the PRCI-M group would use significantly more positive reappraisal (and related strategies) than the control groups six weeks after the start of the waiting period because they had practiced this strategy in the waiting period.

## Method

The Ethical committee of the University of Utrecht provided ethical review and approval for this study and the RCT was registered the Clinical Trials.gov (NCT01701011). The RCT examined the impact of PRCI on emotions, appraisal and coping. PRCI effects on the outcomes of treatment-specific emotions (positive, negative) and global emotional functioning (anxiety, depression) as well as the intervention evaluation have been reported elsewhere (Ockhuijsen et al., 2014) and indicated that the PRCI was associated with significantly more positive emotions during the waiting period. No change in treatment-specific or global emotional functioning was found. The

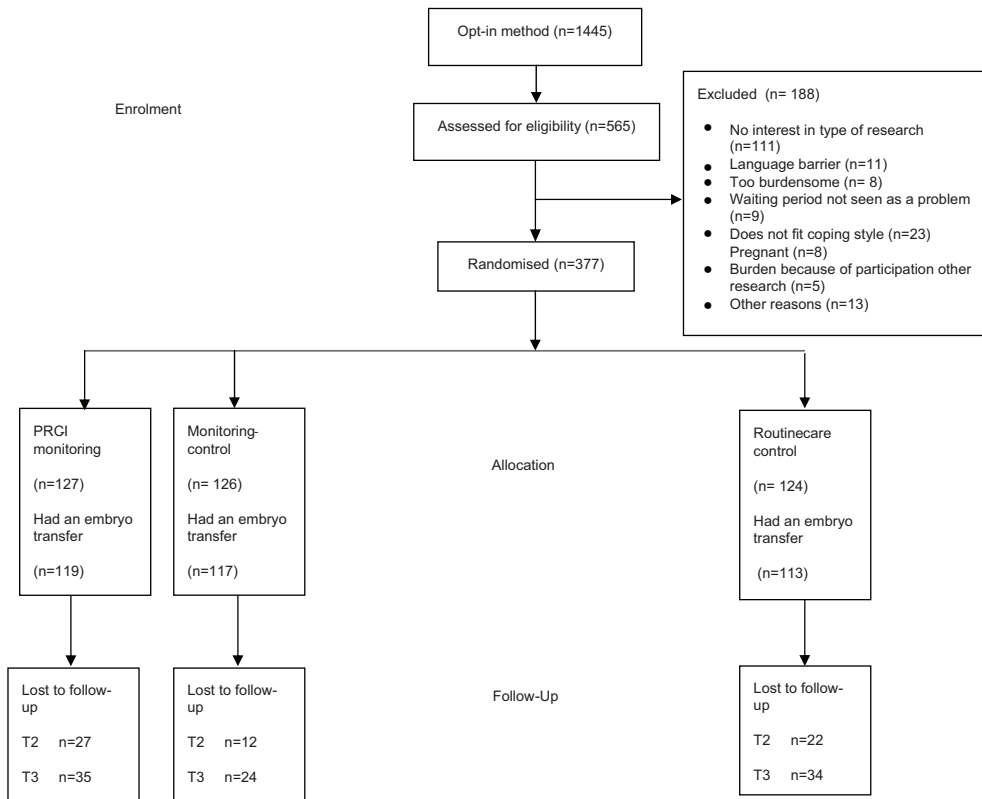


reader is referred to the PRCI study protocol for a more detailed account of the RCT methodology (Ockhuijsen et al., 2013).

## Participants

The sample size calculation for the RCT for emotional wellbeing outcome was based on a medium effect size and 20% attrition rate (Lancastle, 2006) yielding at least 124 women per group. Because emotions and expectations may differ between types of treatment (stimulated, cryopreserved) the type of cycle was used to stratify the population at randomization. Women not speaking the Dutch language were excluded. In total 377 women were randomly assigned to the PRCI-M group ( $n=127$ ), the MC group ( $n=126$ ) or the RCC group ( $n=126$ ). Demographic and medical characteristics were similar between groups at baseline except for previous use of counseling which was more frequent in the PRCI-M (21.4%) and MC groups (27%) than in the RCC group (11.3%). Demographic characteristics showed that the mean age of the women was 34.7 ( $SD=4.8$ ), mean years of living with partner was 8.4 ( $SD=4.3$ ), 68.4% ( $n=258$ ) had no child with current partner but 3.4% ( $n=13$ ) had a child from previous partner, 67.2% ( $n=253$ ) had higher or university level of education. Medical characteristics showed that 19.7% ( $n=74$ ) had other medical problems, duration of infertility was 3.2 years ( $SD=2.2$ ), and duration of fertility treatment was 1.9 years ( $SD=1.8$ ). The percentage of women who had a previous treatment was 72.4% ( $n=273$ ) and for 27.1% ( $n=102$ ) it was a successful previous treatment.

Figure 1 shows the study flow chart. The RCT was conducted over 20 months, between October 2010 and June 2012 in a fertility clinic at a university hospital in the Netherlands, with 1445 invitations to the trial posted to patients. A lack of interest in the research (111/188, 59.0%) was the main reason for non-participation. Of the 377 women who were randomized, 349 had an embryo to transfer ( $n=119$  PRCI-M,  $n=117$  MC,  $n=113$  RCC). Cancellation due to a lack of embryo was not significantly different among the three groups (6.3%, 7.1% and 8.9%, respectively) ( $X^2(2) = .125$ ). Participants remained similar on all characteristics at Time 2 and Time 3.



**Figure 1.** Flow chart for study flow in the three randomized groups.

## Materials

The Background Information Form (BIF) is a 16-item questionnaire used to collect demographic characteristics (age, years living with partner, educational status) and medical history, such as medical problems, outcome of previous pregnancies, infertility diagnosis, duration of infertility and its treatment and treatment success. Women in the PRCI-M and MC groups rated daily appraisals and coping strategies on the Daily Record Keeping (DRK) form. The original DRK comprises a list of emotional and physical symptoms (Boivin & Takefman, 1995) later modified to include coping items (Boivin & Lancaster, 2010) and a broader range of emotions and appraisals (Lancaster, 2006). The coping section included seven coping strategies derived from Stone & Neale's (1984) daily coping measure namely distraction ("I turned my attention away from treatment by thinking about other things or doing some activity"), acceptance ("I accepted there was nothing I could do"), emotional expressions ("I expressed my emotions") and relaxation ("I did something with the

implicit intention of relaxing”). The wishful thinking item (“I wished the situation would go away or somehow be over with”) came from the WCQ (Folkman & Lazarus, 1985) and the problem-solving item (“I made a plan of action and followed it”) from Holahan & Moos (1987). The positive reappraisal item (“I tried to make the most of the situation”) was adapted from Terry & Hynes (1998). Women rated their use of each strategy according to whether the strategy was not used (which scored zero), rarely, sometimes, or frequently used (scored one, two, or three, respectively). Validity of the DRK is shown by findings that overall coping effort varied according to the demands of treatment in expected ways (Lancastle, 2006; Boivin & Lancastle, 2010). The Cronbach alpha coefficient across the waiting period was  $\alpha > .93$  for all strategies.

Five appraisals were assessed using single items. Four were adapted from the Stress Appraisal Measure (SAM) (Peacock & Wong, 1990). These were threat and challenge appraisals (“The waiting period could have a negative impact on me” and “...positive impact...”, respectively), personal control (“I can control what happens in the waiting period”) and overall stressfulness (“I perceive that the waiting period is stressful”). The final appraisal, ability to cope with the waiting period (“I have what it takes to cope with the waiting period”) was from Lancastle (2006). Validity data has shown that the final week of the waiting period in fertility treatment had more negative appraisals than the preceding week (Lancastle, 2006). Reliabilities for the original SAM subscales was satisfactory (Peacock & Wong, 1990) and Cronbachs alpha for the waiting period in the present study was  $\alpha > .92$  for all strategies. Women rated each appraisal by indicating a score of zero if they had not thought about the waiting period in that way or a score of one, two or three if they rarely, sometimes or frequently did that day.

Vaginal bleeding was assessed using a single DRK item, for which zero was the absence of bleeding that day, one, two or three when it was present and did not interfere with daily activities, interfered to some degree, or had a markedly negative effect on daily tasks (respectively).

Finally, women indicated the total number of times the card was read that day. In written and verbal instructions, women were told that the DRK contained a list of different ways of reacting, thinking and coping with the waiting period and given examples of each strategy. Women were asked to complete the DRK at the end of the day, reflecting on the preceding 24 hours, and to leave at least one hour after reading the PRCI card to limit the chance of DRK ratings being artificially and transiently influenced (PRCI-M group).

All three groups completed the Way of Coping Questionnaires (WCQ). The WCQ is based on the cognitive stress and coping model of Lazarus & Folkman (1984) (Edwards & O'Neill, 1998). The WCQ is designed to measure situation-specific coping. Adapted instructions asked women to indicate to what extent they had used each of the coping strategies (Positive Reappraisal, Taking Responsibility, Seeking Support, Problem-Solving, Wishful Thinking, Avoidance) to cope with the given stage of fertility treatment. The 41 items of the Dutch version are rated on a 4-point response scale anchored one (not used) to four (used a great deal). The reliability and validity of the Dutch adaptation of the WCQ was investigated among men and women of different ages (Bramsen, Bleiker, Triemstra, Van Rossum, Sandra M. G., & al., 1995) with Cronbach alpha in the range .65 to .80 for the six subscales. In the present study reliability was satisfactory ( $\alpha > .70$ ) except for taking responsibility ( $\alpha = .652$ ) and avoidance ( $\alpha = .453$ ).

Treatment type and treatment outcome (live birth) was obtained from a medical chart review. The outcome of treatment was live birth according to the standard definition.

### **PRCI Intervention**

The PRCI-M group received the PRCI. The PRCI comprises a leaflet with a detailed explanation about this coping approach and a small laminated card that contains the ten positive reappraisal statements. The leaflet describes the challenges of the waiting period (e.g., possible intrusive thoughts, pregnancy symptom vigilance, anticipatory anxiety and need for coping support). Positive reappraisal coping is described in terms of what it is (“...taking account of good aspects alongside the more negative aspects of the situation”) and is not (“...does not mean pretending that everything is wonderful”). Examples are given and women are encouraged to list some positive aspects of fertility treatment. Instructions for using the PRCI card are provided and advised women to carry the card, read the explanatory leaflet as instructed, and when reading statements to think about how each applied to them personally. Women were instructed to read the PRCI at least twice a day, once in the morning and once in the evening as well as at any other time they wished. The leaflet reminds the users that it could take time for the strategy to become familiar and to persevere in using the card. A detailed description of the development and initial validation studies of the PRCI can be found in Lancaster (2006) and Lancaster & Boivin (2008).

### **Control group and ART treatment**

The control groups completed psychological measures but did not receive the PRCI. All groups underwent ART as per standard procedures at the clinic. Where required,

women underwent ovarian stimulation (7-14 days), thereafter oocytes retrieved from follicles at an optimal time, fertilized with sperm and three days after fertilization, embryos transferred to the uterus. Women then waited for 14 days before using a home pregnancy test to find out if they were pregnant.

### **Procedure**

The opt-in method was used to recruit participants as per conditions of approval declared by the Ethics Committee. Participants were sent an invitation to the trial and asked to contact the research team if interested, using the reply form or email address provided. A researcher responded to patient queries about the study and sent to those still interested an information sheet with a consent form to be returned in accompanying preaddressed stamped envelope. During their first visit to the hospital, more information was given about the logistics of the study by the researcher and a research assistant, using a written protocol. A computer-generated table of random numbers was used to achieve the stratified randomization of the 377 women who met the eligibility criteria. An independent researcher, blind to patient baseline assessment, was responsible for the randomization. To limit demand characteristics, participants were told that they would receive one of three interventions and were not told what intervention was being evaluated. The independent researcher had no contact with participants after randomization (except for scripted reminder text messages). Women were randomized on the day of oocyte retrieval and provided with written information about group assignment on the day of the embryo transfer (ET). At ET women received instructions for the waiting period in an opaque sealed envelope. Clinic staff was blind to group membership. After ET, participants had no further contact with clinic staff, other patients or the researcher during the 14-day waiting period. The PRCI-M and the MC groups completed the DRK daily during the two-week waiting period from the day of ET until the day before the pregnancy test. All groups completed the WCQ as described (Time 1, 2 and 3). All assessments were returned by post weekly.

### **Statistical methods**

IBM SPSS Statistics 20 was used for all statistical analyses. Descriptive statistics were used to describe baseline variables. Equivalence of baseline measures between groups was examined by one-way analyses of variance (ANOVA) for normally distributed variables on interval or ratio level and chi-square for variables on nominal level. If the groups were not comparable on demographic characteristics, medical history, or gynecological variables, those variables were employed as

covariates (or factors) in subsequent analyses. The onset of any bleeding was also used as a covariate in all analyses. A multilevel linear model (MLM) for repeated measures was used to examine the differences between the three groups over time for each coping strategy. The MLM can be conceptualized as a series of interrelated regression models that explain sources of variance at multiple levels of analysis (Hoffman & Rovine, 2007). In the present analyses the model for the daily monitoring coping data modeled a random effect for participants and fixed effects for groups and time with adjustment for vaginal bleeding (spotting), baseline coping strategy. All models were estimated by the method of restricted maximum likelihood (REML) and the compound symmetry covariance structure was chosen for the repeated measures. For the DRK analysis, with 14 repeated measures, we used time as a continuous variable with a linear contrast. Although past research suggests a cubic trend for some coping strategies during the waiting period of ART (e.g., seeking social support, distraction, direct action), the cause of deviation from the otherwise linear trend is due to slope changes after the pregnancy test results are known (i.e., outcome stage) (Boivin & Lancaster, 2010). As the outcome stage was not measured in the present study, we used a linear trend. Summary statistics (F-value, intercept and slope coefficients, confidence intervals) are presented for fixed effects (group, time, time by group). The intercept showed initial status at the start of the waiting period and the slope per day showed the rate of daily change with negative and positive values indicating a decrease or increase (respectively) in appraisal or coping. The model for global WCQ coping had a random intercept for participants and fixed effects for groups and time with adjustment for the baseline global level of coping and previous use of counseling for infertility. The effect of PRCI on treatment outcome (live birth) was examined with a chi-square test. The analysis was performed according to intention to treat.

## Results

### Treatment delivery

Women read the PRCI on average twice a day with a mean of 1.97 times ( $SD=.63$ , range: .29-4.50). The percentage of women who had not used PRCI at least once in the day was 3.8% ( $n=4$ ). The number of times the card was read decreased significantly from day 1 ( $M=2.240$ ,  $SD=.944$ ) to the day before the pregnancy test ( $M=1.639$ ,  $SD=.94$ ,  $F(13, 962)=6.28$ ,  $p < .001$ ).

**Table 1** F-statistics for fixed effects, intercepts and regression coefficients from multilevel model analyses of daily appraisal and coping.

Variable	F-values for fixed effects			Intercept			Slopes		
	Group	Time	Group x Day	MC intercept [95% CI]	PRCI intercept [95% CI]	MC slope per day [95% CI]	PRCI slope [95% CI]		
<b>Appraisal</b>									
Threat	1.819	6.161**	.501	.170 [-.069, .409]	.016 [-.452, .480]	.011 [.002, .020]	.007 [-.015, .029]		
Stressfulness	.220	133.582***	2.106	-.140 [-.470, .190]	-.199 [-.778, .379]	.058 [.046, .070]	.046 [.019, .074]		
Challenge	7.090**	32.216***	7.627**	.091 [-.041, .223]	.299 [.013, .587]	-.006 [-.012, -.001]	-.015 [-.028, -.004]		
Personal control	1.785	125.511***	.004	.585 [-.374, .795]	.433 [-.001, .867]	-.038 [-.047, -.029]	-.038 [-.057, -.0017]		
Ability to cope	.898	55.091***	.005	.548 [.264, .832]	.680 [.122, 1.24]	-.027 [-.036, -.018]	-.027 [-.048, -.005]		
<b>Coping</b>									
Positive Reappraisal	.005	105.00***	5.63**	.418 [.176, .660]	.409 [-.085, .903]	-.043 [-.052, -.034]	-.028 [-.049, -.007]		
Acceptance	1.075	33.63***	4.92*	.944 [.655, 1.23]	.797 [.229, 1.36]	-.030 [-.040, -.020]	-.015 [-.023, -.008]		
Distraction	7.135**	28.44***	9.34**	.711 [.430, .992]	1.05 [.519, 1.58]	-.011 [-.022, -.000]	-.034 [-.059, -.008]		
Relaxing	.159	30.97***	4.92*	.557 [.318, .795]	.509 [.037, .982]	-.032 [-.043, -.021]	-.015 [-.042, .011]		
Express emotions	2.123	1.324	.001	1.53 [1.24, 1.82]	1.72 [1.18, 2.25]	-.005 [-.017, .007]	-.005 [-.032, .022]		
Direct Action	.104	.004	.909	.116 [-.045, .277]	.087 [-.252, .426]	-.002 [-.009, .005]	.002 [-.014, .019]		
Wishful thinking	.313	129.12***	7.06**	.242 [.004, .480]	.309 [-.165, .783]	.060 [.049, .072]	.040 [.013, .067]		

Note. After adjustment for baseline coping level and vaginal bleeding. F = F-value for test of fixed effects. MC=Monitoring-control, PRCI=Positive Reappraisal coping Intervention. ME=main effect. Contrasts for significant interactions shown. \* p < .05 \*\* p < .01 \*\*\* p < .001.

### Effect of PRCI on appraisals during the waiting period

See Table 1 for summary statistics for MLM analyses of daily appraisals. The appraisals threat, stressfulness, challenge, controllability and ability to cope showed main effects of time. Threat and stressfulness showed an increase per day while personal control, ability to cope and challenge appraisals decreased daily. Only challenge showed a significant main effect of group and a group by time interaction. The significant main effect of group showed that the initial status for the PRCI-M group rating was .209 higher than for the MC group (95% CI [.054, .364]). The significant group by time interaction showed the decline in challenge appraisals per day in the PRCI-M group was at a faster rate than in the MC group (see Figure 2a). See Supplemental file 1 for graphs showing the change in adjusted means for appraisal.

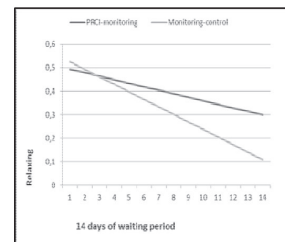
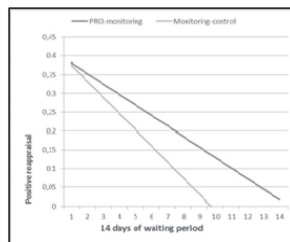
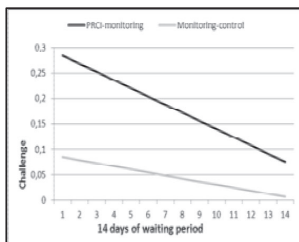


Figure 2a Challenge appraisal Figure 2b Positive reappraisal Figure 2c Relaxing

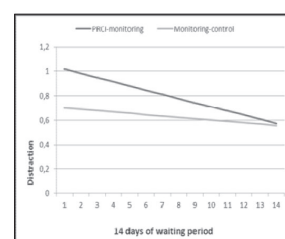
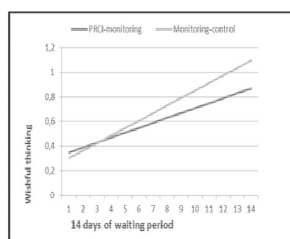
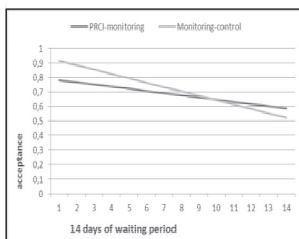


Figure 2d Acceptance Figure 2e Wishful thinking Figure 2f Distraction

**Figure 2.** Estimated slope change as a function of group and time (adjusted) for the significant group by time interaction for daily coping and appraisal.

### Effect of PRCI on coping during the waiting period

See Table 1 for summary statistics for daily coping from the multilevel models. There was a significant main effect of time and interaction for positive reappraisal, acceptance, distraction, relaxing and wishful thinking. Only distraction showed a main effect of group. Effects for express emotions and direct action were not significant. See Figure 2b to 2f for rate of change across time by group for significant interactions.



The regression coefficients for the significant main effect of time for the coping strategy positive reappraisal indicated a decreased per day but the significant group by time interaction showed a slower rate of decrease in PRCI-M group compared to the MC group. The PRCI-M group showed increasingly more positive reappraisal during the fourteen days of the waiting period.

The regression coefficients for the time main effect in other coping strategies showed a decrease per day for acceptance, distraction and relaxing and an increase per day for wishful thinking. The regression coefficients for the significant group by time interaction showed a slower rate of decrease for the PRCI-M group than the MC group on relaxing and acceptance. For relaxing this slower rate of decrease showed that women in the PRCI-M group increasingly used more relaxing (from day 3) compared to the MC group (Figure 2c). For acceptance women in the PRCI-M group initially started with lower acceptance scores than the MC group but only until about day 10 after which there was a crossover (see Figure 2d). The coefficients for the significant group by time interaction for wishful thinking showed that the rate of increase was slower for the PRCI-M group with the MC group showing increasingly more wishful thinking from day 3 compared to the PRCI-M group (Figure 2e). The significant main effect of group on distraction showed that the initial status for the PRCI-M group rating was .339 higher than the MC group (95% CI [.089, .588]). However, the regression coefficients for the interaction on distraction showed that the rate of change for this strategy was faster for PRCI-M than the MC group (see Figure 2f). See Supplemental file 2 for graphs of change in adjusted coping means over time.

### **Effect of PRCI on global coping during the waiting period and at six-weeks after treatment**

Means (SDs) for the WCQ global coping are shown in Table 2 and results presented next. This set of analyses compared all three randomized groups (PRCI-M, MC, RCC).

There was a significant main effect of time for positive reappraisal,  $F(2, 660)=7.51$ ,  $p=.001$ , social support seeking,  $F(2, 665)=7.42$ ,  $p=.001$ , problem solving,  $F(2, 659)=102.57$ ,  $p=.000$ , and avoidance,  $F(2, 670)=10.24$ ,  $p=.000$ . The coping strategies positive reappraisal, social support seeking and problem solving were significantly lower during the waiting period than at other assessment times. Problem solving at the pre-intervention was also significantly lower than at post-intervention and avoidance was significantly lower at the start of treatment than at other assessment times. There was a significant group by time interaction only for the coping strategy

taking responsibility,  $F(4, 660)=3.48$ ,  $p=.008$ . The contrast for the significant group by time interaction revealed that the PRCI-M ( $M=1.537$ ,  $SE=.031$ ) and MC groups ( $M=1.490$ ,  $SE=.029$ ) used significantly less of this coping strategy at the waiting period compared to the control group ( $M=1.646$ ,  $SD=.032$ ). The group main effects were not significant.

**Table 2.** Means (SEs) for global coping on the Dutch Ways of Coping subscales across time in each group, with contrasts for main effect of time.

Variable	Time 1 Pre-intervention n=127	Time 2 Day 10 waiting n=126	Time 3 Post intervention n=124
Positive reappraisal	1.832 (.022) <sup>a</sup>	1.731 (.023) <sup>b</sup>	1.818 (.024) <sup>a</sup>
Taking responsibility	1.587 (.018)	1.553 (.019)	1.572 (.020)
Social support seeking	2.614 (.023) <sup>a</sup>	2.510 (.024) <sup>b</sup>	2.590 (.025) <sup>a</sup>
Problem-solving	2.259 (.021) <sup>a</sup>	1.897 (.023) <sup>b</sup>	2.094 (.023) <sup>c</sup>
Wishful thinking	2.233 (.021)	2.290 (.022)	2.270 (.023)
Avoidance	2.124 (.019) <sup>a</sup>	2.212 (.020) <sup>b</sup>	2.218 (.020) <sup>b</sup>

*Note.* Means with different superscripts are significantly different. Marginal means are shown because all strategies (except taking responsibility) showed only time main effect.

### Treatment outcome

The groups did not differ in the type of treatment they underwent ( $p=.837$ ) with 65.5% ( $n=247$ ) couples undergoing treatment with stimulation. The difference in live birth rate between groups was not significant ( $p=.753$ ). The live birth rate per group was 23.5%, ( $n=28$ ), 21.4% ( $n=25$ ) and 19.5% ( $n=22$ ) for the PRCI-M, MC and RCC groups, respectively.

## Discussion

The results show that the PRCI achieved what it was designed to do, namely to sustain challenge appraisals and the daily use of positive reappraisal coping during the 14 days of waiting for a pregnancy test result following fertility treatment. The PRCI can therefore be recommended as a way of supporting a positive outlook during this waiting period. PRCI benefits occurred in a dynamic context where patients increasingly appraised the waiting period as stressful and made greater appraisals of threat, uncontrollability and inability to cope as the day of the pregnancy test approached. Although the PRCI targeted a specific form of coping, its use was

associated with effects in compatible coping strategies within and across families of coping. PRCI use was not, associated with marked changes in global coping or benefits in physical outcomes (live birth).

The results confirm that the imminent approach of a medical test result makes the waiting period demanding for patients. Women increasingly appraised the waiting period as stressful, uncontrollable and as a potential threat, and reported increased perceptions of being unable to cope. The latter was consistent with time main effects that showed an overall dampening of coping efforts in daily and global coping assessments during the waiting period. These results are consistent with theoretical work on imminence (Lazarus & Folkman, 1984) and research showing increased anticipatory anxiety (tension, worry, nervousness) during the ART waiting period (Boivin & Lancaster, 2010) including an earlier report from the present trial (Ockhuijsen et al., 2014). We propose that imminence is the main driver of these changes in appraisal rather than external cues of the imminent outcome (pregnancy or not) because strong time main effects remained even after controlling for such cues (i.e., bleeding).

The aim of this RCT was to assess the effect of the PRCI on coping strategies and appraisals in women awaiting the outcome of an ART cycle. The results showed that PRCI affected coping and appraisal but provided only partial support for hypotheses. The PRCI achieved what it was designed to do in that it sustained positive reappraisal coping and challenge appraisals. These results were in line with an earlier report from the present trial showing that women using PRCI had a lower decrease in positive emotions during the waiting period than women in the MC group (Ockhuijsen et al., 2014). The term sustained is used because the regression coefficients showed the PRCI effect to be about slowing the decrease in coping effort as the waiting period progressed rather than in increasing coping effort. A decrease could suggest coping is no longer needed but this perspective would be incompatible with the reappraisal findings. Altogether the pattern of results and earlier findings are consistent with theoretical work suggesting that positive reappraisal coping helps people to reinterpret the situation in a more positive light by focusing on positive aspects or its potential for positive benefits (Park & Folkman, 1997; Taylor, 1983). These moderate effects were achieved using an inexpensive self-help tool. The PRCI was designed and tested in the ART setting and future research should examine its effectiveness in other contexts.

The results suggest that PRCI sustains forms of coping that are compatible with positive reappraisal coping whether or not these are in the same or a different family of coping. Interaction effects showed that women using PRCI showed similar

less rapid decrements in strategies related to accommodative coping (acceptance) as well as in strategies from other coping families (relaxing), which could also be interpreted as sustaining coping. The results are compatible with another intervention study showing that teaching emotion-focused strategies produced crossover effects (McQueeney et al., 1997). Overall these results would suggest that encouraging one type of strategy motivates coping efforts more generally across families. The functional classification of coping (Skinner, Edge, Altman, & Sherwood, 2003) is not threatened by these findings but they do imply that families of coping enabling different adaptive processes are not necessarily independent.

Spillover and crossover effects could also be caused by the (in)compatibility of some forms of coping. Distraction could have decreased faster in the PRCI-M group because it was incompatible with positive reappraisal coping. In order to distract, one must avoid thinking about the worrying thought (Phelps et al., 2013), which would be difficult to do if one was trying to simultaneously think about the positive aspects of the negative situation. Similarly, wishful thinking increased during the waiting period, but less so for the PRCI group, which may have reflected that trying to think positively about the situation could be incompatible with wishing it away. In contrast, relaxing often requires one to think of pleasant thoughts to induce the state of calm, which would be compatible with PRCI. The (in)compatibility of some ways of coping has been discussed and argued to be one reason for classification of coping strategies according to functional families (Skinner et al., 2003). The pattern of results suggests that coping interventions should be expected to have spillover and crossover effects. But more research is needed about the causes of such effects and whether such effects might account for goodness-of-fit effects (Tennen et al., 2000).

The crossover effects could also reflect methodological artifact. In terms of distraction, the feasibility and acceptability study reported that PRCI was marginally more distracting than the positive mood induction control (Lancastle & Boivin, 2008) and a qualitative study among women using the PRCI suggested that the PRCI statement "Try to do something that makes me feel good" led to distraction (unpublished, Ockhuijsen). However, the distraction interaction showed that whilst the initial use of PRCI might have been distracting this effect rapidly decreased and PRCI-M was eventually equivalent to the MC group.

The reason for using daily monitoring was to capture coping as a process in time and the results indicate that daily ratings using individual coping items can achieve this goal. Another reason to use daily monitoring was because global assessments based on recall of coping have been shown to be inconsistent with what people

actually do in a given situation (Stone et al., 1984; Tennen et al., 2000). In the present study, the three subscales measured in daily and global assessments showed inconsistent effects. Daily monitoring captured PRCI effects on positive reappraisal coping and wishful thinking but these were not identified in global assessments. Time effects (decreased coping effort during the waiting period) were captured for positive reappraisal in both assessment types but only in daily assessment for wishful thinking. The reverse was true for problem-solving with time effects only captured in global assessments. Overall the results indicate that daily monitoring was more sensitive to PRCI and imminence effects, but it could be argued that daily ways of coping do not lead to more stable global forms of coping.

The lack of consistency could be due to methodological issues such as insensitivity of questionnaires in the fertility context or recall bias in global assessment, as noted previously. However, the WCQ has been used for this population in previous studies (Cousineau et al., 2008; Lancaster & Boivin, 2005). Monitoring itself could have an effect. The only interaction on the WCQ showed that women in the RCC group used taking responsibility significantly more than the PRCI-M and MC group suggesting an effect of monitoring. A no-monitoring control group using the PRCI should be used in future research to clarify such methodological issues. Note however, low reliability on the taking responsibility scale.

The PRCI helped sustain a more positive outlook on the medical waiting period but this outlook was not associated with a reduction in the perceived stressfulness of the situation, a sustained change in global coping or an improved live birth rate with treatment. Earlier findings from the present trial also revealed a lack of effect on negative emotions during the waiting period or on global levels of anxiety or depression (Ockhuijsen et al., 2014). A lack of broader effects was also reported in an evaluation of an active distraction coping intervention, which was found to reduce intrusive thoughts (as designed) but not avoidant thoughts, cancer risk worries or global distress (Phelps et al., 2013). According to Brandtstadter & Renner (1990), in accommodative coping the structure of individual cognitions and valuations is modified to make the given situation appear less negative or more acceptable, which suggests that the effects of this form of coping does not produce genuine decreases in negative mood. Folkman & Lazarus (1985) found that negative (threat) and positive (challenge) emotions co-exist in ambiguous situations. Folkman (1997) argued that the main benefit of positive reappraisal coping was to generate challenge appraisals and consequent positive emotions that helped people to carry on, despite simultaneous threat appraisals and their consequent negative emotions. Our results support the view that threat and challenge appraisals are not poles of a single

continuum; they must be considered as separated but related constructs (Lazarus & Folkman, 1984). It could be that accommodative coping is about making room for good in bad situations. Although women have no control over the outcome of the waiting period, challenge appraisals do tend to be more likely when the person has a sense of control which in the medical waiting periods may mean controlling oneself in the face of continued waiting (Lazarus & Folkman, 1984) rather than in controlling the situation, which was the type of controllability rated in the present study. Thus to capture the full effects of PRCI the measurement of appraisals must be tuned to the multiple ways in which controllability and other appraisals may manifest.

The RCT methodology was rigorous with a clearly defined patient population, satisfactory power, computer generated randomization, medical team blind to condition, assessment and standard care control groups, rigorous outcomes, intention to treat analyses and complete follow-up. Patients were not informed of their group allocation, and although we did not ascertain beliefs about group membership the feasibility and acceptability trial of PRCI showed that patients randomly assigned to PRCI or the daily-monitoring control group were equally likely to think they had been assigned to the intervention (Lancaster, 2006). We did not have a PRCI-only group which makes it difficult to ascertain the effects of the PRCI independent of daily monitoring. It could be that PRCI effects are due to joint effects of using positive reappraisal and recording behavior. It is noteworthy that the only significant group contrast on global assessment was a difference that could be attributable to daily monitoring. Future evaluations of PRCI should aim to include a PRCI-only group.

A strength of this study is that the PRCI intervention was theoretically derived, conceptualized from the cognitive model of stress and coping of Lazarus & Folkman (1984) and developed according to the Medical Research Council framework for developing complex interventions (Campbell et al., 2000). Daily and global assessments were undertaken of theoretically expected changes in coping and using questionnaires with satisfactory psychometric properties. However, the WCQ is not a fertility specific questionnaire and therefore it may have lacked the sensitivity of such questionnaires (e.g., Panagopoulou et al., 2006).

The RCT was powered for the primary outcome (emotional reactions) that took account of potential attrition. In the present study there was attrition of 20% at Time 2 and about 30% at Time 3. The use of multilevel modeling allowed analysis of partial response whilst maintaining power (Hoffman & Rovine, 2007) which served to counter attrition. Maximum likelihood estimation has been shown to provide unbiased and efficient estimates but only when the data are missing at random (Hoffman &

Rovine, 2007). We believe this to be the case because the women who dropped out of the study were not different on demographic and medical characteristics. The analysis for treatment outcome may be underpowered.

The overall balance of strengths and limitations of this large RCT suggest that confidence in the validity of results is warranted. This confidence is additionally justified from the finding that these results generally replicate those obtained in the small feasibility and acceptability trial of the PRCI (e.g., sustaining of positive reappraisal coping, effects on other strategies, challenge appraisals, lack of pregnancy effects), carried out with a sample of women undergoing the same stressor in a different clinic, in another country, and in English (Lancaster, 2006).

Overall, the results suggest that a self-help coping intervention encouraging positive reappraisal can sustain coping during a medical waiting period and support efforts to sustain a more positive outlook during this stage of treatment. Positive reappraisal coping does not, however, appear to change negative appraisals (threat, stress, uncontrollability). Considering the low cost implications of this tool it can be recommended for use in medical waiting contexts to help patients sustain a positive outlook at this time. Future research should examine whether effects are replicated in other populations waiting for potentially threatening medical test results.



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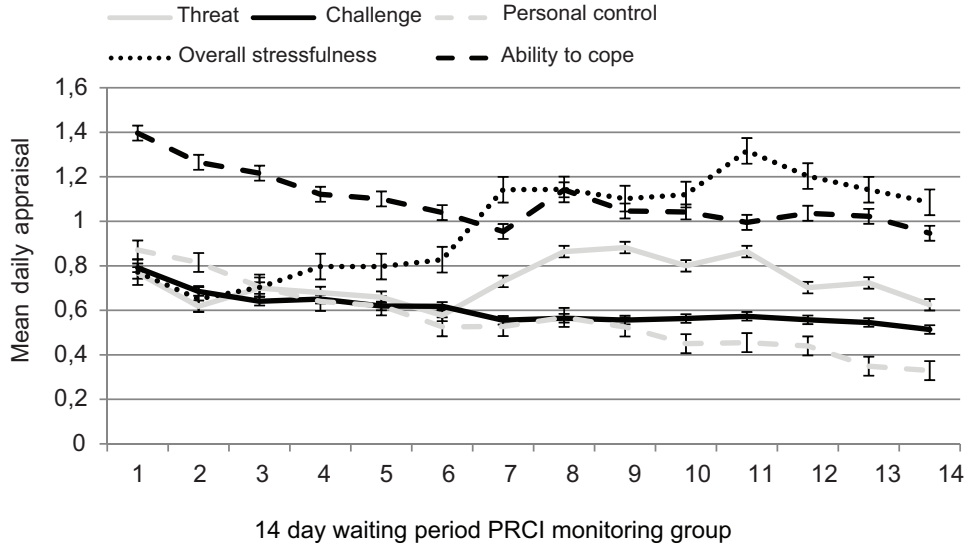


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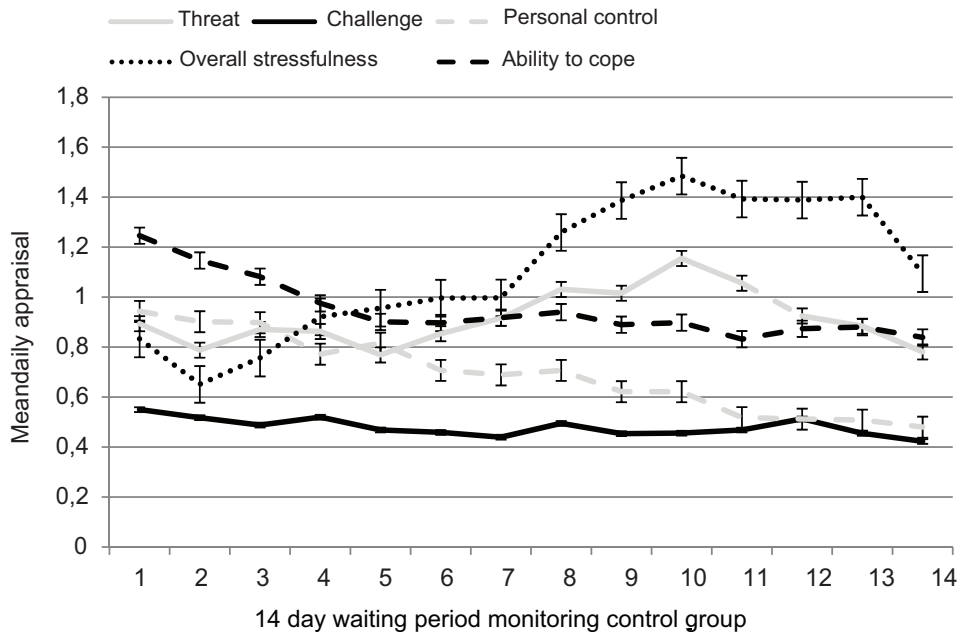
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**Supplemental file 1.** Mean daily appraisal (+/- standard error of the mean) across 14-days of the waiting period in the PRCI-Monitoring and Monitoring-Control group (adjusted).

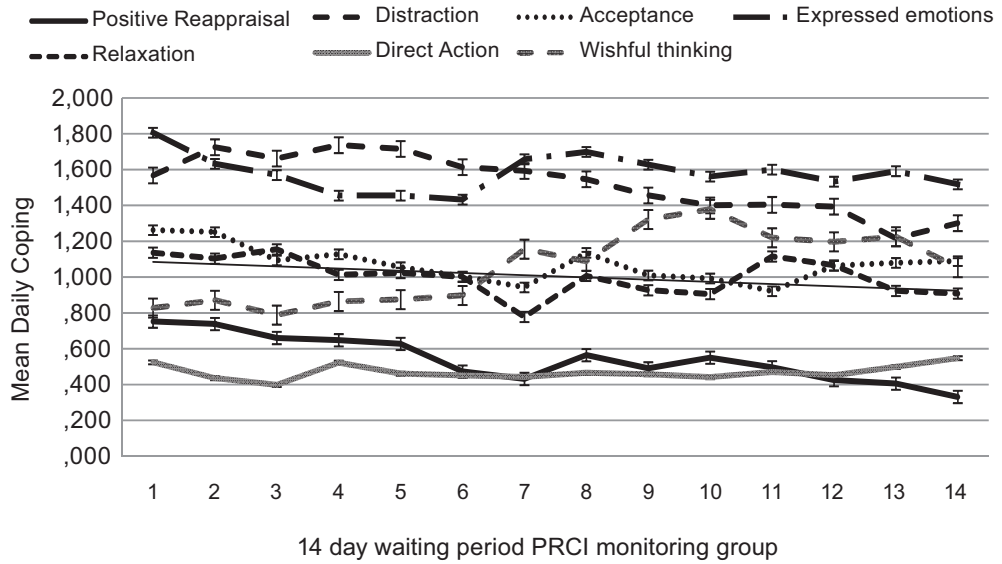


Panel A

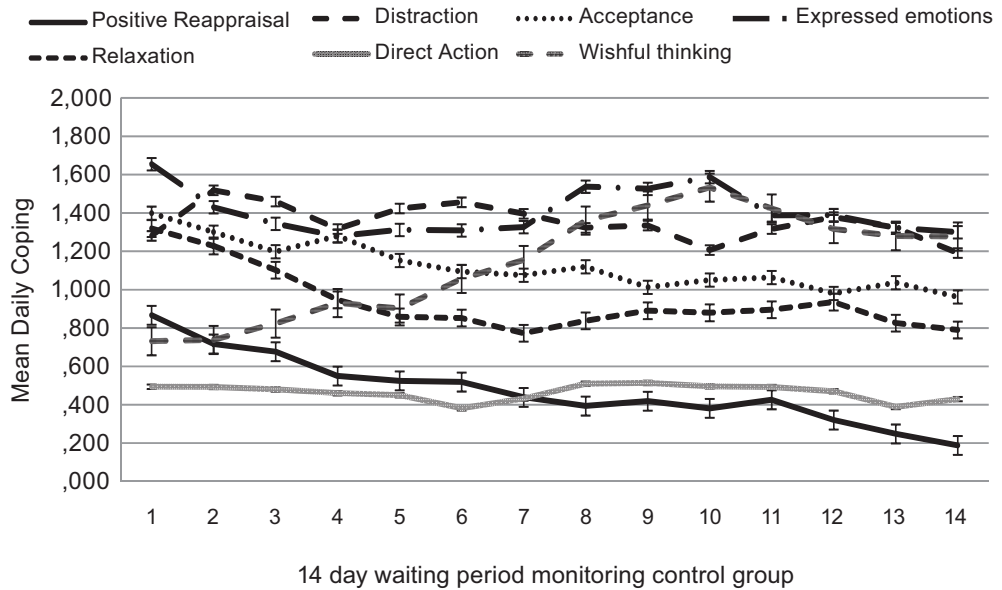


Panel B

**Supplemental file 2.** Mean daily coping (+/- standard error of the mean) across 14-days of the waiting period in the PRCI-Monitoring and Monitoring-Control group (adjusted).



Panel A



Panel B



# Chapter 6

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*Coping after recurrent miscarriage:  
Uncertainty and bracing for the worst*

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## Abstract

**Background:** The aim of this study was to understand how women with single or recurrent miscarriages cope during the waiting periods after miscarriage, waiting for pregnancy or waiting for pregnancy confirmation and to investigate their perception of a 'positive reappraisal' coping intervention designed for these waiting periods. Positive reappraisal is a cognitive strategy to change the meaning of a situation, specifically reinterpreting the situation in a more positive way.

**Methods:** A qualitative methodology was used. Data were obtained from two focus groups comprising nine women with one or more miscarriages.

**Results:** Two core categories, 'uncertainty' and 'bracing', were highlighted during the waiting period for confirmation of an ongoing pregnancy. Women who had experienced a single miscarriage appraised this waiting period as benign and used distraction and coping by social support. Women with recurrent miscarriages could not confidently appraise the waiting period as one that would bring hope or joy and used bracing for the worst as their coping strategy to manage this ambivalence. With this strategy, women tried to control their current emotions, and looked into the future to try to minimise their distress if a further miscarriage occurred. Although all women thought that a 'positive reappraisal' coping intervention would be practical and applicable during waiting periods, only women with recurrent miscarriages actually wanted to use such an intervention.

**Conclusions:** Coping interventions targeting reappraisal of the waiting period stressor situation could help women to cope as they wait for a subsequent pregnancy to be confirmed as ongoing. Coping interventions may need to be tailored, but before any strategy is introduced, further study is needed to identify the most appropriate approach.

**Keywords:** Abortion, Miscarriage, Qualitative Research.



## Background

More than one in 10 pregnancies will end in a miscarriage and this risk increases with age. Further, between 1% and 3% of women will suffer recurrent miscarriages, with an underlying cause found in fewer than 50% of such couples. Miscarriage is a cause of psychosocial distress, as for many women it means more than the loss of a pregnancy. It represents the feeling of a lost baby, a lost future child and a lost motherhood. Miscarriages also cause physical trauma, sudden pain, blood loss and unexpected admission to hospital.<sup>1 2</sup> From their practice, health care workers know that women who have suffered miscarriages potentially experience two subsequent waiting periods: the period between renewed attempts to conceive and conception (waiting for conception), and the period between conception and confirmation that the pregnancy is ongoing (waiting for ongoing pregnancy). Waiting is associated with a build-up of anxiety and stress, which starts because of the uncertainty in timing of the conception and the ongoing pregnancy, but eventually also includes anticipatory anxiety about the outcome, either pregnancy loss or live birth.<sup>3</sup>

Women who have experienced miscarriages may benefit from psychosocial support and counselling during these waiting periods.<sup>1</sup> Several studies have investigated the influence of psychosocial interventions in women who have experienced miscarriage.<sup>4-8</sup> Most have focused on the period immediately following miscarriage.<sup>5-8</sup> There is less information relating to support during the first trimester of a subsequent pregnancy.<sup>4</sup> Interventions such as counselling sessions with nurses,<sup>7</sup> psychological counseling<sup>6</sup> or a weekly ultrasound scan<sup>4</sup> have been shown to reduce anxiety and depressive symptoms. Not all patients use or have access to these interventions and many request adjunct interventions that could be used in addition to such interventions, or as alternatives if they are not readily available.<sup>8</sup>

Lancastle and Boivin<sup>9</sup> recently developed a short self-help Positive Reappraisal Coping Intervention (PRCI) for use during medical waiting periods. It consists of daily reading of 10 positive statements encouraging the use of 'positive reappraisal coping'. This is a cognitive strategy to change the meaning of a situation, in particular, reinterpreting the situation as it stands in a more positive way.<sup>9</sup>

The PRCI is based on the stress theory of Lazarus and Folkman.<sup>10</sup> According to this theory, emotional processes are dependent on actual expectations about the significance and outcome of a specific situation and how people cope following these appraisals.<sup>10</sup> People use a variety of coping strategies to manage stressful events.<sup>10</sup> Problem-focused coping strategies are aimed at confronting and seeking solutions

to a situation, while emotion-focused coping strategies focus on ameliorating the associated level of emotional distress.

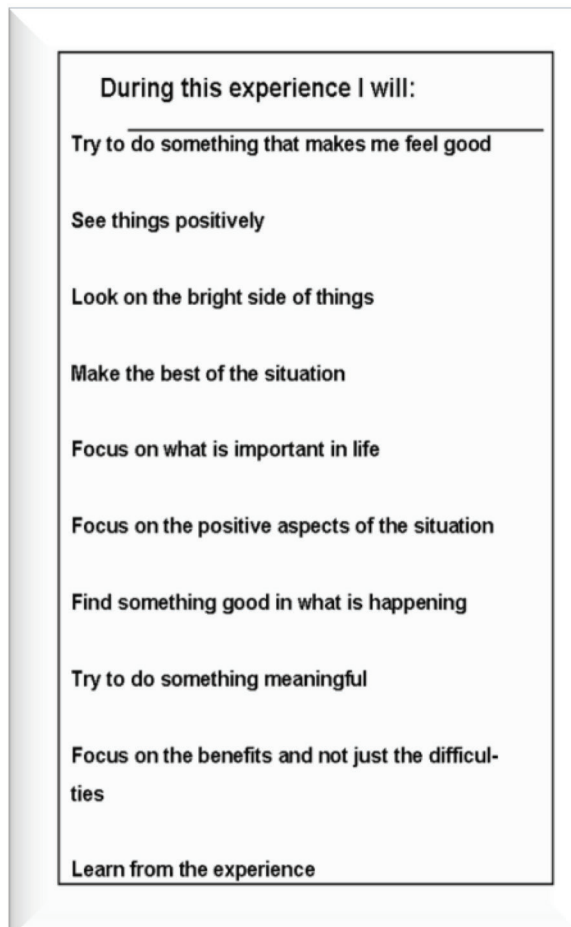
Meaning-based strategies as used in the PRCI (e.g., deriving benefit from adversity or focusing on the positive) are future-orientated strategies that have been shown to be effective where sustained coping efforts are required when a stressor situation is uncontrollable and its outcome unpredictable.<sup>11 12</sup> This is the case in medical waiting periods such as those after experiencing miscarriages. Another future-orientated coping strategy is 'bracing'. Bracing occurs as an attempt to anticipate unpleasant surprises, presumably to avoid disappointment.<sup>13–16</sup> The PRCI was originally developed for the waiting period after embryo transfer in infertility treatment. It consists of a small card (Figure 1) that contains 10 positive reappraisal statements, together with a leaflet with detailed information about the coping techniques. Women are asked to read the PRCI at least twice a day, in the morning and evening, and at any other time that they feel the need to do so. Women have to read the statements and think about how each statement applies to them personally. As conception or confirmation of ongoing pregnancy after a miscarriage often involve a sustained period of waiting, we felt that the PRCI could potentially also be a useful adjunct intervention for women in this patient group. To adapt and further develop the PRCI for women with miscarriages, the UK Medical Research Council medical framework for developing complex interventions was used.<sup>16</sup>

This article presents the results of the first phase of the study, which was to describe the coping strategies of women after miscarriage to determine whether the PRCI intervention could also be applied to this population. To model the intervention, we used a qualitative study design involving two focus groups as recommended for implementation of interventions in novel contexts.<sup>17</sup> In the focus groups we aimed to explore the experience, coping styles and strategies of women during the waiting period for ongoing pregnancy.

## Methods

### Participants

Women attending an Early Pregnancy Unit and/or Recurrent Miscarriage Clinic managed by nurses and doctors at the University Medical Centre Utrecht in The Netherlands were invited to participate in this study. Twenty-five participants, all Dutch-speaking, were approached by telephone and 14 agreed to participate. The main reason for declining was reluctance to talk about this subject in a group setting.



**Figure 1.** Positive Reappraisal Coping Intervention.<sup>9</sup> © 2008 Cardiff University. Figure reproduced with the kind permission of the authors and Cardiff University.

The potential participants were assigned to focus groups based on the number of miscarriages that they had experienced. One focus group comprised women who had experienced a single miscarriage, were currently more than 12 weeks pregnant and were waiting for confirmation of ongoing pregnancy (SM group). Of the seven women invited to this group, one did not attend and two cancelled due to illness. The final sample size in the SM group was therefore four women. The second focus group comprised women with recurrent miscarriages of whom two were over 12 weeks pregnant (RM group). Of the seven women invited to this group, two women did not attend, one because of emotional problems and one for practical reasons.

The final sample size in the RM group was therefore five women. The focus groups took place in a meeting room outside the clinic. Demographic characteristics of the 14 women who agreed to participate are given in Table 1.

**Table 1.** Demographic characteristics of participants in the two focus groups.

Name	Age (years)	Children (n)	Miscarriages (n)	Pregnant	Attendance at focus group
Single miscarriages (SM)					
1) Anna	36	0	1	Yes	Did not attend due to illness
2) Bea	29	0	1	Yes	Did not attend due to illness
3) Cecile	29	0	1	Yes	Yes conception time 3 months, 15 weeks pregnant
4) Diana	29	0	1	Yes	Yes conception time 12 months, 26 weeks pregnant
5) Eva	28	4	1	Yes	Did not attend, unspecified
6) Freya	34	0	1	Yes	Yes conception time 2 months, 21 weeks pregnant
7) Gloria	31	2	1	Yes	Yes conception time 6 months, 26 weeks pregnant
Recurrent miscarriages (RM)					
8) Helen	34	0	3	No	Yes , 5 months after last miscarriage
9) Irene	38	1	3	No	Yes, 3 months after last miscarriage
10) Julia	30	0	3	Yes	Did not attend due to emotional problems
11) Karen	33	1	3	Yes	Yes conception time 2 months, 16 weeks pregnant
12) Lucy	34	1	4	No	Yes, 5 months after last miscarriage
13) Maria	29	1	3	No	Did not attend for practical reasons
14) Nancy	38	0	6	No	Yes, 5 months after miscarriage

### Data collection

An interviewer, note-taker and the researcher, all female, were present during the two focus group sessions. The interviewer had a degree in health science and was experienced in leading focus groups. Notes were taken by a psychologist and the researcher was present to observe.

Data collection took place by semi-structured interview to address issues relevant to miscarriages. The interview schedule broadly followed questions about experiences

and coping strategies around waiting for conception and waiting for ongoing pregnancy. During the focus group session the PRCI was provided and explained, but not used by the women. Questions were asked about the perceptions of the feasibility and acceptability of the PRCI. The central questions for the focus groups were: “How have women with single or recurrent miscarriages experienced and coped during the waiting periods after miscarriage?” and “What is their opinion about the usefulness of the PRCI?”. As most of the women in the RM group were not yet pregnant, their experiences about waiting for an ongoing pregnancy related to past pregnancies that had miscarried. Prompts were developed to ensure that women covered specific categories. The session continued until no new data were gathered, that is, until the data were saturated. The focus groups each lasted 2½ hours with a break of 15 minutes.

### Data analysis

The interviews were tape-recorded and transcribed in full. The method of grounded theory was used to analyse the data of focus groups.<sup>18</sup> In this method, three levels of the coding are used: open, axial and selective coding.<sup>19</sup> The interviews were organised and analysed by thematic analysis assisted by the software programme MAXQDA 10™ (VERBI Software GmbH, Marburg, Germany). To validate the accuracy of the findings, virtual repeatability was used.<sup>20</sup> This was made possible by transcribing the interviews, making field notes and using peer review and peer debriefing with two colleagues proficient in qualitative research to ensure repeatability of findings. One colleague reanalysed the raw data with subsequent consensus discussions with the researcher about emerging categories. Member checking took place during the interviews by asking the participants whether the summaries were a true reflection of their reality.

Illustrative quotations were edited for ease of reading and relevance using the following notation system: ‘...’ refers to omission of some part of the quotation because it is irrelevant to the argument. Where necessary for clarity, additional text (indicated by square brackets) has been included for ease of reading and comprehensibility. Each quotation is followed by a fictitious name (see Table 1), true age and number of miscarriages experienced by the respondent. Translation of the quotations for the purposes of this article was by the researcher and a native English speaker carried out back-translations to verify their accuracy.

## Ethics approval

Permission to conduct the study was obtained from the Ethical Committee of the University of Utrecht, Utrecht, The Netherlands.

## Results

The results of open coding are presented, followed by the axial and selective coding.

### Open-coding categories

Open coding produced the following categories: experiences, appraisal, coping, and PRCI. The categories and their subcategories as indicated by women in the two focus groups are shown in Table 2.

**Table 2.** Categories and subcategories emerging from open coding in the single miscarriage and recurrent miscarriage focus groups.

Category	Single miscarriage group	Recurrent miscarriage group
Waiting period for conception		
Experiences	Time after miscarriage Hope for the future	Time after miscarriage Fear for the future
Waiting period for on-going pregnancy		
Appraisal	Challenge	Uncertainty
Coping	Emotion-focused coping Informing a broader social network	Emotion-focused coping Controlling Bracing Informing a specific social network
PRCI	Practical and applicable No need to use it	Practical and applicable Need to use it

PRCI, Positive Reappraisal coping Intervention.

### Waiting period for conception

#### *Experiences*

Women with the experience of SM or RM reported that the waiting period for ongoing pregnancy was not as stressful as the time immediately after the miscarriage. All women judged the latter period as the worst time. Both groups had feelings of grief because of the loss of a future baby and felt in need of more support during this period.

*“What I found the most difficult were the first weeks after the miscarriage. When I look back, this was the hardest time. You are disappointed and you have physical problems. If I have to face that again I will use all the help there is.” [Helen, 34-3].*

Women who had experienced one miscarriage had the feeling that their miscarriage was just bad luck. They still had hope for the future.

*“It is a bit of a false start feeling. You are positioned in the starting blocks and you think ... but we can have a new opportunity. You have no reason for worrying too much.” [Freya, 34-1]*

Women with RM had fears for the future and some women were afraid of never having another pregnancy or children of their own.

*“What I find difficult is the thought that I might never have children and no family but what is very bad is that what I have now apparently is not enough. I am so busy wondering whether I will ever have children.” [Helen, 34-3]*

## **Waiting period for ongoing pregnancy**

### *Appraisal of the waiting period for ongoing pregnancy*

Women with SM or RM differed in the way they appraised the waiting period for ongoing pregnancy. Women in the SM group were a little uncertain during the waiting period but they still mainly appraised the waiting period as benign or a (positive) challenge rather than a threat with potential for harm.

*“A girlfriend has had four miscarriages. That is a completely different story. Her experiences were quite different. When I compare myself to her, I do not have strong feelings, almost nothing.” [Gloria, 31-1]*

Women in the RM group did not know or were unable to appraise the waiting period: is it benign, a challenge, threat or harm? As a result women in the RM group were very uncertain about how they should regard or feel about the pregnancy.

*“I noticed that two things were present in a subsequent pregnancy. You are reminded of your loss or more losses and that causes extra sadness and I had*

*the feeling that I did not want to lose this child, and on the other hand I wanted to love this child. That makes you very insecure and afraid.” [Julia, 34-3]*

The length of time of the uncertainty depended on the previous experiences. Some women were uncertain for the first weeks while others were uncertain for up to 20 weeks.

*“I had an ultrasound at 7 weeks and then I heard the heartbeat. Only this does not give certainty because the last pregnancy ended at 7 weeks. It [uncertainty] has actually lasted up to 20 weeks before I thought yes, it is now really well.” [Gloria, 31-1]*

Women with RM declared that the uncertainty grew after every new miscarriage.

*“We were actually still not quite accustomed to the idea, and then it went wrong. That is an entirely different approach than when one is very focused on the pregnancy. The second time that it goes wrong ....that happens... but after the second time it is becoming more precarious because then you do not know the cause and I would also not know how you might affect it.” [Lucy, 34-4]*

#### *Coping during the waiting period for ongoing pregnancy*

The coping strategies the two groups used the most were emotion-focused strategies like avoidance, seeking social support, positive reappraisal and distraction. The main difference between women with SM or RM was the reason for using the coping strategies. Women with SM made a point of trying to cope in a different way than during their first pregnancy. For instance, one woman avoided sports during the first pregnancy because she was afraid that it was bad for the baby, however in the second pregnancy she ran a marathon. Some women avoided seeking information on the internet or avoided thinking too much about the baby. Others searched for social support by informing a broader social network sooner about the pregnancy to anticipate a need for support in case of a possible new miscarriage.

*“I told family and friends in both pregnancies, but earlier in the second because they already knew of the previous miscarriage. Yes it helps to talk about it because when it goes wrong again you can have more support from those people.” [Cecile, 29-1]*



Women with RM primarily used the coping strategy of bracing for the future. These women tried to control their emotions and future emotions as much as possible to prepare for the worst outcome. They anticipated negative feelings that could be caused by a new miscarriage in the future. For instance, they avoided thinking and daydreaming about the baby.

*“You notice the thoughts of no planning ahead, no dreaming ... I wanted to be happy really ... I had every reason to but ever since that [miscarriage] you are feeling cautious.” [Lucy, 34-4]*

Women in both groups distracted themselves by going on a holiday or meeting a friend, but it was not always effective. The thought of a possible new miscarriage was frequently on their minds.

*“You try distraction but it does not always work. You try it but you always carry it [the miscarriage] with you, so it is more about killing the time.” [Karen, 33-2]*

Women with RM reported trying to control their social support as much as possible by informing a smaller group of people in case of a subsequent conception. They informed only those people who really could give good support.

*“The more often I became pregnant the fewer people I told [of the pregnancy]. The first time I told everyone who was willing to hear it. The last time I only told a cousin.” [Nancy, 38-6]*

#### *Perceptions of PRCI*

The SM and RM groups thought that the PRCI could be practical and applicable. However, most women with SM did not feel the need to use an intervention whereas most women with RM did. One woman with repeated miscarriage stated:

*“Yes, I would use it, you want to do something. There is nothing else I can do, and now there is something. I think for that reason it can be very helpful.” [Helen, 34-3]*

Women with a single miscarriage could imagine that the PRCI would be useful to other women with more negative miscarriage experiences.

*“Yes if you really have all the negative thoughts and you do not know how to handle it then I think it is an excellent tool ... you focus on the positive things. But for me personally, I would not use it.” [Bea, 29–1]*

Both groups suggested that perhaps the card would be more useful if women additionally kept a diary.

*“I don’t think it is difficult to use. But it might help more if you write something in the morning about the statements and then in the evening you could evaluate.” [Cecil, 29–1]*

### **Axial and selective coding**

The two core categories ‘uncertainty’ and ‘bracing’ emerged out of the data from open coding. These core categories explained the differences between SM and RM in coping and have an association with the open coding categories found.

#### *Uncertainty*

Waiting for ongoing pregnancy is an event that women with SM experienced and coped with differently to women with RM. The more miscarriages a woman had experienced, the more difficult it became in a subsequent pregnancy to confidently appraise the waiting period for ongoing pregnancy. Women with SM still experienced a new pregnancy as benign or a (positive) challenge while women with RM became more uncertain in a subsequent pregnancy. This uncertainty expanded with the increase in the number of miscarriages.

#### *Bracing*

Both groups used emotion-focused coping strategies aimed at regulating emotions they were experiencing, but women with RM used the coping strategy to control or brace against their current emotions and the possible future emotions arising from a negative outcome. SM women just used them to cope in a different way than during their first pregnancy.

#### *Relationship between uncertainty and bracing*

Uncertainty appears when women do not know how to appraise the ‘waiting for ongoing pregnancy’ period. They do not know if the waiting period will be a challenge, threat or harm because the outcome becomes more unpredictable with the increase in the number of miscarriages. The more miscarriages women have experienced

the more the uncertainty grows. It grows because women have less faith that they will ever have an ongoing pregnancy. Women brace as a coping strategy to deal with this uncertainty. Bracing is an attempt to control the emotions and future emotions as much as possible, and to prepare for the worst outcome.

## Discussion

This qualitative study was aimed at exploring the coping strategies in women with single and recurrent miscarriage. We also examined whether a PRCI was perceived as useful for this population. The results show that two core categories, 'uncertainty' and 'bracing', differed between women with RM or SM. The more miscarriages women had experienced, the more likely that bracing was adopted as the core coping strategy to deal with increasing uncertainty about a current or eventual pregnancy. Women thought that coping interventions during the waiting period could be useful and that these could include positive reappraisal tools such as PRCI or other cognitive or psycho-educational interventions.<sup>12</sup>

All women thought that the PRCI could be practical and applicable but most women with SM did not want to use this or any other intervention, in contrast with women with RM who did. This asymmetry may be due to differences between groups in appraisal of the situation. Women with SM felt that the first miscarriage was bad luck, and expected the present pregnancy to continue, lessening the need for additional support. In contrast, women with RM clearly lacked confidence about future outcomes, with perceptions and coping orientated toward potential failure (i.e. bracing for the worst). Another explanation for the difference can be found in the Common Sense Model.<sup>21</sup> This model proposes that people make mental representations of their illness using different sources of information, for instance from memory, social environment and somatic information. Mental representations may change with the increasing number of miscarriages. In this cognitive context, women with RM may benefit from coping strategies targeting reappraisal, such as PRCI. These findings support conclusions from a recent survey on the modes of support likely to be valued by women with RM.<sup>22</sup>

The use of the coping strategy 'brace for the worst', by which women try to control their emotions and future emotions as much as possible, has not previously been described among women with RM. However, in qualitative studies, similar behaviour has been reported such as "holding back emotions"<sup>23</sup> and "emotional cushioning".<sup>24</sup> In a longitudinal, qualitative study among 82 pregnant women who had experienced

loss, a number of comparable coping styles were reported.<sup>25</sup> For example, some women were hesitant to express their growing self-assurance because they were afraid to “jinx” their pregnancy and they delayed the announcement of pregnancy. The women in that study actively pursued many avenues to gain control and cope with the difficulties of their pregnancies. Kiwi<sup>26</sup> argued that patients with recurrent miscarriages might develop a protective emotional shield during pregnancy in an attempt to reduce the pain of impending loss. Norem and Cantor<sup>27</sup> described emotional cushioning as a process by which individuals protect themselves against threats to self-esteem in risky situations. The reason why women with SM did not use bracing is not clear. The differences could be caused by the fact that all women in the SM group were pregnant while most women in the RM group were not. Carroll et al.<sup>15</sup> proposed that bracing was an attempt to avoid disappointment and reflected the cognitive strategy of defensive pessimism. Women with SM still had hope for the future, seeing the first miscarriage as “bad luck”, and therefore experienced the new pregnancy as benign or a challenge.

In risky situations, two strategies can be used: defensive pessimism and an optimistic strategy.<sup>27</sup> Defensive pessimism is discounting of past successes and the lowering of expectations prior to entering a situation. In the optimistic strategy, the expectations are high at the outset with post hoc restructuring of the situation when the outcome is known.<sup>27</sup> It may be that women with SM were already using the coping style of positive reappraisal to deal with the current pregnancy. This optimism may explain the lack of bracing. Clearly all these future-oriented approaches theoretically overlap with bracing (and cushioning). However, our results and those from other studies concur that the particular characteristics of waiting for an ongoing pregnancy provoke specific cognitions and emotions that women may find difficult to manage because they refer to a future unknown, unpredictable and uncontrollable outcome. As such, more research attention should be devoted to this topic in relation to miscarriage and to whether bracing (and other future oriented coping strategies) leads to positive or negative emotions in women with SM or RM.

The uncertainty for women in the RM group increased with every new miscarriage. The relationship between the number of miscarriages and the level of anxiety in a subsequent pregnancy is unclear. Some studies find a positive relationship<sup>2</sup> and others no relationship.<sup>28 29</sup> In the present study, women used mainly emotion-focused coping styles to handle anxiety, which is consistent with the context. Terry and Hynes<sup>30</sup> argue that in low-control situations the use of emotion-focused coping is more effective than problem-focused coping. In contrast to our findings, in a longitudinal study of 82 women pregnant after previous miscarriage, the dominant

form of coping was problem-focused and women appraised their pregnancies as a moderate threat.<sup>30</sup> These differences may be explained by the timing of the assessments. Women entered that study during their 10th to 17th week of pregnancy. Lazarus and Folkman<sup>10</sup> reported that the longer the waiting period, the more the period was likely to be appraised as a threat. While the pregnancy is progressing, the waiting period becomes shorter. Time can be a variable that changes the coping styles.

The main weakness of the present study was the difference between the number of miscarriages and current pregnancy status, since all women in the SM group were currently pregnant compared with just one in the RM group. All women in the RM group had had a miscarriage 3 months or longer ago and they were all waiting for conception. All women in the SM group were at more than 12 weeks of gestation. A further weakness was the non-attendance and consequent reduced sample size. It is likely that non-attendance resulted in a less varied representation of miscarriage experience. The minimum acceptable number of focus groups and the sample size for each group in the literature is ambiguous.<sup>18, 32</sup> Halcomb et al.<sup>32</sup> advise at least two focus groups of each participant type and a group size between four and 12 participants. In our study, we used two focus groups and the final sample size (four and five) was still within an acceptable range.<sup>31</sup>

In conclusion, similarities and differences were found in the experiences of women with SM or RM. Despite the limitations of this study, the two core categories, bracing and uncertainty, were found to be important for women with RM in the waiting period for ongoing pregnancy. More research is required to understand whether modulating these coping strategies might reduce stress in women who have suffered RM. However, the presented findings indicate that the coping strategies adopted by women with recurrent miscarriage as they wait for confirmation of ongoing pregnancy are likely to be amenable to a specifically designed PRCI. A randomised study to assess whether this intervention can improve coping during this stressful waiting period is currently in progress.

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# Chapter 7

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*Pregnancy After Miscarriage: Balancing Between Loss of Control  
and Searching for Control*

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## Abstract

Pregnant women who have had miscarriages face challenges in responding to the loss of the previous pregnancy and the uncertainties of the early pregnancy that follows. The research question in this qualitative study was: How do women experience miscarriage, conception, and the early pregnancy waiting period, and what types of coping strategies do they use during these periods? Twenty-four women were interviewed in a subsequent pregnancy after having a miscarriage. Data analyses resulted in an overarching theme described as “balancing between loss of control and searching for control.” Although women realized there was little they could do to influence the outcome, they searched for strategies to increase the feeling of control in each period of waiting. The results of this study may contribute to interventions to support women during miscarriage and subsequent conception and pregnancy.

**Keywords:** Pregnancy, miscarriage, emotions, coping strategies, qualitative research.

## Introduction

The overall incidence of clinically recognized miscarriages is 15%, but the risk of miscarriage increases with age, rising from 9 % at 20-24 years to 75% at 45 years and older (Rai & Regan, 2006). A spontaneous abortion, or miscarriage, is defined as the spontaneous loss of a clinical pregnancy before 20 completed weeks of gestational age or if gestational age is unknown, the loss of an embryo/fetus of less than 400 g (Zegers-Hochschild et al., 2009). Six percent of women have two or more consecutive miscarriages (Rai & Regan, 2006; Zegers-Hochschild et al., 2009).

Women who become pregnant after miscarriage deal with three different waiting periods: the period from the pregnancy loss until the woman tries to conceive again (miscarriage period), the period between renewing the attempt to conceive and conception (conception period), and the period between conception and confirmation that the pregnancy is viable (pregnancy period). These waiting periods can be experienced as stressful because the outcome of each is unpredictable and difficult to manage (Boivin & Lancaster, 2010). Women with a history of miscarriages are uncertain whether a new pregnancy will occur and, if it does, whether another miscarriage will occur. The uncertainty brings anticipatory anxiety about the outcome (i.e., miscarriage or live birth).

In addition to physical trauma, sudden pain, blood loss, and unexpected admission to a hospital, miscarriages can result in psychosocial distress because of having lost a baby, having lost a future child, and having lost motherhood (Fertl, Bergner, Beyer, Klapp, & Rauchfuss, 2009; Lee & Slade, 1996). In a study of 81 women with recurrent miscarriages, 33% were depressed, 9.9 % moderately depressed, and 7.3% suffering from severe depression, and 21% had anxiety levels that were equal or higher to a typical psychiatric outpatient population (Craig, Tata, & Regan, 2002). Similarly, in a meta-analysis of psychological reactions to miscarriage, psychiatric morbidity was present in 27% of women (Adolfsson, 2011). In a qualitative study, women tried to find an explanation for the cause of the miscarriage but experienced inappropriate medicalization and inadequate professional support and follow up (Simmons, Singh, Maconochie, Doyle, & Green, 2006). However, results are conflicting on the intensity and duration of grief or depression, and on the influence on these reactions of a history of infertility, gestational age of the pregnancy, maternal age, number of prior reproductive losses, absence of living children, and availability of support (Brier, 2008; Lee & Slade, 1996; Lok & Neugebauer, 2007).

Although much is known regarding the experience of miscarriages, research into the conception period after miscarriage is limited. The duration of grief following

miscarriage decreases with a shorter conception waiting period (Brier, 2008), but stress or grief during the miscarriage and conception period does continue in subsequent pregnancy. Pregnant women with a miscarriage history have higher anxiety levels than women with no previous miscarriages (Geller, Kerns, & Klier, 2004; Gong et al., 2012; Tsartsara & Johnson, 2006).

Women with a miscarriage history may adopt a variety of coping strategies to deal with their emotions during the different waiting periods. In a study of 82 women with a history of pregnancy loss, a next pregnancy was appraised as a moderate threat, and women more often used problem-focused coping than emotion-focused coping strategies to deal with stress (Côté-Arsenault, 2007). In a qualitative study of 16 pregnant women with a history of miscarriage, women described distancing themselves from the pregnancy, focusing on pregnancy symptoms, searching for confirming information, and asking for professional and social support (Andersson, Nilsson, & Adolffson, 2012). In a focus group study with a sample of 9 pregnant women with a history of miscarriages, we found that women used a coping strategy of bracing for the worst, as an attempt to control their emotions and future emotions as much as possible in order to be prepared for the worst outcome of another miscarriage (Ockhuijsen, Boivin, van den Hoogen, & Macklon, 2013). Bracing is a future-oriented coping strategy and occurs as an attempt to anticipate unpleasant surprises, presumably to avoid disappointment of a negative outcome (Carroll, Sweeny, & Shepperd, 2006; Shepperd, Findley-Klein, Kwavnick, Walker, & Perez, 2000; Taylor & Shepperd, 1998).

Research to date has focused on either the miscarriage period or the subsequent pregnancy period, and less is known about the conception period between miscarriage and subsequent pregnancy. Furthermore, no research has covered the continuum of miscarriage, subsequent conception, and the early pregnancy waiting period. Therefore, the following question was formulated for this qualitative research: How do women experience the miscarriage, conception, and early pregnancy waiting periods, and what types of coping strategies do they use during these periods? The goal was to inform future interventions to respond to the emotions and enhance the coping strategies of women with a history of miscarriage.

## Methods

### Setting and Sample

Women attending an Early Pregnancy Unit and/or Recurrent Miscarriage Clinic in a university medical center in the Netherlands were invited by telephone to participate in this study. Patients who were interested received verbal and written information from the researcher, and those providing informed consent were included. The inclusion criterion was being pregnant or the wish to become pregnant again, and the sample was intentionally diverse in the number of miscarriages and age, both of which may influence emotions (Bergner, Beyer, Klapp, & Rauchfuss, 2008; Lee & Slade, 1996; Lok & Neugebauer, 2007). Distinctions were therefore made between women with 1, 2, 3 or more miscarriages, and women older or younger than 35 years of age. Exclusion criteria were not speaking the Dutch language, pregnancy after fertility treatment, and having a medical explanation for the miscarriages. Approval to conduct the study was obtained from the Ethical Committee of the university medical center.

Fifty-four women were invited to participate in this study, and 24 agreed to participate. Reasons for declining participation in the study were: participation would be an emotional or physical burden ( $n=11$ ), not knowing whether they wish to become pregnant again ( $n=7$ ), no interest in research ( $n=4$ ), and other reasons ( $n=8$ ). Reasons for participating were helping other women with a miscarriage experience and having the opportunity to tell their own stories.

The number of miscarriages women had experienced varied from 1 to 5 (Median=2). All women in the study were heterosexual and married or partnered. Only one woman had a living child. Age ranged from 27 to 38 years ( $M=33.2$ ,  $SD=3.0$ ). Educational level ranged from secondary school to university.

### Data Collection

All women were interviewed once after eight weeks of pregnancy. All interviews were performed by the same researcher. The duration of the interviews ranged from 40 to 76 minutes ( $M=61.1$ ,  $SD=9.0$ ). The semi-structured, face-to-face interviews were conducted in Dutch and focused on issues relevant to the miscarriage, conception, and pregnancy period. The interview schedule consisted of questions concerning the perspectives of women on emotions and coping strategies. Examples of interview questions were: “How did you experience the miscarriage(s)?” and “How did you cope with the period of waiting for a new pregnancy?” “How do you experience your pregnancy?” and “How do you cope with your current pregnancy?”. Prompts were

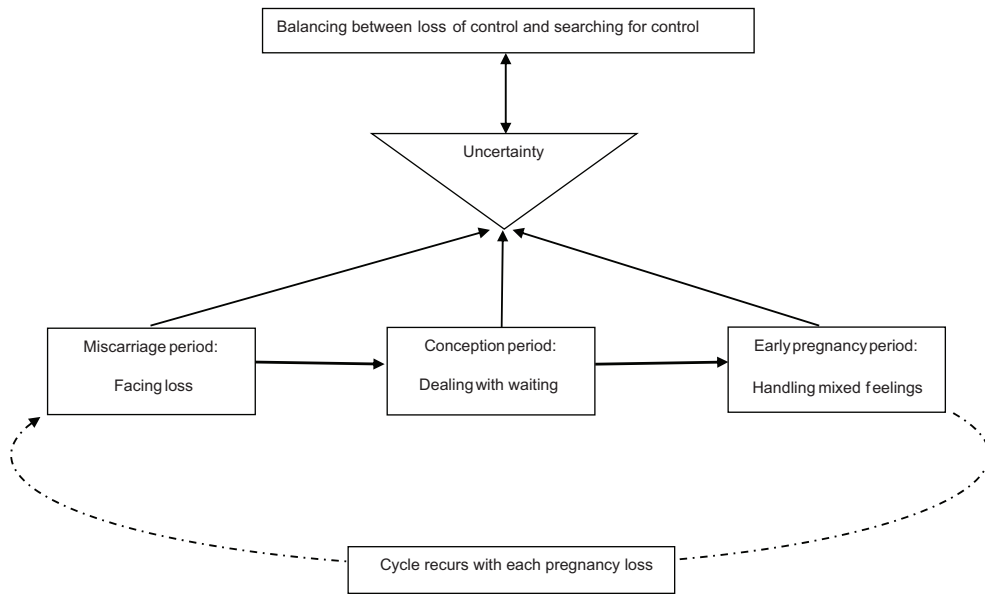
added to research questions to explore preliminary themes that emerged from the early interviews.

### **Data Analysis**

The interviews were tape-recorded and transcribed in full in the Dutch language. The interviews were organized and analyzed with the software program, MAXQDA 10 (Verbi Software GmbH Marburg). Thematic analysis was used to analyze the data (Braun & Clarke, 2006; King & Horrocks, 2010). The first stage was the descriptive stage, in which descriptive codes were identified by reading through the transcripts and highlighting relevant text fragments. The second stage was the interpretive stage, in which descriptive codes were clustered into interpretive themes by grouping together those that seemed to share common meaning. In the third stage, overarching themes were identified from the interpretive themes (King & Horrocks, 2010). Analysis was not a linear process but involved a constant moving back and forward between the coded extracts of data and the initial emerging themes. Themes were refined during further analysis and by discussion among the co-investigators. The analysis phase found its completion by comparison of the established themes with the entire data set (Braun & Clarke, 2006).

Memos and diagrams were developed during and after data analysis (Corbin & Strauss, 2008). To ensure the trustworthiness and quality of the findings, transparency, peer debriefing, and investigator triangulation were used (Holloway & Wheeler, 2010). Transparency was achieved by transcribing the interviews and by making field notes and memos, and peer debriefing by discussing the process of coding and developing themes with colleagues (FdB, AvdH and HO) proficient in qualitative research. The raw data were analyzed by two persons (HO and AvdH) followed by a consensus discussion (investigator triangulation). Member checking took place by asking the participants whether the summaries were an accurate reflection of participants' reality.

In presenting the results, each quotation is followed by age and number of miscarriages of the respondent. The researcher translated the quotations into English for this article, and translations were checked by a native bilingual speaker. The themes were grouped according to time frames following miscarriage, as indicated by women during the interviews, and are shown in Figure 1.



**Figure 1.** Overarching theme and period-specific themes during miscarriage, waiting for conception, and pregnancy after miscarriage.

## Results

### Balancing between Loss of Control and Searching for Control

This overarching theme links the interpretive themes specific to the miscarriage, conception, and pregnancy period. The experience of miscarriage, conception, and pregnancy waiting period was a cyclical process. After miscarriage, women felt that they had lost control over a very important goal in their lives, namely “having a child.” During a subsequent cycle, they feared to be confronted with the same emotions again. The resulting emotions led to uncertainty and imbalance during the different waiting periods. Uncertainty could be intensified due to factors such as the number of miscarriages, being older, a long conception waiting period, duration of pregnancy, absence of clear pregnancy symptoms, and fertility problems in the immediate environment.

In each waiting period, women realized there was little they could do to influence the outcome (i.e., the probability of a miscarriage, the duration of conception time, or occurrence of a viable pregnancy), but they searched for control, using coping strategies to increase the feeling of control to deal with the uncertainty. However, when they thought that they found a balance, for instance by becoming pregnant

again, new uncertainties arose. In order to deal with the renewed uncertainties and feeling of losing control, women searched for new strategies to find a balance again.

### **Facing Loss during the Miscarriage Period**

**Emotions.** After a miscarriage, women experienced all kinds of emotions because of the lost baby and the lost future they would have had with the baby. A miscarriage was perceived as life-threatening, because they had to deal with pain, blood loss, and sometimes treatment in a hospital. Miscarriage brought emotions such as anger, disappointment, sadness, feelings of failure, and anxiety. With every new miscarriage, feelings of uncertainty intensified. Not only the number of miscarriages but also the duration of the pregnancy before the loss affected their uncertainty. For instance, when the miscarriage occurred two weeks after the positive pregnancy test, the woman had hardly habituated to the idea of being pregnant.

*“The first was also an early miscarriage, that was just a disappointment, you do not know very much, you’re still a little inexperienced but it is becoming more difficult every next time.” [29-5]*

Women experienced powerlessness because they were forced to alter their personal goals. They had lived according to a life scheme in which they had planned the pregnancy at a certain moment in their lives, for instance, “I want to become pregnant before I am thirty,” or “I want to have two children who are close in age.”

*“At one point there is a kind of pressure, a self-imposed pressure that we regret that there will be a big age difference between the two children...with the third miscarriage..... I had actually rather waited but the age difference would have been so big.” [32-3]*

The miscarriage led to the feeling of lost control over the important goal of having a child:

*“And the whole society is so constituted that you should have control over everything and I think that’s the big..... that is what makes it so difficult for many people. And you just have no grip on it.” [33-2]*

**Searching for control when facing loss.** During the miscarriage period, women used diverse coping strategies to handle their emotions, including searching



for information, positively reappraising the situation, and seeking social support. They searched for information mainly to find an explanation for the cause of the miscarriage. Sources included the internet, books, and friends. Some women tried to find a medical explanation. However, for none of the women a clear medical reason was identified. On one hand, this was a relief for the women; on the other hand, the message led to the feeling that something was wrong, so they tried to find their own explanations, such as that their miscarriage was caused by their lifestyle, hard work, stress, or that they had failed as a woman.

*“I had worked very hard and I was very tired and I thought, may be that played a role.” [35-2]*

Another strategy was positive reappraisal. They re-evaluated the situation in light of the positive aspects of their lives before and after the miscarriage.

*“After the second miscarriage I prepared myself mentally I realized how good I have it already with a nice family, a good man, we are all healthy, have a good job..... you know, how grateful I should be for everything.” [32-3]*

A third strategy was seeking social support. Support was most needed for the process of grief, and was found in persons who were close to them, such as their partners, parents and (close) friends. Women perceived the most supportive persons to be women who had experienced miscarriages themselves. They felt a lack of support from people who made irrational comments like “the next time you will succeed” or “at least now you know that you can become pregnant.”

*“Well...yes...talked a lot about it with my boyfriend and friends. On the one hand it was fine, on the other hand not. None of my friends have experienced this, so it is quite difficult for them to understand. And then sometimes they said.....well at least you know that you can become pregnant....I got that kind of remark.” [27-3]*

### **Dealing with Waiting during the Conception Period**

**Emotions.** Women realized that other than adapting their lifestyles and timing sexual relations around ovulation, there was nothing they could do to influence the chance of becoming pregnant. They planned the subsequent pregnancy. They used ovulation tests or took their basal body temperatures to determine their fertile

window, and/or they had focused lovemaking. Uncertainty arose when they had to wait a long time until a pregnancy occurred. Women with a long conception waiting period again had the feeling of lost control over the goal of having a child.

*“The last time I was actually very impatient because after that last miscarriage it lasted a year and a half before we were pregnant again. So I thought it would take a year and a half again to become pregnant so we tried again a month after the miscarriage.” [34-3]*

Some women had spent years adapting lifestyle to improve the chance of a healthy pregnancy. During the conception period, women took vitamins and folic acid, stopped drinking alcohol, did not eat raw food, etc. The challenging lifestyle change was one of the reasons why the conception period was very difficult. After so many miscarriages, they wondered if adjusting their lifestyle was all worth it.

An emotion that was characteristic for this period was jealousy. Women with recurrent miscarriage who were waiting for a new pregnancy found it difficult to be confronted with other pregnant women and babies.

*“Just very jealous feelings towards others, very annoying but true....I very quickly began to avoid them.” [32-3]*

They expressed that they felt ashamed for this emotion. Some women forced themselves to attend baby showers, family gatherings, and occasions where they were likely to encounter children. Others avoided these occasions. The feeling of jealousy disappeared when they became pregnant again.

**Searching for control when dealing with waiting.** To achieve a degree of control over their emotions, women mainly used the coping strategies of distraction and seeking support. They used their jobs as a form of distraction but also focused on holidays, sports, and social activities.

*“I just wanted to avoid being too busy with it [becoming pregnant]; that was important for me because the more I was thinking about it, the more upset I became.” [31-2]*

Women searched for social and medical support during the conception waiting period. They had many medical questions, but the support from hospitals in this period was very limited and mainly focused on miscarriage, fertility problems, and pregnancies.

*“What always amazed me is that they [healthcare workers] do not talk about it [duration of the conception time] and especially when it takes a while before you get pregnant.... that phase between miscarriage and pregnancy I considered useless in the hospital, due to the fact that I thought you [health care workers] could give me some advice about at least the good moments, the ovulations. Of course you can search on the internet or read books, but it would have been nice to talk about it and to have some advice.” [34-3]*

Women also searched for alternative forms of support such as psychologists, acupuncturists, homeopaths, yoga teachers, and some used Chinese herbs. Some women took a break after having three miscarriages and waited until they were emotional and physical ready to get pregnant again.

*“Because mentally I knew that I should wait, that’s just better for me to reflect on everything that happened and to have some rest.” [27-3]*

### **Handling mixed feelings during the Pregnancy Period**

**Emotions.** Women reported a clear difference between the emotions in a first pregnancy and in subsequent pregnancies. During the first pregnancy, women had the feeling of living on a cloud. Everything was unreal to them, and they perceived this period as very positive. They fantasized about a future with the baby. They bought clothes for the baby, thought about names, searched on the internet, enrolled for nursery care, and took other preparations in anticipation of the birth. All women were aware of a possible miscarriage, but they had thought it would not happen to them. The first miscarriage came as a surprise.

*“I was living on a pink cloud and in seventh heaven, name all the cliché things, I was really happy and of course you know about miscarriages but I thought it would not happen to me.” [38-2]*

Feelings became mixed in pregnancy after one or more miscarriages. In the beginning of a new pregnancy, positive feelings arose, but very soon these feelings

were mixed with negative feelings, leading to uncertainty. As the number of miscarriages increased, the positive feelings decreased, and the negative feelings started to prevail. Women who had three or more miscarriages said that they did not feel positive at all in the beginning of the current pregnancy. In addition to the number of previous miscarriages, older age, a long conception waiting period, and fertility problems in the immediate environment increased their uncertainty in a next pregnancy. Women with mixed or negative feelings again had the feeling of losing control over having a child. "I feel miserable and stressed. I don't consider this pregnancy as fine. I can't enjoy it." [32-3]

**Searching for control to handle mixed feelings.** As a response to the mixed feelings, women searched for various possibilities to gain a sense of control after becoming pregnant again. They used a range of strategies, including observing and controlling strategies. Observing pregnancy symptoms (i.e. nausea, breast tenderness, tiredness) was very important for all women because they used it as an indicator of the continuing viability of the pregnancy. Certainty was increased when the symptoms were more intense than in the pregnancy that had ended in a miscarriage. Women who did not have stable or increasing pregnancy symptoms felt uncertain. Fluctuating symptoms during the day caused much anxiety and stress.

*"I am observing my body again and every time I think I don't feel my breasts anymore I am instantly afraid that it is wrong again." [31-2]*

Women repeatedly did pregnancy tests in the first weeks of pregnancy to see whether they had the same positive results.

Another important observation was the achievement of a personal milestone. When women reached a gestational point that was beyond previous pregnancies, they became more certain of the pregnancy's wellbeing. Observation of an ultrasound was very important. Ideally, the women wanted to determine the frequency of the ultrasounds, because it would give her a temporary certainty. Because a daily ultrasound was not feasible, they wished for a weekly ultrasound in early pregnancy, and expected that as time progressed, they would have more confidence based on an increasingly visible pregnancy and the feeling of movements of the unborn baby.

*"I think the whole uncertainty will go away at the moment that I can feel the baby itself....that something is moving in me, and as long as that is not there, the fluctuation between fear and joy remains." [29-5]*

Lifestyle adaptations were efforts to control the body. The women did not take any risks, for instance, they stopped engaging in sports or other strenuous physical activities. They improved their nutrition, stopped drinking alcohol, and took more rest or relaxing holidays. All their activities were focused on achieving a steadily progressing and healthy pregnancy.

Bracing was a self-protective strategy used to control emotions. Women with greater uncertainty due to a higher number of miscarriages relied more on this future-oriented coping strategy. The bracing strategies they used were both cognitive and social. They included not envisioning a future with the baby but living in the here and now, blocking thoughts about the pregnancy, distancing themselves from the social environment, controlling social support, reducing commitment to the unborn baby, and avoiding bonding or attachment with the fetus.

Women did not know whether bracing would help them to feel less grief if they had a miscarriage again, but they took no risk:

*“Yes, self-protection, it has been so difficult that I did not want to go through the same hell again if it goes wrong again.” [35-2]*

The more miscarriages they had experienced, the more they anticipated a possible miscarriage in the current pregnancy.

*“I [experience] less that the baby...lives in me....a word [lives] that I will not use soon...I do not allow that thought .....at [a] distance...that picture ... that little heart...with arms and legs and body so beautiful that you can see...I have experienced the previous miscarriages as traumatic.....if it goes wrong .....so that is why I do not see the baby as a living creature....I do not want contact with it.” [32-3]*

Women said that they felt guilty about these feelings.

*“Yes it makes me feel very guilty about it, beforehand, I feel like when the baby might be born that I do injustice to the baby a little.” [32-3]*

Some described bracing as “constructing a wall around them.” Only a limited amount of feelings related to the pregnancy were allowed to trespass the wall.

*“It keeps the joy away...since I have built that wall, just symbolic...it protects you against excessive joy which later you have to turn away...looking forwards to a child that is not going to come...and that wall helps you to keep away positive emotions ...and with the confidence that you are trying to build up, you slowly break down the wall that you earlier had built.” [32-3]*

Another form of bracing was to control the support they would be able to receive if there were to be a sad ending. For example, women who informed only a few people about the first pregnancy informed more people about the second pregnancy, in case it would end in a miscarriage again.

*“Well the advice is to wait twelve weeks before you tell everyone about the pregnancy, but I have noticed that the more people know, the more people there will be to support you.” [38-2]*

In contrast, women who had the feeling that they told too many people about the first pregnancy only informed a limited group of persons during the subsequent pregnancies.

*“There are some people whom I trust who know it already. I just do not want to be congratulated. During the first and second time I had informed more people.” [38-2]*

## **Discussion**

In this qualitative study of emotions and coping strategies of women during miscarriage, conception and early pregnancy waiting period, the overarching theme was “balancing between loss of control and searching for control.” This theme is broader than those found in previous research and links the interpretive themes of the three different waiting periods.

Similar aspects of this broad theme are found in other studies. In a qualitative study, 82 women with a history of perinatal loss were followed through their 25<sup>th</sup> week of gestation. Women used pregnancy calendars to chronicle their personal experiences (Côté-Arsenault, Donato, & Earl, 2006). A see-saw balancing act was the main theme and linked the four themes of fluctuating worry, growing confidence, interpreting signs and managing pregnancy. In another qualitative study of 16 women

with one or recurrent miscarriages, interviews were conducted in a subsequent pregnancy (Andersson et al., 2012). Themes included “distancing herself from her pregnancy” and “focusing on pregnancy symptoms.” An overarching theme of “we are not in control” was found in a phenomenological study of 42 women with a history of miscarriage (Wojnar, Swanson & Adolfsson, 2011). The women reported helplessness, powerlessness and lack of control over sustaining pregnancy while living through the unexpected loss of pregnancy prior to the point of fetal viability. The findings of these studies support the results of the current study. Adding to the existing evidence, we discovered that women make use of a variety of coping strategies to increase the feeling of control.

We identified the themes “facing loss” and “dealing with waiting” in the miscarriage and conception waiting periods. The emotions and coping strategies of those periods also have been found in other qualitative studies, including “trying to find an explanation for the miscarriage” (Simmons et al., 2006), and “problems with encountering other pregnant mothers and babies” (Wojnar et al., 2011).

Control was an important theme in this study and was reflected in specific strategies used by women in this sample. A sense of control is a central element of successful coping (Folkman, 2011). Individuals who are high on perceived control are more competent in handling stressful situations than individuals who doubt their capacities to influence events. Women who are competent in using a variety of control strategies would be expected to be more effective in handling uncertainty and the feeling of lost control than would women who do not use these strategies. More research is needed to confirm this possibility among pregnant women with a history of miscarriage.

A variety of coping strategies exists to manage stressful events (Lazarus & Folkman, 1984). Problem focused coping strategies are aimed at confronting and seeking solutions to the situation and are often used for the changeable aspects of a stressor (Folkman, 2011). Emotion-focused coping strategies focus on ameliorating the associated level of emotional distress and are often used for unchangeable aspects of a stressor (Folkman, 2011). Both coping styles may be used to manage the demands of a stressful encounter (Folkman & Lazarus, 1988).

We found that women used the coping strategy of bracing for the worst to increase the feeling of perceived control over grief that could arise again when confronted with another miscarriage. Bracing can be seen as a form of proactive coping, and it has been investigated in several populations (Shepperd et al., 2000; Taylor & Shepperd, 1998). Similar strategies have been described in other qualitative studies, including “holding back emotions” (Côté-Arsenault & Morrison-Beedy, 2001) and “distancing

herself from her pregnancy” (Andersson et al., 2012). “Emotional cushioning” (Côté-Arsenault & Donato, 2011) was positively correlated with pregnancy anxiety, in a mixed-method study of 63 pregnant women who had previously experienced perinatal loss. The increasing evidence on proactive coping suggests it creates measurable benefits in health and interpersonal outcomes (Folkman, 2011). Because bracing involves avoiding prenatal attachment, future research should focus on the impact of such strategies on bonding, attachment and parenting of the child.

Another important finding of this study is that women need support not only during the miscarriage and subsequent pregnancy period but also during the conception period. Women had many medical questions and said that support from hospitals was limited during this time. Supportive care of professionals can be helpful after miscarriage (Smith, Frost, Levitas, Bradley, & Garcia, 2006; Wojnar, Swanson, & Adolfsson, 2011) and in subsequent pregnancy (Andersson et al., 2012; Côté-Arsenault & Freije, 2004; Musters, Taminiu-Bloem, van den Boogaard, van der Veen, & Goddijn, 2011; Musters et al., 2013), when women are interested in early and frequently repeated ultrasounds,  $\beta$ HCG monitoring, practical advice concerning life style and diet, emotional support in the form of counseling, and medication (Munsters et al., 2011). Future research could focus on developing interventions for the conception waiting period.

The rigor of this study was established by in-depth interviews of 24 purposively selected pregnant women, data collection until no new themes were found, selecting women according to inclusion criteria, and a strong group process for data analysis. Another strength is that all women were interviewed during the first trimester of pregnancy, so key aspects of their experience were captured at the time of the events or soon afterward, reducing the risk of recall bias in retrospective data (Stone et al., 1998; Tennen, Affleck, Armeli, & Carney, 2000).

The transferability of study results is limited by our sample of predominantly highly educated women. Attempts were made to recruit less-educated women without success. Although less-educated women could have different emotions and coping strategies, the relevance of our findings to their experience was supported in a questionnaire study of 177 women, in which no differences were found in women from diverse educational levels in their preferences for supportive care after recurrent miscarriage (Musters et al., 2013).

Another limitation was the narrow age range of the participants. Although we aimed to recruit participants of diverse ages, the mean age was 33.2 years (SD=3.0, range: 27-38), and no women were younger than 27 or older than 38. The risk of having a miscarriage is lower for younger women, which could be a reason that they



were not well-represented (Rai & Regan, 2006), and older women have a decline in fecundity, so fewer would meet the inclusion criterion of pregnancy (Baird et al., 2005). Emotions and coping strategies may vary in different age groups, but we were unable to document such differences.

## Conclusion

This qualitative study gives insights into the experiences of three different waiting periods in women with a history of miscarriages. Women had lost control over a very important goal in their lives, having a child. These women were in need of professional support during all three waiting periods.

The results of this study could inform interventions to assist women to gain control and deal with the uncertainty in each period. The positive reappraisal coping intervention is a cognitive strategy that helps increase the feeling of control during periods of stressful uncertainty (Ockhuijsen, van den Hoogen, Macklon, & Boivin, 2013). This intervention could be refined for women undergoing the uncertainty of miscarriage, conception, and early pregnancy after miscarriage.

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# Chapter 8

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*Exploring a self-help coping intervention  
For pregnant women with a miscarriage history*

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*Submitted*

## Abstract

**Objective:** To investigate whether a Positive Reappraisal Coping Intervention (PRCI) and Daily Record Keeping (DRK) chart are appropriate for use in pregnant women with a history of miscarriage(s).

**Design:** A convergent parallel mixed method study.

**Setting:** An Early Pregnancy Unit and/or Recurrent Miscarriage Clinic in the Netherlands.

**Participants:** Pregnant women with a history of miscarriage(s).

**Methods:** Quantitative and qualitative data were obtained from pregnant women with one or more miscarriages. Women used the PRCI and DRK for three weeks in a subsequent pregnancy. Quantitative data were obtained from the DRK and were analysed by reporting frequencies and means for each case. Qualitative data were collected by semi-structured interviews and were analysed by using thematic analysis.

**Results:** The majority of the women were able to use the PRCI and DRK for three weeks. Women adapted the way in which they used the PRCI and DRK based on their judgment about the effect, the intensity of the emotions they experienced, or whether they felt the effort to use these instruments to be worthwhile or not.

**Conclusion:** This mixed method study is important for the design of any future RCT, it gives insights into how to model and refine the PRCI and DRK, as well as provide information about feasibility, reasons for drop out, and influencing context variables. PRCI and DRK can be used for pregnant women with a miscarriage history. A randomised trial is now required to assess the value of the PRCI in women with recurrent miscarriage.

**Keywords:** Coping intervention, Miscarriage, Pregnancy, Waiting period, Mixed method.



## Introduction

The risk of miscarrying is around fifteen percent and increases with age, 1-5% of women will suffer from recurrent miscarriages (RM) (Rai & Regan, 2006). A miscarriage or spontaneous abortion is defined as the spontaneous loss of a clinical pregnancy before 20 completed weeks of gestational age or, if gestational age is unknown, the loss of an embryo/fetus of less than 400 g (Zegers-Hochschild et al., 2009).

Miscarriage causes considerable distress not only because of the pain, blood loss and sometimes admission to the hospital but also because of the loss of the pregnancy, a baby and motherhood (Lee & Slade, 1996). The symptoms of anxiety and depression, which occur after miscarriage (Craig, Tata, & Regan, 2002; Klock, Chang, Hiley, & Hill, 1997; Magee, MacLeod, Tata, & Regan, 2003), may also extend into a subsequent pregnancy (Fertl, Bergner, Beyer, Klapp, & Rauchfuss, 2009). In a longitudinal study among 143 women, pregnant woman with a history of miscarriage had higher levels of pregnancy related fear and state anxiety during their first trimester compared to pregnant women without miscarriages (Fertl et al., 2009).

Supportive care from professionals can be helpful after a miscarriage (Wojnar, Swanson, & Adolfsson, 2011) but also in a subsequent pregnancy (Andersson, Nilsson, & Adolfsson, 2012; Cote-Arsenault & Freije, 2004; Musters, Taminiu-Bloem, van den Boogaard, van der Veen, & Goddijn, 2011; Musters et al., 2013). An internet survey of 305 women with a history of RM revealed fear of losing a future pregnancy to be the most prevalent concern according to 82% of these women (Séjourné, Callahan, & Chabrol, 2010). Women expressed the need for more supportive care from professionals not only after miscarriages but also in a new pregnancy (Séjourné et al., 2010). Interventions such as counselling sessions with nurses (Swanson, Chen, Graham, Wojnar, & Petras, 2009), psychological counselling (Nikcevic, Kuczmierczyk, & Nicolaidis, 2007) and a weekly ultrasound (Clifford, Rai, & Regan, 1997) are offered after miscarriage. A problem is that most interventions are very time consuming and not all patients are able to use or have access to these interventions. Therefore, while support is often provided to women after miscarriage it is less readily available during a subsequent pregnancy (Clifford et al., 1997; Nikcevic et al., 2007; Rowsell, Jongman, Kilby, Kirchmeier, & Orford, 2001; Swanson et al., 2009).

Lancastle & Boivin (2008) developed a self-help Positive Reappraisal Coping Intervention (PRCI) for use during medical waiting periods. A medical waiting period is common in health care that require patients to wait for results that are

potentially threatening to their well-being (Boivin & Lancaster, 2010). During the waiting period, patients have no control over the outcome, which often causes high levels of anticipatory anxiety and uncertainty that are difficult to cope with (Boivin & Lancaster, 2010).

Positive reappraisal coping is a meaning based coping strategy aimed at changing the meaning of the situation, in particular, reinterpreting the situation in a more positive way (Folkman, 2011; Lazarus & Folkman, 1984). Meaning-based coping strategies have been observed to be effective in contexts that involve a sustained period of unpredictability and uncertainty. Tedlie Moskowitz et al. (1996) and Folkman & Moskowitz (2000) observed that even in very stressful and uncertain situations such as caring for a terminally ill partner with HIV, participants who used meaning-based coping strategies like positive reappraisal also had positive emotions. The PRCI is based on the stress and coping theory of Lazarus & Folkman (1984) which proposes that the emotional response to a stressful situation is partly dependent upon expectations of the significance and outcome of the specific situation. A variety of coping strategies is employed to manage stressful events (Lazarus & Folkman, 1984). Problem focused coping strategies are aimed at confronting and seeking solutions to the situation, while emotion-focused coping strategies focus on improving the associated level of emotional distress. Meaning based strategies as used in PRCI (e.g., deriving benefit from adversity or focusing on the positive) are future orientated strategies that have been shown to be effective in situations that require sustained coping efforts when a stressor situation is uncontrollable and its outcome unpredictable (Folkman, 1997; Folkman & Moskowitz, 2004). This is the case in a subsequent pregnancy after experiencing miscarriages.

The PRCI was originally developed for the waiting period after an embryo transfer in a fertility treatment. The PRCI is a small card that contains ten positive reappraisal statements and a leaflet with a detailed explanation about this coping approach. As waiting for an on-going pregnancy after a previous miscarriage requires a sustained period of waiting, the PRCI could potentially also be a useful adjunct intervention for pregnant women with miscarriage(s) history.

To adapt and further develop the PRCI for women with miscarriages, the medical framework for developing complex interventions by the UK Medical Research Council (MRC) was used (Campbell et al., 2000; Craig et al., 2008). In a previous study, among women with a history of miscarriage(s), coping strategies and the perception of the PRCI was investigated in two focus groups (Ockhuijsen, Boivin, van den Hoogen, & Macklon, 2013). The PRCI could help women to cope as they wait for a subsequent pregnancy to be confirmed as on-going, but it is unclear

whether the PRCI developed or used in other clinical situations may need to be tailored to be effective in this context (Ockhuijsen et al., 2013).

Any study of the possible value of the PRCI in recurrent miscarriage patients will require the regular assessment of emotions and reactions. The Daily Record Keeping (DRK) chart represents such an instrument as it allows the daily rating of emotions and reactions during a pregnancy. The DRK has been shown to be appropriate for monitoring in the context of waiting for the results of fertility treatments, but has not previously been used in pregnant women with a history of miscarriage(s) (Boivin & Takefman, 1995). The aim of this study was to investigate whether a Positive Reappraisal Coping Intervention (PRCI) and Daily Record Keeping (DRK) chart developed for use in assisted conception treatment are appropriate for use in pregnant women with a history of miscarriage(s).

## Methods

### Design

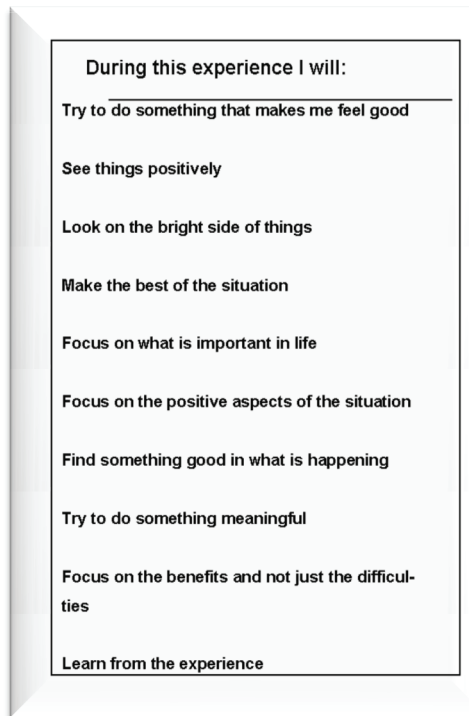
A convergent parallel mixed method study design was used to develop a more complete understanding of the use of the PRCI and DRK. In this design, qualitative and quantitative data are collected and analysed simultaneously, during the same period of the research process. The two sets of results are combined into an overall interpretation. This design also offers the opportunity to check whether the results of the quantitative and qualitative analysis, consisting of detailed views from participants and scores of instruments, are consistent with each other (Creswell, 2014; Holloway & Wheeler, 2010).

### Participants

Women visiting an Early Pregnancy Unit or Recurrent Miscarriage Clinic in a University hospital were invited by telephone to participate in this study. Women who had the wish to become pregnant again and were interested to participate received verbal and written information from the researcher and those providing informed consent were included. Because there is still a debate going on whether age and number of miscarriage influence emotions, distinctions were made in women with 1, 2, 3 or more miscarriages and women older or younger than 35 years of age (Bergner, Beyer, Klapp, & Rauchfuss, 2008; Lee & Slade, 1996; Lok & Neugebauer, 2007). Exclusion criteria were not speaking the Dutch language, pregnancy after fertility treatment and having a medical explanation for the miscarriages.

## Data collection

Women who consented to participate in the study were asked to contact the researcher as soon as possible after a positive pregnancy test. The pregnant women received verbal and written information about the use of the PRCI and DRK. The women used both instruments for three weeks. After this period, an independent investigator (HO) at a location selected by the participant interviewed them. The interview was semi-structured, questions were posed about the usefulness and practicality of the PRCI and DRK. Figure 1 shows the contents of the PRCI card.



**Figure 1.** Coping statements included in the PRCI intervention (contact author JB for complete intervention). © 2008 by Cardiff University. All rights reserved. No part of this document may be reproduced or transmitted in any form or by any means. Electronic, mechanical, photocopying, recording, or otherwise, without prior written permission of authors.

The DRK was used to rate the daily emotions during a subsequent pregnancy. The DRK comprises of 46 possible reactions to a waiting period, including 20 emotions, optimism and pessimism about pregnancy, 12 physical symptoms, five appraisals, and seven coping strategies. The emotional subscale is based on the theory of

Lazarus & Folkman (1984). Women scored each of the 20 emotion adjectives provided on the DRK (e.g., happy, sad, anxious) according to whether, and to what extent, they had felt that way in the previous 24 hours. In the present study, only the scores on positive and negative emotions, frequency of and the effect after reading the PRCI, were reported. Quantitative data were obtained by summing the ratings of the positive and negative emotion subscales that Folkman & Lazarus (1985) proposed to be the emotional counterparts of particular appraisals of a situation. Negative emotions comprised threat (e.g., tense, worried) or harm emotions (e.g., sad, discouraged) whereas positive emotions referred to challenge (e.g., hopeful, positive) or benefit emotions (e.g., content, happy) (Folkman & Lazarus, 1985). Participants were instructed to complete the DRK at the end of the day and at least one hour after reading the PRCI card to limit the chance of DRK ratings being artificially and transiently influenced by completing the DRK.

### **Data analysis**

The IBM SPSS Statistics Package 20 was used to perform the statistical analysis of the DRK. Quantitative data of the DRK were obtained by calculating frequencies and means for each case.

The interviews were tape-recorded and transcribed in full. Thematic analysis was used to analyse the qualitative data (Braun & Clarke, 2006; King & Horrocks, 2010). First, descriptive codes were identified by reading through the transcripts and highlighting relevant material. The second, interpretive stage involved clustering into interpretive codes by grouping together descriptive codes that seems to share common meaning. In the third stage a number of overarching themes are identified built upon the interpretative themes (King & Horrocks, 2010). The interviews were organised and analysed with the software program, MAXQDA 10 (Verbi Software GmbH Marburg). To ensure the trustworthiness and quality of the findings an audit and decision trail was used (Holloway & Wheeler, 2010). A detailed record and description was made before and during the research process, which makes it possible for other researcher to judge the validity of the study. The interviews were fully transcribed, field notes and memos were made, and peer review and debriefing was carried out by three investigators (FdB, AvdH and HO) proficient in qualitative research. One researcher (AvdH) reanalysed the raw data and identified emerging themes with another investigator (HO). Member checking took place during the interviews by asking the participants whether the summaries were an accurate reflection of participants' reality. Method triangulation took place by examining the results of the qualitative and quantitative data sources and their coherence (Creswell,

2014). The researcher translated the quotations from the participants for this article, after which it was checked by a native bilingual speaker.

### Ethical approval

Permission to conduct the study was obtained from the Ethical Committee of the University of Utrecht in the Netherlands.

**Table 1.** Clinical characteristics participants.

Name	Age	Number of pregnancies	Number of children	Number of miscarriages	Duration Pregnancy at interview	Highest education
Agnes	32	2	0	1	10	University
Bea	33	2	0	1	9	University
Claire	35	2	0	1	10	Secondary School to A level
Diana	31	3	0	2	10	Higher Education Qualification
Elly	38	3	0	2	9	University
Fijgje	30	3	0	2	10	University
Gerda	35	3	0	2	10	University
Hilde	27	4	0	3	13	University
Iris	37	5	0	3 & 1 abortion	9	Higher Education Qualification
Jacky	34	4	0	3	9	Higher Education Qualification
Karin	29	6	0	5	11	University
Laura	44	3	0	2	---	---
Marian	35	4	0	3	---	---

### Results

Forty-two women were invited to take part in this study, and 13 agreed to participate. Reasons for declining participation in the study were: perceived burden of participation (n=10), not knowing whether they wish to become pregnant again (n=7), no interest in research (n=4), or other reasons (n=8). Thirteen women received the PRCI and DRK. The duration of the interviews ranged from 59 to 76 minutes. The women included in this study used the PRCI and DRK for three weeks in a subsequent pregnancy. Two of the thirteen women used the PRCI and DRK but did not want to be interviewed due to either having miscarried again or citing a too

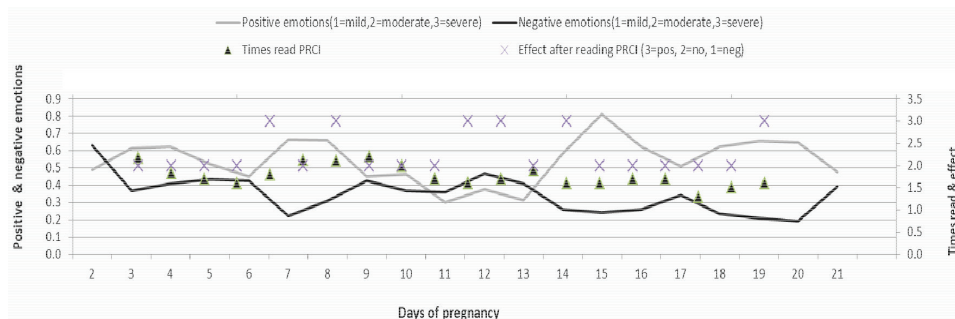
busy schedule. One of these two women did not send back the DRK forms. The clinical characteristics of the participating women are shown in table 1. Women started using the instruments immediately upon obtaining a positive pregnancy test. All women were interviewed after 8 weeks of pregnancy. The women in the study are heterosexual.

### DRK results

In the next section, the results of the quantitative data are presented. Key data are depicted graphically showing positive and negative emotions, frequency of reading the PRCI and perceived effect after reading the PRCI. A varied number of graphs are explained by describing the interview responses of participant about using the instruments.

#### Overall scores of the 12 participating women

The overall analysis of DRK charts showed that women had higher scores for positive than negative emotions, on a mean of 16 out of 21 days (Figure 2). Most participants used the PRCI twice a day, although some used it more, some less. The mean score of using the PRCI per day was 1.78 (SD=0.24). On 6 out of 21 day's women felt a positive effect after reading the PRCI. None of the participants reported the PRCI as having a negative effect on emotions.

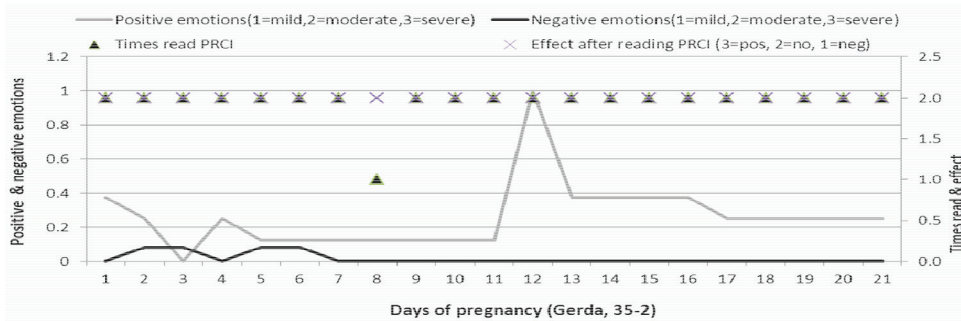


**Figure 2.** Overall scores of the 12 participating women.

#### Example of using PRCI according to leaflet

Gerda used PRCI twice a day for 20 days (Figure 3). During the interview, Gerda described the PRCI as being easy to use in the beginning but it became more difficult for her to use it as the three weeks progressed. The key positive event for her was a positive first ultrasound on day 12 of her pregnancy as this boosted her confidence in

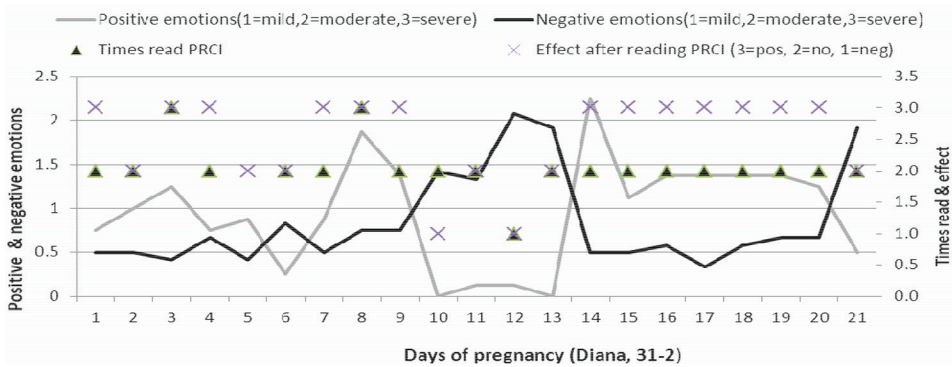
the prognosis for the pregnancy. Gerda reported that she was not aware of an effect of the PRCI but stated she could imagine that it may have subconscious effects.



**Figure 3.** PRCI use according to leaflet.

*Example of an association between perceived effect of PRCI and emotions*

Diana did not always use the PRCI twice a day (Figure 4). On days when there were more positive emotions she perceived an effect and when there were more negative emotions she perceived no effect. During the interview, Diana reported that the use of the PRCI had a positive effect. The PRCI matched with her own coping strategy and although DRK was a confrontation with her emotions, it was easy to use. However, on two days, she reported a negative effect of reading the card. She had vaginal bleeding during these days.

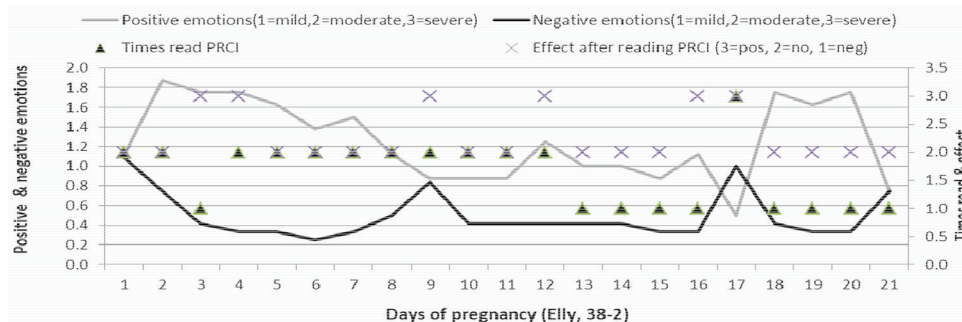


**Figure 4.** Association between perceived effect of PRCI and emotions.



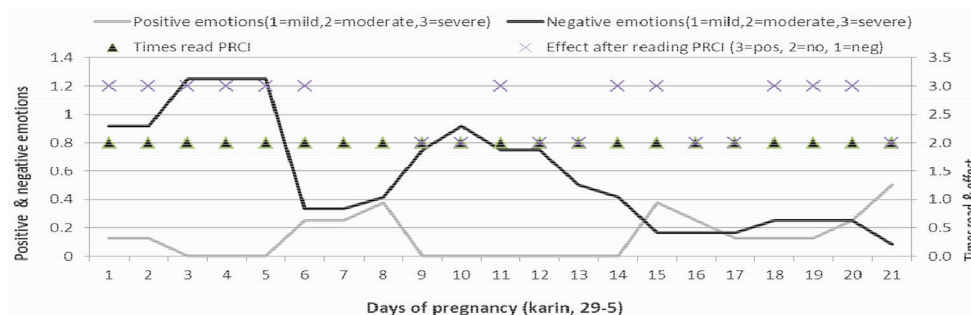
*Examples of disassociation between the perceived effect of PRCI and emotions*

Elly reported higher positive emotions on all days except on day 17 but she experienced a positive effect after reading the PRCI on only 6 days (Figure 5). During the interview, Elly mentioned that she was very positive about the use of the PRCI although she also had to get used to using it. She found it difficult to rate the effect because the effect was not always perceived directly after reading the card but later in the course of the day.



**Figure 5.** Disassociation between the perceived effect of PRCI and emotions.

Although Karin had higher negative than positive emotions on 17 days, she noted a positive effect after reading the card on 12 days (Figure 6). Karin reported that she had had five previous miscarriages and was particularly nervous during the first weeks of her pregnancy. On the days that she felt very uncertain, the PRCI did not appear to help her. However, on days when a positive event occurred, such as a viable ultrasound scan, it had an additional positive effect on her mood.



**Figure 6.** Disassociation between the perceived effect of PRCI and emotions.

## Results of the interviews

The overarching themes that were found in the analysis of the interviews were “adapted use of PRCI and DRK” and “feasibility and practicality of PRCI and DRK.” Interview quotations are displayed within each theme. Each quotation is followed by a fictitious name, age and number of miscarriages of the respondent (see Table 1).

### *Adapted use of the PRCI*

Women had adapted the use of the PRCI, from that was suggested on the leaflet, by reducing the number of days they used the PRCI, increasing or decreasing the times a day they read the PRCI and applying positive reappraisal in their own way and not with the instrument. PRCI use was adapted based on their judgment about the effect of the instrument, the intensity of the emotions they experienced, and depending on whether they felt the effort to use this instrument to be worthwhile or not.

Women, who were positive about the PRCI, reported a positive impact on their emotions. Other women felt that PRCI was aligned with their own coping strategy, as they already used positive reappraisal. For these women, PRCI was easy to use and they used it as suggested on the leaflet.

*“I must say that I found it very enjoyable because I have a history with a lot of positive thinking in it. You know, thinking differently and those kind of things. So it fitted really nice”. [Diana, 31-2]*

The PRCI was also adapted based on women’s judgment about the effect of the PRCI. Some felt that PRCI did had an effect, it encouraged positive thinking, but the effect was only notable on starting using it, and soon disappeared. Some women found a period of three weeks unnecessary or excessive and used PRCI for a shorter period. Women, who felt more confident that the pregnancy was progressing well, stopped using the PRCI or used it just once a day. None of the women experienced a negative effect of the PRCI, but some reported experiencing no effect. Reasons suggested for not feeling an effect was a lack of stress at the time of use or about the pregnancy per se. For these women the motivation to continue with the PRCI was less.

*“I’m really honest. I definitely tried it especially the first week....but it did not have an effect on me”. [Jacky, 34-3]*

*“Yes, I did use it for two weeks with a break of half a week in the middle. I found myself..... I feel good about the pregnancy and I had the thought yes I can use this card but yes ...it ... ehhh ..... I’m feeling good about the pregnancy so I do not have to do those exercises to feel better”. [Agnes, 32-1]*

The frequency of using the PRCI was altered according to the intensity of the emotions women felt. For instance, women who experienced negative emotions were stimulated to use the PRCI more frequently. Other women reminded themselves of the statements on the PRCI or just tried to think positive without using the statements on the card.

*When I felt again that I was restless and tensed, then I tried to turn it in a positive twist for myself....I can start feeling negative all the time but what is the effect....so I was thinking of fun things and good things and then I became really happy and felt calmer”. [Iris, 37-3]*

Women also adapted the PRCI on whether they felt the effort to be worthwhile or not. Women who experienced severe pregnancy symptoms were not able to use PRCI twice a day for three weeks. Women with other time consuming issues like those that had a seriously ill family member did not had the time to use PRCI twice a day.

#### *Adapted use of the DRK*

Some women used the DRK as an instrument to measure emotions while other women adapted it as an intervention.

*“I just registered but there has not been a negative or positive feeling”. [Fijgje, 30-2]*

Women who adapted the DRK as an intervention said that the DRK gave them a kind of awareness and understanding of emotions and it also influenced their emotions. The use of the DRK could have a positive but also a negative effect. Certain statements of the DRK gave women a good feeling for example, “I accepted there was nothing I could do” and “I have what it takes to cope with this experience”. Some women experienced the DRK as a marker of the duration of the pregnancy. Other women felt more positive because they could rate pregnancy symptoms on the DRK.

*“The positive awareness of the fact that it is good. But that’s true in my case and feel good and have the ... for me because I have positive confirmation because of the nausea...that’s where I get confidence from....then it’s a piece of positive awareness of the fact that it goes well”. [Claire, 35-1]*

Women indicated that the use of the DRK could also have a negative effect. If they had registered fewer pregnancy symptoms, they became more uncertain.

*“What I noticed was that when I had fewer symptoms I became uncertain”. [Fijgje, 30-2]*

Other women indicated that it gave negative feelings when they could rate so little positive emotions all those weeks. Seeing the rated list of negative emotions was confrontational. As a response, women started thinking about it and some women tried to control their emotions. For instance, women who mainly rated negative emotions tried to find ways to feel better.

*“That if you rated the negative words that you thought o .... confrontational and also I do not want to feel that way”. [Diana, 31-2]*

The DRK was also adapted based on whether women felt the effort to be worthwhile or not. The reasons were the same as for the PRCI. Women who experienced severe pregnancy symptoms or other time consuming issues were not able to use DRK every day.

#### *Practicality and feasibility of the PRCI and the DRK*

Most women found PRCI and DRK practicable and easy to read. PRCI was not small enough to put in a purse. The completion of the DRK did not take a lot of time, about five minutes a day. Some women found the PRCI and DRK a little old fashioned and suggested how it might be ‘updated’.

*“It would be even nicer if you get such statements sent via your mobile phone. You have to carry the card with you and you can lose it”. [Diana, 31-2]*

In the beginning, some women had to get used to work with the PRCI. Some found it difficult to remember to read the card, others found it a bit artificial or forced.

*“I had to get used to it. It was the first week ... I had put it next to my bed so that I really was aware of it in the morning and evening ... at one point it was more...the second and third week it became much easier. It's becomes a part of your day”. [Hilde, 27-3]*

Not all statements on the PRCI were experienced as good. Women had personal preferences but seven people indicated that the statement “learn from experience” did not fit the situation.

*“There were statements I was annoyed by. “Learn from experience”. I cannot really feel that. No ..... I have no need now for something to learn from this experience”. [Iris, 37-3]*

There was one statement on the PRCI “Try to do something that makes me feel good” that women used to develop the coping strategy distraction. Women really tried to do something that made them feel good like baking cookies.

*“Try to do something that makes me feel good” that is also a nice one, you become aware that you have a choice, look good deep inside and what do I need now.....I will make oatmeal raisin cookies tonight then I will have some goodies all week. So be aware of what I like and I would stand in the kitchen to bake cookies as a distraction”. [Claire, 35-1]*

On the DRK women were asked to rate the effect of the PRCI in minutes. The majority of the women found it difficult to determine the effect. The effect just after reading the PRCI was not always very long but during the course of the day, women reminded themselves about positive thinking.

*“I found it difficult to estimate but then I thought, yes I have been positive for a while and felt more positive or conscious by omitting the negative thought and I thought you have been doing this for half an hour or an hour, so that were the variations I made. Because then it disappears again to the background”. [Bea, 33-1]*

Another problem women mentioned was the rating of the emotions on the DRK. Women found it difficult to distinguish between emotions because of the pregnancy or other emotional events.

*“I found it difficult to separate the pregnancy from other situations within my family. So when completing emotions ... yes I’m really sad, but not because of the pregnancy”. [Agnes, 32-1]*

## Discussion

The aim of this study was to investigate whether a Positive Reappraisal Coping Intervention and Daily Record Keeping chart developed for use in assisted conception treatment are also appropriate for use in pregnant women with a history of miscarriage(s). To investigate these instruments a convergent parallel mixed method study was used. The main findings were that the PRCI and DRK could be used for pregnant women with a history of miscarriage but that women adapted the use of these interventions to fit in with their own needs.

The quantitative and qualitative data supported each other but each method delivers its own unique contribution in understanding how women experienced and used the PRCI and DRK. Outcome from both the quantitative and qualitative data shows that PRCI and DRK can be used for pregnant women with a miscarriage history. Women who are pregnant after having miscarriages can have the feeling of lost control (Andersson et al., 2012). PRCI is developed for waiting periods, where there is no control over the outcome and difficult to cope with. Women found both instruments practicable and feasible, PRCI was never experienced as negative, PRCI sometimes lead to more positive emotions, and some women used PRCI more often when they felt negative.

Some women used DRK as an instrument to measure emotions as intended, whereas other women adapted it and used it as an intervention and consequently experienced a positive or negative effect of rating daily their emotions, physical symptoms, appraisal, and coping. Research shows that self-monitoring has been utilized as a form of intervention or has a therapeutic effect because of the reactivity effects (Korotitsch & Nelson-Gray, 1999; Shiffman, Stone, & Hufford, 2008; Tennen, Affleck, Armeli, & Carney, 2000). Reactivity is defined as the potential for behaviour or experience to be affected by the act of assessing it (Shiffman et al., 2008). Reactivity effects may make an adjunctive contribution to beneficial treatments effects when used in the context of other interventions (Korotitsch & Nelson-Gray, 1999). Computerised methods that do not allow participants to review their recording can minimise this effect (Tennen et al., 2000). Validity and reliability of the DRK has been investigated in different studies (Boivin, 1997) and also in the Netherlands but within a different study population (de Klerk et al., 2005). The findings of this study are important for the design of any future RCT. In developing a RCT, the potential positive or negative impact that may occur by using the DRK should be taken into account. Ultimately, it may influence the outcome of an investigation.

Although clear verbal and written instructions were given about the use of the PRCI, women also adapted their use of this tool. Adaptation of the PRCI was based on the judgment regarding the effect of the PRCI, the intensity of the emotions they experienced, or whether they felt the effort to use the instruments to be worthwhile or not. This finding is consistent with a qualitative study exploring the experiences of participants in a RCT for nicotine vaccination. Throughout the RCT participants tinkered with discourses, objects, and activities to make them serve their individual goals (Wolters, de Wert, van Schayck, & Horstman, 2014). The divergence between individual project and research project obstructed neither process, nearly a third of all participants managed to quit smoking (regardless of whether they were in the intervention or placebo group).

This form of self-adaptation may occur because of how people evaluate their coping resources. The findings of our study are consistent with the stress and coping theory of Lazarus & Folkman (1984) and other functional approaches to coping. According to Folkman (2011) secondary appraisal is the process by which one evaluates the ability of the self to cope with existing resources. Secondary appraisal evaluates the likelihood that a given coping strategy accomplishes what it is supposed to do and the likelihood that one can apply a certain strategy effectively (Folkman, 2011). When women anticipate to use the copings strategy positive reappraisal they evaluate the likelihood that positive reappraisal is effective and whether they can apply it effectively. This evaluative process necessitates an appraisal of self-efficacy. Perceived self-efficacy is concerned with judgments of how well one can execute courses of action required to deal with prospective situations (Bandura, 1982). When a woman is capable of handling positive reappraisal and judges the PRCI as effective, then she will continue using the instrument. Women can increase their sense of self-efficacy by modifying skills (e.g., use PRCI in their own way), and/or increasing actions (e.g., use PRCI more often).

This study combined quantitative and qualitative methods. The value of the quantitative data was that the graphs of the observed DRK results (daily positive and negative emotions) gave insights in the perceived effect after reading the PRCI (ratings of the intervention). Sometimes there was an association between the perceived and observed effect, in other days or for different women there was a disassociation between the perceived and observed effect. The value of the qualitative data is that the different patterns in the graphs could be understood by the information as presented in the interviews. Furthermore, the interviews gave a broader and deeper understanding of how women experienced and used the PRCI and DRK. In this study we found that in some cases there was a disassociation



between the perceived effect or appraisal of PRCI and observed emotional reactions (quantitative DRK ratings). Some women with high negative emotions perceived a positive effect of the PRCI and some women with high positive emotions perceived no effect after reading the card. This difference is likely to be due to the fact that the two methods were targeted at different components of the waiting experience. Negative emotions could seem incongruent with positive evaluations of PRCI (e.g., helpful, useful) if one assumes that emotions were a consequence of using PRCI. However, if strong negative emotions were instead due to waiting and driving the need to use PRCI then positive perceptions of PRCI in a negative emotional environment would be explainable. Reassuringly, PRCI was never perceived to have led to a negative effect. The interviewed women also gave a few possible explanations for the disassociation. Some women were not negative about their pregnancy. They mainly had positive emotions and these emotions were not caused by the use of the PRCI. Other women reported that PRCI did not always have an effect straight after reading the card but during the course of the day. Women also said that they could imagine that PRCI may have subconscious effects which they could not report on the DRK.

The strength of this project is that it is one of the stages that is recommended within the MRC framework for the development of complex interventions (Campbell et al., 2000; Craig et al., 2008). Within this framework, it is advised to model and refine an intervention and assess its feasibility before carrying out a RCT. There is a growing awareness of the role that qualitative research can play alongside Randomised Controlled Trials (RCT) (Lewin, Glenton, & Oxman, 2009). A qualitative method before a trial can be used to develop or refine the intervention, develop appropriate outcome measures, generate hypotheses or explore issues related to the healthcare question (Lewin et al., 2009). The results of this study give insights into how to model and refine the PRCI and DRK, as well as provide information about feasibility, reasons for drop out, and influencing context variables. This information could be useful when designing a RCT for PRCI but also for other types of interventions.

Another strength of this study is the use of a mixed method study design in which both qualitative and quantitative methods were used. Although there is still a debate about whether to combine or not these two approaches with different epistemological and ontological assumptions, a shift already has happened in program evaluation research like education and health care programs (Dattilio, Edwards, & Fishman, 2010; Johnson & Onwuegbuzie, 2004; Ostlund, Kidd, Wengstrom, & Rowa-Dewar, 2011). Although Randomised Controlled Trials constitute an important source of evidence about the efficacy of treatments, clinical settings often differ from those in

which treatments were tested (Dattilio et al., 2010). A RCT is not necessarily able to provide insights or understanding of how individual symptoms are maintained, how a treatment works (mechanism of change) and/or the process around the treatment use (Dattilio et al., 2010). By using a mixed method of combining qualitative and quantitative approaches, similarities and differences between particular aspects of a phenomenon can be explored (Ostlund et al., 2011).

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# Chapter 9

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## *General discussion*

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## General discussion

In healthcare patients often have to deal with many kinds of waiting periods that could be potentially threatening (Lancastle & Boivin, 2008). Waiting periods are stressful because the outcome is often unpredictable, uncontrollable and difficult to cope with (Boivin & Lancastle, 2010). The studies reported in this thesis investigated two different waiting periods, the waiting period following fertility treatment and one in early pregnancy after previous miscarriage. Although many interventions exist to support women during fertility treatment or early pregnancy, few focus on helping women to cope with difficult waiting periods (Ockhuijsen et al., 2013a, Ockhuijsen et al., 2013b). The positive reappraisal coping intervention (PRCI) was developed specially for medical waiting periods (Lancastle, 2006).

The first part of the thesis described the quantitative studies that were focused on the waiting period in an IVF/ICSI treatment. The overall aim was to investigate the effect of the PRCI on psychological well-being of women waiting for the outcome of an IVF/ICSI treatment. The second part of the thesis described the qualitative methods to assess the waiting period in early pregnancy of women with a history of miscarriage. The overall aim was to explore whether the PRCI could also be an adjunct intervention for women with a history of miscarriage in a subsequent pregnancy.

### Main findings of the PRCI for the waiting period in an IVF/ICSI treatment

- Women who used the PRCI and daily record keeping (DRK) during the waiting period of IVF/ICSI treatment reported significantly more positive emotions but not significantly less anxiety, depression or negative emotions.
- Women who used the PRCI and DRK during the waiting period of IVF/ICSI treatment significantly reported more challenge appraisals and increased their use of the coping strategies positive reappraisal, distraction and relaxation.
- Use of the PRCI had no significant effect on treatment outcome when delivered in combination with DRK.
- Women who used the PRCI intervention without DRK during the waiting period of IVF/ICSI treatment had significantly lower anxiety levels during the waiting period and six weeks after the start of the waiting period.



- Use of the PRCI had a significant effect on clinical pregnancies when delivered without concurrent use of the DRK.
- Women who used the PRCI intervention during the waiting period of IVF/ICSI treatment evaluated the PRCI as acceptable and practical, and women perceived a psychological benefit to its use.

### **Main finding of the PRCI for the waiting in early miscarriage**

- Two core categories, “uncertainty” and “bracing”, are important for women facing waiting periods after a history of miscarriage.
- Three interpretive themes described as “facing loss”, “dealing with waiting” and “handling mixed feelings” and one overarching theme described as “balancing between loss of control and searching for control” emerged out of the qualitative data of pregnant women with a history of miscarriage.
- Women with a history of miscarriage were able to use the PRCI and DRK in the first weeks of their pregnancy. PRCI was never described as a negative experience.
- Women adapted the way in which they used the PRCI and DRK based on their judgment about the effect, the intensity of the emotions they experienced, or whether they felt the effort to use these instruments to be worthwhile or not.

### **PRCI for waiting periods**

Quantitative and qualitative data show that waiting periods are stressful and that women are in need of an intervention to make the waiting period bearable. Waiting for the outcome of fertility treatment was perceived to be stressful and was associated with an increase in general anxiety and depression and negative emotions specific to treatment. These results are consistent with other studies on artificial reproductive technology (ART) (Boivin & Takefman, 1995, Boivin & Takefman, 1996, Yong et al., 2000) which show that women appraise the waiting period as a potential threat and as causing related anticipatory negative emotions (e.g., feelings of worry, tension, nervousness).

The results of the studies show that the PRCI achieved what it was designed to do, namely to sustain a positive outlook, sustained challenge appraisals and the daily use of positive reappraisal coping and increased positive emotions during the 14 days of

waiting for a pregnancy test result following fertility treatment. No other RCT studies were found with a comparable coping intervention within the same population. Two RCT's investigated a self-help coping interventions based on distraction techniques during waiting periods but no coping strategies were evaluated (Bennett et al., 2007, Phelps et al., 2013). Participants in the intervention group with high baseline stress had a significant reduction of distress (Bennett et al., 2007) and had significantly lower intrusive thoughts but only among those with low and moderate intrusive worries at baseline distress (Phelps et al., 2013).

The waiting period in early pregnancy was also experienced as stressful. Pregnant women with a history of miscarriage reported changing emotions as gestation progressed. In the beginning of a new pregnancy positive feelings emerged, but very soon these feelings were mixed with negative feelings leading to uncertainty. With the increase of the number of miscarriages, the positive feelings decreased and the negative feelings increased. Other studies confirm these findings. Women with a miscarriage history have higher anxiety levels in a subsequent pregnancy than women with no previous miscarriages (Geller et al., 2004, Gong et al., 2013, Tsartsara & Johnson, 2006).

Women with a history of miscarriages who used the PRCI in the waiting period of a subsequent pregnancy never experienced it as negative. In contrast, the PRCI sometimes lead to more positive emotions, and some women used PRCI more often when they felt negative. Women, who were positive about the PRCI reported a positive impact on their emotions. Other women felt that PRCI was aligned with their own coping strategy, as they already used positive reappraisal. Reasons suggested for not feeling an effect was a lack of stress at the time of use or stress about the pregnancy per se. No comparable interventions for the waiting period in early pregnancy have been found. Several studies have investigated the influence of psychosocial interventions in women who experienced miscarriage (Clifford et al., 1997, Nikcevic et al., 2007, Rowsell et al., 2001, Swanson et al., 2009). Most have focussed on the period immediately following miscarriage (Nikcevic et al., 2007, Rowsell et al., 2001, Swanson et al., 2009). There is less data relating to support during the first trimester of a subsequent pregnancy (Clifford et al., 1997). Interventions such as counselling sessions with nurses (Swanson et al., 2009), psychological counselling (Nikcevic et al., 2007) and a weekly ultrasound (Clifford et al., 1997) have been shown to reduce anxiety and depressive symptoms.

Research supports that pregnant women with a history of miscarriage(s) are in need of supportive care. A telephone interview with women with unexplained recurrent miscarriages, twenty different support options were identified, of which 16 were

preferred for their next pregnancy (Musters et al., 2011). Among the preferred supportive care options were early and frequently repeated ultrasounds,  $\beta$ HCG monitoring, practical advice concerning life style and diet, emotional support in the form of counselling, a clear policy for the upcoming 12 weeks and medication.

## Methodological issues

In this thesis both quantitative and qualitative methods were applied, consistent with the approach advised by the Medical Research Council (MRC) framework (Campbell et al., 2000, Craig et al., 2008). Strengths and limitations of the different studies as well as recommendations for clinical practice and future research are discussed below.

## Strengths

There are several strengths discussed within the different qualitative and quantitative studies. A general strength of the work presented in this thesis is the development of the PRCI which was based on the MRC framework for developing complex interventions (Campbell et al., 2000, Craig et al., 2008). Within this framework, it is advised to model and refine an intervention and assess its feasibility before carrying out a RCT. The original MRC-framework distinguishes five phases but within the iterative phased approach qualitative and quantitative methods are connected (Campbell et al., 2000, Craig et al., 2008). The first stages of the model are examined in another thesis (Lancastle, 2006). In this thesis the effect of the PRCI was investigated for the waiting period in a fertility treatment. A fully-defined intervention was compared to an appropriate alternative using a protocol that is theoretically defensible, reproducible in a study that is adequately controlled with appropriate statistical power.

Because the PRCI had not been previously used in pregnant women with a history of miscarriage, qualitative studies were initially conducted. There is a growing awareness of the role that qualitative research can play alongside randomised controlled trials (RCT) (Lewin et al., 2009). Using qualitative methods before a trial can aid the development or refinement of the intervention, aid the identification of appropriate outcome measures, generate hypotheses and aid the exploration issues related to the healthcare question (Lewin et al., 2009). The results of the presented

studies do not only give insight in how to model and refine the PRCI and DRK, but also provide information about feasibility, reasons for drop out, and influencing contextual variables. This information may be useful when designing a RCT for use of PRCI in early pregnancy.

During the work covered in this thesis, the added value of using qualitative designs before conducting quantitative studies became clear. The RCT about the effectiveness of the PRCI during the waiting period in an IVF/ICSI treatment showed that the PRCI did what it was designed to do namely to sustain a positive outlook (positive emotions, challenge appraisals, use of positive reappraisal coping) but PRCI had no effect on anxiety or depression levels of women waiting for the outcome of their fertility treatment cycle (Ockhuijsen et al., 2014). In a parallel qualitative study, interviews among women with miscarriage showed that the use of the DRK was affecting emotions, as if the DRK itself was an intervention (unpublished data). Women reported during the interview that the DRK gave them a certain awareness and understanding of emotions and may have influenced their emotions. This qualitative study revealed that the use of the DRK could have a positive but also a negative effect. If daily monitoring is perceived to be an intervention then the lack of difference observed in the IVF/ICSI study between the PRCI and the monitoring-control group could have been due to active effects of monitoring or the possibility that active effects attenuated or obscured effects of the PRCI intervention in unknown ways. Further, the PRCI benefits may have arisen secondary to an interaction between PRCI and monitoring. In light of these qualitative findings, it was decided early in our RCT to add a PRCI-comparison group that received the PRCI but did not complete daily monitoring. This group was not randomised so as to avoid undermining the design of the original trial, but followed the same procedures as if randomised. Women in this fourth, non-randomised PRCI-comparison group had significantly lower anxiety levels at day 10 of the waiting period and six weeks after the start of the waiting period compared to the randomised groups and also had a significantly higher clinical pregnancy rate compared to the other three groups. A future RCT in which the PRCI-comparison group is randomised could strengthen this interpretation and could help investigate the potential beneficial effects of daily monitoring of emotional reactions during the waiting period.

Another strength of our study is that not only retrospective assessments but also ecological momentary assessment (EMA) techniques were used. EMA is a collection of methods for obtaining repeated real-time assessments of subjects' behaviour and experience in their natural environments, to minimise recall bias, maximise ecological validity, and document variation over time (Shiffman et al., 2008). In the quantitative

and qualitative studies the DRK chart was used. In the qualitative studies women were interviewed during the waiting period in early pregnancy, only the data about miscarriage and conception waiting period were from a retrospective point of view.

## Limitations

Both the qualitative and quantitative studies presented do suffer from certain limitations. A recurring limitation could be considered to be the samples used in different studies. An optimal sample is not always feasible to obtain due to many factors. Within the quantitative studies, the opt-in method was used to recruit participants on the advice of the Ethics Committee. In this method participants are sent an invitation to the trial and if interested asked to contact the research team using the reply form or email address provided, which differs from the more conventional opt-out approach where all patients are contacted about the trial unless they have contacted the team to indicate that they do not wish to be approached. Although the opt-out method improves recruitment, ethical committees often do not approve this method because repeated contact is too burdensome for participants (Junghans et al., 2005; Treweek et al., 2010). Another limitation concerning samples is the use of a non-randomised group. A non-randomised group is a threat for internal validity due to selection bias and history (Dimitrov & Rumrill, 2003). Post-test differences could be due to characteristic differences between groups. In a qualitative study the sample consisted out of predominantly highly educated women we were not able to recruit lower or middle educated women.

Another limitation concerning samples could be considered to be the participation of patients from only one hospital. We chose to recruit in only one hospital because this university hospital attracts patients from all over the country. However, as there is collaboration with other clinics nationwide inferences about the generalisability of findings can be determined via comparison of patient characteristics collected as part of wider collaborations.

## Recommendations

The results of the different studies need to be considered in light of the strengths and limitations and should also be considered for clinical practice and future research.

The patterns of results, theoretical, empirical and methodological considerations, together indicate that the PRCI, a simple low cost self-help coping intervention, can be offered to women during the waiting period in an IVF/ICSI treatment to sustain a positive outlook on the waiting period. The PRCI not only has an effect on emotions and coping strategies but also is inexpensive and easy to administer. PRCI is self-administered, comprises a sheet of A4, and can be implemented at a time when patients are not in contact with the medical team or other patients for more interpersonal forms of support. Knowledge about the PRCI within a fertility treatment or in pregnant women with a history of miscarriages should be shared and disseminated.

Future research should focus on:

- A randomised control trial with an intervention group that used only the PRCI without daily monitoring.
- The relation between positive emotions and resilience to stress.
- The use of PRCI during other medical waiting periods.
- The development of a Dutch coping questionnaire specific for fertility problems.

Women with a history of miscarriage are in need of support during the different waiting periods. Women with recurrent miscarriage who wait for confirmation of on-going pregnancy use coping strategies that are likely to be amenable to PRCI. Pregnant women with a history of miscarriage found PRCI practicable and feasible and PRCI was never experienced as negative.

Future research should focus on:

- A randomised control trial to assess the effect of PRCI on psychological well-being for women with a history of miscarriage in early pregnancy. Such a study is now underway in the UK.
- The effects and benefits of the use of the coping strategy bracing.
- The developing of interventions for the conception waiting period.

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# Chapter 10

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*Summary*

*Nederlandse samenvatting*

*Dankwoord*

*Curriculum Vitae*

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Patients who make use of healthcare services have to deal with all kind of waiting periods like waiting for the results of a biopsy or waiting for the results of a fertility treatment. Waiting periods can cause high levels of distress because the outcomes of these waiting periods are often unpredictable, uncontrollable and difficult to cope with.

Aim of this thesis was to investigate a Positive Reappraisal Coping Intervention (PRCI) for waiting periods within two different populations. The PRCI is an intervention comprising of an explanatory leaflet and 10 statements, to be read at least once in the morning and once in the evening. The PRCI is investigated among women during an IVF/ICSI treatment and among pregnant women with a history of miscarriages.

## **Chapter 1**

Aim of this first chapter was to describe the background and development of the PRCI, the methodologies used to investigate the PRCI and aims of the thesis. The development of the PRCI is based on the MRC framework for developing complex interventions and based on the stress and coping theory of Lazarus & Folkman.

## **Chapter 2**

In the second chapter a study protocol is described to investigate the PRCI for women waiting for the results of a fertility treatment. The objective of this study was to describe the design and methodological challenges of a three-armed randomised controlled trial (RCT) to investigate the effects of the PRCI on psychological well-being of women waiting for the outcome of their fertility treatment cycle. In this chapter the background of the intervention, recruitment, sample size calculation, randomisation process, study measures and statistical analysis are described. Furthermore strengths and limitations of the study are discussed.

The study protocol also describes the investigation of a fourth non-randomised group (chapter 4). During recruitment for the RCT it was decided to add a fourth non-randomised group, a PRCI-comparison group that received the PRCI and completed the questionnaires but did not complete daily monitoring. The decision to add this group was based on preliminary results of on-going qualitative research with the PRCI and daily monitoring among pregnant women with a history of miscarriages (chapter 8).

### **Chapter 3**

The aim of the study described in chapter 3, was to investigate the effect of the PRCI on anxiety, depression and daily emotions in women awaiting the outcome of an IVF/ICSI treatment. In a three-armed RCT, 377 women were randomised to receive either PRCI and daily emotional monitoring, daily emotional monitoring only, or routine care. To investigate the impact of the PRCI all three groups completed questionnaires at three time points: just before the waiting period, on day 10 of the 14-day waiting period and 6 weeks after the start of the waiting period. To investigate the specific impacts of PRCI on the days of the waiting period the PRCI-monitoring and the monitoring-control group also rated daily, for the 14-day waiting period, their emotions and reactions. Women reported more symptoms of anxiety and depression during the waiting period than before the waiting period. The use of the PRCI did not reduce anxiety or depression, or daily negative emotions during the waiting period but women who used the PRCI reported more positive emotions during the waiting period. Women reported that the intervention was easy to use and had a positive psychological effect. No differences were found between groups in treatment outcome.

### **Chapter 4**

The objective of this study was to evaluate the effects of a PRCI-comparison group that used only PRCI compared to its use combined with monitoring emotions, monitoring emotions alone or no intervention. One hundred and ten participants were recruited after recruitment of the three randomised groups had been completed. Outcomes were compared with those generated by a RCT of the PRCI. Women in the PRCI-comparison group had a significantly lower anxiety at Time 2 and Time 3 but not significantly lower depression levels. The PRCI-comparison group also had a significantly higher clinical pregnancy rate but there were no significant differences in clinical pregnancies with foetal heartbeat.

### **Chapter 5**

In this chapter the effect of the PRCI on coping strategies in three hundred seventy-seven women awaiting the outcome of an in vitro fertilisation cycle was tested in a three-armed randomised controlled trial. Patients were randomised to one of the three experimental groups. Coping strategies like positive reappraisal, acceptance, distraction, relaxing were measured with a Daily Record Keeping (DRK) form and the Way of Coping Questionnaires. Women who used the PRCI intervention during the waiting period of IVF used more positive reappraisal, distraction and relaxation

coping strategies. PRCI produced the effects for which it was designed as it helped sustain a more positive outlook on the waiting period when waiting for potentially threatening medical test results.

## **Chapter 6**

The aim of the qualitative study described in this chapter was to understand how women with single or recurrent miscarriages coped during the waiting period after miscarriage, waiting for pregnancy or waiting for pregnancy confirmation and to investigate their perception of a PRCI designed for waiting periods. Data were obtained from two focus groups comprising women with one or more miscarriages. Two core categories, “uncertainty” and “bracing”, emerged out of the data. Women who had experienced a single miscarriage appraised the waiting period for confirmation of an ongoing pregnancy as benign but women with recurrent miscarriages could not appraise the waiting period as benign and used bracing as their coping strategy. With this coping strategy, women tried to control their emotions, and looked into the future to try to minimize their distress if a further miscarriage occurred. All women thought that the PRCI would be practical and applicable during waiting periods but only women with recurrent miscarriages actually wanted to use such an intervention.

## **Chapter 7**

The aim of the study in chapter 7 was to gain insight into emotions and coping strategies during miscarriage, conception, and early pregnancy waiting period. Twenty four women were interviewed in a subsequent pregnancy after having a miscarriage. Data-analyses resulted in three themes and one overarching theme. The three themes were “facing loss during miscarriage period”, “dealing with waiting during conception period” and “handling mixed emotions during pregnancy period”. The overarching theme “balancing between loss of control and searching for control” relates the themes of the miscarriage, conception, and pregnancy period. Although women realized they lost control and that there is not much they can do to influence the outcome of their efforts, they searched for strategies to increase the feeling of control. The results of this study could lead to developing or refining existing interventions to support women during conception, miscarriage, and pregnancy period.

## **Chapter 8**

In this chapter we described a mixed method study in which we combined quantitative and qualitative data. The objective of this mixed method study was to investigate

whether a PRCI and DRK are appropriate for use in pregnant women with a history of miscarriage(s). Thirteen women used the PRCI and DRK for three weeks in a subsequent pregnancy. Quantitative data were obtained from the DRK and were analysed by reporting frequencies and means for each case. Qualitative data were collected by semi-structured interviews and were analysed by using thematic analysis. The majority of the women were able to use the PRCI and DRK for three weeks. Women adapted the way in which they used the PRCI and DRK based on their judgment about the effect, the intensity of the emotions they experienced, or whether they felt the effort to use these instruments to be worthwhile or not. Some women used DRK as an instrument to measure emotions as intended, whereas other women adapted it and used it as an intervention and consequently experienced a positive or negative effect of rating daily their emotions, physical symptoms and coping.

## **Chapter 9**

The main findings of the thesis are discussed in chapter 9. In addition methodological issues and recommendations for clinical practice and future research are presented.



# Chapter 10

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*Summary*

*Nederlandse samenvatting*

*Dankwoord*

*Curriculum Vitae*

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Patiënten die gebruik maken van de gezondheidszorg krijgen te maken met allerlei wachtperiodes zoals het wachten op de uitslag van een biopsie of het wachten op het resultaat van een vruchtbaarheidsbehandeling. Wachtperiodes kunnen leiden tot hoge stressniveaus en zijn moeilijk om mee om te gaan omdat het uiteindelijke resultaat niet te controleren of te voorspellen is. Doel van dit proefschrift is het onderzoeken van een Positieve herwaardering Coping Interventie (PRCI) voor wachtperiodes in twee verschillende populaties. De PRCI is een interventie die bestaat uit 10 stellingen en een informatiefolder en moet ten minste één keer in de ochtend en één keer in de avond gelezen worden. De PRCI is onderzocht bij vrouwen in een IVF/ICSI-behandeling en bij zwangere vrouwen met een geschiedenis van miskramen.

## **Hoofdstuk 1**

Het doel van dit hoofdstuk is het beschrijven van de achtergrond en de ontwikkeling van de PRCI. De methodes voor het onderzoeken van de PRCI zijn beschreven en er wordt een overzicht gegeven van de doelstellingen van dit proefschrift. De ontwikkeling van de PRCI is gebaseerd op het MRC raamwerk voor het ontwikkelen van complexe interventies en op basis van de stress en coping theorie van Lazarus & Folkman.

## **Hoofdstuk 2**

In het tweede hoofdstuk wordt een beschrijving gegeven van een studie protocol om de PRCI te onderzoeken bij vrouwen die wachten op de resultaten van een IVF /ICSI behandeling. Het doel van deze studie is het beschrijven van het design en de methodologische uitdagingen van een driearmige gerandomiseerde gecontroleerde studie naar de effecten van de PRCI op het psychisch welbevinden van vrouwen die wachten op het resultaat van hun vruchtbaarheidsbehandeling. In dit hoofdstuk zijn de volgende aspecten beschreven: achtergrond van de interventie, werving van deelnemers voor het onderzoek, de berekening van de steekproefgrootte, de randomisatie procedure, de metingen en de statistische analyses. Verder worden sterke en zwakke punten van de studie besproken.

Het studieprotocol beschrijft ook het onderzoek van een vierde niet gerandomiseerde groep (hoofdstuk 4). Tijdens het werven voor de gerandomiseerde studie werd besloten een vierde niet gerandomiseerde groep toe te voegen. Deze vierde groep gebruikt alleen de PRCI zonder de dagelijkse monitoring van emoties. De beslissing om deze groep toe te voegen is gebaseerd op de eerste resultaten van



een kwalitatieve studie over de PRCI en het dagelijks monitoring van emoties bij zwangere vrouwen die miskramen hadden ervaren (hoofdstuk 8).

### **Hoofdstuk 3**

Het doel van deze studie is na te gaan wat het effect is van de PRCI op angst, depressie en dagelijkse emoties bij vrouwen die wachten op het resultaat van een IVF/ ICSI behandeling. In een driearmige studie werden 377 vrouwen gerandomiseerd voor de PRCI en dagelijkse emotionele monitoring, alleen dagelijkse emotionele monitoring of de standaard zorg. Om het effect van de PRCI te onderzoeken hebben drie groepen vragenlijsten ingevuld op drie tijdstippen: vlak voor de wachtperiode, op dag 10 van de 14-daagse wachtperiode na het terugplaatsen van een embryo en 6 weken na het begin van de wachtperiode. Om de specifieke effecten van de PRCI te onderzoeken hebben de vrouwen in de PRCI-monitoring en de monitoring controle groep gedurende de 14-daagse wachtperiode dagelijks hun emoties en reacties geregistreerd. Alle vrouwen hadden meer symptomen van angst en depressie tijdens de wachtperiode dan vóór de wachtperiode. Het gebruik van de PRCI had geen effect op het verminderen van angst, depressie of negatieve emoties maar patiënten die de PRCI gebruikten hadden wel meer positieve emoties tijdens de wachtperiode. Vrouwen rapporteerden dat de interventie eenvoudig was in het gebruik en het had een positief psychologisch effect. Er zijn geen verschillen gevonden tussen de groepen in het uiteindelijke resultaten van de behandeling.

### **Hoofdstuk 4**

Het doel van deze studie is het onderzoeken van de effecten van een PRCI groep die alleen de PRCI gebruikte zonder de dagelijkse monitoring van emoties ten opzichte van groepen die wel dagelijks emoties registreerden of de standaardzorg kregen. Honderdtien vrouwen hebben meegedaan aan dit onderzoek. De resultaten van deze groep zijn vergeleken met de uitkomsten van de driearmige gerandomiseerde gecontroleerde studie. Vrouwen, die alleen de PRCI gebruikten zonder dagelijkse monitoring van emoties, hadden lagere angst niveaus op dag 10 van de wachtperiode en zes weken na het begin van de wachtperiode en ook meer klinische zwangerschappen in vergelijking met de andere drie groepen.

### **Hoofdstuk 5**

In deze driearmige gerandomiseerde gecontroleerde studie is het effect van de PRCI onderzocht op coping strategieën van 377 vrouwen die wachten op het resultaat van een vruchtbaarheidsbehandeling. Patiënten werden gerandomiseerd

in één van de drie experimentele groepen. Coping strategieën zoals positieve herwaardering, acceptatie, afleiding zoeken, ontspanning werden gemeten met een dagelijks registratie formulier (DRK) en een algemene coping vragenlijst. Vrouwen die tijdens de wachtperiode van een IVF/ICSI behandeling de PRCI toepasten, gebruikten vaker de coping strategieën positieve herwaardering, afleiding en ontspanning. PRCI produceert de effecten waarvoor het is ontworpen. PRCI helpt om positiever te blijven tijdens het wachten op een eventuele bedreigende uitkomst van een medische behandeling.

## **Hoofdstuk 6**

Het doel van de kwalitatieve studie die beschreven wordt in dit hoofdstuk is te onderzoeken hoe vrouwen met één of meerdere miskramen omgaan met de wachtperiode na een miskraam, het wachten op een nieuwe zwangerschap en het wachten op een doorgaande zwangerschap. Verder is de mening van deze vrouwen gevraagd over de PRCI die speciaal ontworpen is voor wachtperiodes. De gegevens voor dit onderzoek zijn verkregen met behulp van twee focusgroepen bestaande uit vrouwen met één of meerdere miskramen. Twee belangrijke categorieën, “onzekerheid” en “bracing”, zijn voortgekomen uit de gegevens. Vrouwen die één miskraam hadden ervaren, beoordeelden de wachtperiode voor een doorgaande zwangerschap als onschuldig, maar vrouwen met meerdere miskramen beoordeelden de wachtperiode niet als onschuldig en gebruikten bracing als hun coping strategie. De vrouwen proberen met de coping strategie bracing hun toekomstige emoties te beheersen door te anticiperen op een eventuele nieuwe miskraam. Door bracing te gebruiken hoopten de vrouwen dat het verdriet van een eventuele toekomstige miskraam zou verminderen. Alle vrouwen vonden de PRCI praktisch en toepasbaar voor de wachtperiode, maar alleen vrouwen met meerdere miskramen hadden behoefte aan een dergelijke interventie.

## **Hoofdstuk 7**

Het doel van de studie in hoofdstuk 7 is inzicht te krijgen in de emoties en coping strategieën gedurende de miskraam, conceptie en vroege zwangerschap wachtperiode. Vierentwintig vrouwen zijn geïnterviewd in een zwangerschap nadat ze één of meerdere miskramen hadden ervaren. Data-analyse resulteerde in drie thema's en één overkoepelend thema. De drie thema's zijn “geconfronteerd worden met verlies in de miskraam periode”, “omgaan met wachten tijdens de conceptie periode” en “hanteren van gemengde emoties tijdens de zwangerschap periode”. Het overkoepelende thema “balanceren tussen het verlies van controle en het zoeken

naar controle” verbindt de thema’s van de miskraam, conceptie en zwangerschap periode. Vrouwen met een geschiedenis van miskramen realiseerden zich dat ze de controle verloren hadden en dat ze niet veel konden doen om het resultaat van een wachtperiode te beïnvloeden. Vrouwen zochten naar strategieën om het gevoel van controle te verhogen. De resultaten van dit onderzoek zijn belangrijk voor het ontwikkelen of verfijning van bestaande interventies om vrouwen te ondersteunen tijdens de conceptie, miskraam en zwangerschap wachtperiode.

### **Hoofdstuk 8**

In dit hoofdstuk wordt een zogenaamde mixed method studie beschreven waarin zowel kwantitatieve als kwalitatieve data zijn gebruikt. Het doel van deze mixed method studie was te onderzoeken of de PRCI en DRK ook gebruikt kunnen worden bij zwangere vrouwen met een geschiedenis van miskramen.

Dertien vrouwen met een geschiedenis van miskramen gebruikten de PRCI en DRK gedurende drie weken in het begin van een zwangerschap. Kwantitatieve gegevens werden verkregen met behulp van de DRK. Kwalitatieve gegevens werden verzameld met behulp van semigestructureerde interviews en geanalyseerd door gebruik te maken van thematische analyse. De meerderheid van de vrouwen waren in staat om de PRCI en DRK gedurende drie weken te gebruiken. Vrouwen pasten het gebruik van de PRCI en DRK aan, op basis van hun oordeel over het effect van de PRCI, de intensiteit van de emoties, of dat de inspanning om de instrumenten te gebruiken de moeite waard was. Sommige vrouwen gebruikten de DRK als een instrument voor het meten van emoties zoals bedoeld, andere vrouwen gebruikten de DRK als een interventie en ondervonden een positief of negatief effect door het dagelijks registreren van hun emoties, lichamelijke symptomen en coping strategieën.

### **Hoofdstuk 9**

De belangrijkste bevindingen van het proefschrift worden besproken in hoofdstuk 9. Daarnaast worden de methodologische problemen en aanbevelingen voor de klinische praktijk en toekomstig onderzoek gepresenteerd.



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Na 4 jaar werken aan dit onderzoek is eindelijk het eindpunt in zicht. Gedurende die periode heb ik met veel mensen samengewerkt en nu krijg ik de gelegenheid om deze mensen te bedanken. Zonder jullie hulp was dit niet gelukt!

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Henriëtta, Dorothea, Louisa Ockhuijsen was born in Utrecht, the Netherlands August, 16<sup>th</sup>, 1963. After graduating from secondary school at the “Oosterlicht college” in Utrecht she started her nursing education at Slotervaart Hospital, Amsterdam, which she completed in 1986. After graduating she followed an oncology nursing training at the VU hospital in Amsterdam which she completed in 1989. Hetty worked as an oncology nurse at the VU hospital in Amsterdam until 1993. In 1993 she started working at the University Medical Centre Utrecht at the division Women and Baby. She worked at the gynaecology department as a nurse and senior nurse until 2006. During that time she obtained two bachelor degrees, in management (1999) and Innovations in Health care (2002), at the University of Applied Sciences Utrecht. She graduated cum laude from the University of Utrecht with a Master of Science in Nursing in 2006. In 2006 she started working as a nurse specialist and in 2009 as a nurse researcher at the department of reproductive health at the University Medical Centre Utrecht. Hetty received an ESHRE nursing award in 2008 and 2013. Hetty works as a lecturer in the premaster program of Clinical Health Science.