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The 'Pleasure&Pregnancy' web-based interactive educational programme versus expectant management in the treatment of unexplained subfertility: protocol for a randomised controlled trial

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ABSTRACT

Introduction Many subfertile couples are diagnosed with (relatively) unexplained subfertility and a good prognosis. National professional guidelines (eg, the Netherlands and UK) advise 'expectant management (EM)' for 6–12 months, in which no interaction with healthcare staff is offered. Underpowered studies indicate that face-to-face sex-counselling increases the ongoing pregnancy rates of these couples. In patients with other conditions, web-based interactive educational programmes have the same effect on sexual functioning as face-to-face sex counselling. The 'Pleasure&Pregnancy randomised controlled trial (RCT)' will examine in couples with unexplained subfertility and a good prognosis whether a new web-based interactive educational programme results in a higher chance of naturally conceiving an ongoing pregnancy within 6 months as compared with EM.

Methods and analysis A multicentre RCT with cost-effectiveness analysis will include heterosexual couples diagnosed with (relatively) unexplained subfertility and a good prognosis in Dutch and Belgian secondary or tertiary fertility clinics. Couples will be randomised between 6 months of EM and 6 months of the Pleasure&Pregnancy-programme. This new web-based interactive educational programme includes eight progressive modules of information (on the biology of conception and pleasurable sex) and sensate focus, couple communication and mindfulness exercises. Couples are offered interaction with their coaches via email and can take part in three moderated chat sessions with peers. The primary outcome of this RCT is the probability of naturally conceiving an ongoing pregnancy within 6 months after randomisation. Secondary outcomes include time-to-pregnancy, live birth rate, costs, sexual functioning and personal and relational well-being. Analysis will be according to intention to treat.

Ethics and dissemination This study has been approved by the Medical Ethical Committees of the Academic Medical Centre (the Netherlands) and the Leuven University Hospital (Belgium). The findings of this RCT will be disseminated through presentations at international scientific meetings and peer-reviewed publications.

Trail registration number NTR5709; Pre-results.

Strengths and limitations of the study

- This is an adequately powered multicentre randomised controlled trial (RCT).
- Selection and selective reporting bias has been limited.
- The pathway based on which the programme is expected to work will be examined.
- Acceptance of the hypothesis of this RCT, would have major impact on clinical practice.
- Only the statistician is blinded, which can be considered a limitation.

INTRODUCTION

Subfertility or the inability to conceive after at least 1 year of unprotected intercourse, affects one in 10 heterosexual couples and about half of them will seek medical help.[1] About half of the couples turning to fertility clinics are diagnosed with (relatively) unexplained subfertility as their diagnostic fertility work-up shows tubal patency, an ovulatory cycle and more than three million progressive sperm per ejaculate.[2 3] The prognosis of couples with unexplained subfertility is considered 'good' if the validated model of 'Hunault' predicts at least 30% chance of naturally conceiving a live born child within a year after diagnosis.[3] In these couples, starting with intra-uterine insemination with controlled ovarian stimulation immediately after diagnosis has no added value.[4] Therefore, guidelines of several

national professional associations (eg, the Netherlands, the UK) advise to offer couples with unexplained subfertility and a good prognosis 'expectant management' (EM) rather than medically assisted reproduction (MAR) for at least 6 months in.[3 5 6] None of these guidelines advice to provide couples any interaction with healthcare staff during EM.[3 5 6]

An underpowered randomised controlled trial (RCT) (n=20) and a case-control study (n=17 cases) suggest that offering face-to-face sex-counselling rather than EM increases the ongoing pregnancy rates of couples with unexplained subfertility (respectively: 35% vs 11% within 12 months and 60% vs 11% within 18 months).[7 8] These preliminary findings are plausible as they can be explained by a series of findings from larger scale cohort studies. More specifically, subfertile couples have limited coital frequency (on average 7x/month)[9] and coital frequency affects the probability of natural conception.[10] In addition, sex counselling proved to improve the sexual functioning of couples with other conditions (ie, prostate cancer of men; ie low sexual desire of women)[11 12] and the sexual functioning of subfertile men is associated with their coital frequency.[9]

In heterosexual couples confronted with prostate cancer of the man, web-based interactive educational programmes proved to have the same effect on sexual functioning as more expensive face-to-face sex counselling.[12] Our group recently developed a 6 months 'Pleasure&Pregnancy'-programme, which has yet to be tested.[13]

This web-based interactive educational programme includes eight progressive modules with sensate focus, couple communication and mindfulness exercises and offers information on the biology of conception and interaction with coaches and peers.

METHODS AND ANALYSIS

This protocol, was based on the Standard Protocol Items:Recommendations for Interventional Trials-guidelines.[14]

Aim

The 'Pleasure&Pregnancy'-RCT examines in couples with unexplained subfertility and a good prognosis whether a new web-based interactive educational programme results in a higher probability of a naturally conceived ongoing pregnancy within 6 months than standard EM.

Design

This is a multicentre RCT with cost-effectiveness analysis (CEA). Couples will be allocated (1:1 allocation ratio; computerised randomisation) to the two parallel groups of the 'Pleasure&Pregnancy-programme' and 'EM' and sample size calculations are based on a superiority framework.[15] Only the statistician will be blinded, as the nature of the intervention does not allow blinding couples or recruiters. The flow-chart of this 'Pleasure&Pregnancy-RCT' is presented in figure 1. Recruitment started in June 2016.

Setting

This multicentre RCT will be conducted over a 42 months period in secondary or tertiary fertility clinics in The Netherlands and Belgium, which started in June 2016. So far, 38 clinics have included patients and another two are in the process of obtaining ethical approval. The regularly updated list of participating clinics can be obtained from the study website.[16] Clinics that want to contribute to the Pleasure&Pregnancy-RCT, can contact any of the authors. The RCT is coordinated and monitored by the Dutch Consortium for Healthcare Evaluation in Obstetrics and Gynaecology NVOG Consortium.

Inclusion criteria

Dutch speaking heterosexual couples, in which the woman is between 18 and 38 years old, who are diagnosed with (relatively) unexplained subfertility and have a 'Hunault'-prognosis of at least 30% chance of naturally conceiving a live born child within a year after diagnosis are eligible. In line with the Guidelines of the Dutch Society of Obstetrics and Gynaecology (which allows slight variations in performed diagnostic tests), subfertility is (relatively) unexplained in case of tubal patency, an ovulatory cycle and more than three million progressive sperm per ejaculate.[2 3] Tubal patency can be documented by a negative chlamydia antibody test[4] and/or by a hysterosalpingography, hysterosalpingo-contrast-sonography (HyCoSY) or laparoscopy showing at least one patent tube. Cycles are considered ovulatory if they are regular (ie, duration of 23–35 days with less than 8 days variation) and if ovulation is demonstrated by a basal body temperature curve, a midluteal serum progesterone concentration or by sonographic cycle monitoring.[4] The Hunault-prognosis is calculated based on female age, percentage of progressive sperm, duration of subfertility, type of subfertility (primary or secondary) and referral status (self-referral, secondary or tertiary care referral).[2 17]

Exclusion criteria

Couples in whom the medical history detected somatic or psychological problems interfering with their ability to have intercourse or who are undergoing face-to-face sex-counselling are not eligible for this trial. Other types of counselling or complementary medicine do not affect eligibility.

Sample size

We hypothesise that the Pleasure&Pregnancy-programme will increase the chance of conceiving an ongoing pregnancy within 6 months by increasing pleasurable sex and thereby increasing intercourse frequency and thereby conception rates.

Assuming an ongoing pregnancy rate of 27% in the control group[4] and 35% in the intervention group (ie, based on a case-control study of sex-counselling)[8] and a 10% drop-out rate (ie, based on no drop-out in the

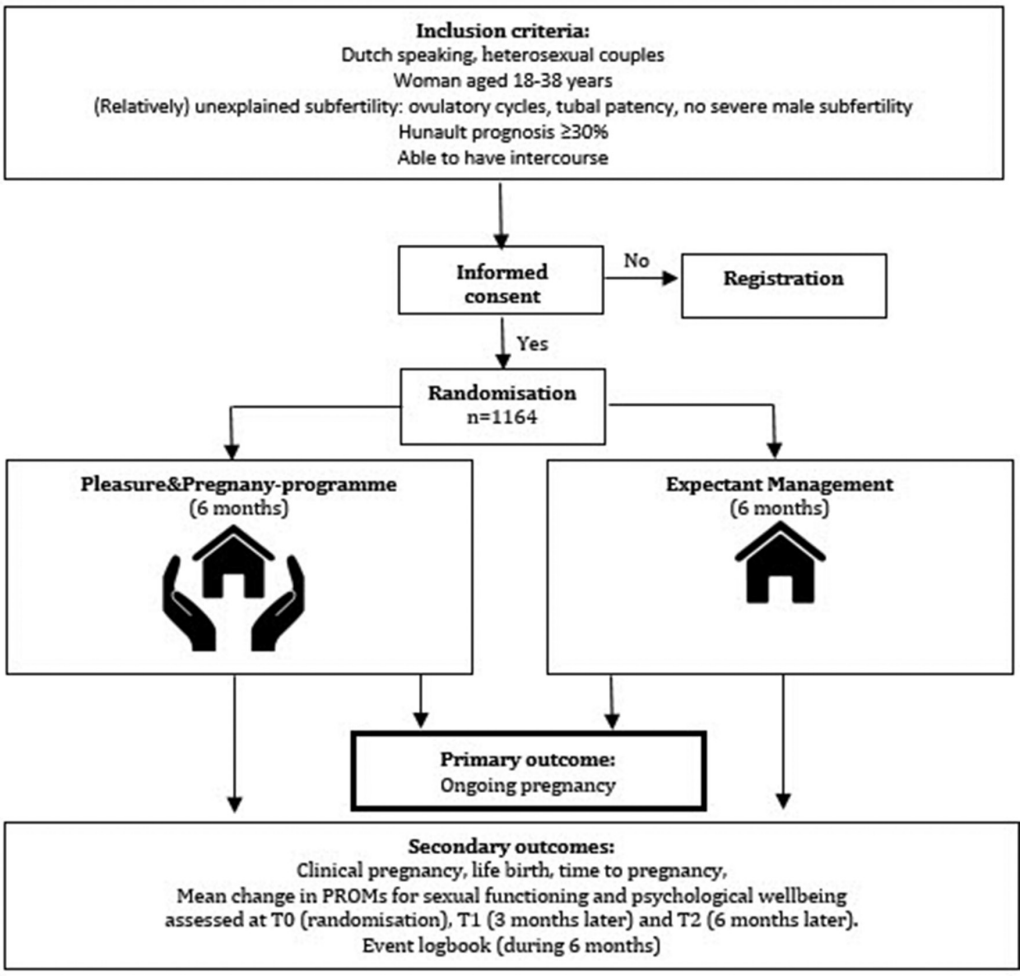

Figure 1 Flow-chart of the Pleasure&Pregnancy-RCT. (PROMs, patient reported outcome measures; RCT, randomised controlled trial).

similar case-control study and on couples' strong wish to conceive),[8] we need 582 couples in each arm of the study or 1164 couples in total (two-sided test, power of 80%, α =0.05).

Attaining this sample size within the 42 months recruitment period of this RCT seems feasible. More specifically, we expect Dutch clinics to diagnose 17 500 eligible couples during the 42 months recruitment period. Based on the prevalence of subfertility and the size of the Dutch population, we expect the incidence of subfertility to be 20 000 couples per year.[18] The probability of diagnosing unexplained subfertility and a good prognosis is 25%.[19] This means that if one third of the Dutch fertility clinics take part and if 50% of eligible patients are willing to participate, 2916 couples could be randomised during our 42 months recruitment period while our required sample size is 1164 couples.

Clinics are likely to take part for the following reasons: (i) physicians prefer taking action while being advised by professional guidelines to delay MAR,[20] (ii) the professional association of Dutch gynaecologists (NVOG) prioritised the objective of this research project over five other objectives[21]; (iii) participation only requires minimal time investments from the participating clinics as the interactions for the new Pleasure&Pregnancy-programme are provided to all patients by the project team (Academic Medical Centre, Amsterdam and University Hospital Leuven, Belgium). We expect many couples to take part as couples going through EM (ie, usual care) have been reported to be desperate for support.[22 23]

Recruitment

Eligible couples are informed and both partners are asked for written informed consent by professionals involved in their healthcare (eg, clinicians, study nurse). Couples declining participation are registered and their rationales are noted. Participants are informed that they may choose to discontinue the Pleasure&Pregnancy-programme once an ongoing pregnancy is diagnosed. Background characteristics of participants are entered in an electronic data base by the recruiters.

Randomisation

A central internet-based randomisation programme, allocates (1:1 allocation ratio) the eligible consenting couples to 6 months of the Pleasure&Pregnancy-programme (ie,

intervention group) or 6 months of 'EM' (ie, control group receiving care as usual) while relying on minimization to ensure a balanced allocation within each clinic. The recruiters cannot access the allocation sequence and only receive the allocation code after having entered the inclusion criteria in the online randomisation programme.

Interventions

In case of randomisation to EM, couples are simply sent home for 6 months to continue to attempt natural conception without being offered interaction with healthcare staff as specified for care as usual by the Dutch guideline (http://nvog-documenten.nl/index.php?pagina=/richtlijn/item/pagina.php&richtlijn_id=869).

In case of randomisation to the Pleasure&Pregnancy-programme, couples are sent home for 6 months to continue to attempt natural conception while having access to the interactive web-based educational Pleasure&Pregnancy-programme. At the time of randomisation couples chose a pseudonym (ie, to guarantee their privacy, also in the group chat sessions) and both partners provide an email address on which to receive a personal access code for the website of the Pleasure&Pregnancy-programme. During the Pleasure&Pregnancy-RCT, we use web-based tracking to follow-up couples' adherence to the Pleasure&Pregnancy-programme.

The Pleasure&Pregnancy-programme was designed based on expert opinion, literature review and patient interviews.[13] The Pleasure&Pregnancy-programme includes eight progressive web-based modules of information and exercises which become available one-by-one with 2 weeks intervals during the first 3.5 months and remain available for the rest of the 6 months' time period. In addition to the modules, a set of frequently asked questions on the biology of conception are answered to prevent behaviour potentially negatively impacting ongoing pregnancy rates (eg, use of lubricants compromises sperm quality).[24] Finally, couples can email the team of coaches (ie, a midwife-researcher, sexologist, gynaecologist and a biologist of the Academic Medical Centre, Amsterdam and the University Hospital of Leuven) and can take part in three facilitated group chat sessions with other anonymised patients. Regarding the modules, the information and exercises aim to increase pleasurable sexual sensations and responses and thereby intercourse frequency and ongoing pregnancy rates. More specifically, couples are informed on correct and misconceptions about how to increase and maintain pleasurable sex. Each module includes three different types of (couple or individual) exercises. Sensate focus exercises teach couples to focus on their own and their partner's pleasurable sexual sensations and responses.[25–27] Mindfulness exercises help couples to decrease cognitive distraction during sexual activity and to decrease performance anxiety and muscles tension.[28 29] Couple communication exercises encourage couples to discuss issues interfering with relational and/or sexual functioning.[27 30]

Outcome measures

The primary outcome of this Pleasure&Pregnancy-RCT is the probability of a naturally conceiving an ongoing pregnancy (defined as a viable intrauterine pregnancy of at least 12 weeks duration confirmed by an ultrasound scan)[31] within 6 months after randomisation. Allied secondary outcomes assessed in couples achieving the primary outcome are the live birth rate and the time to pregnancy. Costs are also assessed. Finally, the sexual functioning and personal and relational well-being of both partners of participating couples is assessed online after sending an email link to a package of patient reported outcome measures (PROMs) at randomisation and 3 and 6 months later. The packages of PROMs include five questionnaires, addressing sexual functioning (n=1; different questionnaire for men and women), personal well-being (n=3) and relational well-being (n=1). The following characteristics of the PROMs are outlined in table 1: outcome, name, source of the used version, number of questions, subscales (minimal and maximal scores and interpretation), reliability measures and demonstrated type of validity. Non-respondents are sent two email reminders and are telephoned by the study nurses of their hospital if needed. In addition, participants are asked to register the following in an online event log calendar: their menstrual period (only women) and when they had coitus and how they experienced it (with the PROM 'QSE' outlined in table 1; women and men).

The same outcomes are followed up in both arms of the Pleasure&Pregnancy-RCT. The follow-up period does, however, differ between non-pregnant and pregnant couples. Non-pregnant couples are followed up from randomisation until 6 months later, unless 2 months need to be added to remind couples of filling out the last package of PROMs. In pregnant couples data are collected until birth or pregnancy termination.

Analysis

The web-based data will all be entered and analysed in the SPSS V.22.0. No interim analysis has been planned and no adverse events are expected due to the nature of the educational intervention. Analysis will be according to intention to treat and p values≤0.05 will be considered to indicate statistically significant differences. To examine whether the randomisation resulted in two balanced groups the following six assessed background characteristics, intercourse frequency and all baseline PROMs will be compared between the intervention and control group: female age, type of infertility (primary/secondary), duration of infertility, intoxications (eg, smoking), body mass index, total motility sperm count and the diagnostic test to verify tubal patency.

Differences in ongoing pregnancy rate will be expressed as relative risks. Kaplan-Meier survival curves for each treatment group will assess time to ongoing pregnancy. PROMs will be processed according to their manuals. Linear mixed models will be used to evaluate treatment, time and interactive effects on all outcomes. Regarding

Table 1 Characteristics of the patient reported outcome measures

Dimensions	Outcome	Name of questionnaire (abbreviation)	Source for the used version of the questionnaire	Questions (n)	(Sub)scales (min-max scores) (Interpretation)	Reliability measures	Demonstrated types of validity
Sexual functioning	Sexual pleasure	Quality of Sexual Experience (QSE)	Dutch: Reciprocally translated by Prof Dr E Laan, University of Amsterdam English similar version[52]	8	Total (8-56) (The higher, the better)	TRR[3] total score: r=0.76 TRR per question: r=0.63–0.75 ITC: α range =0.71-.88 IC per question: α=0.71–0.88[53]*	Known-group validity, convergent validity[53]*
	Sexual functioning of women	Female Sexual Function Index (FSFI)	Dutch[54] English similar version[55]	19	Total score (2.0–36.0) and six subscales: sexual interest/desire (1.2–6.0), sexual arousal (0.0–6.0), lubrication (0.0–6.0), orgasm (0.0–6.0), sexual satisfaction (0.8–6.0), pain (0.0–6.0) (The higher, the better)	IC per subscale: α=0.87–0.98 IC total: α=0.97 TRR per subscale: r=0.71–0.97 TRR total score: r=0.93 ITC per subscale: 0.59–0.95 ITC total: 34–95[56]†	Construct validity, Discriminant validity, Divergent validity[56]†
	Sexual functioning of men	International Index of Erectile Function (IIEF)	Dutch[57] English similar version[58]	15	Total score (5-75) and five subscales: erectile function (1-30), orgasm (0–10), sexual desire (2-10), sexual satisfaction (0–15), overall satisfaction (2-10) (The higher, the better)	IC per domain: α=0.73–0.99 IC total: α>0.90 TRR total: r=0.82 TRR per item: r=0.64–0.84 ITC per domain: r=0.30–0.76[59]*	Construct validity, Discriminant validity, Convergent validity, Divergent validity[59]*
Personal well-being	Overall quality of life (General health)	EuroQol 5D scale (EQ-5D)	Dutch[60] English similar version[61]	6	Total VAS (0–100) and five subscales: mobility (1-3), self-care (1-3), daily activities (1-3), pain (1-3), mood (1-3) (For total VAS: the higher, the better. For subscales: the lower, the better)	IC of the five domains: α=0.85[62 63]* ICC[4]=0.78[64]	Convergent validity, discriminative validity[62]* Criterion, concurrent, construct validity[65]*
	Fertility quality of life	The fertility quality of life (FertiQol; Core FertiQol without treatment module)	Dutch[66] English similar version[67]	24	Total (0–96) and four subscales: emotional (0–24), relational (0–24), mind/body (0–24), social (0–24) (The higher, the better)	IC per subscale: α=0.72–0.91 ITC per domain: r=(−0.29)-(−0.71)[68]‡	Convergent validity[68]‡
	Anxiety and depression	Hospital Anxiety and Depression Scale (HADS)	Dutch[69] English similar version[70]	14	Total (0–42) and two subscales: anxiety (0–21), depression (0–21) (The lower, the better)	IC for total: α>0.82 IC per subscale: α=0.71–0.86 TRR per subscale: r=0.86–0.89 TRR for total: r=0.91[71]† IC per subscale: α=0.75–0.87 ITC per subscale: 0.22–0.55[72]§	Concurrent validity[71]† Convergent validity[72]§

Continued

Table 1 Continued

Dimensions	Outcome	Name of questionnaire (abbreviation)	Source for the used version of the questionnaire	Questions (n)	(Sub)scales (min-max scores) (Interpretation)	Reliability measures	Demonstrated types of validity
Relational well-being	Relation-ship satisfaction	Revised Dyadic Adjustment Scale (R-DAS)	Dutch: Reciprocally translated by Prof Dr E Laan, University of Amsterdam. English similar version[73]	14	Total score (0–69) and three subscales: dyadic consensus (0–30), dyadic satisfaction (0–20), dyadic cohesion (0–19) (The lower, the better)	IC per subscale: α=0.80–0.85 IC total score: α=0.90 TRR per subscale: r=0.80-.89 TRR total score: r=0.95[74]*	Construct validity Criterion validity[74]*

*Study using the most similar version of the questionnaire in another language but not in subfertile patients.
†Study using the same Dutch version of the questionnaire but not in subfertile patients.
‡Study using the same Dutch version of the questionnaire in subfertile patients.
§Study using the most similar version of the questionnaire in another language in subfertile patients.
IC, Internal Consistency; ITC, Item Total Correlation; TRR, Test retest reliability.

PROMs assessed in both partners separately, the factor gender (modelled as fixed effect) and clustering within couples (modelled as random intercepts) will be taken into account. This means that the effect of pregnancy on the quality of life (ie, visual annalogue scale (VAS) EuroQol-5D (EQ-5D) scores) will be evaluated with linear mixed models. In case of an interaction between pregnancy and treatment the difference in quality of life between both groups will be assessed in the women who did not become pregnant.

Economical evaluation

We will conduct a CEA with a time horizon of 6 months after randomisation from the perspectives of the healthcare payer perspective (capturing direct costs).

The costs per ongoing pregnancy in both arms of the RCT (Pleasure&Pregnancy-programme or EM) will be calculated and compared using a decision model taking costs, ongoing pregnancies and change in Quality-adjusted life years (QALYs) into account. The change in QALYs will be based on the responses to the EQ-5D-questionnaire at randomisation and 6 months later. Regarding the costs, actually used resource volumes of the Pleasure&Pregnancy-programme (ie, moderated chats and email interaction with professionals) will be recorded and attached to standardised unit costs (ie, calculated based on actual expenses made by the centralised location of the Academic Medical Centre). In addition, we will conduct a Budget Impact analysis (BIA) from the healthcare payer perspective (capturing direct healthcare costs for Dutch health insurance) and from the societal perspective (additionally capturing indirect healthcare costs due to productivity of patients). The time horizon of this BIA will be 3 years to include costs of, among others: MAR for the couples who did not conceive during the RCT, miscarriage, pregnancy and delivery of singletons and twins, neonatal intensive care unit (NICU) admission and extra care in the first year of the life of a new born baby. For this BIA, we will evaluate three scenarios depending on the implementation rate of the Pleasure&Pregnancy-programme, namely 100%, 85% and 70% of Dutch couples.

Patient and public involvement

The Dutch patient association Freya and the Dutch Society for Obstetrics and Gynaecology (NVOG) confirmed their support for this Pleasure&Pregnancy RCT to the funder. This is not surprising as we started the Pleasure&Pregnancy-programme and RCT based on Dutch patients and gynaecologists sharing that the non-interactive, passive nature of EM was a barrier for implementing EM.[22 23]Patients were consulted during the development of the Pleasure&Pregnancy programme,[13] but not during the design, recruitment and conduct of the Pleasure&Pregnancy RCT. Study participants will be informed on the results of this RCT via the study website.[16] We thank the patients who contributed to the development of the Pleasure&Pregnancy programme and the patient

representatives, who encouraged the funder to fund the Pleasure&Pregnancy RCT.

Ethics and dissemination

The Institutional Review Board (IRB) of the Academic Medical Centre Amsterdam (the Netherlands) and the Medical Ethical Committee of the Leuven University Hospital (Belgium) approved the Pleasure&Pregnancy-RCT (IRB registration numbers: 2015_317; s59666). If important protocol modifications would have to be made, the IRB, recruiters and trial registry will be notified. This trial has been registered in the Netherlands trial register (NTR5709). The findings of this RCT will be disseminated through presentations at international scientific meetings and peer-reviewed publications. We do not intend to collaborate with a medical writer.

DISCUSSION

This protocol outlines our efforts to limit the risk of bias in our RCT. We limited the risk of selection bias in the Pleasure&Pregnancy-RCT with computerised randomisation, allowing random sequence generation. In addition, we will check whether randomisation was successful in equally dividing baseline demographic, medical, sexual and psychosocial confounders between groups. Including sexual confounders (ie, sexual functioning, pleasure and coital frequency) is relevant as they are central to the pathway based on which we expect the programme to work. Including psychosocial confounders is relevant as the effect of psychosocial interventions on pregnancy rates is uncertain.[32–36] We limited the risk of detection and ascertainment bias by blinding the statistician. We cannot blind participants and recruiters as the intervention group receives an additional psychosocial intervention, while the control group will simply be sent home without receiving a placebo intervention. Finally, publishing this protocol, which specifies all outcomes, will prevent selective reporting bias. All outcomes of the Pleasure&Pregnancy-RCT will be assessed reliably. More specifically, ongoing clinical pregnancies are confirmed by ultrasound diagnosis and all included PROMs are assessed with valid and reliable questionnaires. Other strengths of the Pleasure&Pregnancy-RCT are the power calculation, intention-to treat analysis and the standardised format of the intervention. This large scale RCT was not preceded by a pilot-RCT. The feasibility of our Pleasure&Pregnancy-programme was, however, optimised by involving experienced professionals and patients in the development of the programme. For example, a timeline with a gradual build was chosen for the Pleasure&Pregnancy-programme as sexologists wanted to increase the intimacy level of the sensate focus exercises gradually and as interviewed patients shared that their need for self-management strategies increases over time.

The Pleasure&Pregnancy-programme is a comprehensive educational programme,[32] which includes information, couple communication, sensate focus and mindfulness exercises and interaction. The Pleasure&Pregnancy-RCT will primarily test the hypothesis that this programme increases ongoing pregnancy rates when compared with EM. If it is effective, it will be interesting to find out which of its elements contribute to this effect via which pathway. Assessing PROMs prior to, during and at the end of the Pleasure&Pregnancy-programme and using web-based tracking to follow-up couples' adherence to the programme, will help us disentangle the pathway. We expect the Pleasure&Pregnancy-programme to work by increasing pleasurable sex, which increases coital frequency, which in turn increases ongoing pregnancy rates. It is, however, also biologically plausible that improved sexual arousal and pleasure have a direct positive effect on ongoing pregnancy rates. More specifically, in men, orgasms following higher levels of sexual arousal have been associated with better sperm quality.[37] In women, orgasms may enhance passive and active sperm transport.[38 39] Female sexual arousal also enhances lubrication of the vagina, neutralises pH and increases perivaginal vasocongestion, which in turn improves mobility and survival of spermatozoa.[40 41] Vaginal dryness is associated with the use of commercial lubricants, of which some compromise sperm quality.[24 42]

If this RCT proves that the Pleasure&Pregnancy-programme is effective, we will advise to offer an interactive educational programme as first line treatment in couples with (relatively) unexplained subfertility before embarking on MAR. As more couples would be conceiving naturally, the Pleasure&Pregnancy-programme would decrease the 67% of couples returning for MAR after having continued to attempt natural conception for 6 months.[43] This would be highly relevant as MAR is associated with many drawbacks including significant costs, treatment burden and increased probability of multiple pregnancy, obstetric and perinatal complications, congenital abnormalities and long-term health risks for offspring.[44–51] If the Pleasure&Pregnancy-programme increases the number of couples conceiving naturally and/or improves sexual functioning, it would be worthwhile to consider also offering it to couples with other infertility diagnoses at other treatment stages, or even to couples who are interested to improve their sexual functioning. The eHealth format of the Pleasure&Pregnancy-programme will facilitate its low-cost wide-spread implementation.

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