

# Systematic development of a mobile preconception lifestyle programme for couples undergoing *in vitro* fertilisation: The PreLiFe-programme

Boedt T<sup>1,2</sup>, Matthys C<sup>1,3</sup>, Lie Fong S<sup>2,4</sup>, De Neubourg D<sup>5</sup>, Vereeck S<sup>5</sup>, Seghers J<sup>6</sup>, Van der Gucht K<sup>7,8</sup>, Weyn B<sup>9</sup>, David Geerts<sup>10</sup>, Spiessens C<sup>2,4</sup>, Dancet EAF<sup>2,4</sup>.

1) Department of Chronic Diseases and Metabolism, Clinical and Experimental Endocrinology, KU Leuven, Leuven, Belgium

2) Leuven University Fertility Centre, University Hospitals Leuven, Leuven, Belgium

3) Department of Endocrinology, University Hospitals Leuven, Leuven, Belgium

4) Department of Development and Regeneration, KU Leuven, Leuven, Belgium

5) Centre for Reproductive Medicine, Antwerp University Hospital, Edegem, Belgium

6) Department of Movement Sciences, KU Leuven, Leuven, Belgium

7) Leuven Mindfulness Centre, KU Leuven, Leuven, Belgium

8) Faculty of Psychology and Educational Sciences, KU Leuven, Leuven, Belgium

9) Department of Electric Engineering, Leuven, Belgium

10) Meaningful Interactions Lab, KU Leuven, Leuven, Belgium

## Running title:

A mobile lifestyle programme for couples undergoing IVF

## Keywords:

mHealth, telemedicine, preconception, infertility, lifestyle intervention, healthy lifestyle, diet, physical activity, mindfulness, patient-centred care

## Abstract

STUDY QUESTION: Can we develop a preconception lifestyle programme for couples undergoing IVF that is in line with their needs.

SUMMARY ANSWER: A mobile preconception lifestyle programme was systematically developed based on expert opinion, literature and needs of IVF-patients.

WHAT IS KNOWN ALREADY: A healthy lifestyle prior to conception is not only beneficial for the general health of couples, but evidence on its importance for their reproductive health and the health of their children is also emerging. So far, the vast majority of fertility clinics do not offer a lifestyle programme for couples undergoing IVF. Therefore, the present study aimed to develop a lifestyle programme for IVF-couples.

STUDY DESIGN, SIZE, DURATION: The development of the PreLiFe-programme was guided by the steps of the Medical Research Council (MRC) framework for developing complex interventions, a systematic approach for developing theory- and evidence-based health promotion interventions.

PARTICIPANTS, SETTINGS, METHODS: First, the evidence base on lifestyle programmes for IVF-couples was reviewed. Second, several iterations between an expert panel, the literature, and quantitative and qualitative data from IVF-patients identified the content, the format, behaviour change techniques and theory of the programme. Third, the PreLiFe-programme was produced and the expected process and outcomes of a randomized controlled trial assessing it were modelled. Finally, user tests among experts and patients and pilot tests among patients were conducted.

MAIN RESULTS AND ROLE OF CHANCE: The finally developed PreLiFe-programme is a mobile application to be used autonomously by both partners of IVF-couples during the first year of IVF, in combination with motivational interviewing over the telephone every three months (i.e. blended care). The PreLiFe-programme provides advice and skills training on physical activity, diet and mindfulness based stress reduction and is in part tailored based on monitoring and tracking the lifestyle of patients. Based on the literature the expert panel considers it plausible that all three components contribute to IVF-success rates. The PreLiFe-programme is likely to be acceptable to

patients as it meets the need of patients for lifestyle advice and treatment information.

**LIMITATIONS AND REASON FOR CAUTION:** The pilot in IVF-couples had a three months duration. The feasibility of the PreLiFe-programme in other infertile populations and/or upon longer use is yet to be examined. Whether the PreLiFe-programme effectively improves lifestyle and IVF-success rates is currently being examined in a trial randomizing heterosexual couples starting IVF to the PreLiFe-programme or an attention-control group for 12 months.

**WIDER IMPLICATIONS OF THE FINDINGS:** If the PreLiFe-programme improves lifestyle and the chance of IVF-success, it will be a powerful tool and provide guidance for implementing lifestyle programmes in fertility clinics.

**STUDY FUNDING/COMPETING INTERESTS:** Funded by the Research Foundation Flanders (FWO-TBM; reference: T005417N). The authors have no conflict of interest to report.

**TRIAL REGISTRATION NUMBER:** NCT03790449

## Introduction

The life plan for the vast majority of people includes having children. However, one in ten couples are faced with infertility, defined as failure to achieve a clinical pregnancy after 12 months or more of regular unprotected sexual intercourse (Zegers-Hochschild et al., 2017). About half of these couples decide to turn to fertility treatment, including IVF with or without ICSI (Boivin et al., 2007). In Belgium, the live birth rate after three completed IVF/ICSI cycles or one year of IVF is approximately 50% (Peeraer et al., 2014, De Neubourg et al., 2016). However, infertility and its treatment result in a considerable emotional and economic burden for both individuals and society (Wu et al., 2013, Gameiro et al., 2012). Addressing modifiable factors, which can reduce this burden and improve the chance of IVF-success, are therefore important research priorities for the field of reproductive medicine (Gameiro et al., 2013a, Moran et al., 2016). Lifestyle is such a modifiable factor, and following a healthy lifestyle is not only beneficial for the general health of infertile men and women but also for their reproductive health and for the health of their children (Stephenson et al., 2018, Homan et al., 2007). A guideline of the European Society of Human Reproduction and Embryology (ESHRE) highlighted the need for interdisciplinary developed programmes that meet the emotional, relational and cognitive needs of fertility patients, as well as their need for advice on lifestyle behaviour modification (Gameiro et al., 2015). So far, the vast majority of fertility clinics do not yet offer a lifestyle programme to couples undergoing IVF. This might explain why one in three IVF-couples seeks complementary therapy outside of their fertility clinic including lifestyle and/or psychosocial support (Porat-Katz et al., 2016, Smith et al., 2010). Mobile applications have a promising format for lifestyle interventions, proven effective in other patient populations for being time-efficient and empowering patients (Afshin et al., 2016).

This paper describes the systematic development of a preconception lifestyle programme for IVF-couples, the PreLiFe-programme. We aimed to develop an innovative mobile application for IVF-couples based on expert opinion, the needs of IVF-couples, the literature on the relationship between lifestyle and IVF-success, and on behaviour change techniques.

## Materials and Methods

The PreLiFe-programme was developed at Leuven University (Belgium; October 2017 - January 2019), by following the first two stages of the framework of the Medical Research Council (MRC) for developing and evaluating evidence and theory-based complex interventions (Craig et al., 2013). These stages devoted to 'development', and 'feasibility and piloting' and are each split up in three steps (figure 1).

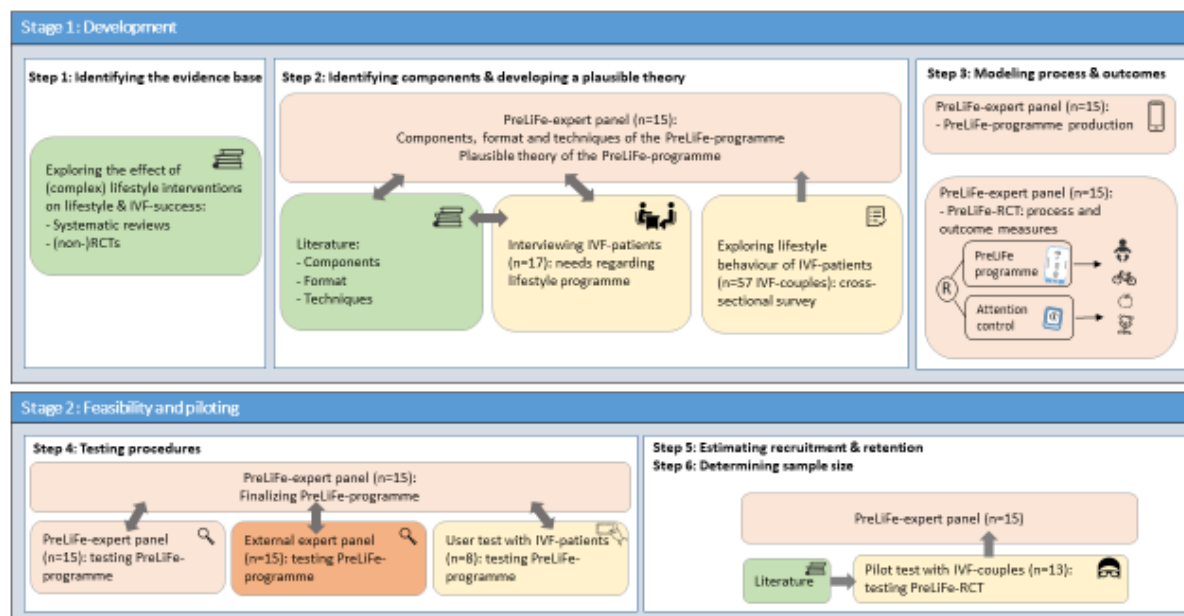


Figure 1. Stages and steps of the development of the PreLiFe-programme

### Stage 1: Development

#### Step 1: Identifying the evidence base

The evidence base on the effect of (complex) interventions focussing on diet and/or physical activity on lifestyle and IVF-success was reviewed until January 2019 (Craig et al., 2013). In line with the hierarchy of evidence systematic reviews and (non-) randomized controlled trials (RCTs) were considered superior to evidence from cohort studies (Evans, 2003).

#### Step 2: Identifying components and developing a plausible theory

Experts, IVF-patients and the literature were consulted during the development of the PreLiFe-programme and a plausible theory of how it can increase IVF-success was developed (Craig et al., 2013).

Involving patients in the development of a novel intervention is in line with the principles of patient-centred care (Corrigan et al., 2001, Crawford et al., 2002, Nilsen et al., 2006).

The repeatedly consulted (i.e. iterative process) interdisciplinary **PreLiFe-expert** panel included 15 persons: physical activity promotion researchers (n=2), nutrition promotion researchers (n=2), psychologists specialized in mindfulness (n=3), sociologists specialized in user experience research (n=2), software developers (n=2), gynaecologists (n=2), an embryologist (n=1) and a midwife specialized in the field of reproductive medicine (n=1). The IVF-patients were consulted in two small scale studies.

First, a qualitative study explored the needs regarding a lifestyle programme of a convenience sample of Dutch speaking heterosexual male and female IVF-patients, volunteering based on a post on the website of the Belgian association for fertility patients and via a flyer in the waiting room of two University fertility clinics. More specifically, the female interviewer (RV, sociologist not involved in fertility care) relied on three open-ended questions <sup>sup</sup> (supplementary table SI) and a topic list for conducting the in-depth interviews of about one hour at the participant's home. The interviews were audio recorded, transcribed and subjected to inductive content analysis by a single researcher (RV). The analysis was not performed with a specialized software and member checking was not performed. Data-collection and analysis were intertwined processes and the sample size was defined by data saturation. Exemplifying interview quotations illustrate the findings. Second, a cross-sectional survey explored the diet and physical activity of Dutch speaking heterosexual couples about to start IVF at a Belgian University fertility clinic with the Food Frequency Questionnaire (FFQ;(Matthys et al., 2015)) and the International Physical Activity Questionnaire (IPAQ;(Craig et al., 2003)). This cross-sectional survey did not assess the distress of IVF-couples, as the decision to address distress with the lifestyle programme was taken afterwards. Moreover, the distress of IVF-couples has been demonstrated by ample previous <sup>stud</sup> studies (Gameiro et al., 2015). The 31-items FFQ questions the frequency and portion size of consumed food and beverages, and allows assessing whether the dietary pattern is in line with WHO and national recommendations (Gezondheidsraad, 2016, WHO, 2018a, GezondLeven, 2018). The 7-items IPAQ questions the frequency and duration of physical activities and allows assessing whether

the amount spent on moderate to vigorous physical activity is in line with recommendations (WHO, 2018b, GezondLeven, 2018). Table I presents the sociodemographic and clinical characteristics of the 84 female and the 73 male IVF-patients consulted during the development and pilot of the PreLiFe-programme.

The **literature** on the relation between lifestyle and IVF-success was reviewed until January 2019. This review was more elaborate than the review presented in step 1 as it: (i) focussed on all components proposed by the PreLiFe-expert panel and patients, rather than only physical activity and/or diet and (ii) included cohort studies examining associations besides (non-)RCTs. In addition, the literature on the format of lifestyle interventions and on behaviour change techniques was consulted.

### **Step 3: Modelling process and outcomes**

The project coordinator (TB) and the PreLiFe-expert panel modelled the complex intervention in detail (i.e. programme production; (Craig et al., 2013)). A team of software engineers and web designers built the mobile application.

The PreLiFe-expert panel selected reliable and valid process and outcome measures for assessing the plausible theory in an RCT.

[illegible]



## *Stage 2: Feasibility and Piloting*

### **Step 4: Testing procedures**

The PreLiFe-expert panel and an external expert panel used the PreLiFe-programme for one week and assessed whether the intended behaviour change techniques were present and identified opportunities for improvement. The external expert panel from Ghent University (n=15) were all health promotion researchers (psychologists, physicians and others with a master of science in health promotion) with a research focus on: physical activity (n=8), nutrition (n=2), mental health (n=5). In addition, eight IVF-patients (also taking part in the interview study; table I) were observed and questioned on feasibility, user-friendliness and opportunities for improvement whilst using the PreLiFe-programme. The female researcher (RV, sociologist not involved in fertility care) relied on the think aloud technique and semi-structured interview questions/tasks, audio recorded the interviews and analysed them in a reflective report per interview (Broekhuis et al., 2019).

### **Step 5: Estimating recruitment and retention**

The PreLiFe-expert panel reviewed the literature on recruitment and retention in RCTs assessing complex lifestyle interventions in the field of reproductive medicine. The PreLiFe-programme and the PreLiFe-RCT were pilot tested for three months among 13 Dutch speaking heterosexual couples about to start IVF in a Belgian University fertility clinic (table I).

### **Step 6: Determining sample size**

The PreLiFe-expert panel based the sample size of the PreLiFe-RCT on the reproductive medicine literature.

## Results

### Step 1: The evidence base

In line with two systematic reviews of RCTs examining the effect of lifestyle interventions on infertile couples' lifestyle and/or IVF-success rate, our review concluded that RCTs were scarce (Anderson et al., 2010, Lan et al., 2017). No RCT examined the effect of a lifestyle intervention in the general population of women and/or men going through IVF (table II). The available RCTs (n=8) focussed exclusively on infertile women who suffered from overweight or obesity, in whom lifestyle interventions improved natural pregnancy rate (odds ratio (OR): 1.87, 95% CI: 1.24 to 2.81)(Lan et al., 2017). The literature review prior to finalizing the PreLiFe-programme in January 2019 identified three non-randomized controlled trials (nRCTs) among IVF-couples, showing that a lifestyle intervention focussing on diet, or on diet and physical activity, improved diet (n=1) or diet and physical activity level (n=2; table II). One nRCT improved the chance of becoming pregnant via natural or IVF-conception (no subgroup analysis; van Dijk et al, 2017) and the others did not examine IVF-success (Homan et al, 2012; Hammiche et al, 2011).

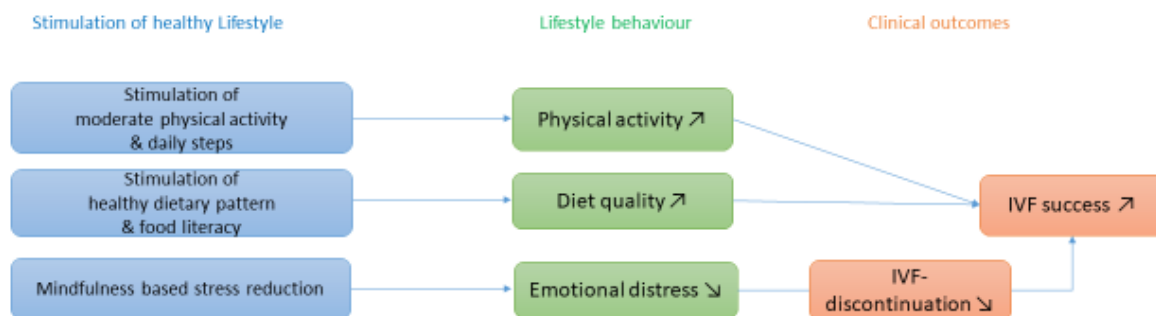
### Step 2: The identified components and developed plausible theory

After several iterations, the expert panel decided on the components, format and techniques of the PreLiFe-programme and finalized a plausible theory of how the novel PreLiFe-programme can improve lifestyle and IVF-success.

#### Components of the PreLiFe-programme

After several iterations between the literature, the interviews with IVF-patients and after the cross-sectional survey in IVF-patients, the PreLiFe-expert panel decided to focus on the following three lifestyle factors: physical activity, diet and mindfulness. The interviews showed that patients want to improve their lifestyle in order to regain control during IVF, as exemplified in the following interview quotation: *'They give very little information, why it fails, what you can do yourself, diet tips, exercise tips? What can you do yourself? That is very important to me'* (Interview 17, woman). Table II outlines the underlying literature and identified needs of IVF-patients, explaining why the expert panel considers it

plausible that each component improves lifestyle behavior and IVF-success. Figure 2 displays the theory based on which the PreLiFe-expert panel considers it plausible that the PreLiFe-programme will improve IVF-success.



**Figure II. The plausible theory of the PreLiFe-programme**

In order to increase its acceptability to patients, the PreLiFe-programme additionally includes reminders for medication, consults and procedural treatment information. This feature has been prioritized by infertile patients (Dancet et al., 2011) and is in line with the needs of interviewed patients, as exemplified by following quotation: *'Step by step information would be very nice'* (Interview 2, man).

Table II. Rationales for the chosen lifestyle components of the complex PreLiFe-programme

Components		Literature*				(Guidelines summarizing) RCTs in healthy individuals or patients with various conditions found that (complex) lifestyle interventions resulted in improved lifestyle & general health	Observational studies in IVF-couples found associations between advised lifestyle behavior and IVF-success rates	IVF-patients: needs identified in qualitative study	Expert panel's final rationale for considering it plausible that the PreLiFe-programme improves lifestyle behavior and IVF-success rates**
		(non-)RCTs in IVF-couples found that (complex) lifestyle interventions resulted in:							
		Improved lifestyle		Improved IVF-success rates					
		RCT	nRCT	RCT	nRCT				
Physical activity (PA)	Stimulating moderate PA		Improved PA ♂️👩 (A,B)		NA	Improved moderate PA level and general health in healthy ♂️ and 👩, 👩 in their perinatal period and ♂️ and 👩 with various conditions*** (C-F)	Positive association between moderate PA in 👩 and IVF-success and between moderate PA in ♂️ and semen quality (G,H)	Need for advice on PA: 'Yes, I have many questions such as: can I stay active during my fertility treatment?' (Interview 10, woman)	Based on the literature an increase in PA and IVF-success rate is plausible, especially as the PreLiFe-programme addresses both partners (J).
	Reducing sedentary behaviour stimulating daily physical activity					Decreased sedentary behaviour and improved general health in healthy ♂️ and 👩, 👩 in their perinatal period and ♂️ and 👩 with various conditions*** (C-F,I)			
Diet	Stimulating healthy dietary pattern & food literacy		Improved diet ♂️👩 (A,B,K)		NA	Improved diet and general health in healthy ♂️ and 👩 and ♂️ and 👩 with various conditions**** (L,M)	Positive association between a healthy dietary pattern in ♂️ and 👩 and IVF-success (N-Q)	Need for dietary advice: 'It might be nice to be provided with menus. Menus consisting of foods that have a positive effect on your fertility.' (Interview 10, woman)	Based on the literature an improvement of diet and IVF-success rate is plausible, especially as the PreLiFe-programme addresses both partners (J,K). The PreLiFe-expert panel expects that the focus on food literacy in addition to dietary pattern will increase the likelihood of an improved diet (R,S). Of note, the only one in three non-RCTs that reported effects on success rates reported an improved pregnancy rate but included naturally besides IVF-conceived pregnancies and did not report sub-group analyses (K).

Mindfulness-based stress reduction (MBSR)	Reduced emotional distress 🧠 (T,U)		Improved IVF-success rate (T)		Reduced emotional distress in healthy 🧠 and 🧠 and 🧠 and 🧠 with various conditions***** (V,W)	Evidence inconclusive on association between emotional distress in 🧠 and 🧠 and IVF-success rate (X,Y)	Need for accessible strategy to reduce emotional distress: <i>‘There should be attention for relaxation and stress release. The mental part is also important. For example, focus on your breath, drink a nice tea... Small, accessible things that support to patients.’</i> (Interview 17, woman)	Based on the literature a decrease in emotional distress and an increase in IVF-success rate is plausible. On the one hand, evidence on the association between distress and IVF-success rate is inconclusive (X,Y). On the other hand, the improved pregnancy rates in the RCT on MBSR (T) might be due to a decrease in IVF-discontinuation, which might in turn increases IVF-success rates. Distress has been reported as a reason for IVF-discontinuation (Z) and IVF-compliance has been related to IVF-success (AA).
<u>Abbreviations:</u> RCT: Randomized controlled trial nRCT: Non-randomized controlled trial PA: Physical activity MBSR: Mindfulness-based stress reduction NA: Not assessed <u>Legend:</u> * Evidence published prior to the finalization of the programme (January 2019) ** Final opinion after several iterations between the literature, patients and experts *** Examples of conditions in which improved physical activity and general health was demonstrated: noncommunicable diseases (NCDs) **** Examples of conditions in which improved diet and general health was demonstrated: NCDs ***** Examples of conditions in which reduced emotional distress was demonstrated: NCDs, psychological problems					<u>References:</u> (A) Homan et al. 2012 (B) Hammiche et al. 2011 (C) WHO fact sheet on physical activity 2018b (D) Harrison et al. 2016 (E) Penedo et al. 2005 (F) Warburton et al. 2017 (G) Ibanez-Perez et al. 2019 (H) Rao et al. 2018 (I) GezondLeven 2018 (J) Best et al. 2016 (K) van Dijk et al. 2017 (L) WHO fact sheet on nutrition 2018a (M) Hoge Gezondheidsraad 2016 (N) Salas-Huetos et al. 2017 (O) Twigt et al. 2012 (P) van Dijk et al. 2016 (Q) Vujkovic et al. 2010 (R) Vidgen et al. 2014 (S) Azevedo Perry et al. 2017 (T) Li et al. 2016 (U) Nery et al. 2019 (V) Gotink et al. 2015 (W) Khoury et al. 2013 (X) Boivin et al. 2011 (Y) Matthiesen et al. 2011 (Z) Gameiro et al. 2012a (AA) Gameiro et al. 2013			

### **Physical activity**

In line with the World Health Organization (WHO) and national recommendations, the PreLiFe-programme stimulates IVF-couples to do at least 150 minutes of moderate physical activity per week and at least 10.000 steps per day (GezondLeven, 2018, WHO, 2018b). The cross-sectional survey showed that only two in three (fe)male IVF-patients perform the recommended 150 minutes of moderate physical activity per week (Supplementary table SII). Based on the literature, the PreLiFe-expert panel considers it plausible that stimulating moderate physical activity and the number of daily steps improves the physical activity level (i.e. nRCTs in IVF-couples and RCTs in other patients populations) and IVF-success (i.e. observed association between physical activity level and IVF-success) of IVF-couples (table II) (Homan et al., 2012, Hammiche et al., 2011, Harrison et al., 2016, Penedo and Dahn, 2005, Warburton and Bredin, 2017, Ibanez-Perez et al., 2019, Rao et al., 2018). The PreLiFe-expert panel expects that advice on physical activity will be acceptable to patients as the interviewed IVF-patients shared their need for advice on physical activity (table II).

### **Diet**

In line with WHO and national recommendations, the PreLiFe-programme stimulates IVF-couples to have a healthy dietary pattern (WHO, 2018a, Gezondheidsraad, 2016, GezondLeven, 2018). Based on expert opinion, the PreLiFe-programme will focus on food literacy in addition to a healthy dietary pattern (table II). Food literacy is an evidence-based model focussing on all practicalities of healthy eating, such as food planning, selecting foods, food preparation and evaluating information about food (Vidgen and Gallegos, 2014, Azevedo Perry et al., 2017, Truman et al., 2017). Healthy dietary pattern and food literacy has been operationalized into 24 goals (Boedt et al., 2019b). The cross-sectional survey showed that depending on the type of food, only 5-42% of (fe)male IVF-patients meet the recommended daily intake (Supplementary table SII). Based on the literature, the PreLiFe-expert panel considers it plausible that stimulating a healthy dietary pattern and food literacy improves the diet (nRCTs in IVF-couples and RCTs in other patients populations) and IVF-success (observed association between diet and IVF-success) of IVF-couples (table II) (Homan et al., 2012, Hammiche et al., 2011, van

Dijk et al., 2016, van Dijk et al., 2017, Gezondheidsraad, 2016, Salas-Huetos et al., 2017, Twigt et al., 2012, Vujkovic et al., 2010). The PreLiFe-expert panel expects dietary advice of IVF-couples to be acceptable to patients as the interviewed IVF-patients shared their need for dietary advice, including recipes (table II).

### ***Mindfulness***

The PreLiFe-programme includes mindfulness-based stress reduction exercises, that stimulate patients to become non-judgmentally aware of thoughts, feelings, and sensations, and increase their capacity to replace automatic, habitual, and often judgmental reactions with more conscious and skilful responses (Maex, 2010, Kabat-Zinn, 2013, Crane et al., 2017). The fact that couples are distressed during IVF is well documented (Cousineau and Domar, 2007)(Gameiro et al, 2015). Based on literature, the PreLiFe-expert panel considers it plausible that mindfulness-based stress reduction lowers distress in IVF-couples (RCTs in IVF-women and RCTs in male and female patients with other conditions) and that it improves IVF-success (RCT in IVF-women)(table II) (Li et al., 2016, Nery et al., 2019, Gotink et al., 2015, Khoury et al., 2013). Of note, the evidence on the association between distress and IVF-success is inconclusive (Boivin et al., 2011, Matthiesen et al., 2011). The PreLiFe-expert panel considers it plausible that mindfulness-based stress reduction improves IVF-success by limiting IVF-discontinuation (table II) (Gameiro et al., 2012, Gameiro et al., 2013b). The PreLiFe-expert panel expects that offering mindfulness-based stress reduction is acceptable to patients, as the IVF-patients interviewed shared their need for an accessible strategy to limit distress (table II).

### **Format of the PreLiFe-programme**

The predefined format of a mobile application was in line with patients' needs for a time efficient intervention, as exemplified by the following interview quotation: *'IVF itself is already time consuming, so please an intervention that does not require visits to the clinic'* (Interview 10, woman). The PreLiFe-expert panel opted for 'blended care' by building the ability to chat with health care professionals into the mobile application. This decision was based on an RCT showing that adding interaction with healthcare professionals to a mobile application improved its effect on lifestyle behaviour (Hurkmans et

al., 2018), and to facilitate implementation (Aarts et al., 2015). Offering the possibility to interact with health care professionals is in line with patients' needs, as exemplified in the following interview quotation: *'We decided to no longer search information on the internet. This drives you crazy after a while. I no longer read information, the physician will tell me what to do'* (Interview 1, woman). In addition, the PreLiFe-expert panel decided to address both partners of IVF-couples, as our cross-sectional survey showed that the dietary pattern of partners is correlated ( $r = .537$ ,  $p = .001$ ) (Boedt et al., 2019). Furthermore, addressing couples, rather than individuals, proved to maximise compliance rates and the effect of lifestyle interventions on behaviour (Best et al., 2017, van Dijk et al., 2017, Black et al., 1990). This approach is also in line with patient's needs as exemplified by the following quote: *'I always join my partner on visits to the clinic. I really try to be involved'* (Interview 4, men).

### Techniques of the PreLiFe-programme

Table III presents the techniques of the PreLiFe-programme and their match with the self-determination theory for human motivation, specifying that the human need for autonomy, competence and relatedness (table III) should be met in order to attain positive behavioural outcomes (Ryan and Deci, 2000).

Table III. Tailored (in italic) and non-tailored techniques of the PreLiFe programme and their match with the self-determination theory for each of the three components		
Self-determination theory		
Autonomy	Competence	Relatedness
PHYSICAL ACTIVITY + DIET + MINDFULLNESS-BASED STRESS REDUCTION		
Self-selection of component	Library	Couple intervention
	Possibility to chat with coach	
	Motivational interviewing by coach via telephone	
PHYSICAL ACTIVITY		
Planning moderate physical activity	Overview of tracked daily steps & planned moderate physical activity	
	Goal to increase daily steps and moderate physical activity by 10%/2 weeks or until 10.000 steps/day and 150 minutes/week	
	Tips aligned with monitoring	
	Overview of achieved goals	
DIET		
Self-selection of 1/3 proposed goals	Proposition of goals based on monitoring	
	Tips aligned with selected goals	
	Overview of achieved goals	



MINDFULNESS BASED STRESS REDUCTION		
No fixed time-frame	Six progressive modules of exercises + additional exercises	
*Physical activity (PA) is monitored at start of intervention with a questionnaire + continuously tracked by moderate PA-planner and pedometer **Diet is monitored at start of the intervention with a questionnaire		

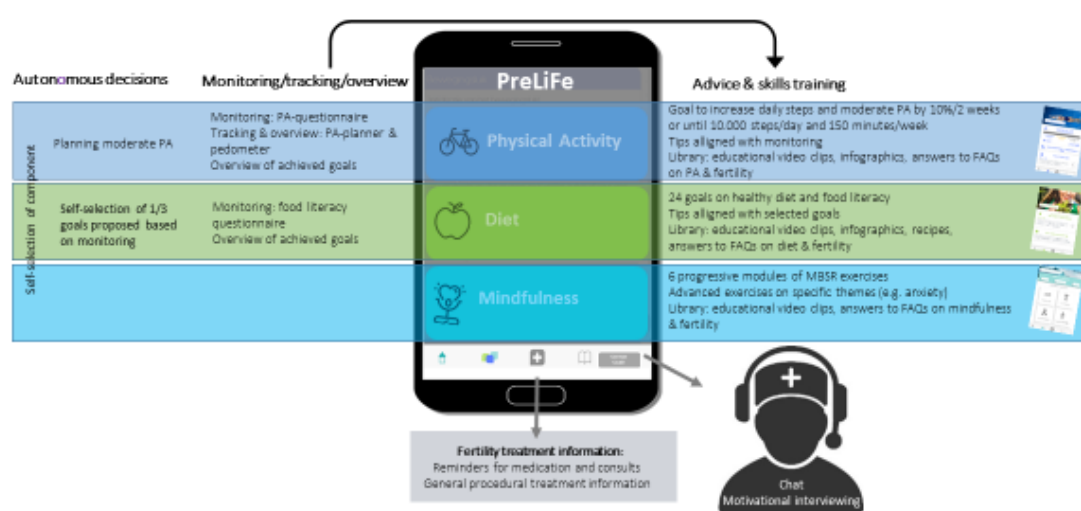
The techniques of the PreLiFe-programme operationalized the following four behaviour change techniques: goal-setting (e.g. 10.000 steps/day), motivational interviewing (i.e. by telephone), tailoring (techniques in *italic* table III) and providing information via imagery (e.g. infographic on preparing a healthy week menu) (Eldredge et al., 2016, Kok et al., 2016). Interestingly, motivational interviewing is especially relevant for applying the self-determination theory in practice (Markland et al., 2005) and has proven to be able to change the lifestyle behaviour of IVF-couples (Homan et al, 2012).

### Step 3: Modelling process & outcomes

#### PreLiFe-Programme

The PreLiFe-programme is a mobile application, developed to be used during the first year of the IVF-treatment trajectory. The PreLiFe-programme was developed to be used autonomously by women and men going through IVF. Both individuals of participating couples receive their own login to download the PreLiFe-programme on their smartphone. A link between the logins of partners ensures that both partners receive the same treatment information. The PreLiFe-programme offers the possibility to send a chat message to a health care professional (i.e. the PreLiFe-coach), who replies within 72 hours. In addition to everything offered by the mobile application, the PreLiFe-coach contacts each patient once every three months (n=4) by telephone to discuss their lifestyle according to the principles of motivational interviewing (Lussier and Richard, 2007). Figure 3 describes the PreLiFe-programme in detail, including for each of the three lifestyle components the autonomous decisions that can be taken, the monitoring or tracking that is performed and the overview thereof that is provided to patients, and finally the given advice and skills training. Besides lifestyle advice, the PreLiFe-programme includes fertility treatment information (figure 3).

The PreLiFe-programme includes a backend server with a secured dashboard interface enabling the PreLiFe-coach to consult the logs and chat function. Regarding physical activity and diet, automated processes tailor the intervention. Monitoring is performed by a physical activity and food literacy questionnaire, and physical activity is tracked by the pedometer of patient's smartphone and the moderate physical activity planner (figure 3). Based on this monitoring and tracking the PreLiFe-programme gives patients an overview and proposes physical activity and dietary goals, which should be selected every two weeks. After two weeks, patients receive a question to evaluate whether the goal was achieved and whether they want to select a new goal. The PreLiFe-programme provides regular tips (every other week for physical activity, every other day for diet) that align with the selected goals (table III; figure 3). Regarding the mindfulness-based stress reduction, the PreLiFe-programme is not tailored automatically. Patients are instructed to follow six progressive modules of guided experiential mindfulness based stress reduction exercises (e.g. body scan) in audio-file format. Patients can opt to do a stress test (i.e. an exercise to be kindly aware of stress in your body (Brewer et al., 2020), and advanced mindfulness exercises on specific themes (e.g. anxiety) are offered.



**Figure III. Detailed description of the PreLiFe-programme with a blended care format**

Abbreviations: FAQs: Frequently asked questions; MBSR: mindfulness based stress reduction; PA: physical activity

## PreLiFe-RCT

As described in detail in the published protocol of the PreLiFe-RCT, the primary outcome is the cumulative ongoing pregnancy rate achieved within 12 months (Boedt et al., 2019a). As secondary outcomes, the following will be assessed in both partners at baseline 3-, 6-, 9- and 12 months later: physical activity, diet, emotional distress, physical health, fertility related quality of life and partners' support (Boedt et al., 2019a). The PreLiFe-programme logs the use of the programme (i.e. frequency and activity per component) and the acceptability of the PreLiFe-programme is questioned 12-months after randomization.

### **Step 4: Testing procedures**

The PreLiFe-expert panel resolved some slight hitches such as language mistakes and aligned the layout and terminology of the different components. The external expert panel confirmed the presence of the behaviour change techniques. As advised by the external expert panel, the following was added: more recipes to support a healthy diet, and additional practical instructions on the physical activity component. The eight IVF-patients taking part in the user tests (table I), would recommend the PreLiFe-programme to friends as they found it attractive and easy to use, as exemplified by the following quotation: *'I think it is very useful. When can I start using this app?'* (User test 3, woman). Patients wanted more information on how the PreLiFe-programme works, as exemplified: *'Does the number of goals increase over time or do you start immediately with three goal'* (User test 2, Man). Instruction movies of the gynaecologists from the recruiting clinics, and of the lifestyle experts, were added.

### **Step 5: Estimating recruitment and retention**

Based on the literature and the pilot test, the PreLiFe-expert panel expects a participation rate of 60% and a dropout rate of 20% (van Dijk et al., 2017, van Dijk et al., 2016, Mutsaerts et al., 2016). Of 18 eligible couples addressed for the pilot, 13 couples were randomized (participation rate: 72%; table I). Three other couples refused as they wanted to focus solely on IVF (n=2), or as the male partner was not interested (n=1). An additional two screen failures were due to a spontaneous pregnancy prior to study intake (n=1) and a male partner not being present at study intake (n=1). Of the seven couples

randomized to the control group, two couples dropped out (15%) due to IVF-discontinuation (n=1) or wanting to focus solely on IVF (n=1). None of the couples of the intervention group dropped-out. Of the six couples randomized to the intervention group, five women and five men started to use the PreLiFe-programme within a month. The PreLiFe-programme was used most intensively during controlled ovarian stimulation for IVF.

### **Step 6: determining sample size by PreLiFe expert panel**

As described in detail in the published protocol of the PreLiFe-RCT, taking account of the literature on cumulative IVF-success rates, IVF-discontinuation rates, study drop-out rates and the plausible effect of lifestyle interventions, led to a sample size of 460 couples (two-sided test; power of 80%; alpha of 5%; study drop-out of 20%) (Boedt et al., 2019a).

## **Discussion**

This paper reports on the thorough development of the PreLiFe-programme, based on expert opinion, literature and needs of IVF-patients. The finally developed PreLiFe-programme is a novel mobile application to be used autonomously by both partners of IVF-couples during the first year of IVF, in combination with motivational interviewing over the telephone every three months (i.e. blended care). The PreLiFe-programme provides advice and skills training on physical activity, diet and mindfulness based stress reduction and is, in part, tailored based on monitoring and tracking of the patient's lifestyle. Based on the literature, the expert panel considers it plausible that all three components contribute to IVF-success rates. The PreLiFe-programme is likely to be acceptable to patients as it meets their needs for lifestyle advice and treatment information.

The PreLiFe-programme was systematically developed and piloted according to the stages and steps of the framework of the Medical Research Council (Craig et al., 2013). Consulting the literature, experts and patients is expected to result in programmes likely to be effective and likely to be implemented in practice (Craig et al., 2013, Eldredge et al., 2016). To the best of our knowledge, this is the first preconception lifestyle programme in line with the needs of IVF-patients regarding content

and format, although the importance of consulting IVF-patients when developing information for them had been highlighted (Aarts et al., 2012, Dancet et al., 2011) and although lifestyle experts had highlighted the need to understand the motivation and context of patients (Barker et al., 2018).


Regarding the consulted literature, prior to finalizing the PreLiFe-programme, trials on the effect of lifestyle interventions in infertile couples were last searched for in January 2019. In the meantime, our group updated the Cochrane systematic review on lifestyle interventions in infertile patients which highlights the need for high-quality studies investigating the effectiveness and safety of preconception advice on a combination of lifestyle factors in men and women with infertility (Boedt et al., 2021).

Interestingly, a recent RCT proved that a mobile application focussing on diet, food supplements, smoking and alcohol improved the lifestyle of both partners of IVF-couples (Oostingh et al., 2020). No significant effects on pregnancy rates were found, but the study was not powered to examine this (Oostingh et al., 2020). Of note, the PreLiFe-expert panel only decided to include mindfulness-based stress reduction exercises for addressing the distress of IVF-couples after having consulted IVF-patients at the end of step 2 of the development of the PreLiFe-programme. Step 1, therefore, only summarizes the evidence base on the effect of interventions focussing on diet and/or physical activity and IVF-couples were only surveyed on their diet and physical activity (step 2). We did, however, catch-up on reviewing RCTs and cohort studies relevant to mindfulness-based stress reduction exercises when finalizing step 2. Table II summarizes the rationales for including all three components of the PreLiFe-programme. We did not catch-up on surveying, as several previous surveys demonstrated the distress of IVF-patients (Gameiro et al., 2015).

Regarding the consulted patients, the content analysis of the patient interviews was performed by one researcher only (i.e. no triangulation) and members checking was not performed. The interviewed patients were, however, consulted again when the first version of the programme had been developed. The PreLiFe-programme was developed and is currently tested in heterosexual couples going through IVF (Boedt et al., 2019a). It would be interesting to test and disseminate the PreLiFe-

programme in a wider target population than only heterosexual couples going through IVF, including couples who have not yet started IVF as well as single and same sex couples.

The Final PreLiFe programme has interesting features. First, it includes effective behaviour change strategies. Second, The PreLiFe-programme addresses both partners of an IVF-couple affected by the couples' condition (infertility), rather than only the woman, which facilitates extra support and maximises compliance (Best et al., 2017, van Dijk et al., 2016). Third, as advised for lifestyle interventions (Barker et al., 2018), our PreLiFe-programme integrates different lifestyle factors into a complex intervention (physical activity, diet and emotional distress) rather than addressing only one. This includes mindfulness exercises that can contribute to self-care and disease management (Greeson and Chin, 2019). Fourth, its blended care format combining a mobile application with motivational interviewing and chats with the PreLiFe-coach proved to be attractive and engaging for other patient populations (Hurkmans et al., 2018), and is also in line with the needs of interviewed IVF-couples. This format empowers patients to actively manage their health (Afshin et al., 2016) and will enable low-cost widespread implementation of our PreLiFe-programme. The mobile application might, however, give rise to technical problems, such as a mobile phone that has reached its data limit. In addition, patients are likely to want to use the chat function for fertility treatment-related questions while the messaging system is meant for lifestyle-related questions.

This paper outlines the development of the PreLiFe-programme. This detailed description of our lifestyle programme will be informative for other groups developing or selecting preconception lifestyle interventions. Whether the PreLiFe-programme indeed improves the lifestyle or IVF-success rates in IVF-couples is currently being evaluated in an  allocating Belgian heterosexual couples starting IVF to the PreLiFe-programme or an attention-control group for 12 months (Boedt et al., 2019a). If this programme proves to be effective on reproductive and lifestyle outcomes in IVF-couples, it will be a powerful tool and provide guidance for implementing lifestyle programmes as standard care in fertility clinics.

## Data availability statement

The International Committee of Medical Journal Editors (ICMJE) recommendations will be followed: Individual de-identified participant data underlying this manuscript will be shared upon a reasonable request to the corresponding author (christophe.matthys@uzleuven.be) from investigators having their project approved by an independent review and signing a data access agreement.

## Acknowledgements

We would like to thank Steve De Backer for the technical development and support of the PreLiFe-programme; Roos Voorend and Jan Derboven for contributing to the patient centred design of the PreLiFe-programme; Edel Maex, for contributing to the development of the mindfulness part of our PreLiFe-programme; An Bogaerts for contributing to the development of the physical activity part of our PreLiFe-programme; the Nutrition Unit of University Hospitals Leuven for contributing to the development of the diet part of our PreLiFe-programme; An DeSmet for guiding the external expert panel; the advisory committee of our FWO—TBM project for their guidance and advice and all the patients participating in the patient centred design research, user tests and pilot tests.

## Authors' roles

All authors contributed substantially to the development of the PreLiFe-programme. TB, SLF, DDN, SV, CS and DG made an essential effort for the acquisition of the patient data. TB, DG and EAFD analysed and interpreted the data. TB, CM and EAFD prepared this manuscript and all authors read, revised and approved the final manuscript.

## Funding

This work was funded by the Research Foundation Flanders (FWO-TBM; reference: T005417N).

**Conflict of interest**

Authors have no conflict of interest to report



## References

- AARTS, J. W., FABER, M. J., COHLEN, B. J., VAN OERS, A., NELEN, W. L. & KREMER, J. A. 2015. Lessons learned from the implementation of an online infertility community into an IVF clinic's daily practice. *Hum Fertil (Camb)*, 18, 238-47.
- AARTS, J. W., VAN DEN HAAK, P., NELEN, W. L., TUIL, W. S., FABER, M. J. & KREMER, J. A. 2012. Patient-focused internet interventions in reproductive medicine: a scoping review. *Hum Reprod Update*, 18, 211-27.
- AFSHIN, A., BABALOLA, D., MCLEAN, M., YU, Z., MA, W., CHEN, C. Y., ARABI, M. & MOZAFFARIAN, D. 2016. Information Technology and Lifestyle: A Systematic Evaluation of Internet and Mobile Interventions for Improving Diet, Physical Activity, Obesity, Tobacco, and Alcohol Use. *J Am Heart Assoc*, 5.
- ANDERSON, K., NORMAN, R. J. & MIDDLETON, P. 2010. Preconception lifestyle advice for people with subfertility. *Cochrane database of systematic reviews (Online)*, CD008189.
- AZEVEDO PERRY, E., THOMAS, H., SAMRA, H. R., EDMONSTONE, S., DAVIDSON, L., FAULKNER, A., PETERMANN, L., MANAFO, E. & KIRKPATRICK, S. I. 2017. Identifying attributes of food literacy: a scoping review. *Public Health Nutr*, 20, 2406-2415.
- BARKER, M., DOMBROWSKI, S. U., COLBOURN, T., FALL, C. H. D., KRIZNIK, N. M., LAWRENCE, W. T., NORRIS, S. A., NGAIZA, G., PATEL, D., SKORDIS-WORRALL, J., SNIEHOTTA, F. F., STEEGERS-THEUNISSEN, R., VOGEL, C., WOODS-TOWNSEND, K. & STEPHENSON, J. 2018. Intervention strategies to improve nutrition and health behaviours before conception. *Lancet*, 391, 1853-1864.
- BEST, D., AVENELL, A. & BHATTACHARYA, S. 2017. How effective are weight-loss interventions for improving fertility in women and men who are overweight or obese? A systematic review and meta-analysis of the evidence. *Hum Reprod Update*, 1-25.
- BLACK, D. R., GLEESER, L. J. & KOOYERS, K. J. 1990. A meta-analytic evaluation of couples weight-loss programs. *Health Psychol*, 9, 330-47.
- BOEDT, T., DANCET, E., LIE FONG, S., PEERAER, K., DE NEUBOURG, D., PELCKMANS, S., VAN DE VIJVER, A., SEGHERS, J., VAN DER GUCHT, K., VAN CALSTER, B., SPIESSENS, C. & MATTHYS, C. 2019a. Effectiveness of a mobile preconception lifestyle programme in couples undergoing in vitro fertilisation (IVF): the protocol for the PreLiFe randomised controlled trial (PreLiFe-RCT). *BMJ Open*, 9, e029665.
- BOEDT, T., DANCET, E., PEERAER, K., LIE FONG, S., SPIESSENS, C. & MATTHYS, C. The diet quality of couples undergoing IVF. 34th Annual Meeting of the European-Society-of-Human-Reproduction-and-Embryology (ESHRE), 2019 Barcelona Spain Human Reproduction 188-188.
- BOEDT, T., VANHOVE, A. C., VERCOE, M. A., MATTHYS, C., DANCET, E. & LIE FONG, S. 2021. Preconception lifestyle advice for people with infertility. *Cochrane Database Syst Rev*, 4, Cd008189.
- BOEDT, T., VOOREND, R., DERBOVEN, J., DANCET, E., SPIESSENS, C. & MATTHYS, C. Development of a food literacy intervention for couples trying to conceive. 13th European Nutrition Conference: Malnutrition in an obese world: European Perspectives, 2019b Dublin, Ireland.
- BOIVIN, J., BUNTING, L., COLLINS, J. A. & NYGREN, K. G. 2007. International estimates of infertility prevalence and treatment-seeking: potential need and demand for infertility medical care. *Hum Reprod*, 22, 1506-12.
- BOIVIN, J., GRIFFITHS, E. & VENETIS, C. A. 2011. Emotional distress in infertile women and failure of assisted reproductive technologies: meta-analysis of prospective psychosocial studies. *BMJ*, 342, d223.
- BREWER, J. A., ROY, A., DELUTY, A., LIU, T. & HOGE, E. A. 2020. Can mindfulness mechanistically target worry to improve sleep disturbances? Theory and study protocol for app-based anxiety program. *Health Psychol*, 39, 776-784.

- BROEKHUIS, M., VAN VELSEN, L. & HERMENS, H. 2019. Assessing usability of eHealth technology: A comparison of usability benchmarking instruments. *Int J Med Inform*, 128, 24-31.
- CORRIGAN, J., DONALDSON, M., KOHN, L., MAGUIRE, S. & PIKE, K. 2001. Crossing the Quality Chasm. A New Health System for the 21st Century. *Institute of Medicine, National Academy of Sciences, National Academy Press*.
- COUSINEAU, T. M. & DOMAR, A. D. 2007. Psychological impact of infertility. *Best Pract Res Clin Obstet Gynaecol*, 21, 293-308.
- CRAIG, C. L., MARSHALL, A. L., SJÖSTRÖM, M., BAUMAN, A. E., BOOTH, M. L., AINSWORTH, B. E., PRATT, M., EKELUND, U., YNGVE, A., SALLIS, J. F. & OJA, P. 2003. International physical activity questionnaire: 12-country reliability and validity. *Med Sci Sports Exerc*, 35, 1381-95.
- CRAIG, P., DIEPPE, P., MACINTYRE, S., MICHIE, S., NAZARETH, I. & PETTICREW, M. 2013. Developing and evaluating complex interventions: the new Medical Research Council guidance. *Int J Nurs Stud*, 50, 587-92.
- CRANE, R. S., BREWER, J., FELDMAN, C., KABAT-ZINN, J., SANTORELLI, S., WILLIAMS, J. M. & KUYKEN, W. 2017. What defines mindfulness-based programs? The warp and the weft. *Psychol Med*, 47, 990-999.
- CRAWFORD, M. J., RUTTER, D., MANLEY, C., WEAVER, T., BHUI, K., FULOP, N. & TYRER, P. 2002. Systematic review of involving patients in the planning and development of health care. *Bmj*, 325, 1263.
- DANCET, E. A., VAN EMPEL, I. W., ROBER, P., NELEN, W. L., KREMER, J. A. & D'HOOGHE, T. M. 2011. Patient-centred infertility care: a qualitative study to listen to the patient's voice. *Hum Reprod*, 26, 827-33.
- DE NEUBOURG, D., BOGAERTS, K., BLOCKEEL, C., COETSIER, T., DELVIGNE, A., DEVREKER, F., DUBOIS, M., GILLAIN, N., GORDTS, S. & WYNS, C. 2016. How do cumulative live birth rates and cumulative multiple live birth rates over complete courses of assisted reproductive technology treatment per woman compare among registries? *Hum Reprod*, 31, 93-9.
- ELDREDGE, L., MARKHAM, C., RUITER, R., FERNANDEZ, M., KOK, G. & PARCEL, G. 2016. *Planning health promotion programs. An intervention mapping approach*, San Fransisco CA, Jossey-Bass A Wiley Brand.
- EVANS, D. 2003. Hierarchy of evidence: a framework for ranking evidence evaluating healthcare interventions. *J Clin Nurs*, 12, 77-84.
- GAMEIRO, S., BOIVIN, J., DANCET, E., DE KLERK, C., EMERY, M., LEWIS-JONES, C., THORN, P., VAN DEN BROECK, U., VENETIS, C., VERHAAK, C. M., WISCHMANN, T. & VERMEULEN, N. 2015. ESHRE guideline: routine psychosocial care in infertility and medically assisted reproduction-a guide for fertility staff. *Hum Reprod*, 30, 2476-85.
- GAMEIRO, S., BOIVIN, J. & DOMAR, A. 2013a. Optimal in vitro fertilization in 2020 should reduce treatment burden and enhance care delivery for patients and staff. *Fertil Steril*, 100, 302-9.
- GAMEIRO, S., BOIVIN, J., PERONACE, L. & VERHAAK, C. M. 2012. Why do patients discontinue fertility treatment? A systematic review of reasons and predictors of discontinuation in fertility treatment. *Hum Reprod Update*, 18, 652-69.
- GAMEIRO, S., VERHAAK, C. M., KREMER, J. A. & BOIVIN, J. 2013b. Why we should talk about compliance with assisted reproductive technologies (ART): a systematic review and meta-analysis of ART compliance rates. *Hum Reprod Update*, 19, 124-35.
- GEZONDHEIDSRAAD, H. 2016. Voedingsaanbevelingen voor België. HGR n 9285.
- GEZONDLEVEN. 2018. <https://www.gezondleven.be/> [Online]. [Accessed].
- GOTINK, R. A., CHU, P., BUSSCHBACH, J. J., BENSON, H., FRICCHIONE, G. L. & HUNINK, M. G. 2015. Standardised mindfulness-based interventions in healthcare: an overview of systematic reviews and meta-analyses of RCTs. *PLoS One*, 10, e0124344.
- GREESON, J. M. & CHIN, G. R. 2019. Mindfulness and physical disease: a concise review. *Curr Opin Psychol*, 28, 204-210.

- HAMMICHE, F., LAVEN, J. S., VAN MIL, N., DE COCK, M., DE VRIES, J. H., LINDEMANS, J., STEEGERS, E. A. & STEEGERS-THEUNISSEN, R. P. 2011. Tailored preconceptional dietary and lifestyle counselling in a tertiary outpatient clinic in The Netherlands. *Hum Reprod*, 26, 2432-41.
- HARRISON, C. L., BROWN, W. J., HAYMAN, M., MORAN, L. J. & REDMAN, L. M. 2016. The Role of Physical Activity in Preconception, Pregnancy and Postpartum Health. *Semin Reprod Med*, 34, e28-37.
- HOMAN, G., LITT, J. & NORMAN, R. J. 2012. The FAST study: Fertility ASsessment and advice Targeting lifestyle choices and behaviours: a pilot study. *Hum Reprod*, 27, 2396-404.
- HOMAN, G. F., DAVIES, M. & NORMAN, R. 2007. The impact of lifestyle factors on reproductive performance in the general population and those undergoing infertility treatment: a review. *Hum Reprod Update*, 13, 209-23.
- HURKMANS, E., MATTHYS, C., BOGAERTS, A., SCHEYS, L., DEVLOO, K. & SEGHERS, J. 2018. Face-to-Face Versus Mobile Versus Blended Weight Loss Program: Randomized Clinical Trial. *JMIR Mhealth Uhealth*, 6, e14.
- IBANEZ-PEREZ, J., SANTOS-ZORROZUA, B., LOPEZ-LOPEZ, E., MATORRAS, R. & GARCIA-ORAD, A. 2019. An update on the implication of physical activity on semen quality: a systematic review and meta-analysis. *Arch Gynecol Obstet*.
- KABAT-ZINN, J. 2013. *Full catastrophe living, revised edition: how to cope with stress, pain and illness using mindfulness meditation.*, Hachette UK.
- KHOURY, B., LECOMTE, T., FORTIN, G., MASSE, M., THERIEN, P., BOUCHARD, V., CHAPLEAU, M. A., PAQUIN, K. & HOFMANN, S. G. 2013. Mindfulness-based therapy: a comprehensive meta-analysis. *Clin Psychol Rev*, 33, 763-71.
- KOK, G., GOTTLIEB, N. H., PETERS, G. J., MULLEN, P. D., PARCEL, G. S., RUITER, R. A., FERNANDEZ, M. E., MARKHAM, C. & BARTHOLOMEW, L. K. 2016. A taxonomy of behaviour change methods: an Intervention Mapping approach. *Health Psychol Rev*, 10, 297-312.
- LAN, L., HARRISON, C. L., MISSO, M., HILL, B., TEEDE, H. J., MOL, B. W. & MORAN, L. J. 2017. Systematic review and meta-analysis of the impact of preconception lifestyle interventions on fertility, obstetric, fetal, anthropometric and metabolic outcomes in men and women. *Hum Reprod*, 32, 1925-1940.
- LI, J., LONG, L., LIU, Y., HE, W. & LI, M. 2016. Effects of a mindfulness-based intervention on fertility quality of life and pregnancy rates among women subjected to first in vitro fertilization treatment. *Behav Res Ther*, 77, 96-104.
- LUSSIER, M. T. & RICHARD, C. 2007. The motivational interview: in practice. *Can Fam Physician*, 53, 2117-8.
- MAEX, E. 2010. *In de maalstroom van je leven*, Belgium, Lannoo Meulenhoff.
- MARKLAND, D., RYAN, R., TOBIN, V. & ROLLNICK, S. 2005. Motivational Interviewing and Self-Determination Theory. *Journal of Social and Clinical Psychology - J SOC CLIN PSYCHOL*, 24, 811-831.
- MATTHIESEN, S. M., FREDERIKSEN, Y., INGERSLEV, H. J. & ZACHARIAE, R. 2011. Stress, distress and outcome of assisted reproductive technology (ART): a meta-analysis. *Hum Reprod*, 26, 2763-76.
- MATTHYS, C., MEULEMANS, A. & SCHUEREN, B. V. D. 2015. Development and validation of general FFQ for use in clinical practice. *Annals of Nutrition and Metabolism*, 67 (S1), 239-239.
- MORAN, L. J., SPENCER, L., RUSSELL, D. L., HULL, M. L., ROBERTSON, S. A., VARCOE, T. J., DAVIES, M. J., BROWN, H. M., RODGERS, R. J. & PRACTITIONERS, R. R. I. C. O. F. A. C. 2016. Research Priorities for Fertility and Conception Research as Identified by Multidisciplinary Health Care Practitioners and Researchers. *Nutrients*, 8.
- MUTSAERTS, M. A., VAN OERS, A. M., GROEN, H., BURGGRAAFF, J. M., KUCHENBECKER, W. K., PERQUIN, D. A., KOKS, C. A., VAN GOLDE, R., KAAIJK, E. M., SCHIERBEEK, J. M., OOSTERHUIS, G. J., BROEKMANS, F. J., BEMELMANS, W. J., LAMBALK, C. B., VERBERG, M. F., VAN DER VEEN, F., KLIJN, N. F., MERCELINA, P. E., VAN KASTEREN, Y. M., NAP, A. W., BRINKHUIS, E. A., VOGEL, N. E., MULDER, R. J., GONDRIE, E. T., DE BRUIN, J. P., SIKKEMA, J. M., DE GREEF, M.

- H., TER BOGT, N. C., LAND, J. A., MOL, B. W. & HOEK, A. 2016. Randomized Trial of a Lifestyle Program in Obese Infertile Women. *N Engl J Med*, 374, 1942-53.
- NERY, S. F., PAIVA, S. P. C., VIEIRA É, L., BARBOSA, A. B., SANT'ANNA, E. M., CASALECHI, M., DELA CRUZ, C., TEIXEIRA, A. L. & REIS, F. M. 2019. Mindfulness-based program for stress reduction in infertile women: Randomized controlled trial. *Stress Health*, 35, 49-58.
- NILSEN, E. S., MYRHAUG, H. T., JOHANSEN, M., OLIVER, S. & OXMAN, A. D. 2006. Methods of consumer involvement in developing healthcare policy and research, clinical practice guidelines and patient information material. *Cochrane Database Syst Rev*, Cd004563.
- OOSTINGH, E. C., KOSTER, M. P. H., VAN DIJK, M. R., WILLEMSSEN, S. P., BROEKMANS, F. J. M., HOEK, A., GODDIJN, M., KLIJN, N. F., VAN SANTBRINK, E. J. P., STEEGERS, E. A. P., LAVEN, J. S. E. & STEEGERS-THEUNISSEN, R. P. M. 2020. First effective mHealth nutrition and lifestyle coaching program for subfertile couples undergoing in vitro fertilization treatment: a single-blinded multicenter randomized controlled trial. *Fertil Steril*, 114, 945-954.
- PEERAER, K., DEBROCK, S., LAENEN, A., DE LOECKER, P., SPIESSENS, C., DE NEUBOURG, D. & D'HOOGHE, T. M. 2014. The impact of legally restricted embryo transfer and reimbursement policy on cumulative delivery rate after treatment with assisted reproduction technology. *Hum Reprod*, 29, 267-75.
- PENEDO, F. J. & DAHN, J. R. 2005. Exercise and well-being: a review of mental and physical health benefits associated with physical activity. *Curr Opin Psychiatry*, 18, 189-93.
- PORAT-KATZ, A., PALTIEL, O., KAHANE, A. & ELDAR-GEVA, T. 2016. The effect of using complementary medicine on the infertility-specific quality of life of women undergoing in vitro fertilization. *Int J Gynaecol Obstet*, 135, 163-167.
- RAO, M., ZENG, Z. & TANG, L. 2018. Maternal physical activity before IVF/ICSI cycles improves clinical pregnancy rate and live birth rate: a systematic review and meta-analysis. *Reprod Biol Endocrinol*, 16, 11.
- RYAN, R. M. & DECI, E. L. 2000. Self-determination theory and the facilitation of intrinsic motivation, social development, and well-being. *Am Psychol*, 55, 68-78.
- SALAS-HUETOS, A., BULLÓ, M. & SALAS-SALVADÓ, J. 2017. Dietary patterns, foods and nutrients in male fertility parameters and fecundability: a systematic review of observational studies. *Hum Reprod Update*, 1-19.
- SMITH, J. F., EISENBERG, M. L., MILLSTEIN, S. G., NACHTIGALL, R. D., SHINDEL, A. W., WING, H., CEDARS, M., PASCH, L. & KATZ, P. P. 2010. The use of complementary and alternative fertility treatment in couples seeking fertility care: data from a prospective cohort in the United States. *Fertil Steril*, 93, 2169-74.
- STEPHENSON, J., HESLEHURST, N., HALL, J., SCHOENAKER, D., HUTCHINSON, J., CADE, J. E., POSTON, L., BARRETT, G., CROZIER, S. R., BARKER, M., KUMARAN, K., YAJNIK, C. S., BAIRD, J. & MISHRA, G. D. 2018. Before the beginning: nutrition and lifestyle in the preconception period and its importance for future health. *Lancet*, 391, 1830-1841.
- TRUMAN, E., LANE, D. & ELLIOTT, C. 2017. Defining food literacy: A scoping review. *Appetite*, 116, 365-371.
- TWIGT, J. M., BOLHUIS, M. E., STEEGERS, E. A., HAMMICHE, F., VAN INZEN, W. G., LAVEN, J. S. & STEEGERS-THEUNISSEN, R. P. 2012. The preconception diet is associated with the chance of ongoing pregnancy in women undergoing IVF/ICSI treatment. *Hum Reprod*, 27, 2526-31.
- VAN DIJK, M. R., HUIJGEN, N. A., WILLEMSSEN, S. P., LAVEN, J. S., STEEGERS, E. A. & STEEGERS-THEUNISSEN, R. P. 2016. Impact of an mHealth Platform for Pregnancy on Nutrition and Lifestyle of the Reproductive Population: A Survey. *JMIR Mhealth Uhealth*, 4, e53.
- VAN DIJK, M. R., KOSTER, M. P. H., WILLEMSSEN, S. P., HUIJGEN, N. A., LAVEN, J. S. E. & STEEGERS-THEUNISSEN, R. P. M. 2017. Healthy preconception nutrition and lifestyle using personalized mobile health coaching is associated with enhanced pregnancy chance. *Reprod Biomed Online*.
- VIDGEN, H. A. & GALLEGOS, D. 2014. Defining food literacy and its components. *Appetite*, 76, 50-9.

- VUJKOVIC, M., DE VRIES, J. H., LINDEMANS, J., MACKLON, N. S., VAN DER SPEK, P. J., STEEGERS, E. A. & STEEGERS-THEUNISSEN, R. P. 2010. The preconception Mediterranean dietary pattern in couples undergoing in vitro fertilization/intracytoplasmic sperm injection treatment increases the chance of pregnancy. *Fertil Steril*, 94, 2096-101.
- WARBURTON, D. E. R. & BREDIN, S. S. D. 2017. Health benefits of physical activity: a systematic review of current systematic reviews. *Curr Opin Cardiol*, 32, 541-556.
- WHO. 2018a. *Healthy Diet* [Online]. <https://www.who.int/news-room/fact-sheets/detail/healthy-diet>. [Accessed].
- WHO. 2018b. *Physical Activity* [Online]. [www.who.int/news-room/fact-sheets/detail/physical-activity](http://www.who.int/news-room/fact-sheets/detail/physical-activity). [Accessed].
- WU, A. K., ELLIOTT, P., KATZ, P. P. & SMITH, J. F. 2013. Time costs of fertility care: the hidden hardship of building a family. *Fertil Steril*, 99, 2025-30.
- ZEGERS-HOCHSCHILD, F., ADAMSON, G. D., DYER, S., RACOWSKY, C., DE MOUZON, J., SOKOL, R., RIENZI, L., SUNDE, A., SCHMIDT, L., COOKE, I. D., SIMPSON, J. L. & VAN DER POEL, S. 2017. The International Glossary on Infertility and Fertility Care, 2017. *Hum Reprod*, 32, 1786-1801.

## Figure legends

Figure 1: Stages and steps of the development of the PreLiFe-programme. 

Figure 2: The plausible theory of the PreLiFe-programme

Figure 3: Detailed description of the PreLiFe-programme with a blended care

format. Abbreviations: FAQs: frequently asked questions; MBSR: mindfulness based stress reduction; PA: physical activity



### Supplementary table SI: The three open-ended questions and topic list used for the interviews with IVF-patients on their needs regarding a lifestyle programme

#### Open-ended questions:

- 1) Based on your experiences with having fertility problems, to which extend do you need/want advice regarding your lifestyle?
- 2) If we were to develop an application with lifestyle advice for IVF-couples, how could the format of such programme deal with the two partners of a couple?
- 3) How do you feel about apps?

#### Topics related to question 1:

- Dietary advice
  - Interest in diet
  - Content
    - Useful tips on diet
    - Advice on selecting food\*

- Advice on preparing food\*
  - Advice on interpreting information on food\*
  - Advice on planning food\*
  - Advice on eating food\*
- Format
  - Phrasing of tips
  - Potential of app for healthy diet
  - Interest in (digital) interaction with professional regarding diet
- Physical activity
  - Interest in physical activity
  - Content
    - Advice on exercising
    - Advice on daily physical activity
    - Advice on sedentary behaviour\*
  - Format
    - Potential of app for physical activity
    - Interest in (digital) interaction with professional regarding physical activity
- Other components?
- Other component: Ways to cope with emotional distress\*
  - Content
    - Most stressful treatment aspects\*
    - Used strategies for coping with emotional distress\*
    - Interest in mindfulness\*
  - Format
    - Potential of app for coping with emotional distress\*
    - Interest in (digital) interaction with professional regarding coping with emotional distress\*
- Other component: Fertility treatment advice\*
  - Content
    - Elements of IVF requiring more general information\*
    - Elements of IVF requiring more personalized feedback\*
  - Format
    - Potential of app for fertility treatment advice\*
    - Interest in (digital) interaction with professional regarding IVF\*
- Format: general
  - Advice on different lifestyle components separate or intertwined
  - Certain lifestyle components need certain format of advice
  - Interaction speed

#### Topics related to question 2:

- Exercising together with partner
- Preparing food/eating together with partner
- Deal with emotional distress together with partner\*
- Search/digest fertility treatment information together with partner\*
- Format for dealing with partners of the same couple

#### Topics related to question 3:

- Used devices
- Challenges of certain devices

- Favourite apps
- Dealing with notifications

---

\*Topics added throughout the intertwined process of data-collection and analysis

<b>Supplementary table SII: Percentage of women and men participating in our cross-sectional survey with diet and physical activity in line with recommendations</b>		
<b>Recommended daily intake (RDI) according to food based dietary recommendations (A,B)</b>	<b>% of women that meet RDI (n=57)</b>	<b>% of men that meet RDI (n=57)</b>
<b>Water: 1500 ml/day</b>	28% *	42% *
<b>Vegetables: 300g/day</b>	5% *	6% *
<b>Fruit: 250g/day</b>	10% *	6% *
<b>Meat: 100g/day</b>	27% **	22% **
<b>Rest group of ultraprocessed foods: max 10% of total food intake/day</b>	21%**	15%**
<b>Recommended weekly physical activity (RPA) according to physical activity recommendations (A,C)</b>	<b>% of women that meet RPA (n=57)</b>	<b>% of men that meet RPA (n=57)</b>
<b>Moderate to vigorous physical activity: 150 minutes/week</b>	62%	66%
<b>Legend:</b> * too low intake ** too high intake <b>(A)</b> GezondLeven 2018 <b>(B)</b> WHO fact sheet on nutrition 2018a <b>(C)</b> WHO fact sheet on physical activity 2018b		