RESEARCH PROTOCOL

PReCARE

1 March 2023

PROTOCOL TITLE 'PReCARE - Evaluation of a PReparatory eHealth intervention for patients with a low SEP in CArdiac REhabilitation: a pilot study.'

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Laboratory sites <*if applicable*>	***Not applicable***
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LIST OF ABBREVIATIONS AND RELEVANT DEFINITIONS

CR	**Cardiac Rehabilitation**
DSMB	**Data Safety Monitoring Board**
eHealth	**Technologies for Health**
EudraCT	**European drug regulatory affairs Clinical Trials**
IC	**Informed Consent**
METC	**Medical research ethics committee (MREC); in Dutch: medisch-ethische toetsingscommissie (METC)**
(S)AE	**(Serious) Adverse Event**
SEP	**Socio-economic Position**
Sponsor	**The sponsor is the party that commissions the organisation or performance of the research, for example a pharmaceutical company, academic hospital, scientific organisation or investigator. A party that provides funding for a study but does not commission it is not regarded as the sponsor, but referred to as a subsidising party.**
SUSAR	**Suspected Unexpected Serious Adverse Reaction**
WMO	**Medical Research Involving Human Subjects Act (in Dutch: Wet Medisch-wetenschappelijk Onderzoek met Mensen**

SUMMARY

Rationale: Health disparities between socioeconomic classes are growing. People with a low socioeconomic position (SEP) display unhealthier lifestyles, resulting in an increased risk of cardiovascular diseases. Cardiac rehabilitation (CR) is less successful for patients with a low SEP. A possible cause is that patients with a low SEP display lower levels of patient activation (being able to manage your health) when compared to people with a high SEP. Improving patient activation for patients with a low SEP seems therefore important to facilitate their success within their CR. In a preliminary study we found that patients indeed have a passive attitude towards their condition, especially during the so-called 'waiting period' (the period between discharge from the hospital and start of the rehabilitation). Activating patients in this period could be beneficial for the success of their upcoming rehabilitation as well as their long-term health. Therefore, we have developed a tailored eHealth intervention aimed at improving patient activation levels by supporting patients with a low SEP during their waiting period.

Objective: To assess the feasibility of a tailored eHealth intervention for cardiac patients with a low SEP. Secondly, to explore its effect on patient activation levels and feelings of certainty and guidance compared to usual care.

Study design: Randomized pilot study

Study population: Sixty Patients with a low SEP (>18 years) who are eligible for participation in CR and have been referred to CR by their cardiologist; 30 patients in the intervention group and 30 in the control group.

Intervention (if applicable): Patients will be enrolled in the intervention group based on randomization. The intervention group will use an eHealth application during the waiting period before CR starts. The app asks patients to engage with preparatory messages daily. Messages are pre-made and consist of videos about the rehabilitation, written tips and spoken success stories. The control group will go through the usual waiting period before the start of CR.

Main study parameters/endpoints:

- Feasibility of the intervention in terms of usage, acceptability and experience. Usage will be determined based on the number of days used, length of use (period from first to last day use), number of viewed messages and time spent per visit. Acceptability will be measured using a self-designed questionnaire (9 items) based on the USE questionnaire (Lund, 2001). Finally, experience will be determined based on a thematic analysis of several qualitative semi-structured interviews.

Secondary parameters/endpoints:

- Patient activation measured using the PAM-13 questionnaire. We use the Dutch translation of this questionnaire consisting of 13 items with a 4-point Likert scale.

- Feelings of certainty and guidance using a self-designed questionnaire (9 items).

Nature and extent of the burden and risks associated with participation, benefit and group relatedness: Both intervention and control group will receive CR as usual, as recommended by guidelines. Before CR starts, participants in the intervention group are asked to use an eHealth application daily. The app shows daily messages provided by representatives of different disciplines within CR. Use of the app per day depends on the length of messages but can range between 5 and 10 minutes per day. The content of the app is developed in collaboration with healthcare workers at the rehabilitation center. Patients in the control group do not have this eHealth application in their waiting period.

Both groups will be asked to fill in a questionnaire at two moments:
T_1: Face-to-face group meeting within one week after declaring interest in the study, in which informed consent will be signed, about demographics, certainty, guidance and activation consisting of 25 questions and taking approximately 8 minutes.
T_2: At the start of the rehabilitation (usually after 2 to 6 weeks from T_1) about:

Control: Certainty, guidance, and activation consisting of 22 questions taking approximately 7 minutes.

Intervention: Acceptability, certainty, guidance, and activation, consisting of 31 questions and taking approximately 10 minutes

To minimize the burden for participants, at the start of the study, participants can indicate their preferred medium for filling in the questionnaires (email or postal mail) for T_2. Additional semi-structured interviews (regarding experience, 30 minutes) will be held at T_2 with a subset (estimated: $N \approx 10$) of the participants in the intervention group. Participants are free to choose where they want to do the interviews, either at the CR center, or at their home. Finally, to minimize the burden of the participants using the intervention, we will clarify that reading the messages is not obligatory and that they can be read at any time during the day. We take additional precautions regarding the SEP of our participants:
we will be clear about the nature of the research while avoiding stigmatization. We will do this by avoiding words that imply marginalization in our communications (e.g. IC form). We will ensure our communications, written as well as verbal, are clear and understandable.

1. INTRODUCTION AND RATIONALE

Health disparities between socioeconomic classes are growing (RIVM, 2017). People with a low SEP display unhealthier lifestyles, resulting in an increased risk of cardiovascular diseases (Stringhini et al., 2010). Following a cardiac event, CR programs have proven to reduce the risk of re-hospitalization and premature death (Balady et al., 2007; Piepoli et al., 2010). Evidence points out that CR is less beneficial for patients with a low SEP as they experience more obstacles (Shanmugasegaram, Oh, Reid, McCumber, & Grace, 2013) and therefore are less adherent to the CR program (Valencia, Savage, & Ades, 2011) compared to patients with a high SEP. A possible cause for this is that patients with a low SEP display lower levels of patient activation than patients with a high SEP (J. H. Hibbard et al., 2008; Michie, Jochelson, Markham, & Bridle, 2009). Patient activation comprises the knowledge, skills, and confidence needed to self-manage a chronic condition, such as a cardiovascular disease (J. H. Hibbard, Greene, Shi, Mittler, & Scanlon, 2015).

In a preliminary qualitative study, we identified that patients with a low SEP have a passive attitude, especially during the waiting period between discharge from the hospital and start of the CR. In this study, in which we performed semi-structured interviews with healthcare providers (N = 7) and cardiac patients with a low SEP (N = 7), we showed that feelings of uncertainty and lack of guidance resulted in this passive start of their rehabilitation. Getting the patients to be more active during the preparation period may benefit their rehabilitation on the short term (becoming active directly after a cardiac event has proven crucial for the patients' health (Leon et al., 2005) and benefit their health and wellbeing on the long term (supporting the patient to properly prepare and acquire the needed self-management skills could improve their rehabilitation outcomes (Erskine et al., 2018).

Improving patient activation, especially for patients with a low SEP during their waiting period, seems of key importance to facilitate success within their CR. Nevertheless, due to rising financial pressure regarding healthcare and CR treatment, it is practically not feasible to offer additional guidance and support during the waiting period. Therefore, integrating this in a practically feasible, tailored, and accessible eHealth intervention could lead to positive effects on activation levels during the waiting period, hence improving the overall success of their rehabilitation. While there is evidence of effective eHealth interventions aimed at improving the activation of cardiac patients (Frith et al., 2021), no studies exist that specifically focus on patients with a low SEP. People with a low SEP are more dependent on directions from their healthcare provider and display lower levels of certainty and self-efficacy compared to people with high SEP (Mirowsky & Ross, 2003; Schröder, Fink, & Richter, 2018; Yin et al., 2012). We have developed an eHealth intervention to improve patient activation, certainty and guidance in people with low SEP through a user-centered design process at a CR facility. The overall aim of this pilot study is to assess the feasibility of this newly developed eHealth intervention in patients with a low SEP. Secondly, we explore the effects on patient activation, certainty and guidance during their waiting period before the start of CR. The results could provide insight into the potential and further development of such an intervention to aid the CR.

2. OBJECTIVES

Primary Objective:

To study the feasibility of the newly developed tailored eHealth intervention for cardiac patients with a low SEP.

Secondary Objective(s):

- To explore the effect of the tailored eHealth intervention for cardiac patients with a low SEP on patient activation levels during the waiting period compared to usual care.
- To explore the effect of the tailored eHealth intervention for cardiac patients with a low SEP on their feeling of certainty and guidance during the waiting period compared to usual care.

3. STUDY DESIGN

The study concerns a mono-center randomized pilot study. The study will take place at the CR center 'Capri Hartrevalidatie' with sites in Rotterdam and The Hague. Outcome measures are assessed at 2 time points: (T_1) after declaring interest in the study and signing informed consent, (T_2) at the start of CR (usually after 2 - 6 weeks from T_1). Participants will be randomized into intervention (using the app) and control group.

4. STUDY POPULATION

4.1 Population (base)

We aim to include a total of 60 patients (age >18 years) with a low SEP eligible for participation in CR and who are referred by their cardiologist to Capri Hartrevalidatie. These patients will be divided in either control group (N = 30) or intervention group (N = 30).

4.2 Inclusion criteria

To be eligible to participate in this study, a subject must meet all the following criteria:

- The patient is eligible for participation in CR
- The patient has agreed to sharing his/her contact details and be contacted for research purposes
- The patient is aged 18 years or above
- The patient signs an IC
- The patient is sufficient in the Dutch language
- The patient has access to a mobile phone with internet
- The patient is identified as someone with a low SEP, which will be determined by the socioeconomic status of the neighbourhood

To be eligible to participate in the semi-structured interview, a subject must meet the following criteria:

- The patient enrolled and participated in the intervention group
- The patient provided consent to participate in the interview during T_1

4.3 Exclusion criteria

A potential subject who meets any of the following criteria will be excluded from participation in this study:

- Upon referral, the medical status of the patient is screened by a physician of the CR center. Patients with severe physical, psychological, or cognitive impairments will not be included in the study.

4.4 Sample size calculation

We aim to include 30 patients per group, resulting in a total population of 60 cardiac patients. A paper by NCSS (NCSS, 2022) reviewed several studies that provide sample size recommendations for pilot studies of various purposes. For feasibility studies, these sample size recommendations range from 10 to 35 per group. Capri Hartrevalidatie Rotterdam has approximately 140 referrals each month, of which 60 are expected to fit our inclusion criteria. We expect a participation rate of 25%, which results in 15 participants each month. We expect our recruitment period to last approximately 4

months. A sample size of 30 per group would therefore be feasible and we expect to gain a clear image of the feasibility of the intervention and make an estimation about the effect size regarding activation.

For the semi-structured interviews, we will approach a subset of the intervention group. The size of this subset will be determined based on when theoretical saturation within the responses is reached. Theoretical saturation is reached when during interviewing no additional data is found whereby new properties of qualitative themes (codes) are identified (see analysis ch. 10) (Saunders et al., 2018). We expect to reach saturation after about 10 patients.

5. TREATMENT OF SUBJECTS

5.1 Investigational product

Intervention: The app (figure 1)

The app is a digital, tailored intervention aimed at activating patients with a low SEP during their waiting period between discharge from hospital and start of their CR by providing certainty and guidance. In addition, the intervention is designed to provide feelings of autonomy over intervention usage and facilitate its own engagement on long and short term.

The intervention emphasizes a calendar-based progression using the metaphor of a train on a journey. The goal of the intervention is to reach the end-goal: the start of the rehabilitation. Progression towards this end-goal is made automatically as time advances, which could provide the feeling of certainty. Because waiting times vary based on different factors (e.g., capacity of rehabilitation center, condition of patient and personal circumstances), the timeframe in which the intervention is used can vary (generally between 2 and 6 weeks). The flexible end-goal of the intervention is therefore designed to offer support regardless of the length of the waiting period.

The intervention provides guidance by providing the patient with a set of daily messages. These messages are pre-made by representatives of different disciplines within CR (e.g., cardiologist, physiotherapist, dietician). The messages contain discipline-related information and suggestions as well as a perspective on peer experiences. Each day, the patient is free to choose which and the number of messages to engage with. Engagement is not required to make progress, yet persuasive elements tailored towards the specific needs of people with a low SEP will encourage the patient to engage nevertheless.

Completed messages will be added to the *done pile*, providing a sense of completion which could contribute to feelings of certainty. Participants are encouraged to fill the *done pile* till a predetermined level, which once it is reached provides them with an aesthetical upgrade of their done pile. This upgrade raises the bar for the upcoming level of the *done pile* to be reached while also providing a sense of reward. Through this, the intervention makes use of short-term goals and rewards, which are persuasive mechanisms known to be specifically effective for people with a low SEP (Michie, Johnston, Francis, Hardeman, & Eccles, 2008; Teuscher et al., 2015; Troelstra, Magnée, Koopman, & Nagelhout, 2020).

Once every two weeks, the patient will receive a registration link through the application that allows them to sign up for a physical meeting. This meeting will be facilitated by the investigator at the CR center. The goal of this meeting is for patients to meet fellow peers

and exchange experiences about their waiting period and usage of the app. The patient is free to choose whether to register for the meeting or not.

In the 'help' section of the app the patient finds information (phone number and email) that can be used to contact the investigator (in case of research related questions). The participant is asked to contact their cardiologist at the hospital in case they have medical questions.

The intervention will be used from T_1 until the start of the rehabilitation. However, after the start of the rehabilitation, patients still have access to its contents.

Data and privacy

The data collected within the app will remain on the user's device. Data that will be stored in the application are: username, date of start of rehabilitation, and usage history. To answer our research question regarding the feasibility of the design, only usage data will be exported from the application. The usage data will be collected on general level and will therefore not be relatable to individual participants.

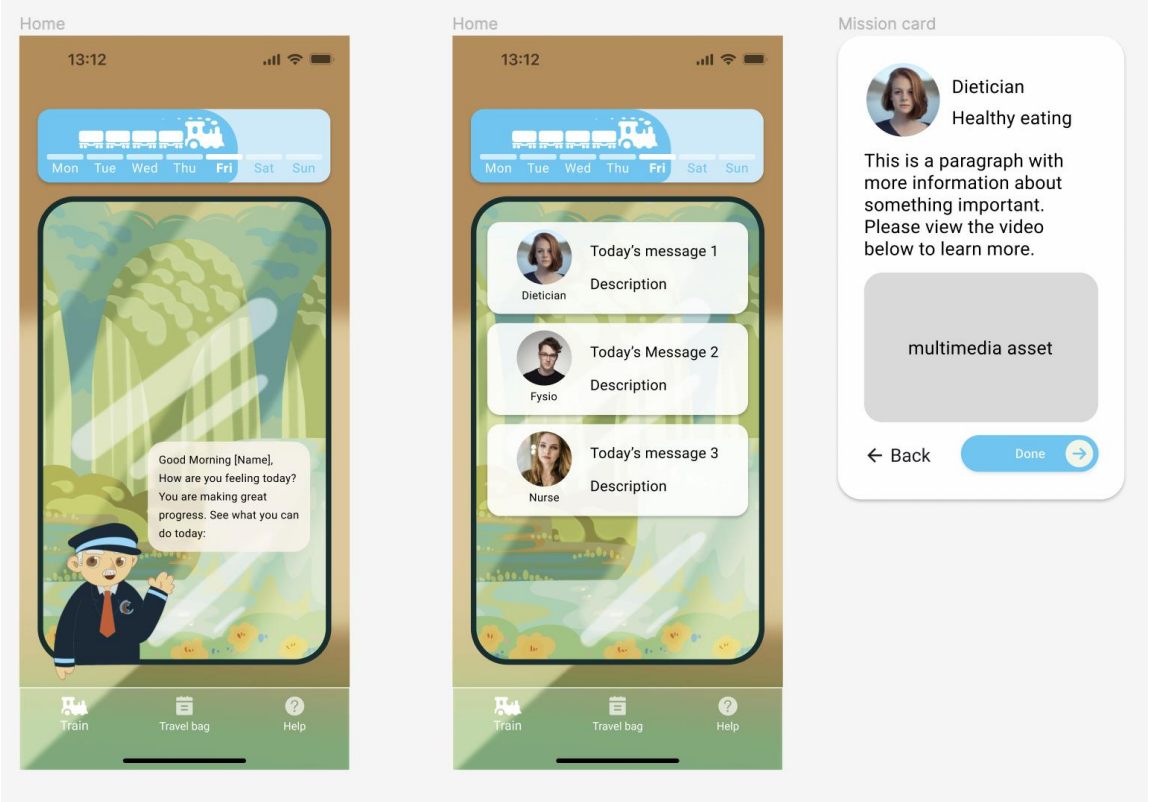

Figure 1. Impression of main screens of the intervention.

5.2 Use of co-intervention

Not applicable

5.3 Escape medication

Not applicable

6. INVESTIGATIONAL PRODUCT

Not applicable

6.1 Name and description of investigational product(s)

6.2 Summary of findings from non-clinical studies

6.3 Summary of findings from clinical studies

6.4 Summary of known and potential risks and benefits

6.5 Description and justification of route of administration and dosage

6.6 Dosages, dosage modifications and method of administration

6.7 Preparation and labelling of Investigational Medicinal Product

6.8 Drug accountability

7. NON-INVESTIGATIONAL PRODUCT

Not applicable

7.1 Name and description of non-investigational product(s)

7.2 Summary of findings from non-clinical studies

7.3 Summary of findings from clinical studies

7.4 Summary of known and potential risks and benefits

7.5 Description and justification of route of administration and dosage

7.6 Dosages, dosage modifications and method of administration

7.7 Preparation and labelling of Non Investigational Medicinal Product

7.8 Drug accountability

8. METHODS

8.1 Study parameters/endpoints

8.1.1 Main study parameter/endpoint

Feasibility

We will investigate the feasibility of our intervention by looking at the usage, acceptability and experience of the intervention.

- Usage will be determined based on (1) number of days used, (2) length of use (period from first to last day of use), (3) number of viewed messages and (4) time spent per visit
- Acceptability will be determined through a self-designed questionnaire based on the USE questionnaire, which relates to Usefulness, Satisfaction and Usability (Lund, 2001). The questionnaire will consist of 9 items on a 5-point Likert scale. We chose to adapt and shorten the questionnaire to better fit with this specific application and to minimize the burden on our participants.
- Experience will be determined through qualitative semi-structured interviews.

8.1.2 Secondary study parameters/endpoints

Patient Activation

We will explore the effect on patient activation levels by using the Dutch translation of the PAM13 questionnaire (Rademakers, Nijman, van der Hoek, Heijmans, & Rijken, 2012). This questionnaire contains 13 items with a 4-point Likert scale. The questions cover topics such as responsibility about health, knowing what to do with prescribed medication and knowing how to prevent health complaints.

Certainty and guidance

We will explore the effect of the tailored eHealth intervention for cardiac patients on their feeling of certainty and guidance during the waiting period. We will do this with self-designed questions with a 5-point Likert scale regarding the concepts related to certainty and guidance. These are the key concepts that resulted from an earlier study we performed and are the drivers on which the intervention is developed. These concepts are the following: certainty, fear of movement, hope, future perspective, information, and direction. These self-designed questions are based on existing questionnaires regarding motivation (MOT-Q), experienced emotional comfort (PEECE), and expectancy (CEQ). We chose to include self-designed questions instead of full validated questionnaires as this better fitted with the exploratory nature of our pilot study and minimizes the burden on participants.

8.1.3 Other study parameters

Demographics

- Sex (Questionnaire)
- Age (Questionnaire)
- Chronic condition (Patient file)
- Educational status (Questionnaire)
- Occupational status and occupation (Questionnaire)

8.2 Randomisation, blinding and treatment allocation

Randomization will take place after the participant has signed informed consent during T_1. Allocations to intervention or control will be done using the Castor research platform. We will choose variable block sizes (two and four).

8.3 Study procedures

Outcome measures will be assessed at 2 points in time (see figure 2).

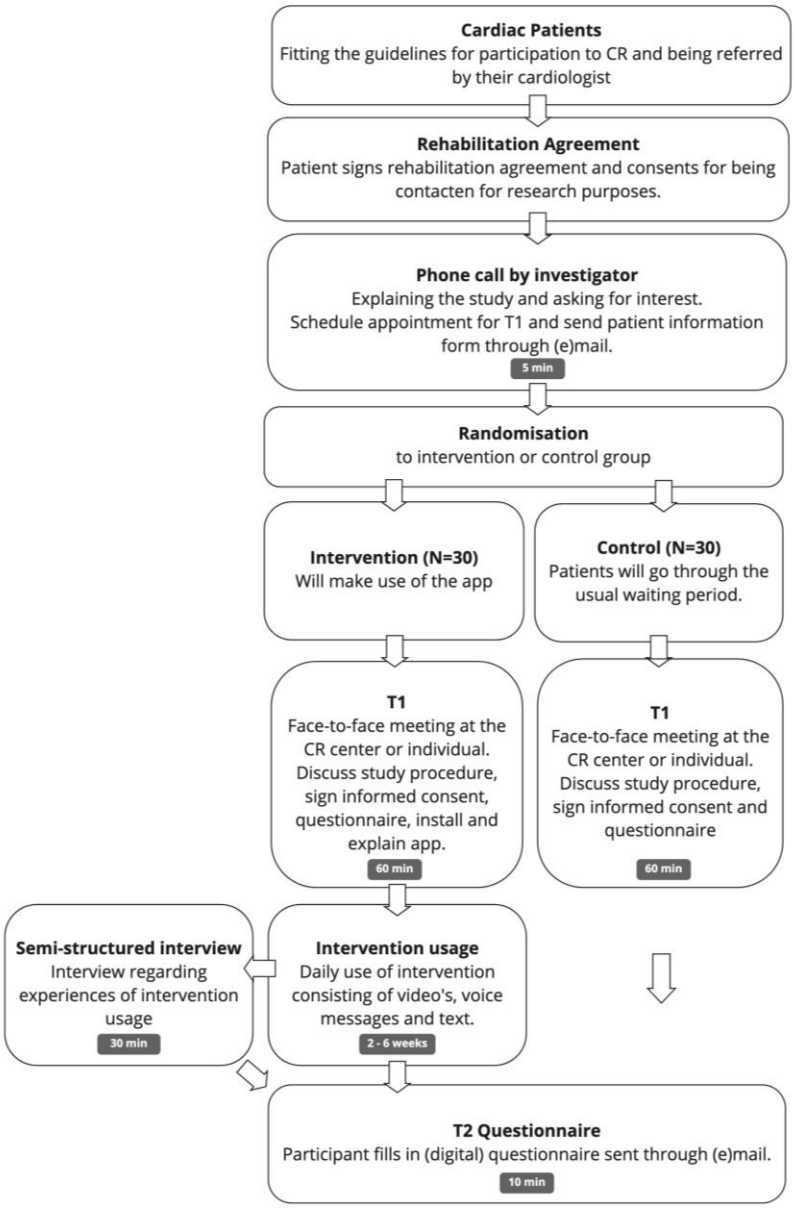

Figure 2 – Flowchart of study procedures

8.4 Withdrawal of individual subjects

Subjects can leave the study at any time for any reason if they wish to do so without any consequences. The investigator can decide to withdraw a subject from the study for urgent medical reasons.

8.4.1 Specific criteria for withdrawal

Not applicable

8.5 Replacement of individual subjects after withdrawal

Subjects who drop out of the study will not be replaced.

8.6 Follow-up of subjects withdrawn from treatment

Subjects withdrawn from the study will be treated according to the usual care. Subjects are not required to indicate their reason to stop participating, but if they do provide reason for dropping out, we will register it and include it in our analysis concerning the feasibility and acceptability of the eHealth intervention.

8.7 Premature termination of the study

If serious adverse events occur that are unacceptable, the study will be prematurely terminated. Patients will then be informed by the investigator and treated according to the usual care. Results will be reported to the accredited METC and the hospital board.

9. SAFETY REPORTING

9.1 Temporary halt for reasons of subject safety

In accordance to section 10, subsection 4, of the WMO, the sponsor will suspend the study if there is sufficient ground that continuation of the study will jeopardise subject health or safety. The sponsor will notify the accredited METC without undue delay of a temporary halt including the reason for such an action. The study will be suspended pending a further positive decision by the accredited METC. The investigator will take care that all subjects are kept informed.

9.2 AEs, SAEs and SUSARs

9.2.1 Adverse events (AEs)

Adverse events are defined as any undesirable experience occurring to a subject during the study, whether or not considered related to the experimental intervention. All adverse events reported spontaneously by the subject or observed by the investigator or his staff will be recorded.

9.2.2 Serious adverse events (SAEs)

A serious adverse event is any untoward medical occurrence or effect that

- results in death;
- is life threatening (at the time of the event);
- requires hospitalisation or prolongation of existing inpatients' hospitalisation;
- results in persistent or significant disability or incapacity;
- is a congenital anomaly or birth defect; or
- any other important medical event that did not result in any of the outcomes listed above due to medical or surgical intervention but could have been based upon appropriate judgement by the investigator.

An elective hospital admission will not be considered as a serious adverse event.

The investigator will report all SAEs to the sponsor without undue delay after obtaining knowledge of the events. The sponsor will report the SAEs through the web portal *ToetsingOnline* to the accredited METC that approved the protocol, within 7 days of first knowledge for SAEs that result in death or are life threatening followed by a period of maximum of 8 days to complete the initial preliminary report. All other SAEs will be reported within a period of maximum 15 days after the sponsor has first knowledge of the serious adverse events.

9.2.3 Suspected unexpected serious adverse reactions (SUSARs)

Not applicable

9.3 Annual safety report

Not applicable

9.4 Follow-up of adverse events

All AEs will be followed until they have abated, or until a stable situation has been reached. Depending on the event, follow up may require additional tests or medical procedures as indicated, and/or referral to the general physician or a medical specialist. SAEs need to be reported till end of study within the Netherlands, as defined in the protocol

9.5 Data Safety Monitoring Board (DSMB)

Not applicable

10. STATISTICAL ANALYSIS

10.1 Primary study parameter(s)

For the primary research question about feasibility, we will analyze quantitative data on usage and acceptability and qualitative data on patient experience. Regarding usage, we will investigate the measures of central tendency and variability for number of days used, length of use (period from first to last day of use), number of viewed messages and time spent per visit. Acceptability will be determined by investigating the measures for central tendency and variability of each item individually and for the overarching concepts: usefulness, usability and satisfaction (5 point likert scale).

Qualitative data on patient experience will be analyzed using a thematic analysis. Interviews will be transcribed verbatim after which we will code individual quotations with corresponding interpretations. Subsequently, we will combine codes into overarching themes that will be used to complement the quantitative results.

The quantitative descriptive statistics combined with the qualitative data on experience will allow us to make a judgement about the feasibility of the intervention.

10.2 Secondary study parameter(s)

For the secondary research question about patient activation levels, we will evaluate patient activation scores between the two groups. The PAM-13 item responses will result in total raw score, ranging from 13 to 52, which we will convert to the linear interval scale of patient activation scores, ranging from 0 (lowest activation) to 100 (highest activation) using instructions (Judith H. Hibbard, Mahoney, Stockard, & Tusler, 2005). We will evaluate the normal distribution with tests for skewness and kurtosis. Second, we will perform T-tests (parametric or non-parametric) to compare the differences in outcome measures between low SEP groups (intervention group and control group) and over time (T_1, T_2). Descriptive statistics will be used to report demographics and baseline characteristics. For all statistical comparisons, the level of significance will be set at $p \leq 0.05$. Analyses will be carried out in the statistical software package SPSS. When our method would appear to be unsuitable during the analysis, for example with an abundance of missing values, we will reevaluate our analysis strategy. We will use a similar analysis procedure using t-tests on the results of the 5-point Likert scales of the individual concepts for the secondary research question about certainty and guidance.

10.3 Other study parameters

Not applicable

10.4 Interim analysis (if applicable)

Not applicable

11. ETHICAL CONSIDERATIONS

11.1 Regulation statement

The study will be conducted according to the principles of the Declaration of Helsinki (64th WMA General Assembly, Fortaleza, Brazil, October 2013) and in accordance with the Medical Research Involving Human Subjects Act (WMO).

11.2 Recruitment and consent

The postal codes of patients that are referred to the CR center will be sent by an employee of the CR center to the investigator who will use them to determine the neighborhood SEP associated with each code. The matching postal codes will be sent back to the employee. Thereafter, the employee will ask, during a routine phone call, for the patient's permission to share his/her contact information and be contacted for research purposes. For those patients that agree, contact information will be sent to the investigator. Subsequently, the patient will be approached by phone by the investigator to identify their interest and for verbal explanation of the research procedure. Patients are explained that the decision of participation does not influence further treatment policy. After declaring their interest in participating in the study, the patient will receive an information letter through mail or email. An appointment will be made for T_1. While making the appointment we will consider the time the patients need to think about their participation in the study, with a least a minimum of two days. One day prior to T_1, participants will be contacted by the investigator and are given the opportunity to ask questions. If patients do not agree to participate, their participation will be cancelled and they will receive usual care. If patients do agree to participate, at T_1 the patient is asked to sign the IC form. The IC form will be signed twice, and one version is given to the patient. Even after agreement, patients are free to stop their participation at any time, without giving a reason for their choice to stop.
T_1 will be organized as a weekly group meeting at their CR facility. However, patients that would not like to participate in this group meeting or do not want to travel to the CR facility, will have the option to choose for an individual meeting at the patient's place of preference instead.

11.3 Objection by minors or incapacitated subjects (if applicable)

Not applicable

11.4 Benefits and risks assessment, group relatedness

The intervention program does not involve additional risks for the participants. Patients will not receive other care than described in the guidelines for CR. Patients will have no direct benefit from participating in this study, other than the expected benefits on patient activation, certainty and guidance. To minimize the burden for participants, at T_1, they will have the opportunity to propose a for them convenient location if they do not wish to partake in the group meeting. For T_2 they have the option to indicate their preferred

method of delivery of the questionnaire (email or mail). See figure 2 for total expected time for each research activity. Participating in the intervention will also ask additional time of the patients. Yet, the patients are allowed to perform the activities at a for them convenient moment. In addition, in our preliminary study we found participants usually have a time abundance during their waiting period and might therefore not mind the additional time expense. The study is group-related because it cannot be conducted without the participation of subjects with a low SEP. We take additional precautions regarding our participants with a low SEP. We will be clear about the nature of the research while avoiding stigmatization. We will do this by avoiding words that imply marginalization in our communications (e.g., IC form). In addition, we will ensure our communications, written as well as verbal, are clear and understandable.

11.5 Compensation for injury

The sponsor/investigator has a liability insurance which is in accordance with article 7 of the WMO.

The sponsor (also) has an insurance which is in accordance with the legal requirements in the Netherlands (Article 7 WMO). This insurance provides cover for damage to research subjects through injury or death caused by the study.

The insurance applies to the damage that becomes apparent during the study or within 4 years after the end of the study.

11.6 Incentives (if applicable)

CR is covered by health insurance. T_1 will be situated at the CR facility. The patients will all receive a 15-euro gift voucher that covers for possible travel expenses and provides a small compensation for participation in the study. At T_2, the measurements can be performed from a distance, so no extra travel expenses are made.

12. ADMINISTRATIVE ASPECTS, MONITORING AND PUBLICATION

12.1 Handling and storage of data and documents

Study outcomes and patient data collected within the app will be handled in compliance with the GDPR and UAVG and the privacy rules of Erasmus MC. Questionnaire data will be collected using paper and an electronic data capture system (Castor). The paper surveys will be scanned and manually added to the database within a V storage drive at Erasmus MC protected with usernames and passcodes. The physical documents will be stored at a protected location at the CR facility. The interview recordings and their transcripts will be uploaded to the same storage drive. We will use voice-editing software to make voices in the recordings unidentifiable. IC forms will be scanned and uploaded to the same storage drive. Physical copies will be saved at a protected location at the CR facility. Members of the research team will have access to the storage drive. All personal data will be given a designated code-number. Only this code-number will be used for data analysis, study-reports, or publications. Only members of the researcher team will have access to the code-list and accompanying key. Data that can be reduced to a subject can only be examined by certified persons after permission of this subject. These certified persons are employees of the research-team of Erasmus MC and employees of the inspection of healthcare and members of the METC. Inspection can be necessary to examine the reliability and quality of the study. Data will be made available for sharing after the project. Data are available for research purposes. Data will be stored for 15 years. After this, data will be destroyed.

12.2 Monitoring and Quality Assurance

At least once every 2 months (with the first visit within the first 2 months after start), an independent researcher will randomly check accuracy, inclusion criteria, compliance, IC's, SAE's and completeness of at least 10% of the data. Findings will be reported to the principal investigator and head of the department. If needed, the principal investigator will take action and talk to responsible people or change protocols.
At the end of data collection, all collected data will be checked by the investigator on completeness and accuracy. Afterwards 10% of the data will be checked by a second independent researcher. All mistakes will be reported and corrected. After this, the data base will be closed to start the analyses.

12.3 Amendments

Not applicable

12.4 Annual progress report

The sponsor/investigator will submit a summary of the progress of the trial to the accredited METC once a year. Information will be provided on the date of inclusion of the first subject, numbers of subjects included and numbers of subjects that have completed

the trial, serious adverse events/ serious adverse reactions, other problems, and amendments.

12.5 Temporary halt and (prematurely) end of study report

The investigator/sponsor will notify the accredited METC of the end of the study within a period of 8 weeks. The end of the study is defined as the last patient's last visit.

The sponsor will notify the METC immediately of a temporary halt of the study, including the reason of such an action.

In case the study is ended prematurely, the sponsor will notify the accredited METC within 15 days, including the reasons for the premature termination.

Within one year after the end of the study, the investigator will submit a final study report with the results of the study, including any publications/abstracts of the study, to the accredited METC.

12.6 Public disclosure and publication policy

The study will be registered in a clinical trial registration (clinicaltrials.gov) before the first patient is recruited. The results of the current project will be written up for publication and submitted to peer-reviewed, international psychological or engineering journals.

13. STRUCTURED RISK ANALYSIS

Not applicable

13.1 Potential issues of concern

Not applicable

13.2 Synthesis

Not applicable

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