Project no: 689043
Acronym : SELFBACK
Title: A decision support system for self-management of low back pain
Activity: PHC-28-2015 Predictive modelling RIA

Work Package 5:	Randomised controlled trial
Deliverable D5.1:	The trial (TRIAL) protocol
Organisation name of deliverable lead:	UoSD
Author(s):	Louise Fleng Sandal, Mette Jensen Stochkendahl, Per Kjær, Jan Hartvigsen, Barbara Nicholl, Frances Mair, Karen Wood, Paul Jarle Mork, Kerstin Bach, Tomasz Szczepanski, Tom Ivar Nilsen, Charlotte Nørregaard Rasmussen, Malene Jagd Svendsen, Kay Cooper, Morten Villumsen, Karen Søgaard
Reviewer(s):	Charlotte Rasmussen, Ottar Vasseljen
Participants:	NTNU, GLA, RGU, NFA
Type:	Report
Dissemination Level:	PU
Version:	1.1
Total no of pages:	44
Project Start date:	1. January 2016
Contractual delivery date:	31 March 2018
Actual delivery date:	12 October 2018
Keywords:	Protocol, RCT, digital decision support system, app, low back pain, outcomes and effect measures.
Status:	Submitted

Abstract
This deliverable describes the protocol for the pilot study, the randomised controlled trial and process evaluation. The randomised controlled trial is an international multi-centre trial with two parallel arms to evaluate the effectiveness of the SELFBACK decision support system (DSS) in addition to usual care versus usual care only in terms of pain-related disability at three months (primary

This project has received funding from the European Union Horizon 2020 research and innovation programme under grant agreement No 689043.

endpoint). This document describes in detail the methods applied and plans for data management and analysis.

Document History

Version	Date	Author(s)	Description
0.1	08/02/17	MJS	Initial version with bullet points to the main methodological components in tabular view
0.2	12/06/17	MJS	Updated version with bullet points to the main methodological components in tabular view
0.3	10/07/17	LFS, MJS	Protocol in plain text started, based on the item checklist from the SPIRIT guideline, 2013
0.4	22/08/17	LFS, JH, MJS, KS, GS	First draft of full protocol circulated at UoSD to clear up obvious mistakes.
0.5	31/08/17	LFS, JH, MJS, KS, GS	Updated version from initial read through.
0.6	15/09/17	All medical partners	Updated after comments and suggestions from all medical partners.
0.7	07/11/17	All medical partners	Updated version after Amsterdam meeting Nov 6th
0.8	29/01/18	All medical partners	Updated version after Skype calls in the fall on unresolved issues in the protocol – final version for commenting before progressing with ethics applications
0.9	12/02/18	All medical partners	Updated after comments from medical partners. Version to be used/scaled down to ethics applications
0.10	21/02/18	All medical partners	Protocol document revised additional comments from MV, PM, TN, BN, KW, then revised from long protocol version into deliverable D.5.1 draft
0.11	05/03/18	Review by OV, CNR	Drafted deliverable in internal review by Ottar Vasseljen and Charlotte Nørregaard Rasmussen
0.12	23/03/18	All medical partners	Deliverable revised after comments in internal review.
0.13	25/03/18	PJM, KB	Minor revisions
1.0	31/03/18	KB, PJM	D5.1 Submitted to the EC
1.0.1	06/09/18	LFS	Minor revision to include the effect of Amendment - AMD-689043-10 (change of pilot and RCT side from UoSD, NTNU and GLA to UoSD and NTNU)
1.1	12/10/18	KB, PJM	Review and revised D5.1 submitted to the EC

Table of Contents

1 Protocol for the SELFBACK trial

Effectiveness of an app-delivered self-management program for reducing pain-related disability in people with low back pain - a protocol for the SELFBACK randomised controlled trial.

This protocol follows the recommendation for items from the Standard Protocol items: Recommendation for Intervention Trials (SPIRIT, 2013) [1] and Consolidated Standards Of Reporting Trials (CONSORT, 2010) guidelines [2]. Additionally the E-health extension to the CONSORT checklist has been used as a guideline for describing the digital intervention [3].

Protocol version: 1.1

Trial registration:
Trial registry will be completed at www.clinicaltrials.gov. The pilot study and randomised controlled trial (RCT) will be registered separately and before patient recruitment is initiated.

Roles and responsibilities:
The partners involved in the SELFBACK project include:

- The Norwegian University of Science and Technology (NTNU), Trondheim, Norway
- The University of Glasgow (GLA), Glasgow, Scotland
- The Robert Gordon University (RGU), Aberdeen, Scotland
- Trade eXpansion (TRX), Tommerup, Denmark
- National Research Centre for the Working Environment (NFA), Copenhagen, Denmark
- Health Leads BV (HLE), Amsterdam, Netherlands
- University of Southern Denmark (UoSD), Odense, Denmark

NTNU is leading the development of the underlying structure for the database and decision support system (DSS), RGU has been leading the physical activity monitoring and TRX has been leading the mobile app development. The medical partners (from NTNU, GLA, RGU, NFA and UoSD) have provided content for the app. The RCT is a multi-centre trial, patients are recruited at NTNU and UoSD; UoSD is lead in the planning and conducting of the RCT; UoSD is lead in the process evaluation with support from GLA and NFA. NTNU is leading the overall project.

Funding
The SELFBACK project has received funding from the European Union Horizon 2020 research and innovation programme under grant agreement no 689043. The funding body supervises the conduct of the overall project, but is not involved in the planning, implementation and interpretation of data from the RCT.

2 Introduction

Low back pain (LBP) is worldwide a major contributor to years lived with pain and disability. In the Global Burden of Disease studies of 2010 and 2015, it was estimated that pain in the low back and neck are the leading causes of years lived with disability in most countries [4, 5]. In the vast majority of people experiencing LBP specific pathoanatomical causes cannot be identified and therefore more than 85% of people seen in primary care are categorised as having "non-specific" LBP [6]. The economic costs of health-care, sickness absence, lost ability to work, social benefits and treatment costs of non-specific LBP are high, and can be considered a societal burden [7-9].

Clinical guidelines recommend patient education, exercise therapy, multidisciplinary treatments and combined physical and psychological interventions as management of persisting LBP [10-12]. Although national clinical guidelines differ in scope and context, the recommendation for managing LBP seem to be persistent over time and generally consistent across countries [10-15]. Self-management programmes that include elements of such recommended treatment components have been suggested as a promising option for chronic conditions including non-specific LBP [16]. Self-management may be defined as the individual's ability to care for their own health by managing their symptoms, physical and psychological consequences and impact on life [16]. However, as self-management is broadly defined, the content of self-management programmes varies [17]. Adherence to self-management programmes is influenced by a variety of factors, such as tailoring of the programme to the individual and support to persist with self-management [18], which in turn may influence the effect of self-management. In LBP, the effectiveness of self-management has been reported to be moderate for pain and small to moderate for disability [17, 19].

Digital solutions, such as mobile applications (apps), have been suggested as promising platforms for supporting self-management of chronic conditions [20, 21]. Within recent years, a vast amount of apps has been introduced to the commercial market for self-management of LBP. A systematic review identified 61 apps and concluded that available apps have poor quality, included poor quality information from questionable sources and that none of the apps had been tested for effectiveness [22]. The SELFBACK project aims to fill this knowledge gap by developing an evidence-based and data-driven decision support system (DSS) delivered via a smartphone app to facilitate, improve and reinforce self-management of non-specific LBP. The DSS suggests self-management plans consisting of physical activity advice, patient education and recommendations for physical exercise tailored to the individual's specific health information. The effectiveness of the DSS will be evaluated in a RCT. Additionally, a pilot study (section 8) and a process evaluation in parallel to the RCT (section 9) [23] are planned.

2.1 Objectives

The objective is to evaluate the effectiveness of the SELFBACK DSS in addition to usual care versus usual care only in a RCT. Primary outcome is pain-related disability at three months

(primary endpoint). We hypothesise that participants randomised to using the SELFBACK app in addition to usual care will have at least two points difference in pain-related disability at three months, measured by the Roland-Morris Disability Questionnaire (RMDQ), compared to participants receiving usual care only.

The effectiveness of the intervention on secondary outcomes, such as quality of life, use of non-prescriptive medication, sleep problems, functional ability and pain intensity, will be assessed at three months. We will also evaluate more long-term effects on these outcomes at six and nine months.

3 Methods

3.1 Trial design

The SELFBACK study is designed as an international multi-centre superiority RCT with two parallel groups, testing the relative effectiveness of the SELFBACK DSS in addition to usual care (intervention group) versus usual care only (control group) for participants with non-specific LBP.

3.2 Study setting

The recruitment of participants will be conducted in two countries: Trondheim, Norway (NO), and Odense, Denmark (DK). In NO, participants will be recruited from general practice, physiotherapy and chiropractic clinics. In DK, recruitment will be from general practice, physiotherapy and chiropractic clinics as well as from the SpineCenter in the Region of Southern Denmark. The SpineCenter is an outpatient hospital that consults patients with back pain referred from primary practice. The SpineCenter provides diagnostic assessment of patients and prescribes treatment plans according to national treatment guideline. Patients seen at the SpineCenter without serious pathologies are referred to the SELFBACK study.

3.3 Selection criteria

Participants must meet all of the following eligibility criteria:

- Seeking care from primary health-care practice or a specialised outpatient hospital facility (DK) for non-specific LBP within the past 8 weeks
- LBP of any duration
- Mild-to severe pain-related disability rated as 16 or below on the PROMIS-PF4 function scale [24-26].
- Age: ≥18 years
- Own and regularly use a smart phone (with at least Android 4.4+ or iOS7.0+) with internet access (Wi-Fi and/or mobile data)
- Have a working email address and have access to a computer with internet access to complete questionnaires in a web browser.

Presence of any of the following criteria will exclude participants from enrolling in the RCT:

- Not interested
- Unable to speak, read or write in the national language (English/ Danish/ Norwegian)
- Cognitive impairment or learning disabilities
- Pathology, such as fracture, cancer, inflammatory diseases, and signs of radiculopathy (severe leg pain, loss of leg strength, or loss of or altered sensation in a myotomal or dermatomal distribution)
- Serious mental illness, such as major depression, schizophrenia, and psychosis

- Terminal illness
- Unable to take part in exercise/physical activity (such as non-ambulatory patients, use of walking aids/assistance, unable to get down and up from the floor independently)
- Fibromyalgia (diagnosed by a HCP)
- Pregnancy
- Previous back surgery
- Ongoing participation in other research trials for LBP management

The assessment of whether the criteria are considered limiting participation is performed either by the referring healthcare professionals (HCP) during the recruitment phase (see green box in Figure **1**) or by participant self-report during the screening call (see blue box in Figure **1**).

3.4 Identification and recruitment of participants by health care professionals (HCP)

The recruitment period starts February 2019. A total of 350 participants are to be recruited to the RCT. Of these, 75% (n=262) will be recruited in DK and 25% in NO (n=88). In each country, collaborations with local clinics and HCP (i.e. general practitioners, physiotherapists and chiropractors) will be established to facilitate recruitment. The number of clinics and HCPs needed to ensure a sufficient recruitment rate will be informed by the pilot study (August–November 2018) (further described in section 8).

The recruitment process is outlined in the green box in Figure **1**. Patients seeking care due to non-specific LBP will be invited to participate in the trial. The HCP will refer potentially eligible participants based on a short description of eligibility. Final eligibility will be assessed by the research team in a screening phone call (blue box in Figure **1**). The referral to the SELFBACK trial will take place after the HCP has performed routine diagnostic assessment or treatment (usual care). Participants are recruited through two pathways, 1) registry data or 2) live recruitment.

For 1), recruitment from registries will be conducted at the SpineCenter in DK. For the registry recruitment in DK, a list of patients will be extracted on a monthly basis from the SpineCenter's registry, who consulted in the past month with LBP according to the inclusion criteria. These patients receive an invitation to participate in the project along with written information on the project, describing two ways to contact the research team, if interested: 1) by email address, or 2) telephone call or text message.

For 2), the live recruitment of participants, the HCP identifies patients seen in their clinical practice who are eligible for self-management of LBP. The HCP briefly informs the patient about the project and provides the patient with written information. This information is similar to that given in the registry recruitment. If interested, patients can contact the research team by 1) email or 2) telephone (call or text message). Additionally for NO,

participants can provide their contact information on a sign-up sheet at the clinic after seeing their HCP to be contacted by the researchers.

3.5 Screening for eligibility by researchers

The screening process is outlined in the blue box in Figure **1**. Participants, who have indicated that they are interested in the project, are contacted via telephone by a researcher in the SELFBACK team. During this telephone call, oral information about the trial is given to the participant and questions about the project and project participation can be answered. A detailed eligibility screening is performed via a pre-defined screening form including the inclusion and exclusion criteria above. If eligible and willing to participate, the participants give their verbal consent to participate and are invited to see a researcher at a research facility, in their home, or a place at the participants' convenience. In advance of the face-to-face meeting, an email entailing a link to the web-based baseline questionnaire is sent to the participant, so that this can be answered in advance of the face-to-face meeting. Also, if the participant has not received the written information yet, this will be sent electronically.

3.6 Enrolment and signed informed consent

The enrolment process is outlined in the grey box in Figure **1**. At a face-to-face meeting with the researcher, oral information about the trial will be repeated to the participant and any questions answered. If a participant declines participation at the face-to-face meeting, the researcher will ensure that the baseline questionnaire that was completed in advance is deleted. If a participant accepts the invitation to participate, the informed consent form is signed and randomisation is performed online via a web-based randomisation system (see section 3.7), and the researcher informs the participant of the results of the randomisation and gives instructions according to the group allocation. If randomised to a) the SELFBACK DSS in addition to usual care, participants are given a wearable device and instructions and assistance on how to download, install and pair the wearable device with the app and how to connect the apps on the smartphone. Moreover, the participant is given information about the follow-up assessments and information on how to contact the researcher if needed. If randomised to b) usual care, participants are instructed on the principles of usual care, and are given the same information as the SELFBACK intervention group about the follow-up assessments and how to get in touch with the researcher if needed.

3.7 Randomisation

Participants are randomised to either a) SELFBACK DSS in addition to usual care or b) usual care only. The randomisation is performed as a block randomisation with permuted blocks of random size (4 to 8 participants) and stratified by country and care provider (i.e. general practitioner, physiotherapist, chiropractor, or SpineCenter). The allocation ratio between the SELFBACK DSS in addition to usual care and the usual care groups is 1:1. Randomisation will be

performed by a web-based randomisation system (WebCRF) developed and administered by Unit of Applied Clinical Research, Faculty of Medicine and Health Sciences, NTNU, Trondheim, Norway. This unit is not otherwise involved in the trial management or trial conduct. A data processor agreement will be contracted with the Unit of Applied Clinical Research concerning their role and responsibilities in the project. The WebCRF system will track recruitment rates and hold a minimal data set on all screened participants (variables included: a participant id number, country, care provider, recruitment site, age, gender). The flow of participants through the trial is described in Figure **1**.

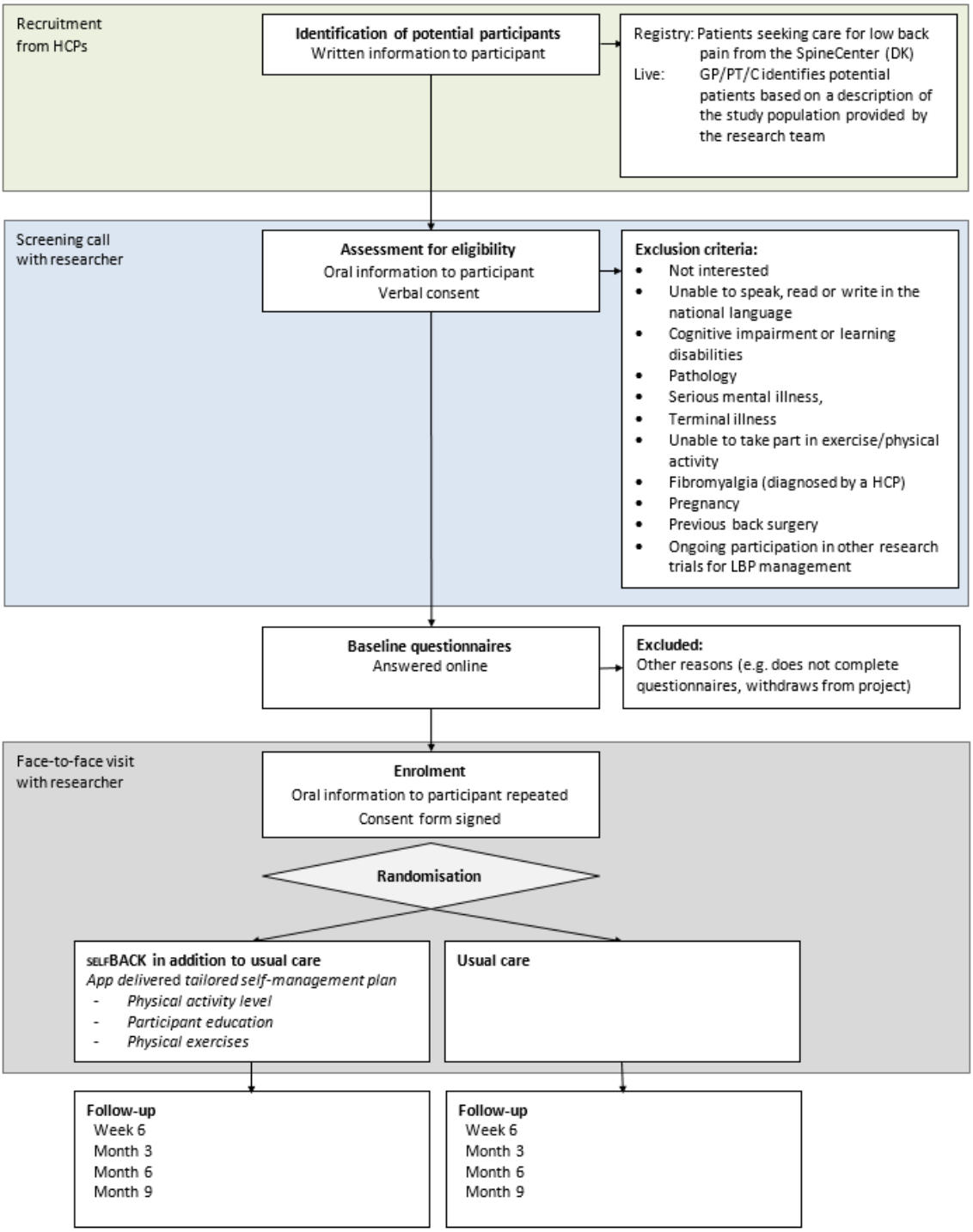

Figure 1: Participant flow through SELFBACK trial. Abbreviations: GP: general practitioner, PT: physiotherapist, C: chiropractor, HCP: Health care provider, LBP: Low Back Pain

3.8 Blinding

The study is a single-blinded study. Participants are not blinded to group allocation. The analysis and interpretation of the study results will be performed by researchers blinded to group allocation. Once the study is completed, a copy of the data will be extracted in pseudonymised form for statistical analyses. All personal information that may lead back to specific participants (i.e. e-mail address, username etc.) will be removed from the data. The information concerning group allocation will be added to the dataset with the intervention and control group will be randomly labelled A and B. The randomisation key (i.e. document entailing information on which group is which) is kept at the Unit of Applied Clinical Research at NTNU. They will provide the randomisation key to the research team once a blinded interpretation of the results is finalized (see section 6.2).

4 Interventions

4.1 Usual care

Participants randomised to usual care will follow any diagnostic or treatment-related pathway (e.g. receive information, advice or treatment) as instructed by their HCP. They are also allowed to seek care, treatment or help elsewhere as normal. After the completion of the trial at 9 months, participants who have completed all follow-up assessments are contacted and offered a wearable device similar to the SELFBACK intervention group.

4.2 SELFBACK in addition to usual care

The SELFBACK intervention is a digital DSS for self-management of LBP provided to the participant via a smartphone app (SELFBACK app). In addition, the participant is provided with a wearable device (i.e., a step-detecting wristband) that interacts with the SELFBACK app. Based on the step count and participant's self-reported data, the SELFBACK app provides individually tailored self-management plans including educational messages, physical activity advice and exercise recommendations matched to the participant's health status, as generated by the DSS. Importantly, the project adheres to the HONcode principle [27, 28], i.e., the intervention is not intended to replace follow-up by HCP, but to supplement the ordinary care by the HCP, and the participant is informed accordingly. Thus, participants randomised to the SELFBACK intervention may continue to seek care, treatment or help as normal.

The content of the intervention was developed using Intervention Mapping (IM). IM is a six-step process with each step consisting of several tasks, which, once completed, inform the next step, as detailed by Bartholomew et al. [29]. The IM process aims to facilitate participation and consultation from all relevant stakeholders. It provides a structure for the integration of theory, empirical findings from the literature, and information collected from the target population. In short, the first step of the IM process of this project consisted of a review of international clinical practice guidelines for management of LBP. The guidelines consistently endorse important elements such as education about LBP, and uptake of evidence-based self-management behaviours by participants; including physical activity and specific exercises as well as cognitive behavioural therapy (CBT) to promote self-management for people with LBP [10, 12-15]. Additionally, literature on self-management of LBP and studies on physical activity, exercise or education (including CBT) was reviewed for inspiration for specific content for each component. Finally, patient leaflets and other patient information delivered through websites or apps were reviewed for content of self-management for LBP. The IM process for the SELFBACK intervention will be described in detail elsewhere (deliverable 3.8 IMAP, delivery date M33).

4.2.1 The digital DSS

The SELFBACK system constitutes a data-driven predictive DSS that uses the Case-Based Reasoning (CBR) methodology [30] to capture and reuse participant cases in order to suggest the most suitable self-management plan for participants. The data sources for the CBR system comprise 1) the initial participant data collected by the baseline web-based questionnaire, 2) a weekly question and answering session (tailoring) by the participant in the SELFBACK app (including pain, function, fear-avoidance, workability, sleep, self-efficacy, stress, health belief and barriers), and 3) the step-detecting wearable. On a weekly basis, this information is used to customize the self-management plan by matching the characteristics of the current participant case with existing successful participant cases in the SELFBACK case-base. The weekly tailoring questions will only be given if relevant for the participant. As an example, if a participant has indicated sleep problems at baseline, then a tailoring question will be asked in appropriate time-intervals, and, based on the answer, a set of educational messages on e.g. sleep hygiene will be offered to the participant. Consequently, the DSS will deliver an individualised self-management plan for the coming week via the SELFBACK app. All interaction between the participant and the SELFBACK DSS happens via the SELFBACK app. There is no interaction between the DSS and HCPs. The architecture of the DSS and the interaction between the participant, the wearable device, the SELFBACK app and the database is outlined in Figure 2. A full description of the DSS is published elsewhere [31] and demonstrated in deliverable 3.2 CBRa (M18).

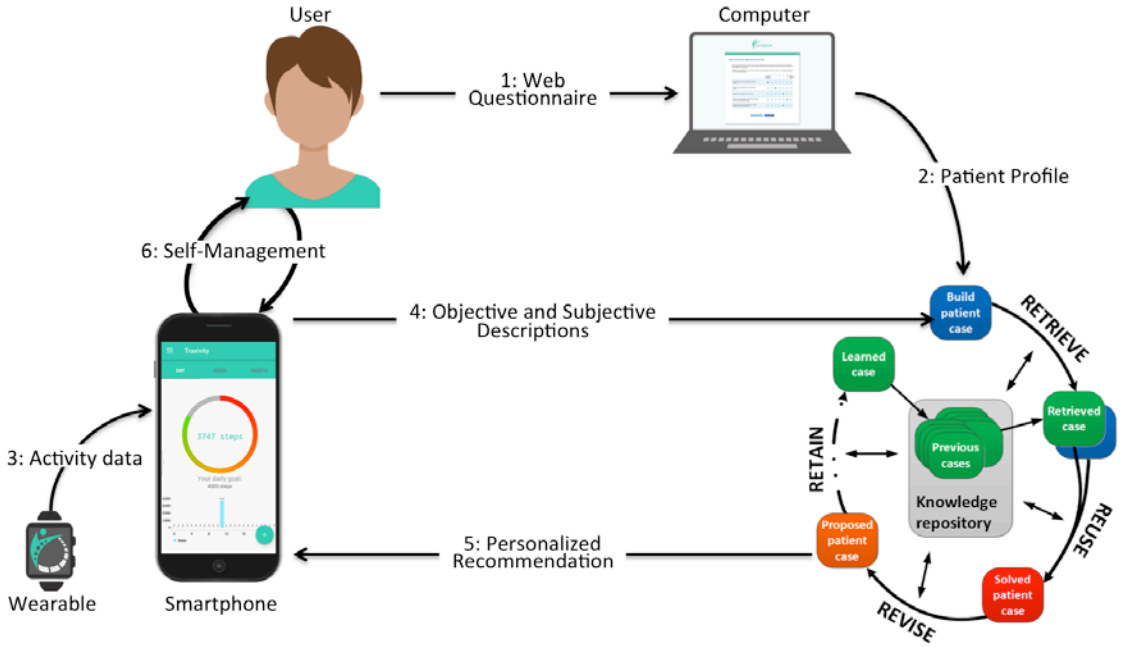

Figure 2: Overview of the SELFBACK decision support system.

4.2.2 Wearable device and supporting apps

The Xiaomi Mi Band 2 wristband was chosen as the wearable device. The wristband tracks the physical activity in terms of step counts and synchronizes them with the GoogleFit app on Android devices and Apple HealthKit app on iOS devices throughout the day. The wristband registers movement in all three planes (frontal, horizontal and sagittal) via an ADI (Analog Devices, Inc.) ultra low-power acceleration sensor and computes step-count from this information. It connects to the phone via Bluetooth (V4.2 BLE) and requires Android 4.4+ / iOS 7.0+.[1] The wearable device is to be worn on the participant's wrist continuously while participating in the intervention. In order to connect the wristband and step count function to the SELFBACK app, the MiFit app is required to be installed on the participant's smartphone. Additionally, Apple HealthKit needs to be activated on iOS devices, and GoogleFit needs to be activated or downloaded if not preinstalled on Android devices. The apps: MiFit, Apple HealthKit and GoogleFit, are freely available, and can be downloaded without cost for the participant. An account needs to be created for the apps for every participant. An installation guide will be developed to help participants install and connect apps, and a researcher will be present at the time of installation to ensure the correct setup.

4.2.3 The SELFBACK self-management plans

The DSS builds the self-management plan from three types of content: 1) physical activity level (i.e., step count) and goals, 2) a bank of physical exercises, and 3) a bank of educational material. An overview of the available content is presented in Figure 3.

Physical activity

Physical activity is tracked as described for the wearable device (see section 4.2.2). The SELFBACK app prompts the participant to set a goal for physical activity by suggesting a gradual increase in daily steps if the past week's goal was achieved. A 10% increase is suggested, until a goal of 10.000 steps per day is reached. The participant is allowed to adjust the suggested goal, before accepting it. During the week, the participant is able to see the achieved step-count per day and track his/her progress. The lowest step count goal that is possible to set will be 3000 steps per day. This limit is based on average step count numbers from previous studies in workplace pedometer intervention (average ~6000 steps) [32] and home-based pedometer intervention in older adults with knee problems (average ~3500 steps) [33]. The minimum step count goal of 3000 per day was chosen to reflect that participants in the trial have functional disability that may also affect their physical activity level. Based on the achieved daily step count from previous week, the step count goal for the coming week is adjusted, and educational messages and notifications aimed to motivate more physical activity is pushed to the participant through the app.

[1]More details: https://xiaomi-mi.com/news-and-actions/mi-band-2-review-new-xiaomi-fitness-tracker-with-oled-display/

Exercise programme

The physical exercise material is compiled of 70 exercises organised in 6 targets (back-, abdominal-, gluteal-, and core muscle strength, pain relief and flexibility). Each participant is given an individualised exercise programme, the default recommendation is to perform exercises in 3-5 sessions per week of 20 minutes (e.g. four exercises with an estimated duration of five min per exercise). The number of exercises is adjusted according to the participant's indication of time available for doing exercise and to the anticipated level of difficulty defined by baseline questionnaire. An exercise programme will always include either 1) a strength exercise for abdominal and back extensor muscles, or 2) one strength exercise for the core muscles. Additionally, exercises targeting strength in hip and gluteal muscles, flexibility of the spine, or pain-relieving exercises may be included in the programme. If a participant presents with an acute pain flare-up or high pain ratings, the app will offered pain-relieving exercises only until an acceptable pain level is achieved.

An exercise is presented to the participant in the app as a short video accompanied by a written instruction that includes recommendations on number of sets and repetitions. The participant will be prompted in the app to report completed number of sets and repetitions per exercise. The DSS will offer a new exercise at a more difficult or easier level in the coming week, based on the level of completion registered. In addition, participants are able to request new exercises (at the same level of difficulty and within the same group of exercises) if they experience problems completing the suggested exercise. The included exercises were extracted from studies identified in international guidelines for treatment of LBP [10, 34], and systematic reviews on effect of exercises in LBP treatment [35-40]. The organisation, targets and progression of exercises were guided by consensus discussions among experienced clinicians and researchers within the SELFBACK project team. This process will be described in detail in deliverable 3.8 (IMAP), due in M33.

Education

The educational material is structured under 14 main categories ("information about LBP", "understanding mind-body", "self-management for LBP", "thoughts, behaviour, attitude and feeling", "fitting in self-management in a busy life", "first aid when your back hurts", "LBP and comorbidities", "goal-setting and action planning", "pacing and graded activity", "problem solving", "relaxation", "sleep and LBP", "social support" and "overcoming barriers for self-management of LBP"). For each main category, a tree-structure of educational messages has been created. Every short message is about 140 characters long. Some messages may include links to longer, more explanatory text (max 500 characters) or tools that can be used to help with self-managing LBP, e.g. goal setting tool, sleep advice, etc. Some short messages are also rewritten into "quizzes", where the educational content is rephrased into a yes or no type question. When answering a quiz, a follow-up answer is displayed to the participant stating the correct answer with additional explanation. A total of 230 short messages or quizzes are available in the educational material.

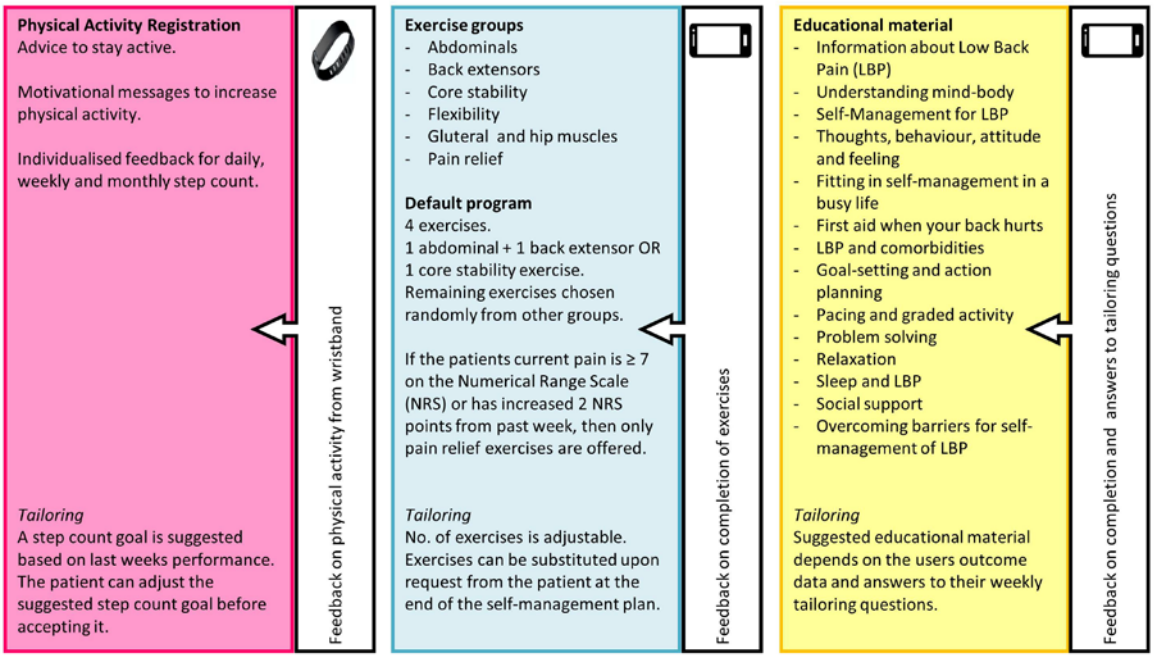

Figure 3: Overview of available content within the selfBACK app

4.2.4 SELFBACK mobile app

The individually tailored self-management plan is delivered via the SELFBACK app. The SELFBACK app is developed by TRX in close collaboration with the other SELFBACK partners. The development of the first version of the app has been completed (by Dec 2017). The final version of the app is scheduled for demonstration by June 2018. The SELFBACK app will be tested in the pilot study (section 8). Upon completion of the pilot study, any feedback from the participants will be implemented into the app; however the core content and features will remain as described above. Hereafter, the app and DSS will be frozen and tested in the RCT. To increase transparency and facilitate replicability of the intervention, the version of the app and DSS used in the RCT will be preserved. A short video representation of the app will be made publicly available after the RCT has been completed.

4.2.5 Access, frequency and mode of delivery

The participants access their self-management plan via the SELFBACK app and enter data into the DSS by answering tailoring questions in the app and by wearing the connected wearable device. These data are combined with the participant self-reported outcome as outlined in Figure 2. The participant is encouraged to use the SELFBACK app daily or at least once a week, in order to be offered a new self-management plan for the coming week. The app will send push-notifications reminding the participant to open the app and view the new self-management plan. The participant can disable or adjust the frequency of notifications in the app settings. The goal of the intervention is that participants learn to self-manage their LBP, which may potentially result in participants discontinuing their use of the app. Consequently, discontinuation is not necessarily a sign of low compliance but may indicate a high self-

management level. Nevertheless, to accommodate fluctuations in use of the app a "welcome back" sequence is constructed to guide participants back into the intervention if they re-open the app after having discontinued use for more than 4 weeks.

4.2.6 Ancillary and post-trial management

All participants randomised to the SELFBACK intervention are allowed to continue their use of the wearable device after the trial. However, the access to the SELFBACK app will cease after the 9 months follow-up, by disabling the participants username, thereby restricting login to the app. All participants randomised to the usual care group are given a wearable device after completing all follow-up assessments. No further post-trial management is planned.

5 Outcomes

All outcomes are collected at baseline, six weeks, three, six and nine months. Additionally, participant characteristics and demographic variables are collected at baseline. Participant characteristics include age, gender, height, weight, and relevant comorbidities. The demographic variables include family relations, ethnicity, educational status, employment, and work characteristics if employed. The outcomes included into the study was based on recommendations for LBP trials [41-43] and described in deliverable 1.2 (QUEST), delivered M6.

5.1 Primary outcome

The Roland Morris Disability Questionnaire (RMDQ) assesses pain-related disability [44]. The questionnaire includes 24 items asking participants to indicate if they experience functional impairments by answering "yes" or "no" to a series of descriptions of functional abilities [45]. The RMDQ score range from 0 to 24, where a higher score indicates higher levels of disability due to LBP [45, 46]. The RMDQ is a validated and recommended tool for measuring pain-related disability in LBP populations [42, 46, 47]. The minimal clinically important difference for the RMDQ has been reported to be five points in LBP population with baseline scores ranging between 14-16 points [48]. The SELFBACK trial aims to detect a two point difference after three months. This is less than the suggested five point reduction stated as minimally clinically important. Also, if the two point difference does not exceed the measurement error of the RMDQ, the results will then be difficult to apply on an individual level in clinical practice. The measurement error of the RMDQ has been reported to range between 1.4-3.7 in studies comparing the RMDQ to the Oswestry Disability Index, with 3 studies reporting measurement error to range between 1.4 to 1.8 and one study reporting 3.7 {Chiarotto, 2016 #2816}. Given that the SELFBACK intervention is an add-on to usual care and supposed to be a supplement to existing treatment rather than a substitution, a smaller difference can be justified.

5.2 Secondary outcomes

The *average* and *worst LBP intensity* within the past week will be assessed by asking "Please indicate your average/worst low back pain level during the last week" using an 11-point numerical rating scale (NRS) ranging from zero to 10. The NRS scale is a valid and commonly used outcome for measuring pain in adults [41, 49, 50]. *Pain duration* measures length of participants' current back pain episode and total duration of time with LBP by asking "What is the length of time you have had low back pain during this episode?" with scoring ranging from less than 1 week to more than 12 weeks and "What is the total length of time that you have had low back trouble during the last 12 months?" with scoring ranging from 0 days to everyday. Measures of pain intensity and duration are recommended as a core set of outcomes for LBP trials [41]. *Pain medication* evaluates the frequency of non-prescription

pain medication use for LBP by asking "How many days during the last week have you taken non-prescription pain medication for low back pain?"

The *Fear-Avoidance Belief Questionnaire (FABQ)* assesses participant's beliefs about how physical activity and work affect their LBP [51]. The FABQ is a 5-item questionnaire, where the participants score their beliefs about their LBP on an ordinal scale ranging from zero [completely disagree] to six [completely agree]. The *Pain Self-Efficacy Questionnaire* (PSEQ) assesses the participant's level of confidence in carrying out specific activities despite their pain [52, 53]. The PSEQ is a 10-item questionnaire scored on an ordinal scale ranging from zero [completely disagree] to six [completely agree].

Activity Limitation evaluates if LBP has limited work and leisure time activities. The questionnaire consists of two single items with response options "yes" and "no." *Work Ability* is measured by a single-item and rated on an 11-point NRS scale ranging from zero [completely unable to work] to 10 [work ability at its best] [54].

Self-reported physical activity is evaluated by a revised version of *Saltin-Grimby Physical Activity Level Scale*, where participants indicate their amount of time per week performing leisure activities with four levels of intensity ranging from sedentary to vigorous physically active [55]. Function is evaluated by the *Patient Specific Functional Scale* (PSFS) where the participants, on up to two self-selected activities, are asked to rate if they are unable to do or are having difficulty with the their ability to perform self-selected activities regarded as important by the participants themselves [56, 57]. The ability to carry out the activity/activities is rated from zero [unable to perform] to 10 [able to perform].

Sleep is assessed by self-report using four items concerning problems with falling asleep, waking up repeatedly, waking up too early, and feeling sleepy during the day [58]. Items are scored in three categories; [seldom or never], [sometimes] or [several times a week]. The information retrieved from these four items approximates the information necessary to diagnose insomnia according to the DSM-V criteria [59]. Stress is evaluated with the *Perceived Stress Scale* (PSS), a 10-item questionnaire asking about frequency of thoughts and feelings related to perceived stress [60]. Participants indicate their frequency of experiencing stress-related issues on a 5-point Likert scale, ranging from [never] to [very often].

Three outcome measures are included to assess general health and perception of illness. Health-related quality of life is evaluated with the *EuroQoL 5-dimension* (EQ-5D) questionnaire [61]. A 5-point Likert scale ranging from [no problems] to [complete inability] is used to assess the health-related quality of life within each of the five dimension (i.e., mobility, self-care, activities, pain/discomfort and anxiety/depression). The *Brief Illness Perception Questionnaire* (BIPQ) [63] evaluates the participants' illness perception in an 8-item questionnaire. Items are scored on an ordinal scale ranging from zero [no problems] to 10 [worst severity] [63]. The *Patient Health Questionnaire-8* (PHQ-8) is an 8-item questionnaire used to evaluate the participants' depressive symptoms [64]. Items are scored on a 4-point Likert scale scoring frequency of experiencing symptoms of depression [64]. Also, a single item question for *Patient's Global Perceived Effect* will be asked at all follow-ups,

where participants are asked to rate improvement or deterioration of their LBP compared to before the intervention.

Participants randomised to the SELFBACK DSS in addition to usual care are also asked a set of tailoring questions weekly in order to individualise their self-management plan. The tailoring questions include items on pain (NRS for pain intensity [42]), function (item 5 from the Chronic Pain Grade Questionnaire [65]), fear-avoidance (1-item Tampa [66]), work ability (1-item WAI [54]), sleep (single item, modified from s-HUNT-Q [58]), pain self-efficacy (item 5 and 9 from PSEQ [67]), stress (4-items from PSS [60]), symptoms of depression (2 items from PHQ-8 [64]), and barriers for self-management (single item, customised to SELFBACK). In total, this comprises 17 tailoring questions; however, participants will only be asked a maximum of 7 questions per week (most commonly 4 questions). The selection of the relevant questions is based on a set of rules implemented in the backend of DSS that take into account the progression of the self-management process and the individual participant characteristics, deliverable 3.4 RULE, M18.

6 Statistics

6.1 Sample size estimations

The study is designed as a superiority trial with two parallel groups, SELFBACK in addition to usual care versus usual care only, and will test the hypothesis that the SELFBACK in addition to usual care (intervention group) will have a two points reduction in pain related disability (RMDQ) compared to the usual care (control group) over the three months intervention period. The sample size calculations have been performed in two ways. First, we conducted a simple calculation assuming only one follow-up measure and a standard deviation (SD) of the RMDQ score of six points. The expected SD was informed by previous high-quality studies in DK and UK investigating similar LBP populations [68-71]. Based on these calculation we estimated that a sample size of 382 (191 in each group) was necessary to detect a two point difference with 90% power and a two-sided alpha level of 0.05.

We then performed a simulation using 1000 repetitions of a mixed model regression for repeated measures, assuming 1) three data points per participant (i.e. baseline, six weeks and, three months), 2) an effect of treatment of two points, 3) an SD of six points, and 4) a correlation between repeated measures of 0.4. The latter was based on information from previous trials with repeated measures for the RMDQ in similar LBP populations [72, 73]. As in the simple calculations reported above, we used an alpha level of 0.05. Based on these assumptions, sample size calculations showed that 250 participants (i.e. 125 participants in each group) gave a power of 92% (95% confidence interval [CI 90-93]) to detect a two point difference in RMDQ between study groups at three months. Furthermore, simulations assuming that a two point difference between groups is observed at both follow up time points (six weeks and three months) indicated that a sample size of 180 (90 in each group) will give a power of 94% (95% CI, 92-95). Taken together, these sample size calculation indicate that a sample size of ~250 persons (125 in each group) will be sufficient under the given assumptions if the statistical analyses utilise the repeated measure design. A recent systematic review showed that attritions rates ranged between 4-94% for digital self-management interventions lasting between two weeks and 12 months in LBP populations [74]. To allow for a 30% drop out rate at three months follow-up we aim at including a total of 350 participants in the trial; 175 participants in each arm.

6.2 Statistical analysis

The primary analysis will estimate mean group difference with 95% CI in RMDQ score over the first three months of the nine months intervention period between the SELFBACK in addition to usual care versus usual care only. The analyses will be conducted according to the intention to treat principle using a linear mixed model for repeated measures. This model includes all available data for all participants at each time point (i.e. baseline, six weeks, and three months). In the regression model, individual participants will be specified as a random effect, accounting for the within subject covariance structure. The effect of group and time will be specified as fixed effects using a joint variable of intervention and time. The analysis

will investigate the effect of the intervention as constant over time, as well as an interaction between time and group allocation. Here, baseline levels are pooled over the two study groups assuming that any baseline differences are due to chance [75]. All effects will be estimated both crude and adjusted for the two variables used for stratification in the randomisation i.e. country and care provider [76].

Any missing values are inherently accounted for in the mixed model approach [77], but multiple imputation methods and complete case analysis will be applied in sensitivity analyses. Other sensitivity analyses will include adjustment for other factors suggested by any baseline imbalance (e.g. age, sex, educational level, and pain duration). Additional plans for per-protocol analysis and within subject effects over time will be specified in the statistical analysis plan for the trial. Which outcome to use to assess adherence to the SELFBACK intervention will be informed by and decided after the pilot study. Possible modifiers of the effect of intervention on the primary outcome will be assessed in supplementary analyses stratified by gender, age groups, socioeconomic status and different levels of LBP severity etc., and accompanied by tests of statistical interaction.

Secondary outcomes will be analysed using a similar approach as described above for the primary outcome, with linear mixed models for repeated measures. Analyses of more long-term effects based on data from six and nine months follow-up will also be analysed according to the above description for the primary outcome. The precision of the estimates from the statistical analyses will be assessed by 95% CI.

To increase the transparency, a statistical analysis plan will be agreed upon and made publically available before the inclusion of participants is completed (deadline: before recruitment to the RCT starts, i.e. end Jan 2019.). Also, to reduce the risk of biased interpretation of results the following procedure will be undertaken: Two interpretations will be drafted based on a review of the primary outcome data with groups arbitrary labelled as A and B [78]. One interpretation assumes that A is the SELFBACK DSS in addition to usual care and B is usual care, the other interpretation assumes that A is the usual care and B is the SELFBACK DSS in addition to usual care. After agreeing on both interpretations, the randomisation code is then broken and the correct interpretation will be chosen.

7 Data collection and management

The outlined data collection and data management is valid for the pilot study (see section 8), RCT and process evaluation (see section 9).

7.1 Data collection

Outcome measures are collected at baseline, six weeks, three, six and nine months. Data collection is performed online, and consequently all data are entered directly into the SELFBACK database by the participants. The website created for data collection will be extensively tested before the start of the trial in order to ensure that all items of the outcome questionnaires are included, that the structure from the original questionnaires are kept in the online version, and that the scoring for each included questionnaire is consistent with the original scoring instructions. Time to complete the baseline questionnaire is approximately 20-25 minutes, the follow-up questionnaires are less in extent and time to complete is approximately 20 min.

For baseline, six weeks, three, six and nine months follow-up, participants will be sent an email with a link that directs them to the logon to the SELFBACK questionnaire website using their username and password provided at the start of the trial. To ensure as high a response rate as possible in the follow-up questionnaires, reminder e-mails will be sent after one and two weeks. If still no answer, a researcher will call the participant and ask if he/she is willing to answer some questions on the phone. The outcomes assessed during this telephone call will be the RMDQ.

In addition to the outcomes obtained at baseline and follow-ups answered via a website, participants in the intervention group will in the app answer a set of tailoring questions on a weekly basis (described in section 4.2.1). These answers will be tracked over time and used in secondary analysis of the trial data.

7.2 Data management

A data management plan entailing an overview of the generated data, data collection schemes and descriptions of each data collection form (baseline, six weeks, three, six and nine months follow-up) for the SELFBACK trial is available from the authors upon request.

7.2.1 Handling personally identifiably data

Upon enrolment into the trial, a trial identification number for the participant is created. A key document entailing the trial identification number, home address, the webCRF id, SELFBACK username, participant's name, email address, phone number, and date of birth is kept securely on university servers at each research facility. Only researchers connected to the recruitment and conduct of the trial have access to these documents and will only have access to this information for participants in their own country.

In order to minimise the potential for error in the data collection, we chose to automate the data collection process. Consequently, email addresses for all included participants will

be stored on secure servers at NTNU, enabling the DSS to automatically send emails to the participants containing links to the questionnaire website. The SELFBACK DSS and app only holds the SELFBACK username and email-address, all other personally identifiable data are kept separate from the DSS and SELFBACK app.

A precondition for the enrolment process as described in section 3.5 is that all national ethical committees and data protection agencies approve the storage of all participants' emails at NTNU, regardless of participants' nationality.

7.2.2 Data security for data transfer from the web questionnaire to the servers

In the following, descriptions of the security for the servers, the web questionnaire and transmission between the two are described.

All outcome data from all participants, regardless of nationality, are stored on a secure server (an mySQL database server). The SELFBACK DSS runs from the SELFBACK server. When the DSS complies a new self-management plan for a participant it requests outcome data for that specific participant from the mySQL server, and consequently the username, email and outcome data are stored together. However, all outcome data are stored in a coded format and labelled using arbitrary names. Consequently, the data are unreadable without the codebook. The codebook is kept securely and separately from the mySQL and SELFBACK server.

The mySQL and SELFBACK servers are physically located at Department of Computer Science, NTNU, NO. The servers are firewall protected. The entire virtual machine is backed-up on a daily basis, and back-ups are kept for a one year period. Data storage is compliant with existing European law.

The mySQL and SELFBACK servers can only be accessed by the assigned staff at NTNU's Department of Computer Science (Kerstin Bach, Tomasz Szczepanski, Ilya Ashikhmin) and the IT administrator at NTNU. Additional access can only be approved by the responsible project leader, Kerstin Bach. Researchers connected to the recruitment of participants, data collection and conduct of the trial are not allowed to add data or to review, access, or make changes in original participant data. Finally, no information concerning group allocation is held on the mySQL or SELFBACK servers. This information is kept in the WebCRF system (as described in section 3.7), which is separate from the entire SELFBACK. A figure of the data flow can be seen in Figure 4.

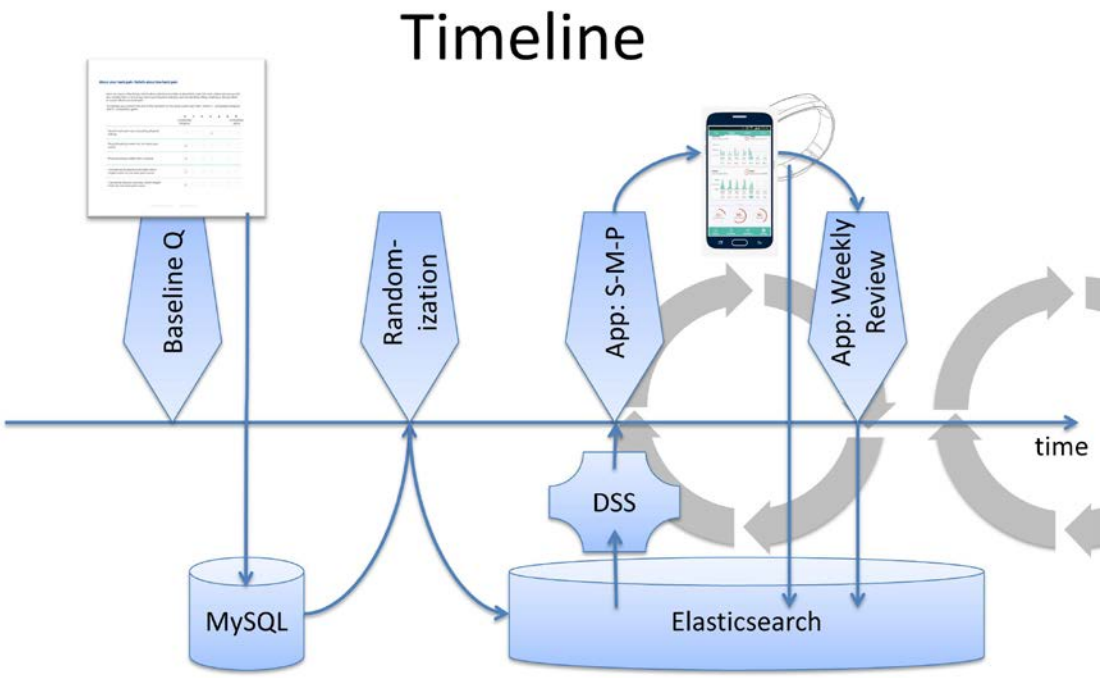

Figure 4: overview of dataflow the SELFBACK. Q: questionnaire, S-M-P: self-management plan, DSS: decision support system. MySQL = mySQL database server, Elasticsearch = the SELFBACK server.

7.2.3 Data security in transmission from the SELFBACK app to the SELFBACK server

In the following, detailed descriptions of the security for the SELFBACK server, the SELFBACK app and transmission between the two are described.

Data from the SELFBACK app is protected from unauthorized use, disclosure or modification by following the latest recommended security guidelines from the device manufacturers[2]. A secure data transfer is ensured by an encrypted communication between clients (participants) and mySQL and SELFBACK servers by using HTTPS (Hyper Text Transfer Protocol Secure) and SSL (Secure Sockets Layer) certificate and by storing sensitive information in the keychain/keystore. The HTTPS is a way of transferring information with links rather than writing the actual information. The links are only accessed when a series of security mechanisms are met. The SSL certificate is granted by an external third party that authenticates NTNU as an institution that can be trusted. A token (key) authentication will also be required from the participant on every communication with the SELFBACK server when using the app. Also, the AES (Advanced Encryption Standard) 256 crypto engine that is

[2] https://static.googleusercontent.com/media/enterprise.google.com/en//android/static/files/android-for-work-security-white-paper.pdf
https://www.apple.com/business/docs/iOS_Security_Guide.pdf

built into the hardware's (smartphone) flash storage and main memory is used, making file encryption highly efficient. On first launch of the app, a 256-bit encryption key is generated. Similarly, for any data stored locally on the smartphone, we will use the encryption key to store the data encrypted. Additionally, a feature in the app will be implemented to completely wipe the stored data on the device when the user signs out or removes the app from their phone. Lastly, safety is ensured by digital signing in on both android and iOS phones before installation of the app.

The mechanisms described above ensure a secure communication channel between the SELFBACK app and the SELFBACK servers. Further, an OAuth2 authentication is used to ensure that a participant's information is only accessible for themselves and not accessible for other participants. In the OAuth2 authentication, participants enter their username and password to authenticate them and access their information. The participant's password is private and if lost, a new password can be requested.

7.3 Access to data

Ownership of the data collected in the SELFBACK trial is shared between the participating partners (NTNU, GLA, RGU, TRX, NFA, HLE, UoSD). A data steering committee will be established, who will be competent to decide over the use of the data. The steering committee will comprise one member from each participating partner. The SELFBACK consortium supports the concept of data sharing and enquires from outside research partners to use the data are welcomed and will be discussed and decided upon by the steering committee. All personal identifiable data collected in the trial will be kept for five years (see more in section 7.2.1). These data are kept to be able to track any adverse events reported post completion of the trial, and to enable the project to contact enrolled participants should any plan of additional long-term follow-ups be funded. After this five year period the data set will be fully anonymised. The anonymised full data set will be kept for at least 30 years for research purposes and will be used to create a data model that can inform the further development of a potential commercial version of the SELFBACK app. Data will be stored at NTNU, NO.

8 Pilot testing

In order to secure a timely completion of the RCT, a pilot study is conducted starting August 2018 and ending no later than December 1st 2018. The primary reason for conducting the pilot study is to test a fully operative version of the SELFBACK intervention as well as to gain information about practical procedures regarding recruitment and screening as described in this protocol. Consequently, the pilot study will provide information on the number of recruitment sites needed in each country and may also identify challenges to the recruitment process that can be adjusted before the RCT.

The pilot will be conducted with the methods described for the RCT in this protocol. Recruitment will run until 70-80 participants are recruited, but no longer than two months irrespective of the number of participants recruited. The distribution of participants in the pilot study is 15-20 participants in NO, and 45-60 participants in DK. All participants in the pilot study will be given the SELFBACK app in addition to usual care (intervention). Outcomes will be collected at baseline and after 6 weeks. Hereafter, included participants will discontinue their use of the app. Data collected during participants' use of the SELFBACK app will be added to the case base of the DSS for better similarity measures and improved decision support to the RCT. The outcome data collected is not included in the RCT analyses. The pilot study will also inform on which variable to be selected as a measure of adherence for the RCT. The process evaluation (see section 9) is included in the pilot. Here data on app usage and participants' experiences with the app from interviews will inform on any adjustments needed in the app prior to the RCT.

9 Process evaluation

As an integrated part of the RCT, a process evaluation will be conducted, which will let us explore how the digital self-management intervention will be implemented and received by users. We intend to follow the RE-AIM framework [79] and include a theoretically informed qualitative component.

The key aims of the process evaluation are:

- To document the implementation of the intervention;
- To identify and describe users of the SELFBACK system
- To map the participants' satisfaction and experience with using the SELFBACK DSS;
- To describe barriers and facilitators to initial and sustained engagement with the SELFBACK app to promote self-management of LBP.
- To describe the experience and self-management of LBP in participants in the usual care group.

Key Outputs from our Process Evaluation will be:

- Details of participant perspectives regarding usability and utility of the SELFBACK system, self-management and the effectiveness of the SELFBACK system for participants with LBP
- Identification of key barriers and facilitators to initial interaction and sustained engagement with the SELFBACK system
- Identification of self-management strategies (before and after hearing about the SELFBACK study) for those in the usual care group.

9.1 Methods

The RE-AIM framework emphasises five key aspects: 1) Reach; 2) Efficacy; 3) Adoption; 4) Implementation; and 5) Maintenance.

The ***'Reach'*** of the intervention refers to the proportion of the target population participating in the intervention. As part of our RCT, we will be following recommendations outlined in the CONSORT guidelines [2]. We will therefore record details of the number of invites sent out for trial participation and acceptance rates. We will record details of the basic sociodemographic details of those invited and of those who eventually agree to trial participation. The flow of participants through the trial is described in Figure 1. We will be able to see how many people fail the eligibility screening and why and how many proceed into the trial. This information will provide valuable information about interest in the proposed intervention and likely eligibility rates amongst those interested in using the SELFBACK system including details of why interested respondents are deemed ineligible.

'Efficacy' refers to the success rate of the intervention if implemented as planned. We hypothesise that in our RCT the SELFBACK in addition to usual care group will experience a

two point reduction in pain-related disability as measured using the RMDQ compared to the usual care group at three months. We also have a number of secondary outcome measures and therefore as part of our RCT design we have a number of clear measures of efficacy. In addition, as part of the process evaluation we explicitly intend to address "efficacy" from the user perspective by examining user satisfaction with the SELFBACK intervention. We intend to invite participants using the SELFBACK app to complete the Virtual Care Climate Questionnaire (VCCQ) [80]. In addition three single items on overall rating of the SELFBACK app, ease of use of the app, and recommendation to other, will be asked to the intervention group in the same way commercial apps often do.

'Adoption' refers to what proportion of the participants will adopt or use the SELFBACK app. This is likely to differ with type of setting in which the intervention is implemented, as the barriers and facilitators to their adoption will vary in different settings and how participants believe they can adapt any given intervention to suit their needs. We will examine adoption in the different countries in which SELFBACK is delivered, DK and NO through examination of the background analytics data within the app, which will allow us to see what proportion of participants engage with the app from the outset and to what extent they use the app in the first month.

'Implementation' describes to what extent the intervention is implemented in the real world as intended. This is usually described as examining how effectively and consistently any given intervention is delivered in any particular context (e.g. primary or secondary care) by staff. As the SELFBACK system intervention is not being delivered by HCPs but instead is a self-management app, we will instead focus on how the SELFBACK system app becomes embedded and integrated into the daily routines of participants with LBP. We will use semi-structured interviews, underpinned by Normalisation Process Theory (NPT), a conceptual framework that seeks to determine the mechanisms through which an intervention become embedded into an individual's daily routines.

'Maintenance' refers to the extent to which engagement with the intervention is sustained over time and usually refers to maintenance at both the individual and system level. Due to the nature of the SELFBACK intervention, our focus will be on the concept of maintenance at the individual level. We will aim to examine this via use of app analytics data to monitor usage of the app by individual participants. We will also examine engagement and achievement of physical activity goals via analysis of data from the wearable tracking physical activity to assess to what extent participants can maintain behaviour changes as promoted in SELFBACK. In addition, we will explore this issue via qualitative interviews with participants who have used the SELFBACK app.

9.2 Theoretical frameworks

When a new intervention like SELFBACK is introduced it seeks to influence how people think, act and organise themselves. So for the SELFBACK intervention to be successful, it needs to change participants' thinking and behaviour in order to improve outcomes. While implementation failure may be partly due to problems of achieving behavioural changes,

there could also be other socio-organisational reasons for such failure. These include time constraints, such as the time taken to operationalise SELFBACK advice, and individual preferences. Wider societal and contextual barriers are also present, e.g., whether a participant's wider social network supports a participant in engaging with the SELFBACK system or not.

Within the SELFBACK project, the NPT is used to help understand and evaluate the factors that promote or inhibit uptake, utilisation and sustained use of SELFBACK. NPT is a sociological theory that has been widely promoted as a means to understand the factors that influence how new technologies or therapies become implemented, embedded and integrated into routine use or not. The theory has four main constructs: 1) coherence, the sense making work that participants undertake that influences whether they are willing to embed a new practice in their lives; 2) cognitive participation, the work that participants undertake to engage with the new practice; 3) collective action, the work that participants do to enact a new practice; 4) reflexive monitoring, the appraisal work that participants undertake to determine whether the new practice is worth sustaining or how it must be reconfigured to fit their needs (see Figure 5).

We will use NPT to inform interview guides for use with both participants using the SELFBACK app and usual care participants. Semi-structured interviews will be audiotaped, with participants' consent, and transcribed. The transcriptions will provide the data for analysis that will be analysed using a framework approach underpinned by the NPT serving as the underpinning conceptual framework. The interviews will provide valuable knowledge about the sustainability of SELFBACK in a participant's real world context and hence provide essential information about the chances for successful implementation. In terms of usual care participants, NPT will serve to help understand experiences of LBP and facilitators and barriers to LBP self-management.

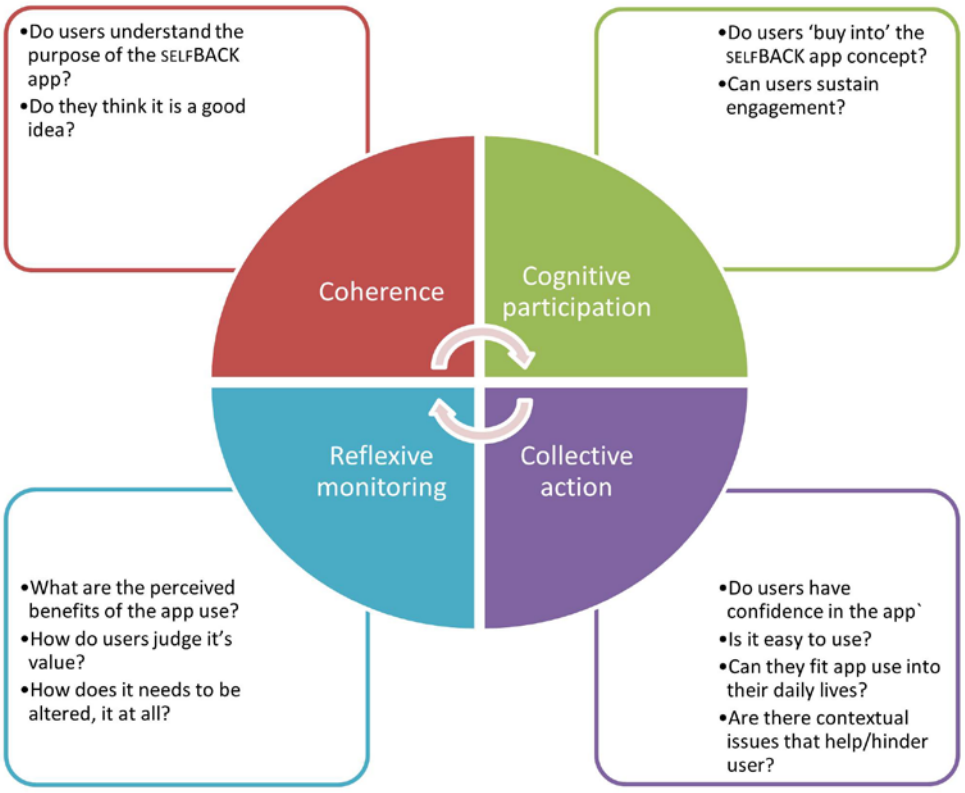

Figure 5: Four constructs of Normalization Process Theory (NPT) and associated question from the process evaluation.

9.3 Data collection for the process evaluation

Quantitative Data Collection

Quantitative data to be collected across the three countries will include: the VCCQ [80] in a 15-item version concerning perceived support for autonomy in a virtual care setting, three rating questions (on overall rating, ease of use and recommendation to others) using a 5-point system. These data are collected via an online survey service from NTNU. The participant will receive an email entailing a link to complete the questionnaire, as opposed to the baseline and follow-up questionnaires, where the participant logs in using username and password, here the participant authenticates him/her by entering in their username.

In addition to the questionnaires, data on physical activity (step count) and data analytics (where user permission is granted) on app usage will be collected. We will look to identify non-engagers, participants who have not achieved much change and users who have achieved large changes in their physical activity.

We anticipate data analytics on app usage would examine the following:

- Frequency of log-ins to SELFBACK app over study period
- Duration and frequency of app use
- Patterns of use (linking frequency and duration of use of different sections of the app across the study period)

- What sections are used and how often
- Frequency of use of the SELFBACK "toolbox" area
- Frequency of use of the ”first aid kit” section
- Frequency of looking at notifications
- Number of self-management plans created / adjusted / completed
- Updates to the app downloaded

For the pilot study, all recruited participants will receive the SELFBACK in addition to usual care, and therefore all are eligible to contribute quantitative data to the process evaluation. For the RCT, only the participants in the SELFBACK in addition to usual care group will contribute quantitative data. The time-points and outcomes collected for the process evaluation for the pilot and RCT are outlined in Table 1. Within the app, app usage data is per default registered, and the participants are explicitly made aware of this in the consent form. App usage data will be collected and stored via the *Matomo* service, an open-source analytics platform. All data will be stored in a de-identifiable manner and only linked to the individual participant via the SELFBACK system.

Qualitative Data Collection

Semi-structured interviews with a purposive sample of participants from across the two countries, DK and NO will be undertaken. These interviews will collect information from the participants about their experiences of self-management and of using the SELFBACK app to promote self-management of LBP. The interviews will also explore barriers and facilitators to engagement with the SELFBACK system and embedding its use within daily routines.

We aim to identify high, moderate and low or non-users of SELFBACK (assessed from data on app usage) and participants from both sexes and across age groups and deprivation levels to enable us to explore issues of engagement and utilisation in order to maximise learning about influences on use of the SELFBACK app. In the pilot study, we will also speak with key implementers involved in recruitment across the sites in order to understand their views on barriers and facilitators to uptake of the study. Interviews will be undertaken either in person or via telephone and will be audio-taped with participant consent, and then transcribed to provide data for qualitative analyses.

For the pilot study, we expect to interview approximately nine participants across the recruiting sites (two in NO and seven in DK). The interviews will be conducted after the data collection at six weeks.

For the RCT, we expect to interview approximately 40 intervention participants from the SELFBACK in addition to usual care in total (30 and 10, at the DK and NO sites, respectively). Interviews will be conducted 4-6 months after the start of the intervention (i.e. after assessing the primary outcome at three months follow up). Also for the RCT, we will undertake semi-structured interviews with 10 participants (DK site) from the usual care group. The interview schedules for this group will cover their experience of LBP self-management and whether they have changed their behaviour/management of LBP since

entering the SELFBACK study. Interviews with the participants from the usual care group will be conducted at convenient times across the study period (after baseline data collection). The time-points and outcomes collected for the process evaluation for the pilot and RCT are outlined in Table 1.

Table 1	Pilot	RCT
Quantitative		*SELFBACK in addition to usual care*
• **VCCQ**	4-6 weeks	4 months
• **Three rating questions**	4-6 weeks	4 months
• **App usage data**		
• **Physical activity (step count)**		
Qualitative		*SELFBACK in addition to usual care*
• **Semi-structured interviews, underpinned by NPT**	After 6 weeks	4-6 months
		Usual care
		At convenience

Table 1: Outcomes collected and time-point for process evaluation in pilot and RCT study. Abbreviations: RCT, Randomised Controlled Trial; VCCQ, Virtual Climate care Questionnaire; NPT, Normalisation Process Theory.

9.4 Analyses

Quantitative

Simple descriptive statistics will be used to examine questionnaire data and information on app usage and physical activity.

Qualitative

We will analyse the qualitative data collected using a framework approach underpinned by NPT as described above. We will follow the 5 stages of framework analysis described by Ritchie and Lewis [81]: familiarization, identifying a thematic framework, indexing, charting, and mapping and interpretation. The distribution of codes will be recorded, and importantly, any data that falls outside of the coding frame will be identified and examined to determine if important concepts or ideas are being missed by using the chosen theoretical framework. Transcripts will be analysed in their original language.

Coding will be undertaken by researchers at each of the recruiting sites, but in order to ensure consensus on themes and coding we will arrange 'coding clinics' where the coding framework and a proportion of the data will be double coded to ensure that data analysis is robust and that we were open to identifying themes that fall outside the NPT framework. In this way, we will ensure the coding is iterative and responsive to the data and avoid inappropriate 'shoe-horning' of the qualitative data collected. In the case of transcripts being used for double coding, translation into English will be required.

10 Trial management

10.1 Research ethics approval

Approval for the pilot study, RCT and process evaluation will be sought at the relevant ethical committees in DK and NO separately. In DK the approval is obtained from the Regional Scientific Ethical Committee for Southern Denmark, in NO from the Regional Committee for Medical and Health Research Ethics. Correspondingly, approval from institutional review boards and/or data protection agencies will be applied for nationally. In DK, approval is obtained from the Danish Data Protection Agency through application to the University of Southern Denmark's legal office and in NO from the National Data Protection Authority and/or the Centre for Research Data. All approvals from ethical committees and/or data protection agencies must be obtained no later than June 2018.

10.2 Protocol amendments

Any amendments to the protocol will be registered with a detailed description of the change marked with date of implementation. Any amendments to the protocol will be filed with the relevant ethical committees or data protection agencies and registered in the clinical trial registry (www.clinicaltrials.gov) for transparency.

10.3 Trial monitoring

10.3.1 Harms

No serious adverse events are expected for this trial. As the suggested self-management plans may include advice to increase physical activity and exercise volume, increased muscle soreness and transient increase in joint pain are expected adverse events. Such adverse events are known in exercise interventions and as they are transient, they pose no harm to the participants. Additionally, participants are informed that such events may occur and that they are normal. Further, any detection of unusual pain increase is automatically noted and reacted to by the DSS, and a suggestion to adjust volume of physical activity or exercise and advice on handling muscle pain is given to the participant. In addition, within the app a "caution" checklist can be consulted if participants are experiencing worsening of symptoms or pain flare-ups. In the checklist, participants are advised to seek care with their primary HCP or emergency clinics as they normally would. Consequently, as serious adverse events are unexpected, no interim analysis or a priori defined stopping rules are defined or implemented for this trial.

For each country a telephone hotline will be established, where participants can seek technical support for any questions relating to the use of the app or wearable device during office hours or by leaving a message asking to be contacted the following work day. Also, the app will contain a Frequently Asked Questions (FAQ) section that can guide participants with technical issues. Should a participant call the telephone hotline concerning any worsening of symptoms, the participant will be advised to seek care from their HCP as they normally

would. All enquiries to this telephone hotline will be recorded and discussed in an internal audit (see section 10.3.2) and reported with the study results.

10.3.2 Auditing

On a monthly basis, a researcher from each recruiting country (DK, NO), a representative from the app development company (TRX), a technical partner connected to the DSS system and primary investigator of the trial will review the recruitment, enrolment, data collection, conduct of the intervention, completion of the trial, reported adverse events and discuss appropriate actions to any inconsistencies or unexpected events. The purpose of this internal audit is to detect any inconsistency between the planned trial conduct and the performed trial conduct as well as suggesting measures to address such inconsistencies.

10.4 Declaration of interests

The overall aim of the SELFBACK project is to develop a digital DSS and mobile app to support participants to self-manage their LBP. The results and experiences from the pilot and RCT will inform the further development of the app, which may be introduced into a commercial market. In order to secure an unbiased interpretation and dissemination of the RCT, the interpretation of the results will be performed blind to group allocation. Upon publication of study results, this commercial potential in the app development will be clearly stated and the publication will undergo peer-review to ensure methodological and scientific rigor.

10.5 Dissemination policy

The results of this RCT will be reported in accordance with the CONSORT 2010 reporting guideline and the 2013 amendment CONSORT-EHEALTH checklist for reporting web-based and mobile-based RCTs [2, 82]. Data collection is expected to be complete by July 2020 and dissemination of trial results is planned from then.

11 Discussion

11.1 Scientific justification

This protocol describes an RCT assessing the effectiveness of a mobile app to help non-specific LBP participants self-manage their condition. A vast number of mobile apps for managing LBP are already available on the commercial market [22], and m- and e-health solutions have been described as promising platforms for supporting participants in managing chronic conditions [20, 21]. In a recent systematic review, nine studies were identified describing digital m- and e-health self-management interventions for LBP population [74]. Few studies reported their theoretical underpinnings for the included content and consequently, the evidence base for digital self-management interventions for LBP is weak [74, 83]. There is a need for studying digital self-management for LBP patients in rigorous study designs and with larger focus on describing the evidence behind the provided content and its theoretical underpinnings. The SELFBACK DSS is data driven, it describes the development of the intervention and its theoretical underpinnings, its content is evidence based and its effect will be investigated in the current trial.

11.2 Novelty and impact

The SELFBACK intervention builds on a digital DSS and CBR methodology, this means that the SELFBACK system is a learning system and the knowledge base grows with increasing number of available cases in the case base. Consequently, every time a participant completes their weekly self-management plan, the experiences with that self-management plan for this specific participant will be stored as a case in the SELFBACK system. Thus, over time the DSS "learns" from experience resulting in improved self-management plans for similar (future) participant cases. This learning cycle in the CBR methodology may result in a more crude composition of self-management plans for participants included in the start of the trial compared to participants enrolled in the latter part of the trial, when the DSS will have learned from the previous participants. However, a set of carefully described rules has been developed based on current evidence to tailor the initial self-management plans to different participant profiles (cases) from existing patient cohorts. To test if there is a difference in the self-management advice given at different time-points in the intervention, a participant case can be fed into the DSS system at such different time-points to evaluate the learning effect acquired by the system.

11.3 Methodological considerations

The SELFBACK project adheres to the HONcode principle [27, 28], i.e., it is not intended as a substitution for consulting HCPs, but as an add-on to usual care. It is important to recognise that usual care will differ for participants both within and across study centres (countries) of this trial. This is a very common problem in trials where usual care is comparator. However, it is also a reflection of how LBP is managed in a real life setting. The process evaluation may

inform on perceptions of usual care as interviews are performed with participants from the usual care only group as well as with participants using the SELFBACK app in addition to usual care.

Variation in the content and volume of the intervention is expected for participants using SELFBACK. The intervention is based on recommended treatment components: exercise, physical activity and educational material, but it is very likely that some components of the content will appeal more for some participants than others. Similarly, the content given to each individual participant is tailored to that specific participant, rather than providing the same package for all participants. Consequently, should the RCT show the SELFBACK in addition to usual care to be more effective than usual care, the trial design does not allow analyses of which part of the intervention that may be causal of such an effect.

There is consensus on a core set of domains to measure in clinical trials for LBP; pain intensity, health related quality of life and physical functioning [41, 42, 47]. Recently recommendations have been given for which measurement instruments to use in these domains [26, 41]. The primary outcome for this trial is physical functioning, measured with RMDQ, which follows these recommendations [41]. The CONSORT statement [2] states that clinical trials should choose one outcome as primary and base the study conclusion on that result. However, the methodological rigour in choosing one outcome as primary outcome does not necessarily reflect that patients may have a more complex experience of having LBP than what can be measured with just one outcome [85]. Patients may, for example, report improvements in physical function but at the same time report increased pain intensity [85]. A wide range of secondary outcomes have been included in the SELFBACK trial that can inform on similarities or contradictions in health outcomes from the intervention. It can also be discussed how self-management is best measured. At this time, there are no back pain specific outcome measure designed to measure self-management and consequently, we chose the RMDQ as primary outcome measure, which is a clinical outcome, widely used and recommended for the study population.

The process evaluation is integrated within the RCT and aims to identify crucial factors that may influence the expected impact of the SELFBACK system and to understand current self-management strategies for those in the usual care group. Patient acceptance and patterns of use of the SELFBACK system are factors that will influence the expected impact in the SELFBACK intervention. We have tried to ensure high usability of SELFBACK by involving potential users during the developmental phase. Also, an IM process has been undertaken and logic models developed to provide the theoretical underpinnings for the SELFBACK system. The process evaluation will enable an examination of factors identified as key, particularly barriers and facilitators, to uptake, utilisation and implementation of the SELFBACK system within the lives of those with LBP. The thorough process evaluation integrated in the RCT will enhance the credibility of the findings from our trial and at the same time provide important input for improving the SELFBACK system in order to enhance both the commercial potential and the apps impact. It will also provide important input to the possible process of extending the generic part of the SELFBACK system to other

conditions and diseases where symptom progression depends on quality and extent of self-management (e.g., diabetes, osteoarthritis, rheumatoid arthritis, cardiovascular disease etc.).

11.4 Changes to the protocol from the original grant application

This protocol has developed from the original work planned in the grant application. To minimise the risk of an inconclusive outcome at the end of the trial, we have added an additional follow-up point at six weeks and also, the primary endpoint of the RCT was changed from nine months to three months. It is important to recognize that the follow-ups at six and nine months are not omitted from the study, these will inform on the long-term effect of the intervention. The inclusion of an additional follow-up and earlier endpoint for the primary outcome will ensure that the project is able to detect a relatively small difference (two points on RMDQ) between groups and that the study has high power to detect such a difference. Also, the data collection for the primary outcome is expected to be completed earlier, by January 2020 rather than July 2020. Consequently, there is still time to complete the data collection as described and report the results within the project period, should the RCT unexpectedly be delayed due to insufficient recruiting of participants.

A clinician's dashboard is described in the overall project. The specification and design document for the clinician's dashboard is described in deliverable 4.3 (SPECW), and a demonstration of the web based clinicians dashboard will be submitted with deliverable 4.8 (DEMCD). The clinician's dashboard is not included in the RCT. However, work is currently in progress planning different means to involve clinicians in reviewing the quality of the participants' self-management plans as suggested by the DSS. The initial self-management plans for participants are drafted to match "seed-cases" identified in pre-existing cohorts of LBP patients (deliverable 1.3/4/5 CASEa/b/c). The content of the self-management plans will be based on LBP treatment guidelines as well as reviewed by experienced clinicians within the project. For the educational content, information from the baseline questionnaire will result in specific targeted educational messages. For physical activity, for the first week the volume of steps is based on recommendations for physical activity. Hereafter, the participants suggested step goal will be based on previous week's achievement. In the weekly tailoring session, the participant is able to adjust the step goal within the app before accepting it. For the exercise, experienced clinicians and LBP researchers within the consortium discussed and grouped the exercises and proposed the rule of how to combine exercises in the default programme. Finally, the exercise in the first week's self-management plan was carefully selected by clinicians (physiotherapists) to match the characteristics of the seed-cases, as clinicians normally would in clinical practice. A more detailed description of the intervention development and structure is described in deliverable 3.8, IMAP.

12 REFERENCES

1. Chan, A.W., et al., *SPIRIT 2013 statement: defining standard protocol items for clinical trials.* Ann Intern Med, 2013. **158**(3): p. 200-7.
2. Schulz, K.F., D.G. Altman, and D. Moher, *CONSORT 2010 Statement: updated guidelines for reporting parallel group randomised trials.* Trials, 2010. **11**: p. 32.
3. Eysenbach, G. and C.-E. Group, *CONSORT-EHEALTH: improving and standardizing evaluation reports of Web-based and mobile health interventions.* J Med Internet Res, 2011. **13**(4): p. e126.
4. Collaborators, G.B.D.D.I.I.P., *Global, regional, and national incidence, prevalence, and years lived with disability for 310 diseases and injuries, 1990-2015: a systematic analysis for the Global Burden of Disease Study 2015.* Lancet, 2016. **388**(10053): p. 1545-1602.
5. Buchbinder, R., et al., *Placing the global burden of low back pain in context.* Best Pract Res Clin Rheumatol, 2013. **27**(5): p. 575-89.
6. Deyo, R.A. and J.N. Weinstein, *Low back pain.* New England Journal of Medicine, 2001. **344**(5): p. 363-70.
7. Walker, B.F., R. Muller, and W.D. Grant, *Low back pain in Australian adults: the economic burden.* Asia Pac J Public Health, 2003. **15**(2): p. 79-87.
8. Dagenais, S., J. Caro, and S. Haldeman, *A systematic review of low back pain cost of illness studies in the United States and internationally.* Spine J, 2008. **8**(1): p. 8-20.
9. Maniadakis, N. and A. Gray, *The economic burden of back pain in the UK.* Pain, 2000. **84**(1): p. 95-103.
10. Pillastrini, P., et al., *An updated overview of clinical guidelines for chronic low back pain management in primary care.* Joint Bone Spine, 2012. **79**(2): p. 176-85.
11. Savigny, P., et al., *Early management of persistent non-specific low back pain: summary of NICE guidance.* BMJ, 2009. **338**: p. b1805.
12. Koes, B.W., et al., *An updated overview of clinical guidelines for the management of non-specific low back pain in primary care.* Eur Spine J, 2010. **19**(12): p. 2075-94.
13. Chou, R., et al., *Diagnosis and treatment of low back pain: a joint clinical practice guideline from the American College of Physicians and the American Pain Society.* Ann Intern Med, 2007. **147**(7): p. 478-91.
14. Stochkendahl, M.J., et al., *National Clinical Guidelines for non-surgical treatment of patients with recent onset low back pain or lumbar radiculopathy.* Eur Spine J, 2018. **27**(1): p. 60-75.
15. NICE, t.N.I.f.H.a.C.E., *Low back pain and sciatica in over 16s: assessment and management. Assessment and non-invasive treatments.* 2016.
16. Barlow, J., et al., *Self-management approaches for people with chronic conditions: a review.* Patient Educ Couns, 2002. **48**(2): p. 177-87.
17. Oliveira, V.C., et al., *Effectiveness of self-management of low back pain: systematic review with meta-analysis.* Arthritis Care Res (Hoboken), 2012. **64**(11): p. 1739-48.
18. Liddle, S.D., G.D. Baxter, and J.H. Gracey, *Chronic low back pain: Patients' experiences, opinions and expectations for clinical management.* Disability and Rehabilitation, 2007. **29**(24): p. 1899-909.
19. Du, S., et al., *Self-management program for chronic low back pain: A systematic review and meta-analysis.* Patient Education and Counseling, 2017. **100**(1): p. 37-49.
20. Zhao, J., B. Freeman, and M. Li, *Can mobile phone apps influence people's health behavior change? An evidence review.* J Med Internet Res, 2016. **18**(11): p. e287.
21. Beatty, L. and S. Lambert, *A systematic review of internet-based self-help therapeutic interventions to improve distress and disease-control among adults with chronic health conditions.* Clin Psychol Rev, 2013. **33**(4): p. 609-22.
22. Machado, G.C., et al., *Smartphone apps for the self-management of low back pain: A systematic review.* Best Practice & Research Clinical Rheumatology, 2017.
23. group, s., *Grant Agreement No 689043 selfBACK*. 2015.
24. Cella, D., et al., *The Patient-Reported Outcomes Measurement Information System (PROMIS) developed and tested its first wave of adult self-reported health outcome item banks: 2005-2008.* J Clin Epidemiol, 2010. **63**(11): p. 1179-94.
25. Cella, D., et al., *The Patient-Reported Outcomes Measurement Information System (PROMIS): progress of an NIH Roadmap cooperative group during its first two years.* Med Care, 2007. **45**(5 Suppl 1): p. S3-S11.
26. Chiarotto, A., C.B. Terwee, and R.W. Ostelo, *Choosing the right outcome measurement instruments for patients with low back pain.* Best Practice & Research Clinical Rheumatology, 2017.
27. Boyer, C., et al., *The Health On the Net Code of Conduct for medical and health Websites.* Computers in Biology and Medicine, 1998. **28**(5): p. 603-610.
28. *Health On the Net Foundation (HONcode).* 2017-24-07]; Available from: http://www.hon.ch/HONcode/

29. Bartholomew, L.K., G.S. Parcel, and G. Kok, *Intervention mapping: a process for developing theory- and evidence-based health education programs.* Health Educ Behav, 1998. **25**(5): p. 545-63.
30. Aamodt, A. and E. Plaza, *Case-based reasoning: foundational issues, methodological variations, and system approaches.* AI Communications, 1994. **7**(1): p. 39-59.
31. Bach, K., et al., *Case Representation and Similarity Assessment in the SELFBACK Decision Support System.* Case-Based Reasoning Research and Development, Iccbr 2016, 2016. **9969**: p. 32-46.
32. Mansi, S., et al., *Investigating the effect of a 3-month workplace-based pedometer-driven walking programme on health-related quality of life in meat processing workers: a feasibility study within a randomized controlled trial.* BMC Public Health, 2015. **15**: p. 410.
33. Talbot, L.A., et al., *A Home-Based Pedometer-Driven Walking Program to Increase Physical Activity in Older Adults with Osteoarthritis of the Knee: A Preliminary Study.* Journal of the American Geriatrics Society, 2003. **51**: p. 387-392.
34. Bernstein, I.A., et al., *Low back pain and sciatica: summary of NICE guidance.* Bmj, 2017. **356**: p. i6748.
35. Steffens, D., et al., *Prevention of Low Back Pain: A Systematic Review and Meta-analysis.* JAMA Intern Med, 2016: p. 1-10.
36. Saragiotto, B.T., et al., *Motor control exercise for chronic non-specific low-back pain.* Cochrane Database Syst Rev, 2016. **1**: p. CD012004.
37. Macedo, L.G., et al., *Motor control exercise for acute non-specific low back pain.* Cochrane Database Syst Rev, 2016. **2**: p. CD012085.
38. Gordon, R. and S. Bloxham, *A Systematic Review of the Effects of Exercise and Physical Activity on Non-Specific Chronic Low Back Pain.* Healthcare (Basel), 2016. **4**(2).
39. Searle, A., et al., *Exercise interventions for the treatment of chronic low back pain: a systematic review and meta-analysis of randomised controlled trials.* Clin Rehabil, 2015. **29**(12): p. 1155-67.
40. van Middelkoop, M., et al., *Exercise therapy for chronic nonspecific low-back pain.* Best Pract Res Clin Rheumatol, 2010. **24**(2): p. 193-204.
41. Chiarotto, A., et al., *Core outcome measurement instruments for clinical trials in nonspecific low back pain.* Pain, 2018.
42. Chiarotto, A., et al., *Core outcome domains for clinical trials in non-specific low back pain.* Eur Spine J, 2015. **24**(6): p. 1127-42.
43. Deyo, R.A., et al., *Report of the NIH Task Force on research standards for chronic low back pain.* J Pain, 2014. **15**(6): p. 569-85.
44. Roland, M. and R. Morris, *A study of the natural history of low-back pain. Part II: development of guidelines for trials of treatment in primary care.* Spine (Phila Pa 1976), 1983. **8**(2): p. 145-50.
45. Roland, M. and R. Morris, *A study of the natural history of back pain. Part I: development of a reliable and sensitive measure of disability in low-back pain.* Spine (Phila Pa 1976), 1983. **8**(2): p. 141-4.
46. Smeets, R., et al., *Measures of function in low back pain/disorders: Low Back Pain Rating Scale (LBPRS), Oswestry Disability Index (ODI), Progressive Isoinertial Lifting Evaluation (PILE), Quebec Back Pain Disability Scale (QBPDS), and Roland-Morris Disability Questionnaire (RDQ).* Arthritis Care Res (Hoboken), 2011. **63 Suppl 11**: p. S158-73.
47. Deyo, R.A., et al., *Outcome measures for low back pain research. A proposal for standardized use.* Spine (Phila Pa 1976), 1998. **23**(18): p. 2003-13.
48. Jordan, K., et al., *A minimal clinically important difference was derived for the Roland-Morris Disability Questionnaire for low back pain.* J Clin Epidemiol, 2006. **59**(1): p. 45-52.
49. Hawker, G.A., et al., *Measures of adult pain: Visual Analog Scale for Pain (VAS Pain), Numeric Rating Scale for Pain (NRS Pain), McGill Pain Questionnaire (MPQ), Short-Form McGill Pain Questionnaire (SF-MPQ), Chronic Pain Grade Scale (CPGS), Short Form-36 Bodily Pain Scale (SF-36 BPS), and Measure of Intermittent and Constant Osteoarthritis Pain (ICOAP).* Arthritis Care Res (Hoboken), 2011. **63 Suppl 11**: p. S240-52.
50. Jensen, M.P., P. Karoly, and S. Braver, *The measurement of clinical pain intensity: a comparison of six methods.* Pain, 1986. **27**(1): p. 117-26.
51. Waddell, G., et al., *A Fear-Avoidance Beliefs Questionnaire (FABQ) and the role of fear-avoidance beliefs in chronic low back pain and disability.* Pain, 1993. **52**(2): p. 157-68.
52. Nicholas, M.K., *Pain self efficacy questionnaire (PSEQ).* 1989.
53. Nicholas, M.K., *The pain self-efficacy questionnaire: Taking pain into account.* Eur J Pain, 2007. **11**(2): p. 153-63.
54. Ahlstrom, L., et al., *The work ability index and single-item question: associations with sick leave, symptoms, and health--a prospective study of women on long-term sick leave.* Scand J Work Environ Health, 2010. **36**(5): p. 404-12.

55. Grimby, G., et al., *The "Saltin-Grimby Physical Activity Level Scale" and its application to health research.* Scand J Med Sci Sports, 2015. **25 Suppl 4**: p. 119-25.
56. Stratford, P., M.D. Westaway, and J. Binkley, *Assessing disability and change on individual patients: a report of a patient specific measure.* Physiotherapy Canada, 1995. **47**: p. 258-263.
57. Hefford, C., et al., *The Patient-Specific Functional Scale: Validity, Reliability, and Responsiveness in Patients With Upper Extremity Musculoskeletal Problems.* Journal of Orthopaedic & Sports Physical Therapy, 2012. **42**(2): p. 56-65.
58. Engstrøm, M., et al., *The Reliabilty of a New Sleep Screening Questionnaire for Large Population-Based Studies: The Third Nord-Trøndelag Health Study.* The Open Sleep Journal, 2011. **4**: p. 14-19.
59. American Psychiatric Association, D.S.M.T.F. and A. American Psychiatric, *Diagnostic and statistical manual of mental disorders: DSM-5.* 5. ed. 2013, Arlington, Va: American Psychiatric Association.
60. Cohen, S., T. Kamarck, and R. Mermelstein, *A global measure of perceived stress.* J Health Soc Behav, 1983. **24**(4): p. 385-96.
61. Brooks, R., *EuroQol: the current state of play.* Health Policy, 1996. **37**(1): p. 53-72.
62. Soer, R., et al., *Clinimetric properties of the EuroQol-5D in patients with chronic low back pain.* Spine J, 2012. **12**(11): p. 1035-9.
63. Hallegraeff, J.M., et al., *Measurement of acute nonspecific low back pain perception in primary care physical therapy: reliability and validity of the brief illness perception questionnaire.* BMC Musculoskelet Disord, 2013. **14**: p. 53.
64. Kroenke, K., et al., *The PHQ-8 as a measure of current depression in the general population.* J Affect Disord, 2009. **114**(1-3): p. 163-73.
65. Von Korff, M., et al., *Grading the severity of chronic pain.* Pain, 1992. **50**(2): p. 133-49.
66. Verwoerd, A.J., et al., *A single question was as predictive of outcome as the Tampa Scale for Kinesiophobia in people with sciatica: an observational study.* J Physiother, 2012. **58**(4): p. 249-54.
67. Nicholas, M.K., B.E. McGuire, and A. Asghari, *A 2-item short form of the Pain Self-efficacy Questionnaire: development and psychometric evaluation of PSEQ-2.* J Pain, 2015. **16**(2): p. 153-63.
68. Khan, K.A., et al., *Mapping between the Roland Morris Questionnaire and generic preference-based measures.* Value Health, 2014. **17**(6): p. 686-95.
69. Hill, J.C., et al., *Comparison of stratified primary care management for low back pain with current best practice (STarT Back): a randomised controlled trial.* The Lancet, 2011. **378**(9802): p. 1560-1571.
70. Konstantinou, K., et al., *Characteristics of patients with low back and leg pain seeking treatment in primary care: baseline results from the ATLAS cohort study.* BMC Musculoskelet Disord, 2015. **16**: p. 332.
71. da, C.M.C.L., et al., *The prognosis of acute and persistent low-back pain: a meta-analysis.* CMAJ, 2012. **184**(11): p. E613-24.
72. Hestbaek, L., et al., *Low back pain in primary care: a description of 1250 patients with low back pain in danish general and chiropractic practice.* Int J Family Med, 2014. **2014**: p. 106102.
73. Lauridsen, H.H., et al., *Danish version of the Oswestry disability index for patients with low back pain. Part 2: Sensitivity, specificity and clinically significant improvement in two low back pain populations.* Eur Spine J, 2006. **15**(11): p. 1717-28.
74. Nicholl, B.I., et al., *Digital Support Interventions for the Self-Management of Low Back Pain: A Systematic Review.* J Med Internet Res, 2017. **19**(5): p. e179.
75. Fitzmaurice, G.M., N.M. Laird, and J.H. Ware, *Linear Mixed Effects Models*, in *Applied Longitudinal Analysis*. 2004, John Wilet & Sons, Inc. : USA, New Jersey. p. 187-237.
76. Kahan, B.C. and T.P. Morris, *Reporting and analysis of trials using stratified randomisation in leading medical journals: review and reanalysis.* BMJ, 2012. **345**: p. e5840.
77. Ranstam, J., et al., *Alternative analyses for handling incomplete follow-up in the intention-to-treat analysis: the randomized controlled trial of balloon kyphoplasty versus non-surgical care for vertebral compression fracture (FREE).* BMC Med Res Methodol, 2012. **12**: p. 35.
78. Jarvinen, T.L., et al., *Blinded interpretation of study results can feasibly and effectively diminish interpretation bias.* J Clin Epidemiol, 2014. **67**(7): p. 769-72.
79. *RE-AIM.* [cited 2018; Available from: www.re-aim.org.
80. Smit, S.E., et al., *The Virtual Care Climate Questionnaire: Development and Validation of a Questionnaire Measuring Perceived Support for Autonomy in a Virtual Care Setting.* J Med Internet Res, 2017. **19**(5): p. e155.
81. Ritchie, J. and J. Lewis, *Qualitative research practice: a guide for social science students and researchers.* 2003, London: Sage.
82. Eysenbach, G., *CONSORT-EHEALTH: implementation of a checklist for authors and editors to improve reporting of web-based and mobile randomized controlled trials.* Stud Health Technol Inform, 2013. **192**: p. 657-61.

83. Dario, A.B., et al., *Effectiveness of telehealth-based interventions in the management of non-specific low back pain: a systematic review with meta-analysis.* Spine J, 2017. **17**(9): p. 1342-1351.
84. Kongsted, A., L. Hestbaek, and P. Kent, *How can latent trajectories of back pain be translated into defined subgroups?* BMC Musculoskelet Disord, 2017. **18**(1): p. 285.
85. Froud, R., et al., *Primary outcome measure use in back pain trials may need radical reassessment.* BMC Musculoskeletal Disorders, 2015. **16**(1): p. 88.