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Title:

eVISualisation (eVIS) of Physical Activity and Pain to improve Physical Health in patients with chronic pain participating in Swedish Interdisciplinary Pain Rehabilitation Programs: study protocol for a registry-based randomized controlled clinical trial.

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Keywords: Chronic pain, Individualized physical activity level, Interdisciplinary Pain Rehabilitation Programs, Internal pilot study, Physical health, Registry-based randomized clinical trial, Study protocol.

ABSTRACT

Introduction: Living with chronic pain often involves negative consequences. Interdisciplinary Pain Rehabilitation Programs (IPRPs), a subset of Interdisciplinary Treatment (IDT) are considered to be superior to single-treatment measures in patients with chronic pain. However, effects emerge sub-optimal and as many as 30% of patients deteriorate in some outcomes. A novel intervention, eVISualisation (eVIS) of physical activity and pain, has been systematically developed to facilitate patients in reaching and maintaining recommended individualized physical activity levels. The aim is to transparently report on methodology, outcome assessments, and processes for a registry-based randomized controlled trial (R-RCT) initiated as an internal pilot study.

Methods and analysis: In the R-RCT, recruitment of approximately 400 patients with chronic pain who are registered at primary and specialized IPRP units (n=15) in Sweden will be performed. Participants will be randomly allocated to either IPRP + eVIS or to control group that will receive IPRP only. eVIS entails objectively measured physical activity (steps) and patient-reported outcomes (pain intensity, affect on daily activities, pharmaceutical consumption) collected and visualized in the web application PATRON. Data from the initial 30 participants completing the study period (6 months) will be included in a pilot study designed to evaluate recruitment- and randomization processes, standardized effect size, sample size, characteristics of outcomes, and follow-up rates of the R-RCT. Outcome variables will be extracted from PATRON and from six national registries. Multivariate statistics and repeated measures analyses will be performed. Quality Adjusted Life Years (QALYs) and Incremental Cost Effectiveness Ratio (ICER) will be calculated for cost effectiveness evaluation.

Ethics/dissemination: The Swedish Ethics Review Board granted approval (Dnr 2021/02109). Results will be disseminated through peer-review journals.

Trial registration number: The trial is registered at ClinicalTrials.gov. At the time of submission, a trial registration number had not yet been assigned due to pending review.

Protocol version: 1 (1)

Strengths and limitations of the study

- The proceeding internal pilot study will enable rare prerequisites to improve the robustness of the R-RCT design, decrease the risk of adverse events, and aid interpretations of the main trial.
- This study will evaluate the effectiveness of a systematically developed health-promoting intervention (eVIS) that targets individualized physical activity levels in patients with chronic pain who are participating in interdisciplinary pain rehabilitation programs in Sweden.
- The intervention is based on objectively measured physical activity levels, patient-reported clinical outcomes, and mechanisms that facilitate behavior change, in accordance with current guidelines that are provided by authorities in the chronic pain management field.
- The nature of the intervention precludes blinding of patients and the IPRP team.

INTRODUCTION

Chronic pain and physical activity

Chronic musculoskeletal pain (>3 months), including neck/shoulder/back pain or widespread pain, is a major global health and socioeconomic burden.[1-2] Living with chronic pain is often associated with reduced levels of wellbeing and the health-related quality of life of this group has been reported to be among the lowest of any medical condition.[3] To date, physical activity (i.e. any bodily movement that requires energy expenditure) and exercise (i.e. structured and planned physical activity aimed to increase fitness)[4] have been shown to prevent and/or treat several of our noncommunicable diseases including chronic pain,[5] due to their beneficial effects on general health, pain intensity, physical and psychological functioning, and health-related quality of life.[5-8] WHO's physical activity guidelines provide clear outlines for the recommended amount (volume, intensity, type, duration) of physical activity required for adults living with chronic disabilities such as chronic pain.[9] These recommendations encourage engaging in physical activity for a minimum of 150-300 minutes/week at a moderate intensity level to assimilate health benefits, such as improved functional health and health-related quality of life.[9] Despite the growing evidence of health benefits related to physical activity, participation and adherence to recommendations are often low in patients living with chronic pain,[10-11] which may result in sub-optimal levels of physical activity. This lack of adherence to recommendations may be partly explained by the indicated association between high pain scores and low patient-reported activity levels among patients with chronic pain and/or the documented reports of the negative impact of depression on physical activity levels.[12] In addition, it is well known that behavior change is difficult, and that each individual's own participation is essential.[13] It has been shown that behavior change towards a beneficial physical activity level may be facilitated by individuals self-monitoring their physical activity.[14] The use of objective measures increases the likelihood of the effectiveness of interventions designed to promote physical activity.[14] By adding goal setting, feedback, and a focus on achieved goals, effectiveness can be further improved.[14-17]

Interdisciplinary Pain Rehabilitation Programs

Interdisciplinary pain rehabilitation programs (described as a subset of Interdisciplinary Treatment [IDT]), are defined as "multimodal treatment provided by a multidisciplinary team (including at least 3 professions), collaborating in assessment and treatment using a shared biopsychosocial model and goals"[18]. The IPRP approach adopts the principles of behavioral therapy and incorporates not only physical activity and exercise, but also psychological measures, pharmaceutical treatment and patient education.[19] Physical activity and exercise are central measures in IPRPs as they target physical deconditioning by improving levels of physical activity, and also reducing pain severity and improving physical function and quality of life.[5] Interdisciplinary pain rehabilitation programs are considered to be superior to single-treatment measures for patients with chronic pain.[19 20] However, their effectiveness is only slightly better and in the majority of cases only a small effect is seen.[20-24] In addition, up to 30% of patients deteriorate in some outcomes despite completing an IPRP.[19, 24-25] Sustainable treatment effects seem to vary according to patient clinical features at baseline, such as poor employment status, high pain levels, and low functioning, all of which predict low physical health at follow-up.[22-26]

Many efforts have been made to find effective interventions that improve the health of chronic pain patients. To facilitate individualized physical activity levels within the Swedish IPRP setting, an eVISualisation (eVIS) of physical activity and pain intervention has been systematically developed in collaboration with patients with chronic pain, clinicians, and researchers in the field. eVIS is designed to target facilitating mechanisms for behavior change, such as outcome expectations, self-monitoring, self-evaluation, and self-efficacy,[27-29] which are theoretically framed by the Social Cognitive Theory.[29] In eVIS, objectively measured physical activity tracking using a wrist-worn activity tracker[30] (Fitbit Versa 2) is combined with a daily activity goal (steps/day) and daily patient reports of known important clinical outcome assessments: pain intensity and its affect on daily activities[31-35] and pharmaceutical consumption. Data is collected and visualized in a purpose-developed web application, Pain And TRaining ON-line (PATRON), which can be used by the patient and the IPRP-team to follow and adjust individual physical activity levels.

Despite interventions of this kind having highly promising potential, they are rarely systematically developed specifically for their target patient group and thereafter validated,

meaning that there is a lack of crucial information regarding both their feasibility and true effectiveness. To increase the robustness of this planned R-RCT and to avoid problems such as under-power,[36] an internal randomized pilot study will be conducted to evaluate the intervention's feasibility within the IPRP setting by assessment of planned methods and procedures with the specific purpose of improving and strengthening the R-RCT design.[36-39] In this trial, the UK National Institute for Health Research's (NIHR) definitions of the terms *pilot study* (i.e., "a smaller version of the main study") and *feasibility study* (i.e., "evaluation of pieces of research done before the main study") are applied.[40] The aim of this paper is to transparently clarify and report on the study designs, aims, outcome assessments, and procedures for a planned R-RCT (including an internal randomized pilot study) to prospectively evaluate clinical effectiveness and the cost effectiveness of eVIS as a supplement to IPRPs for patients living with chronic pain compared to standard IPRPs.

METHODS AND ANALYSIS

Trial design and setting

This two-armed multi-site registry-based randomized controlled clinical trial (R-RCT) will be conducted in specialized and primary IPRPs in Sweden, and include approximately 400 (n=200, n=200) patients (number will be definitively determined after the pilot study is finalized) with chronic musculoskeletal non-malignant pain. As indicated, an internal randomized controlled pilot study (n=15, n=15) will be incorporated as the initial phase of the main trial.[38, 41] This trial will comply with the Consolidated Standards of Reporting Trials (CONSORT)[37] and with the Standard Protocol Items: Recommendations for Interventional Trials (SPIRIT)[42]. A completed SPIRIT 2013 Checklist can be found in the additional files. See Figure 1 for study design and enrollment details.

Insert Figure 1 here.

Figure 1. CONSORT 2010 Flow diagram chart of study design and enrollment.

Eligibility criteria

In this trial, the patient-related, care process- and caregiver-related inclusion criteria for receiving Swedish IPRP will be applied, as patients entering the trial must be accepted for IPRP. Principal IPRP inclusion criteria are: patients of working age with persistent or intermittent pain lasting ≥3 months with pain affecting daily activities to a large extent, completed systematic assessment (including screening for psychosocial risk factors and differential diagnosis) and non-pharmacological optimization. Inclusion criteria for Swedish IPRPs is outlined in detail elsewhere.[43] Due to the nature of the intervention, patients must be able to hear, see, and comprehend spoken and written Swedish, and have daily access to a computer, smartphone, or tablet. Patients who need to use a walking aid indoors will be excluded, as will patients living with pain caused by systemic disease or malignancies.

Recruitment

Interdisciplinary Pain Rehabilitation Program Units

A balanced distribution of approximately 15 IPRP units in primary and specialized care in Sweden will be included in the trial. IPRP units reporting to the Swedish National Quality Registry for Pain Rehabilitation (SQRP) have been approached by email with study information (aim, rationale, methods etc.) and an invitation to participate in one of several online digital information meetings that will further present the study (planned for August/September 2021). Study representatives will approach healthcare staff at potential IPRP units by telephone or email to formally offer participation. Operation managers at each unit will be asked to provide written consent by e-mail.

Participants

In order to give potential participants additional time to consider taking part in the trial before they visit the IPRP unit, healthcare staff at the units will be encouraged to provide a general information sheet about the trial in the summon to the initial IPRP assessment. Members of IPRP teams (primarily physiotherapists but also occupational therapists, physicians, nurses etc.) will identify potential participants selected for an IPRP based on outlined criteria and provide them with verbal and written details of the study (information sheets and the project's web address). All participants will provide written informed consent prior to joining the study, which will be managed by the IPRP team. Detailed verbal and written information about the voluntary

nature of participation and the indisputable right to discontinue participation in the trial at any time will be provided. Detailed checklists and forms will support these procedures, and these will be easily accessible on the project web site.

Intervention

Participation in the intervention group involves regular IPRP supplemented with eVIS for a coherent time span of six months, IPRP time included. Participants are not prohibited from taking part of other health care programs during the study period. Interdisciplinary pain rehabilitation programs vary in interventions, duration, composition, and intensity[23-24] and can be performed either individually or in group format. In this trial, participation in a an IPRP will be supplemented by eVIS, a health promoting intervention containing three elements designed to facilitate individualized physical activity level.

The data collection element

Outcome assessments of physical activity level (steps/day) will be objectively collected by a wrist-worn population-specifically validated activity tracker, Fitbit Versa 2.[30] This data will be combined with activity goal setting (steps/day), daily patient reports of pain intensity (0-10), affect of pain on daily activities (0-10), pharmacological consumption (name, dose, number, and form), and (optional) free-text comments in the web application PATRON that can be accessed via computer, smartphone, or tablet. The data collection element is designed to target facilitating mechanisms for behavior change, such as outcome expectations, self-monitoring, self-evaluation, and self-efficacy.[27-29]

The visualisation element

The outcome assessments described above are graphically visualized in relation to daily activity goals for the patient and the IPRP team in three different graphs (1/7/28 days). The visualisation element provides prerequisites for knowledge acquisition and self-monitoring, and self-evaluation as data is visualized in relation to individual goals to improve patient self-efficacy.

The communication element

The graphs will provide support for the patient and the IPRP team in goal setting, reinforcement, knowledge acquisition, self-monitoring, and self-efficacy by facilitating informed discussions

on physical activity levels in relation to daily patient-reported clinical assessments (described in Data collection element) and daily physical activity goals.

Control

Participation in the control group involves taking part in a regular IPRP plus making daily ratings of pain intensity, affect of pain on daily activities, and pharmaceutical consumption (corresponding as in intervention group) in PATRON for six months, including the time that the IPRP is being carried out. The control group will not use the wrist-worn activity tracker or have access to PATRON's visualizing or communication features.

Patient and Public Involvement Statement

In an early phase of developing the web application PATRON, patients living with chronic pain and representatives from patient organizations were invited to participate to the development. In this stage, PATRON was presented and carefully discussed with patients and representatives from patient organizations as well as with web application developers and researchers, resulting in important alterations were made in an early phase.

Outcome assessments

According to the Initiative on Methods, Measurement, and Pain Assessment in Clinical Trials (IMMPACT), physical health, emotional health, and pain intensity are three of six identified core outcome domains that should be considered when designing research studies aiming to evaluate the efficacy and effectiveness of chronic pain treatments.[31, 44] It is specifically recommended that a health survey such as RAND-36 should be incorporated into treatment as a clinical outcome assessment of physical health in clinical trials.[33-34] Outcome assessments for evaluating feasibility will be performed on data from the IPRP baseline and after the study period is completed (six months). In the main trial, assessments of effectiveness will be performed on data from the IPRP baseline and from the 12-month follow-up. The cost effectiveness assessments will be based on data from the IPRP baseline, from the 12-month IPRP follow-up and again 24 and 36 months after the IPRP is completed. A detailed overview of outcome assessments can be found in Table 1.

Table 1. Overview of study period, measurement time points, outcome assessments (***bold and italics)***, instruments, and data sources (*italics*).

	Study period						
	Enrolment	Allocation		Post-allocation			
	-t_1	**0**	**Baseline**	**t1**	**t2**	**t3**	**t4**
Enrolment	X						
Written and verbal study information	X						
Eligibility screen	X						
Informed consent	X						
Allocation/randomization		X					
Interventions							
Intervention, eVIS (6 months)			X	X			
Control (6 months)			X	X			
Outcome assessments							
Personal characteristics							
Sex, age, country of origin, family composition, beliefs of restored health (*SQRP, ITR*)			X				
Disposable-, earned- and net income (*ITR*)			X		X	X	X
Education level and education orientation (*PER, ITR*)			X		X	X	X
Diagnosis (*PATR*)			X		X	X	X
Volume and reason for inpatient care (*PATR*)			X		X	X	X
Pain characteristics							
Pain intensity (last 7 days), NRS (*SQRP-PC and SC*)			X		X		
Pain intensity (today), NRS (*PATRON*)			X	X			
Pain type, location, duration (*SQRP-PC and SC)*			X				
Pain interference (*PATRON*)			X				
Multidimensional measures							
Physical health, RAND-36 PCS health survey (*PATRON*)			X	X	X	X	X
Physical health, RAND-36 PCS health survey (*SQRP-SC only*)			X		X		
Emotional health, RAND-36 MCS health survey (*PATRON*)			X	X	X	X	X
Emotional health, RAND-36 MCS health survey (*SQRP- SC only*)			X		X		

Overall emotional distress, HAD(S) (*SQRP-PC and SC*)	X		X		
Pain catastrophizing, PCS (*SQRP-PC and SC*)	X		X		
Psychosocial consequences, MPI-S (*SQRP-PC and SC*)	X		X		
Pain acceptance, CPAQ-8 (*SQRP-PC only*)	X		X		
Perceived life Satisfaction, LiSat (*SQRP-PC and SC*)	X		X		
Functional level, FRI (*SQRP-SC only*)	X		X		
Physical activity					
Objective measures of steps per day (*Fitbit Versa 2*)	X	X			
Patient-reported measures (*SQRP- PC and SC*)	X		X		
Work					
Return to work (partially or full time) every month (*SSIA*)			X	X	X
Number of days with sick benefit during study period (*SSIA*)			X	X	X
Number of days in work before new sick leave during study period (*SSIA*)			X	X	X
Length of total sick leave during study period (*SSIA*)			X	X	X
Perceived work ability, WAI (*SQRP-PC and SC*)	X		X		
Sleep quality, ISI *(SQRP-SC only)*	X		X		
Pharmaceutical consumption					
Name, dose, size, prize of prescribed pharmaceuticals (*PHAR, PATRON [not size, prize]*)			X	X	X
Prescribed pharmaceuticals collected from pharmacies, (*PHAR*)			X	X	X
Cost of prescribed pharmaceuticals included in benefit program (*PHAR*)			X	X	X
Health care consumption *(PATR)*			X	X	X
Feasibility outcomes, *Questionnaire*		X			
Treatment integrity, *Questionnaire*		X	X		

Abbreviations: -t^1 = pre recruitment period, t^1 = completed study period (6 months), t^2 = follow-up 12 months after completed Interdisciplinary Pain Rehabilitation Program (IPRP), t^3 = 24 months after completed IPRP, t^4 = 36 months after completed IPRP, eVIS = eVISualisation of physical activity and pain intervention, SQRP = the Swedish national quality registry for pain rehabilitation, SQRP-PC = , the Swedish national quality registry for pain rehabilitation primary care, SQRP-SC = the Swedish national quality registry for pain rehabilitation specialized care, NRS = Numeric Rating Scale, PATRON = Pain and training online (web application), RAND-36 PCS = physical health domain , RAND-36 MCS = mental health domain, HAD(S) = Hospital Anxiety and Depression Scale, PCA = Pain Catastrophizing Scale, MPI-S = Multidimensional Pain Inventory -Swedish Version, CPAQ-8 = The Chronic Pain and Acceptance Questionnaire, LiSat = Life Satisfaction Scale, WAI = Work Ability Index, FRI = Functional rating scale, ISI = Insomnia Severity Index, SSIA = the Swedish Social Insurance Agency's registry, PATR = the Patient registry, PHAR = the Pharmaceutical registry, ITR = the Income- and taxation registry, PER = the Population education registry.

Feasibility outcomes, pilot study

The trial will be initiated as a full-scale registry-based internal randomized controlled pilot study. In this initial step, the recruitment process and more specifically the willingness of clinicians to recruit participants, willingness of patients to be recruited, number of eligible participants, contact ways, procedure of gaining consent, and sufficiency of provided recruitment material etc. will be evaluated. Also, the randomization process and the willingness of participants to be randomized and the type of randomization (block size, cluster, details of restrictions) will be evaluated. Furthermore, the standardized effect size and sample size estimation with Cohen's *d*, characteristics [mean, SD] of the primary outcome assessment in the main trial will be calculated after completed study period. In addition, follow-up rates (response rates to questionnaires, rates of treatment integrity, fidelity) will contribute with important aspects of the trial's feasibility in the intended setting.[38, 41]

Primary outcome, main trial

The R-RCT will prospectively evaluate the *clinical effectiveness* of eVIS supplementing IPRPs regarding improvements in our primary outcome assessment *Physical health* collected by the physical health domain in RAND-36 health survey[3, 45] at the 12-month IPRP follow-up after completing the IPRP. The RAND-36 is, for this population, a valid health survey measuring health-related quality of life in two dimensions, physical health (PCS) and mental health (MCS), mediated by eight subscales.[45]

Secondary outcomes, main trial

In the main trial, secondary outcomes will be extracted from Fitbit Versa 2, PATRON and collapsed with data from six national registries (all listed below) at 6, 12, 24, and 36 months after the IPRP is completed.

Objectively measured secondary outcomes collected using Fitbit Versa 2

Objectively measured physical activity levels will be collected daily during the study period using a wrist-worn activity tracker (Fitbit Versa 2). The Fitbit device measures and estimates a range of physical activity outcomes such as number of steps, heart rate, energy expenditure, floors climbed, physical activity level, and sleep.[30, 46] In this trial, participants' step count per

day will automatically be synchronized to PATRON during the study period (six months). The use of steps per day is considered to be a valid quantification of physical activity levels and this is acknowledged by the Swedish Health Authority.[47]

Patient-reported secondary outcomes collected through PATRON

Data on physical and mental health collected using the RAND-36 health survey will be collected through PATRON at 6, 12 and 24 months after IPRP. Pain intensity ("*rate your average pain during the last 24 hours*") will be measured daily using the Numeric Rating Scale (NRS 0-10), a 11-point Likert scale[48] incorporated in the web application PATRON. Pain interference on daily activities is a recommended outcome domain.[32] In PATRON, assessments of affect of pain on daily activities ("*rate how much your daily activities are affected by pain*") will be measured using an 11-point Likert Scale (0-10). This question in PATRON has been modified based on the Multidimensional Pain Inventory Swedish version and its items on pain interference,[49] and validated in our previous study (in manuscript). Data on daily pharmaceutical consumption will be collected in PATRON (name, dose, number, and form). Voluntary free text comments will supplement patient reporting by providing additional information regarding perceived mental and physical health (only in the intervention group).

Secondary outcomes collected through the Swedish national quality registry for pain rehabilitation

In Sweden, 90% of IPRP units routinely collect patient-reported data from standardized questionnaires and report to SQRP, a database initiated in 1998 that contains data from chronic non-malignant pain patients participating in IPRPs.[23, 50] The registry consists of two parts; the primary care SQRP (SQRP-PC) and the specialized SQRP (SQRP-SC). The primary care SQRP is supplied with data from affiliated primary care IPRP units (n=42, reported data from 505 patients in 2020). The specialized care SQRP, receives data from affiliated specialized care IPRP units (n=45, reporting data from 7427 patients in 2020). Data in both registries are collected at baseline, when the IPRP is completed, and at 12-month follow-ups, the content of data collected in the registries differs somewhat. In this trial, registry data from both registries will be collected and used to describe demographics such as age, sex, height, weight, education level, and work.[23, 50] Participants partaking in an IPRP in SC will also routinely complete the RAND-36 health survey at baseline and at their 12-month follow-up after they have completed their program. Data on pain intensity ("*last 7 days*") (NRS 0-10)[48] will be retrieved from SQRP-PC and SQRP-SC alongside other pain characteristics including pain location (36 anatomical

predefined areas, 18 on the left side, 18 on the right side), pain duration, and pain type (intermittent or continuous). Data on self-rated physical and mental health is collected by the RAND-36 health survey[3, 45] in SQRP-SC and the EuroQol-5 dimensions (EQ-5D) collected routinely in SQRP-PC and SQRP-SC will be used. The EQ-5D is a standard instrument used in health economic evaluations and contains five items each with three ordered response categories, and a 0-100 index.[51]

Measures of self-rated physical activity are collected in SQRP-PC using the National Board of Health and Welfare's three questions on physical activity (0 - >300 minutes/week), exercise (0 - >120 minutes/week), and sedentary behavior (0 - 15 hours/day).[52] In SQRP-SC, data is collected by the Godin-Shepard leisure-time physical activity questionnaire (number of times/week that strenuous/moderate/light exercise is performed).[53] Data on overall emotional distress (0 - 3), pain catastrophizing (0 - 4), and psychosocial consequences (0 - 6) of living with pain are collected in SQRP-PC and SQRP-SC using the Hospital Anxiety and Depression Scale (HADS),[45, 54] the Pain Catastrophizing Scale (PCS),[55] and the Multidimensional Pain Inventory Scale Swedish version (MPI-S, 0 - 6).[49] Level of pain acceptance (0 - 6) is collected in SQRP-PC using the Chronic Pain and Acceptance Questionnaire (CPAQ-8).[56] Perceived life satisfaction (1-6) is collected by the Life Satisfaction Scale (LiSat)[57] in both registries. Data on perceived work ability (0 - 10) is collected by the Work Ability Index (WAI)[58] and functional levels (0 - 4) by the Functional Rating Scale (FRI)[59] is collected in SQRP-SC only. Data on patient-reported sleep quality (0 - 4) is collected by the Insomnia Severity Index (ISI)[60] in SQRP-SC.

Secondary outcomes collected through other national registries

Data will be collected from the Swedish Social Insurance Agency's registry on diagnosis, reasons for sick leave, type of financial compensation, number of sick days, and sickness benefit (days and hours) during the study period. In addition, data on days in work (partial or full time) per month in total before a new sick leave period and length of total sick leave during the study period will be retrieved from the registry. Data will be retrieved from the Patient registry on diagnosis and healthcare consumption (total number of days in care etc.). Retrieved data from the Pharmaceutical registry will provide information on prescribed pharmaceutical names, doses, sizes, and prices that have been collected from pharmacies, their costs, and whether the pharmaceutical is included in the subsidized pharmaceutical program. Data on disposable and earned income as well as net income will be retrieved from the Income and taxation registry. In addition, demographic data such as sex, age, marital status, citizenship, education level, and

number of children in the family will be collected. Data on education level and education orientation (focus) in addition to limited demographic data (sex, age) will be collected from the Population registry.

Sample size

A sample size for the pilot study of at least n=30 is considered sufficient for planned pilot study analyses since it will not involve hypothesis testing and sample size calculation *per se*.[39] An interim sample size and power calculation was performed and based on data on RAND-36 outcomes reported by patients living with chronic pain 12 months after taking part in IPRP treatment.[22] A clinically meaningful difference on our primary outcome has previously been reported to be ≥3 points.[24] In this trial, the null hypothesis is that there will be no difference (<15% with ≥3 points improvement) between the intervention group and the control group with regard to proportional improvement in the PCS domain of RAND-36 health survey when assessed at the 12-month follow-up after the completion of the IPRP. The calculation was performed in R, using a calculation method for simple randomization and for independent observations. The preliminary power calculation allows a dropout rate of 20% and requires a total sample size of approximately n=400 to have an 80% power to detect a 15% difference (≥3p) between the groups regarding our primary outcome Physical health. Physical health is measured using the RAND-36 health survey at the 12-month follow-up measurement point after the completion of the IPRP. The significance level is set to 0.05 and is two-tailed. The sample size calculation may be re-calculated after the pilot study is completed.

Allocation

A simple randomization design with a (random) block size of 4 and 6 will be applied and evaluated in the pilot study in order to allocate participants to either the intervention or control group.[61-63] A computer-generated randomization schedule will be created using a random number table to allocate participants to one of the two treatment arms; intervention group (IPRP supplemented by eVIS) or control group (IPRP with daily patient reports in PATRON). The schedule will be generated by an experienced researcher, who is not directly involved in the trial. Sequentially numbered opaque sealed envelopes will be used to ensure allocation

concealment. Allocation will take place at the IPRP unit and will be conducted by members of the IPRP team.

Blinding/masking

Neither the IPRP team delivering the intervention nor participants will be blinded to allocation to either group due to the nature of the intervention.

Data collection methods

Besides objectively measured data of physical activity level, patient-reported data will be collected from PATRON and from six Swedish registries at the IPRP baseline and at 6, 12, and 24 months after completed IPRP. In addition, patient-reported data regarding cost effectiveness will be retrieved 36 months after the IPRP is completed. In this trial, data will be retrieved from SQRP, the Swedish social insurance agency's registry, the Patient registry, the Pharmaceutical registry, the Income- and taxation registry, and the Population education registry to enable a broad investigation into the intervention's effectiveness.

To enable sufficient pilot study analyses, as well as assessment of the primary outcome Physical health (PCS) in RAND-36, members of the IPRP team will be asked to provide self-reported data on feasibility outcomes (outlined below) using a purpose-developed questionnaire with specific questions targeting the IPRP-team perspective.[38] If deemed required, data collection will be supplemented by individual or group interviews. A detailed overview of assessments, time points, and data sources can be found in Table 1.

Data management

In order to connect individual-level data from different registries to PATRON data, we will seek assistance from the National Board of Health and Welfare who will provide a consecutive number key. This key will be stored at the National Board of Health and Welfare for three years (longer if needed). The procedure is initiated by sending PATRON data to the National Board of Health and Welfare and participants' social security numbers will be sent there by SQRP. The National Board of Health and Welfare creates the consecutive number key and connects ordered data with own registry data (the Patient registry and the Pharmaceutical registry). The

National Board of Health and Welfare will then send a data order to the remaining registries (the Swedish Social Insurance Agency's registry, the Income and taxation registry, and the Population education registry) and un-identified data will be sent to the principal investigator to be stored in Dalarna University's secured server.

Intervention fidelity

The following measures have been and will be taken to increase intervention fidelity: A systematical intervention development with a clarified theoretical base explaining suggested mechanisms has been undertaken throughout the development process. Healthcare staff at the IPRP units will be provided with comprehensive written information (easily accessed online) that includes step-by-step instructions on how to initiate and deliver the intervention while maintaining a high level of integrity. Before the study starts, all participating healthcare staff at the IPRP units will take part in a standardized provider training session online. Also, recurring web-based meeting opportunities will be provided, where IPRP-team members will be encouraged to discuss experienced or perceived difficulties, and a questionnaire will be sent out after the study period with the aim of assessing treatment fidelity (treatment integrity and treatment differentiation) by gathering data on how treatment was delivered (manner *versus* treatment manual, intervention's alignment to intended theoretical base). This will allow results to be interpreted and will facilitate practical implementation.[64-65] During the on-going study period, researchers will be automatically notified of non-wear time (Fitbit Versa 2) and any absence of patient reports in PATRON. In these cases, researchers will contact the relevant participant via email or telephone to ask if they need help or support. If a participant decides to discontinue the trial, he or she will be asked if they are willing to grant permission for the collected data up to that point to be used in the trial.

Statistical methods

A statistical analysis plan (SAP) will expand on statistical principles, statistical analyses, the planned handling of missing data, possible additional analyses (subgroups etc.), and interim analyses. In both the pilot study and the R-RCT, descriptive statistical analyses will be performed to provide transparent reporting of characteristics of both participants and participating IPRP units. In addition, IPRP units will be prompted to register the number of

patients they ask to participate, those excluded based on eligibility criteria, and those who decline participation. Analyses of pilot outcomes and primary and secondary outcomes will be performed based on PATRON data and registry data. The clinical effectiveness of eVIS will be analyzed for each outcome using multivariate statistical and repeated measures analyses as a preliminary plan. Both the intention-to-treat and the per-protocol sample will be analyzed, but the intention-to-treat analysis will be considered as the primary analysis. All p-values will be presented. If a p-value is <0.05, the null hypothesis will be rejected and eVIS will be considered effective according to the outlined hypothesis. To perform cost-effectiveness calculations, data on health-related quality of life measured by EQ-5D will be retrieved from SQRP. EQ-5D is the standard instrument used to evaluate health costs and cost effectiveness. Calculations of quality-adjusted life-years (QALYs) will be performed by multiplying health-state utility (measured using the EQ-5D Index score) by time spent in this specific health state.[66-67] In addition, calculations of the incremental cost effectiveness ratio (ICER) will be made as the difference in the cost of two interventions divided by their effect.[68]

Data monitoring

Trial data will be monitored and regularly assessed for integrity and errors. All data monitoring will be performed completely independently from sponsors and competing interests. An independent data monitoring committee (DMC) will be appointed to critically review data safety in the trial. Veronica Sjöberg (VS) will be responsible for the monitoring of all data collected in the internal pilot study. A data management plan (DMP) will be outlined by the first author (VS) and implemented by the principal investigator (LV) to ensure sound data structure (folder structure, file naming, organization), and data storing.

Harms and adverse events

Participating patients and healthcare staff at the participating IPRP units will be encouraged to report any adverse events such as unexpected side effects or symptom deterioration,[69] which will also be reported to the Swedish Ethical Board Review.

Ethics and dissemination

The trial is registered in ClinicalTrials.gov and was approved by the Swedish Ethics Review Board in May 2021 (Dnr 2021/02109). The trial will be conducted in compliance to the Helsinki Declaration.[70] Important protocol modifications will be communicated to the Swedish Ethics Review Board as well as to all participating IPRP units and participants. To protect confidentiality, all data will be coded by an individual code, and the encryption key will be stored separately. Data will be stored at an intended project server at Dalarna University, which is secured by regular backups and only accessible by researchers in the trial after approval from the principal investigator. Results of the internal pilot study and the main trial will be submitted for publication in peer-reviewed journals and communicated in national and international research networks, as well as in relevant clinical settings, including patient associations.

CONCLUSION

This trial has been designed to provide robust data on the feasibility and effectiveness of a systematically developed intervention named eVIS. eVIS is designed to facilitate patients in IPRP reaching and maintaining individualized levels of physical activity recommended to them by involving both objective and patient-reported data, as well as mitigating behavior-change mechanisms.

Author contribution statement

LV and BÄ are responsible for the conception of the trial. LV is the principal investigator and is involved in all methodological decisions. VS, ET, AM, JW, RLM, BÄ, MH, MB, and LV all contributed to study design and were all involved in the development processes (the evaluation of criterion validity of the wrist-worn activity tracker and the evaluations of the content validity and clinical feasibility) of the intervention. RLM performed the preliminary power and sample size calculations and was involved in all associated decisions. VS wrote the first draft of the manuscript and was responsible for revising the manuscript's intellectual content based on all co-authors conscientious input. All authors read and approved the final version of the manuscript. For this article, no ghost authors, guest authors, or professional writers have or will

be used. Author eligibility is and will be based upon the ICMJE Recommendations for the Conduct, Reporting, Editing, and Publication of Scholarly work in Medical Journals.

Trial status

The recruitment process of IPRP units have been initiated in June 2021. Recruitment of participants are anticipated to start in September 2021 and the trial is planned to be completed on 31 December 2024.

Funding

This trial is funded by the Swedish Research Council for Health, Working Life and Welfare (2017-00491), the Research Council (2018-02455), the Swedish Association for Survivors of Polio, Accident, and Injury (2020-03), and research funding from Dalarna University (No grant number). The funders had no role in study design and will have no role in any part of the implementation of the study or the reporting of its results.

Competing interests

None declared.

Access to data

This is a protocol describing a trial design. No data collection has yet been initiated. All authors will have access to the final trial dataset.

Additional files:

- Completed SPIRIT 2013 Checklist
- Patient consent form (in Swedish)

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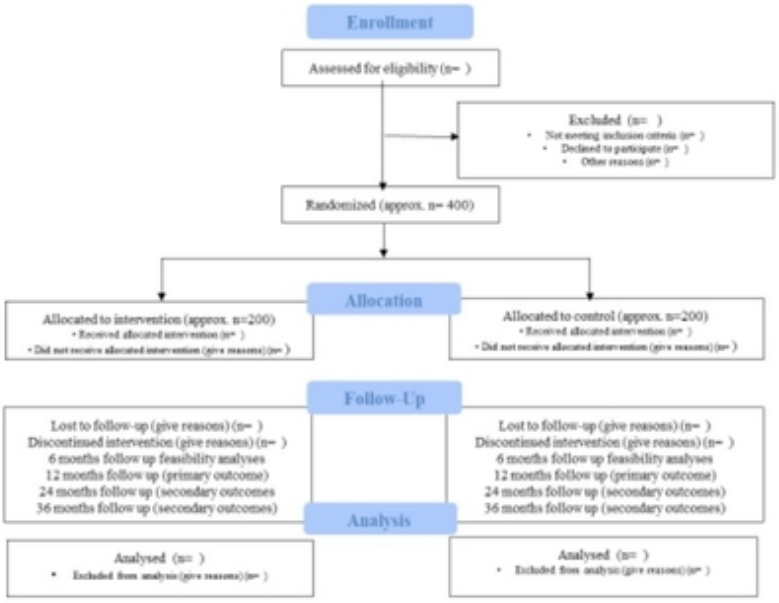

Figure 1. CONSORT 2010 Flow diagram chart of study design and enrollment.

21x17mm (600 x 600 DPI)

SPIRIT 2013 Checklist: Recommended items to address in a clinical trial protocol and related documents*

Section/ item	Item No	Description	Page number
Administrative information			
Title	1	Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym	1
Trial registration	2a	Trial identifier and registry name. If not yet registered, name of intended registry	2, 18
	2b	All items from the World Health Organization Trial Registration Data Set	NA
Protocol version	3	Date and version identifier	2
Funding	4	Sources and types of financial, material, and other support	20
Roles and responsibilities	5a	Names, affiliations, and roles of protocol contributors	1, 19
	5b	Name and contact information for the trial sponsor	20 (not contact info)
	5c	Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities	20
	5d	Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data management team, and other individuals or groups overseeing the trial, if applicable (see Item 21a for data monitoring committee)	18
Introduction			
Background and rationale	6a	Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention	4-6

	6b	Explanation for choice of comparators	17-18
Objectives	7	Specific objectives or hypotheses	6, 17-18
Trial design	8	Description of trial design including type of trial (eg, parallel group, crossover, factorial, single group), allocation ratio, and framework (eg, superiority, equivalence, noninferiority, exploratory)	6
Methods: Participants, interventions, and outcomes			
Study setting	9	Description of study settings (eg, community clinic, academic hospital) and list of countries where data will be collected. Reference to where list of study sites can be obtained	6
Eligibility criteria	10	Inclusion and exclusion criteria for participants. If applicable, eligibility criteria for study centres and individuals who will perform the interventions (eg, surgeons, psychotherapists)	7
Interventions	11a	Interventions for each group with sufficient detail to allow replication, including how and when they will be administered	8-9
	11b	Criteria for discontinuing or modifying allocated interventions for a given trial participant (eg, drug dose change in response to harms, participant request, or improving/worsening disease)	18-19
	11c	Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return, laboratory tests)	17
	11d	Relevant concomitant care and interventions that are permitted or prohibited during the trial	8
Outcomes	12	Primary, secondary, and other outcomes, including the specific measurement variable (eg, systolic blood pressure), analysis metric (eg, change from baseline, final value, time to event), method of aggregation (eg, median, proportion), and time point for each outcome. Explanation of the clinical relevance of chosen efficacy and harm outcomes is strongly recommended	9-14 Table 1
Participant timeline	13	Time schedule of enrolment, interventions (including any run-ins and washouts), assessments, and visits for participants. A schematic diagram is highly recommended (see Figure)	Table 1, 10-11

Sample size	14	Estimated number of participants needed to achieve study objectives and how it was determined, including clinical and statistical assumptions supporting any sample size calculations	15
Recruitment	15	Strategies for achieving adequate participant enrolment to reach target sample size	7, 17
Methods: Assignment of interventions (for controlled trials)			
Allocation:			15
Sequence generation	16a	Method of generating the allocation sequence (eg, computer-generated random numbers), and list of any factors for stratification. To reduce predictability of a random sequence, details of any planned restriction (eg, blocking) should be provided in a separate document that is unavailable to those who enrol participants or assign interventions	17-18
Allocation concealment mechanism	16b	Mechanism of implementing the allocation sequence (eg, central telephone; sequentially numbered, opaque, sealed envelopes), describing any steps to conceal the sequence until interventions are assigned	17-18
Implementation	16c	Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions	15
Blinding (masking)	17a	Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how	16
	17b	If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during the trial	16
Methods: Data collection, management, and analysis			
Data collection methods	18a	Plans for assessment and collection of outcome, baseline, and other trial data, including any related processes to promote data quality (eg, duplicate measurements, training of assessors) and a description of study instruments (eg, questionnaires, laboratory tests) along with their reliability and validity, if known. Reference to where data collection forms can be found, if not in the protocol	16-18

	18b	Plans to promote participant retention and complete follow-up, including list of any outcome data to be collected for participants who discontinue or deviate from intervention protocols	17
Data management	19	Plans for data entry, coding, security, and storage, including any related processes to promote data quality (eg, double data entry; range checks for data values). Reference to where details of data management procedures can be found, if not in the protocol	16
Statistical methods	20a	Statistical methods for analysing primary and secondary outcomes. Reference to where other details of the statistical analysis plan can be found, if not in the protocol	17-18
	20b	Methods for any additional analyses (eg, subgroup and adjusted analyses)	17-18
	20c	Definition of analysis population relating to protocol non-adherence (eg, as randomised analysis), and any statistical methods to handle missing data (eg, multiple imputation)	17-18
Methods: Monitoring			
Data monitoring	21a	Composition of data monitoring committee (DMC); summary of its role and reporting structure; statement of whether it is independent from the sponsor and competing interests; and reference to where further details about its charter can be found, if not in the protocol. Alternatively, an explanation of why a DMC is not needed	18
	21b	Description of any interim analyses and stopping guidelines, including who will have access to these interim results and make the final decision to terminate the trial	17-18
Harms	22	Plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial conduct	18
Auditing	23	Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor	20
Ethics and dissemination			

Research ethics approval	24	Plans for seeking research ethics committee/institutional review board (REC/IRB) approval	18-19
Protocol amendments	25	Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators, REC/IRBs, trial participants, trial registries, journals, regulators)	18-19
Consent or assent	26a	Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32)	7
	26b	Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable	NA
Confidentiality	27	How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial	18-19
Declaration of interests	28	Financial and other competing interests for principal investigators for the overall trial and each study site	20
Access to data	29	Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators	20
Ancillary and post-trial care	30	Provisions, if any, for ancillary and post-trial care, and for compensation to those who suffer harm from trial participation	No
Dissemination policy	31a	Plans for investigators and sponsor to communicate trial results to participants, healthcare professionals, the public, and other relevant groups (eg, via publication, reporting in results databases, or other data sharing arrangements), including any publication restrictions	18-19
	31b	Authorship eligibility guidelines and any intended use of professional writers	19
	31c	Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code	20
Appendices			

Informed consent materials	32	Model consent form and other related documentation given to participants and authorised surrogates	See supplementary files [In Swedish]
Biological specimens	33	Plans for collection, laboratory evaluation, and storage of biological specimens for genetic or molecular analysis in the current trial and for future use in ancillary studies, if applicable	NA

BMJ Open

Effectiveness of the eVISualisation of physical activity and pain intervention (eVIS) in Swedish Interdisciplinary Pain Rehabilitation Programs: study protocol for a registry-based randomized controlled clinical trial

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Title:

Effectiveness of the eVISualisation of physical activity and pain intervention (eVIS) in Swedish Interdisciplinary Pain Rehabilitation Programs: study protocol for a registry-based randomized controlled clinical trial

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ABSTRACT

Introduction: Living with chronic pain often involves negative consequences. Interdisciplinary Pain Rehabilitation Programs (IPRPs), a subset of Interdisciplinary Treatment is considered superior to single-treatment measures in patients with chronic pain. Despite this, effects emerge sub-optimal and more than 20% of patients deteriorate in patient reported physical health outcomes after IPRP. A novel e-Health intervention, eVISualisation (eVIS) of physical activity and pain, has been systematically developed to facilitate patients in reaching and maintaining recommended individualized physical activity levels. The aim is to transparently report on methodology, outcome assessments, and processes for a registry-based randomized controlled trial (R-RCT) initiated as a pilot study.

Methods and analysis: In the R-RCT, recruitment of approximately 400 patients with chronic pain at primary and specialized IPRP units (n=15) in Sweden will be performed. Participants will be randomly allocated to either IPRP + eVIS or to control group that will receive IPRP only. eVIS entails objectively measured physical activity (steps) and patient-reported outcomes (pain intensity, interference of pain on daily activities, pharmaceutical consumption) collected and visualized in the web application PATRON. Data from the initial 30 participants completing the study period (6 months) will be included in a pilot study designed to evaluate key feasibility outcomes (recruitment- and randomization processes, implementation process, treatment integrity, data collection procedure, and preliminary outcome measures). Outcome variables will be extracted from PATRON and from six national registries. Multivariate statistics and repeated measures analyses will be performed. Quality Adjusted Life Years (QALYs) and Incremental Cost Effectiveness Ratio (ICER) will be calculated for cost effectiveness evaluation.

Ethics/dissemination: The Swedish Ethics Review Board granted approval (Dnr 2021/02109). Results will be disseminated through peer-review journals.

Trial registration number: The trial was prospectively registered at ClinicalTrials.gov with trial registration number NCT05009459.

Protocol version: 1

Strengths and limitations of the study

- A proceeding pilot study will enable improvements of design and feasibility of subsequent R-RCT.
- The eVIS-intervention has been developed, evaluated, and improved, based on data provided from patients, clinicians, and researchers in different fields.
- The intervention targets physical activity modalities in IPRP and is designed to enable a more individualized IPRP treatment.
- The intervention is based on objectively measured physical activity levels, patient-reported clinical outcomes, and mechanisms that facilitate behavior change, in accordance with current guidelines that are provided by authorities in the chronic pain management field.
- The nature of the intervention precludes blinding of patients and the IPRP team.

INTRODUCTION

Chronic musculoskeletal pain (>3 months), including neck/shoulder/back pain or widespread pain, is a major global health and socioeconomic burden.[1 2] Living with chronic pain is often associated with reduced levels of wellbeing and the health-related quality of life of this group has been reported to be among the lowest of any medical condition.[3] To date, physical activity (i.e. any bodily movement that requires energy expenditure) and exercise (i.e. structured and planned physical activity aimed to increase fitness)[4] have been shown to prevent and/or treat several of our noncommunicable diseases including chronic pain,[5] due to their beneficial effects on general health, pain intensity, physical and psychological functioning, and health-related quality of life.[5-8] Despite the growing evidence of health benefits related to physical activity, participation and adherence to physical activity recommendations, such as WHO´s physical activity guidelines, are often low in patients living with chronic pain.[9-12] This may partly be explained by the indicated association between high pain scores and low patient-reported activity levels among patients with chronic pain and/or the documented reports of the negative impact of depression on physical activity levels.[13] In addition, it is well known that behavior change is difficult, and that each individual's own participation is essential.[14] It has been shown that behavior change towards a beneficial physical activity level may be facilitated by individuals self-monitoring their physical activity.[15] The use of objective measures increases the likelihood of the effectiveness of interventions designed to promote physical activity.[15] By adding goal setting, feedback, and a focus on achieved goals, effectiveness can be further improved.[15-18]

Interdisciplinary pain rehabilitation programs (described as a subset of Interdisciplinary Treatment [IDT]), is defined as "multimodal treatment provided by a multidisciplinary team (at least 3 professions), collaborating in assessment and treatment using a shared biopsychosocial model and goals"[19]. The IPRP approach adopts the principles of behavioral therapy and incorporates besides physical activity and exercise, also psychological measures, pharmaceutical treatment and patient education.[20] Physical activity and exercise are central measures in IPRPs as it targets the physical deconditioning by improving levels of physical activity, and also reduces pain severity and improved physical function and quality of life, without causing any severe adverse events.[5] Interdisciplinary pain rehabilitation programs are considered to be superior to single-treatment measures (e.g., physical treatments, education interventions, surgery, etc.) for patients with chronic pain supporting positive effects on pain intensity and activity disability.[20 21] However, IPRP effectiveness is only slightly better and in

the majority of cases only a small effect is seen.[21-25] In addition, up to 25% of patients report deterioration in physical health after completing IPRP and after 12 months follow up, regardless of duration of IPRP.[20 25 26] Sustainable treatment affects seem to vary according to patient clinical features at baseline, such as poor employment status, high pain levels, and low functioning, all of which predict low physical health at follow-up.[23 27] Many efforts have been made to find effective interventions that improve the health of chronic pain patients. To facilitate individualized physical activity levels within the Swedish IPRP setting, an eVISualisation (eVIS) of physical activity and pain intervention has been systematically developed according to the Medical Research Council´s recently updated framework for development and evaluation of complex interventions. [28 29] In accordance with the framework, the eVIS-interventions were designed and planned in close collaboration with stakeholders. eVIS is designed to target facilitating mechanisms for behavior change, such as outcome expectations, self-monitoring, self-evaluation, and self-efficacy,[30-32] which are theoretically framed by the Social Cognitive Theory.[32] In eVIS, objectively measured physical activity tracking using a wrist-worn activity tracker[33] (Fitbit Versa 2) is combined with a daily activity goal (steps/day) and daily patient reports of known important clinical outcome assessments: pain intensity and its interference on daily activities[34-38] and pharmaceutical consumption. Data is collected and visualized in a purpose-developed web application, Pain And TRaining ON-line (PATRON), which can be used by the patient and the IPRP-team to follow and adjust individual physical activity levels. Despite interventions of this kind having highly promising potential to relive pain and improve disability in this patient group,[39]interventions are rarely systematically developed and validated specifically for their target patient group, leaving crucial information of feasibility and true effectiveness unknown. To increase the robustness of this planned R-RCT and to avoid an underpowered trial and gain knowledge of population variation,[40] an randomized pilot study will be conducted to evaluate the intervention's feasibility within the IPRP setting with the specific purpose of improving and strengthening the R-RCT design.[40-43] In this trial, the UK National Institute for Health Research's (NIHR) definitions of the terms *pilot study* (i.e., "a smaller version of the main study") and *feasibility study* (i.e., "evaluation of pieces of research done before the main study") are applied.[44] The aim of this paper is to transparently clarify and report on study designs, aims, outcome assessments, and procedures for a planned R-RCT (including an randomized pilot study) which prospectively will evaluate clinical effectiveness and cost effectiveness of eVIS supplement to IPRPs for patients living with chronic pain compared to standard IPRPs.

METHODS AND ANALYSIS

Trial design and setting

This two-armed pragmatic multi-site registry-based randomized controlled clinical trial (R-RCT) will be conducted in specialized and primary IPRPs in Sweden, and include approximately 400 (n=200, n=200) patients (number will be definitively determined after the pilot study is finalized) with chronic musculoskeletal non-malignant pain. As indicated, an randomized controlled pilot study (n=15, n=15) will be incorporated as the initial phase of the main trial in order to evaluate the intervention´s methodology and design.[29 42 45] This trial will comply with the Consolidated Standards of Reporting Trials (CONSORT)[41] and with the Standard Protocol Items: Recommendations for Interventional Trials (SPIRIT)[46]. A completed SPIRIT 2013 Checklist can be found in the additional files. See Figure 1 for study design and enrollment details.

Insert Figure 1 here.

Figure 1. CONSORT 2010 Flow diagram chart of study design and enrollment.

Eligibility criteria

In this trial, the patient-related, care process and caregiver-related inclusion criteria for receiving Swedish IPRP will be applied, as patients entering the trial must be accepted for IPRP. Principal IPRP inclusion criteria are patients in working age with persistent or intermittent pain lasting ≥3 months with pain affecting daily activities to a large extent, completed systematic assessment (including screening for psychosocial risk factors and differential diagnosis) and non-pharmacological optimization. Inclusion criteria for Swedish IPRPs is outlined in detail elsewhere.[47] Due to the nature of the intervention, patients must be able to hear, see, and comprehend spoken and written Swedish, and have daily access to a computer, smartphone, or tablet. Patients who need to use a walking aid indoors will be excluded.

Recruitment

Interdisciplinary Pain Rehabilitation Units

Approximately 15 IPRP units in primary and specialized care in Sweden will be included in the trial. IPRP units reporting to the Swedish National Quality Registry for Pain Rehabilitation (SQRP) have been approached by email with study information (aim, rationale, methods etc.) and an invitation to participate in one of several online digital information meetings that will further present the study (planned from August 2021). Study representatives will approach healthcare staff at potential IPRP units by telephone or email to formally offer participation. Operation managers at each unit will be asked to provide written consent by e-mail.

Participants

In order to give potential participants additional time to consider taking part in the trial before they visit the IPRP unit, healthcare staff at the units will be encouraged to provide a general information sheet about the trial in the summon to the IPRP assessment. Members of IPRP teams (primarily physiotherapists but also occupational therapists, physicians, nurses etc.) will identify potential participants selected for IPRP based on outlined criteria and provide them with verbal and written details of the study (information sheets and the project's web address). All participants will provide written informed consent (see supplementary file) prior to joining the study, which will be managed by the IPRP team. Detailed verbal and written information about the voluntary nature of participation and the indisputable right to discontinue participation in the trial at any time will be provided. Detailed checklists and forms will support these procedures, and these will be easily accessible on the project web site.

Intervention

Participation in the intervention group involves regular IPRP supplemented with eVIS for a coherent time span of six months, IPRP time included. As the duration and intensity of IPRPs greatly vary from a couple of weeks up to four months[25], a six month study period ensures time of independent use of eVIS after completed IPRP. Participants are not prohibited to take part of other health care during study period. Interdisciplinary pain rehabilitation programs vary in interventions, duration, composition, intensity[24 25] and can be performed either individually or in group format. In this trial, participation in a IPRP will be supplemented by eVIS, a health

promoting intervention containing three elements designed to facilitate individualized physical activity level (Figure 2).

The data collection element

Outcome assessments of physical activity level (steps/day) will be objectively collected by a wrist-worn activity tracker, Fitbit Versa 2. This device has been population-specifically validated and the measurement of step rate is indicated as valid for measurement in this population. [33] Data on step rate will be automatically synchronized to the web application PATRON where pain intensity (0-10), [48] interference of pain on daily activities (0-10),[49] pharmacological consumption (name, dose, number, and form), and (optional) free-text comments will be reported by the patient daily. The web application can be accessed via computer, smartphone, or tablet. A daily activity goal (steps/day) is formulated by the patient in collaboration with the IPRP-team and revised accordingly.

The data collection element is designed to target facilitating mechanisms for behavior change, such as outcome expectations, self-monitoring, self-evaluation, and self-efficacy.[30-32] The visualisation element

Objectively measured physical activity levels, patient-report on pain intensity and interference of pain on daily activity are graphically visualized in relation to patient daily activity goal. Three different graphs (1/7/28 days) are available. The visualisation element provides prerequisites for increased knowledge acquisition, self-monitoring, and self-evaluation as data is visualized over time and in relation to each other and to the individual daily activity goal in order to improve patient self-efficacy.

The communication element

The graphs in the visualisation element together with compiled data on pharmacological consumption will provide novel support for the patient and the IPRP team towards an individualized goal setting process by reinforcement, knowledge acquisition, self-monitoring, and self-efficacy. The support is facilitated by objectively measured physical activity levels visualized in relation known factors important in pain rehabilitation. Based on data in eVIS, patient and IPRP-team get unique information of factors affecting physical activity levels. This addition to IPRP provides possibilities to investigate barriers to physical activity and fine-tune individualized treatment.

Insert Figure 2 here

Figure 2. Schematic illustration of the eVIS-intervention´s three elements: i) the data collection element of physical activity level (steps/day), patient-reports of interference of pain on daily activities, pain intensity and pharmacological consumption, ii) the visualisation element of collected data in different graphs and compilations of data, and iii) the communication element.

Control

Participation in the control group involves taking part in regular IPRP plus making daily ratings of pain intensity, interference of pain on daily activities, and pharmaceutical consumption (corresponding as in intervention group) in PATRON for six months, including the time that the IPRP is being carried out. The control group will not use the wrist-worn activity tracker or have access to PATRON's visualizing or communication features.

Patient and Public Involvement Statement

In an early developing phase, stakeholders (patients living with chronic pain, representatives from patient organizations and clinicians experienced in pain rehabilitation) were invited to contribute to the intervention development. In this phase, the web application PATRON and eVIS was presented and carefully discussed with stakeholders as well as with web application developers and researchers. Several needs for improvement were identified, such as a need of an addition of pharmaceutical report function, designated web pages and graphical changes in planned interfaces.

Outcome assessments

According to the Initiative on Methods, Measurement, and Pain Assessment in Clinical Trials (IMMPACT), physical health, emotional health, and pain intensity are three of six identified core outcome domains that should be considered when designing research studies aiming to evaluate effectiveness of chronic pain treatments.[34 50] It is specifically recommended that a health survey such as RAND-36 should be incorporated into treatment as a clinical outcome assessment of physical health in clinical trials.[36 37] Outcome assessments for evaluating

feasibility will be performed on data from the IPRP baseline and after the study period is completed (six months) for the first 30 participants (n=15 +, n=15). In the main trial, assessments of effectiveness will be performed on data from the IPRP baseline and from the 12-month follow-up. The cost effectiveness assessments will be based on data from the IPRP baseline, from the 12-month IPRP follow-up and again 24 and 36 months after the IPRP is completed. A detailed overview of outcome assessments can be found in Table 1.

Table 1. Overview of study period, measurement time points, outcome assessments (***bold and italics)***, instruments, and data sources (*italics*).

	Study period						
	Enrolment	Allocation	Post-allocation				
	-t_1	**0**	**Baseline**	**t1**	**t2**	**t3**	**t4**
Enrolment	X						
Written and verbal study information	X						
Eligibility screen	X						
Informed consent	X						
Allocation/randomization		X					
Interventions							
Intervention, eVIS (6 months)			X	X			
Control (6 months)			X	X			
Outcome assessments							
Personal characteristics							
Sex, age, country of origin, family composition, beliefs of restored health (*SQRP, SS*)			X				
Disposable-, earned- and net income (SS)			X		X	X	X
Education level and education orientation (*SPR, SS*)			X		X	X	X
Diagnosis (*NPR*)			X		X	X	X
Volume and reason for inpatient care (*NPR*)			X		X	X	X
Pain characteristics							
Pain intensity (last 7 days), NRS (*SQRP-PC and SC*)			X		X		
Pain intensity (today), NRS (*PATRON*)			X	X			
Pain type, location, duration (*SQRP-PC and SC)*			X				
Pain interference (*PATRON*)			X				
Multidimensional measures							
Physical health, RAND-36 PCS health survey (*PATRON*)			X	X	X	X	X
Physical health, RAND-36 PCS health survey (*SQRP-SC only*)			X		X		
Emotional health, RAND-36 MCS health survey (*PATRON*)			X	X	X	X	X
Emotional health, RAND-36 MCS health survey (*SQRP- SC only*)			X		X		

Overall emotional distress, HAD(S) (*SQRP-PC and SC*)	X		X		
Pain catastrophizing, PCS (*SQRP-PC and SC*)	X		X		
Psychosocial consequences, MPI-S (*SQRP-PC and SC*)	X		X		
Pain acceptance, CPAQ-8 (*SQRP-PC only*)	X		X		
Perceived life Satisfaction, LiSat (*SQRP-PC and SC*)	X		X		
Functional level, FRI (*SQRP-SC only*)	X		X		
Physical activity					
Objective measures of steps per day (*Fitbit Versa 2*)	X	X			
Patient-reported measures (*SQRP- PC and SC*)	X		X		
Work					
Return to work (partially or full time) every month (*SSIA*)			X	X	X
Number of days with sick benefit during study period (*SSIA*)			X	X	X
Number of days in work before new sick leave during study period (*SSIA*)			X	X	X
Length of total sick leave during study period (*SSIA*)			X	X	X
Perceived work ability, WAI (*SQRP-PC and SC*)	X		X		
Sleep quality, ISI *(SQRP-SC only)*	X		X		
Pharmaceutical consumption					
Name, dose, size, prize of prescribed pharmaceuticals (*SPDR, PATRON [not size, prize]*)			X	X	X
Prescribed pharmaceuticals collected from pharmacies, (*SPDR*)			X	X	X
Cost of prescribed pharmaceuticals included in benefit program (*SPDR*)			X	X	X
Health care consumption *(NPR)*			X	X	X
Feasibility outcomes, *Questionnaire*		X			
Treatment integrity, *Questionnaire*		X	X		

Abbreviations: -t^1 = pre recruitment period, t^1 = completed study period (6 months), t^2 = follow-up 12 months after completed Interdisciplinary Pain Rehabilitation Program (IPRP), t^3 = 24 months after completed IPRP, t^4 = 36 months after completed IPRP, eVIS = eVISualisation of physical activity and pain intervention, SQRP = the Swedish national quality registry for pain rehabilitation, SQRP-PC = , the Swedish national quality registry for pain rehabilitation primary care, SQRP-SC = the Swedish national quality registry for pain rehabilitation specialized care, NRS = Numeric Rating Scale, PATRON = Pain and training online (web application), RAND-36 PCS = physical health domain , RAND-36 MCS = mental health domain, HAD(S) = Hospital Anxiety and Depression Scale, PCA = Pain Catastrophizing Scale, MPI-S = Multidimensional Pain Inventory -Swedish Version, CPAQ-8 = The Chronic Pain and Acceptance Questionnaire, LiSat = Life Satisfaction Scale, WAI = Work Ability Index, FRI = Functional rating scale, ISI = Insomnia Severity Index, SSIA = the Swedish Social Insurance Agency's registry, NPR = the National Patient Register, SPDR = the Swedish Prescribed Drug Register, SS = Statistics Sweden, SPR = the Swedish Population Register.

Feasibility outcomes, pilot study

The trial will be initiated as a full-scale registry-based randomized controlled pilot study. In this initial step, feasibility will be evaluated from data provided from the first 30 participants completing the study period and in the following key areas: the unit´s recruitment capabilities, the randomization process, implementation process, participant response to intervention which is outlined in Table 2. In addition, the data collection procedure and the preliminary outcome measures (standardized effect size, sample size estimation with Cohen's *d*, characteristics [mean, SD]) in main trial will be evaluated.[42 45] In addition to feasibility outcomes, characteristics of the units IPRP will be collected

Table 2. Overview of key feasibility outcomes in pilot study.

Key feasibility outcomes
Recruitment capability
Volume of total eligible patients
Number recruited/week
Eligibility screening procedure
Proportion accepted/declined
Personal characteristics of included and excluded participants
Pain characteristics of included and excluded participants
Procedure of collecting consent
Randomization process
Delivery envelopes
Storage of envelopes
Procedure of opening envelopes
Patients´ reaction to allocation
Implementation process
Response rate RAND-36 PCS
Compliance rate (use of Fitbit Versa 2, intervention group only)
Compliance rate (patient reported outcomes in PATRON)
Treatment integrity
Reported adverse events
Data collection procedure
Access to PATRON data
Access to RAND-36 data
Preliminary outcome measures
Characteristics primary outcome
Missing data
Changes from baseline to finalized study period

Abbreviations: RAND-36 PCS = physical health domain in RAND-36, PATRON = Pain and training online (web application).

Primary outcome, main trial

The R-RCT will prospectively evaluate the clinical effectiveness of eVIS supplementing IPRPs regarding improvements in our primary outcome assessment Physical health collected by the physical health domain in RAND-36 health survey[3 51] at the 12-month IPRP follow-up after completing the IPRP. The RAND-36 is, for this population, a valid health survey measuring health-related quality of life in two dimensions, physical health (PCS) and mental health (MCS), mediated by eight subscales.[51]

Secondary outcomes, main trial

In the main trial, secondary outcomes will be extracted from Fitbit Versa 2, PATRON and collapsed with data from six national registries (all listed below) at 12, 24, 36 months after the IPRP is completed.

Objectively measured secondary outcomes collected using Fitbit Versa 2

Objectively measured physical activity levels will be collected daily during the study period using a wrist-worn activity tracker (Fitbit Versa 2). The Fitbit device measures and estimates a range of physical activity outcomes such as number of steps, heart rate, energy expenditure, floors climbed, physical activity level, and sleep.[33 52] In this trial, participants' step count per day will automatically be synchronized to PATRON during the study period (six months). The use of steps per day is considered to be a valid quantification of physical activity levels and this is acknowledged by the Swedish Health Authority.[53]

Patient-reported secondary outcomes collected through PATRON

Data on physical and mental health collected by RAND-36 health survey will be collected through PATRON at 6, 12 and 24 months after IPRP. Pain intensity ("*rate your average pain during the last 24 hours*") will be measured daily using the Numeric Rating Scale (NRS 0 = *no pain at all* to 10 = *pain as bad as it could be*), a 11-point Likert scale[48] incorporated in the web application PATRON. Pain interference on daily activities is a recommended outcome domain.[35] In PATRON, assessments of interference of pain on daily activities will be measured by the question "*rate how much your daily activities are affected by pain*" using an 11-point Likert Scale (0 = *not at all* to 10 = *to a very large extent*). This question in PATRON has been modified based on the Multidimensional Pain Inventory Swedish version and its items on pain interference,[49] and validated in our previous study (in manuscript). Data on daily pharmaceutical consumption will be collected in PATRON (name, dose, number, and form).

Voluntary free text comments will supplement patient reporting by providing additional information regarding perceived mental and physical health (only in the intervention group).

Secondary outcomes collected through the Swedish national quality registry for pain rehabilitation

In Sweden, 90% of IPRP units routinely collect patient-reported data from standardized questionnaires and report to SQRP, a database initiated in 1998 that contains data from chronic non-malignant pain patients participating in IPRPs.[24 54] The registry consists of two parts; the primary care SQRP (SQRP-PC) and the specialized SQRP (SQRP-SC). The primary care SQRP is supplied with data from affiliated primary care IPRP units (n=42, reported data from 505 patients in 2020). The specialized care SQRP, receives data from affiliated specialized care IPRP units (n=45, reporting data from 7427 patients in 2020). Data in both registries are collected at baseline, when the IPRP is completed, and at 12-month follow-ups, the content of data collected in the registries differs somewhat. In this trial, registry data from both registries will be collected used to describe demographics such as age, sex, height, weight, education level, and work.[24 54] Participants partaking in an IPRP in SC will also routinely complete the RAND-36 health survey at baseline and at their 12-month follow-up after they have completed their program. Data on pain intensity ("*last 7 days*") (NRS 0-10)[48] will be retrieved from SQRP-PC and SQRP-SC alongside other pain characteristics including pain location (36 anatomical predefined areas, 18 on the left side, 18 on the right side), pain duration, and pain type (intermittent or continuous). Data on self-rated physical and mental health is collected by the RAND-36 health survey[3 51] in SQRP-SC and the EuroQol-5 dimensions (EQ-5D) collected routinely in SQRP-PC and SQRP-SC will be used. The EQ-5D is a standard instrument used in health economic evaluations and contains five items each with three ordered response categories, and a 0-100 index.[55]

Measures of self-rated physical activity is collected in SQRP-PC and SC using the National Board of Health and Welfare's three questions on physical activity (0 - >300 minutes/week), exercise (0 - >120 minutes/week), and sedentary behavior (0 - 15 hours/day).[56] and in SQRP-PC by the Godin-Shepard leisure-time physical activity questionnaire (number of times/week that strenuous/moderate/light exercise.[57] Data on overall emotional distress (0 - 3), pain catastrophizing (0 - 4), and psychosocial consequences (0 - 6) of living with pain are collected in SQRP-PC and SQRP-SC using the Hospital Anxiety and Depression Scale (HADS),[51 58] the Pain Catastrophizing Scale (PCS),[59] and the Multidimensional Pain Inventory Scale Swedish version (MPI-S, 0 - 6).[49] Level of pain acceptance (0 - 6) is collected in SQRP-PC using the

Chronic Pain and Acceptance Questionnaire (CPAQ-8).[60] Perceived life satisfaction (1-6) is collected by the Life Satisfaction Scale (LiSat)[61] in both registries. Data on perceived work ability (0 - 10) is collected by the Work Ability Index (WAI)[62] and functional levels (0 - 4) by the Functional Rating Scale (FRI)[63] is collected in SQRP-SC only. Data on patient-reported sleep quality (0 - 4) is collected by the Insomnia Severity Index (ISI)[64] in SQRP-SC.

Secondary outcomes collected through other national registries

Data will be collected from the Swedish Social Insurance Agency's registry on diagnosis, reasons for sick leave, type of financial compensation, number of sick days, and sickness benefit (days and hours) during the study period. In addition, data on days in work (partial or full time) per month in total before new sick leave period and length of total sick leave during the study period will be retrieved from the registry. Data will be retrieved from the Patient registry on diagnosis and healthcare consumption (total number of days in care etc.). Retrieved data from the Swedish Prescribed Drug Register will provide information on prescribed pharmaceutical names, doses, sizes, and prices that have been collected from pharmacies, their costs, and whether the pharmaceutical is included in the subsidized pharmaceutical program. Data on disposable and earned income as well as net income will be retrieved from Statistics Sweden. In addition, demographic data such as sex, age, marital status, citizenship, education level, and number of children in the family will be collected. From the Swedish Population Register, data on education level and education orientation (focus) in addition to limited demographic data (sex, age) will be collected.

Sample size

A sample size for the pilot study of at least n=30 is considered sufficient for planned feasibility analyses since it will not involve hypothesis testing and sample size calculation *per se*.[43 65 66] For the main trial, a preliminary power calculation are based on assumptions from previous research reporting on proportions of patients that report a clinically meaningful difference of ≥3 points in the physical health domain in RAND-36, 12-months after completed IPRP. [25] The calculation was performed in R, using a calculation method for simple randomization and for independent observations. The preliminary power calculation allows a dropout rate of 20% and requires a total sample size of approximately n=400 to have an 80% power to detect a 15% difference (≥3p) between the groups in the outcome physical health. Physical health is measured by the RAND-36 health survey at the 12-month follow-up measurement point after the

completion of the IPRP. The significance level is set to 0.05 and is two-tailed. The sample size calculation may be re-calculated after the pilot study is completed. In this trial, the null hypothesis is that there will be no difference between the intervention group and the control group (<15% with ≥3 points improvement) with regard to proportional improvement in the PCS domain of RAND-36 health survey when assessed at the 12-month follow-up after the completion of the IPRP.

Allocation

A permuted block randomization design with a random block size of 4 and 6 and an 1:1 allocation ratio will be applied and evaluated in the pilot study in order to allocate participants to either the intervention or control group.[67-69] A computer-generated randomization schedule will be created using a random number table to allocate participants to one of the two treatment arms; intervention group (IPRP supplemented by eVIS) or control group (IPRP with daily patient reports in PATRON). The schedule will be generated by an experienced researcher, who is not directly involved in the trial. Sequentially numbered opaque sealed envelopes will be used to ensure allocation concealment. Allocation will take place at the IPRP unit and will be conducted by members of the IPRP team after initial assessment.

Blinding/masking

Neither the IPRP team delivering the intervention nor participants will be blinded to allocation to either group due to the nature of the intervention.

Data collection methods

Besides objectively measured data of physical activity level, patient-reported data will be collected from PATRON and from six Swedish registries at the IPRP baseline and at 6, 12 and 24 months after completed IPRP. In addition, patient-reported data regarding cost effectiveness will be retrieved 36 months after the IPRP is completed. In this trial, data will be retrieved from SQRP, the Swedish social insurance agency's registry, the Patient registry, the Pharmaceutical registry, the Income- and taxation registry, and the Population education registry to enable a broad investigation into the intervention's effectiveness.

To enable sufficient pilot study analyses, as well as assessment of the primary outcome Physical health (PCS) in RAND-36, members of the IPRP team will be asked to provide self-reported data on feasibility outcomes (outlined below) using a purpose-developed questionnaire with specific questions targeting the IPRP-team perspective.[42] If deemed required, data collection will be supplemented by individual or group interviews. A detailed overview of assessments, time points, and data sources can be found in Table 1.

Data management

In order to link individual-level data from different registries to PATRON data, we will seek assistance from the National Board of Health and Welfare who will provide a consecutive number key. This key will be stored at the National Board of Health and Welfare for three years (longer if needed). The procedure is initiated by sending PATRON data to the National Board of Health and Welfare and participants' social security numbers will be sent there by SQRP. The National Board of Health and Welfare creates the consecutive number key and connects ordered data with own registry data (the Patient registry and the Pharmaceutical registry). The National Board of Health and Welfare will then send a data order to the remaining registries (the Swedish Social Insurance Agency's registry, Statistics Sweden, and the Population education registry) and encoded data will be sent to the principal investigator to be stored in Dalarna University's secured server.

Intervention fidelity

The following measures have been and will be taken to increase intervention fidelity: A systematical intervention development with a clarified theoretical base explaining suggested mechanisms has been undertaken throughout the development process. [29]Healthcare staff at the IPRP units will be provided with comprehensive written information (easily accessed online) that includes step-by-step instructions on how to initiate and deliver the intervention while maintaining a high level of integrity. Before the study starts, all participating healthcare staff at the IPRP units will take part in a standardized provider training session online. Also, recurring web-based meeting opportunities will be provided, where IPRP-team members will be encouraged to discuss experienced or perceived difficulties, and a questionnaire will be sent out after the study period with the aim of assessing treatment fidelity (treatment integrity and

treatment differentiation) by gathering data on how treatment was delivered (manner *versus* treatment manual, intervention's alignment to intended theoretical base). This will allow results to be interpreted and will facilitate practical implementation.[70 71] During the on-going study period, researchers will be automatically notified of non-wear time (Fitbit Versa 2) and any absence of patient reports in PATRON. In these cases, researchers will contact the relevant participant via email or telephone to ask if they need help or support. If a participant decides to discontinue the trial, he or she will be asked if they are willing to grant permission for the collected data up to that point to be used in the trial.

Statistical methods

A statistical analysis plan (SAP) will expand on statistical principles, statistical analyses, the planned handling of missing data, possible additional analyses (subgroups etc.) and interim analyses. In both the pilot study and the R-RCT, descriptive statistical analyses will be performed to provide transparent reporting of characteristics of both participants and participating IPRP units. In addition, IPRP units will be prompted to register the number of patients they ask to participate, those excluded based on eligibility criteria, and those who decline participation. Analyses of pilot data (ratings of key feasibility outcomes) made by IPRP-teams on a four-point Likert scale (i.e.1= strongly disagree, 2= disagree, 3= agree, 4= strongly agree) will be calculated as proportions in four categories for each item. Ratings ≥3 will be considered as acceptable feasibility. Analyses of primary and secondary outcomes in main trial will be performed based on PATRON data and registry data. The clinical effectiveness of eVIS will be analyzed for each outcome using multivariate statistical and repeated measures analyses as a preliminary plan. Both the intention-to-treat and the per-protocol sample will be analyzed, but the intention-to-treat analysis will be considered as the primary analysis. All p-values will be presented. If a p-value is ≤0.05, the null hypothesis will be rejected and eVIS will be considered effective according to the outlined hypothesis. To perform cost-effectiveness calculations, data on health-related quality of life measured by EQ-5D will be retrieved from SQRP. EQ-5D is the standard instrument used to evaluate health costs and cost effectiveness. Calculations of quality-adjusted life-years (QALYs) will be performed by multiplying health-state utility (measured using the EQ-5D Index score) by time spent in this specific health state.[72 73] In addition, calculations of the incremental cost effectiveness ratio (ICER) will be made as the difference in the cost of two interventions divided by their affect.[74]

Data monitoring

Trial data will be monitored and regularly assessed for integrity and errors. All data monitoring will be performed completely independently from sponsors and competing interests. An independent data monitoring committee (DMC) will be appointed to critically review data safety in the trial. Veronica Sjöberg (VS) will be responsible for the monitoring of all data collected in the pilot study. A data management plan (DMP) will be outlined by the first author (VS) and implemented by the principal investigator (LV) to ensure sound data structure (folder structure, file naming, organization), and data storing.

DISCUSSION

This article describes a protocol for a R-RCT trial of a novel e-Health intervention. The trial will contribute to establish evidence for the effectiveness of individualized physical activity and exercise among patients living with chronic pain and participating in IPRP. The methodology and feasibility of the trial will be evaluated in an early phase by a pilot study, which will contribute to optimized robustness of the subsequent R-RCT-trial and enable further refinement of the intervention. Despite many efforts have been taken to develop health promoting interventions for this patient group, it is rare that such interventions are systematically developed and includes both objective and patient reported outcomes. The eVIS-intervention is developed according to MRC´s framework for development and evaluation of complex interventions.[29] It consists of both objectively measured physical activity level (steps/day), and patients own reports on pain intensity, interference on daily activities and individual daily activity goal, all joint in the web application named PATRON. This enables known facilitating mechanisms for behavior change (e.g., as self-monitoring etc.)[32] whilst including several core outcome domains.[34 75] The agile development process has enabled continuous evaluation and improvement of the intervention based on data provided from patients, clinicians, and researchers in different fields. Objectively measured constructs of physical activity by Fitbit devices have been criticized due to lack of accuracy of measurements of time spent in moderate to vigorous physical activity (MVPA) where various devices overestimate the measurement[76]. Preceding this study, our research group performed an evaluation of Fitbit Versa´s criterion validity of measuring energy expenditure, heart rate and step count among patients living with chronic pain. Results confirmed previous study results in adjacent patient groups reporting that

Fitbit Versa systematically overestimated energy expenditure, however, measurements of step count both in laboratory and in free-living setting were valid.[33]

In this trial participants will be recruited at IPRP units nationally distributed. All units adopt to core IPRP content regarding modalities, but it is well-known that both duration and intensity greatly vary which may limit generalization of the results.[25] To achieve maximum external validity, we will collect data on the specific characteristics of all participating units and include this in the final analyses. Unknown engagement in other out-patient treatments under study period, may be a potential source of bias, though data on in-patient engagement will be known through registry data from the Patient registry. Non-adherence to daily self-report in PATRON can be expected and may differ between intervention- and control group (differential missing). Measures will be taken to optimize adherence in both groups such as regular auditing of registrations in PATRON followed by personal emails with encouragement to follow protocol. To minimize the risk of contamination between groups, and to ensure that the study will be carried out in compliance with the study protocol, all participating staff at the IPRP-units will participate in a study-specific course including sessions regarding Good Clinical Practice prior entering the trial. Results generated from the pilot study and the subsequent effectiveness trial will inform pain management field with new knowledge on eVIS´s potential to increase pain rehabilitation program´s effectiveness by individualized physical activity levels among patients living with chronic pain.

Harms and adverse events

Participating patients and healthcare staff at the participating IPRP units will be encouraged to report any adverse events such as unexpected side effects or symptom deterioration,[77] which will also be reported to the Swedish Ethical Board Review.

Ethics and dissemination

The trial is prospectively registered in ClinicalTrials.gov (trial registration number NCT05009459) and was approved by the Swedish Ethics Review Board in May 2021 (Dnr 2021/02109). The trial will be conducted in compliance to the Helsinki Declaration.[79] Important protocol modifications will be communicated to the Swedish Ethics Review Board as well as to all participating IPRP units and participants. To protect confidentiality, all data will be coded

by an individual code, and the encryption key will be stored separately. Data will be stored at an intended project server at Dalarna University, which is secured by regular backups. No unauthorized persons will have access to data, e.g., data will only be accessible by researchers in the trial after approval from the principal investigator. Results of the pilot study and the main trial will be submitted for publication in peer-reviewed journals and communicated in national and international research networks, as well as in relevant clinical settings, including patient associations.

Author contribution statement

LV and BÄ are responsible for the conception of the trial. LV is the principal investigator and is involved in all methodological decisions. VS, ET, AM, JW, RLM, BÄ, MH, MB, and LV all contributed to study design and were all involved in the development processes (the evaluation of criterion validity of the wrist-worn activity tracker and the evaluations of the content validity and clinical feasibility) of the intervention. RLM performed the preliminary power and sample size calculations and was involved in all associated decisions. VS wrote the first draft of the manuscript, was responsible for revising the manuscript's intellectual content based on all co-authors conscientious input and conducted manuscript revision according to peer-reviewer´s comments. All authors read and approved the final version of the manuscript. For this article, no ghost authors, guest authors, or professional writers have or will be used. Author eligibility is and will be based upon the ICMJE Recommendations for the Conduct, Reporting, Editing, and Publication of Scholarly work in Medical Journals.

Trial status

Recruitment of participants was initiated late October 2021 and the trial is planned to be completed on 31 December 2024.

Funding

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number). The funders had no role in study design and will have no role in any part of the implementation of the study or the reporting of its results.

Competing interests

None declared.

Access to data

This is a protocol describing a trial design. All authors will have access to the final trial dataset.

Supplementary files:

- Completed SPIRIT 2013 Checklist
- Patient consent form (in Swedish)

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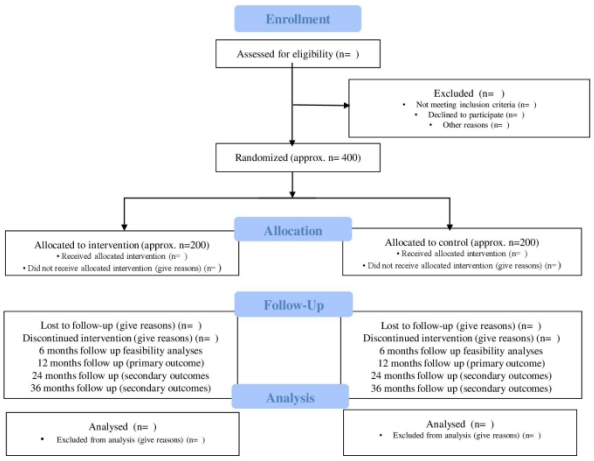

Figure 1. CONSORT 2010 Flow diagram chart of study design and enrollment.

338x190mm (200 x 200 DPI)

Figure 2. Schematic illustration of the eVIS-intervention´s three elements: i) the data collection element of physical activity level (steps/day), patient-report of pain interference on daily activities, pain intensity and pharmacological consumption, ii) the visualisation element of collected data in different graphs and compilations of data, and iii) the communication element.

338x190mm (300 x 300 DPI)

HÖGSKOLAN DALARNA

Deltagarkod _____

Samtycke till att delta i projektet

Jag har fått muntlig och skriftlig informationen om projektet och har haft möjlighet att ställa frågor. Jag får behålla den skriftliga informationen.

☐ Jag samtycker till att delta i projektet **Utvärdering av eVISualisering av fysisk aktivitet och smärta (eVIS) som tillägg till multimodal smärtrehabilitering**

☐ Jag samtycker till att Socialstyrelsen sammanför data från de i forskningspersonsinformationen nämnda svenska register med den data som samlas in via forskningsprojektet (PATRON, aktivitetsklockan och hälsoenkäten RAND36)

☐ Jag samtycker till att uppgifter om mig behandlas på det sätt som beskrivs i forskningspersonsinformationen.

Ort och datum **Underskrift**

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SPIRIT 2013 Checklist: Recommended items to address in a clinical trial protocol and related documents*

Section/ item	Item No	Description	Page number in Main document (clean copy)
Administrative information			
Title	1	Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym	1
Trial registration	2a	Trial identifier and registry name. If not yet registered, name of intended registry	2, 21
	2b	All items from the World Health Organization Trial Registration Data Set	NA
Protocol version	3	Date and version identifier	2
Funding	4	Sources and types of financial, material, and other support	22
Roles and responsibilities	5a	Names, affiliations, and roles of protocol contributors	1, 22
	5b	Name and contact information for the trial sponsor	22 (not contact info)
	5c	Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities	22
	5d	Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data management team, and other individuals or groups overseeing the trial, if applicable (see Item 21a for data monitoring committee)	19
Introduction			

Background and rationale	6a	Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention	4-6
	6b	Explanation for choice of comparators	16-17
Objectives	7	Specific objectives or hypotheses	5-6, 16-17
Trial design	8	Description of trial design including type of trial (eg, parallel group, crossover, factorial, single group), allocation ratio, and framework (eg, superiority, equivalence, noninferiority, exploratory)	6
Methods: Participants, interventions, and outcomes			
Study setting	9	Description of study settings (eg, community clinic, academic hospital) and list of countries where data will be collected. Reference to where list of study sites can be obtained	6
Eligibility criteria	10	Inclusion and exclusion criteria for participants. If applicable, eligibility criteria for study centres and individuals who will perform the interventions (eg, surgeons, psychotherapists)	6-7
Interventions	11a	Interventions for each group with sufficient detail to allow replication, including how and when they will be administered	7-9
	11b	Criteria for discontinuing or modifying allocated interventions for a given trial participant (eg, drug dose change in response to harms, participant request, or improving/worsening disease)	18-19
	11c	Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return, laboratory tests)	18-19
	11d	Relevant concomitant care and interventions that are permitted or prohibited during the trial	7-8
Outcomes	12	Primary, secondary, and other outcomes, including the specific measurement variable (eg, systolic blood pressure), analysis metric (eg, change from baseline, final value, time to event), method of aggregation (eg, median, proportion), and time point for each outcome. Explanation of the clinical relevance of chosen efficacy and harm outcomes is strongly recommended	9-16 Table 1 Table 2

Participant timeline	13	Time schedule of enrolment, interventions (including any run-ins and washouts), assessments, and visits for participants. A schematic diagram is highly recommended (see Figure)	Table 1 Figure 1
Sample size	14	Estimated number of participants needed to achieve study objectives and how it was determined, including clinical and statistical assumptions supporting any sample size calculations	16-17
Recruitment	15	Strategies for achieving adequate participant enrolment to reach target sample size	7, 18-19
Methods: Assignment of interventions (for controlled trials)			
Allocation:			15
Sequence generation	16 a	Method of generating the allocation sequence (eg, computer-generated random numbers), and list of any factors for stratification. To reduce predictability of a random sequence, details of any planned restriction (eg, blocking) should be provided in a separate document that is unavailable to those who enrol participants or assign interventions	17-18
Allocation concealment mechanism	16 b	Mechanism of implementing the allocation sequence (eg, central telephone; sequentially numbered, opaque, sealed envelopes), describing any steps to conceal the sequence until interventions are assigned	17
Implementation	16 c	Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions	17
Blinding (masking)	17 a	Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how	17
	17 b	If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during the trial	NA
Methods: Data collection, management, and analysis			

Data collection methods	18a	Plans for assessment and collection of outcome, baseline, and other trial data, including any related processes to promote data quality (eg, duplicate measurements, training of assessors) and a description of study instruments (eg, questionnaires, laboratory tests) along with their reliability and validity, if known. Reference to where data collection forms can be found, if not in the protocol	Table 1 9-16
	18b	Plans to promote participant retention and complete follow-up, including list of any outcome data to be collected for participants who discontinue or deviate from intervention protocols	18-19
Data management	19	Plans for data entry, coding, security, and storage, including any related processes to promote data quality (eg, double data entry; range checks for data values). Reference to where details of data management procedures can be found, if not in the protocol	20
Statistical methods	20a	Statistical methods for analysing primary and secondary outcomes. Reference to where other details of the statistical analysis plan can be found, if not in the protocol	19
	20b	Methods for any additional analyses (eg, subgroup and adjusted analyses)	19
	20c	Definition of analysis population relating to protocol non-adherence (eg, as randomised analysis), and any statistical methods to handle missing data (eg, multiple imputation)	19
Methods: Monitoring			
Data monitoring	21a	Composition of data monitoring committee (DMC); summary of its role and reporting structure; statement of whether it is independent from the sponsor and competing interests; and reference to where further details about its charter can be found, if not in the protocol. Alternatively, an explanation of why a DMC is not needed	20
	21b	Description of any interim analyses and stopping guidelines, including who will have access to these interim results and make the final decision to terminate the trial	19
Harms	22	Plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial conduct	21

Auditing	23	Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor	20
Ethics and dissemination			
Research ethics approval	24	Plans for seeking research ethics committee/institutional review board (REC/IRB) approval	18-19
Protocol amendments	25	Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators, REC/IRBs, trial participants, trial registries, journals, regulators)	21-22
Consent or assent	26 a	Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32)	7
	26 b	Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable	NA
Confidentiality	27	How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial	18-19
Declaration of interests	28	Financial and other competing interests for principal investigators for the overall trial and each study site	20
Access to data	29	Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators	20
Ancillary and post-trial care	30	Provisions, if any, for ancillary and post-trial care, and for compensation to those who suffer harm from trial participation	No
Dissemination policy	31 a	Plans for investigators and sponsor to communicate trial results to participants, healthcare professionals, the public, and other relevant groups (eg, via publication, reporting in results databases, or other data sharing arrangements), including any publication restrictions	21-22
	31 b	Authorship eligibility guidelines and any intended use of professional writers	22
	31 c	Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code	23

Appendices			
Informed consent materials	32	Model consent form and other related documentation given to participants and authorised surrogates	See supplementary files [In Swedish]
Biological specimens	33	Plans for collection, laboratory evaluation, and storage of biological specimens for genetic or molecular analysis in the current trial and for future use in ancillary studies, if applicable	NA

BMJ Open

Effectiveness of the eVISualisation of physical activity and pain intervention (eVIS) in Swedish Interdisciplinary Pain Rehabilitation Programs: study protocol for a registry-based randomized controlled clinical trial

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Effectiveness of the eVISualisation of physical activity and pain intervention (eVIS) in Swedish Interdisciplinary Pain Rehabilitation Programs: study protocol for a registry-based randomized controlled clinical trial.

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Keywords: Chronic pain, Individualized physical activity level, Interdisciplinary Pain Rehabilitation Programs, Pilot study, Physical health, Registry-based randomized clinical trial, Study protocol.

ABSTRACT

Introduction: Living with chronic pain often involves negative consequences. Interdisciplinary Pain Rehabilitation Programs (IPRPs) is considered superior to single-treatment measures in patients with chronic pain. Despite this, effects emerge sub-optimal and more than 20% of patients deteriorate in patient reported physical health outcomes after IPRP. A novel e-Health intervention, eVISualisation of physical activity and pain (eVIS), was systematically developed to facilitate individualization of physical activity levels. By adding elements of data collection, visualization, and communication of objectively measured physical activity and patient-reported outcomes (pain intensity, interference of pain, pharmaceutical consumption) to existing treatment modalities in IPRP, the IPRP team acquires prerequisites to adapt advice and physical activity prescriptions and to evaluate set activity goals. The overall aim is two-fold. First, the aim is to evaluate the feasibility of the subsequent registry-based randomized controlled clinical trial (R-RCT). Secondly, the aim is to prospectively evaluate the effectiveness of the eVIS-intervention as a supplement to IPRP on our defined primary (physical health) and secondary outcomes.

Methods and analysis: In the R-RCT, recruitment of 400 patients with chronic pain will be performed at 15 IPRP units . A random allocation to either IPRP + eVIS or to control group that will receive IPRP only will be performed. . Data from the initial 30 participants completing the study period (6 months) will be included in a pilot study where key feasibility outcomes (recruitment, randomization, , implementation, , treatment integrity, data collection procedure, preliminary outcome measures) will be evaluated. Outcome variables will be extracted from PATRON and from six national registries. Multivariate statistics and repeated measures analyses will be performed. Quality Adjusted Life Years (QALYs) and Incremental Cost Effectiveness Ratio (ICER) will be calculated for cost effectiveness evaluation.

Ethics/dissemination: The Swedish Ethics Review Board granted approval (Dnr 2021/02109). Results will be disseminated through peer-review journals.

Trial registration number: NCT05009459.

Protocol version: 1

Strengths and limitations of the study

- A proceeding pilot study will enable improvements of design and feasibility of a subsequent R-RCT
- The eVIS-intervention has been developed, evaluated, and improved, based on data provided from patients, clinicians, and researchers in different fields.
- The intervention targets physical activity modalities in IPRP and is designed to enable a more individualized IPRP treatment.
- The intervention is based on objectively measured physical activity levels, patient-reported clinical outcomes, and mechanisms that facilitate behavior change, in accordance with current guidelines that are provided by authorities in the chronic pain management field.
- The nature of the intervention precludes blinding of patients and the IPRP team.

INTRODUCTION

Chronic musculoskeletal pain (>3 months), including neck/shoulder/back pain or widespread pain, is a major global health and socioeconomic burden.[1 2] Living with chronic pain is often associated with reduced levels of wellbeing and the health-related quality of life of this group has been reported to be among the lowest of any medical condition.[3] To date, physical activity (i.e. any bodily movement that requires energy expenditure) and exercise (i.e. structured and planned physical activity aimed to increase fitness)[4] have been shown to prevent and/or treat several of our noncommunicable diseases including chronic pain,[5] due to their beneficial effects on general health, pain intensity, physical and psychological functioning, and health-related quality of life.[5-8] Despite the growing evidence of health benefits related to physical activity, participation and adherence to physical activity recommendations, such as WHO´s physical activity guidelines, are often low in patients living with chronic pain.[9-12] This may partly be explained by the indicated association between high pain scores and low patient-reported activity levels among patients with chronic pain and/or the documented reports of the negative impact of depression on physical activity levels.[13] In addition, it is well known that behavior change is difficult, and that each individual's own participation is essential.[14] It has been shown that behavior change towards a beneficial physical activity level may be facilitated by individuals self-monitoring their physical activity.[15] The use of objective measures increases the likelihood of the effectiveness of interventions designed to promote physical activity.[15] By adding goal setting, feedback, and a focus on achieved goals, effectiveness can be further improved.[15-18]

Interdisciplinary pain rehabilitation programs (described as a subset of Interdisciplinary Treatment), is defined as "multimodal treatment provided by a multidisciplinary team (at least 3 professions), collaborating in assessment and treatment using a shared biopsychosocial model and goals"[19]. The IPRP approach adopts the principles of behavioral therapy and incorporates besides physical activity and exercise, also psychological measures, pharmaceutical treatment and patient education.[20] Physical activity and exercise are central measures in IPRPs as it targets the physical deconditioning by improving levels of physical activity, and also reduces pain severity and improved physical function and quality of life, without causing any severe adverse events.[5] Interdisciplinary pain rehabilitation programs are considered to be superior to single-treatment measures (e.g., physical treatments, education interventions, surgery, etc.) for patients with chronic pain supporting positive effects on pain intensity and activity disability.[20 21]

However, IPRP effectiveness is only slightly better and in the majority of cases only a small effect is seen.[21-25] In addition, up to 25% of patients report deterioration in physical health after completing IPRP and after 12 months follow up, regardless of duration of IPRP.[20 25 26] Sustainable treatment affects seem to vary according to patient clinical features at baseline, such as poor employment status, high pain levels, and low functioning, all of which predict low physical health at follow-up.[23 27] Many efforts have been made to find effective interventions that improve the health of chronic pain patients. To facilitate individualized physical activity levels within the Swedish IPRP setting, an eVISualisation (eVIS) of physical activity and pain intervention has been systematically developed according to the Medical Research Council´s recently updated framework for development and evaluation of complex interventions. [28 29] In accordance with the framework, the eVIS-interventions was designed and planned in close collaboration with stakeholders. eVIS is designed to target facilitating mechanisms for behavior change, such as outcome expectations, self-monitoring, self-evaluation, and self-efficacy,[30-32] which are theoretically framed by the Social Cognitive Theory.[32] In eVIS, objectively measured physical activity tracking using a wrist-worn activity tracker[33] (Fitbit Versa 2) is combined with a daily activity goal (steps/day) and daily patient reports of known important clinical outcome assessments: pain intensity and its interference on daily activities[34-38] and pharmaceutical consumption. Data is collected and visualized in a purpose-developed web application, Pain And TRaining ON-line (PATRON), which can be used by the patient and the IPRP team to follow and adjust individual physical activity levels. Despite interventions of this kind having highly promising potential to relive pain and improve disability in this patient group,[39]interventions are rarely systematically developed and validated specifically for their target patient group, leaving crucial information of feasibility and true effectiveness unknown. Therefore, the overall aim of this study is two-fold. First, the aim is to evaluate the feasibility (recruitment capability, eligibility screening procedure, randomization, implementation process, response rate, compliance rate, changes in primary- and secondary outcomes from start to end of study period, differences between treatment groups in primary outcome) of a subsequent registry-based randomized controlled clinical trial (R-RCT) within the IPRP setting in order to gain knowledge of population variation, increase robustness and to avoid underpower. [40-43] Secondly, the aim is to prospecively evaluate the effectiveness of the eVIS-intervention as a supplement to IPRP on our defined primary (physical health) and secondary outcomes, 12 months after completed IPRP compared to IPRP as usually provided. In addition, the aim is to evaluate the cost effectiveness of eVIS supplementing IPRP at 12 and 36 months follow up

after completed IPRP, and to prospectively evaluate differences in opioid consumtion at start of IPRP compared to six months after completed IPRP.

4240-43In this trial, the UK National Institute for Health Research's (NIHR) definitions of the terms *pilot study* (i.e., "a smaller version of the main study") and *feasibility study* (i.e., "evaluation of pieces of research done before the main study") are applied.[44] The aim of this paper is to transparently clarify and report on study designs, aims, outcome assessments, and procedures for a planned R-RCT (including an randomized pilot study) which prospectively will evaluate clinical effectiveness and cost effectiveness of eVIS as a supplement to IPRPs for patients living with chronic pain compared to standard IPRPs.

METHODS AND ANALYSIS

Trial design and setting

This two-armed pragmatic multi-site R-RCT will be conducted in specialized and primary IPRPs in Sweden, and include approximately 400 (n=200, n=200) patients (number will be definitively determined after the pilot study is finalized) with chronic musculoskeletal non-malignant pain. As indicated, an randomized controlled pilot study (n=15, n=15) will be incorporated as the initial phase of the main trial in order to evaluate the intervention´s methodology and design.[29 41 45] This trial will comply with the Consolidated Standards of Reporting Trials (CONSORT)[40] and with the Standard Protocol Items: Recommendations for Interventional Trials (SPIRIT)[46]. A completed SPIRIT 2013 Checklist can be found in the additional files. See Figure 1 for study design and enrollment details.

Insert Figure 1 here.

Figure 1. CONSORT 2010 Flow diagram chart of study design and enrollment.

Eligibility criteria

In this trial, the patient-related, care process and caregiver-related inclusion criteria for receiving Swedish IPRP will be applied, as patients entering the trial must be accepted for IPRP.

Principal IPRP inclusion criteria are patients in working age with persistent or intermittent pain lasting ≥3 months with pain affecting daily activities to a large extent, completed systematic assessment (including screening for psychosocial risk factors and differential diagnosis) and non-pharmacological optimization. Inclusion criteria for Swedish IPRPs is outlined in detail elsewhere.[47] Due to the nature of the intervention, patients must be able to hear, see, and comprehend spoken and written Swedish, and have daily access to a computer, smartphone, or tablet. Patients who need to use a walking aid indoors will be excluded.

Recruitment

Interdisciplinary Pain Rehabilitation Units

Approximately 15 IPRP units in primary and specialized care in Sweden will be included in the trial. IPRP units reporting to the Swedish National Quality Registry for Pain Rehabilitation (SQRP) have been approached by email with study information (aim, rationale, methods etc.) and an invitation to participate in one of several online digital information meetings that will further present the study (initated August 2021). Study representatives will approach healthcare staff at potential IPRP units by telephone or email to formally offer participation. Operation managers at each unit will be asked to provide written consent by e-mail.

Participants

In order to give potential participants additional time to consider taking part in the trial before they visit the IPRP unit, healthcare staff at the units will be encouraged to provide a general information sheet about the trial in the summon to the IPRP assessment. Members of IPRP teams (primarily physiotherapists but also occupational therapists, physicians, nurses etc.) will identify potential participants selected for IPRP based on outlined criteria and provide them with verbal and written details of the study (information sheets and the project's web address). All participants will provide written informed consent (see supplementary file) prior to joining the study, which will be managed by the IPRP team. Detailed verbal and written information about the voluntary nature of participation and the indisputable right to discontinue participation in the trial at any time will be provided. Detailed checklists and forms will support these procedures, and these will be easily accessible on the project web site.

Intervention

Participation in the intervention group involves regular IPRP supplemented with eVIS for a coherent time span of six months, IPRP time included. As the duration and intensity of IPRPs greatly vary from a couple of weeks up to four months[25], a six month study period ensures time of independent use of eVIS after completed IPRP. Participants are not prohibited to take part of other health care during study period. Interdisciplinary pain rehabilitation programs vary in interventions, duration, composition, intensity[24 25] and can be performed either individually or in group format. In this trial, participation in a IPRP will be supplemented by eVIS, a health promoting intervention containing three elements designed to facilitate individualized physical activity level (Figure 2).

The data collection element

Outcome assessments of physical activity level (steps/day) will be objectively collected by a wrist-worn activity tracker, Fitbit Versa 2. This device has been population-specifically validated and the measurement of step rate is indicated as valid for measurement in this population. [33] Data on patient´s physical activity level quantified as steps/day, will be automatically synchronized to the web application PATRON where pain intensity (0-10), [48] interference of pain on daily activities (0-10),[49] pharmacological consumption (name, dose, number, and form), and (optional) free-text comments will be reported by the patient daily. The web application can be accessed via computer, smartphone, or tablet. A daily activity goal (steps/day) is formulated by the patient in close collaboration with the IPRP team and revised accordingly. The daily activity goal in eVIS is individually set based on patient's individual prerequisites and re-evaluated regularly as part of the communication element (described below). In the process of setting a daily activity goal, the IPRP team are encouraged to consider international guidelines of step rate as a quantification of beneficial physical activity levels [50] as well as patient´s personal barriers and resources to perform physical activity. The data collection element is designed to target facilitating mechanisms for behavior change, such as outcome expectations, self-monitoring, self-evaluation, and self-efficacy.[30-32]

The visualisation element

Objectively measured physical activity levels, patient-report on pain intensity and interference of pain on daily activity are graphically visualized separately or alongside each other, in relation to the daily activity goal. Three different graphs (1/7/28 days) are available. The visualisation element provides additional prerequisites for increased knowledge acquisition, self-monitoring,

and self-evaluation as data is visualized over time and in relation to each other and to the individual daily activity goal in order to improve patient self-efficacy.

The communication element

The graphs in the visualisation element together with compiled data on pharmacological consumption will provide a novel decision basis for the patient and the IPRP team. This addition to existing treatment modalities traditionally provided in Swedish IPRP (e.g. physical activity, cardio training, weight training, mobility training, stability training, motivating conversation education, advice etc.). enables prerequisites for the IPRP team to integrate behavioral changing techniques (e.g. reinforcement, knowledge acquisition, self-monitoring, self-efficacy) into existing treatment options. By such integration, knowledge of patient's personal barriers and resources in factors important in pain rehabilitation may be visualized and if necessary, assessed. The IPRP team as well as the patients are encouraged to explore the visualisation element of eVIS at each visit at the IPRP unit. This in order to utilize data into the treatment by adjusting advise or prescriptions.

Insert Figure 2 here

Figure 2. Schematic illustration of the eVIS-intervention´s three elements: i) the data collection element of physical activity level (steps/day), patient-reports of interference of pain on daily activities, pain intensity and pharmacological consumption, ii) the visualisation element of collected data in different graphs and compilations of data, and iii) the communication element.

Control

Participation in the control group involves taking part in regular IPRP plus making daily ratings of pain intensity, interference of pain on daily activities, and pharmaceutical consumption (corresponding as in intervention group) in PATRON for six months, including the time that the IPRP is being carried out. The control group will not use the wrist-worn activity tracker as this may affect their physical activity behavior [51]. Nor will they have access to PATRON's visualizing or communication features.

Patient and Public Involvement Statement

In an early developing phase, stakeholders (patients living with chronic pain, representatives from patient organizations and clinicians experienced in pain rehabilitation) were invited to contribute to the intervention development. In this phase, the web application PATRON and eVIS was presented and carefully discussed with stakeholders as well as with web application developers and researchers. Several needs for improvement were identified, such as a need of an addition of pharmaceutical report function, designated web pages and graphical changes in planned interfaces.

Outcome assessments

According to the Initiative on Methods, Measurement, and Pain Assessment in Clinical Trials (IMMPACT), physical health, emotional health, and pain intensity are three of six identified core outcome domains that should be considered when designing research studies aiming to evaluate effectiveness of chronic pain treatments. [35-37] It is specifically recommended that a health survey such as RAND-36 should be incorporated into treatment as a clinical outcome assessment of physical health in clinical trials.[36 37] Outcome assessments for evaluating feasibility will be performed on data from the IPRP baseline and after the study period is completed (six months) for the first 30 participants (n=15 +, n=15). In the main trial, assessments of effectiveness will be performed on data from the IPRP baseline and from the 12-month follow-up. The cost effectiveness assessments will be based on data from the IPRP baseline, from the 12-month IPRP follow-up and again 24 and 36 months after the IPRP is completed. A detailed overview of outcome assessments can be found in Table 1.

Table 1. Overview of study period, measurement time points, outcome assessments (***bold and italics)***, instruments, and data sources (*italics*).

	Study period						
	Enrolment	Allocation	Post-allocation				
	-t_1	**0**	**Baseline**	**t1**	**t2**	**t3**	**t4**
Enrolment	X						
Written and verbal study information	X						
Eligibility screen	X						
Informed consent	X						
Allocation/randomization		X					
Interventions							
Intervention, eVIS (6 months)			X	X			
Control (6 months)			X	X			
Outcome assessments							
Personal characteristics							
Sex, age, country of origin, family composition, beliefs of restored health (*SQRP, SS*)			X				
Disposable-, earned- and net income (*SS*)			X		X	X	X
Education level and education orientation (*SPR, ITR*)			X		X	X	X
Diagnosis (NPR			X		X	X	X
Volume and reason for inpatient care (*NPR*)			X		X	X	X
Pain characteristics							
Pain intensity (last 7 days), NRS (*SQRP-PC and SC*)			X		X		
Pain intensity (today), NRS (*PATRON*)			X	X			
Pain type, location, duration (*SQRP-PC and SC)*			X				
Pain interference (*PATRON*)			X				
Multidimensional measures							
Physical health, RAND-36 PCS health survey (*PATRON*)			X	X	X	X	X
Physical health, RAND-36 PCS health survey (*SQRP-SC only*)			X		X		
Emotional health, RAND-36 MCS health survey (*PATRON*)			X	X	X	X	X
Emotional health, RAND-36 MCS health survey (*SQRP- SC only*)			X		X		

Overall emotional distress, HAD(S) (*SQRP-PC and SC*)	X		X		
Pain catastrophizing, PCS (*SQRP-PC and SC*)	X		X		
Psychosocial consequences, MPI-S (*SQRP-PC and SC*)	X		X		
Pain acceptance, CPAQ-8 (*SQRP-PC only*)	X		X		
Perceived life Satisfaction, LiSat (*SQRP-PC and SC*)	X		X		
Functional level, FRI (*SQRP-SC only*)	X		X		
Physical activity					
Objective measures of steps per day (*Fitbit Versa 2*)	X	X			
Patient-reported measures (*SQRP- PC and SC*)	X		X		
Work					
Return to work (partially or full time) every month (*SSIA*)			X	X	X
Number of days with sick benefit during study period (*SSIA*)			X	X	X
Number of days in work before new sick leave during study period (*SSIA*)			X	X	X
Length of total sick leave during study period (*SSIA*)			X	X	X
Perceived work ability, WAI (*SQRP-PC and SC*)	X		X		
Sleep quality, ISI *(SQRP-SC only)*	X		X		
Pharmaceutical consumption					
Name, dose, size, prize of prescribed pharmaceuticals (*SPDR, PATRON [not size, prize]*)			X	X	X
Prescribed pharmaceuticals collected from pharmacies, (*SPDR*)			X	X	X
Cost of prescribed pharmaceuticals included in benefit program (*SPDR*)			X	X	X
Health care consumption *(NPR)*			X	X	X
Feasibility outcomes, *Questionnaire*		X			
Treatment integrity, *Questionnaire*		X	X		

Abbreviations: -t^1 = pre recruitment period, t^1 = completed study period (6 months), t^2 = follow-up 12 months after completed Interdisciplinary Pain Rehabilitation Program (IPRP), t^3 = 24 months after completed IPRP, t^4 = 36 months after completed IPRP, eVIS = eVISualisation of physical activity and pain intervention, SQRP = the Swedish national quality registry for pain rehabilitation, SQRP-PC = , the Swedish national quality registry for pain rehabilitation primary care, SQRP-SC = the Swedish national quality registry for pain rehabilitation specialized care, NRS = Numeric Rating Scale, PATRON = Pain and training online (web application), RAND-36 PCS = physical health domain , RAND-36 MCS = mental health domain, HAD(S) = Hospital Anxiety and Depression Scale, PCA = Pain Catastrophizing Scale, MPI-S = Multidimensional Pain Inventory -Swedish Version, CPAQ-8 = The Chronic Pain and Acceptance Questionnaire, LiSat = Life Satisfaction Scale, WAI = Work Ability Index, FRI = Functional rating scale, ISI = Insomnia Severity Index, SSIA = the Swedish Social Insurance Agency's registry, NPR = the National Patient Register, SPDR = the Swedish Prescribed Drug Register, SS = Statistics Sweden, SPR = the Swedish Population Register.

Feasibility outcomes, pilot study

The trial will be initiated as a full-scale registry-based randomized controlled pilot study. In this initial step, feasibility will be evaluated from data provided from the first 30 participants completing the study period and in the following key areas: the unit´s recruitment capabilities, the randomization process, implementation process, participant response to intervention which is outlined in Table 2. In addition, the data collection procedure and the preliminary outcome measures (standardized effect size, sample size estimation with Cohen's *d*, characteristics [mean, SD]) in main trial will be evaluated.[41 45] In addition to feasibility outcomes, characteristics of the IPRP units will be collected

Table 2. Overview of key feasibility outcomes in pilot study.

Key feasibility outcomes
Recruitment capability
Volume of total eligible patients
Number recruited/week
Eligibility screening procedure
Proportion accepted/declined
Personal characteristics of accepted and declined participants
Pain characteristics of accepted and declined participants
Procedure of collecting consent
Randomization process
Delivery envelopes
Storage of envelopes
Procedure of opening envelopes
Patients´ reaction to allocation
Implementation process
Response rate RAND-36 PCS
Compliance rate (use of Fitbit Versa 2, intervention group only)
Compliance rate (patient reported outcomes in PATRON)
Treatment integrity
Reported adverse events
Data collection procedure
Access to PATRON data
Access to registry data
Access to RAND-36 data
Preliminary outcome measures
Characteristics, mean (SD)
Missing data
Changes from baseline to finalized study period

Abbreviations: RAND-36 PCS = physical health domain in RAND-36, PATRON = Pain and training online (web application).

Primary outcome, main trial

The R-RCT will prospectively evaluate the *clinical effectiveness* of eVIS supplementing IPRPs regarding improvements in our primary outcome assessment *Physical health* collected by the

physical health domain in RAND-36 health survey[3 52] at the 12-month IPRP follow-up after completing the IPRP. The RAND-36 is, for this population, a valid health survey measuring health-related quality of life in two dimensions, physical health (PCS) and mental health (MCS), mediated by eight subscales.[52]

Secondary outcomes, main trial

In the main trial, secondary outcomes will be extracted from Fitbit Versa 2, PATRON and collapsed with data from six national registries (all listed below) at 12, 24, 36 months after the IPRP is completed.

Objectively measured secondary outcomes collected using Fitbit Versa 2

Objectively measured physical activity levels will be collected daily during the study period using a wrist-worn activity tracker (Fitbit Versa 2). The Fitbit device measures and estimates a range of physical activity outcomes such as number of steps, heart rate, energy expenditure, floors climbed, physical activity level, and sleep.[33 53] In this trial, participants' step count per day will automatically be synchronized to PATRON during the study period (six months). The use of steps per day is considered to be a valid quantification of physical activity levels and this is acknowledged by the Swedish Health Authority.[54]

Patient-reported secondary outcomes collected through PATRON

Data on physical and mental health collected by RAND-36 health survey will be collected through PATRON at 6, 12 and 24 months after IPRP. Pain intensity ("*rate your average pain during the last 24 hours*") will be measured daily using the Numeric Rating Scale (NRS, 0 = *no pain at all* to 10 = *pain as bad as it could be*), a 11-point Likert scale[48] incorporated in the web application PATRON. Pain interference on daily activities is a recommended outcome domain.[35] In PATRON, assessments of interference of pain on daily activities will be measured by the question "*rate how much your daily activities are affected by pain*" using an 11-point Likert Scale (0 = *not at all* to 10 = *to a very large extent*). This question in PATRON has been modified based on the Multidimensional Pain Inventory Swedish version and its items on pain interference,[49] and validated in our previous study (in manuscript). Data on daily pharmaceutical consumption will be collected in PATRON (name, dose, number, and form). Voluntary free text comments will supplement patient reporting by providing additional information regarding perceived mental and physical health (only in the intervention group).

Secondary outcomes collected through the Swedish national quality registry for pain rehabilitation

In Sweden, 90% of IPRP units routinely collect patient-reported data from standardized questionnaires and report to SQRP, a database initiated in 1998 that contains data from chronic non-malignant pain patients participating in IPRPs.[24 55] The registry consists of two parts; the primary care SQRP (SQRP-PC) and the specialized SQRP (SQRP-SC). The primary care SQRP is supplied with data from affiliated primary care IPRP units (n=42, reported data from 505 patients in 2020). The specialized care SQRP, receives data from affiliated specialized care IPRP units (n=45, reporting data from 7427 patients in 2020). Data in both registries are collected at baseline, when the IPRP is completed, and at 12-month follow-ups, the content of data collected in the registries differs somewhat. In this trial, registry data from both registries will be collected used to describe demographics such as age, sex, height, weight, education level, and work.[24 55] Participants partaking in an IPRP in SC will also routinely complete the RAND-36 health survey at baseline and at their 12-month follow-up after they have completed their program. Data on pain intensity ("*last 7 days*") (NRS 0-10)[48] will be retrieved from SQRP-PC and SQRP-SC alongside other pain characteristics including pain location (36 anatomical predefined areas, 18 on the left side, 18 on the right side), pain duration, and pain type (intermittent or continuous). Data on self-rated physical and mental health is collected by the RAND-36 health survey[3 52] in SQRP-SC and the EuroQol-5 dimensions (EQ-5D) collected routinely in SQRP-PC and SQRP-SC will be used. The EQ-5D is a standard instrument used in health economic evaluations and contains five items each with three ordered response categories, and a 0-100 index.[56]

Measures of self-rated physical activity is collected in SQRP-PC and SC using the National Board of Health and Welfare's three questions on physical activity (0 - >300 minutes/week), exercise (0 - >120 minutes/week), and sedentary behavior (0 – 15 hours/day).[57] and in SQRP-PC by the Godin-Shepard leisure-time physical activity questionnaire (number of times/week that strenuous/moderate/light exercise.[58] Data on overall emotional distress (0 – 3), pain catastrophizing (0 – 4), and psychosocial consequences (0 – 6) of living with pain are collected in SQRP-PC and SQRP-SC using the Hospital Anxiety and Depression Scale (HADS),[52 59] the Pain Catastrophizing Scale (PCS),[60] and the Multidimensional Pain Inventory Scale Swedish version (MPI-S, 0 – 6).[49] Level of pain acceptance (0 – 6) is collected in SQRP-PC using the Chronic Pain and Acceptance Questionnaire (CPAQ-8).[61] Perceived life satisfaction (1-6) is collected by the Life Satisfaction Scale (LiSat)[62] in both registries. Data on perceived work

ability (0 – 10) is collected by the Work Ability Index (WAI)[63] and functional levels (0 – 4) by the Functional Rating Scale (FRI)[64] is collected in SQRP-SC only. Data on patient-reported sleep quality (0 – 4) is collected by the Insomnia Severity Index (ISI)[65] in SQRP-SC.

Secondary outcomes collected through other national registries

Data will be collected from the Swedish Social Insurance Agency's registry on diagnosis, reasons for sick leave, type of financial compensation, number of sick days, and sickness benefit (days and hours) during the study period. In addition, data on days in work (partial or full time) per month in total before new sick leave period and length of total sick leave during the study period will be retrieved from the registry. Data will be retrieved from the National Patient Register on diagnosis and healthcare consumption (total number of days in care etc.). Retrieved data from the Swedish Prescribed Drug Register will provide information on prescribed pharmaceutical names, doses, sizes, and prices that have been collected from pharmacies, their costs, and whether the pharmaceutical is included in the subsidized pharmaceutical program. Data on disposable and earned income as well as net income will be retrieved from Statistics Sweden. In addition, demographic data such as sex, age, marital status, citizenship, education level, and number of children in the family will be collected. From the Population registry, data on education level and education orientation (focus) in addition to limited demographic data (sex, age) will be collected.

Sample size

A sample size for the pilot study of at least n=30 is considered sufficient for planned feasibility analyses since it will not involve hypothesis testing and sample size calculation *per se.*[43 66 67] For the main trial, a preliminary power calculation are based on assumptions from previous research reporting on proportions of patients that report a clinically meaningful difference of ≥3 points in the physical health domain in RAND-36, 12-months after completed IPRP. [25] The calculation was performed in R, using a calculation method for simple randomization and for independent observations. The preliminary power calculation allows a dropout rate of 20% and requires a total sample size of approximately n=400 to have an 80% power to detect a 15% difference (≥3p) between the groups in the outcome physical health. Physical health is measured by the RAND-36 health survey at the 12-month follow-up measurement point after the completion of the IPRP. The significance level is set to 0.05 and is two-tailed. The sample size calculation may be re-calculated after the pilot study is completed. In this trial, the null

hypothesis is that there will be no difference between the intervention group and the control group (<15% with ≥3 points improvement) with regard to proportional improvement in the PCS domain of RAND-36 health survey when assessed at the 12-month follow-up after the completion of the IPRP.

Allocation

A permuted block randomization design with a random block size of 4 and 6 and an 1:1 allocation ratio will be applied and evaluated in the pilot study in order to allocate participants to either the intervention or control group.[68-70] A computer-generated randomization schedule will be created using a random number table to allocate participants to one of the two treatment arms; intervention group (IPRP supplemented by eVIS) or control group (IPRP with daily patient reports in PATRON). The schedule will be generated by an experienced researcher, who is not directly involved in the trial. Sequentially numbered opaque sealed envelopes will be used to ensure allocation concealment. Allocation will take place at the IPRP unit and will be conducted by members of the IPRP team after initial assessment.

Blinding/masking

Neither the IPRP team delivering the intervention nor participants will be blinded to allocation to either group due to the nature of the intervention.

Data collection methods

Besides objectively measured data of physical activity level, patient-reported data will be collected from PATRON and from six Swedish registries at the IPRP baseline and at 6, 12 and 24 months after completed IPRP. In addition, patient-reported data regarding cost effectiveness will be retrieved 36 months after the IPRP is completed. In this trial, data will be retrieved from SQRP, the Swedish social insurance agency's registry, the Patient registry, the Swedish Prescribed Drug Register , the Income- and taxation registry, and the Swedish Population Register to enable a broad investigation into the intervention's effectiveness.

To enable sufficient pilot study analyses, as well as assessment of the primary outcome Physical health (PCS) in RAND-36, members of the IPRP team will be asked to provide self-reported

data on feasibility outcomes (outlined below) using a purpose-developed questionnaire with specific questions targeting the IPRP team perspective.[41] If deemed required, data collection will be supplemented by individual or group interviews. A detailed overview of assessments, time points, and data sources can be found in Table 1.

Data management

In order to link individual-level data from different registries to PATRON data, we will seek assistance from the National Board of Health and Welfare who will provide a consecutive number key. This key will be stored at the National Board of Health and Welfare for three years (longer if needed). The procedure is initiated by sending PATRON data to the National Board of Health and Welfare and participants' social security numbers will be sent there by SQRP. The National Board of Health and Welfare creates the consecutive number key and connects ordered data with own registry data (the National Patient Register and the Swedish Prescribed Drug Register). The National Board of Health and Welfare will then send a data order to the remaining registries (the Swedish Social Insurance Agency's registry, Statistics Sweden, and the Swedish Population Register) and encoded data will be sent to the principal investigator to be stored in Dalarna University's secured server.

Intervention fidelity

The following measures have been and will be taken to increase intervention fidelity: A systematical intervention development with a clarified theoretical base explaining suggested mechanisms has been undertaken throughout the development process. [29]Healthcare staff at the IPRP units will be provided with comprehensive written information (easily accessed online) that includes step-by-step instructions on how to initiate and deliver the intervention while maintaining a high level of integrity. Before the study starts, all participating healthcare staff at the IPRP units will take part in a standardized provider training session online. Also, recurring web-based meeting opportunities will be provided, where IPRP team members will be encouraged to discuss experienced or perceived difficulties, and a questionnaire will be sent out after the study period with the aim of assessing treatment fidelity (treatment integrity and treatment differentiation) by gathering data on how treatment was delivered (manner *versus* treatment manual, intervention's alignment to intended theoretical base). This will allow results

to be interpreted and will facilitate practical implementation.[71] [72] During the on-going study period, researchers will be automatically notified of non-wear time (Fitbit Versa 2) and any absence of patient reports in PATRON. In these cases, researchers will contact the relevant participant via email or telephone to ask if they need help or support. If a participant decides to discontinue the trial, he or she will be asked if they are willing to grant permission for the collected data up to that point to be used in the trial.

Statistical methods

A statistical analysis plan (SAP) will expand on statistical principles, statistical analyses, the planned handling of missing data, possible additional analyses (subgroups etc.) and interim analyses. In both the pilot study and the R-RCT, descriptive statistical analyses will be performed to provide transparent reporting of characteristics of both participants and participating IPRP units. In addition, IPRP units will be prompted to register the number of patients they ask to participate, those excluded based on eligibility criteria, and those who decline participation. Analyses of pilot data (ratings of key feasibility outcomes) made by IPRP teams on a four-point Likert scale (i.e.1= strongly disagree, 2= disagree, 3= agree, 4= strongly agree) will be calculated as proportions in four categories for each item. Ratings ≥3 will be considered as acceptable feasibility. Analyses of primary and secondary outcomes in main trial will be performed based on PATRON data and registry data. The clinical effectiveness of eVIS will be analyzed for each outcome using multivariate statistical and repeated measures analyses as a preliminary plan. Both the intention-to-treat and the per-protocol sample will be analyzed, but the intention-to-treat analysis will be considered as the primary analysis. All p-values will be presented. If a p-value is ≤0.05, the null hypothesis will be rejected and eVIS will be considered effective according to the outlined hypothesis. To perform cost-effectiveness calculations, data on health-related quality of life measured by EQ-5D will be retrieved from SQRP. EQ-5D is the standard instrument used to evaluate health costs and cost effectiveness. Calculations of quality-adjusted life-years (QALYs) will be performed by multiplying health-state utility (measured using the EQ-5D Index score) by time spent in this specific health state.[73] [74] In addition, calculations of the incremental cost effectiveness ratio (ICER) will be made as the difference in the cost of two interventions divided by their affect.[75]

Data monitoring

Trial data will be monitored and regularly assessed for integrity and errors. All data monitoring will be performed completely independently from sponsors and competing interests. An independent data monitoring committee (DMC) will be appointed to critically review data safety in the trial. Veronica Sjöberg (VS) will be responsible for the monitoring of all data collected in the pilot study. A data management plan (DMP) will be outlined by the first author (VS) and implemented by the principal investigator (LV) to ensure sound data structure (folder structure, file naming, organization), and data storing.

DISCUSSION

This article describes a protocol for a R-RCT trial of a novel e-Health intervention. The trial will contribute to establish evidence for the effectiveness of individualized physical activity and exercise among patients living with chronic pain and participating in IPRP. The methodology and feasibility of the trial will be evaluated in an early phase by a pilot study, which will contribute to optimized robustness of the subsequent R-RCT-trial and enable further refinement of the intervention. Despite many efforts have been taken to develop health promoting interventions for this patient group, it is rare that such interventions are systematically developed and includes both objective and patient reported outcomes. The eVIS-intervention is developed according to MRC´s framework for development and evaluation of complex interventions.[29] It consists of both objectively measured physical activity level (steps/day), and patients own reports on pain intensity, interference on daily activities and individual daily activity goal, all joint in the web application named PATRON. This enables known facilitating mechanisms for behavior change (e.g., as self-monitoring etc.)[32] whilst including several core outcome domains.[34 76] The agile development process has enabled continuous evaluation and improvement of the intervention based on data provided from patients, clinicians and researchers in different fields. Objectively measured constructs of physical activity by Fitbit devices have been criticized due to lack of accuracy of measurements of time spent in moderate to vigorous physical activity (MVPA) where various devices overestimate the measurement[77]. Preceding this study, our research group performed an evaluation of Fitbit Versa´s criterion validity of measuring energy expenditure, heart rate and step count among patients living with chronic pain. Results confirmed previous study results in adjacent patient groups reporting that

Fitbit Versa systematically overestimated energy expenditure, however, measurements of step count both in laboratory and in free-living setting were valid.[33]

In this trial participants will be recruited at IPRP units nationally distributed. All units adopt to core IPRP content regarding modalities, but it is well-known that both duration and intensity greatly vary which may limit generalization of the results.[25] To achieve maximum external validity, we will collect data on the specific characteristics of all participating units and include this in the final analyses. Unknown engagement in other out-patient treatments under study period, may be a potential source of bias, though data on in-patient engagement will be known through registry data from the National Patient register. Non-adherence to daily self-report in PATRON can be expected and may differ between intervention- and control group (differential missing). Measures will be taken to optimize adherence in both groups such as regular auditing of registrations in PATRON followed by personal emails with encouragement to follow protocol. To minimize the risk of contamination between groups, and to ensure that the study will be carried out in compliance with the study protocol, all participating staff at the IPRP units will participate in a study-specific course prior entering the trial. Results generated from the pilot study and the subsequent effectiveness trial will inform pain management field with new knowledge on eVIS´s potential to increase pain rehabilitation program´s effectiveness by individualized physical activity levels among patients living with chronic pain.

Harms and adverse events

Participating patients and healthcare staff at the participating IPRP units will be encouraged to report any adverse events such as unexpected side effects or symptom deterioration,[78] which will also be reported to the Swedish Ethical Board Review.

Ethics and dissemination

The trial is prospectively registered in ClinicalTrials.gov (trial registration number NCT05009459) and was approved by the Swedish Ethics Review Board in May 2021 (Dnr 2021/02109). The trial will be conducted in compliance to the Helsinki Declaration.[79] Important protocol modifications will be communicated to the Swedish Ethics Review Board as well as to all participating IPRP units and participants. To protect confidentiality, all data will be coded by an individual code, and the encryption key will be stored separately. Data will be stored at

an intended project server at Dalarna University, which is secured by regular backups. No unauthorized persons will have access to data, e.g., data will only be accessible by researchers in the trial after approval from the principal investigator. Results of the pilot study and the main trial will be submitted for publication in peer-reviewed journals and communicated in national and international research networks, as well as in relevant clinical settings, including patient associations.

Author contribution statement

LV and BÄ are responsible for the conception of the trial. LV is the principal investigator and is involved in all methodological decisions. VS, ET, AM, JW, RLM, BÄ, MH, MB, and LV all contributed to study design and were all involved in the development processes (the evaluation of criterion validity of the wrist-worn activity tracker and the evaluations of the content validity and clinical feasibility) of the intervention. RLM performed the preliminary power and sample size calculations and was involved in all associated decisions. VS wrote the first draft of the manuscript, was responsible for revising the manuscript's intellectual content based on all co-authors conscientious input and conducted manuscript revisions according to peer-reviewer´s comments. All authors read and approved the final version of the manuscript. For this article, no ghost authors, guest authors, or professional writers have or will be used. Author eligibility is and will be based upon the ICMJE Recommendations for the Conduct, Reporting, Editing, and Publication of Scholarly work in Medical Journals.

Trial status

Recruitment of participants was initiated late October 2021 and the trial is planned to be completed on 31 December 2024.

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number). The funders had no role in study design and will have no role in any part of the implementation of the study or the reporting of its results.

Competing interests

None declared.

Access to data

This is a protocol describing a trial design. All authors will have access to the final trial dataset.

Supplementary files:

- Completed SPIRIT 2013 Checklist
- Patient consent form (in Swedish)

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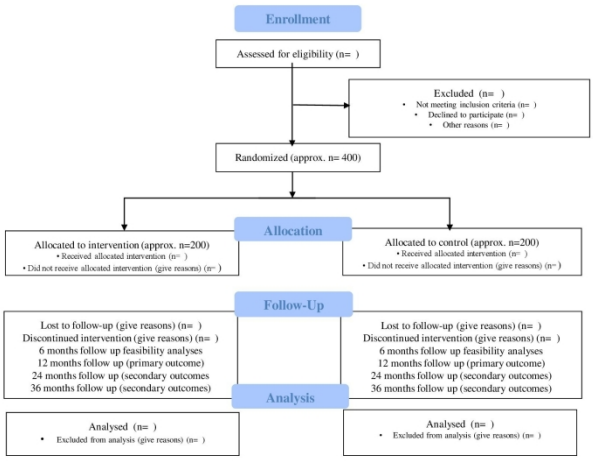

Figure 1. CONSORT 2010 Flow diagram chart of study design and enrollment.

338x190mm (200 x 200 DPI)

Figure 2. Schematic illustration of the eVIS-intervention´s three elements: i) the data collection element of physical activity level (steps/day), patient-report of pain interference on daily activities, pain intensity and pharmacological consumption, ii) the visualisation element of collected data in different graphs and compilations of data, and iii) the communication element.

338x190mm (300 x 300 DPI)

SPIRIT 2013 Checklist: Recommended items to address in a clinical trial protocol and related documents*

Section/ item	Item No	Description	Page number in Main document (clean copy)
Administrative information			
Title	1	Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym	1
Trial registration	2a	Trial identifier and registry name. If not yet registered, name of intended registry	2, 21
	2b	All items from the World Health Organization Trial Registration Data Set	NA
Protocol version	3	Date and version identifier	2
Funding	4	Sources and types of financial, material, and other support	22
Roles and responsibilities	5a	Names, affiliations, and roles of protocol contributors	1, 22
	5b	Name and contact information for the trial sponsor	22 (not contact info)
	5c	Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities	22
	5d	Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data management team, and other individuals or groups overseeing the trial, if applicable (see Item 21a for data monitoring committee)	19
Introduction			

Background and rationale	6a	Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention	4-6
	6b	Explanation for choice of comparators	16-17
Objectives	7	Specific objectives or hypotheses	5-6, 16-17
Trial design	8	Description of trial design including type of trial (eg, parallel group, crossover, factorial, single group), allocation ratio, and framework (eg, superiority, equivalence, noninferiority, exploratory)	6
Methods: Participants, interventions, and outcomes			
Study setting	9	Description of study settings (eg, community clinic, academic hospital) and list of countries where data will be collected. Reference to where list of study sites can be obtained	6
Eligibility criteria	10	Inclusion and exclusion criteria for participants. If applicable, eligibility criteria for study centres and individuals who will perform the interventions (eg, surgeons, psychotherapists)	6-7
Interventions	11a	Interventions for each group with sufficient detail to allow replication, including how and when they will be administered	7-9
	11b	Criteria for discontinuing or modifying allocated interventions for a given trial participant (eg, drug dose change in response to harms, participant request, or improving/worsening disease)	18-19
	11c	Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return, laboratory tests)	18-19
	11d	Relevant concomitant care and interventions that are permitted or prohibited during the trial	7-8
Outcomes	12	Primary, secondary, and other outcomes, including the specific measurement variable (eg, systolic blood pressure), analysis metric (eg, change from baseline, final value, time to event), method of aggregation (eg, median, proportion), and time point for each outcome. Explanation of the clinical relevance of chosen efficacy and harm outcomes is strongly recommended	9-16 Table 1 Table 2

Participant timeline	13	Time schedule of enrolment, interventions (including any run-ins and washouts), assessments, and visits for participants. A schematic diagram is highly recommended (see Figure)	Table 1 Figure 1
Sample size	14	Estimated number of participants needed to achieve study objectives and how it was determined, including clinical and statistical assumptions supporting any sample size calculations	16-17
Recruitment	15	Strategies for achieving adequate participant enrolment to reach target sample size	7, 18-19
Methods: Assignment of interventions (for controlled trials)			
Allocation:			15
Sequence generation	16 a	Method of generating the allocation sequence (eg, computer-generated random numbers), and list of any factors for stratification. To reduce predictability of a random sequence, details of any planned restriction (eg, blocking) should be provided in a separate document that is unavailable to those who enrol participants or assign interventions	17-18
Allocation concealment mechanism	16 b	Mechanism of implementing the allocation sequence (eg, central telephone; sequentially numbered, opaque, sealed envelopes), describing any steps to conceal the sequence until interventions are assigned	17
Implementation	16 c	Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions	17
Blinding (masking)	17 a	Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how	17
	17 b	If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during the trial	NA
Methods: Data collection, management, and analysis			

Data collection methods	18a	Plans for assessment and collection of outcome, baseline, and other trial data, including any related processes to promote data quality (eg, duplicate measurements, training of assessors) and a description of study instruments (eg, questionnaires, laboratory tests) along with their reliability and validity, if known. Reference to where data collection forms can be found, if not in the protocol	Table 1 9-16
	18b	Plans to promote participant retention and complete follow-up, including list of any outcome data to be collected for participants who discontinue or deviate from intervention protocols	18-19
Data management	19	Plans for data entry, coding, security, and storage, including any related processes to promote data quality (eg, double data entry; range checks for data values). Reference to where details of data management procedures can be found, if not in the protocol	20
Statistical methods	20a	Statistical methods for analysing primary and secondary outcomes. Reference to where other details of the statistical analysis plan can be found, if not in the protocol	19
	20b	Methods for any additional analyses (eg, subgroup and adjusted analyses)	19
	20c	Definition of analysis population relating to protocol non-adherence (eg, as randomised analysis), and any statistical methods to handle missing data (eg, multiple imputation)	19
Methods: Monitoring			
Data monitoring	21a	Composition of data monitoring committee (DMC); summary of its role and reporting structure; statement of whether it is independent from the sponsor and competing interests; and reference to where further details about its charter can be found, if not in the protocol. Alternatively, an explanation of why a DMC is not needed	20
	21b	Description of any interim analyses and stopping guidelines, including who will have access to these interim results and make the final decision to terminate the trial	19
Harms	22	Plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial conduct	21

Auditing	23	Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor	20
Ethics and dissemination			
Research ethics approval	24	Plans for seeking research ethics committee/institutional review board (REC/IRB) approval	18-19
Protocol amendments	25	Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators, REC/IRBs, trial participants, trial registries, journals, regulators)	21-22
Consent or assent	26 a	Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32)	7
	26 b	Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable	NA
Confidentiality	27	How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial	18-19
Declaration of interests	28	Financial and other competing interests for principal investigators for the overall trial and each study site	20
Access to data	29	Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators	20
Ancillary and post-trial care	30	Provisions, if any, for ancillary and post-trial care, and for compensation to those who suffer harm from trial participation	No
Dissemination policy	31 a	Plans for investigators and sponsor to communicate trial results to participants, healthcare professionals, the public, and other relevant groups (eg, via publication, reporting in results databases, or other data sharing arrangements), including any publication restrictions	21-22
	31 b	Authorship eligibility guidelines and any intended use of professional writers	22
	31 c	Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code	23

Appendices			
Informed consent materials	32	Model consent form and other related documentation given to participants and authorised surrogates	See supplementary files [In Swedish]
Biological specimens	33	Plans for collection, laboratory evaluation, and storage of biological specimens for genetic or molecular analysis in the current trial and for future use in ancillary studies, if applicable	NA

BMJ Open

Effectiveness of the eVISualisation of physical activity and pain intervention (eVIS) in Swedish Interdisciplinary Pain Rehabilitation Programs: study protocol for a registry-based randomized controlled clinical trial

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Title:

Effectiveness of the eVISualisation of physical activity and pain intervention (eVIS) in Swedish Interdisciplinary Pain Rehabilitation Programs: study protocol for a registry-based randomized controlled clinical trial

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Keywords: Chronic pain, Individualized physical activity level, Interdisciplinary Pain Rehabilitation Programs, Pilot study, Physical health, Registry-based randomized clinical trial, Study protocol

ABSTRACT

Introduction: Living with chronic pain often involves negative consequences. Interdisciplinary Pain Rehabilitation Programs (IPRPs) is considered superior to single-treatment measures in patients with chronic pain. Despite this, effects emerge sub-optimal and more than 20% of patients deteriorate in patient reported physical health outcomes after IPRP. A novel e-Health intervention, eVISualisation of physical activity and pain (eVIS), was systematically developed to facilitate individualization of physical activity levels. By adding elements of data collection, visualization, and communication of objectively measured physical activity and patient-reported outcomes (pain intensity, interference of pain, pharmaceutical consumption) to existing treatment modalities in IPRP, the IPRP team acquires prerequisites to adapt advice and physical activity prescriptions and to evaluate set activity goals. The overall aim is two-fold. First, the aim is to evaluate the feasibility of the subsequent registry-based randomized controlled clinical trial (R-RCT). Secondly, the aim is to prospectively evaluate the effectiveness of the eVIS-intervention as a supplement to IPRP on our defined primary (physical health) and secondary outcomes.

Methods and analysis: In the R-RCT, recruitment of 400 patients with chronic pain will be performed at 15 IPRP units. A random allocation to either IPRP + eVIS or to control group that will receive IPRP only will be performed. Data from the initial 30 participants completing the study period (6 months) will be included in a pilot study where key feasibility outcomes (recruitment, randomization, , implementation, treatment integrity, data collection procedure, preliminary outcome measures) will be evaluated. Outcome variables will be extracted from PATRON and from six national registries. Multivariate statistics and repeated measures analyses will be performed. Quality Adjusted Life Years (QALYs) and Incremental Cost Effectiveness Ratio (ICER) will be calculated for cost effectiveness evaluation.

Ethics/dissemination: The Swedish Ethics Review Board granted approval (Dnr 2021/02109). Results will be disseminated through peer-review journals.

Trial registration number: NCT05009459.

Protocol version: 1

Strengths and limitations of the study

- A proceeding pilot study will enable improvements of design and feasibility of a subsequent R-RCT
- The eVIS-intervention has been developed, evaluated, and improved, based on data provided from patients, clinicians, and researchers in different fields.
- The intervention targets physical activity modalities in IPRP and is designed to enable a more individualized IPRP treatment.
- The intervention is based on objectively measured physical activity levels, patient-reported clinical outcomes, and mechanisms that facilitate behavior change, in accordance with current guidelines that are provided by authorities in the chronic pain management field.
- The nature of the intervention precludes blinding of patients and the IPRP team.

INTRODUCTION

Chronic musculoskeletal pain (>3 months), including neck/shoulder/back pain or widespread pain, is a major global health and socioeconomic burden.[1 2] Living with chronic pain is often associated with reduced levels of wellbeing and the health-related quality of life of this group has been reported to be among the lowest of any medical condition.[3] To date, physical activity (i.e. any bodily movement that requires energy expenditure) and exercise (i.e. structured and planned physical activity aimed to increase fitness)[4] have been shown to prevent and/or treat several of our noncommunicable diseases including chronic pain,[5] due to their beneficial effects on general health, pain intensity, physical and psychological functioning, and health-related quality of life.[5-8] Despite the growing evidence of health benefits related to physical activity, participation and adherence to physical activity recommendations, such as WHO´s physical activity guidelines, are often low in patients living with chronic pain.[9-12] This may partly be explained by the indicated association between high pain scores and low patient-reported activity levels among patients with chronic pain and/or the documented reports of the negative impact of depression on physical activity levels.[13] In addition, it is well known that behavior change is difficult, and that each individual's own participation is essential.[14] It has been shown that behavior change towards a beneficial physical activity level may be facilitated by individuals self-monitoring their physical activity.[15] The use of objective measures increases the likelihood of the effectiveness of interventions designed to promote physical activity.[15] By adding goal setting, feedback, and a focus on achieved goals, effectiveness can be further improved.[15-18]

Interdisciplinary pain rehabilitation programs (described as a subset of Interdisciplinary Treatment), is defined as "multimodal treatment provided by a multidisciplinary team (at least 3 professions), collaborating in assessment and treatment using a shared biopsychosocial model and goals"[19]. The IPRP approach adopts the principles of behavioral therapy and incorporates besides physical activity and exercise, also psychological measures, pharmaceutical treatment and patient education.[20] Physical activity and exercise are central measures in IPRPs as it targets the physical deconditioning by improving levels of physical activity, and also reduces pain severity and improved physical function and quality of life, without causing any severe adverse events.[5] Interdisciplinary pain rehabilitation programs are considered to be superior to single-treatment measures (e.g., physical treatments, education interventions, surgery, etc.) for patients with chronic pain supporting positive effects on pain intensity and activity disability.[20 21]

However, IPRP effectiveness is only slightly better and in the majority of cases only a small effect is seen.[21-25] In addition, up to 25% of patients report deterioration in physical health after completing IPRP and after 12 months follow up, regardless of duration of IPRP.[20 25 26] Sustainable treatment affects seem to vary according to patient clinical features at baseline, such as poor employment status, high pain levels, and low functioning, all of which predict low physical health at follow-up.[23 27] Many efforts have been made to find effective interventions that improve the health of chronic pain patients. To facilitate individualized physical activity levels within the Swedish IPRP setting, an eVISualisation (eVIS) of physical activity and pain intervention has been systematically developed according to the Medical Research Council´s recently updated framework for development and evaluation of complex interventions. [28 29] In accordance with the framework, the eVIS-interventions was designed and planned in close collaboration with stakeholders. eVIS is designed to target facilitating mechanisms for behavior change, such as outcome expectations, self-monitoring, self-evaluation, and self-efficacy,[30-32] which are theoretically framed by the Social Cognitive Theory.[32] In eVIS, objectively measured physical activity tracking using a wrist-worn activity tracker[33] (Fitbit Versa 2) is combined with a daily activity goal (steps/day) and daily patient reports of known important clinical outcome assessments: pain intensity and its interference on daily activities[34-38] and pharmaceutical consumption. Data is collected and visualized in a purpose-developed web application, Pain And TRaining ON-line (PATRON), which can be used by the patient and the IPRP team to follow and adjust individual physical activity levels. Despite interventions of this kind having highly promising potential to relive pain and improve disability in this patient group,[39]interventions are rarely systematically developed and validated specifically for their target patient group, leaving crucial information of feasibility and true effectiveness unknown. Therefore, the overall aim of this study is two-fold. First, the aim is to evaluate the feasibility (recruitment capability, eligibility screening procedure, randomization, implementation process, response rate, compliance rate, changes in primary- and secondary outcomes from start to end of study period, differences between treatment groups in primary outcome) of a subsequent registry-based randomized controlled clinical trial (R-RCT) within the IPRP setting in order to gain knowledge of population variation, increase robustness and to avoid underpower. [40-43] Secondly, the aim is to prospecively evaluate the effectiveness of the eVIS-intervention as a supplement to IPRP on our defined primary (physical health) and secondary outcomes, 12 months after completed IPRP compared to IPRP as usually provided. In addition, the aim is to evaluate the cost effectiveness of eVIS supplementing IPRP at 12 and 36 months follow up

after completed IPRP, and to prospectively evaluate differences in opioid consumtion at start of IPRP compared to six months after completed IPRP.

[4240-43]In this trial, the UK National Institute for Health Research's (NIHR) definitions of the terms *pilot study* (i.e., "a smaller version of the main study") and *feasibility study* (i.e., "evaluation of pieces of research done before the main study") are applied.[44] The aim of this paper is to transparently clarify and report on study designs, aims, outcome assessments, and procedures for a planned R-RCT (including an randomized pilot study) which prospectively will evaluate clinical effectiveness and cost effectiveness of eVIS as a supplement to IPRPs for patients living with chronic pain compared to standard IPRPs.

METHODS AND ANALYSIS

Trial design and setting

This two-armed pragmatic multi-site R-RCT will be conducted in specialized and primary IPRPs in Sweden, and include approximately 400 (n=200, n=200) patients (number will be definitively determined after the pilot study is finalized) with chronic musculoskeletal non-malignant pain. As indicated, an randomized controlled pilot study (n=15, n=15) will be incorporated as the initial phase of the main trial in order to evaluate the intervention´s methodology and design.[29 41 45] This trial will comply with the Consolidated Standards of Reporting Trials (CONSORT)[40] and with the Standard Protocol Items: Recommendations for Interventional Trials (SPIRIT)[46]. A completed SPIRIT 2013 Checklist can be found in the additional files. See Figure 1 for study design and enrollment details.

Insert Figure 1 here.

Figure 1. CONSORT 2010 Flow diagram chart of study design and enrollment.

Eligibility criteria

In this trial, the patient-related, care process and caregiver-related inclusion criteria for receiving Swedish IPRP will be applied, as patients entering the trial must be accepted for IPRP.

Principal IPRP inclusion criteria are patients in working age with persistent or intermittent musculoskeletal and or generalized pain lasting ≥3 months with pain affecting daily activities to a large extent, completed systematic assessment (including screening for psychosocial risk factors and differential diagnosis) and non-pharmacological optimization. Inclusion criteria for Swedish IPRPs is outlined in detail elsewhere.[47] Due to the nature of the intervention, patients must be able to hear, see, and comprehend spoken and written Swedish, and have daily access to a computer, smartphone, or tablet. Patients who need to use a walking aid indoors will be excluded.

Recruitment

Interdisciplinary Pain Rehabilitation Units

Approximately 15 IPRP units in primary and specialized care in Sweden will be included in the trial. IPRP units reporting to the Swedish National Quality Registry for Pain Rehabilitation (SQRP) have been approached by email with study information (aim, rationale, methods etc.) and an invitation to participate in one of several online digital information meetings that will further present the study (initiated August 2021). Study representatives will approach healthcare staff at potential IPRP units by telephone or email to formally offer participation. Operation managers at each unit will be asked to provide written consent by e-mail.

Participants

In order to give potential participants additional time to consider taking part in the trial before they visit the IPRP unit, healthcare staff at the units will be encouraged to provide a general information sheet about the trial in the summon to the IPRP assessment. Members of IPRP teams (primarily physiotherapists but also occupational therapists, physicians, nurses etc.) will identify potential participants selected for IPRP based on outlined criteria and provide them with verbal and written details of the study (information sheets and the project's web address). All participants will provide written informed consent (see supplementary file) prior to joining the study, which will be managed by the IPRP team. Detailed verbal and written information about the voluntary nature of participation and the indisputable right to discontinue participation in the trial at any time will be provided. Detailed checklists and forms will support these procedures, and these will be easily accessible on the project web site.

Intervention

Participation in the intervention group involves regular IPRP supplemented with eVIS for a coherent time span of six months, IPRP time included. As the duration and intensity of IPRPs greatly vary from a couple of weeks up to four months[25], a six month study period ensures time of independent use of eVIS after completed IPRP. Participants are not prohibited to take part of other health care during study period. Interdisciplinary pain rehabilitation programs vary in interventions, duration, composition, intensity[24 25] and can be performed either individually or in group format. In this trial, participation in a IPRP will be supplemented by eVIS, a health promoting intervention containing three elements designed to facilitate individualized physical activity level (Figure 2).

The data collection element

Outcome assessments of physical activity level (steps/day) will be objectively collected by a wrist-worn activity tracker, Fitbit Versa 2. This device has been population-specifically validated and the measurement of step rate is indicated as valid for measurement in this population. [33] Data on patient´s physical activity level quantified as steps/day, will be automatically synchronized to the web application PATRON where pain intensity (0-10), [48] interference of pain on daily activities (0-10),[49] pharmacological consumption (name, dose, number, and form), and (optional) free-text comments will be reported by the patient daily. The web application can be accessed via computer, smartphone, or tablet. A daily activity goal (steps/day) is formulated by the patient in close collaboration with the IPRP team and revised accordingly. The daily activity goal in eVIS is individually set based on patient's individual prerequisites and re-evaluated regularly as part of the communication element (described below). In the process of setting a daily activity goal, the IPRP team are encouraged to consider international guidelines of step rate as a quantification of beneficial physical activity levels [50] as well as patient´s personal barriers and resources to perform physical activity. The data collection element is designed to target facilitating mechanisms for behavior change, such as outcome expectations, self-monitoring, self-evaluation, and self-efficacy.[30-32]

The visualisation element

Objectively measured physical activity levels, patient-report on pain intensity and interference of pain on daily activity are graphically visualized separately or alongside each other, in relation to the daily activity goal. Three different graphs (1/7/28 days) are available. The visualisation element provides additional prerequisites for increased knowledge acquisition, self-monitoring,

and self-evaluation as data is visualized over time and in relation to each other and to the individual daily activity goal in order to improve patient self-efficacy.

The communication element

The graphs in the visualisation element together with compiled data on pharmacological consumption will provide a novel decision basis for the patient and the IPRP team. This addition to existing treatment modalities traditionally provided in Swedish IPRP (e.g. physical activity, cardio training, weight training, mobility training, stability training, motivating conversation education, advice etc.). enables prerequisites for the IPRP team to integrate behavioral changing techniques (e.g. reinforcement, knowledge acquisition, self-monitoring, self-efficacy) into existing treatment options. By such integration, knowledge of patient's personal barriers and resources in factors important in pain rehabilitation may be visualized and if necessary, assessed. The IPRP team as well as the patients are encouraged to explore the visualisation element of eVIS at each visit at the IPRP unit. This in order to utilize data into the treatment by adjusting advise or prescriptions.

Insert Figure 2 here

Figure 2. Schematic illustration of the eVIS-intervention´s three elements: i) the data collection element of physical activity level (steps/day), patient-reports of interference of pain on daily activities, pain intensity and pharmacological consumption, ii) the visualisation element of collected data in different graphs and compilations of data, and iii) the communication element.

Control

Participation in the control group involves taking part in regular IPRP plus making daily ratings of pain intensity, interference of pain on daily activities, and pharmaceutical consumption (corresponding as in intervention group) in PATRON for six months, including the time that the IPRP is being carried out. The control group will not use the wrist-worn activity tracker as this may affect their physical activity behavior [51]. Nor will they have access to PATRON's visualizing or communication features.

Patient and Public Involvement Statement

In an early developing phase, stakeholders (patients living with chronic pain, representatives from patient organizations and clinicians experienced in pain rehabilitation) were invited to contribute to the intervention development. In this phase, the web application PATRON and eVIS was presented and carefully discussed with stakeholders as well as with web application developers and researchers. Several needs for improvement were identified, such as a need of an addition of pharmaceutical report function, designated web pages and graphical changes in planned interfaces.

Outcome assessments

According to the Initiative on Methods, Measurement, and Pain Assessment in Clinical Trials (IMMPACT), physical health, emotional health, and pain intensity are three of six identified core outcome domains that should be considered when designing research studies aiming to evaluate effectiveness of chronic pain treatments. [35-37] It is specifically recommended that a health survey such as RAND-36 should be incorporated into treatment as a clinical outcome assessment of physical health in clinical trials.[36 37] Outcome assessments for evaluating feasibility will be performed on data from the IPRP baseline and after the study period is completed (six months) for the first 30 participants (n=15 +, n=15). In the main trial, assessments of effectiveness will be performed on data from the IPRP baseline and from the 12-month follow-up. The cost effectiveness assessments will be based on data from the IPRP baseline, from the 12-month IPRP follow-up and again 24 and 36 months after the IPRP is completed. A detailed overview of outcome assessments can be found in Table 1.

Table 1. Overview of study period, measurement time points, outcome assessments (***bold and italics)***, instruments, and data sources (*italics*).

	Study period						
	Enrolment	Allocation	Post-allocation				
	-t_1	**0**	**Baseline**	**t1**	**t2**	**t3**	**t4**
Enrolment	X						
Written and verbal study information	X						
Eligibility screen	X						
Informed consent	X						
Allocation/randomization		X					
Interventions							
Intervention, eVIS (6 months)			X	X			
Control (6 months)			X	X			
Outcome assessments							
Personal characteristics							
Sex, age, country of origin, family composition, beliefs of restored health (*SQRP, SS*)			X				
Disposable-, earned- and net income (*SS*)			X		X	X	X
Education level and education orientation (*SPR, ITR*)			X		X	X	X
Diagnosis (NPR			X		X	X	X
Volume and reason for inpatient care (*NPR*)			X		X	X	X
Pain characteristics							
Pain intensity (last 7 days), NRS (*SQRP-PC and SC*)			X		X		
Pain intensity (today), NRS (*PATRON*)			X	X			
Pain type, location, duration (*SQRP-PC and SC)*			X				
Pain interference (*PATRON*)			X				
Multidimensional measures							
Physical health, RAND-36 PCS health survey (*PATRON*)			X	X	X	X	X
Physical health, RAND-36 PCS health survey (*SQRP-SC only*)			X		X		
Emotional health, RAND-36 MCS health survey (*PATRON*)			X	X	X	X	X
Emotional health, RAND-36 MCS health survey (*SQRP- SC only*)			X		X		

Overall emotional distress, HAD(S) (*SQRP-PC and SC*)	X		X		
Pain catastrophizing, PCS (*SQRP-PC and SC*)	X		X		
Psychosocial consequences, MPI-S (*SQRP-PC and SC*)	X		X		
Pain acceptance, CPAQ-8 (*SQRP-PC only*)	X		X		
Perceived life Satisfaction, LiSat (*SQRP-PC and SC*)	X		X		
Functional level, FRI (*SQRP-SC only*)	X		X		
Physical activity					
Objective measures of steps per day (*Fitbit Versa 2*)	X	X			
Patient-reported measures (*SQRP- PC and SC*)	X		X		
Work					
Return to work (partially or full time) every month (*SSIA*)			X	X	X
Number of days with sick benefit during study period (*SSIA*)			X	X	X
Number of days in work before new sick leave during study period (*SSIA*)			X	X	X
Length of total sick leave during study period (*SSIA*)			X	X	X
Perceived work ability, WAI (*SQRP-PC and SC*)	X		X		
Sleep quality, ISI *(SQRP-SC only)*	X		X		
Pharmaceutical consumption					
Name, dose, size, prize of prescribed pharmaceuticals (*SPDR, PATRON [not size, prize]*)			X	X	X
Prescribed pharmaceuticals collected from pharmacies, (*SPDR*)			X	X	X
Cost of prescribed pharmaceuticals included in benefit program (*SPDR*)			X	X	X
Health care consumption *(NPR)*			X	X	X
Feasibility outcomes, *Questionnaire*		X			
Treatment integrity, *Questionnaire*		X	X		

Abbreviations: -t^1 = pre recruitment period, t^1 = completed study period (6 months), t^2 = follow-up 12 months after completed Interdisciplinary Pain Rehabilitation Program (IPRP), t^3 = 24 months after completed IPRP, t^4 = 36 months after completed IPRP, eVIS = eVISualisation of physical activity and pain intervention, SQRP = the Swedish national quality registry for pain rehabilitation, SQRP-PC = , the Swedish national quality registry for pain rehabilitation primary care, SQRP-SC = the Swedish national quality registry for pain rehabilitation specialized care, NRS = Numeric Rating Scale, PATRON = Pain and training online (web application), RAND-36 PCS = physical health domain , RAND-36 MCS = mental health domain, HAD(S) = Hospital Anxiety and Depression Scale, PCA = Pain Catastrophizing Scale, MPI-S = Multidimensional Pain Inventory -Swedish Version, CPAQ-8 = The Chronic Pain and Acceptance Questionnaire, LiSat = Life Satisfaction Scale, WAI = Work Ability Index, FRI = Functional rating scale, ISI = Insomnia Severity Index, SSIA = the Swedish Social Insurance Agency's registry, NPR = the National Patient Register, SPDR = the Swedish Prescribed Drug Register, SS = Statistics Sweden, SPR = the Swedish Population Register.

Feasibility outcomes, pilot study

The trial will be initiated as a full-scale registry-based randomized controlled pilot study. In this initial step, feasibility will be evaluated from data provided from the first 30 participants completing the study period and in the following key areas: the unit´s recruitment capabilities, the randomization process, implementation process, participant response to intervention which is outlined in Table 2. In addition, the data collection procedure, and the preliminary outcome measures (standardized effect size, sample size estimation with Cohen's *d*, characteristics [mean, SD]) in main trial will be evaluated.[41 45] In addition to feasibility outcomes, characteristics of the IPRP units will be collected

Table 2. Overview of key feasibility outcomes in pilot study.

Key feasibility outcomes
Recruitment capability
Volume of total eligible patients
Number recruited/week
Eligibility screening procedure
Proportion accepted/declined
Personal characteristics of accepted and declined participants
Pain characteristics of accepted and declined participants
Procedure of collecting consent
Randomization process
Delivery envelopes
Storage of envelopes
Procedure of opening envelopes
Patients´ reaction to allocation
Implementation process
Response rate RAND-36 PCS
Compliance rate (use of Fitbit Versa 2, intervention group only)
Compliance rate (patient reported outcomes in PATRON)
Treatment integrity
Reported adverse events
Data collection procedure
Access to PATRON data
Access to registry data
Access to RAND-36 data
Preliminary outcome measures
Characteristics, mean (SD)
Missing data
Changes from baseline to finalized study period

Abbreviations: RAND-36 PCS = physical health domain in RAND-36, PATRON = Pain and training online (web application).

Primary outcome, main trial

The R-RCT will prospectively evaluate the *clinical effectiveness* of eVIS supplementing IPRPs regarding improvements in our primary outcome assessment *Physical health* collected by the

physical health domain in RAND-36 health survey[3 52] at the 12-month IPRP follow-up after completing the IPRP. The RAND-36 is, for this population, a valid health survey measuring health-related quality of life in two dimensions, physical health (PCS) and mental health (MCS), mediated by eight subscales.[52]

Secondary outcomes, main trial

In the main trial, secondary outcomes will be extracted from Fitbit Versa 2, PATRON and collapsed with data from six national registries (all listed below) at 12, 24, 36 months after the IPRP is completed.

Objectively measured secondary outcomes collected using Fitbit Versa 2

Objectively measured physical activity levels will be collected daily during the study period using a wrist-worn activity tracker (Fitbit Versa 2). The Fitbit device measures and estimates a range of physical activity outcomes such as number of steps, heart rate, energy expenditure, floors climbed, physical activity level, and sleep.[33 53] In this trial, participants' step count per day will automatically be synchronized to PATRON during the study period (six months). The use of steps per day is considered to be a valid quantification of physical activity levels and this is acknowledged by the Swedish Health Authority.[54]

Patient-reported secondary outcomes collected through PATRON

Data on physical and mental health collected by RAND-36 health survey will be collected through PATRON at 6, 12 and 24 months after IPRP. Pain intensity ("*rate your average pain during the last 24 hours*") will be measured daily using the Numeric Rating Scale (NRS, 0 = *no pain at all* to 10 = *pain as bad as it could be*), a 11-point Likert scale[48] incorporated in the web application PATRON. Pain interference on daily activities is a recommended outcome domain.[35] In PATRON, assessments of interference of pain on daily activities will be measured by the question "*rate how much your daily activities are affected by pain*" using an 11-point Likert Scale (0 = *not at all* to 10 = *to a very large extent*). This question in PATRON has been modified based on the Multidimensional Pain Inventory Swedish version and its items on pain interference,[49] and validated in our previous study (in manuscript). Data on daily pharmaceutical consumption will be collected in PATRON (name, dose, number, and form). Voluntary free text comments will supplement patient reporting by providing additional information regarding perceived mental and physical health (only in the intervention group).

Secondary outcomes collected through the Swedish national quality registry for pain rehabilitation

In Sweden, 90% of IPRP units routinely collect patient-reported data from standardized questionnaires and report to SQRP, a database initiated in 1998 that contains data from chronic non-malignant pain patients participating in IPRPs.[24 55] The registry consists of two parts; the primary care SQRP (SQRP-PC) and the specialized SQRP (SQRP-SC). The primary care SQRP is supplied with data from affiliated primary care IPRP units (n=42, reported data from 505 patients in 2020). The specialized care SQRP, receives data from affiliated specialized care IPRP units (n=45, reporting data from 7427 patients in 2020). Data in both registries are collected at baseline, when the IPRP is completed, and at 12-month follow-ups, the content of data collected in the registries differs somewhat. In this trial, registry data from both registries will be collected used to describe demographics such as age, sex, height, weight, education level, and work.[24 55] Participants partaking in an IPRP in SC will also routinely complete the RAND-36 health survey at baseline and at their 12-month follow-up after they have completed their program. Data on pain intensity ("*last 7 days*") (NRS 0-10)[48] will be retrieved from SQRP-PC and SQRP-SC alongside other pain characteristics including pain location (36 anatomical predefined areas, 18 on the left side, 18 on the right side), pain duration, and pain type (intermittent or continuous). Data on self-rated physical and mental health is collected by the RAND-36 health survey[3 52] in SQRP-SC and the EuroQol-5 dimensions (EQ-5D) collected routinely in SQRP-PC and SQRP-SC will be used. The EQ-5D is a standard instrument used in health economic evaluations and contains five items each with three ordered response categories, and a 0-100 index.[56]

Measures of self-rated physical activity is collected in SQRP-PC and SC using the National Board of Health and Welfare's three questions on physical activity (0 - >300 minutes/week), exercise (0 - >120 minutes/week), and sedentary behavior (0 – 15 hours/day).[57] and in SQRP-PC by the Godin-Shepard leisure-time physical activity questionnaire (number of times/week that strenuous/moderate/light exercise.[58] Data on overall emotional distress (0 – 3), pain catastrophizing (0 – 4), and psychosocial consequences (0 – 6) of living with pain are collected in SQRP-PC and SQRP-SC using the Hospital Anxiety and Depression Scale (HADS),[52 59] the Pain Catastrophizing Scale (PCS),[60] and the Multidimensional Pain Inventory Scale Swedish version (MPI-S, 0 – 6).[49] Level of pain acceptance (0 – 6) is collected in SQRP-PC using the Chronic Pain and Acceptance Questionnaire (CPAQ-8).[61] Perceived life satisfaction (1-6) is collected by the Life Satisfaction Scale (LiSat)[62] in both registries. Data on perceived work

ability (0 – 10) is collected by the Work Ability Index (WAI)[63] and functional levels (0 – 4) by the Functional Rating Scale (FRI)[64] is collected in SQRP-SC only. Data on patient-reported sleep quality (0 – 4) is collected by the Insomnia Severity Index (ISI)[65] in SQRP-SC.

Secondary outcomes collected through other national registries

Data will be collected from the Swedish Social Insurance Agency's registry on diagnosis, reasons for sick leave, type of financial compensation, number of sick days, and sickness benefit (days and hours) during the study period. In addition, data on days in work (partial or full time) per month in total before new sick leave period and length of total sick leave during the study period will be retrieved from the registry. Data will be retrieved from the National Patient Register on diagnosis and healthcare consumption (total number of days in care etc.). Retrieved data from the Swedish Prescribed Drug Register will provide information on prescribed pharmaceutical names, doses, sizes, and prices that have been collected from pharmacies, their costs, and whether the pharmaceutical is included in the subsidized pharmaceutical program. Data on disposable and earned income as well as net income will be retrieved from Statistics Sweden. In addition, demographic data such as sex, age, marital status, citizenship, education level, and number of children in the family will be collected. From the Population registry, data on education level and education orientation (focus) in addition to limited demographic data (sex, age) will be collected.

Sample size

A sample size for the pilot study of at least n=30 is considered sufficient for planned feasibility analyses since it will not involve hypothesis testing and sample size calculation *per se.*[43 66 67] For the main trial, a preliminary power calculation are based on assumptions from previous research reporting on proportions of patients that report a clinically meaningful difference of ≥3 points in the physical health domain in RAND-36, 12-months after completed IPRP. [25] The calculation was performed in R, using a calculation method for simple randomization and for independent observations. The preliminary power calculation allows a dropout rate of 20% and requires a total sample size of approximately n=400 to have an 80% power to detect a 15% difference (≥3p) between the groups in the outcome physical health. Physical health is measured by the RAND-36 health survey at the 12-month follow-up measurement point after the completion of the IPRP. The significance level is set to 0.05 and is two-tailed. The sample size calculation may be re-calculated after the pilot study is completed. In this trial, the null

hypothesis is that there will be no difference between the intervention group and the control group (<15% with ≥3 points improvement) with regard to proportional improvement in the PCS domain of RAND-36 health survey when assessed at the 12-month follow-up after the completion of the IPRP.

Allocation

A permuted block randomization design with a random block size of 4 and 6 and an 1:1 allocation ratio will be applied and evaluated in the pilot study in order to allocate participants to either the intervention or control group.[68-70] A computer-generated randomization schedule will be created using a random number table to allocate participants to one of the two treatment arms; intervention group (IPRP supplemented by eVIS) or control group (IPRP with daily patient reports in PATRON). The schedule will be generated by an experienced researcher, who is not directly involved in the trial. Sequentially numbered opaque sealed envelopes will be used to ensure allocation concealment. Allocation will take place at the IPRP unit and will be conducted by members of the IPRP team after initial assessment.

Blinding/masking

Neither the IPRP team delivering the intervention nor participants will be blinded to allocation to either group due to the nature of the intervention.

Data collection methods

Besides objectively measured data of physical activity level, patient-reported data will be collected from PATRON and from six Swedish registries at the IPRP baseline and at 6, 12 and 24 months after completed IPRP. In addition, patient-reported data regarding cost effectiveness will be retrieved 36 months after the IPRP is completed. In this trial, data will be retrieved from SQRP, the Swedish social insurance agency's registry, the Patient registry, the Swedish Prescribed Drug Register , the Income- and taxation registry, and the Swedish Population Register to enable a broad investigation into the intervention's effectiveness.

To enable sufficient pilot study analyses, as well as assessment of the primary outcome Physical health (PCS) in RAND-36, members of the IPRP team will be asked to provide self-reported

data on feasibility outcomes (outlined below) using a purpose-developed questionnaire with specific questions targeting the IPRP team perspective.[41] If deemed required, data collection will be supplemented by individual or group interviews. A detailed overview of assessments, time points, and data sources can be found in Table 1.

Data management

In order to link individual-level data from different registries to PATRON data, we will seek assistance from the National Board of Health and Welfare who will provide a consecutive number key. This key will be stored at the National Board of Health and Welfare for three years (longer if needed). The procedure is initiated by sending PATRON data to the National Board of Health and Welfare and participants' social security numbers will be sent there by SQRP. The National Board of Health and Welfare creates the consecutive number key and connects ordered data with own registry data (the National Patient Register and the Swedish Prescribed Drug Register). The National Board of Health and Welfare will then send a data order to the remaining registries (the Swedish Social Insurance Agency's registry, Statistics Sweden, and the Swedish Population Register) and encoded data will be sent to the principal investigator to be stored in Dalarna University's secured server.

Intervention fidelity

The following measures have been and will be taken to increase intervention fidelity: A systematical intervention development with a clarified theoretical base explaining suggested mechanisms has been undertaken throughout the development process. [29]Healthcare staff at the IPRP units will be provided with comprehensive written information (easily accessed online) that includes step-by-step instructions on how to initiate and deliver the intervention while maintaining a high level of integrity. Before the study starts, all participating healthcare staff at the IPRP units will take part in a standardized provider training session online. Data on each participant's number of entries in PATRON will be available throughout the study in order to collect data on treatment fidelity. During the on-going study period, researchers will be automatically notified of non-wear time (Fitbit Versa 2) and any absence of patient reports in PATRON. In these cases, researchers will contact the relevant participant via email or telephone to ask if they need help or support. If a participant decides to discontinue the trial, he or she will

be asked if they are willing to grant permission for the collected data up to that point to be used in the trial. Also, recurring web-based meeting opportunities will be provided, where IPRP team members will be encouraged to discuss experienced or perceived difficulties, and a questionnaire will be sent out after the study period with the aim of assessing treatment fidelity (treatment integrity and treatment differentiation) by gathering data on how treatment was delivered (manner *versus* treatment manual, intervention's alignment to intended theoretical base). This will allow results to be interpreted and will facilitate practical implementation.[71 72]

Statistical methods

A statistical analysis plan (SAP) will expand on statistical principles, statistical analyses, the planned handling of missing data, possible additional analyses (subgroups etc.) and interim analyses. In both the pilot study and the R-RCT, descriptive statistical analyses will be performed to provide transparent reporting of characteristics of both participants and participating IPRP units. In addition, IPRP units will be prompted to register the number of patients they ask to participate, those excluded based on eligibility criteria, and those who decline participation. Analyses of pilot data (ratings of key feasibility outcomes) made by IPRP teams on a four-point Likert scale (i.e.1= strongly disagree, 2= disagree, 3= agree, 4= strongly agree) will be calculated as proportions in four categories for each item. Ratings ≥3 will be considered as acceptable feasibility. Analyses of primary and secondary outcomes in main trial will be performed based on PATRON data and registry data. The clinical effectiveness of eVIS will be analyzed for each outcome using multivariate statistical and repeated measures analyses as a preliminary plan. Both the intention-to-treat and the per-protocol sample will be analyzed, but the intention-to-treat analysis will be considered as the primary analysis. All p-values will be presented. If a p-value is ≤0.05, the null hypothesis will be rejected and eVIS will be considered effective according to the outlined hypothesis. To perform cost-effectiveness calculations, data on health-related quality of life measured by EQ-5D will be retrieved from SQRP. EQ-5D is the standard instrument used to evaluate health costs and cost effectiveness. Calculations of quality-adjusted life-years (QALYs) will be performed by multiplying health-state utility (measured using the EQ-5D Index score) by time spent in this specific health state.[73 74] In addition, calculations of the incremental cost effectiveness ratio (ICER) will be made as the difference in the cost of two interventions divided by their affect.[75]

Data monitoring

Trial data will be monitored and regularly assessed for integrity and errors. All data monitoring will be performed completely independently from sponsors and competing interests. An independent data monitoring committee (DMC) will be appointed to critically review data safety in the trial. Veronica Sjöberg (VS) will be responsible for the monitoring of all data collected in the pilot study. A data management plan (DMP) will be outlined by the first author (VS) and implemented by the principal investigator (LV) to ensure sound data structure (folder structure, file naming, organization), and data storing.

DISCUSSION

This article describes a protocol for a R-RCT trial of a novel e-Health intervention. The trial will contribute to establish evidence for the effectiveness of individualized physical activity and exercise among patients living with chronic pain and participating in IPRP. The methodology and feasibility of the trial will be evaluated in an early phase by a pilot study, which will contribute to optimized robustness of the subsequent R-RCT-trial and enable further refinement of the intervention. Despite many efforts have been taken to develop health promoting interventions for this patient group, it is rare that such interventions are systematically developed and includes both objective and patient reported outcomes. The potential measurement errors of self-reported constructs of physical activity are well known and this trial contributes to introducing objective measurement methods in a clinical context. The eVIS-intervention is developed according to MRC´s framework for development and evaluation of complex interventions.[29] It consists of both objectively measured physical activity level (steps/day), and patients own reports on pain intensity, interference on daily activities and individual daily activity goal, all joint in the web application named PATRON. This enables known facilitating mechanisms for behavior change (e.g., as self-monitoring etc.)[32] whilst including several core outcome domains.[34] [76] The agile development process has enabled continuous evaluation and improvement of the intervention based on data provided from patients, clinicians, and researchers in different fields. Objectively measured constructs of physical activity by Fitbit devices have been criticized due to lack of accuracy of measurements of time spent in moderate to vigorous physical activity (MVPA) where various devices overestimate the measurement[77]. Preceding this study, our research group performed an

evaluation of Fitbit Versa´s criterion validity of measuring energy expenditure, heart rate and step count among patients living with chronic pain. Results confirmed previous study results in adjacent patient groups reporting that Fitbit Versa systematically overestimated energy expenditure, however, measurements of step count both in laboratory and in free-living setting were valid.[33]

In this trial participants will be recruited at IPRP units nationally distributed. All units adopt to core IPRP content regarding modalities, but it is well-known that both duration and intensity greatly vary which may limit generalization of the results.[25] To achieve maximum external validity, we will collect data on the specific characteristics of all participating units and include this in the final analyses. Unknown engagement in other out-patient treatments under study period, may be a potential source of bias, though data on in-patient engagement will be known through registry data from the National Patient register. Non-adherence to daily self-report in PATRON can be expected and may differ between intervention- and control group (differential missing). Measures will be taken to optimize adherence in both groups such as regular auditing of registrations in PATRON followed by personal emails with encouragement to follow protocol. To minimize the risk of contamination between groups, and to ensure that the study will be carried out in compliance with the study protocol, all participating staff at the IPRP units will participate in a study-specific course prior entering the trial. Results generated from the pilot study and the subsequent effectiveness trial will inform pain management field with new knowledge on eVIS´s potential to increase pain rehabilitation program´s effectiveness by individualized physical activity levels among patients living with chronic pain.

Harms and adverse events

Participating patients and healthcare staff at the participating IPRP units will be encouraged to report any adverse events such as unexpected side effects or symptom deterioration,[78] which will also be reported to the Swedish Ethical Board Review.

Ethics and dissemination

The trial is prospectively registered in ClinicalTrials.gov (trial registration number NCT05009459) and was approved by the Swedish Ethics Review Board in May 2021 (Dnr 2021/02109). The trial will be conducted in compliance to the Helsinki Declaration.[79] Important

protocol modifications will be communicated to the Swedish Ethics Review Board as well as to all participating IPRP units and participants. To protect confidentiality, all data will be coded by an individual code, and the encryption key will be stored separately. Data will be stored at an intended project server at Dalarna University, which is secured by regular backups. No unauthorized persons will have access to data, e.g., data will only be accessible by researchers in the trial after approval from the principal investigator. Results of the pilot study and the main trial will be submitted for publication in peer-reviewed journals and communicated in national and international research networks, as well as in relevant clinical settings, including patient associations.

Author contribution statement

LV and BÄ are responsible for the conception of the trial. LV is the principal investigator and is involved in all methodological decisions. VS, ET, AM, JW, RLM, BÄ, MH, MB, and LV all contributed to study design and were all involved in the development processes (the evaluation of criterion validity of the wrist-worn activity tracker and the evaluations of the content validity and clinical feasibility) of the intervention. RLM performed the preliminary power and sample size calculations and was involved in all associated decisions. VS wrote the first draft of the manuscript, was responsible for revising the manuscript's intellectual content based on all co-authors conscientious input and conducted manuscript revisions according to peer-reviewer´s comments. All authors read and approved the final version of the manuscript. For this article, no ghost authors, guest authors, or professional writers have or will be used. Author eligibility is and will be based upon the ICMJE Recommendations for the Conduct, Reporting, Editing, and Publication of Scholarly work in Medical Journals.

Trial status

Recruitment of participants was initiated late October 2021 and the trial is planned to be completed on 31 December 2024.

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Competing interests

None declared.

Access to data

This is a protocol describing a trial design. All authors will have access to the final trial dataset.

Supplementary files:

- Completed SPIRIT 2013 Checklist
- Patient consent form (in Swedish)

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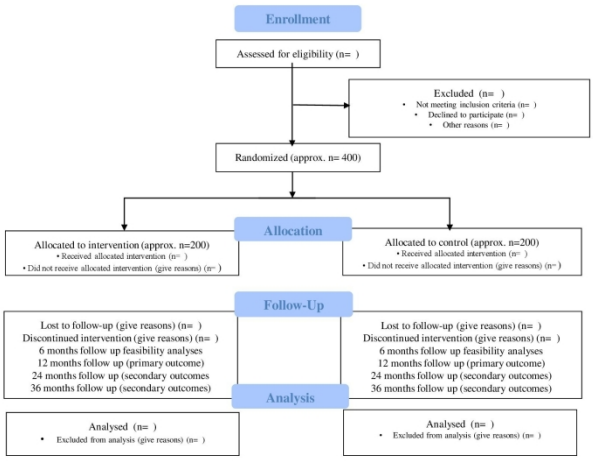

Figure 1. CONSORT 2010 Flow diagram chart of study design and enrollment.

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Figure 2. Schematic illustration of the eVIS-intervention´s three elements: i) the data collection element of physical activity level (steps/day), patient-report of pain interference on daily activities, pain intensity and pharmacological consumption, ii) the visualisation element of collected data in different graphs and compilations of data, and iii) the communication element.

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SPIRIT 2013 Checklist: Recommended items to address in a clinical trial protocol and related documents*

Section/ item	Item No	Description	Page number in Main document (clean copy)
Administrative information			
Title	1	Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym	1
Trial registration	2a	Trial identifier and registry name. If not yet registered, name of intended registry	2, 21
	2b	All items from the World Health Organization Trial Registration Data Set	NA
Protocol version	3	Date and version identifier	2
Funding	4	Sources and types of financial, material, and other support	22
Roles and responsibilities	5a	Names, affiliations, and roles of protocol contributors	1, 22
	5b	Name and contact information for the trial sponsor	22 (not contact info)
	5c	Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities	22
	5d	Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data management team, and other individuals or groups overseeing the trial, if applicable (see Item 21a for data monitoring committee)	19
Introduction			

Background and rationale	6a	Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention	4-6
	6b	Explanation for choice of comparators	16-17
Objectives	7	Specific objectives or hypotheses	5-6, 16-17
Trial design	8	Description of trial design including type of trial (eg, parallel group, crossover, factorial, single group), allocation ratio, and framework (eg, superiority, equivalence, noninferiority, exploratory)	6
Methods: Participants, interventions, and outcomes			
Study setting	9	Description of study settings (eg, community clinic, academic hospital) and list of countries where data will be collected. Reference to where list of study sites can be obtained	6
Eligibility criteria	10	Inclusion and exclusion criteria for participants. If applicable, eligibility criteria for study centres and individuals who will perform the interventions (eg, surgeons, psychotherapists)	6-7
Interventions	11a	Interventions for each group with sufficient detail to allow replication, including how and when they will be administered	7-9
	11b	Criteria for discontinuing or modifying allocated interventions for a given trial participant (eg, drug dose change in response to harms, participant request, or improving/worsening disease)	18-19
	11c	Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return, laboratory tests)	18-19
	11d	Relevant concomitant care and interventions that are permitted or prohibited during the trial	7-8
Outcomes	12	Primary, secondary, and other outcomes, including the specific measurement variable (eg, systolic blood pressure), analysis metric (eg, change from baseline, final value, time to event), method of aggregation (eg, median, proportion), and time point for each outcome. Explanation of the clinical relevance of chosen efficacy and harm outcomes is strongly recommended	9-16 Table 1 Table 2

Participant timeline	13	Time schedule of enrolment, interventions (including any run-ins and washouts), assessments, and visits for participants. A schematic diagram is highly recommended (see Figure)	Table 1 Figure 1
Sample size	14	Estimated number of participants needed to achieve study objectives and how it was determined, including clinical and statistical assumptions supporting any sample size calculations	16-17
Recruitment	15	Strategies for achieving adequate participant enrolment to reach target sample size	7, 18-19
Methods: Assignment of interventions (for controlled trials)			
Allocation:			15
Sequence generation	16 a	Method of generating the allocation sequence (eg, computer-generated random numbers), and list of any factors for stratification. To reduce predictability of a random sequence, details of any planned restriction (eg, blocking) should be provided in a separate document that is unavailable to those who enrol participants or assign interventions	17-18
Allocation concealment mechanism	16 b	Mechanism of implementing the allocation sequence (eg, central telephone; sequentially numbered, opaque, sealed envelopes), describing any steps to conceal the sequence until interventions are assigned	17
Implementation	16 c	Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions	17
Blinding (masking)	17 a	Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how	17
	17 b	If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during the trial	NA
Methods: Data collection, management, and analysis			

Data collection methods	18a	Plans for assessment and collection of outcome, baseline, and other trial data, including any related processes to promote data quality (eg, duplicate measurements, training of assessors) and a description of study instruments (eg, questionnaires, laboratory tests) along with their reliability and validity, if known. Reference to where data collection forms can be found, if not in the protocol	Table 1 9-16
	18b	Plans to promote participant retention and complete follow-up, including list of any outcome data to be collected for participants who discontinue or deviate from intervention protocols	18-19
Data management	19	Plans for data entry, coding, security, and storage, including any related processes to promote data quality (eg, double data entry; range checks for data values). Reference to where details of data management procedures can be found, if not in the protocol	20
Statistical methods	20a	Statistical methods for analysing primary and secondary outcomes. Reference to where other details of the statistical analysis plan can be found, if not in the protocol	19
	20b	Methods for any additional analyses (eg, subgroup and adjusted analyses)	19
	20c	Definition of analysis population relating to protocol non-adherence (eg, as randomised analysis), and any statistical methods to handle missing data (eg, multiple imputation)	19
Methods: Monitoring			
Data monitoring	21a	Composition of data monitoring committee (DMC); summary of its role and reporting structure; statement of whether it is independent from the sponsor and competing interests; and reference to where further details about its charter can be found, if not in the protocol. Alternatively, an explanation of why a DMC is not needed	20
	21b	Description of any interim analyses and stopping guidelines, including who will have access to these interim results and make the final decision to terminate the trial	19
Harms	22	Plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial conduct	21

Auditing	23	Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor	20
Ethics and dissemination			
Research ethics approval	24	Plans for seeking research ethics committee/institutional review board (REC/IRB) approval	18-19
Protocol amendments	25	Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators, REC/IRBs, trial participants, trial registries, journals, regulators)	21-22
Consent or assent	26 a	Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32)	7
	26 b	Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable	NA
Confidentiality	27	How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial	18-19
Declaration of interests	28	Financial and other competing interests for principal investigators for the overall trial and each study site	20
Access to data	29	Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators	20
Ancillary and post-trial care	30	Provisions, if any, for ancillary and post-trial care, and for compensation to those who suffer harm from trial participation	No
Dissemination policy	31 a	Plans for investigators and sponsor to communicate trial results to participants, healthcare professionals, the public, and other relevant groups (eg, via publication, reporting in results databases, or other data sharing arrangements), including any publication restrictions	21-22
	31 b	Authorship eligibility guidelines and any intended use of professional writers	22
	31 c	Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code	23

Appendices			
Informed consent materials	32	Model consent form and other related documentation given to participants and authorised surrogates	See supplementary files [In Swedish]
Biological specimens	33	Plans for collection, laboratory evaluation, and storage of biological specimens for genetic or molecular analysis in the current trial and for future use in ancillary studies, if applicable	NA