

BMJ Open Serious gaming during multidisciplinary rehabilitation for patients with complex chronic pain or fatigue complaints: study protocol for a controlled trial and process evaluation

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ABSTRACT

Introduction Many individuals suffer from chronic pain or functional somatic syndromes and face boundaries for diminishing functional limitations by means of biopsychosocial interventions. Serious gaming could complement multidisciplinary interventions through enjoyment and independent accessibility. A study protocol is presented for studying whether, how, for which patients and under what circumstances, serious gaming improves patient health outcomes during regular multidisciplinary rehabilitation.

Methods and analysis A mixed-methods design is described that prioritises a two-armed naturalistic quasi-experiment. An experimental group is composed of patients who follow serious gaming during an outpatient multidisciplinary programme at two sites of a Dutch rehabilitation centre. Control group patients follow the same programme without serious gaming in two similar sites. Multivariate mixed-modelling analysis is planned for assessing how much variance in 250 patient records of routinely monitored pain intensity, pain coping and cognition, fatigue and psychopathology outcomes is attributable to serious gaming. Embedded qualitative methods include unobtrusive collection and analyses of stakeholder focus group interviews, participant feedback and semistructured patient interviews. Process analyses are carried out by a systematic approach of mixing qualitative and quantitative methods at various stages of the research.

Ethics and dissemination The Ethics Committee of the Tilburg School of Social and Behavioural Sciences approved the research after reviewing the protocol for the protection of patients' interests in conformity to the letter and rationale of the applicable laws and research practice (EC 2016.25t). Findings will be presented in research articles and international scientific conferences.

Trial registration number A prospective research protocol for the naturalistic quasi-experimental outcome evaluation was entered in the Dutch trial register (registration number: NTR6020; Pre-results).

INTRODUCTION

Background and rationale

Video games are vividly debated to their behavioural and clinical outcomes, which

Strengths and limitations of this study

- The novelty of the intervention and study methods is a strength.
- Using a pragmatic approach to study serious gaming when deployed in a regular healthcare setting enables to understand under what conditions serious gaming will (not) work.
- Study limitations come with the naturalistic design, due to pragmatic reasons, that prevents random treatment assignment and stringent diagnostic methods.

may be negative or positive depending on game content and player attributes.^{1,2} Serious (health) games primarily target promotion of health benefits.³ A new serious game, called LAKA, aims to facilitate patient learning about living with complex chronic somatic complaints.⁴ Based on the results of a feasibility study, LAKA is deployed in a regular healthcare setting, as an additional component of outpatient multidisciplinary rehabilitation. The current protocol presents an innovative mixed-methods study for gaining insight into the effectiveness of serious gaming as a complementary modality during regular multidisciplinary rehabilitation.

Using a variety of definitions and measures of pain and disability, the worldwide prevalence estimates for chronic pain range between 7% and 64%.^{5–9} Individuals are in chronic pain (CP) when complaints persist beyond the usual 3 to 6 months of organic recovery.¹⁰ Functional somatic syndromes (FSS) are diagnosed in individuals that seek medical help for functional disturbance and chronic somatic symptoms without a satisfactory explanation by organ pathology

or disease.¹¹ CP and FSS may have a biological explanation in central nervous system sensitisation.^{12–13} Predisposition to these disorders is probably determined by a combination of genetic factors and personality characteristics.^{14–15} Symptom patterns are often precipitated by trauma or social factors.^{16–18} Maladaptive thoughts, feelings and behaviour are assumed to maintain the symptoms.^{17–19–21} Regarding treatment, support has been found for a stepped care approach with active biopsychosocial treatment when monodisciplinary treatments are insufficient.¹⁷ Randomised controlled trials that compared symptoms and functioning after multidisciplinary rehabilitation versus alternative treatments in patients with CP or chronic fatigue syndrome generally reported up to medium-sized differences.^{22–25} Nonetheless, recent research addresses improvement of biopsychosocial intervention models,^{26–27} ‘matching’ and ‘blending’ therapeutic strategies and delivery modes^{28–29} and promotion of patient engagement.³⁰ As such, access, reach, adherence and effectiveness of biopsychosocial interventions may be enhanced.

Serious gaming could be of aid here. Previously investigated strategies are ‘exergaming’ to improve motivation for physical activity,³¹ ‘brain training games’ against dullness in the remediation of cognitive functions,³² ‘virtual reality’ for safety in graded activity or exposure³³ and ‘health behaviour gaming’ for fun while addressing behavioural antecedents.³ In the fields of rehabilitation and pain management, virtual environments have shown promise in reducing acute pain by distraction, or in activity management to restore physical functioning.^{34–35} Despite of promising results for various monodisciplinary applications of gaming and simulation, no evident application seems to exist for supporting biopsychosocial adjustment processes in patients with CP or FSS.^{2–3–32–37} Outcome improvement after treatment in patients with CP or FSS may be mediated by changes in aspects of self (beliefs about illness and fear avoidance, catastrophising and psychological flexibility), coping behaviour and affect.^{38–39} Features that distinguish serious games from traditional modes include covert learning techniques, interactivity, storytelling, sound effects, visuals and ‘debriefings’. They could offer relative benefits for behavioural change processes through distinctive attentional (presence), affective (enjoyment) and metacognitive processes.^{40–43} Further research into gaming mechanisms is needed⁴² and may also inform about how biopsychosocial intervention mechanisms could be strengthened.

However, within the outcome evaluation of multidisciplinary interventions several complicating factors arise. These consist of outcome multidimensionality and dependency on implementation in actual healthcare settings.^{44–45} In other words, characteristics at the levels of organisation, care providers, patients and interventions all affect outcome levels.^{46–47} Therefore, ideally, multiple sources of information are used to evaluate to what extent, for whom, when and under what circumstances an innovation of multidisciplinary treatment

improves outcomes in patients with CP or FSS.^{48–49} For example, some intervention studies show different outcomes of a computer-delivered therapy when applied in different countries.⁵⁰ This is also an important issue for the outcomes of serious gaming, which are clearly sensitive to context factors.^{51–52} Therefore, ‘debriefings’ are suggested as a method for discussing and exploiting game-play experiences and strengthening learning outcomes.⁵³ Previous studies leave uncertainties about how to effectively organise instructional support, that is, via software or delivered by (trained) healthcare staff, via internet or face-to-face, in groups or individually. There is strong consensus that adequately powered clinical trials are needed to determine the effectiveness of serious gaming.^{2–3–37} Moreover, pragmatic trials and realist evaluation principles are needed to determine how serious gaming relates to patient outcomes depending on how it is deployed in actual healthcare settings.

Study aims

Here we describe the protocol for outcome and process evaluations of complementary serious gaming during regular multidisciplinary rehabilitation for patients with CP or FSS, which holds three study aims. The first aim is to investigate the effectiveness of serious gaming as a treatment complement. We question to what extent multidisciplinary rehabilitation with an additional serious gaming component is more effective than multidisciplinary rehabilitation without serious gaming for symptom reduction and clinically relevant improvement. Primarily, interdependent outcome domains of pain, fatigue and emotional functioning (pain intensity, pain coping and cognition, fatigue complaints and psychological distress) are studied, because they are considered to be relevant and plausible for the intervention and population.^{27–45} Secondary outcomes are patients’ impression of overall improvement, general subjective health and satisfaction with functioning and treatment.

Second, we aim to understand which innovation, patient, provider and organisation level factors influence the outcomes of serious gaming for patients. Innovation level factors could be design quality and compatibility with user routines. Patient level facilitators or barriers could be demographic, health status and intervention history factors. Serious gaming outcomes could also depend on complex provider behaviour by attitude, skill and/or time constraints. Finally, outcomes of serious gaming could be influenced by its organisation in a clinical setting. Therefore, we pose the question: what are the barriers and facilitators of outcome improvement through serious gaming according to patients, providers and other stakeholders? Furthermore, we question how variation in serious gaming outcomes can be decomposed with plausible patient level differences and/or delivery conditions within the treatment setting (ie, size of a debriefing group).

The third aim concerns how serious gaming contributes to patient outcomes. For this, we explore various

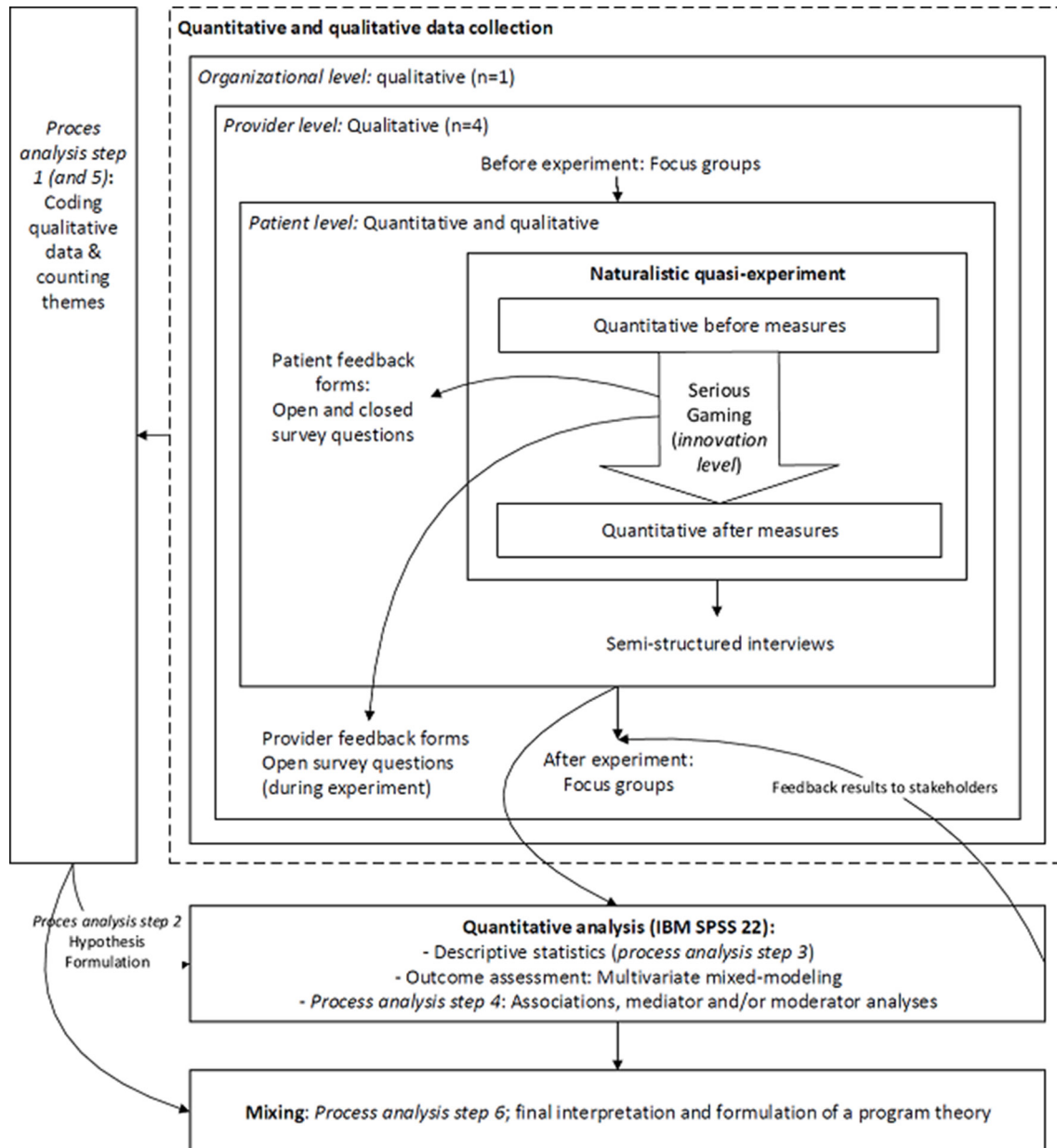


Figure 1 Overview of the mixed-methods design.

serious gaming mechanisms, being the subjective experiences and objective performances in context that may affect health outcomes. In addition, plausible linear effects between mechanisms and patient outcome variables are investigated. Achievement of all three research aims will inform the further development of a valid and practical programme theory of serious gaming outcomes in regular healthcare for patients with CP or FSS.

METHODS AND ANALYSIS

Study design and procedure

An embedded experimental mixed-methods design is created by an integrated multidisciplinary research team (MV, HV, MJ, AZ, AM) to address all three research aims in a single study (see [figure 1](#)). For studying the first research aim, which is to estimate patient level outcome

improvement due to serious gaming during regular outpatient rehabilitation, a two-armed naturalistic quasi-experiment is prioritised (displayed at the centre of [figure 1](#)). A serious gaming intervention is deployed for usage by all patients, at two sites of a Dutch outpatient rehabilitation clinic. Therefore, an intervention group is constituted of patients who receive the multidisciplinary rehabilitation programme with an additional serious gaming intervention. The control group consists of patients who simultaneously follow the same programme in two similar sites of the same clinic without serious gaming. Codified quantitative data from patient records will be retrieved and analysed to examine between group outcome differences. The protocol for the naturalistic quasi-experiment was entered in the Dutch trial register (NTR6020).



Embedding qualitative methods before, concurrently to and after the quasi-experiment suits our second and third study aims. This mixed-method design is ideal for examining intervention processes, understanding mechanisms related to variables and supporting programme theory development.⁵⁴ Herein, no intermediate qualitative results are communicated with providers and implementers during the experiment. Data collection started in April 2016 and is planned to end in March 2017, quantitative outcome data will be retrieved when concurrently collected qualitative data are analysed (February 2017).

Recruitment

Sites and professionals

Two intervention sites where serious gaming is deployed participate in the study. For the recruitment of control subjects, two other sites (out of 18 sites as part of the same treatment centre) are selected based on similarity with regard to patient characteristics, facilities, protocols, history, personnel, location in or near a city in the southern Netherlands, and no other research projects planned during the intervention period. The treatment centre provides rehabilitation care covered by health insurance in association with a university medical centre. Professional study participants are local stakeholders of serious gaming, including experts, implementers and providers.

Patients

Patient candidates received an indication of eligibility for outpatient multidisciplinary rehabilitation from a rehabilitation physician and completed half of their rehabilitation programme at a participating site. Physician indications of eligibility are followed, which are based on the results of diagnostic surveys, physical and psychological investigations and clinical interviewing. Accordingly, patient participant inclusion criteria are: being between 18 and 67 years of age, reporting the presence of pain for more than 6 months or fatigue complaints or a musculoskeletal disease for more than 3 months, having no (more) indication for another (cost-) effective medical treatment and have concomitant psychosocial problems. Patients are excluded from participation if: psychiatric symptoms are not adequately controlled, there is significant risk of psychological decompensation through a rehabilitation treatment, language or communication problems make it impossible to follow rehabilitation and/or demonstrable inability to change behaviour (due to personality disorders, third party liabilities or otherwise). An information letter, consent form and verbal explanation are provided by local care providers. The recruitment process is monitored to ensure that all candidates are invited.

Interventions

Multidisciplinary rehabilitation programme

The outpatient multidisciplinary rehabilitation programme includes common biopsychosocial approaches and incorporates a focus on well-being and

participation.²⁶ The standardised 16-week programme consists of on average 95 hours of individual or group sessions that are organised in modules and centrally assigned to individual patients based on diagnostic findings. Each patient is treated by a team of two physiotherapists and two registered master's degree psychologists. Psychotherapeutic techniques include cognitive behavioural therapy and psychodynamic approaches. For all patients, treatment contains rationales, goal setting and feedback, social support, exposure treatment, behavioural repetition and substitution, skills training (in relaxation, social skills and meditation) and identity development techniques. Allocation of physical therapy, cognitive restructuring, eye movement desensitisation and an intensive 2-day well-being course depend on diagnostic findings for physical status, psychopathological symptoms⁵⁵ and fear avoidance beliefs,⁵⁶ post-traumatic stress and psychological well-being.

Serious gaming

Theory and change techniques of the serious game LAKA

Developer assumptions for the game LAKA have been documented throughout development and related to conceptual frameworks (see appendix).⁵⁷ Serious gaming is proposed to promote practice for well-being improvement and for identifying and diminishing distortions and biases of self. This may be helpful for patients with CP or FSS in reducing the burden of their symptoms.⁵⁸ Based on a review of information about the design rationale, functionality, validity proof (before outcome evaluation) and data protection measures of LAKA, an independent jury awarded three out of five attainable stars for quality (see appendix).⁵⁹

The serious game LAKA promotes practice through an Avatar model. Before the game starts, participants are invited to identify with an Avatar of their chosen gender and name (table 1). The storyline introduces an Avatar who recently experienced physical and social deterioration, senses an urgency to change and engages in a trip around the world to learn about 'the art of living'. Player tasks are: to explore and select virtual action plans for 'encounters' with non-playing characters, to evaluate their 'satisfaction' about chosen actions and to perform skills training in focused attention and open-monitoring meditation exercises.⁶⁰ Encounter scenarios model uncertain events resulting in varying Avatar states depending on action plans chosen by players. Encounters are increasingly influenced by distant cultural meanings to challenge anticipation of the course of events (eg, depending on the scenario, agreeable responding can result in a pleasant interaction or involvement in a scam). Players receive global feedback on the extent to which chosen actions correspond with a reference model for values (see appendix). Self-reflective elements are interspersed with short casual action and puzzle games, images and information associated with the location of the Avatar. These

**Table 1** Features, dose and tasks

Features	Dose (in game frequency)	Tasks
Introduction	1	<ul style="list-style-type: none"> – Choose Avatar gender and name – Receive instruction: to identify with the personal Avatar – Introduction to Avatar storyline – Receive task instructions from LAKA (non-playing character with a mentoring role)
Encounters (see online supplementary appendix 1) for screenshot and user interface)	16	– Select action plans for the Avatar in encounters with non-playing characters (each instance offers five optional action plans, which are modelled after a reference set of values: generosity, moral discipline, patience, enthusiastic perseverance).
Mood scenarios	8	<ul style="list-style-type: none"> – Select action plans for the Avatar when subjected to an adverse event. – Given the adverse scenario: think of what your own affective state would be in this situation and bear in mind the depicted emotional state of the Avatar.
Reflections	4	<ul style="list-style-type: none"> – Assess satisfaction about selected Avatar actions on a scale of 0–10. – Receive feedback from LAKA on chosen action plans. – Receive feedback about the correspondence between satisfaction rating and LAKA assessment.
Attention training	3	– Guided (focused attention and open-monitoring) meditation exercises for mental stability.
Tours	16	– Skip or listen to ‘tour-guide’ voice-overs informing about pictures of the location visited by the Avatar.
Loading screens	-	– See where travel destinations are located on a geographical map.
Mini games	8	<ul style="list-style-type: none"> – Action games: steering a vehicle (by using tilt mechanism of tablet pc or keyboard arrow controls) to arrive at the next encounter (reference: ‘rocket bird’). – Puzzle: fix a road by connecting parts of the road to arrive at the next encounter (reference: ‘plumber games’).
Festive closing	1	– Replay of ‘extreme’ responses throughout the game.

features are included to vary game play, and can be skipped.

Mode of delivery

In accordance with patient suggestions for optimal reach, the rehabilitation clinic delivers professional assistance and the occasion for playing the serious game LAKA on site, besides downloading and playing on a home computer.⁴ Suitable rooms with Wi-Fi connection, tablet computers with LAKA installed and headphones are provided. Four 1-hour sessions of serious gaming are planned for one to six patients simultaneously during weeks 9–12 of their rehabilitation programme. The sessions are scheduled in connection with other therapy sessions to ease coordination with daily activities. Staff members are available for consultation on accessing serious gaming (ie, for technical issues and adaptation to special needs). Experienced therapists (one physiotherapist, and three psychologists) facilitate the first session (introduce LAKA and instruct to complete the game independently during sessions 2 and 3) and the fourth session (debriefing). The goal of the debriefings is to discuss experiences of game play, technology acceptance and learning transfer to daily life. For external validity, no specific roles were assigned to other local stakeholders for the delivery of

serious gaming (ie, to observe ‘natural’ problem solving by implementers).

Programme theory

The framework of context, mechanism, outcome (CMO) configurations is used to structure ongoing development of a programme theory for serious gaming as a complement during multidisciplinary rehabilitation.⁶¹ To illustrate, a patient with an active coping style self-exposed for a short amount of time to unsupported serious gaming during multidisciplinary rehabilitation (context), experienced enjoyment and discrepancy regarding valued self-identities (mechanism) and expected this to contribute to health improvement (outcome).⁴ Timely building blocks for CMO configurations for serious gaming are deduced from the literature. Besides by symptom categorisation, serious gaming outcomes were interpreted by frameworks of rehabilitation mechanisms as self-improvements (see online supplementary appendix 1).^{27 45 57 58 62 63} Two comprehensive implementation models are used for the classification of context factors, such as planning and compatibility relative to other treatment components.^{64 65} Finally, mechanisms of serious gaming are discerned as gaming behaviours (frequency, length and performance of game play) and user experiences of gaming, simulation and information systems. More specifically, subjective

Table 2 Quantitative outcome measures

Variables	Measures	Time of measurement
Primary outcomes		
Current pain intensity	1-item Numerical Rating Scale 0–10	Baseline, intermediate, post-treatment
Pain coping and cognition	Pain Coping and Cognitions List	
Fatigue	Checklist Individual Strength	
Psychopathological symptoms	Symptom Check List	
Secondary outcomes		
Clinically relevant improvement	Patient Global Impression of Change	Intermediate, post-treatment
General subjective health	“What do you think of your current health in general?”	
Perceived functioning	“Please indicate how satisfied you are with your current level of functioning.”	
Treatment satisfaction	Three Likert scale items, that is, “Would you recommend this treatment centre to other rehabilitation patients?”	Post-treatment

Patient variables are demographic, health status and treatment history information (see [table 3](#)).

mechanisms may involve sense of presence,⁶⁶ technology acceptance,⁶⁷ positive and negative affect,⁶⁸ game-based learning⁶⁹ and perceived ‘learning transfer’ to daily life.⁵³

Measures

Quantitative data

Outcome and case-mix variables are retrieved from routinely administered clinical patient records after all participants have completed their rehabilitation programme. All patient variables are collected by the clinic through a standardised and secured web-surveying procedure, including facilitation of patients without convenient computer access and promotion of follow-up completion.^{4 70} Outcomes are monitored at the indication of eligibility (at baseline), after 8 weeks of treatment (intermediate) and again after 16 weeks of treatment

(post). Relevant and valid measures were available for assessing the primary outcomes (see [table 2](#)). These endpoints include a numerical rating scale for current pain intensity,⁷¹ the pain coping and cognitions list,⁷² fatigue as assessed by the Checklist Individual Strength⁶³ and psychopathological symptoms as measured by the Symptom Checklist.⁵⁵ Secondary measures focus on clinical relevance, such as patients’ global impression of improvement after treatment.⁴⁵ Another widely used single item Likert scale rating is used for measuring general health (poor to excellent).⁷³ Finally, numerical rating scale items are available to assess patients’ satisfaction about treatment and functioning (see [table 2](#)).

Intervention mechanisms may cover subjective experiences and objective behaviours of serious gaming (see

Table 3 Patient characteristics

Variables	Variables (measurement)
Age	Years of age (calculated from registered date of birth)
Gender	% Female
Socioeconomic status	Highest education level, source of income (categorical rating items)
Coping style	Utrecht Coping List ⁸¹ (validated questionnaire)
Environment	Presence of problems with regard to social life, financial situation, trauma, work situation (categorical rating items)
Symptoms	Duration (months; calculated from the date of onset), course (categorical rating item) and pain location (standard physical examination report)
Physical status	Body mass index, blood pressure, musculoskeletal conditions (standard physical examination report)
Other treatment	(Changes of) presence of medication usage, frequency of healthcare visits, previous visits to health providers (medical specialists, physiotherapists and/or psychologist) (categorical rating items)
Treatment (modules) received	Automatic logs of session presence (determined from absence registrations by healthcare providers)

**Table 4** Quantitative indicators for mechanisms

Variables	Measures	Respondents	Time of measurement
Reach, dose, gaming performance	Data logs: frequency, timing, length, progress and scores of play	Intervention group	During serious gaming (automatic)
Acceptability and playability	Selection of UTAUT2* items (perceived usefulness, ease of use, trust, enjoyment) Selection of EGameFlow items (clear goals, challenge, perceived learning)	Intervention group	Post-serious gaming
Positive and negative affect	PANAS-SF	Intervention group	Post-serious gaming
Presence (general, involvement and realism)	Igroup Sense of Presence Questionnaire item for general sense of presence and subscales for involvement and realism.	Intervention group	Post-serious gaming
Learning transfer	Numerical rating scale (0–10): “Use the following slider to indicate to what extent you expect that the LAKA sessions contribute to your daily life”.	Intervention group	Post-serious gaming
Values (expressed in thoughts and behaviour)	Values questionnaire†: 5-point Likert scales, that is, “If I find it necessary, I'll intervene to help or to protect others”.	Intervention and control groups	Baseline, intermediate, post-treatment

*Unified theory of acceptance and use of technology.

†Psychometric properties are still under investigation. Empirical support for good scale internal consistency and strong associations with psychological well-being in rehabilitating patients were documented in a report for the Dutch Committee on Test Affairs (COTAN). PANAS-SF, Positive and Negative Affect Scale—Short Form.

table 4). Automatic registrations in patient files enable objective assessment of serious gaming frequency, duration, progress and performance. Moreover, a short survey was composed in collaboration with the rehabilitation centre to measure subjective experiences shortly after serious gaming. This survey contains items on perceptions of using a serious game (regarding usefulness, ease of use, trust, enjoyment, goal clarity, challenge and learning^{4 67 69}), the 10-item short form of the positive and negative affect scale,⁷⁴ the involvement and realism scales from the Igroup Presence Questionnaire⁶⁶ and (0–10) numerical rating scale item on perceived learning transfer. A reminder was sent to intervention group participants if the survey was not completed within a week after their last gaming session. Finally, a questionnaire on patient values may be used to explore relationships between mechanisms and outcomes of serious gaming.

Qualitative data

Protocols for focus group and semistructured patient interviews are informed by the CMO building blocks and principles for interviewing in realist evaluation.⁷⁵ Accordingly, the interviewer starts with an open and explorative style, but may sometimes take an explanatory role to raise discussion about programme theory elements when CMO configurations become better delineated. Providers are expected to be especially knowledgeable about context and mechanisms of serious gaming, while patients may say the most about context and outcomes. Purposive sampling of participants is used until reaching a point of data saturation.

All interviews are tape recorded and verbatim transcribed. Transcripts and a summary of findings are sent to participants by e-mail to enable them to check if their views are accurately reflected.

Stakeholder (focus group) interviewing

Four focus group interviews are held, two before and two after the naturalistic experiment, to involve stakeholders in the ongoing development of serious gaming and programme theory. Participant selection and topics are based on actual data needs. Heterogeneous groups of care providers, implementers and experts (in information and communication technology, well-being and serious gaming) are invited for the first and last discussion meetings. The first interview focused on the research goals for an open discussion. The last group interview will focus on programme theory for member checking and refinement. Homogenous groups of provider participants may be invited for the second and third focus groups for more in-depth information. Provider participants are asked to share positive and/or negative feedback about serious gaming via a secured web form. This includes information on the occurrence and management of adverse events and/or unintended effects during serious gaming.

Patient interviewing

Two open interview questions about gaming experience and perceived learning transfer are added to the post-gaming survey for intervention group participants. Patient participants with high and low scores on a 1-item numerical rating scale (0–10) for perceived learning transfer are invited for a semistructured interview after their



rehabilitation treatment. These interviewees are asked to describe their health outcomes during rehabilitation and to list the three most important reasons why serious gaming did, or did not, contribute positively or negatively to this process. A point of saturation is reached if the three factors (context and/or mechanisms) mentioned are all richly described. Control group interviewees are matched to some of the intervention group interviewees to compare rehabilitation outcome changes for similar cases with versus without serious gaming.

Analysis

Statistical outcome evaluation

Quantitative data will be imported in SPSS V.22, described after statistical inferences and analysed on intention-to-treat basis. All case-mix variables are described for individual study participants, as well as the differences between intervention group and control group participants. Multivariate mixed-linear modelling techniques will be used to evaluate the extent to which serious gaming predicts variance in patient outcome levels between the intermediate and final outcome assessments of the rehabilitation programme. Effective sample size and intraclass coefficients will be calculated to determine dependency on hierarchical patterns in outcome variation by care provider levels. An optimal prediction model will be specified, correcting for potential unbalances between the study groups (at baseline and/or intermediate) and/or important higher level random effects.

Process analyses

A programme theory will be created after a sequence of analysis steps. In each step, analyses will be performed completely by MV and in part by MJ or AZ (independent coding of interviews and rerunning syntax), and discussions will be held involving a third author (HV) to resolve differences and find agreement about the results. First, concurrently collected qualitative data analyses will be performed to identify plausible CMO configurations from the perspectives stakeholders. All qualitative data will be coded in vivo and higher order coded using CMO building blocks to determine configurations. Second, a selection of key CMO configurations will be made based on counts of the number of participants supporting them in their open text responses to the postgaming survey. Hypotheses will contain specific expectations of (linear) relationships implied by the CMOs. If needed, additional provider or site level data (ie, debriefing session group sizes) will be retrieved from clinical administration records. Third, quantitative data will be screened by testing internal consistency in SPSS or data triangulation with qualitative data if possible. Fourth, hypotheses will be tested with available and valid quantitative data. Fifth, data from the last focus group will be coded. Sixth, quantitative and qualitative findings will be mixed for an overall interpretation and drawing final conclusions.

Power calculation

From practical, theoretical and statistical perspectives, a powerful primary outcome assessment was anticipated by focusing on recruiting a sufficient number of individual patients from the four participating treatment facilities. The rehabilitation centre (n=1), intervention sites (n=2), as well as the number of time-points (3), are practically fixed. Analysis of unpublished pilot data suggested that variation in baseline to post-treatment outcome changes between treatment locations might be negligible relative to individual variation within sites (intraclass correlations <0.05).

G*Power was used for sample-size calculations.⁷⁶ A required sample size of 212 participants was calculated for determining a small to medium effect by means of a multivariate analysis of variance test of global effects. Effect size estimation was based on meta-analysis results for the effects of serious games on cognition, motivation and psychological outcomes.³ The following parameters were inserted: for power (1-Beta)=0.8; effect-size $f^2(V)=0.0625$; type 2 error probability (alpha)=0.05; number of dependent variables=5; and number of groups=2. By the same standards, it was checked if the determined sample size would also be sufficient for independent univariate tests of variance on each of the primary outcomes.

Anticipating some level dependence and/or randomly missing data (pain coping and cognition measures are not filled out by patients reporting 0 pain intensity at baseline), 250 patient participants will be recruited. Assuming 20% treatment and study attrition rates and an average weekly inflow of nine patients starting with their treatment within each of the four facilities, outcome data are available 6 months after recruiting the first patient.

ETHICS AND DISSEMINATION

Ethical approval for the mixed-methods protocol was obtained from the psychological ethics committee of Tilburg School of Social and Behavioural Sciences (EC-2016.25t). In the absence of a legal obligation for medical ethics review, independent judgement was provided on the protection of patient rights by conformity to the letter and rationale of the applicable laws and research practice. Patient participants are consented before participation, that is before receiving the additional (5–10 min) survey (intervention group), being invited for a semistructured interview or retrieving their codified data. Participants were protected against harm by regular clinical safety measures throughout. Professional participants are also consented before participation in qualitative data collections. Under supervision of MJ, MV is responsible for safe storage and the accessibility of (codified) research data to all authors. Qualitative and quantitative results will be presented and discussed together in one or more research article(s) and at one or more international



scientific conferences. A summary of study results will be provided to the study participants.

DISCUSSION

The novelty of the serious gaming intervention and study methods are strengths of the proposed evaluation but imply limitations as well. LAKA is the first serious game that promotes practice for self-process enhancement under highly prevalent adverse conditions such as CP or FSS. CMO configurations may be identified that are transferable to other populations and settings where similar approaches to behavioural change are beneficial.⁷⁷ However, internal and external validity are threatened due to divergence from the golden standard procedures of a (cluster) randomised controlled (multicentre) trial. Instead, pragmatic considerations for the deployment of serious gaming during rehabilitation in two sites of a single Dutch centre led treatment allocation, recruitment and data collection methods. Different comparisons with serious gaming (ie, usual care, waiting list or text-based computer-based intervention), more elaborate diagnostic assessment and outcome measurements including role participation and long-term follow-up are precluded. Still, conditional optimisation of quasi-experimental methods is a legitimate strategy for obtaining evidence on the effectiveness of an intervention.⁷⁸ Apparent confounding factors (ie, differences in usual treatment received) should be controlled for by appropriate methods. By the emergence of practical limitations, study strengths shift towards dealing with questions of process. The realist evaluation principles and mixed-methods used in this study are increasingly accepted in scientific communities as means to compensate for practical limitations and to build programme theories that enhance future predictions of intervention effects across patients and healthcare settings.

Legitimate application of mixed methods is promoted by the protocol in various ways. First, participant recruitment and selection methods for quantitative and qualitative examinations allow a strong representation of patients receiving biopsychosocial treatment in a regular outpatient setting. This differs from studies in which the eligibility of applicants for computer-based intervention depends on motivation and/or ability to use a computer or internet facilities.^{79 80} Second, perspectives of insiders (patients, healthcare providers and developers) and outsiders (independent experts and members of the research team) will be used. Third, relevant theoretical constructs are specified before quantitative and qualitative data collections to prevent process analysis results being strongly affected by the sequencing of qualitative and quantitative methods. Fourth, predefined steps structure data convergence and switches in epistemological paradigms when qualitative methods are used to propose quantitative results (in advance) and to explain them (afterwards).

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Correction notice This paper has been amended since it was published Online First. Owing to a scripting error, some of the publisher names in the references were replaced with 'BMJ Publishing Group'. This only affected the full text version, not the PDF. We have since corrected these errors and the correct publishers have been inserted into the references.

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Contributors MV, HV, AM, and MJ conceived the protocol. MV drafted the work, which was critically revisited by HV, AZ, AM and MJ for important intellectual content. All authors have given their final approval of the version to be published and agree to be accountable for all aspects of the work.

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Serious gaming during multidisciplinary rehabilitation for patients with complex chronic pain or fatigue complaints: study protocol for a controlled trial and process evaluation

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