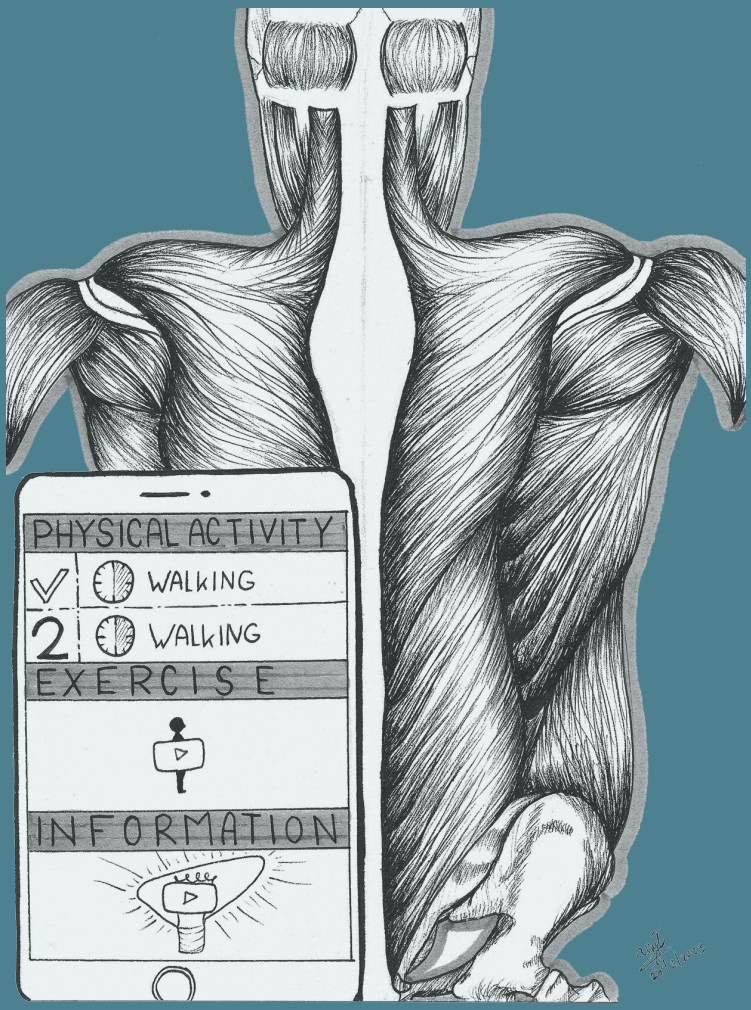
e-Exercise Low Back Pain

Stratified blended physiotherapy for patients with nonspecific low back pain



TJARCO KOPPENAAL

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e-Exercise Low Back Pain: Stratified blended physiotherapy for patients with nonspecific low back pain
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e-Exercise Low Back Pain

Stratified blended physiotherapy for patients with nonspecific low back pain

e-Exercise Lage Rugpijn

Gestratificeerde blended fysiotherapie voor patiënten met aspecifieke lage rugpijn
(met een samenvatting in het Nederlands)

Proefschrift

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Jacob Theodoor Koppenaal

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te Groningen

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“If I have seen further it is by standing on the shoulders of Giants”

– Isaac Newton (1642-1726) –

Voor Pa

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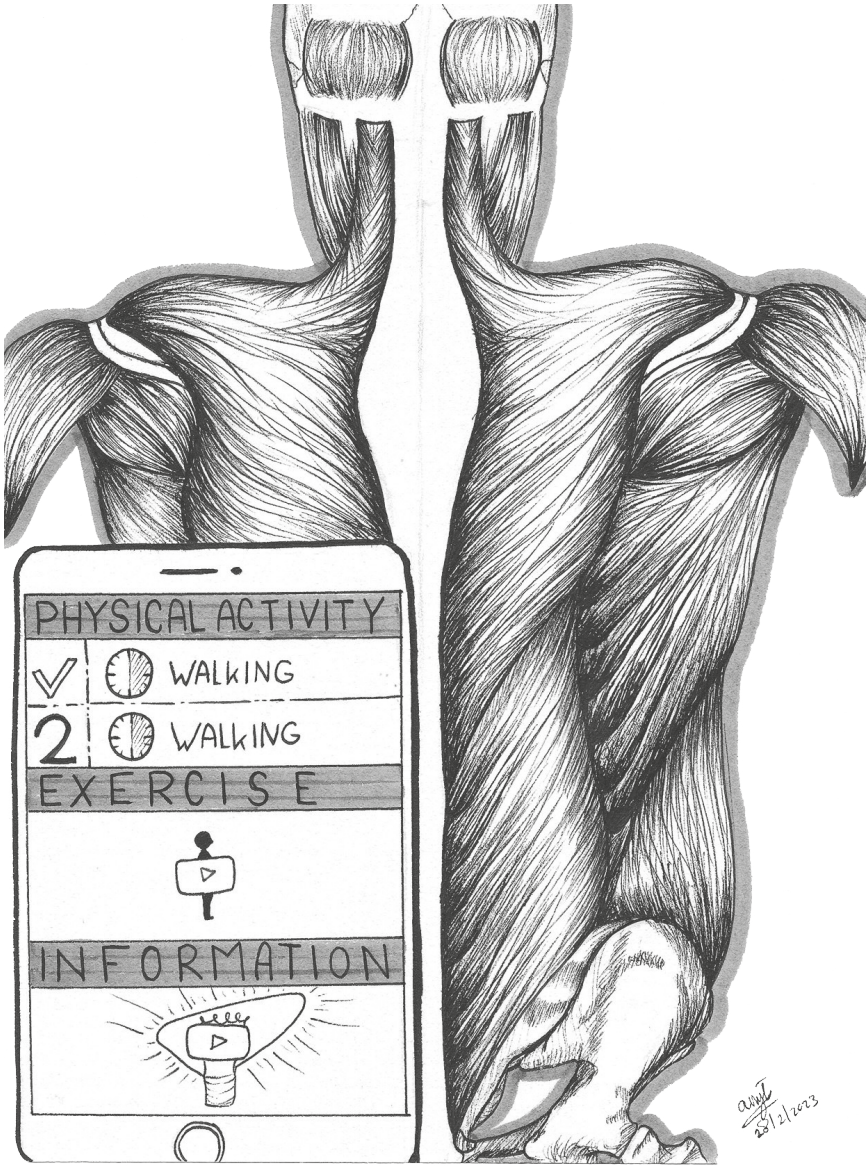
PHYSICAL ACTIVITY
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WALKING
EXERCISE
INFORMATION

1

General introduction

Authorship statement

The idea and set-up of the general introduction were mine; I conducted the literature search and wrote the general introduction. During the whole process I asked for and implemented input and feedback from my supervisory team.

Nonspecific low back pain – Epidemiology and definition

Low back pain (LBP) is a leading contributor to the global burden of years lived with disabilities, and this burden is rising due to the increasing and ageing population[1]. The annual prevalence of activity-limiting LBP is estimated to be 1.4-20% in adults living in high-income countries. Among all adults, 50-80% experience one or more episodes of activity-limiting LBP during their lifetime[2,3].

LBP is considered to be a symptom rather than a disease and is defined as the occurrence of pain in the lumbosacral region between the lower ribs and the buttock creases and is occasionally associated with neurological symptoms in the buttocks or legs[4]. Similar to other symptoms, e.g., headache or dizziness, LBP can have many causes and can result from a number of known or unknown abnormalities or diseases. There are two common forms of LBP: specific LBP and nonspecific LBP. A small proportion of patients with LBP have specific LBP, which can be caused by a specific pathology or trauma, e.g., by a malignancy, vertebral fracture, or inflammatory disorder. However, approximately 90% of patients have nonspecific LBP, meaning that no specific patho-anatomical cause of the pain can be determined[5,6].

Nonspecific LBP is a common condition and recurrent episodes occur frequently. It is one of the most common reasons for a patient to consult primary care[7]. In the Netherlands and in many other countries, patients with nonspecific LBP have direct access to primary care, and consultation or treatment by a general practitioner and/or a physiotherapist is common[8,9]. This thesis focuses on the primary care physiotherapy treatment of patients with nonspecific LBP.

Nonspecific low back pain – Prognosis

In recent years, nonspecific LBP has been increasingly classified as a long-lasting condition featuring a variable clinical course rather than separated and unrelated episodes[10,11]. Approximately half of patients suffering from nonspecific LBP in the context of primary care experience low-to-moderate ongoing or fluctuating pain, while other patients rapidly or gradually recover, and yet other patients develop persistent severe LBP (Figure 1)[10,11].

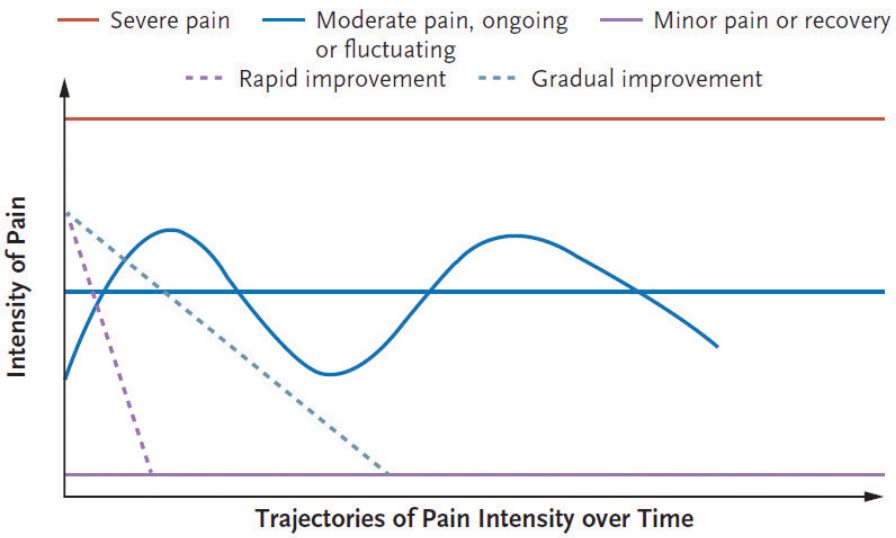

Figure 1. Simplified principal trajectories of pain intensity among patients with LBP (adapted from Kongsted et al.[10])

There is strong evidence to suggest that most episodes of nonspecific LBP improve considerably within a period as brief as a matter of days or as long as six weeks[12]. However, 66% of primary care patients with nonspecific LBP experience some degree of pain after three months, and as many as 65% of such patients continue to experience some degree of pain one year after onset[12,13]. In addition, recurring episodes of nonspecific LBP are common. Approximately 33% of these patients experience a recurrent episode of nonspecific LBP within one year, and 40% experience activity limitations or consult a healthcare professional due to recurring episodes[14]. Factors that contribute to the development of persistent disabling LBP are diverse and include biological, psychological, societal, and work-related factors. The prognostic factors of older age, poor general health, increased psychological or psychosocial stress, poor relations with colleagues, physically heavy work, worse baseline functional disability, sciatica, and the presence of social/work compensation were consistently associated with poor outcomes[15]. However, models to predict LBP outcome in individual patients are heterogeneous, and on average, the explained variance of these models is low[16,17]. As a result, it remains unclear which prognostic factors, or combination of factors, truly contribute to the development of persistent disabling LBP.

Nonspecific low back pain – Management

By definition, in nonspecific LBP a specific patho-anatomical cause cannot be identified. As a result, there are no specific treatments that can be provided. Instead, primary care management by the general practitioner and/or the physiotherapist focuses on reducing pain and its associated disability. Many national and international clinical LBP guidelines

recommend a similar evidence-based primary care approach to the management of nonspecific LBP. In general, recommendations include the use of a biopsychosocial framework and a nonpharmacological approach, including patient education and advice concerning returning to normal activities, to guide the management of nonspecific LBP. For patients who are at risk of developing persistent LBP, the prescription of home-based exercises and/or supervised exercise therapy and psychological treatments is recommended[6,18–22].

To provide more detail, early physiotherapy management for all patients with nonspecific LBP should comprise advice concerning the nonspecific nature of LBP, reassurance that a medically serious cause for LBP is highly unlikely, promotion of self-management, and encouragement to stay active, i.e., by continuing to engage in ordinary activities and work routines[18,21,22]. During the early stages of management, supervised exercise therapy by a physiotherapist is only needed when patients' progress is slow or when a patient is at risk of developing persistent LBP[23].

Long-term physiotherapy management for patients with nonspecific LBP should focus on improving physical functioning and reducing LBP-related pain and disability. A key feature of long-term physiotherapy management is exercise therapy, either on its own or combined with education focusing on the patients' individual needs, which is tailored to the patients' capabilities[18,22–25]. Supplementary passive management options, e.g., manipulation, massage or mobilization therapy by a physiotherapist, can be considered for patients who do not respond to initial treatment[18,22]. Furthermore, psychological treatment, e.g., graded activity or cognitive behavioural therapy, can be considered an option for the long-term management of patients with persistent nonspecific LBP who do not respond to other treatment options[18,21,22].

Nonspecific low back pain – Costs

The costs of LBP related to healthcare use and productivity loss in the context of paid work, e.g., due to absences from work and reduced productivity at work, are enormous[26]. In 2017, the annual costs of neck pain and LBP within the healthcare sector in the Netherlands were estimated to be 937 million Euros. That is, almost 14% of the healthcare costs incurred due to musculoskeletal complaints and approximately 1% of the total healthcare costs in the Netherlands in 2017. Of these annual costs, approximately 114 million Euros were made in primary care, approximately 583 million Euros were made in secondary care, approximately 102 million Euros were made in alternative medicine, and approximately 79 million Euros were made as medication expenditures. For the total costs of neck pain and LBP made in primary care, approximately 75 million Euros were spent by patients for care given by the general practitioner care, and approximately 37 million Euros were spent for care given by the physiotherapist[27]. In 2020, when a patient with LBP was treated by a physiotherapist,

the reported average number of face-to-face sessions was 6.7, and the reported average treatment duration was 13.2 weeks[28].

Nonspecific low back pain – Challenges in management

Physiotherapy is considered a valuable aspect of the recommended primary care management of nonspecific LBP[18–22]. Early referral to guideline adherent physiotherapy for patients with nonspecific LBP has been shown to be able to lower health care utilization and costs[29]. However, the effect sizes of physiotherapy in patients with nonspecific LBP are typically small[6,19,25,30]. To illustrate, among adults with recent-onset of nonspecific LBP, early physiotherapy did result in a statistically significant improvement in disability; however, the improvement was modest and did not surpass the minimum clinically important difference compared with usual care, i.e., education about the favourable prognosis of nonspecific LBP and the advice to remain active[31]. The current challenge is to optimize the available treatment strategies to increase the effectiveness of physiotherapy in patients with nonspecific LBP and reduce the socioeconomic burden of nonspecific LBP. Careful consideration of which patients can benefit from physiotherapy for nonspecific LBP, how to tailor treatment to modifiable risk factors to prevent the development of persistent nonspecific LBP, and how to support patients' adherence to recommended management is needed to be able to design the optimal care process for individual patients with nonspecific LBP. These challenges are perfectly in line with the current transition of the Dutch healthcare policy towards adequate insured health care services for everyone in the Netherlands, i.e., in Dutch "*passende zorg*", to be able to maintain the accessibility and quality of affordable healthcare for all patients[32,33].

Current clinical guidelines on the primary care management of nonspecific LBP have emphasized three topics that can potentially optimize the effectiveness of physiotherapy in patients with nonspecific LBP, i.e., (1) a patient-centred approach, (2) stimulating patients' self-management, and (3) supporting patients' adherence to prescribed management[34–36].

First, a patient-centred approach for the management of nonspecific LBP ensures that management is focussed on the individual patients' context and modifiable risk factors related to the development of persistent nonspecific LBP[35,36]. As a result, the patient will feel empowered and will acquire the skills and knowledge to develop a long-term strategy to actively manage his nonspecific LBP instead of a short-term cure for the problem[19,37]. In the past decade, a stratified primary care approach for nonspecific LBP has gained increasing attention, and this approach can be useful to facilitate patient-centred management of nonspecific LBP. As part of a stratified care approach, a screening tool is used to determine the patients' risk of developing persistent LBP. Based on the results of this initial screening, treatment is adapted to the patients' risk of developing persistent LBP. An example of a screening tool for identifying patients at

risk of delayed recovery, which is suggested in the most recent LBP guideline of the royal Dutch Society for Physiotherapy, is the Keele STarT Back Screening Tool[22,38]. Although inconclusive, research from the United Kingdom suggests that such a stratified primary care approach could improve physical functioning and satisfaction with care among patients with LBP while possibly reducing the costs of healthcare in both physiotherapy[39] and primary care settings[40,41].

Second, since nonspecific LBP has been increasingly recognized as a long-lasting condition with a variable clinical course, it is essential for patients with nonspecific LBP to be guided towards self-management[10,11,19,21]. Self-management is defined as "the ability to manage symptoms, treatment, physical and psychosocial consequences, and lifestyle changes inherent in living with a chronic condition"[42]. Stimulating patients' self-management skills can help empower patients to take responsibility for their long-lasting conditions, temporary acute complaints and recurrent episodes and can allow them to manage their own health on a daily basis[36,43]. Consequently, an improvement in patients' self-management skills can help to reduce the burdens of nonspecific LBP by reducing care-seeking behaviour, the costs associated with treatment, and the costs associated with taking time off work[44]. From previous studies, we know that adequate self-management skills are effective in reducing pain and symptoms and improving physical functioning and quality of life for different types of chronic diseases, e.g., cancer, chronic obstructive pulmonary disease, knee osteoarthritis, and chronic LBP[45–50]. In addition, some evidence has suggested that self-management support interventions can reduce health service utilization without compromising patient health outcomes[51].

Finally, the effectiveness of physiotherapy in patients with nonspecific LBP also depends on patient adherence to prescribed (home) exercises and recommended physical activities. Previous research has shown that 45% to 70% of patients do not adhere to prescribed exercises and physical activity recommendations, whereas adherent patients with LBP have a reduced risk of recurrent episodes of nonspecific LBP[52–55]. In addition, poor adherence to exercise can have implications for treatment effectiveness and costs[56]. Several systematic reviews have investigated the different factors that contribute to patient adherence. For example, both Jack et al.[57] and Essery et al.[52] found strong evidence that poor adherence can be due to patient-related factors, including low motivation, pain, poor self-efficacy, limited past experience with exercise, and reduced social support. Additionally, the benefits of home-exercise programs may not be immediately recognized by patients.

Blended care – Advantages of integrating an app into face-to-face physiotherapy

An emerging strategy for optimizing primary care physiotherapy management for patients with nonspecific LBP is the application of eHealth. EHealth is defined as "the use of information and communication technology in support of health and health-related fields"[58]. The integration of online applications, such as websites and apps, into face-

to-face care provided by a physiotherapist, i.e., so-called “blended care”, is promising and offers several advantages to overcome the previously reported challenges in the management of patients with nonspecific LBP[59,60]:

First, the design of an app has the potential to stimulate patients’ self-management and encourage adherence to prescribed (home) exercises and recommended physical activities[59,61,62]. According to the Capability Opportunity Motivation-Behaviour (COM-B) model (Figure 2)[63,64], behaviour occurs when the following three factors are obtained: (1) the capability to perform the behaviour (e.g., physical strength, knowledge, skills, and stamina), (2) the opportunity to perform the behaviour (e.g., physical accessibility, affordability, social acceptability, and sufficient time), and (3) sufficiently strong motivation to perform the behaviour. Online applications, e.g., websites and apps, have the capacity to influence these three factors via persuasive design features, i.e., interactive information technology designed to change users’ attitudes or behaviours[59,65,66]. Persuasively designed online applications can offer dialogue support and system credibility support. Dialogue support aims to keep the patient active and motivated to use the online application in a manner that can ensure that the user continues to perform the intended behaviour. This task can be accomplished by means of features such as personalized feedback concerning user performance, rewards for performing certain behaviours, and reminders[59,65,67]. Furthermore, online applications can also be persuasive by providing credible and verifiable information concerning a health condition in question, i.e., in the form of system credibility support. For example, self-management information pertaining to nonspecific LBP can be provided by an authority such as a physiotherapist, patient or opinion leader[59,65].

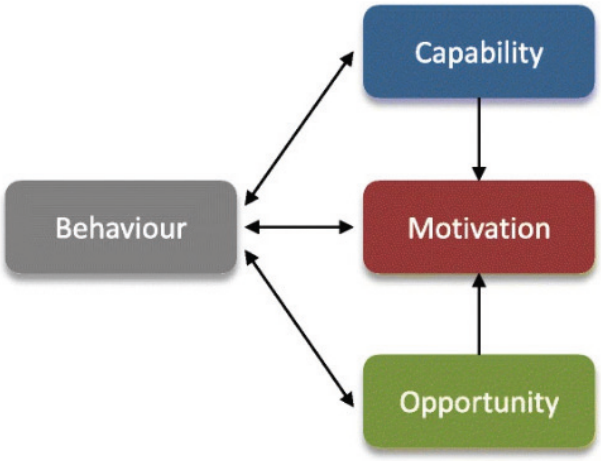

Figure 2. Capability Opportunity Motivation-Behaviour (COM-B) model

Second, apps have the possibility of stimulating patients' self-management and exercise adherence anytime and anywhere, whereas face-to-face guidance by a physiotherapist is limited to a certain number of sessions and specific appointments. The opportunity for patients to have constant access to the online component of their intervention was positively perceived by patients in a previous study of blended physiotherapy intervention for patients with osteoarthritis[68,69]. Patients indicated that they had the ability to continue their treatment between face-to-face sessions in a structured way in the context of their home environment, which improved adherence and continuity of care. In addition, from previous studies, we know that online applications using personalized exercise programs, video instructions and reminders to exercise can increase adherence to exercise recommendations, provide guidance concerning the quality of patient performance, facilitate remote support, and help improve therapist-patient interactions in the context of home-based exercising[61,70].

Finally, the integration of an app into face-to-face care enables patients' individual health behaviour to be monitored between face-to-face sessions. As a result, the physiotherapist is provided with information that can improve his or her ability to coach the patient and to optimize and tailor face-to-face care to the patients' individual needs[62,71,72]. Taking into account patients' individual context, knowledge, needs, goals, progress and preferences will improve patient-centred care and help to build patients' self-efficacy to take control in the management of their complaints and ultimately be responsible for their personal health[36,37,73].

To date, several related systematic reviews and meta-analyses have been published concerning the added value of online self-management interventions for nonspecific LBP. However, these studies have predominantly focussed on nonblended interventions, i.e., independent online applications without face-to-face guidance from a health care professional[74–78]. For example, Machado et al.[75] reviewed apps aimed at the self-management of LBP and evaluated the quality of their content. Nicholl et al.[74] summarized the evidence concerning the use of digital strategies to support the self-management of LBP. Dario et al.[76], Garg et al.[78], and Du et al.[77] all investigated whether online self-management interventions were effective in improving patient-relevant outcomes. Unfortunately, there is considerable heterogeneity with respect to the quality and applicability of the online applications involved in these studies[74,75]. Furthermore, evidence regarding the effectiveness of online self-management interventions appears to be inconclusive, especially in the long term, and the cost-effectiveness of such interventions remains unknown[74,76–78]. As a result, little is known about the added value of blended care interventions, in which the strength of both face-to-face physiotherapy guidance and online applications are combined.

In addition, it is important to realize that online self-management interventions are not a one-size-fits all solution and that matching the appropriate digital content to the

individual patient's needs is reported as a challenge[74,79]. The main recommendations of these studies include the development of interventions in close collaboration with healthcare professionals, researchers, and patients to ensure that app content is accurate, evidence-based, and engaging. Furthermore, it was recommended to integrate online self-management interventions into face-to-face care to optimize their effects and to study the cost-effectiveness of such interventions[74–76]. Finally, it is important to study how an online self-management intervention can be tailored to the individual patient to optimize its added value. As mentioned earlier, in face-to-face physiotherapy, a tool that can be used for matching the appropriate content of face-to-face care to the individual patient is already available, i.e., the Keele STarT Back Screening Tool[38]. However, for the online aspect of self-management interventions, this is a relatively undeveloped territory. It is possible that the Keele STarT Back Screening Tool[38] has the same potential for matching the content of blended care interventions to the individual patient as in face-to-face care. Therefore, we developed e-Exercise LBP (Box 1), a stratified blended physiotherapy intervention for patients with nonspecific LBP[80].

A brief history of 'e-Exercise LBP'

e-Exercise LBP (Box 1) is the product of a multiphase and iterative codesign development process following the Center for eHealth Research (CeHRes) Roadmap (Figure 3)[81]. The CeHRes roadmap is based on the principles of participatory design, which means that e-Exercise LBP was developed via a process of cocreation involving physiotherapists, patients, software developers, opinion leaders in the field of LBP, and a commercial eHealth entrepreneur.

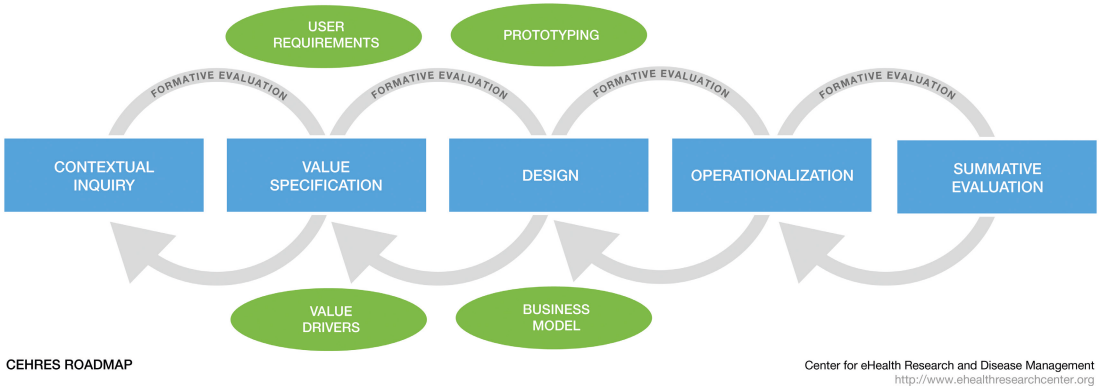

Figure 3. Center for eHealth Research (CeHRes) Roadmap

Box 1. The e-Exercise Low Back Pain Intervention

e-Exercise LBP is a stratified blended physiotherapy intervention comprising a smartphone app that is integrated with face-to-face physiotherapy treatment. Both the contents of the smartphone app and the face-to-face physiotherapy treatment are based on the LBP guidelines provided by the Royal Dutch Society for Physiotherapy. The duration and content of the stratified blended physiotherapy intervention are based on the patients' risk of developing persistent LBP (low, medium, or high) as measured using the Keele STarT Back Screening Tool.

The **smartphone app** contains the following features. (i) An *information module* containing 12 weekly self-management themes (text and video), including assignments related to the aetiology of LBP, physical activity, patient experiences, pain management, and psychosocial factors pertaining to LBP. (ii) An *exercise module* containing a home-based exercise program per patient's prognostic risk profile, which features video instructions. The selection, frequency and number of repetitions can be adjusted by the physiotherapist to address the patient's specific functional limitations. (iii) A *physical activity module* containing a goal-oriented training program consisting of three sessions per week, which is intended to help the patient maintain or improve his or her level of physical activity for a self-chosen type of activity (e.g., cycling or walking). The training program starts with a 3-day baseline test and can be optionally supported by graded activity functionality featuring tailored feedback.
For patients at "low risk" of developing persistent LBP, the smartphone application offers support for 3 weeks. For "medium" and "high risk" patients, this support is extended to 12 weeks. Thereafter, the content of the smartphone application remains available to the patients. For "low risk" patients, the smartphone application only contains the information and exercise modules. For "medium and high risk" patients, the physical activity module is added. The graded activity functionality can be enabled for "medium risk" patients who avoid physical activity due to nonspecific LBP. For "high risk" patients the graded activity functionality is always activated.

During **face-to-face care**, the physiotherapist tailors the e-Exercise LBP intervention to the patients' identified risk of developing persistent LBP (i.e., low, medium or high). Patients are asked to schedule their exercises and physical activities via the smartphone application, following which the smartphone application sends automatic pop-up reminders at the appropriate time. Physiotherapists are able to monitor patients' use of the smartphone application, keep track of evaluated assignments, and select other types of exercises. Given this information, the physiotherapist should be able to evaluate the progress and attitudes of the patients during the period between face-to-face sessions, optimize the content of the smartphone application to suit patients' individual needs, and tailor face-to-face care. Physiotherapists are encouraged to provide approximately 2 face-to-face physiotherapy sessions to patients who are labelled "low risk", 8 sessions to patients who are labelled "medium risk", and 12 sessions to patients who are labelled "high risk". After completing the e-Exercise LBP programme, the patient receives reminders from the smartphone application every 2 weeks for up to 6 months to continue to adopt a physically active lifestyle.

E-Exercise LBP is an adapted version of a previously developed and evaluated e-Exercise intervention for patients with hip and/or knee osteoarthritis (e-Exercise OA) that showed promising results[69,82,83]. Patients treated with e-Exercise OA experienced improvements in terms of physical functioning, pain, tiredness, quality of life and self-efficacy[83]. Moreover, these patients exhibited highly positive attitudes towards and were satisfied with the availability of information and assignments anytime and anywhere. The majority of these participants adhered to the online component of e-Exercise OA, illustrating its applicability[68]. Physiotherapists indicated that the intervention's integration into face-to-face physiotherapy and the persuasive design of e-Exercise OA appeared to play an important role in optimizing patient adherence. In addition, physiotherapists suggested that regular use of similar interventions in multiple conditions would enhance the applicability of e-Exercise and facilitate the uptake in physiotherapists' daily routine. Given that the management of nonspecific LBP is similar to the management of hip and/or knee osteoarthritis, i.e., that relevant recommendations include education, exercise and physical activity, it was hypothesized that e-Exercise would also be beneficial for patients with nonspecific LBP[79].

As a result, the first three steps of the CeHRes Roadmap, i.e., contextual inquiry, value specification and design, were followed in the development of e-Exercise LBP[80]. In summary, patients indicated that physical activity and exercises were important aspects of the treatment of nonspecific LBP, and a platform featuring video-supported exercise recommendations would enable them to accomplish exercises at home. Physiotherapists suggested the inclusion of a graded activity module. Both physiotherapists and experts recommended to combine the STarT Back Screening Tool with recommendations concerning the average number of treatment sessions per risk group. Finally, the proof of concept for the e-Exercise LBP prototype was tested in a multicentre feasibility study[80]. The results of this study showed that the e-Exercise LBP prototype was feasible, and initial evidence concerning the prototype's effectiveness in reducing disability and pain was demonstrated. Based on the results of the feasibility study and end-user (patients and physiotherapists) usability experiences, the e-Exercise LBP prototype was further improved in preparation for operationalization and evaluation, i.e., steps 4 and 5 of the CeHRes Roadmap. This thesis describes the results of the use of e-Exercise LBP in daily physiotherapy practice, i.e., operationalization, and evaluates its effect on clinical and economic outcome measures, i.e., summative evaluation.

Aim of this thesis

In summary, e-Exercise LBP aims to improve the physical functioning of patients with nonspecific LBP by offering a stratified blended-care physiotherapy approach. In addition to an improvement in patients' physical functioning, this stratified blended-care approach is hypothesized to positively influence patients' self-management skills and their adherence to exercise and physical activity recommendations regarding the management of nonspecific LBP. In the long term, it is hypothesized that improvements

in patients' self-management skills and their adherence to the management of nonspecific LBP could result in improved handling of recurring episodes of nonspecific LBP, which could in turn result in a reduction in societal and/or healthcare costs.

Therefore, the aim of this thesis is to evaluate the effectiveness and cost-effectiveness of e-Exercise LBP, a stratified blended physiotherapy intervention, compared to face-to-face physiotherapy for patients with nonspecific LBP.

Outline of this thesis

Chapter 2 presents the critical appraisal and comparison of the measurement properties of all language versions of the Quebec Back Pain Disability Scale. The results of this systematic review were helpful in determining whether the Quebec Back Pain Disability Scale was an adequate measurement instrument to measure physical functioning in patients with nonspecific LBP. **Chapter 3** describes the study protocol of a multicentre cluster randomized controlled trial study to investigate the effectiveness and cost-effectiveness of stratified blended physiotherapy in patients with nonspecific LBP. **Chapter 4** presents the results concerning the short-term (3 months) effectiveness of stratified blended physiotherapy (e-Exercise LBP) compared to face-to-face physiotherapy. **Chapter 5** presents the results concerning the long-term (12 months) effectiveness and cost-effectiveness of e-Exercise LBP. In this study, cost-effectiveness is discussed from both the societal and healthcare perspectives. **Chapter 6** identifies the characteristics and health outcomes that were associated with activation for self-management in patients with nonspecific LBP. The results of this cross-sectional study increase the understanding of what determinants are associated with activation for self-management in patients with nonspecific LBP. This information is a first step in helping physiotherapists easily recognize people with a potentially lower degree of activation for self-management, which can be helpful as a means of personalizing and individually tailoring future self-management interventions more effectively. Finally, **Chapter 7** presents a general discussion of the entire e-Exercise Low Back Pain project. In this chapter, the main findings are reviewed, methodological considerations are discussed, and implications for clinical practice, education, and recommendations for future research are presented. This dissertation ends with a summary in both English and Dutch.

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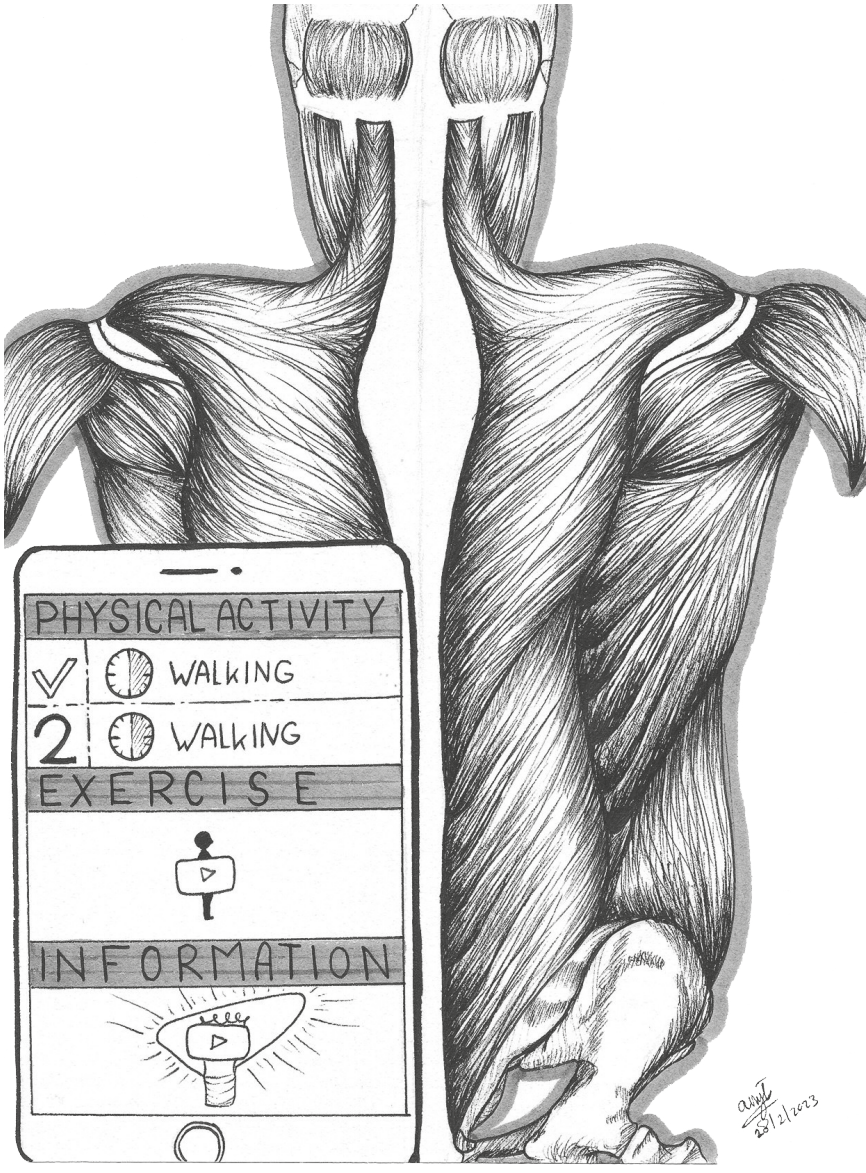
PHYSICAL ACTIVITY
WALKING
2
WALKING
EXERCISE
INFORMATION

2

Measurement properties of the Quebec Back Pain Disability Scale in patients with nonspecific low back pain:

Systematic review

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Authorship statement

I contributed to defining the research question, proposed the methodology and the design of the study under supervision of Dr Speksnijder. I provided the project management and contributed in the data collection and data analysis. I wrote the first draft of the manuscript and implemented the contribution of the co-authors up to the first submission of the manuscript. After rejection, Dr Speksnijder updated the literature search and revised the manuscript up to final publication (therefore, I am second author). I contributed in the data analysis of the updated literature search and reviewed the final version of the manuscript.

ABSTRACT

Background

The Quebec Back Pain Disability Scale (QBPDS) has been translated into different languages, and several studies on its measurement properties have been done.

Purpose

The purpose of this review was to critically appraise and compare the measurement properties, when possible, of all language versions of the QBPDS by systematically reviewing the methodological quality and results of the available studies.

Methods

Bibliographic databases (PubMed, Embase, CINAHL, and PsycINFO) were searched for articles with the key words "Quebec," "back," "pain," and "disability" in combination with a methodological search filter for finding studies on measurement properties concerning the development or evaluation of the measurement properties of the QBPDS in patients with nonspecific low back pain. Assessment of the methodological quality was carried out by the reviewers using the COnsensus-based Standards for the selection of health Measurement INstruments (COSMIN) checklist for both the original language version of the QBPDS in English and French and all translated versions. The results of the measurement properties were rated based on criteria proposed by Terwee et al.

Results

The search strategy resulted in identification of 1,436 publications, and 27 articles were included in the systematic review. There was limited-to-moderate evidence of good reliability, validity, and responsiveness of the QBPDS for the different language versions, but for no language version was evidence available for all measurement properties.

Conclusions

For research and clinical practice, caution is advised when using the QBPDS to measure disability in patients with nonspecific low back pain. Strong evidence is lacking on all measurement properties for each language version of the QBPDS.

BACKGROUND

One of the leading causes of disability worldwide is low back pain (LBP). Most of the time, LBP is benign and self-limiting and can be considered as nonspecific LBP, as no specific musculoskeletal pathology is found[1-3]. It occurs in similar proportions in all cultures, interferes with quality of life and work performance, and is the most common reason for medical consultation[4,5].

To measure the construct of disability in patients with LBP, several self-report back-specific questionnaires have been developed. They are recommended by the World Health Organization as instruments to evaluate the efficacy of treatments[4]. Two of the most commonly investigated questionnaires are the Roland-Morris Disability Questionnaire (RMDQ)[6-10] and the Oswestry Low Back Pain Disability Index (ODI)[11-15]. However, previous systematic reviews on available questionnaires to measure disability in patients with LBP indicate that the Quebec Back Pain Disability Scale (QBPDS)[16-18] is another well-validated and often recommended questionnaire[17,19-21]. The QBPDS also is commonly used in randomized controlled trials[20,22-24].

The QBPDS (Appendix 1) was developed in 1995 in English and French[16,17,25,26]. Contrary to the RMDQ and ODI, the QBPDS is based on a conceptual model of disability[16,17,27] The developers of the QBPDS used the World Health Organization's definition of disability as "any restriction or lack of ability to perform an activity in a manner or within the range considered normal for a human being[28,29]." Disability was operationally defined in terms of difficulty experienced while performing simple tasks[17,30,31] During the development of the QBPDS, factor analysis of 46 items showed that the QBPDS had a 6- or 7-factor structure, with 53% of the variance explained by the first factor[17]. The decision to include 20 items in the final instrument was based on item analysis and practical considerations, which resulted in a 6-factor structure[17]. These 20 items represented 6 correlated factors, which are selected and based on the following requirements: (1) all types of physical activities relevant to back pain should be represented, including bed/rest, sitting/standing, ambulation, movement, bending/stooping, and handling large or heavy objects; and (2) the QBPDS should be highly reliable and discriminative over a wide range of disability levels, while also being practical and acceptable to both patients and clinicians[17].

The 20 QBPDS items are scored on a 6-point scale (0="not difficult at all," 5="unable to do"). The total score is calculated by a summation of the scores for each item and ranges from 0 ("not being disabled") to 100 ("being maximally disabled")[16,17].

The QBPDS has been translated into different languages and adapted to different cultures. Studies have been performed on its measurement properties in these different adapted language versions[32,33]. A systematic review on this topic could be useful because

a review on cross-cultural adaptations of the McGill Pain Questionnaire showed there is often limited evidence for the measurement properties of translated or adapted language versions. Therefore, the results from translated questionnaires should be interpreted with caution[34,35]. For the QBPDS, such a review has not yet been undertaken.

Studies of high methodological quality are needed to guarantee appropriate conclusions about measurement properties. The COSMIN checklist was developed to appraise the methodological quality of studies on measurement properties of health status questionnaires[36,37]. The purpose of this review was to critically appraise and compare the measurement properties, when possible, of the different language versions of the QBPDS for measuring disability in patients with nonspecific LBP by systematically reviewing the methodological quality and results of the available studies.

METHOD

Search strategy

The following computerized bibliographic databases were searched up to September 18, 2014: PubMed (1966–2014), Embase (1974–2014), CINAHL (EBSCOhost) (1981–2014), and PsycINFO (OvidSPhost) (1806–2014). The databases were searched with the key words "Quebec," "back," "pain," and "disability" in combination with a methodological search filter for finding studies on measurement properties (Appendix 2)[38]. Reference lists were screened to identify additional relevant studies.

Selection criteria

Two reviewers (T.K., M.S.) independently assessed titles, abstracts, and reference lists of the studies retrieved by the literature search. Only full-text original articles were included, primarily concerning the development or evaluation of the measurement properties of the QBPDS. Articles in all languages were included.

For inclusion, the QBPDS had to be evaluated in adult patients (>18 years of age) with general, nonspecific LBP. Studies in patients with sciatica without any reference to a specific cause were included as well. Studies in patients with sciatica due to a specific cause (e.g., nerve root comprise) or LBP due to specific causes (e.g., neurological disorder, ankylosing spondylitis, fracture) were excluded. There was no minimum sample size for inclusion.

In case of disagreement between the 2 reviewers, a third reviewer (C.B.T.) made the decision regarding inclusion of the article. Both primary reviewers (T.K., M.S.) are senior physical therapists and scientists, and the third reviewer (C.B.T.) is a senior epidemiologist, which made this an optimal team for selecting articles for this review.

Quality assessment

Assessment of the methodological quality of the included studies was carried out using the COSMIN checklist[36,39]. The COSMIN checklist consists of 9 boxes with methodological standards for how each measurement property should be assessed. Each item in a box can be scored on a 4-point scale (i.e., "poor," "fair," "good," or "excellent"), which is an additional feature of the COSMIN checklist[40]. An overall score for the methodological quality of a study was determined by taking the lowest rating of any of the items in the 9 boxes. None of the studies used item response theory (IRT), so the IRT box was not used.

Data extraction and assessment of (methodological) quality were independently performed by 2 reviewers (T.K. and C.B.T. for 17 of the included articles[8-10,15-18,21,23,25-27,29,33,41-43] and C.M.S. and C.B.T. for 10 of the included articles[5,7,14,24,30,31,35,37,44,45]). In case of disagreement, a third reviewer made the decision (C.M.S. for data extraction and quality assessment performed by T.K. and C.B.T. and T.K. for data extraction and quality assessment performed by C.M.S. and C.B.T.). Two reviewers (C.M.S. and C.B.T.) are senior epidemiologists and, therefore, trained in psychometrics. One reviewer (C.B.T.) is one of the developers of the COSMIN checklist, and the other reviewers (C.M.S. and T.K.) were trained by the COSMIN team on quality appraisal and data extraction.

Measurement properties

The measurement properties are divided over 3 domains: reliability (including internal consistency, reliability, and measurement error), validity (including content validity, construct validity [i.e., structural validity, hypotheses testing, and cross-cultural validity], and criterion validity), and responsiveness. Hypotheses testing was done for the original version of the QBPDS developed by Kopec and colleagues[16,17] by correlating the QBPDS with the RMDQ, ODI, Medical Outcomes Study 36-Item Short-Form survey (SF-36), and pain rated on a visual analogue scale (VAS-pain), so we extracted data on the correlations of the QBPDS with these instruments for all language versions. Also related to pain, data on the correlation of the QBPDS with the Numeric Rating Pain Scale (NRPS) were included.

Part of cross-cultural validity testing concerns translation. The quality of the translation was determined by using items 4 to item 11 of the COSMIN cross-cultural validity box.

There is no gold standard for health status questionnaires available. Consequently, no level of evidence related to criterion validity can be determined for the QBPDS. The measurement properties and interpretability have been defined and discussed in detail elsewhere[46,47] Interpretability is not a measurement property, but rather an important characteristic of a measurement instrument[46].

Data synthesis, levels of evidence, and meta-analyses

When the quality of the translation was at least fair, we determined the quality of the measurement properties by applying levels of evidence, as defined in Table 1. The possible overall rating for a measurement property is "positive," "indeterminate," or "negative," accompanied with a level of evidence ("strong," "moderate," "limited," "conflicting," and "unknown"). To give a positive or negative rating for the results of the measurement properties, criteria for good measurement properties were used, based on criteria proposed by Terwee et al[48] (Table 2).

Meta-analyses were not performed because there were no more than 2 studies per measurement property per language version. Moreover, it is more important to evaluate whether the results are above a defined cut-off (e.g., ICC>.70) than to estimate the exact pooled value of the parameter.

Table 1. Levels of evidence for summary statements on measurement property based on overall quality[59]

Level	Rating[a]	Criteria
strong	**+++ or ---**	Consistent findings in multiple studies of good methodological quality OR in one study of excellent methodological quality
moderate	**++ or --**	Consistent findings in multiple studies of fair methodological quality OR in one study of good methodological quality
limited	**+ or -**	One study of fair methodological quality
conflicting	**+/-**	Conflicting findings
unknown	**?**	Only studies of poor methodological quality

[a] + = positive rating; ? = indeterminate rating; - = negative rating

Table 2. Quality criteria for measurement properties (Based on Terwee et al.[48])

Property	Rating[a]	Quality Criteria
Reliability		
Internal consistency	+	Cronbach's alpha(s) ≥ 0.70
	?	Cronbach's alpha not determined
	-	Cronbach's alpha(s) < 0.70
Reliability	+	ICC / weighted Kappa ≥ 0.70 OR Pearson's r ≥ 0.80
	?	Neither ICC / weighted Kappa, nor Pearson's r determined
	-	ICC / weighted Kappa < 0.70 OR Pearson's r < 0.80
Measurement error	+	MIC > SDC OR MIC outside the LOA
	?	MIC not defined
	-	MIC ≤ SDC OR MIC equals or inside LOA

Table 2. Continued

Property	Rating[a]	Quality Criteria
Validity		
Content validity	+	The target population considers all items in the questionnaire to be relevant AND considers the questionnaire to be complete
	?	No target population involvement
	-	The target population considers items in the questionnaire to be irrelevant OR considers the questionnaire to be incomplete
Construct validity		
Structural validity	+	Factors should explain at least 50% of the variance
	?	Explained variance not mentioned
	-	Factors explain < 50% of the variance
Hypothesis testing	+	Correlation with an instrument measuring the same construct ≥ 0.50 OR at least 75% of the results are in accordance with the hypotheses AND correlation with related constructs is higher than with unrelated constructs
	?	Solely correlations determined with unrelated constructs
	-	Correlation with an instrument measuring the same construct < 0.50 OR < 75% of the results are in accordance with the hypotheses OR correlation with related constructs is lower than with unrelated constructs
Cross-cultural validity	+	Original factor structure confirmed OR no important DIF between language versions
	?	Confirmatory factor analysis not applied and DIF not assessed
	-	Original factor structure not confirmed OR important DIF found between language versions
Criterion validity	+	Convincing arguments that gold standard is "gold" AND correlation with gold standard ≥ 0.70
	?	No convincing arguments that gold standard is "gold" OR doubtful design or method
	-	Correlation with gold standard < 0.70, despite adequate design and method

Table 2. Continued

Property	Rating[a]	Quality Criteria
Responsiveness		
Responsiveness	+	Correlation with an instrument measuring the same construct ≥ 0.50 OR at least 75% of the results are in accordance with the hypotheses OR AUC ≥ 0.70 AND correlation with related constructs is higher than with unrelated constructs
	?	Solely correlations determined with unrelated constructs
	-	Correlation with an instrument measuring the same construct < 0.50 OR < 75% of the results are in accordance with the hypotheses OR AUC < 0.70 OR correlation with related constructs is lower than with unrelated constructs

[a] + = positive rating; ? = indeterminate rating; - = negative rating
MIC = minimal important change; SDC = smallest detectable change; LoA = limits of agreement; ICC = intraclass correlation coefficient; DIF = differential item functioning; AUC = area under the curve

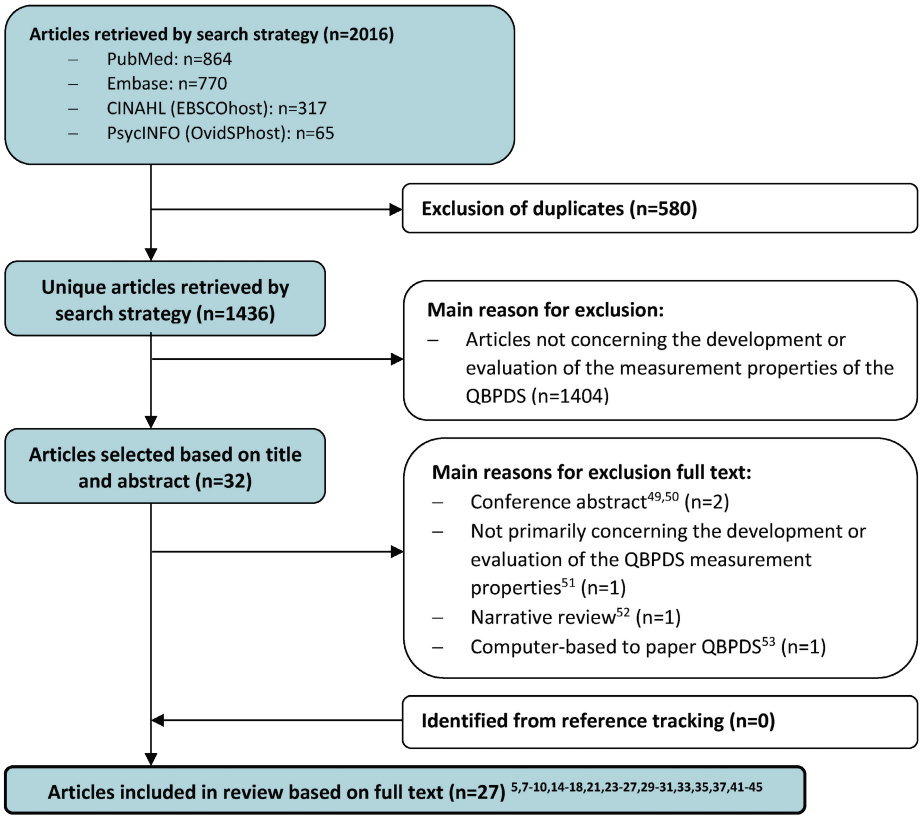
RESULTS

General

The search strategy resulted in 1,436 unique publications, of which 32 articles were selected based on title and abstract. Based on the full text of these articles, 5 articles[49–53] were excluded, mainly because the articles were not about the development or evaluation of the measurement properties of the QBPDS.

Reference tracking did not result in additional articles. Finally, 27 articles[5,7-10,14-18,21,23-27,29-31,33,35,37,41-45] were included (Figure 1).

The general characteristics of these studies are presented in Table 3. One study resulted in 2 publications and, therefore, is mentioned only once in Tables 3 and 4[16,17]. Rater scores for each criterion within each COSMIN quality appraisal boxes summarized in Table 4 can be requested from the first author.



* September 18, 2014

Figure 1. Flowchart of search and selection

Table 3. Characteristics of included studies

Study	Language	Population	Duration of complaints ± SD		
Alnahhal et al.[44]	Arabic (Gaza strip; Palestine)	Nonspecific LBP	8.4 ± 5.9 (yr)		
Bendeddouche et al.[45]	Arabic (Morocco)	Nonspecific chronic LBP (>3 mo)	58.4 ± 65.9 (mo)		
Wei et al.[31]	Chinese	Nonspecific LBP (≥6 wk)	18.3 ± 6.4 (wk)		
Demoulin et al.[10]	Dutch	Nonspecific chronic LBP (>3 mo)	24 (mo) (IQR: 12-72)		
Mens et al.[23]	Dutch	Nonspecific lumbopelvic pain since pregnancy	-		
Reneman et al.[26]	Dutch	Chronic nonspecific LBP	9.8 ± 11.3 (mo) (R: 2-72)		
Schoppink et al.[33]	Dutch	Chronic LBP	0-6 mo 7-12 mo 13-24 mo >25 mo	14% 6% 8% 72%	
van der Roer et al.[29]	Dutch	Nonspecific LBP	-		
Davidson et al.[8]	English (Australia)	LBP		UG	IG
			<1wk	4.2%	17.3%
			1-6wk	21.3%	42.2%
			6wk-6mo	23.4%	51.1%
			>6mo	19.2%	17.3%
Fritz et al.[15]	English (USA)	Acute LBP (<3 wk)	6.2 ± 5.3 (days) (R: 0-19)		
Hicks et al.[18]	English (USA)	Current LBP	31.8 ± 23.4 (wk)		
Kopec et al.[16,17*]	English (Canada) & French (Canada)	Back pain	<1wk 1-6wk 6wk-3mo 3mo-1yr >1yr	3.3% 16.5% 12.8% 22.7% 43.8%	
Wilhelm et al.[42]	French (European)	Chronic LBP	-		
Yvanes-Thomas et al.[43]	French (European	Chronic LBP	8 ± 5 (yr)		

Setting	N	Mean age ± SD (yr)	Male (%)
Physiotherapy department of different hospitals	148	33.4 ± 9.2	66.9
Hospital	64	47.6 ± 12.3	37.5
Orthopedic department of a hospital	114	49.9 ± 9.2	43.9
Rehabilitation center	223	43 (IQR: 33-49)	52.8
Outpatient clinic of a rehabilitation center	FG: 44 SG: 56	FG: 31.7 ± 3.2 SG: 33.5 ± 4.9	0
Outpatient university rehabilitation center	64	38.0 ± 8.9 (R: 23-58)	84
General practice	120	39.7 ± 10.4 (R: 21-60)	60
Sixty eight primary care physiotherapy practices	442	46.0 ± 14.0	46.8
Physical therapy outpatient departments of 3 hospitals, 3 community health services and 4 private physical therapy practices	UG: 47 IG: 52	UG: 55 ± 17 (R: 19-83) IG: 49 ± 16 (R: 20-80)	UG: 36.2 IG: 26.9
Physical therapy	67	39.2 ± 9.7 (R: 21-58)	57
Four continuing care home retirement communities	107	79.6 ± 5.7	28.1
Private and hospital-based physiotherapy clinics, physiatry center, family group practice, orthopedic-, pain- and rheumatology clinic	242	<20 0.8% 20-29 18.2% 30-39 24.4% 40-49 26.0% 50-59 13.6% 60+ 16.9%	49.6
Retrospective examination of medical records of low back outpatients in a physical medicine and rehabilitation department	30	41.6 (R: 29-59)	63.3
Hospital pain clinic	32	42 ± 8	66

Table 3. Continued

Study	Language	Population	Duration of complaints ± SD	
Christakou et al.[5]	Greek	Chronic LBP (>8 mo)	39.3 ± 37.4 (mo)	
Valasek et al.[37]	Hungarian	Chronic LBP (>4 mo)	4-6mo 7-12mo 13-24mo >24mo	34.6% 24.1% 12.0% 29.3%
Suh et al.[35]	Korean	Chronic LBP	21.2 ± 9.4 (mo)	
Mousavi et al.[25]	Persian	Chronic LBP	7.0 ±8.8 (yr) (R: 0.8-40)	
Misterska et al.[24]	Polish	LBP due to spinal disc herniation and degenerative changes	45.9 ± 55.5 (mo)	
Rodrigues et al.[27]	Portuguese (Brazil)	LBP	3-6mo 6-12mo 12-18mo 18-24mo >2yr	3.7% 9.2% 5.5% 11.1% 70.3%
Cruz et al.[7]	Portuguese (Europe)	Nonspecific chronic LBP (>3 mo)	3-6 mo 6-12 mo 12-24 mo > 24 mo	13.6% 9.1% 11.4% 65.9 %
Vieira et al.[30]	Portuguese (Europe)	Chronic LBP (>3 mo)	UG: ≤24mo n=15; >24mo n=29 IG: ≤24mo n=26;>24mo n=50	
De Beer et al.[9]	Tswana	LBP		
Bicer et al.[41]	Turkish	Chronic LBP (>6 mo)	7.11 ± 6.0 (yr) (R: 0.50-25)	
Düger et al.[14]	Turkish	Chronic LBP		
Melikoglu et al.[21]	Turkish	LBP (>3 wk)	50.9 ± 50.3 (mo)	

***** One study, evaluating the measurement properties of the QBPDS, resulted in two publications and is therefore mentioned once

LBP = low back pain; UG = unchanged group; IG = improved group; FG = first group; SG = second group; N = included population; IQR = interquartile range; R = range; SD = standard deviation; yr = year; wk = week; mo = month; % = percentage

Setting	N	Mean age ± SD (yr)	Male (%)
Private rehabilitation and/or physiotherapy clinic	130	41.1 ± 11.6	46.2
Outpatient clinic of the national center for spinal disorder	133	48.1 ± 15.3	42
Hospital	80	48.8 ± 7.5	35
Physical therapy unit of a large hospital	100	40.1 ± 11.6 (R: 17-68)	45
Hospital	111	41.4 ± 11.1 (R: 21-60)	55.3
Orthopeadics and traumatology clinic	54	44.3 ± 12.1	30
Sixteen outpatient clinics	132	46.6 ± 12.7 (R: 18-65)	27.3
Sixteen different clinical settings	UG: 41 IG: 76	UG: ≤49 n=22; >49 n=22 IG: ≤49 n=39; >49 n=37	UG: 20.5 IG: 31.6
Five hospitals	100	42 ± 9.1 (R: 23-63)	5
Outpatient clinics of physical medicine and rehabilitation department of a university hospital	83	43.6 ± 10.2 (R: 18-69)	24.1
Physical therapy and rehabilitation	55	37.8 ± 5.1	0
University medical faculty physical medicine and rehabilitation department	100	45.4 ± 15.1	26

Table 4. Methodological quality of each study per measurement property (COSMIN Checklist[36])

Study	Language	Internal Consistency	Reliability	Measurement Error
Alnahhal et al.[44]	Arabic (Gaza strip; Palestine)	**poor**	**fair**	
Bendeddouche et al.[45]	Arabic (Morocco)	**poor**	**fair**	**fair**
Wei et al.[31]	Chinese	**poor**	**fair**	**fair**
Demoulin et al.[10]	Dutch			**fair**
Mens et al.[23]	Dutch			
Reneman et al.[26]	Dutch			
Schoppink et al.[33]	Dutch	**poor**	**good**	**good**
Van der Roer et al.[29]	Dutch			**fair**
Davidson et al.[8]	English (Australia)		**fair**	**fair**
Fritz et al.[15]	English (USA)		**poor**	**poor**
Hicks et al.[18]	English (USA)		**good**	**good**
Kopec et al.[16],[17*]	English & French (Canada)	**good**	**poor**	
Wilhelm et al.[42]	French (Europe)			
Yvanes-Thomas et al.[43]	French (Europe)	**poor**		
Christakou et al.[5]	Greek	**fair**	**fair**	
Valasek et al.[37]	Hungarian	**good**	**fair**	**fair**
Suh et al.[35]	Korean	**poor**	**poor**	**poor**
Mousavi et al.[25]	Persian	**poor**	**fair**	
Misterska et al.[24]	Polish	**poor**	**fair**	
Rodrigues et al.[27]	Portuguese (Brazil)	**poor**	**good**	**good**
Cruz et al.[7]	Portuguese (Europe)	**good**	**good**	
Vieira et al.[30]	Portuguese (Europe)			**fair**
De Beer et al.[9]	Tswana	**poor**	**fair**	
Bicer et al.[41]	Turkish	**poor**		
Düger et al.[14]	Turkish			
Melikoglu et al.[21]	Turkish	**fair**	**fair**	

* One study, evaluating the measurement properties of the QBPDS, resulted in two publications and is therefore mentioned once

Content Validity	Structural Validity	Hypotheses Testing	Translation	Cross-cultural Validity	Criterion Validity	Responsiveness
		poor	poor			
		poor	fair			
		fair	fair			
						fair
						poor
		fair				
		poor	poor			poor
						fair
						fair
		good				
fair	good	poor				poor
		poor				poor
poor		poor				
fair	fair	fair	good			
	good	fair	fair			
		poor	excellent			
		fair	excellent			
		poor	poor			
		fair	good			
	good	good	poor			
						good
		poor	fair			
		poor	poor			
		poor				
		fair	excellent			

Table 5. Data synthesis[48]; Levels of evidence overall quality of the QBPDS measurement properties per language

Language	Internal Consistency	Reliability	Measurement Error	Content Validity	Structural Validity
Arabic (Gaza strip; Palestine)[44]	?	+	n/a	n/a	n/a
Arabic (Morocco)[45]	?	+	?*	n/a	n/a
Chinese[31]	?	+	?*	n/a	n/a
Dutch[10,23,26,29,33]	?	++	--	n/a	n/a
English[8,15,16,17,18]	++	++	?*	+	++
French[16,17,42,43]	++	?	n/a	+	++
Greek[5]	+	+	n/a	+	+
Hungarian[37]	++	+	?*	n/a	++
Korean[35]	?	?	?	n/a	n/a
Persian[25]	?	+	n/a	n/a	n/a
Polish[24]	?	+	n/a	n/a	n/a
Portuguese (Brazil)[27]	?	++	?*	n/a	n/a
Portuguese (Europe)[7,30]	++	++	-	n/a	++
Tswana[9]	?	+	n/a	n/a	n/a
Turkish[41]	?	n/a	n/a	n/a	n/a
Turkish[14]	n/a	n/a	n/a	n/a	n/a
Turkish[21]	+	+	n/a	n/a	n/a

+++ or --- = strong evidence positive/negative result; ++ or -- = moderate evidence positive/negative result; + or - = limited evidence positive/negative result; +/- = conflicting evidence; ? = result indeterminate or unknown, due to poor methodological quality; ?* = result unknown, due to lacking information about the minimal important change (MIC); n/a = no information available; QBPDS = Quebec Back Pain Disability Questionnaire; RMDQ = Roland-Morris Disability Questionnaire; ODI = Oswestry Low Back Pain Disability Index; VAS = Visual Analogue Scale; NRPS = Numeric Rating Pain Scale

Hypothesis testing				Transla-tion	Cross-cultural Validity	Criterion Validity	Respon-siveness
RMDQ	ODI	SF-36	VAS-pain/ NRPS				
n/a	?	n/a	?	?	n/a	n/a	n/a
?	n/a	n/a	?	+	n/a	n/a	n/a
n/a	+	n/a	+	+	n/a	n/a	n/a
+	+	n/a	?	?	n/a	n/a	+
?	?	++	?	n/a	n/a	n/a	+
?	?	?	?	n/a	n/a	n/a	?
+	n/a	n/a	n/a	++	n/a	n/a	n/a
n/a	+	n/a	+	+	n/a	n/a	n/a
n/a	?	?	?	+++	n/a	n/a	n/a
+	+	+	-	+++	n/a	n/a	n/a
n/a	?	n/a	n/a	?	n/a	n/a	n/a
+	n/a	n/a	+	++	n/a	n/a	n/a
++	n/a	n/a	--	?	n/a	n/a	++
n/a	n/a	n/a	?	+	n/a	n/a	n/a
n/a	n/a	n/a	?	?	n/a	n/a	n/a
n/a	?	n/a	?	n/a	n/a	n/a	n/a
n/a	+	n/a	-	+++	n/a	n/a	n/a

Methodological quality

Overall, the methodological quality of the studies was fair (Table 4). The reviewers (T.K., C.B.T., C.M.S.) came to an agreement on all quality assessments. Only 2 studies[5,43] adequately described the measurement properties of the QPBDS. Twenty-four studies[5,8-10,14-18,21,23-27,29-31,33,35,41-45] did not describe how missing items were handled, and 20 studies[5,8-10,14,15,18,21,23,24,26,27,29,30,35,41-45] did not describe the number or percentage of missing responses. Three studies[25,42,43] had an inadequate sample size (<50).

The QBPDS was translated into Palestinian Arabic[44], Moroccan Arabic[45], Chinese[31], Dutch[33], French[17], Greek[5], Hungarian[37], Korean[35], Persian[25], Polish[24], Brazilian Portuguese[27], European Portuguese[7], Tswana[9], and Turkish[14,21,41]. The original English and French versions of the QBPDS developed by Kopec and colleagues[16,17] were used in 3 studies[8,15,18] and 2 studies[42,43], respectively. The Dutch version was used in 5 studies[10,23,26,29,33]. The European Portuguese version was used in 2 studies[7,30]. All 3 studies using a Turkish version[14,21,41] used different translations. All other language versions were used in only 1 study[5,9,24,25,27,31,35,37,44,45].

The results per measurement property of the QBPDS are discussed below. The results from studies of poor methodological quality (Table 4 and Appendix 3) are not mentioned because they may be biased. The data synthesis of the results and accompanying levels of evidence is presented in Table 5.

Reliability

Internal consistency

Sixteen studies[5,7,9,16,21,24,25,27,31,33,35,37,41,43-45] assessed the degree of the interrelatedness among the items of the QBPDS, expressed by Cronbach α. The studies using the English-French[16,17], Hungarian[37], and European Portuguese[7] language versions were of good quality, and the studies using the Greek[5] and one of the Turkish[21] language versions were of fair quality (Table 4). All 5 studies had positive results. The unidimensionality of the QBPDS was confirmed for the European Portuguese version by showing one predominant common factor explaining 52.1% of the variance[7]. The Cronbach α for the whole scale in these 5 studies ranged from .89[5] to .96[5,16,17].

We found moderate evidence for positive internal consistency of the English, French, Hungarian, and European Portuguese language versions of the QBPDS and limited evidence for positive internal consistency of the Greek and Turkish language versions.

Reliability

Reliability (proportion of the total variance in the measurements that is due to “true” differences among patients) was evaluated in 17 studies[5,7-9,15-18,21,24,25,27,31,33,35,37,44,45]. All of these studies evaluated the test-retest reliability of the QBPDS. One of these studies also conducted an inter-rater reliability study, as the QBPDS was administered twice

by 2 different researchers[27]. Eleven studies[5,7,16-18,27,31,33,35,37,44,45] used an appropriate time interval (2–14 days) between the first and second QBPDS administrations. The reliability studies concerning the Dutch[33], English[18], Brazilian Portuguese[27], and European Portuguese[7] language versions were of good quality. The studies on the Palestinian Arabic[44], Moroccan Arabic[45], Chinese[31], English[8], Greek[5], Hungarian[37], Persian[25], Polish[24], Tswana[9], and Turkish[21] language versions were of fair quality. All of these studies[5,7-9,18,21,24,25,27,31,33,37,44,45] had positive results and showed ICCs for test-retest reliability ranging from .70[7] to .99[31]. The study on the Brazilian Portuguese language version[27] was of good quality and evaluated both inter-rater and intra-rater reliability. The ICCs were .96 and .93, respectively. The study on the Palestinian Arabic language version[44] was of fair quality and showed weighted kappa values of .86 and .98 for the 2 different time points in that study.

We found moderate evidence for positive reliability for the Dutch, English, Brazilian Portuguese, and European Portuguese language versions of the QBPDS and limited evidence for positive reliability for the Palestinian Arabic, Moroccan Arabic, Chinese, Greek, Hungarian, Persian, Polish, Tswana, and Turkish language versions.

Measurement error

The measurement error consists of the systematic and random error of a patient's score, which is not attributed to true changes in the construct of disability. Measurement error is calculated using data from a test-retest reliability study and is expressed in the unit of measurement of the scale (number of points on the QBPDS)[47]. Measurement error was evaluated in 12 studies[8,10,15,18,27,29-31,33,35,37,45]. Seven studies[18,27,31,33,35,37,45] used an appropriate time interval (2–14 days) between the first and second administrations of the QBPDS. The studies concerning the Dutch[33], English[18], and Brazilian Portuguese[27] language versions were of good quality. In the study on the English language version[18], the smallest detectable change (SDC; 1.65*√2*standard error of measurement [SEM]) was 11 points (14.5% scored below 11 points, and 0.66% scored above 89 points). In the study on the Dutch language version[33], the limits of agreement (LOA) ranged from -15.6 to 16.4. In the study on the Brazilian Portuguese language version[27], the intra-observer LOA ranged from -1.4 to 2.8 points, and the inter-observer LOA ranged from -1.6 to 2.7 points.

In 5 fair-quality studies[8,10,29,30,37] (2 concerning the Dutch version, 1 concerning the English version, 1 concerning the Hungarian version, and 1 concerning the European Portuguese language version), SDC also was determined. In the Dutch language version study by Demoulin et al[10], the SDC (1.96*√2*SEM) was 15.8 points. In the Dutch study by van der Roer et al[29], the SDC (1.96*√2*SEM) was 32.9 points (95% confidence interval [CI]=24.6, 49.8) in patients with acute or subacute LBP and 24.6 points (95% CI=19.9, 32.4) in patients with chronic LBP. In the English study[8], the SDC (1.96*√2*SEM) was 19 points (95% CI=15, 31) in patients with LBP. In the Hungarian study[37], the SDC (1.96*√2*SEM)

was 14.4 points in patients with chronic LBP. In the study on the European Portuguese language version[30] in patients with acute or subacute LBP, the SDC (1.65*√2*SEM) was 19 points. In 2 other fair studies (Moroccan Arabic[45] and Chinese[31]), LOA also were reported. The intra-observer LOA of the Moroccan Arabic language version[45] ranged from -19.3 to 20.7 points. The intra-observer LOA of the Chinese language version[31] ranged from -17.1 to 18.1 points.

We found moderate evidence for a negative measurement error for the Dutch language version. However, for the Moroccan Arabic, Chinese, English, Hungarian, and Brazilian Portuguese language versions of the QBPDS, we could not perform a best evidence synthesis because of the lack of a minimal important change (MIC).

Validity

Content validity (including face validity)

The aim of the study by Kopec et al[17] was to develop a new scale of functional disability associated with back pain. All 20 items of the QBPDS reflect disabilities in performing activities in LBP well (Appendix 1). The studies on the Palestinian Arabic[44] and Greek[5] language versions concluded that the QBPDS assesses the intended construct. In particular, patients agreed that the scale seemed to be a reasonable test for evaluating the functional disability of patients with LBP. In all other studies, it was not reported whether patients agreed that the scale appeared to be a reasonable test for evaluating the functional disability of patients with LBP.

Three studies[5,17,43] evaluated the degree to which the content of the QBPDS is an adequate reflection of construct disability. Two studies (English-French[16,17] and Greek[5]) were of at least fair quality. From the study on the development of the QBPDS[16,17] and the study using the Greek version[5] of the QBPDS, it can be deduced that all items were considered relevant to measure the construct disability in a population of patients with LBP, as rated by experts and patients, and no important items were missing. We found limited evidence for positive content validity for the English, French, and Greek language versions of the QBPDS.

Construct validity (including structural validity, hypothesis testing, and cross-cultural validity)

To assess structural validity, 3 methodologically good studies (English-French[16,17], Hungarian[37], European Portuguese[7]) and 1 fair study (Greek[5]) assessed whether the scores of the QBPDS are an adequate reflection of the dimensionality of construct disability. The studies on the English-French[16,17] and the European Portuguese[7] language versions suggested that the 20-item scale could be considered approximately unidimensional. The study on the Hungarian language version[37] showed a 4-factor structure of the 20 items. The studies on the original English-French version[16,17] and the Greek language version[5] showed a 6-factor structure of the 20 items.

We found moderate evidence for positive structural validity for the English, French, Hungarian, and European Portuguese language versions of the QBPDS and limited evidence for positive structural validity for the Greek language version of the QBPDS.

Twenty studies[5,7,9,14,16,18,21,24-27,31,33,35,37,41-45] tested hypotheses of the relation between the QBPDS and other measurement tools. However, in 17 studies[5,7,9,14,18,21,24-27,31,33,35,41-44], hypotheses were vaguely or not described. Only 12 of the 20 studies[5,7,14,18,21,24-26,33,41-43] adequately described the construct of the comparator instrument. Two studies (English[18] and European Portuguese[7]) were of good quality, and 7 studies (Chinese[31], Dutch[26], Greek[5], Hungarian[37], Persian[25], Brazilian Portuguese[27], and Turkish[21]) were of fair quality. In the studies on the Dutch[26], Greek[5], Persian[25], Brazilian Portuguese[27], and European Portuguese[7] versions, the relation between the QBPDS and the RMDQ was tested. The correlations between the QBPDS and RMDQ ranged from .60[25,26] to .85[27], as supposed. The relation between the QBPDS and the ODI was tested in the studies using the Chinese[31], Dutch[26], Hungarian[37], Persian[25], and Turkish[21] language versions. The correlations between the QBPDS and ODI ranged, as supposed, from .67[21] to .90[31]. The studies using the English[18] and Persian language versions[25] showed correlations between the QBPDS and SF-36 ranging from .64[18] to .69[25], as we expected. The studies using the Chinese[31], Hungarian[37], Brazilian Portuguese[27], European Portuguese[7], and Turkish[21] language versions showed correlations between the QBPDS and VAS-pain ranging from .37[21] to .87[31].

Correlations with the VAS-pain were expected to be lower than the correlations with disability measures, and indeed the correlation with the VAS-pain was .37 in one study on the Turkish language version[21] and .38 in the study on the European Portuguese language version[7]. However, in the studies on the Chinese[31], Hungarian[37], and Brazilian Portuguese[27] language versions, the correlations of the QBPDS with the VAS-pain were higher than expected (.62[37], .75[27], and .87[31]). Also, the correlation of the QBPDS with the bodily pain subscale of the SF-36 was .50 in the study on the English language version[18] and .62 in the study on the Persian language version[25]. As expected, low correlations were found between the QBPDS and the SF-36 mental health (.25[18] and .40[25]) and role-emotional functioning (.26[18] and .37[25]) subscales.

We found moderate evidence for positive construct validity for the English language version related to the SF-36. For the Tswana language version, we found moderate evidence for positive construct validity related to the RMDQ and negative construct validity related to the VAS-pain. Limited evidence was found for positive construct validity for the Chinese (ODI, VAS-pain), Dutch (RMDQ, ODI), Greek (RMDQ), Hungarian (ODI, VAS-pain), Persian (RMDQ, ODI, SF-36), Portuguese Brazilian (RMDQ, VAS-pain), and Turkish (ODI) language versions. However, we also found limited evidence for negative construct validity for the Persian and Turkish language versions related to VAS-pain.

For cross-cultural validity and translation, none of the included studies assessed whether the performance of the items on a translated QBPDS were an adequate reflection of the performance of the original QBPDS (cross-cultural validity) (e.g., by using multiple group factor analyses of evaluating differential item functioning).

In 15 studies[5,7,9,17,21,24,25,27,31,33,35,37,41,44,45], a translation of the QBPDS was described. The QBPDS was translated into Palestinian Arabic[44], Moroccan Arabic[45], Chinese[31], Dutch[33], French[17], Greek[5], Hungarian[37], Korean[5], Brazilian Portuguese[27], European Portguese[7], Persian[25], Polish[24], Tswana[9], and Turkish[14,21,41]. The Korean[35], Persian[25], and Turkish[21] translation studies were of excellent quality; the Brazilian Portuguese[27] and Greek[5] translation studies were of good methodological quality; and the Moroccan Arabic[45], Chinese[31], Hungarian[37], and Tswana[9] translation studies were of fair methodological quality. We found no evidence for cross- cultural validity.

Criterion validity

As stated in the Method section, no gold standard for health status questionnaires is available.

Responsiveness

Eight studies[8,10,15–17,23,30,33,42] evaluated the ability of the QBPDS to detect change over time in the construct of disability. One study on the European Portuguese language version[30] was of good quality and showed an area under the receiver operating characteristic (ROC) curve (AUC) of 0.74. In the European Portuguese language version[30], the AUC was interpreted as the probability of correctly discriminating between "clinically stable" (score<4) and "clinically improved" (score>5) patient outcomes, based on the change in scores on the Patient Global Improvement Change Scale (PGIC-PT; ordinal scale from 1 to 7[54]). One study on the Dutch language version[10] and 2 studies on the English language version[8,15] were of fair quality and showed positive results, with AUCs of .85[10], .74[8], and .87[15]. In the Dutch language version[10], the AUC was interpreted as the probability of correctly discriminating between "clinically stable" and "clinically improved" patient outcomes, using a change score (score>6) and an unchanged score (score=3–5) of the following ordinal scale: 1="worse than ever," 2="much worsened," 3="slightly worsened," 4="unchanged," 5="slightly improved," 6="much improved," and 7="completely recovered." In the English language version of the QBPDS in the study by Davidson and Keating[8], the AUC was interpreted as the probability of correctly discriminating between "unchanged" and "improved" patient outcome, using a change score (score<3) and an unchanged score (score=4–6) of the following ordinal scale: 1="completely gone," 2="much better," 3="better," 4="a little better," 5="about the same," 6="a little worse," and 7="much worse." In the English language version of the QBPDS in the study by Fritz and Irrgang[15]. The AUC was interpreted as the probability of correctly discriminating between "clinically stable" and "clinically improved" patient outcomes based on the 15-point rating scale of Jaeschke et al[55], using a change score

(score>3) and an unchanged score (score=-3 to 3) of the following ordinal scale: 1="completely gone," 2="much better," 3="better," 4="a little better," 5="about the same," 6="a little worse," and 7="much worse."

In 3 of these studies, patients were treated by physical therapists for LBP[8], acute LBP[15], and chronic LBP[30]. In one study[10], patients were treated by a multidisciplinary team for chronic LBP.

We found moderate evidence for positive responsiveness for the European Portuguese language version and limited evidence for positive responsiveness for the Dutch and English language versions of the QBPDS.

Interpretability: MIC

In one study on the European Portuguese language version[30] and 2 studies on the Dutch language version[10,29], the MIC of the QBPDS was estimated. These 3 studies used the ROC method to determine the MIC. In the European Portuguese study by Vieira et al[30] and the Dutch study by Demoulin et al[10], the MIC was determined by identifying the point closest to the upper left corner on the ROC curve. In the Dutch study by van der Roer et al[29], the MIC was determined by the optimal cut-off point as that point that yields the lowest overall misclassification.

In the European Portuguese language version of the QBPDS[30], the AUC was interpreted as the probability of correctly discriminating between "clinically stable" (score<4) and "clinically improved" (score>5) patient outcomes, based on the change in the PGIC-PT (ordinal scale from 1 to 7[54]) score. In the Dutch study by Demoulin et al[10], the AUC was interpreted as the probability of correctly discriminating between "clinically stable" and "clinically improvement" patient's outcome, using a change score (score>6) and an unchanged score (score=3–5) of the following ordinal scale: 1="worse than ever," 2="much worsened," 3="slightly worsened," 4="unchanged," 5="slightly improved," 6="much improved," and 7="completely recovered." In the Dutch study by van der Roer et al[29], the AUC was interpreted as the probability of correctly discriminating between "stable" and "improved" patient outcomes, using a change score (score <2) and an unchanged score (score=3–5) of the following ordinal scale: 1="completely recovered," 2="much improved," 3="slightly improved," 4="no change," 5="slightly worsened," 6="much worse."

In the study on the European Portuguese version[30], the MIC was defined as 6.5 points (AUC=0.74) for patients with chronic LBP after 6 weeks. In one Dutch study[10], the MIC was defined as 5 points (AUC=0.85) or an 18.1% change from baseline (AUC=0.86) after 10 weeks in patients with chronic LBP who received multidisciplinary rehabilitation. In the other Dutch study[29], the MIC was defined as 17.5 points (AUC=0.74) for patients with acute or subacute LBP and 8.5 points for patients with chronic LBP after 12 weeks[29].

Patients of the 2 last-mentioned studies received physical therapy. An expert panel recommended an MIC of 20 points or a change of 30% from baseline[22].

In 3 of these studies, patients were treated by physical therapists for LBP[8], acute LBP[15], and chronic LBP[30]. In one study[10], patients were treated by a multidisciplinary team for chronic LBP.

DISCUSSION

There is limited-to-moderate evidence for good reliability, validity, and responsiveness of the QBPDS for different language versions. However, there is no complete evidence for all measurement properties in any language version of the QBPDS. Because of the wide ranges in SDC and MIC values, it is difficult to determine whether the QBPDS can distinguish true changes from the systematic and random error of a score in individual patients.

Concerning the degree to which the QBPDS measures the construct of disability[7,18], the construct of the QBPDS also seems to be correlated to bodily pain[18]. By using the term "difficulty," possibly both the constructs disability and pain are measured by the QBPDS.

Limitations

A limitation of this study is that we were not able to differentiate among study settings, follow-up durations, interventions, and subacute, acute, and chronic LBP. There were not enough studies to enable distinctions among these groups. Therefore, we are not sure that the same results apply to, for example, patients with acute and chronic LBP. One study of poor quality (because of a small sample size) measuring patients with acute LBP showed an ICC of .55[15]. This finding may suggest that the reliability of the QBPDS is not as good in patients with acute LBP, but more evidence is needed in good-quality studies.

For this systematic review, we were interested in all language versions; however, we used only English terms in our search string to identify relevant articles, which could have limited the inclusion of non-English studies.

The QBPDS was translated into 14 different languages[5,7,9,17,21,24,25,27,31,33,35,37,41,44,45]. The translation of the original version was of at least good quality in 5 studies[5,21,25,27,35]. However, cross-cultural validity has not been assessed. It is therefore unknown if the translated versions of the QBPDS assesses disability in the same manner as its original version. Cross-cultural validity can be assessed by determining if the factor structure of the translated version equals the original factor structure (in a multiple-group

factor analysis), or by assessing if there is differential item functioning between the 2 versions[47]. Differential item functioning means that patients with the same true score on the construct have the same score on the measurement instrument item[39].

We recommend these statistical analyses for each language version to show if the scores of the translated QBPDS versions can be interpreted in the same way as the original version of the QBPDS developed by Kopec and colleagues[16,17].

The decision to include 20 items in the final instrument was based on item analysis and practical considerations, which resulted in a 6-factor structure[17]. Two good-quality studies, one on the original English-French version[16,17] and one on the European Portuguese version[7], suggested that the 20-item scale could be considered approximately unidimensional, explaining 52% to 53% of the variance. However, another good-quality study using the Hungarian version[37] showed a 4-factor structure (everyday activities, ambulation, sitting/carrying, and bed/rest) of the 20 QBPDS items, and the fair-quality studies on the original English-French version[17] and the Greek language version[5] showed a 6-factor structure (movement, handling of large/ heavy objects, bending/stooping, ambulation, sit/stand, and bed/rest) of the 20 QBPDS items. An explanation for these different results may be low cross-cultural validity. As the dimensional structure of the QBPDS, therefore, is not entirely clear, the results on internal consistency should be interpreted with caution because unidimensionality is a prerequisite for a clear interpretation of the internal consistency statistics[56].

Future research

For almost all measurement properties, additional studies are needed. Foremost, studies are needed to determine cross-cultural validity so that scores related to different language versions of the QBPDS can be compared with each other.

We recommend adequate factor analyses for each language version in future studies of the QBPDS. Also, IRT analyses are recommended to investigate the internal structure of the QBPDS.

Studies that determine the reliability to determine “true” differences between patients and measurement error to distinguish true changes from systematic and random error also are needed[46,57]. Regarding interpretability, only 3 studies[10,29,30] of at least fair quality determined the MIC of the QBPDS, and their results varied widely. Because of the wide range in SDC and MIC values, it is difficult to conclude whether the SDC is larger or smaller than the MIC. It is recommended, therefore, that future research should focus on determining the MIC and SDC in all language versions. Until there is more evidence regarding the MIC, we recommend using the conservative guidelines as recommended by the expert panel (an MIC of 20 points or a change of 30% from baseline)[22].

Furthermore, more high-quality studies on responsiveness are needed. Most studies assessing responsiveness of the QBPDS did not formulate or only vaguely formulated hypotheses regarding expected correlations in advance[8,16,33,42]. Without specific hypotheses, the risk of bias is high because retrospectively it is tempting to come up with alternative explanations for low correlations instead of concluding that the questionnaire is not responsive[48]. We, therefore, recommend performing additional high-quality studies, testing specific hypotheses regarding the correlation of changes in the QBPDS with changes in other disability questionnaires, pain measures, and measures of psychosocial functioning.

The original version of the QBPDS was in English and French. For these language versions, research of at least good methodological quality is needed for every measurement property mentioned by the COSMIN checklist[36]. Internal consistency, reliability, measurement error, structural validity, and hypotheses testing have to be investigated once again by a study of at least good quality. Thereby, content validity, criterion validity, responsiveness, and interpretability have to be investigated once by a study of excellent methodological quality or at least twice by good methodological studies.

It is advisable to perform similar reviews for the RMDQ and the ODI to enhance the comparability among the different questionnaires. Finally, future research should focus on comparing the QBPDS, RMDQ, and ODI with newly developed, IRT-based instruments, such as the Patient-Reported Outcomes Measurement Information System (PROMIS) Physical Functioning instruments (http://www.nihpromis.org) The PROMIS offers major advantages, such as the possibility of computer adaptive testing and comparability of scores across patient populations. Research has shown that the PROMIS has better measurement properties than traditional questionnaires[58]. Although the PROMIS is a generic questionnaire, it may be as responsive as disease-specific questionnaires when used as a computerized adaptive test, and its responsiveness should be investigated in future studies.

For research and clinical practice, we advise using the QBPDS with caution to measure disability in patients with nonspecific LBP. Strong evidence is lacking on all measurement properties for each language version of the QBPDS.

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Appendix 1. Quebec Back Pain Disability Scale (Kopec et al[16,17])[a]

This questionnaire is about the way your back pain is affecting your daily life. People with back problems may find it difficult to perform some of their daily activities. We would like to know if you find it difficult to perform any of the activities listed below, because of your back. For each activity there is a scale of 0 to 5. Please choose one response option for each activity (do not skip any activities) and circle the corresponding number.

Today, do you find it difficult to perform the following activities because of your back?

	Not difficult at all	Minimally difficult	Somewhat difficult	Fairly difficult	Very difficult	Unable to do
1. Get out of bed	0	1	2	3	4	5
2. Sleep through the night	0	1	2	3	4	5
3. Turn over in bed	0	1	2	3	4	5
4. Ride in a car	0	1	2	3	4	5
5. Stand up for 20-30 minutes	0	1	2	3	4	5
6. Sit in a chair for several hours	0	1	2	3	4	5
7. Climb one flight of stairs	0	1	2	3	4	5
8. Walk a few blocks (300-400 m)	0	1	2	3	4	5
9. Walk several kilometers	0	1	2	3	4	5
10. Reach up to high shelves	0	1	2	3	4	5
11. Throw a ball	0	1	2	3	4	5
12 Run one block (about 100m)	0	1	2	3	4	5
13. Take food out of the refrigerator	0	1	2	3	4	5
14 Make your bed	0	1	2	3	4	5
15. Put on socks (pantyhose)	0	1	2	3	4	5
16. Bend over to clean the bathtub	0	1	2	3	4	5
17. Move a chair	0	1	2	3	4	5
18. Pull or push heavy doors	0	1	2	3	4	5
19. Carry two bags of groceries	0	1	2	3	4	5
20. Lift and carry a heavy suitcase	0	1	2	3	4	5

[a] QBPDS © Jacek A. Kopec, 1995. All rights reserved. Used with permission from © Mapi Research Trust, Lyon, France: https://eprovide.mapi-trust.org.

Appendix 2. Search strategy

Search	Query
#7	Search **(#5 NOT #6)**
#6	Search **((“animals”[MeSH Terms] NOT “humans”[MeSH Terms]))**
#5	Search **(#3 NOT #4)**
#4	Search **((“addresses”[Publication Type] OR “biography”[Publication Type] OR “case reports”[Publication Type] OR “comment”[Publication Type] OR “directory”[Publication Type] OR “editorial”[Publication Type] OR “festschrift”[Publication Type] OR “interview”[Publication Type] OR “lectures”[Publication Type] OR “legal cases”[Publication Type] OR “legislation”[Publication Type] OR “letter”[Publication Type] OR “news”[Publication Type] OR “newspaper article”[Publication Type] OR “patient education handout”[Publication Type] OR “popular works”[Publication Type] OR “congresses”[Publication Type] OR “consensus development conference”[Publication Type] OR “consensus development conference, nih”[Publication Type] OR “practice guideline”[Publication Type]) NOT (“animals”[MeSH Terms] NOT “humans”[MeSH Terms]) OR (cancer[sb] OR veterinary[sb] OR aids[sb] OR bioethics[sb] OR jsubsetd OR jsubsets OR jsubsete OR jsubsetq OR jsubsetqis))**
#3	Search **(#1 AND #2)**
#2	Search **((instrumentation[sh] OR methods[sh] OR Validation Studies[pt] OR Comparative Study[pt] OR “psychometrics”[MeSH] OR psychometr*[tiab] OR clinimetr*[tw] OR clinometr*[tw] OR “outcome assessment (health care)”[MeSH] OR outcome assessment[tiab] OR outcome measure*[tw] OR “observer variation”[MeSH] OR observer variation[tiab] OR “Health Status Indicators”[Mesh] OR “reproducibility of results”[MeSH] OR reproducib*[tiab] OR “discriminant analysis”[MeSH] OR reliab*[tiab] OR unreliab*[tiab] OR valid*[tiab] OR coefficient[tiab] OR homogeneity[tiab] OR homogeneous[tiab] OR “internal consistency”[tiab] OR (cronbach*[tiab] AND (alpha[tiab] OR alphas[tiab])) OR (item[tiab] AND (correlation*[tiab] OR selection*[tiab] OR reduction*[tiab])) OR agreement[tiab] OR precision[tiab] OR imprecision[tiab] OR “precise values”[tiab] OR test-retest[tiab] OR (test[tiab] AND retest[tiab]) OR (reliab*[tiab] AND (test[tiab] OR retest[tiab])) OR stability[tiab] OR interrater[tiab] OR inter-rater[tiab] OR intrarater[tiab] OR intra-rater[tiab] OR intertester[tiab] OR inter-tester[tiab] OR intratester[tiab] OR intra-tester[tiab] OR interobserver[tiab] OR inter-observer[tiab] OR intraobserver[tiab] OR intra-observer[tiab] OR intertechnician[tiab] OR inter-technician[tiab] OR intratechnician[tiab] OR intra-technician[tiab] OR interexaminer[tiab] OR inter-examiner[tiab] OR intraexaminer[tiab] OR intra-examiner[tiab] OR interassay[tiab] OR inter-assay[tiab] OR intraassay[tiab] OR intra-assay[tiab] OR interindividual[tiab] OR inter-individual[tiab] OR intraindividual[tiab] OR intra-individual[tiab] OR interparticipant[tiab] OR inter-participant[tiab] OR intraparticipant[tiab] OR intra-participant[tiab] OR kappa[tiab] OR kappa’s[tiab] OR kappas[tiab] OR repeatab*[tiab] OR ((replicab*[tiab] OR repeated[tiab]) AND (measure[tiab] OR measures[tiab] OR findings[tiab] OR result[tiab] OR results[tiab] OR test[tiab] OR tests[tiab])) OR generaliza*[tiab] OR generalisa*[tiab] OR concordance[tiab] OR (intraclass[tiab] AND**

Appendix 2. Continued

Search	Query
	correlation*[tiab]) OR discriminative[tiab] OR "known group"[tiab] OR factor analysis[tiab] OR factor analyses[tiab] OR dimension*[tiab] OR subscale*[tiab] OR (multitrait[tiab] AND scaling[tiab] AND (analysis[tiab] OR analyses[tiab])) OR item discriminant[tiab] OR interscale correlation*[tiab] OR error[tiab] OR errors[tiab] OR "individual variability"[tiab] OR (variability[tiab] AND (analysis[tiab] OR values[tiab])) OR (uncertainty[tiab] AND (measurement[tiab] OR measuring[tiab])) OR "standard error of measurement"[tiab] OR sensitiv*[tiab] OR responsive*[tiab] OR ((minimal[tiab] OR minimally[tiab] OR clinical[tiab] OR clinically[tiab]) AND (important[tiab] OR significant[tiab] OR detectable[tiab]) AND (change[tiab] OR difference[tiab])) OR (small*[tiab] AND (real[tiab] OR detectable[tiab]) AND (change[tiab] OR difference[tiab])) OR meaningful change[tiab] OR "ceiling effect"[tiab] OR "floor effect"[tiab] OR "Item response model"[tiab] OR IRT[tiab] OR Rasch[tiab] OR "Differential item functioning"[tiab] OR DIF[tiab] OR "computer adaptive testing"[tiab] OR "item bank"[tiab] OR "cross-cultural equivalence"[tiab]))
#1	Search **(Quebec[tiab] AND (pain[tiab] OR back*[tiab] OR disability[tiab] OR scale[tiab])) OR QBPDS[tw]**

Appendix 3. Measurement properties of the QBPDS from studies of at least fair methodological quality (Table 4) used to determine the level of evidence (Table 1 & Table 2)

Study	Language	Internal Consistency	Reliability	Measurement Error
Alnahhal et al.[44]	Arabic (Gaza strip; Palestine)		**+**: weighted kappa = 0.86-0.98	
Bendeddouche et al.[45]	Arabic (Morocco)		**+**: ICC= 0.96	**?**: LOA = -19.3 to 20.7 MIC = n/a
Wei et al.[31]	Chinese		**+**: ICC = 0.99	**?**: LOA = -17.1 to 18.1 MIC = n/a
Demoulin et al.[10]	Dutch			**-**: SDC = 15.8 MIC = 5
Mens et al.[23]	Dutch			
Reneman et al.[26]	Dutch			
Schoppink et al.[33]	Dutch		**+**: ICC = 0.90	**?**: LOA = -15.6 to 16.4 MIC = n/a
van der Roer et al.[29]	Dutch			(Sub)acute LBP: **-**: SDC = 32.9 MIC = 17.5 Chronic LBP: **-**: SDC = 24.6 MIC = 8.5
Davidson et al.[8]	English (Australia)		**+**: ICC = 0.80	**?**: SDC = 19 MIC = n/a
Fritz et al.[15]	English (USA)			
Hicks et al.[18]	English (USA)		**+**: ICC = 0.94	**?**: SDC = 11.04 MIC = n/a
Kopec et al.[16,17]*	English & French(Canada)	**+**: Cr.α = 0.96		
Wilhelm et al.[42]	French (Europe)			
Yvanes-Thomas et al.[43]	French (Europe)			
Christakou et al.[5]	Greek	**+**: Cr.α = 0.89-0.96	**+**: ICC = 0.92	
Valasek et al.[37]	Hungarian	**+**: Cr.α = 0.95	**+**: ICC = 0.92	**?**: SDC = 14.4 MIC = n/a
Suh et al.[35]	Korean			

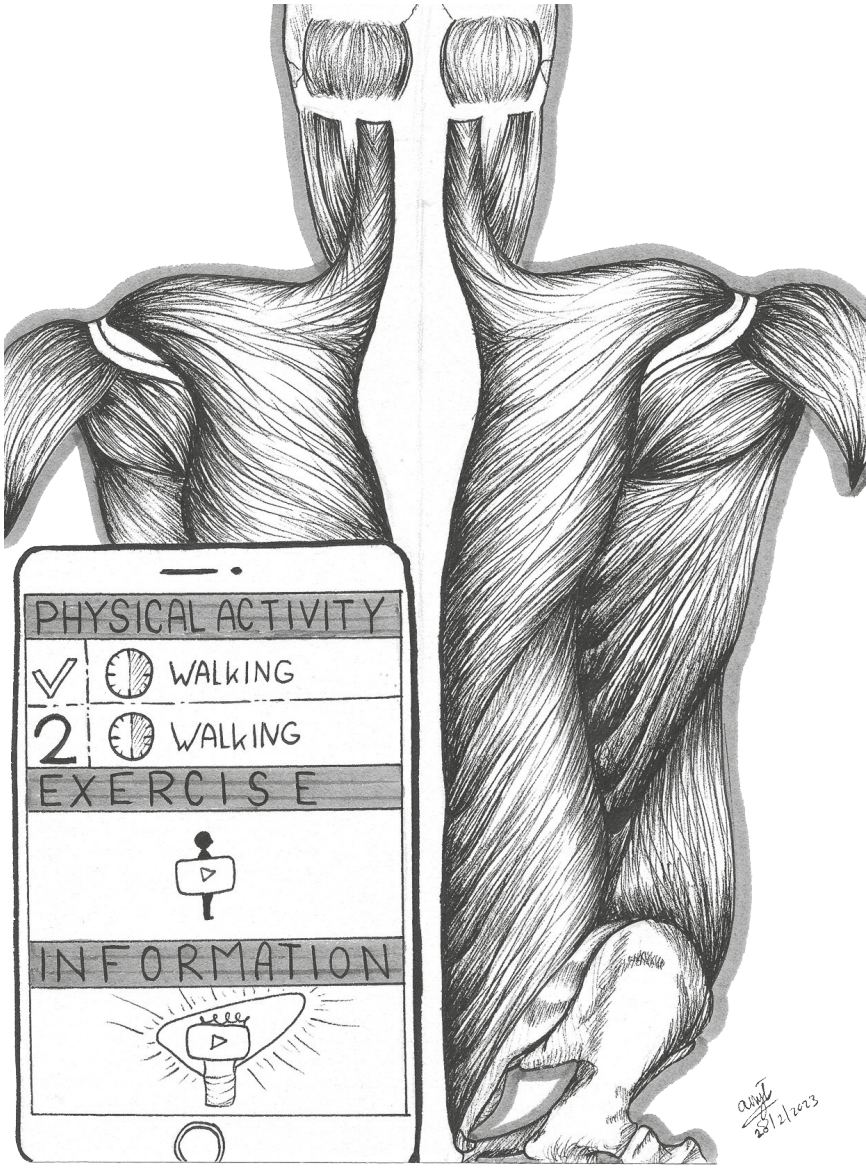
Content Validity	Structural Validity	Hypotheses Testing	Cross-cultural Validity	Criterion Validity	Responsive-ness
		+: r ODI = 0.90 +: r VAS = 0.87			
					+: AUC = 0.85
		+: r RMDQ = 0.60 +: r ODI = 0.74			
					+: AUC = 0.74
					+: AUC = 0.87
		+: r SF-36 = 0.64			
+	+: 7 factors accounting for 74% of the total variance				
+	+: 6 factors accounted for 82% of the total variance	+: r RMDQ = 0.70			
	+: 4 factors accounting for 71% of the total variance	+: r ODI = 0.81 +: r VAS = 0.62			

Appendix 3. Continued

Study	Language	Internal Consistency	Reliability	Measurement Error
Mousavi et al.[25]	Persian		+: ICC = 0.86	
Misterska et al.[24]	Polish		+: ICC = 0.93	
Rodrigues et al.[27]	Portuguese (Brazil)		IA-R: +: ICC = 0.93 IE-R: +: ICC = 0.96	IA-R: ?: MD LOA = -1.4 to 2.8 MIC = n/a IE-R: ?: MD LOA = -1.6 to 2.7 MIC = n/a
Cruz et al.[7]	Portuguese (Europe)	+: Cr.α = 0.95	+: ICC = 0.70	
Vieira et al.[30]	Portuguese (Europe)			-: SDC = 19 MIC = 6.5
De Beer et al.[9]	Tswana		+: ICC = 0.91	
Bicer et al.[41]	Turkish			
Düger et al.[14]	Turkish			
Melikoglu et al.[21]	Turkish	+: Cr.α = 0.94-0.95	+: ICC = 0.92	

* One study, evaluating the measurement properties of the QBPDS, resulted in two publications and is therefore mentioned once.
+ = positive rating; ? = indeterminate rating; - = negative rating; Cr.α = Cronbach's alpha; AUC = area under the curve; ICC = intraclass correlation coefficient; IE-R = Inter-rater reliability; IA-R = Intra-rater reliability; LOA = limits of agreement; LBP = low back pain; MD = minimal detectable; MIC = minimal important change; n/a = no information available; ODI = Oswestry Low Back Pain Disability Index; r = correlation; RMDQ = Roland-Morris Disability Questionnaire; SDC = smallest detectable change; VAS = visual analogue scale

Content Validity	Structural Validity	Hypotheses Testing	Cross-cultural Validity	Criterion Validity	Responsive-ness
		+: r SF-36 = 0.69 +: r ODI = 0.76 +: r RMDQ = 0.60 -: r VAS = 0.46			
		+: r RMDQ = 0.85 +: r VAS = 0.75			
	+: 1 factor accounting for 52% of the total variance *or* 4 factors accounting for 70% of the total variance	+: r RMDQ = 0.62 -: r VAS = 0.38			
					+: AUC = 0.74
		-: r VAS_0 = 0.37 -: r VAS_1 = 0.44 +: r ODI_0 = 0.67 +: r ODI_1 = 0.68			


PHYSICAL ACTIVITY
WALKING
2
WALKING
EXERCISE
INFORMATION

3

Effectiveness and cost-effectiveness of stratified blended physiotherapy in patients with nonspecific low back pain:

Study protocol of a cluster randomized controlled trial

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Authorship statement

I made a substantial contribution to the design of this study and have drafted the first version of the manuscript or substantively revised it. During the whole process I asked for and implemented input and feedback from the co-authors of this study.

ABSTRACT

Background

Patient education, advice on returning to normal activities and (home-based) exercise therapy are established treatment options for patients with nonspecific low back pain (LBP). However, the effectiveness of physiotherapy interventions on physical functioning and prevention of recurrent events largely depends on patient self-management, adherence to prescribed (home-based) exercises and recommended physical activity behaviour. Therefore we have developed e-Exercise LBP, a blended intervention in which a smartphone application is integrated within face-to-face care. E-Exercise LBP aims to improve patient self-management skills and adherence to exercise and physical activity recommendations and consequently improve the effectiveness of physiotherapy on patients' physical functioning. The aim of this study is to investigate the short- (3 months) and long-term (12 and 24 months) effectiveness on physical functioning and cost-effectiveness of e-Exercise LBP in comparison to usual primary care physiotherapy in patients with LBP.

Methods

This paper presents the protocol of a prospective, multicentre cluster randomized controlled trial. In total 208 patients with LBP pain were treated with either e-Exercise LBP or usual care physiotherapy. E-Exercise LBP is stratified based on the risk for developing persistent LBP. Physiotherapists are able to monitor and evaluate treatment progress between face-to-face sessions using patient input from the smartphone application in order to optimize physiotherapy care. The smartphone application contains video-supported self-management information, video-supported exercises and a goal-oriented physical activity module. The primary outcome is physical functioning at 12-months follow-up. Secondary outcomes include pain intensity, physical activity, adherence to prescribed (home-based) exercises and recommended physical activity behaviour, self-efficacy, patient activation and health-related quality of life. All measurements will be performed at baseline, 3, 12 and 24 months after inclusion. An economic evaluation will be performed from the societal and the healthcare perspective and will assess cost-effectiveness of e-Exercise LBP compared to usual physiotherapy at 12 and 24 months.

Discussion

A multi-phase development and implementation process using the Center for eHealth Research Roadmap for the participatory development of eHealth was used for development and evaluation. The findings will provide evidence on the effectiveness of blended care for patients with LBP and help to enhance future implementation of blended physiotherapy.

Trial Registration

ISRCTN, ISRCTN94074203. Registered 20 July 2018 – Retrospectively registered.

Keywords

E-health; Nonspecific low back pain; Physiotherapy; Telemedicine

BACKGROUND

Low back pain (LBP) is the most common cause of disability in western society[1]. LBP causes a significant economic burden and is responsible for high direct healthcare costs as well as high indirect costs due to time lost from work[2]. LBP can be caused by a specific pathology or trauma; however, in more than 90% of cases an underlying disease is absent[3,4]. The clinical course of this so-called 'nonspecific LBP' varies; some people recover within a couple of days or weeks, and other people experience persistent disabling symptoms leading to chronic LBP[2,5,6]. Both national and international clinical LBP guidelines endorse patient education, advice on returning to normal activities and the prescription of home-exercises and/or supervised exercise therapy[7-10].

However, the effectiveness of physiotherapy in patients with LBP does not solely depend on providing the most adequate physiotherapy interventions. It also highly depends on patients' adherence to prescribed (home) exercises and recommended physical activity behaviour[11,12]. Earlier research showed that 45–70% of patients do not adhere to prescribed exercises and physical activity recommendations[13-15], whereas adherent patients with LBP who continue a physically active lifestyle have a reduced risk of recurrent LBP[16]. Therefore, supporting self-management and adherence in patients with LBP is expected to be essential for the effectiveness of physiotherapy interventions on patients' physical functioning and prevention of recurrent events.

Online applications, such as websites and apps, provide new solutions to support patients' ability to manage their physical functioning in their home environment, and are promising to support self-management and adherence to prescribed (home) exercises between face-to-face sessions[17-20]. Consequently, the integration of online applications into healthcare, so-called blended care[21], is expected to have several advantages for patients with LBP. Firstly, a blended intervention can stimulate self-management and exercise adherence to prescribed (home) exercises and recommended physical activity behaviour in patients with LBP by its 24/7 online support and persuasive design[20,22-24]. Secondly, the use of online applications enables monitoring and coaching of the patients' individual health behaviour and provides the physiotherapist with information to optimize and tailor face-to-face care to the patients' individual needs[22,23,25-27].

Despite all these benefits, matching the appropriate blended treatment for the individual patient is reported as a challenge[28]. To resolve this challenge within traditional face-to-face guidance, stratification tools have gained more attention in the last decade. Within a stratified-care approach, the treatment is matched upon the patients' risk of developing persistent LBP, for example determined with the Keele STarT Back Screening Tool[29]. Research showed that such an approach results in improved physical functioning and satisfaction with care among patients with LBP while reducing costs of healthcare in both physiotherapy[30] and primary care settings[31,32]. Whereas the STarT Back Screening

Tool can be used for matching the appropriate content of the face-to-face care to the individual patient, this tool also might have the same potential for matching the right digital content to the individual patient. Up until now, no other groups have used a stratification tool for personalization of blended physiotherapy as a whole.

Recently, the authors' research group developed e-Exercise LBP, a blended and stratified intervention, in co-creation with patients, physiotherapists and experts[33]. E-Exercise LBP consists of face-to-face physiotherapy treatment, in which eCoaching is integrated using a smartphone application. E-Exercise LBP aims to improve patients' physical functioning by offering a blended stratified-care approach, and consequently influencing patients' self-management skills and adherence to exercise and physical activity recommendations in a positive way. At the long-term, e-Exercise LBP could result in an improved handling of recurrent LBP and direct and indirect costs. This blended care intervention is an adapted version of previously developed and evaluated blended physiotherapy programs[34,35]. A pilot study using a prototype of the e-Exercise LBP intervention in 41 patients with LBP demonstrated feasibility and proof-of-concept on functional disability and pain[33]. Based on the results of the pilot study and end-user (patients and physiotherapist) usability experiences, the e-Exercise LBP program was further improved in preparation for the current study.

This study aims to investigate the short- (3 months) and long-term (12 and 24 months) effectiveness on physical functioning and cost-effectiveness of e-Exercise LBP, a primary care based personalized stratified blended care intervention, in comparison to usual primary care physiotherapy in patients with nonspecific LBP.

METHOD/DESIGN

Study design

A prospective, multicentre cluster randomized controlled trial (RCT) will be conducted. The study has been approved by the Medical Research Ethics Committee of the University Medical Center Utrecht, the Netherlands (ISRCTN 94074203) for all centre sites. Within primary care, e-Exercise LBP will be compared to usual physiotherapy care. A flow diagram of the study protocol is shown in Figure 1.

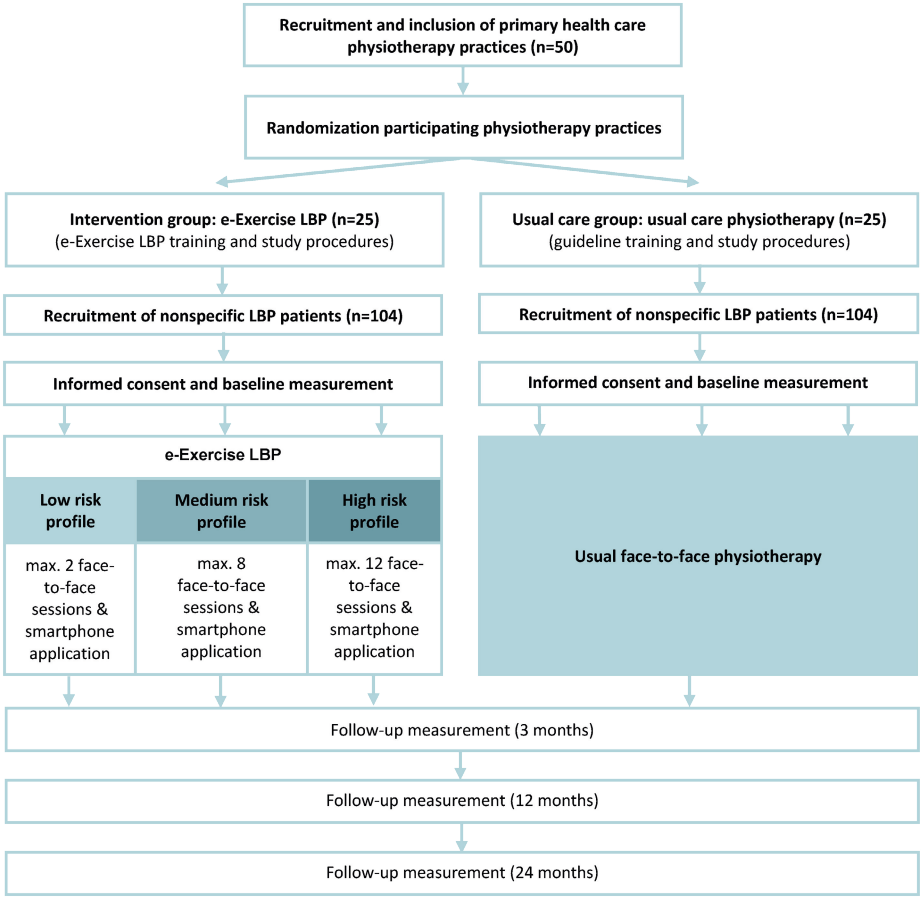

Figure 1. RCT study procedures

Participants

Primary care physiotherapy practices

Primary care physiotherapy practices will be invited by letter to participate in the study. Contact details of potential participating practices will be obtained from the professional network of the authors and a previous e- Exercise study[35]. Additionally, a recruitment advertisement will be placed in the online newsletter of The Royal Dutch Association for Physiotherapy (KNGF). Primary care physiotherapy practices are eligible to participate if at least five patients with nonspecific LBP consult the practice for physiotherapy treatment each month. Each participating physiotherapy practice will be asked to enrol at least two physiotherapists in order to ensure continuity of care. All primary care physiotherapists, regardless of professional experience and education or specialization (e.g. manual therapist) are eligible to participate.

Patients

All patients with LBP who visit a participating physiotherapy practice will be invited to participate in the study.

Eligibility criteria of patients include: (i) being a patient requesting physiotherapy treatment for LBP, defined as pain in the lumbosacral region (sometimes associated with radiating pain to the buttock or leg)[10,36], (ii) age 18 years or older, (iii) possessing a smartphone or tablet with access to the internet, (iv) mastery of the Dutch language.

Exclusion criteria include: (i) a specific cause of LBP determined through medical imaging or a medical doctor (e.g. osteoporotic fractures, spinal nerve compromise, malignancy, ankylosing spondylitis, canal stenosis, or severe spondylolisthesis), (ii) serious comorbidities (e.g., malignancy, stroke), (iii) current pregnancy, because of the prevalence of pelvic girdle pain as a specific form of LBP.

Study procedure

Physiotherapy practices that are willing to participate in the study will be screened on eligibility by a researcher (TK or RA). Cluster randomization will be performed at the level of the participating physiotherapy practices. Each practice will be randomly assigned to the intervention (e- Exercise LBP) or the usual care group by an independent researcher using an a priori created computer-generated random sequence table. Physiotherapists in the intervention group will receive two 4-h training sessions about e-Exercise LBP and the study procedures. In the usual care group, physiotherapists will receive one 4-h training session in current best evidence practice according to the guideline LBP of the Royal Dutch Association for Physiotherapy (KNGF)[10] and the study procedures.

Physiotherapists, or their colleagues who will handle the initial registration of the patient, will orally inform potentially eligible patients about the study. Interested patients will receive the patient information letter by e-mail and will be contacted by one of the researchers (TK or RA) by phone prior to the first physiotherapy appointment. When a patient is willing to participate, a face-to-face appointment with one of the researchers (TK or RA) will be scheduled to screen in- and exclusion criteria and to provide written informed consent. After signing informed consent, the patient's physiotherapist will be informed about the patient's participation.

During the study period, both patient groups can still receive care from any other healthcare professional.

Interventions

E-exercise LBP

A multi-phase development process based on the Center for eHealth Research (CeHRes) Roadmap[37] was used for development of the e-Exercise LBP intervention[33]. The e-Exercise LBP intervention integrates eCoaching using a smartphone application within face-to-face physiotherapy. The content is based on recommendations from national and international guidelines[7,8,10], and preferences and needs of patients and physiotherapists[33]. The principles of stratified care are used to personalize e-Exercise LBP to individual needs[30,31].

Smartphone application The smartphone application consists of three modules (Table 1): (i) An *information module* containing 12 weekly self-management themes (text and video), including assignments, about the aetiology of LBP, physical activity, patient experiences, pain management, and psychosocial factors related to LBP. (ii) An *exercise module* including a home-based video-instructed exercise program per prognostic risk profile. The selection, frequency and repetitions can be adjusted by the physiotherapist to address the patient's specific functional limitations. (iii) A *physical activity module* containing a goal-oriented training program consisting of three sessions a week, to maintain or improve the level of physical activity for a self-chosen type of activity (e.g., cycling or walking). The training program starts with a 3-day baseline test, and can be optionally supported by graded activity functionality with tailored feedback, which was previously studied in two osteoarthritis studies[35,38].

In patients having a "low risk" for developing persistent LBP the smartphone application will offer support for 3 weeks. In "medium" – and "high risk" patients the support will be 12 weeks. Afterwards the content of the smartphone application will remain available for the patients. In "low risk" patients the smartphone application will only contain the information – and exercise modules. In "medium – and high risk" patients the physical activity module will be added. The results of the baseline test of the physical activity module will be used by the physiotherapist and patient to set a goal to reach within 11 weeks. The graded activity functionality can be switched on in "medium risk" patients who avoid physical activity because of LBP. For "high risk" patients the graded activity functionality will always be activated. Print screens of the smartphone application are given in Appendix 1.

Face-to-face care During the first face-to-face session, the physiotherapist will tailor the e-Exercise LBP intervention to the patients' identified risk for developing persistent LBP (i.e. low, medium or high), using the Keele STarT Back Screening Tool[29,39,40] (Figure 1, Table 1). Patients are asked to schedule their exercises and physical activities in the smartphone application, after which the smartphone application will sent automatic pop-up reminders accordingly. Physiotherapists will be able to monitor patients' use of the smartphone application, monitor evaluated assignments, and select other types

of exercises. With this information, the physiotherapist will be able to evaluate the progress and beliefs of the patients between face-to-face sessions, optimize the content of the smartphone application to patients' individual needs, and tailor face-to-face care.

Physiotherapists are recommended to provide two face-to-face physiotherapy sessions to patients labelled as "*low risk*", 8 sessions for patients labelled as "*medium risk*", and 12 sessions for patients labelled as "*high risk*". The objective of face-to-face care is to reassure the patient, provide information about LBP, instruct on self-management options, and underline the importance of adequate physical activity behaviour in accordance with the guideline LBP of the Royal Dutch Association for Physiotherapy (KNGF)[10]. Additionally, in medium- and high risk patients, the physiotherapist can consider to provide evidence-based interventions (e.g., passive or active joint mobilization) as recommended by the guideline LBP of the Royal Dutch Association for Physiotherapy (KNGF)[10]. In high risk patients, the physiotherapist will address patient specific psychosocial risk factors using a cognitive behavioural therapy approach, and pain education will be given[41,42]. However, with respect to the physiotherapists' clinical competences, physiotherapists are allowed to deviate from the e-Exercise protocol.

After completing e-Exercise LBP, the patient will receive fortnightly reminders from the smartphone application for up to 6 months to continue a physically active lifestyle.

Usual care

Patients in the usual care group will receive face-to-face usual care following the recommendations of the guideline LBP of the Royal Dutch Association for Physiotherapy (KNGF)[10]. Although eCoaching applications are not recommended in the guideline, physiotherapists from the usual care group are instructed to treat people without using any eCoaching applications. According to the guideline, the physiotherapy treatment includes information, exercises, and recommendations regarding physical activity. Practical content considerations will be made by the physiotherapists themselves with respect to their clinical expertise. The number of sessions will differ per patient.

Table 1. Overview e-Exercise LBP intervention

Mode of delivery	Low-risk profile	Medium-risk profile	High-risk profile
Smartphone application			
- Duration	3 weeks	12 weeks	12 weeks
- Information module	Knowledge-based platform with several LBP self-management information themes (directly available)	12 weekly self-management themes, including assignments	12 weekly self-management themes, including assignments, pain education and psychosocial risk factors

Table 1. Continued

Mode of delivery	Low-risk profile	Medium-risk profile	High-risk profile
- Exercise module	3-4 home-based exercises tailored to the patient's specific functional limitations	3-4 home-based exercises tailored to the patient's specific functional limitations	3-4 home-based exercises tailored to the patient's specific functional limitations
- Physical activity module	Physical activity recommendations in accordance with the KNGF guideline LBP	A 3-day baseline test to determine current level of physical activity. An 11-week, 3 times per week, goal-oriented training program to maintain or improve the level of physical activity. In patients avoiding physical activity due to LBP a graded activity functionality can be activated	A 3-day baseline test to determine current level of physical activity. An 11-week, 3 times per week, goal-oriented training program to maintain or improve the level of physical activity using a graded activity approach
Face-to-face care			
- Sessions	2 sessions	Max. 8 sessions	Max. 12 sessions
- Content	Reassurance, information about LBP, instruction on self-management options, and the importance of adequate physical activity behaviour	Content similar as low risk and additionally: The physiotherapist can consider to provide evidence-based interventions (e.g. passive or active joint mobilization) as recommended by KNGF guideline LBP	Content similar as medium risk and additionally: The physiotherapist will address patient's specific psychosocial risk factors using a cognitive-behavioural approach and pain education will be given
Integration of face-to-face care and smartphone application			
- First session	Provide information about LBP and instruction on home-based exercises addressing patient's specific functional limitations using the smartphone application	Provide information about LBP, instruction on home-based exercises addressing patient's specific functional limitations, and instruction on 3-day baseline test using the smartphone application	Provide information about LBP, instruction on home-based exercises addressing patient's specific functional limitations, and instruction on 3-day baseline test using the smartphone application

Table 1. Continued

Mode of delivery	Low-risk profile	Medium-risk profile	High-risk profile
- Middle sessions		Evaluation of progress with smartphone application and optimizing face-to-face care	Evaluation of progress with smartphone application and optimizing face-to-face care
- Final session	Evaluate the progress with smartphone application and give recommendations to prevent recurrent episodes of LBP and maintain or improve the physical activity level	Evaluate the progress with smartphone application and give recommendations to prevent recurrent episodes of LBP and maintain or improve the physical activity level	Evaluate the progress with smartphone application and give recommendations to prevent recurrent episodes of LBP and maintain or improve the physical activity level

LBP = low back pain; KNGF = Royal Dutch Association for Physiotherapy; Max. = Maximum

Measurements

Four time points (baseline, 3, 12 and 24 months) will be used for data collection of the primary and secondary outcomes using an online questionnaire. Baseline measurement will be conducted face-to-face and follow-up measurements preferably through online communication, e.g., Skype or FaceTime. When follow-up measurements through online communication are not possible, follow-up measurements will be conducted face-to-face. At all four time points participants will receive an accelerometer (Activ8) for the objective measurement of physical activity. Participants will be instructed to wear the Activ8 for five consecutive weeks at baseline and eight consecutive days at all following time points, except during sleeping, showering, bathing or swimming. For the economic evaluation, patients will be asked to complete eight retrospective 3-monthly online cost questionnaires. All of these questionnaires will have a 3-month recall period to cover the full duration of follow-up (i.e., 24 months). No financial incentives to complete questionnaires or to wear accelerometers will be offered. Table 2 gives a summary of all outcome measures and time points.

Primary outcome measure

The primary outcome measure is *physical functioning* and is derived from the internationally accepted "Core Outcome Set" (COS) for research into patients with nonspecific LBP. The other recommended outcomes are included as secondary parameters, i.e., pain intensity, health-related quality of life, psychological functioning and pain interference[43-45] (Table 2). All selected measurement instruments in the current study are determined to be valid and reliable in previous research.

Physical functioning due to pain in LBP patients is assessed by the Oswestry Disability Index (ODI), version 2.1a[44-46].

Secondary outcome measures

Pain intensity is measured with an 11-point Numeric Rating Scale (NRS) for the average LBP intensity in the last week[44,45,47].

Physical activity is objectively measured using a 3-axial accelerometer, the Activ8 (ACTIV8, Valkenswaard, The Netherlands)[48]. The Activ8 is a valid instrument to detect sedentary behaviour (combination of lying and sitting), standing, walking, running, and cycling. Additionally, MET-values are given. The Activ8 measures with 12.5 Hz, an epoch of 1 s a sample interval of 5 s. Every 5 min a summary is stored of the different postures and MET-values[49]. In addition, participants are requested to fill out a short activity diary about unusual activities and reasons for device removal.

Patient self-reported adherence to prescribed home exercises is measured by the Exercise Adherence Rating Scale (EARS). Besides that, the EARS measures the exercise prescription and the reasons for (non-)adherence[50].

Physiotherapist based assessment of adherence to prescribed home exercises is measured by the Exercise Adherence Scale (EXAS). The EXAS is an interview-based questionnaire which is used by the physiotherapist during face-to-face care to determine both the qualitative performance of the recommended home exercises and the agreement between recommended home exercises and patient reported adherence[51].

Adherence to the smartphone application is measured in the experimental group only by means of quantitative data about usage (e.g., completed modules). The data is automatically stored on the backend of the smartphone application.

Fear avoidance beliefs about physical activity and work is measured using the Fear-Avoidance Beliefs Questionnaire (FABQ). The FABQ assesses the fear of movement/(re) injury and consists of items related to physical activity and work[52].

Pain catastrophizing is measured by the Pain Catastrophizing Scale (PCS) The PCS is a self-report measurement tool that provided a valid index of catastrophizing in clinical and non-clinical populations[53,54].

Self-efficacy, i.e., the patients beliefs in their efficacy to influence events that affect their lives[55], is measured using the General Self-efficacy Scale (GSE Scale)[56-58].

Patient activation is assessed by the Dutch version of the short form Patient Activation Measure (PAM 13-Dutch)[59,60]. The Pam 13-Dutch assesses patient (or consumer) self-reported knowledge, skills and confidence for self-management of one's health or chronic condition.

The number of recurrent LBP episodes is measured by the number of self-reported LBP episodes during the follow-up period. A recurrent LBP episode is defined as return of LBP with a minimum duration of 24 h after a period of at least 4 weeks without pain[61].

Other measures

Patient characteristics, i.e., age, gender, educational level, profession, employment status, and medical history related to LBP over the past 2 years, are measured using an online questionnaire. Besides that, relevant clinical variables such as duration of current complaints, Body Mass Index, past surgeries, risk of developing persistent LBP, the presence of central sensitivity, and possible comorbidities are collected.

Content and number of physiotherapy sessions are measured trough registration forms, developed by the researchers. The registration forms collect information on the number and content of face-to-face sessions, adherence to face-to-face sessions and deviations from the study protocol and are completed by the physiotherapists.

Table 2. Schedule of enrolment, interventions, and assessments

	STUDY PERIOD								
	Enrolment	Allocation	Post-allocation						Close-out
TIMEPOINT	0m	0m	3m	6m	9m	12m	15m	18m	21m	24m
ENROLMENT:										
Eligibility screen	X									
Informed consent	X									
Allocation		X								
INTERVENTIONS:										
e-Exercise LBP		⟷								
Usual care		⟷								
ASSESSMENTS:										
Patient characteristics										
Age		X								
Gender		X								
BMI		X								
Educational level, profession and employment status		X								
Medical history related to LBP, past surgeries and co-morbidities		X								
Duration of LBP complaints		X								
Risk of developing persistent LBP		X								
Central sensitivity		X								
Primary outcome measure										
Physical functioning (ODI)		X	X			X				X

Table 2. Continued

	STUDY PERIOD									
	Enrolment	Allocation	Post-allocation							Close-out
TIMEPOINT	0m	0m	3m	6m	9m	12m	15m	18m	21m	24m
Secondary outcome measure										
Pain intensity (11-point NRS)		X	X			X				X
Physical activity (Activ8)		X	X			X				X
Patient self-reported Adherence to prescribed exercises (EARS)		X	X			X				X
PT assessed adherence to prescribed exercises (EXAS)		⟷								
Adherence to the smartphone application (Backend application)		⟷	⟷	⟷	⟷	⟷	⟷	⟷	⟷	⟷
Fear avoidance beliefs (FABQ)		X	X			X				X
Pain catastrophizing (PCS)		X	X			X				X
Self-efficacy (GSE Scale)		X	X			X				X
Patient activation (PAM 13-Dutch)		X	X			X				X
Number of recurrent LBP episodes (Questionnaire)			X			X				X
Economic evaluation										
Health related quality of life (EQ-5D-5L)		X	X			X				X
LBP related costs (Cost questionnaire)		X	X	X	X	X	X	X	X	X
Other measures										
Content and number of PT sessions (Registration form)		⟷								

⟷ Indicator for a period; duration of the period is not limited to length of the indicator and dependent on duration of interventions and use of smartphone application

LBP = low back pain; BMI = Body Mass Index; ODI = Oswestry Disability Index; NRS = Numeric Rating Scale; EARS = Exercise Adherence Rating Scale; PT = Physiotherapist; EXAS = Exercise Adherence Scale; FABQ = Fear-Avoidance Beliefs Questionnaire; PCS = Pain Catastrophizing Scale; GSE scale = General Self-efficacy Scale; PAM = Patient Activation Measure; EQ-5D-5L = EuroQol 5D

Sample size calculation

The required sample size was calculated according to the recommendations of Campbell et al. (2010) for cluster randomized trials[62,63], taking into account repeated measures of the primary outcome measure physical functioning on the ODI during follow-up[64]. An intracluster correlation coefficient of 0.05 was used[65,66]. Additionally, to detect a clinical relevant difference between groups at 12 months following baseline, a difference of > 6 points in physical functioning on the ODI[67,68] and a standard deviation of 14.5[69] were used in the sample size calculation. For the repeated measures of physical functioning on the ODI a correlation of 0.5 is estimated between baseline and follow-up measurements until 12 months follow-up[64]. Based on these assumptions (using a power of 80% and $\alpha = 0.05$) and average cluster size of 5, in total 165 patients are needed. With an expected dropout rate of 20% a total of 207 participating patients (104 patients per arm) are needed.

Statistical analysis

Descriptive statistics (e.g., means and proportions) will be used to explore baseline comparability. To investigate selective attrition, general characteristics and primary baseline variables of dropouts and non-dropouts will be compared All analyses will be performed according to the 'intention-to-treat' principle. Missing data for all outcomes and cost measures will be imputed using 'Multivariate Imputation by Chained Equations' under the assumption that data are missing at random given baseline confounders. For all analysis, a two-tailed significance level of $p < 0.05$ is considered to be statistically significant. All analyses will be carried out using IBM SPSS Statistics version 24.0 (Amork, New York, USA).

Effectiveness

The primary purpose of this study is to estimate the effectiveness of e-Exercise LBP for improving physical functioning compared to usual primary care physiotherapy in patients with LBP. The primary analysis time point for the study will be 12 months following baseline, however 3- and 24-month changes will also be evaluated. To evaluate the overall effectiveness of e-Exercise LBP, differences in change scores per group and time period will be estimated on primary and secondary outcomes using linear mixed models (LMM) with random effects to control for correlation within patients and physiotherapists[70,71]. The three-level hierarchy will exist of repeated measurements (level 1), nested within patients (level 2), nested within physiotherapists (level 3). Analysis will be controlled for baseline variables that have been shown to be related to physical functioning, e.g., age, gender, pain severity scores, duration of pain[72-74].

In addition, a per-protocol analysis that only includes patients of the intervention group which were adherent to the smartphone application and the entire usual care group will be performed. Patients will be considered to be adherent to the smartphone application if they used the application for at least 2/3rd of the duration (i.e., 2 out of 3 week for

the "low-risk" profile and 8 out of 12 weeks for the "medium- and high-risk" profile)[35,75]. Per-protocol analyses will be performed using LMM with the same 3-level structure, and will be controlled for the same variables as the primary analysis.

Economic evaluation

An economic evaluation will be performed from the societal and the healthcare perspective and will assess the cost-effectiveness of e-Exercise LBP compared to usual physiotherapy at 12 and 24 months.

Identification, measurement and valuation of costs When the societal perspective is applied intervention, healthcare, informal care, unpaid productivity, and paid productivity costs will be included. When the healthcare perspective is applied, only costs accruing to the formal Dutch healthcare sector will be included. The costs of e-Exercise LBP will be estimated using a bottom-up micro-costing approach[76]. Information on the patients' other kinds of resource use will be collected using eight 3-monthly retrospective cost questionnaires with 3-month recall periods. Healthcare utilization, unpaid productivity, and informal care will be valued in accordance with the "Dutch Manual of Costing"[77]. Paid productivity losses comprise of absenteeism (i.e., sickness absence) and presenteeism (i.e., reduced productivity while at work). Absenteeism was measured using a modified version of the IMTA Productivity Cost Questionnaire (iPCQ). Absenteeism will be valued in accordance with the "Friction Cost Approach" (FCA), using gender-specific price weights[78,79]. Presenteeism will be measured using the "World Health Organization – Work Performance Questionnaire" as well as the "Productivity and Disease Questionnaire", and valued using gender-specific price weights as well[78-81].

Measurement and valuation of health-related quality of life The patients' health states will be measured using the EuroQol-5D-5L (EQ-5D-5L)[82-85]. This questionnaire comprises of five health dimensions, i.e., mobility, self-care, usual activities, pain/discomfort and anxiety/depression. Per health dimension, patients are asked to indicate their severity level. Health states will be converted into utility values using the Dutch tariff[86] and Quality Adjusted Life Years (QALYs) will be estimated using linear interpolation between measurement points.

Statistical analyses Missing cost and effect data will be imputed using 'Multivariate Imputation by Chained Equations' and the results will be pooled using Rubin's rules[87]. Cost differences (ΔC) and effect differences (ΔE) will be estimated using LMM, and will be corrected for the same baseline variables as the effectiveness analysis. To account for the highly skewed nature of cost data, bias-corrected and accelerated bootstrapping with 5000 replications will be used to estimate 95% confidence intervals around the cost differences (ΔC). Incremental cost-effectiveness ratios (ICERs) will be calculated by dividing the difference in costs by the difference in effects (ΔC/ΔE). Uncertainty

surrounding the ICERs will be graphically illustrated by plotting bootstrapped cost-effect pairs on cost-effectiveness planes and by estimating cost-effectiveness acceptability curves. To test the robustness of the study results, several sensitivity analyses will be performed[88].

Timeline

Recruitment of physiotherapy practices began in January 2018. The trial started in July 2018. Until January 2020 patients are able to enrol in the study. The follow-up will last until January 2022. Analysis of short-term effectiveness will start in March 2020, analysis of 12-month (cost-)effectiveness will start in January 2021.

DISCUSSION

This paper describes the design and methods of the e-Exercise LBP trial. The aim of the presented study is to investigate the short-term as well as the long-term effectiveness and cost-effectiveness of e-Exercise LBP compared to usual physiotherapy in patients with LBP. E-Exercise LBP is a stratified blended care intervention in which an eCoaching smartphone application is integrated into primary care face-to-face physiotherapy.

A major strength of this study is that the e-Exercise LBP trial is part of a multi-phase development and implementation process which was based on the Center for eHealth Research (CeHRes) Roadmap[37]. This holistic framework provides guidance during the participatory development of eHealth in order to enhance future implementation. As part of the development of the e-Exercise LBP intervention, needs and values of end-users and various stakeholders (e.g., physiotherapists, developers) were used to develop the first prototype[33]. Next, the prototype was tested on feasibility in a pilot study[33]. Based on experiences of patients and physiotherapists several important adaptations were made to the prototype of the e-Exercise LBP intervention. A first important adaptation is the development of a smartphone application, which was based on the web-based application used in the prototype. Secondly, the content of the smartphone application was stratified to match the stratification of face-to-face care for patients at low, medium or high risk for developing persistent LBP. As a result, the content of the smartphone application for low-risk patients was provided immediately instead of spread out over 12 weeks. The graded activity functionality was made mandatory for patients with a high risk for developing persistent LBP. On top of that, each information theme was enriched with an assignment in order to stimulate self-reflection. Overall, we believe that the improved smartphone application with various options for physiotherapists to personalize the content of the application, might help to improve patients' level of physical functioning in patients with LBP.

Besides further development of the e-Exercise LBP intervention, several important methodological considerations were made with respect to the study design of the e-Exercise LBP trial. A first consideration was the use of a cluster-randomized controlled design to avoid contamination between the e-Exercise LBP intervention and usual physiotherapy care at the level of the participating physiotherapist. Cluster-randomization at the level of the participating physiotherapy practices ensures that each participating physiotherapist working in the same physiotherapy practice delivers the same intervention[89]. The influence of clustering will be corrected using LMM in the statistical analysis.

Since the e-Exercise LBP intervention aims to improve physical functioning, this outcome measurement was selected as primary outcome measurement. Intervention duration will last up to 3 months, but a 12-month evaluation will provide insight in the effectiveness of e-Exercise LBP on the long-term. However, with respect to the cost-effectiveness, it is hypothesized that patients who followed e-Exercise LBP are able to manage recurrent complaints independently, resulting in reduced healthcare usage or sickness absence. Since a 12-month follow-up might be too short to study this hypothesis, we added a 24-month follow-up focusing on the management of recurrent complaints.

Because the study design is well-considered, several potential operational issues are taken into account. An important operational issue is the physiotherapists' training in the e-Exercise LBP intervention. From previous studies we learned that implementing a blended intervention into daily routine is a complex process that changes existing routines[28]. Therefore, training of the participating physiotherapists in the e-Exercise LBP intervention has been expanded from a 4-h training session to two 4-h training sessions. Additionally, Siilo, a secure messenger for healthcare professionals to communicate and share information, will be used during the study to be able to provide direct assistance to participating physiotherapists. And finally, instruction videos were created to support physiotherapists in using the e-Exercise LBP intervention. Another important operational issue is the possible increased risk of drop-outs during this study due to the 24-month follow-up period and the 11 questionnaires that have to be completed during this period. To minimize this risk, a researcher (TK or RA) will conduct the follow-up assessments at 3, 12 and 24 months in person, i.e., by phone, Skype or face-to-face. A final operational issue is the belief that e-Exercise LBP will not provide a solution for all patients having LBP, nor for all physiotherapists treating patients with LBP. Therefore, selection bias could occur, e.g., participants or physiotherapists having low digital literacy skills, or have a more negative attitude towards technology in general, are less likely to be included in this study.

However, with respect to our digitalized society it is expected that the majority of patients with LBP can benefit from the e-Exercise LBP intervention. The results of this study will help to understand whether blended physiotherapy for patients with LBP can be implemented on this basis.

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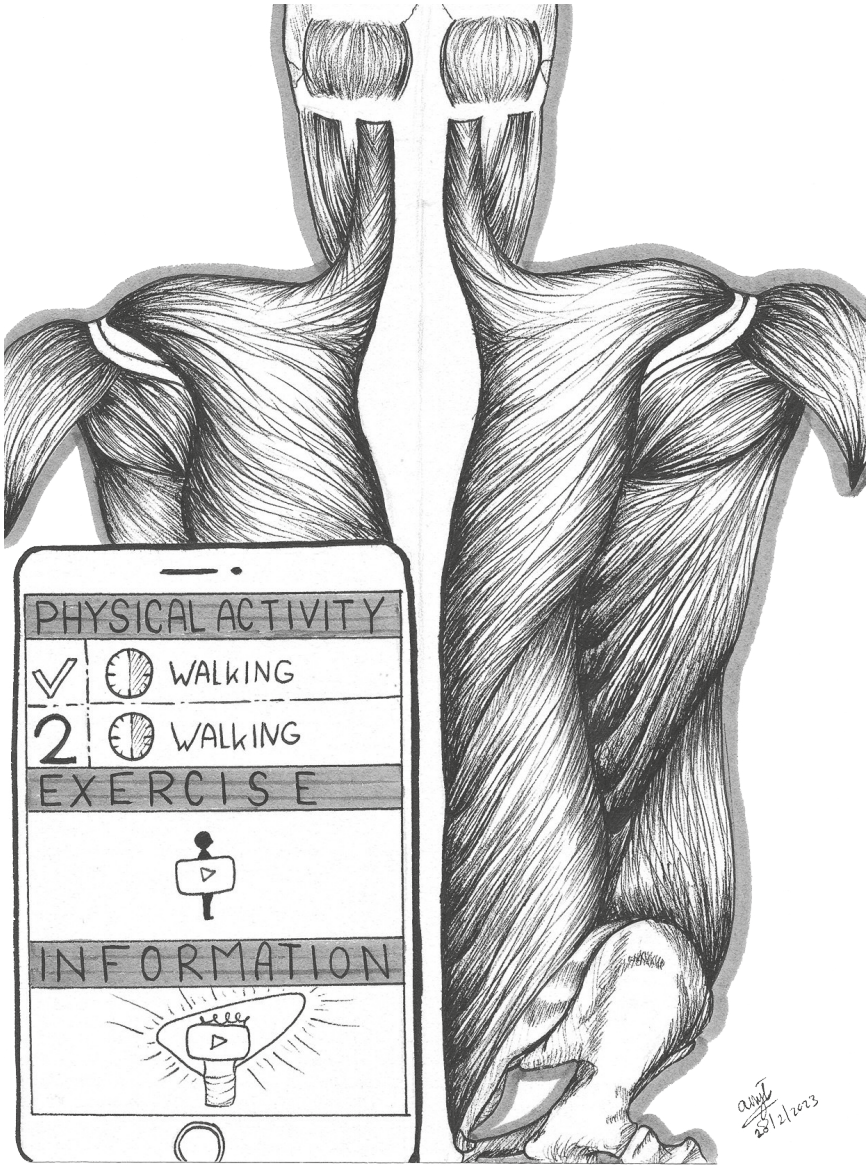
Appendix 1. Print screens of the smartphone application


PHYSICAL ACTIVITY
WALKING
2
WALKING
EXERCISE
INFORMATION

4

The 3-month effectiveness of a stratified blended physiotherapy intervention in patients with nonspecific low back pain:

Cluster randomized controlled trial

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Authorship statement

I participated in the development of the design of the study, conducted the study, performed data management, and performed the statistical analyses. I drafted and revised the manuscript and implemented the contribution of the co-authors and external reviewers up to final publication. During the whole process I asked for and implemented input and feedback from the other contributors to this study.

ABSTRACT

Background

Patient education, home-based exercise therapy, and advice on returning to normal activities are established physiotherapeutic treatment options for patients with nonspecific low back pain (LBP). However, the effectiveness of physiotherapy interventions on health-related outcomes largely depends on patient self-management and adherence to exercise and physical activity recommendations. e-Exercise LBP is a recently developed stratified blended care intervention comprising a smartphone app integrated with face-to-face physiotherapy treatment. Following the promising effects of web-based applications on patients' self-management skills and adherence to exercise and physical activity recommendations, it is hypothesized that e-Exercise LBP will improve patients' physical functioning.

Objective

This study aims to investigate the short-term (3 months) effectiveness of stratified blended physiotherapy (e-Exercise LBP) on physical functioning in comparison with face-to-face physiotherapy in patients with nonspecific LBP.

Methods

The study design was a multicenter cluster randomized controlled trial with intention-to-treat analysis. Patients with nonspecific LBP aged ≥18 years were asked to participate in the study. The patients were treated with either stratified blended physiotherapy or face-to-face physiotherapy. Both interventions were conducted according to the Dutch physiotherapy guidelines for nonspecific LBP. Blended physiotherapy was stratified according to the patients' risk of developing persistent LBP using the Keele STarT Back Screening Tool. The primary outcome was physical functioning (Oswestry Disability Index, range 0-100). Secondary outcomes included pain intensity, fear-avoidance beliefs, and self-reported adherence. Measurements were taken at baseline and at the 3-month follow-up.

Results

Both the stratified blended physiotherapy group (104/208, 50%) and the face-to-face physiotherapy group (104/208, 50%) had improved clinically relevant and statistically significant physical functioning; however, there was no statistically significant or clinically relevant between-group difference (mean difference −1.96, 95% CI −4.47 to 0.55). For the secondary outcomes, stratified blended physiotherapy showed statistically significant between-group differences in fear-avoidance beliefs and self-reported adherence. In patients with a high risk of developing persistent LBP (13/208, 6.3%), stratified blended physiotherapy showed statistically significant between-group differences in physical functioning (mean difference −16.39, 95% CI −27.98 to −4.79) and several secondary outcomes.

Conclusions
The stratified blended physiotherapy intervention e-Exercise LBP is not more effective than face-to-face physiotherapy in patients with nonspecific LBP in improving physical functioning in the short term. For both stratified blended physiotherapy and face-to-face physiotherapy, within-group improvements were clinically relevant. To be able to decide whether e-Exercise LBP should be implemented in daily physiotherapy practice, future research should focus on the long-term cost-effectiveness and determine which patients benefit most from stratified blended physiotherapy.

Trial Registration
ISRCTN Registry 94074203; https://doi.org/10.1186/ISRCTN94074203

Keywords
E-Health; Nonspecific low back pain; Physiotherapy; Blended care; Mobile phone

INTRODUCTION

Low back pain (LBP)–related disability and the related socioeconomic burden remain high despite the many treatment options and healthcare resources available for LBP[1]. LBP can be caused by a specific pathology or trauma; however, in >90% of cases, an underlying disease is absent[2]. The clinical course of this so-called *nonspecific LBP* varies and, as expected, is often less favourable; some patients recover within a couple of days or weeks, and other patients experience persistent disabling symptoms leading to chronic LBP. Up to 65% of primary care patients with LBP still experience pain 1 year after onset[3,4].

Clinical practice guidelines recommend a patient-centred approach for the management of LBP[5,6]. This approach identifies patients with an increased likelihood of delayed recovery at an early stage and stratifies the treatment accordingly[6-8]. An example of a tool for identifying individuals at risk of delayed recovery is the Keele STarT Back Screening Tool[9,10]. In general, in patients who have a *low risk* for delayed recovery, early management comprises advice, reassurance, and education about the nonspecific nature of their LBP and encouragement to stay active. For individuals at *medium risk* for developing persistent LBP, personalized and supervised exercise therapy should be considered. For the *high-risk* group, this exercise therapy can be supported by a graded activity approach or cognitive behavioural components[8,11]. In addition to a patient-centred and stratified approach, patients' adherence to prescribed (home-based) exercises and recommended physical activity behaviour is crucial for the effectiveness of care[12]. Earlier research showed that 45% to 70% of patients do not adhere to prescribed exercises and physical activity recommendations, whereas adherent patients with LBP have a reduced risk of recurrent LBP[13,14].

Within the treatment of patients with LBP, *blended care* is a promising new and understudied field[15]. Blended care refers to the integration of web-based and offline components within the treatment process and requires that both components contribute equally to the treatment process[16,17]. The integration of web-based components, such as websites and apps, provides new solutions to monitor and coach patients' individual health behaviours and support the optimization of face-to-face care tailored to the patients' individual needs[18-20]. Thereafter, web-based components can be an effective means of stimulating adherence to prescribed exercises at home between face-to-face sessions and possibly increase self-management of LBP[21,22]. Until now, evidence on patient-centred and stratified care has not been integrated into blended care. Therefore, we recently developed e-Exercise LBP, a stratified blended intervention in which a smartphone app is integrated within face-to-face physiotherapy treatment, and established its feasibility and proof of concept for the treatment of functional disability and pain[23]. e-Exercise LBP is an adapted version of previously developed and evaluated blended physiotherapy programs[24,25]. Following the promising effects

of web-based applications for patients' self-management skills and adherence to exercise and physical activity recommendations, it is hypothesized that e-Exercise LBP will improve patients' physical functioning. However, the effectiveness of e-Exercise LBP in comparison with primary care physiotherapy still needs to be determined. The primary aim of this study is to investigate the short-term (3 months) effectiveness of stratified blended physiotherapy (e-Exercise LBP) on physical functioning in comparison with face-to-face physiotherapy in patients with nonspecific LBP.

METHODS

Design and ethical considerations

The e-Exercise LBP study was a prospective multicenter cluster randomized controlled trial. The study protocol was approved by the medical research ethics committee of the University Medical Center Utrecht, the Netherlands (18-085/D), and registered at the onset of patient enrolment (ISRCTN 94074203). From January 2018 to June 2018, 122 physiotherapists working in 58 primary care physiotherapy practices were recruited and randomized to either stratified blended physiotherapy (e-Exercise LBP) or face-to-face physiotherapy. Details of the design and methods of the study have been published previously[26]. This study is reported according to the CONSORT (Consolidated Standards of Reporting Trials) statement for cluster randomized trials.

Recruitment

Setting and randomization

Physiotherapists were recruited by an invitational letter sent to the professional network of the authors and physiotherapists who participated in a previous e-Exercise study[24]. In addition, an advertisement was placed in the web-based newsletter of the Royal Dutch Society for Physiotherapy. Physiotherapy practices could participate with ≥1 physiotherapist, regardless of professional experience and education or specialization (e.g., manual therapy). Physiotherapists were cluster randomized at the level of practice to avoid contamination. Treatment allocation was concealed and performed by an independent researcher using a computer-generated, a priori created, random sequence table and in a 1:1 allocation ratio. Physiotherapists and patients were not blinded to the group allocation.

The physiotherapists in the stratified blended physiotherapy group received two 4-hour training sessions on e-Exercise LBP and the study procedures. In the face-to-face physiotherapy group, physiotherapists received a 4-hour training session in current best practices according to the LBP guidelines of the Royal Dutch Society for Physiotherapy[11] and the study procedures.

Patients

Patients with LBP who contacted a participating physiotherapy practice were orally informed about the study and invited to participate. Interested patients received a patient information letter by email and an informative phone call by one of the researchers (TK or RMA) before the first appointment. When a patient was willing to participate after the phone call, a face-to-face appointment was scheduled (by TK or RMA) to obtain written informed consent and verify eligibility. The eligibility criteria were as follows: (1) being a patient requesting physiotherapy treatment for nonspecific LBP, defined as pain in the lumbosacral region (sometimes associated with radiating pain to the buttock or leg)[11]; (2) aged ≥18 years; (3) possessing a smartphone or tablet (iOS or Android operating system) with access to the internet; and (4) mastery of the Dutch language. The exclusion criteria were as follows: (1) a specific cause of LBP determined through medical imaging or a medical physician, (2) serious comorbidities (e.g., malignancy or stroke), and (3) current pregnancy because of the prevalence of pelvic girdle pain as a specific form of LBP.

Intervention

Experimental: Stratified blended physiotherapy (e-Exercise LBP)

Patients allocated to the stratified blended physiotherapy group received blended physiotherapy, comprising a smartphone app integrated within face-to-face physiotherapy treatment[23,26]. Both the contents of the smartphone app and the face-to-face physiotherapy treatment are based on the recommendations of the LBP guidelines of the Royal Dutch Society for Physiotherapy[11]. The duration and content of the stratified blended physiotherapy intervention were based on the patients' risk for developing persistent LBP (*low, medium, or high*) using the Keele STarT Back Screening Tool[9,10]. The smartphone app contains video-supported self-management information, video-supported exercises, and a goal-oriented physical activity module. Both the contents of face-to-face care and the smartphone app were tailored by the physiotherapists to the patients' individual needs and progress (Table 1). Although physiotherapists were recommended to treat according to the stratified blended physiotherapy protocol, they were free to deviate from the protocol with respect to their clinical competence. Print screens of the smartphone app are provided in Appendix 1.

Control: Face-to-face physiotherapy

Patients in the face-to-face physiotherapy group received only face-to-face care following the recommendations of the LBP guidelines of the Royal Dutch Society for Physiotherapy[11]. The guideline distinguishes between three different patient profiles based on the clinical course of recovery (i.e., normal recovery, abnormal recovery without predominant psychosocial factors, and abnormal recovery with predominant psychosocial factors) but does not use a specific tool to stratify care a priori. The content of face-to-face physiotherapy was the same as the stratified blended care intervention (i.e., information, exercises, and recommendations regarding physical

activity). However, no recommendations or restrictions were provided with regard to the number of face-to-face sessions. Although web-based applications, such as websites and apps, are not recommended in the guidelines, physiotherapists were instructed to treat people without using any web-based applications to assure contrast between both groups. Practical content considerations were made by the physiotherapists themselves with respect to their clinical expertise.

Measurements

Patients received a web-based questionnaire and an accelerometer at baseline and after 3 months of follow-up. Baseline measurements were conducted face to face and follow-up measurements through web-based communication (e.g., FaceTime) or face to face when requested. No financial incentives were offered to complete the measurements. In the case of an unfilled questionnaire, patients were reminded after 7 and 14 days.

Table 1. Overview of the stratified blended physiotherapy intervention (e-Exercise low back pain [LBP])

Mode of delivery	Low-risk profile	Medium-risk profile	High-risk profile
Smartphone application			
- Duration	3 weeks	12 weeks	12 weeks
- Information module	Knowledge-based platform with several LBP self-management information themes (directly available)	12 weekly self-management themes, including assignments	12 weekly self-management themes, including assignments, pain education, and psychosocial risk factors
- Exercise module	3 to 4 home-based exercises tailored to the patient's specific functional limitations	3 to 4 home-based exercises tailored to the patient's specific functional limitations	3 to 4 home-based exercises tailored to the patient's specific functional limitations
- Physical activity module	Physical activity recommendations in accordance with the LBP guidelines of the Royal Dutch Association for Physiotherapy	A 3-day baseline test to determine the current level of physical activity; an 11-week, 3-times per week, goal-oriented training program to maintain or improve the level of physical activity; in patients avoiding physical activity because of LBP, a graded activity functionality can be activated	A 3-day baseline test to determine the current level of physical activity; an 11-week, 3-times per week, goal-oriented training program to maintain or improve the level of physical activity using a graded activity approach
Face-to-face care			
- Sessions	2 sessions	Maximum of 8 sessions	Maximum of 12 sessions
- Content	Reassurance, information about LBP, instruction on self-management options, and the importance of adequate physical activity behaviour	Content similar to low risk, and in addition, the physiotherapist can consider providing evidence-based interventions (e.g., passive or active joint mobilization) as recommended by guideline LBP of the Royal Dutch Association for Physiotherapy	Content similar to medium risk, and in addition, the physiotherapist will address the patient's specific psychosocial risk factors using a cognitive behavioural approach, and pain education will be given

Table 1. Continued

Mode of delivery	Low-risk profile	Medium-risk profile	High-risk profile
Integration of face-to-face care and smartphone application			
- First session	Provide information about LBP and instructions on home-based exercises addressing patient's specific functional limitations using the smartphone app	Provide information about LBP, instructions on home-based exercises addressing patient's specific functional limitations, and instructions on 3-day baseline test using the smartphone app	Provide information about LBP, instructions on home-based exercises addressing patient's specific functional limitations, and instructions on 3-day baseline test using the smartphone app
- Middle sessions	N/A[a]	Evaluation of progress with the smartphone app and optimizing face-to-face care	Evaluation of progress with the smartphone app and optimizing face-to-face care
- Final session	Evaluate the progress with the smartphone app and give recommendations to prevent recurrent episodes of LBP and maintain or improve the physical activity level	Evaluate the progress with the smartphone app and give recommendations to prevent recurrent episodes of LBP and maintain or improve the physical activity level	Evaluate the progress with the smartphone app and give recommendations to prevent recurrent episodes of LBP and maintain or improve the physical activity level

[a] N/A = not applicable

Outcome measures

Primary outcome

Physical functioning because of pain was assessed using the Oswestry Disability Index (ODI; version 2.1a)[27,28]. The ODI was derived from the internationally accepted core outcome set for research into patients with nonspecific LBP[28]. A higher score (0-100) indicates increased functional disability.

Secondary outcomes

Pain intensity was measured using an 11-point numeric rating scale for the average LBP intensity in the last week (0=no pain and 10=worst possible pain)[28,29].

Physical activity was objectively measured using Activ8 (2M Engineering)[30]. Patients were instructed to wear the Activ8 for 5 consecutive weeks starting at baseline and 8 consecutive days at the 3-month follow-up, except during sleeping, showering, bathing, or swimming. For the purpose of this study, only the first 7 days at both the baseline and 3-month follow-up were used. Accelerometer data were eligible if patients had worn the

meter for at least 3 days for ≥10 hours a day[31]. For each patient, the mean time spent in moderate to vigorous physical activity (all activities >3.0 metabolic equivalents[32]) in minutes per day was computed by summation and divided by the number of eligible wearing days.

Fear-avoidance beliefs about physical activity and work were measured using the Fear-Avoidance Beliefs Questionnaire[33]. A higher score (range 0-96) indicates stronger fear and avoidance beliefs about how physical activity and work negatively affect LBP.

Pain catastrophizing was measured using the Pain Catastrophizing Scale[34]. A higher score (range 0-55) indicates a higher level of catastrophizing.

Self-efficacy was measured using the General Self-Efficacy Scale[35,36]. A higher score (range 10-40) indicates greater or stronger perceived self-efficacy.

Self-management ability was assessed using the Dutch version of the short form Patient Activation Measure[37]. A higher score (range 0-100) indicates a higher level of self-management.

Health-related quality of life was measured using the EuroQol-5D-5L[38]. A higher score (range 0-100) indicates a higher health-related quality of life.

Patient self-reported adherence to prescribed home exercises was measured using the Exercise Adherence Rating Scale[39]. A higher score (range 0-24) indicates better adherence.

Other measures

Physiotherapists were asked to complete a registration form about the number of face-to-face sessions and report the applied treatment modalities per session. Patient characteristics and relevant clinical variables were assessed as part of the baseline questionnaire.

Data analysis

Overview

Descriptive statistics were used to explore baseline comparability and describe patients' general characteristics, the number of face-to-face physiotherapy sessions, and the treatment modalities. To investigate selective attrition, general characteristics and primary baseline variables of dropouts and non-dropouts were compared. All analyses were performed according to the *intention-to-treat* principle. Missing value analyses were performed by assuming the missing at random assumption. Multiple imputation was applied using multivariate imputation by chained equations with predictive mean matching for missing data in all outcomes. A total of 36 imputed data sets were generated, corresponding to the highest missing value percentage[40]. For all analyses, a 2-tailed significance level of $P<.05$ was considered statistically significant.

Analyses of effectiveness

Linear mixed models (LMMs) with random effects to control for correlation within patients and physiotherapy practices[41] were used to determine the short-term

effectiveness of stratified blended physiotherapy compared with face-to-face physiotherapy on primary and secondary outcome measures. Regression coefficients with 95% CIs signifying the differences between stratified blended physiotherapy and face-to-face physiotherapy were estimated. Analyses were adjusted for predefined confounders (e.g., age, gender, and duration of pain[42-44]) that changed the between-group estimate by ≥10%. In addition, analyses were also adjusted for variables with a substantial difference at baseline that changed the regression coefficient for the between-group estimate by ≥10%. Potential interaction terms were explored. In the case of a statistically significant interaction term, stratified LMM analyses, controlling for the same variables as the primary analysis, were performed for the effect modifier.

Sample size

The power calculation was based on the recommendations of Campbell et al[45] for cluster randomized trials and performed for the physical functioning primary outcome at the primary end point of the e-Exercise LBP study (i.e., 12-month follow-up). In addition, repeated measures of the primary outcome during follow-up were taken into account[46]. An intraclass correlation coefficient of 0.05 was assumed. In addition, to detect a clinically relevant difference between groups at the 12-month follow-up, a difference of >6 points in physical functioning (ODI)[47,48], and an SD of 14.5[49] were used in the sample size calculation. For the repeated measures of physical functioning, a correlation of 0.5 was estimated between baseline and follow-up measurements until the 12-month follow-up[46]. On the basis of these assumptions (power 80%; α=.05) and an average cluster size of 5, a total of 165 patients were needed. With an expected dropout rate of 20%, a total of 208 participating patients (n=104 per arm) were needed.

RESULTS

Flow of participants, therapists and centers trough the study

From June 2018 to December 2019, 434 eligible patients with LBP were asked to participate in 58 physiotherapy practices. In 22 physiotherapy practices allocated to stratified blended physiotherapy and 20 practices allocated to face-to-face physiotherapy, 47.9% (208/434) patients were included (Figure 1).

Baseline characteristics of the patients are presented in Table 2. The stratified blended physiotherapy group comprised more men, more patients with a low level of education, and more patients with a duration of LBP >12 months. No other relevant differences in characteristics were seen between groups. At baseline, complete data on outcome measures were available from 97.1% (101/104) of the patients in the stratified blended physiotherapy group and 99% (103/104) of the patients in the face-to-face physiotherapy group, and eligible accelerometer data were available from 84.6% (88/104) and 83.7%

(87/104), respectively. Of the 208 patients, 4 (1.9%) ineligible patients (n=2, 50% in the stratified blended physiotherapy group and 2, 50% in the face-to-face physiotherapy group) were unjustified included, did not receive the allocated intervention and were therefore excluded from all analyses.

At the 3-month follow-up, complete data on outcome measures were available from 86.5% (90/104) of the patients in the stratified blended physiotherapy group and 93.3% (97/104) of the patients in the face-to-face physiotherapy group, and eligible accelerometer data were available from 74% (77/104) and 76% (79/104) of these patients, respectively.

Number and treatment modalities of physiotherapy sessions

In total, 189 physiotherapist registration forms were returned (n=95, 50.3% stratified blended physiotherapy and n=94, 49.7% in face-to-face physiotherapy). Table 3 shows the number and treatment modalities of the face-to-face physiotherapy sessions. Patients in the stratified blended physiotherapy group received an average of 4.81 (SD 2.94) face-to-face sessions. For the *low-*, *medium-*, and *high-risk* groups, the average number of sessions was 3.77 (SD 2.54), 5.65 (SD 2.65), and 7.67 (SD 3.54), respectively. Patients in the face-to-face physiotherapy group received an average of 4.94 (SD 2.26) face-to-face sessions. The average number of sessions for the *low-*, *medium-*, and *high-risk* groups was 4.88 (SD 2.02), 5.09 (SD 2.51), and 4.33 (SD 4.16), respectively.

In general, education was the main treatment modality during the face-to-face sessions in both treatment groups. No remarkable differences in treatment modalities were found between the 2 groups or between the different risk groups of developing persistent LBP.

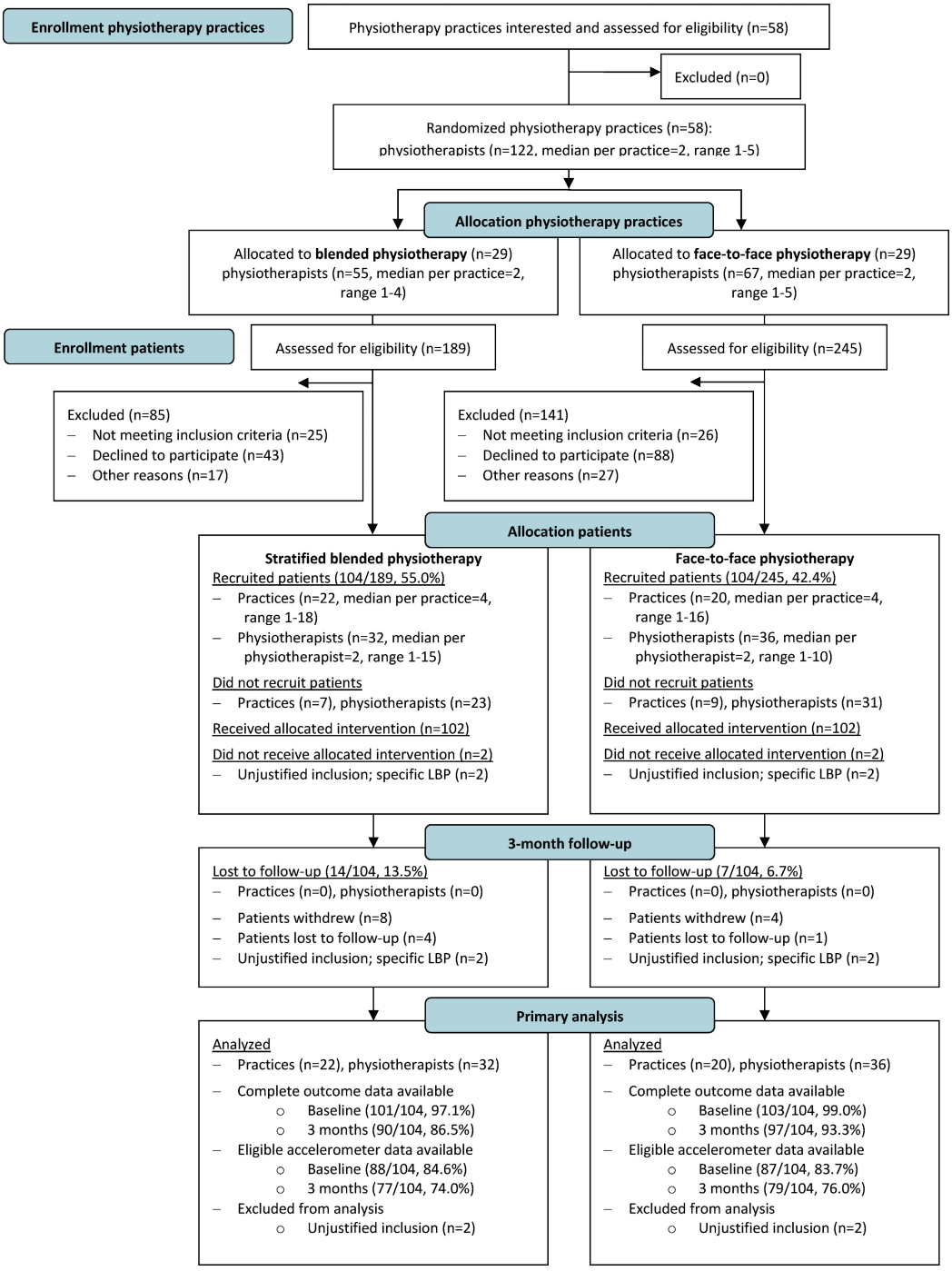

Figure 1. Flow diagram of the e-Exercise low back pain study

Table 2. Baseline demographic and clinical characteristics for patients from the stratified blended physiotherapy group and face-to-face physiotherapy group (N=208)

Characteristics	Baseline	
	Stratified blended physiotherapy (n=104)	Face-to-face physiotherapy (n=104)
Gender (female), n (%)	45 (43.3)	57 (54.8)
Age (years), mean (SD)	48.10 (15.08)	47.26 (13.58)
BMI (kg/m^2), mean (SD)	25.78 (3.79)	26.31 (5.11)
Presence of comorbidities (yes), n (%)	38 (36.5)	28 (26.9)
Past LBP[a] surgery, n (%)		
None	100 (96.2)	101 (97.1)
Lumbar fusion	0 (0)	1 (1)
Lumbar discectomy	4 (3.9)	2 (1.9)
Educational level, n (%)		
Low	22 (21.2)	13 (12.5)
Middle	33 (31.7)	36 (34.6)
High	49 (47.1)	55 (52.9)
Duration of LBP complaints, n (%)		
0 to 6 weeks	37 (35.6)	49 (47.1)
6 to 12 weeks	11 (10.6)	19 (18.3)
12 weeks to 12 months	9 (8.7)	9 (8.7)
>12 months	47 (45.2)	27 (26)
Central sensitization (score 0-100), mean (SD)	30.88 (13.38)	30.17 (12.19)
Physical functioning (score 0-100), mean (SD)	19.37 (15.64)	20.38 (13.99)
Pain intensity (average score 7 days 0-10), mean (SD)	5.61 (1.99)	5.36 (2.01)
Physical activity (MVPA[b] minutes/day), mean (SD)	80.34 (36.75)	74.82 (40.94)
Health-related quality of life (score 0-100), mean (SD)	67.90 (18.08)	69.75 (17.63)
Fear-avoidance beliefs (score 0-96), mean (SD)	27.86 (16.03)	25.08 (16.18)
Pain catastrophizing (score 0-52), mean (SD)	11.06 (9.30)	10.21 (8.75)
Self-efficacy (score 10-40), mean (SD)	32.13 (4.36)	33.12 (3.62)
Patient activation (score 0-100), mean (SD)	62.48 (12.38)	64.75 (12.68)

[a] LBP = low back pain; [b] MVPA = moderate to vigorous physical activity

Table 3. Number and treatment modalities of face-to-face physiotherapy sessions for patients from the stratified blended physiotherapy group and face-to-face physiotherapy group

Category	Stratified blended physiotherapy (risk of developing persistent LBP[a])				Face-to-face physiotherapy (risk of developing persistent LBP)			
	Low (n=52)	Medium (n=34)	High (n=9)	Total (n=95)	Low (n=57)	Medium (n=34)	High (n=3)	Total (n=94)
Number of sessions, mean (SD)	3.77 (2.54)	5.65 (2.65)	7.67 (3.54)	4.81 (2.94)	4.88 (2.02)	5.09 (2.51)	4.33 (4.16)	4.94 (2.26)
Treatment modalities, n (%)[b]								
Education	42 (81)	24 (71)	6 (67)	72 (76)	43 (75)	25 (74)	2 (67)	70 (74)
Strength exercises	9 (17)	3 (9)	1 (11)	13 (14)	7 (12)	6 (18)	0 (0)	13 (14)
Stability exercises	14 (27)	5 (15)	4 (44)	23 (24)	14 (25)	11 (32)	0 (0)	25 (27)
Endurance training	1 (2)	0 (0)	0 (0)	1 (1)	3 (5)	0 (0)	0 (0)	3 (3)
Functional exercises	3 (6)	0 (0)	0 (0)	3 (3)	4 (7)	0 (0)	0 (0)	4 (4)
Active mobilization	15 (29)	10 (29)	2 (22)	27 (28)	22 (39)	11 (32)	2 (67)	35 (37)
Passive mobilization	12 (23)	16 (47)	3 (33)	31 (33)	15 (26)	9 (26)	1 (33)	25 (27)
Massage	4 (8)	8 (24)	2 (22)	14 (15)	9 (19)	5 (15)	0 (0)	14 (15)

[a] LBP = low back pain; [b] Amount (%) of patients who received the treatment modality as part of the face-to-face physiotherapy session for ≥60% of the total number of face-to-face physiotherapy sessions

Is stratified blended physiotherapy effective compared with face-to-face physiotherapy?

In the mixed model analyses, log likelihood ratios of naive models and models that included a random intercept for both physiotherapy practice and physiotherapist were similar. Therefore, physiotherapy practice or physiotherapist was not included as a level in the LMM analyses. At 3 months, LMM analyses showed no clinically relevant or statistically significant between-group difference in the primary outcome of physical functioning (mean difference [MD] −1.96, 95% CI −4.47 to 0.55). For the secondary outcomes, a statistically significant between-group difference was found in favour of stratified blended physiotherapy for fear-avoidance beliefs (MD −4.29, 95% CI −7.22 to −1.37) and patients' self-reported adherence to prescribed home exercises (MD 0.73, 95% CI 0.06-1.39). Within-group analyses showed clinically relevant and statistically significant improvements in physical functioning (MD −11.48, 95% CI −15.06 to −7.91), average pain intensity (MD −2.38, 95% CI −3.00 to −1.76), and fear-avoidance beliefs (MD −5.14, 95% CI −9.22 to −1.06) in the stratified blended physiotherapy group. In the face-to-face physiotherapy group, clinically relevant and statistically significant improvements in physical functioning (MD −11.22, 95% CI −14.64 to −7.80) and average pain intensity (MD −2.51, 95% CI −3.11 to −1.90) were found (Table 4).

As indicated by a statistically significant interaction term, the patients' risk of developing persistent LBP was an effect modifier of the between-group differences on the primary outcome of physical functioning. In patients with a high risk of developing persistent LBP, the stratified analysis showed a statistically significant between-group difference in favour of stratified blended physiotherapy on physical functioning (MD –16.39, 95% CI –27.98 to –4.79), average pain intensity (MD –3.43, 95% CI –6.55 to –0.31), and fear-avoidance beliefs (MD –14.51, 95% CI –28.21 to –0.81). In patients with a medium risk of developing persistent LBP, a statistically significant between-group difference was found in favour of stratified blended physiotherapy on fear-avoidance beliefs (MD –5.93, 95% CI –11.45 to –0.40). In patients with a low risk of developing persistent LBP, no statistically significant between-group differences were found (Table 5).

Table 4. Unadjusted and adjusted primary and secondary outcome measures: improvements and differences within and between groups (N=204)

Outcome	Stratified blended physiotherapy (n=102)			Face-to-face physiotherapy (n=102)			Between group differences[a]	
	Measurements, mean (SD)		Unadjusted with-in-group differences	Measurements, mean (SD)		Unadjusted with-in-group differences	Unadjusted	Adjusted[b]
	Baseline	3 months	Mean (95% CI) *P* value	Baseline	3 months	Mean (95% CI) *P* value	Mean (95% CI) *P* value	Mean (95% CI) *P* value
Physical functioning (range 0-100)								
	19.39 (15.56)	7.91 (9.64)	−11.48 (−15.06 to −7.91) <.001	20.20 (13.90)	8.97 (10.75)	−11.22 (−14.64 to −7.80) <.001	−0.83 (−3.43 to 1.77) .53	−1.98 (−4.49 to 0.53) .12
Pain intensity (average score 7 days; range 0-10)								
	5.67 (1.94)	3.29 (2.42)	−2.38 (−3.00 to −1.75) <.001	5.40 (2.00)	2.90 (2.36)	−2.51 (−3.11 to −1.90) <.001	0.31 (−0.35 to 0.98) .36	0.08 (−0.57 to 0.74) .80
Physical activity (MVPA[c] min/day)								
	81.97 (38.52)	78.58 (44.45)	−3.37 (−15.63 to 8.88) .59	75.70 (41.89)	71.24 (40.34)	−4.42 (−16.91 to 8.07) .49	3.49 (−8.38 to 15.36) .56	3.62 (−8.27 to 15.51) .55
Fear-avoidance beliefs (range 0-96)								
	27.92 (16.01)	22.77 (13.38)	−5.14 (−9.25 to −1.04) .01	25.51 (16.24)	24.82 (16.92)	−0.70 (−5.26 to 3.87) .77	−3.73 (−6.63 to −0.82) .01	−4.29 (−7.22 to −1.37) <.001
Pain catastrophizing (range 0-52)								
	11.02 (9.30)	8.97 (8.05)	−2.04 (−4.50 to 0.43) .11	10.33 (8.76)	9.16 (9.84)	−1.17 (−3.74 to 1.40) .37	−0.63 (−2.58 to 1.32) .53	−0.96 (−2.95 to 1.02) .34

Table 4. Continued

Outcome	Stratified blended physiotherapy (n=102)			Face-to-face physiotherapy (n=102)			Between group differences[a]	
	Measurements, mean (SD)		Unadjusted with-in-group differences	Measurements, mean (SD)		Unadjusted with-in-group differences	Unadjusted	Adjusted[b]
	Baseline	3 months	Mean (95% CI) *P* value	Baseline	3 months	Mean (95% CI) *P* value	Mean (95% CI) *P* value	Mean (95% CI) *P* value
Self-efficacy (range 10-40)								
	32.05 (4.38)	32.02 (4.27)	−0.03 (−1.24 to 1.19) .97	33.12 (3.63)	32.58 (3.99)	−0.54 (−1.59 to 0.52) .32	0.12 (−0.82 to 1.06) .81	0.14 (−0.82 to 1.10) .77
Health-related quality of life (range 0-100)								
	67.70 (18.09)	71.44 (20.07)	3.73 (−1.68 to 9.14) .18	69.75 (17.71)	72.57 (21.06)	2.82 (−2.56 to 8.20) .31	−0.65 (−6.38 to 5.08) .82	0.95 (−4.80 to 6.69) .75
Patient activation (range 0-100)								
	62.43 (12.37)	62.45 (11.89)	0.02 (−3.42 to 3.46) .99	64.72 (12.65)	64.39 (12.71)	−0.33 (−3.84 to 3.18) .85	−0.83 (−3.94 to 2.27) .60	−0.79 (−3.95 to 2.36) .62
Adherence to prescribed home exercises (range 0-24)[d]								
	N/A[e]	11.96 (2.43)	N/A	N/A	11.18 (2.17)	N/A	0.78 (0.13 to 1.44) .02	0.73 (0.06 to 1.39) .03

[a] Difference between baseline and 3 months in stratified blended physiotherapy versus face-to-face physiotherapy; [b] Adjusted for baseline and duration of low back pain complaints (<12 vs >12 weeks); [c] MVPA = moderate to vigorous physical activity; [d] Patient self-reported adherence to prescribed home exercises could only be measured after the treatment period; [e] N/A = not applicable

Table 5. Adjusted primary and secondary outcome measures: improvements and differences between groups stratified for the risk of developing persistent low back pain (LBP; N=204)

Outcome measure	Risk of developing persistent LBP					
	Low risk (n=120)		Medium risk (n=71)		High risk (n=13)	
	Between-group difference, mean (95% CI)[a]	*P* value	Between-group difference, mean (95% CI)[b]	*P* value	Between-group difference, mean (95% CI)[b]	*P* value
Physical functioning (range 0-100)	−0.82 (−2.92 to 1.27)	.44	−3.48 (−8.99 to 2.03)	.22	−16.39 (−27.98 to −4.79)	.01
Pain intensity (average score 7 days; range 0-10)	0.30 (−0.52 to 1.13)	.47	0.01 (−1.08 to 1.11)	.98	−3.43 (−6.55 to −0.31)	.03
Physical activity (MVPA[b] minutes/day)	3.80 (−12.05 to 19.65)	.64	1.08 (−16.70 to 18.86)	.91	39.50 (−1.24 to 80.24)	.06
Fear-avoidance beliefs (range 0-96)	−2.70 (−6.22 to 0.82)	.13	−5.93 (−11.45 to −0.40)	.04	−14.51 (−28.21 to −0.81)	.04
Pain catastrophizing (range 0-52)	0.28 (−2.03 to 2.59)	.81	−2.66 (−5.73 to 0.41)	.09	−14.47 (−31.89 to 2.94)	.10
Self-efficacy (range 10-40)	−0.58 (−1.76 to 0.60)	.33	0.85 (−0.92 to 2.62)	.35	1.50 (−4.02 to 7.02)	.60
Health-related quality of life (range 0-100)	1.26 (−7.15 to 9.68)	.77	0.84 (−6.47 to 8.15)	.82	15.84 (−3.92 to 35.61)	.12
Patient activation (range 0-100)	−2.22 (−6.38 to 1.93)	.29	1.85 (−3.27 to 6.97)	.48	7.49 (−1.35 to 16.34)	.10
Adherence to prescribed home exercises (range 0-24)	0.82 (−0.01 to 1.65)	.05	0.86 (−0.35 to 2.08)	.16	−1.19 (−3.37 to 0.99)	.28

[a] Difference between baseline and 3 months in stratified blended physiotherapy versus face-to-face physiotherapy per risk group and adjusted for baseline and duration of low back pain complaints (<12 vs >12 weeks); [b] MVPA = moderate to vigorous physical activity

DISCUSSION

Principal findings

This study evaluated the short-term (3 months) effectiveness of the stratified blended physiotherapy intervention e-Exercise LBP on physical functioning in comparison with face-to-face physiotherapy in patients with nonspecific LBP. In contrast to our expectations, the study results showed no statistically significant between-group difference in physical functioning and most of the secondary outcome measures. Only fear-avoidance beliefs and patient self-reported adherence to prescribed home exercises improved significantly in patients who were allocated to stratified blended physiotherapy. When looking at the different prognostic risk groups in patients with a high risk of developing persistent LBP, a statistically significant between-group difference in favour of stratified blended physiotherapy on physical functioning, average pain intensity, and fear-avoidance beliefs was found; however, these results come with some uncertainty.

Interpretation of the findings

The results of this study complement the findings from previous systematic reviews of randomized controlled trials that showed that in the short term, web-based applications could reduce LBP-related pain and disability; however, when compared with other interventions, the results are inconclusive[15,22,50]. A possible explanation for these inconclusive findings is the considerable heterogeneity in the studied characteristics and comparators, which hampers a clear comparison. For example, in our study, we integrated a web-based application within face-to-face guidance and compared it with face-to-face physiotherapy. Previous studies in this research area have focused predominantly on web-based applications as a stand-alone intervention without the face-to-face guidance of a health care professional[15,22,50]. Only a few studies have investigated web-based applications as an adjunct to face-to-face guidance, and the results regarding the added value of these combined interventions have been inconclusive[15,51]. Similar to our study, Sandal et al[51] investigated a smartphone app as an adjunct to face-to-face guidance. The app was tailored using artificial intelligence and did not influence face-to-face guidance. In this study, the reported between-group difference was statistically significant in favour of the combined intervention when compared with face-to-face guidance alone; however, the difference was small and of uncertain clinical significance.

Another example of heterogeneity in research on web-based applications is the large variation in delivery modes and duration. Similar to e-Exercise LBP, most web-based applications tailored the content of the intervention using patient characteristics and focused on self-management support, home-based exercise, and physical activity prescription[15,22,50]. However, the e-Exercise LBP app provided this content in weekly information modules and daily reminders to exercise and physical activity

recommendations during a 3- or 12-week duration[26]; the duration in other studies ranged from 3 weeks to 1 year. In addition, the delivery modes showed large variation; that is, from no specific recommendations to multiple web- or telephone-based coaching sessions[15,22,50].

Thus, looking at the different characteristics of web-based applications, such as the role of the health care professional within the intervention and the delivery mode and duration, future research needs to focus on the comparison of web-based applications with different characteristics to obtain a better understanding of which elements work the best.

In our study, the short-term within-group improvements in physical functioning and average pain intensity of stratified blended physiotherapy were comparable with face-to-face physiotherapy, both of which were statistically significant and clinically meaningful. Patients in the stratified blended physiotherapy group improved on average 11.48 (95% CI −15.06 to −7.91) points (59.5%) in physical functioning, and patients in the face-to-face physiotherapy group improved by an average of 11.22 (95% CI −14.64 to −7.80) points (56%). For average pain intensity, these improvements were 2.38 (95% CI −3.00 to −1.76) points (42.8%) and 2.51 (95% CI −3.11 to −1.90) points (46.9%), respectively. As physical functioning and average pain intensity decreased by >30%, the improvements in both groups were considered clinically meaningful[52]. At the moment, e-Exercise LBP cannot be considered an alternative to face-to-face physiotherapy as this study was conducted as a superiority trial. To be able to value the true potential of e-Exercise LBP, the meaningful within-group improvements must be considered from the perspective of the additional effort and costs needed to implement such an intervention in daily physiotherapy practice. Future cost-effectiveness analyses will provide more insight into the long-term economic benefits of stratified blended physiotherapy. On the other hand, given the additional effort and costs, the potential of e-Exercise LBP needs to be considered from the perspective of future health care. It is expected that technology will be increasingly integrated into care for patients who are suitable to use it. Future studies need to determine which patients benefit most from a stratified blended physiotherapy approach.

The e-Exercise LBP intervention significantly increased patients' self-reported adherence to prescribed home exercises, as hypothesized. In addition, it resulted in a significant reduction of fear-avoidance beliefs when compared with face-to-face physiotherapy. The between-group difference in patients' self-reported adherence to prescribed home exercises was 3.3% points in favour of the e-Exercise LBP intervention. For fear-avoidance beliefs, the between-group difference was −4.6% points in favour of the e-Exercise LBP intervention. Although there are no established cutoffs for the minimum clinically important between-group differences in these outcomes, we consider the between-group differences as small. The difference in adherence might

be explained by the benefits of integrating a smartphone app. The 24/7 availability of the app and functionality to remind the patient to perform scheduled exercises might have stimulated the patients to adhere to their prescribed home exercises in a better way than in the face-to-face physiotherapy group[18,53]. Further research on the long-term clinical relevance of adherence to home exercises as prescribed in e-Exercise LBP is ongoing.

The reduction of fear-avoidance beliefs complements evidence from a systematic review and meta-analysis that concluded that patient education provides reassurance for patients with acute or subacute LBP[54]. In our study, this reduction in the stratified blended physiotherapy group might be explained by the information module of the smartphone app. As the information module provides the patient with self-management information about LBP, the patient can reread the advice and reassurance given in the face-to-face sessions by the physiotherapist about their LBP at all times. As a result, the harmless and nonspecific nature of LBP is possibly remembered in a better way[55]. Long-term results should indicate whether this reduction in fear-avoidance beliefs also influences physical functioning, the handling of recurrent complaints, and costs a patient incurs because of LBP.

Several explanations are possible to clarify why the additional benefits of stratified blended physiotherapy were not found. A first explanation is that the added value of a stratified approach in itself must be critically evaluated. Although clinical practice guidelines have adopted and advocated a stratified care approach for several years to improve patient outcomes, the added value of this approach is, at present, unclear. On the basis of previous recommendations, we decided to use the Keele STarT Back Screening Tool to create a matched web-based application[10]. Our results show that, after specific training, treatment intensity (i.e., the number of face-to-face sessions) in the e-Exercise LBP group was in line with the patient's risk profile, which was not the case in our control group. However, this difference in treatment intensity did not lead to relevant between-group differences. This seems to be in line with more recent studies evaluating the stratified approach according to the Keele STarT Back Screening Tool. The results from these studies are not convincing regarding the added value of such a stratified approach[56,57]. Future research should focus on determining whether this concerns the added value of the tool itself or the added value of a stratified care approach in general.

In addition, stratified blended physiotherapy might not be suitable for every patient. Earlier research has shown that it is difficult to determine what works best for each individual patient[22,50]. In our study, we did not take into account the patient's suitability for blended care to determine the optimal personalized blended treatment[58]. As a result, patients might have received stratified blended physiotherapy without being suitable for it; for example, a lack of motivation or digital literacy skills. Consequently, this could

have resulted in the suboptimal effectiveness of our stratified blended physiotherapy intervention when compared with face-to-face physiotherapy. For future studies on blended care, it is recommended to use patients' suitability for blended care as inclusion criteria or criteria to match treatment. The Dutch Blended Physiotherapy Checklist[58] could be a useful aid in this process.

A third explanation might be the relatively high proportion of patients with a low risk of developing persistent LBP in this study. For this group, earlier research has shown that providing advice as a single intervention is likely to reassure the patient with LBP but does not result in different management of pain and disability in the short term[54,59]. In addition, for this group, a stratified approach is beneficial from an economic perspective rather than in terms of clinical outcomes, as many of these patients recover completely within 2 to 3 weeks but nevertheless receive unnecessary treatment[57,60,61].

A final explanation is the timing of our follow-up measurement at 3 months only. Given the favourable course of LBP[62] and the rationale that stratified blended physiotherapy will stimulate patients' self-management and adherence[21,22], patients in the stratified blended physiotherapy group might recover faster, which is not captured by a single follow-up measurement at 3 months. Therefore, for future studies that aim to investigate postintervention effectiveness, it is recommended to measure the clinical outcomes immediately after the intervention is completed and to monitor the time to recovery.

Strengths and limitations

This study had several important strengths. It is the next step in a multiphase development and implementation process based on the Center for eHealth Research Roadmap[63]. After developing a prototype and testing its feasibility in a pilot study[23], this study determined the short-term effectiveness of the final stratified blended physiotherapy protocol and showed its potential compared with face-to-face physiotherapy. The pragmatic, multicenter, cluster randomized controlled trial design allowed for the evaluation of stratified, blended physiotherapy in comparison with face-to-face physiotherapy in a real-world situation. The baseline characteristics of both treatment groups and the distribution of the different prognostic risk groups of developing persistent LBP reflect the characteristics of patients with LBP normally being treated in primary care physiotherapy[60], which enhances the generalizability of our results. The use of measurement instruments recommended in the core outcome set for research into patients with nonspecific LBP[28] and a low dropout rate (10.1%) guaranteed the internal validity of the results.

Nevertheless, this study also had a few limitations. First, the results seem to suggest that patients' risk of developing persistent LBP could be an effect modifier of the between-group differences on the primary outcome. Especially in the highest risk group,

consistent between-group differences were seen in both the primary and secondary outcomes, supporting the rationale for stratified blended physiotherapy. As it was not the primary aim of this study, the sample size calculation did not take interaction into account, the numbers were small, and therefore, the results should be interpreted with caution. Second, as we conducted a pragmatic study, the experiences of physiotherapists in either using web-based applications or treating patients with nonspecific LBP were not considered inclusion criteria for physiotherapy practices. However, given both the complexity of blended care[17] and the complexity of treating patients with nonspecific LBP[4], it can be expected that more experienced physiotherapists are able to deliver better treatment than less experienced physiotherapists. Therefore, experience might have influenced our analysis. Finally, 4 included patients were excluded from the analysis after being diagnosed with specific LBP. As this number is low and occurred equally in both treatment groups (2 in each group), we expect that this has not influenced the results[64].

CONCLUSIONS

The stratified blended physiotherapy intervention e-Exercise LBP is not more effective than face-to-face physiotherapy in patients with nonspecific LBP in improving physical functioning in the short term. For both stratified blended physiotherapy and face-to-face physiotherapy, within-group improvements were clinically relevant. To be able to decide whether e-Exercise LBP should be implemented in daily physiotherapy practice, future research should focus on the long-term cost-effectiveness and determine which patients benefit most from stratified blended physiotherapy.

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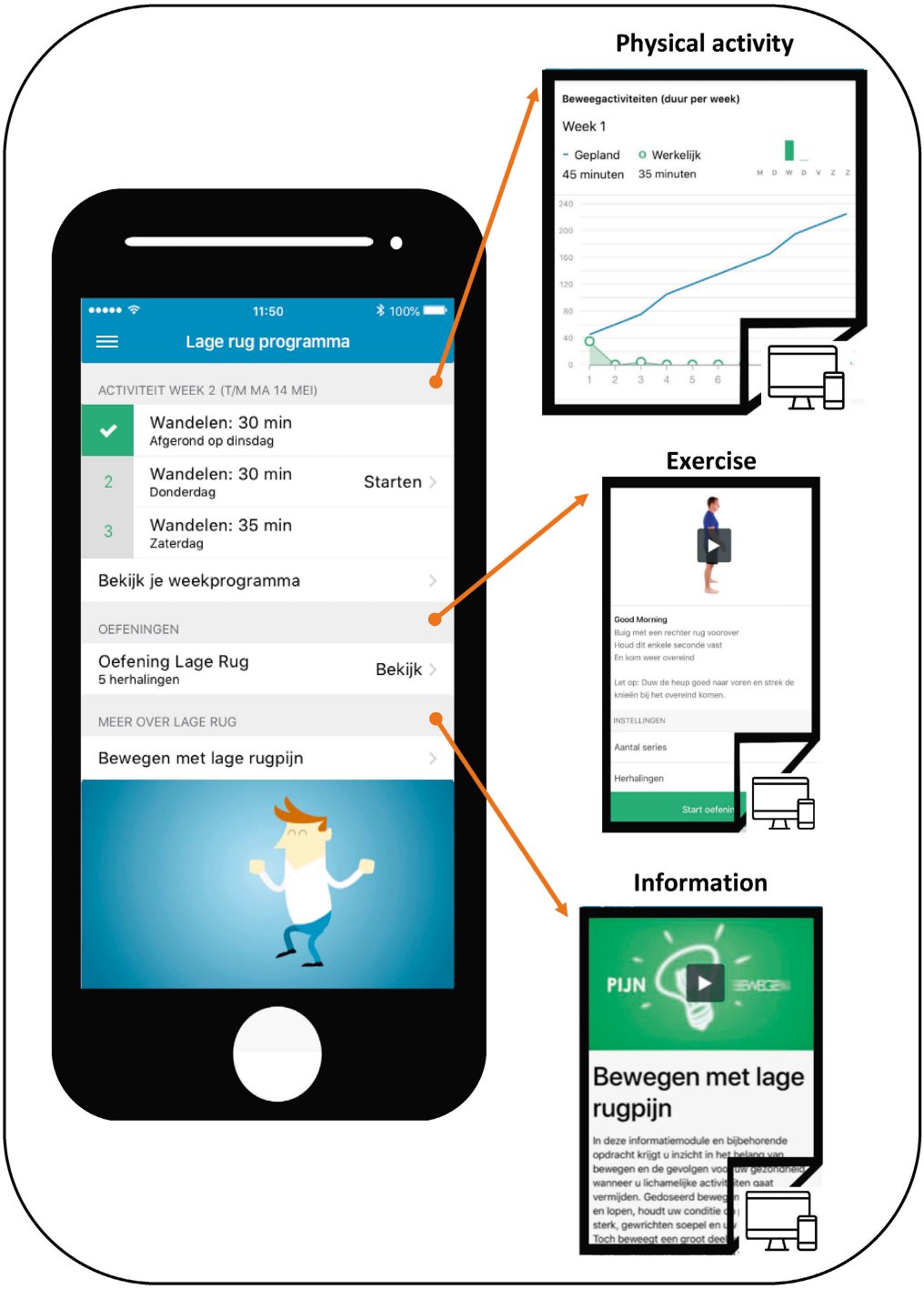
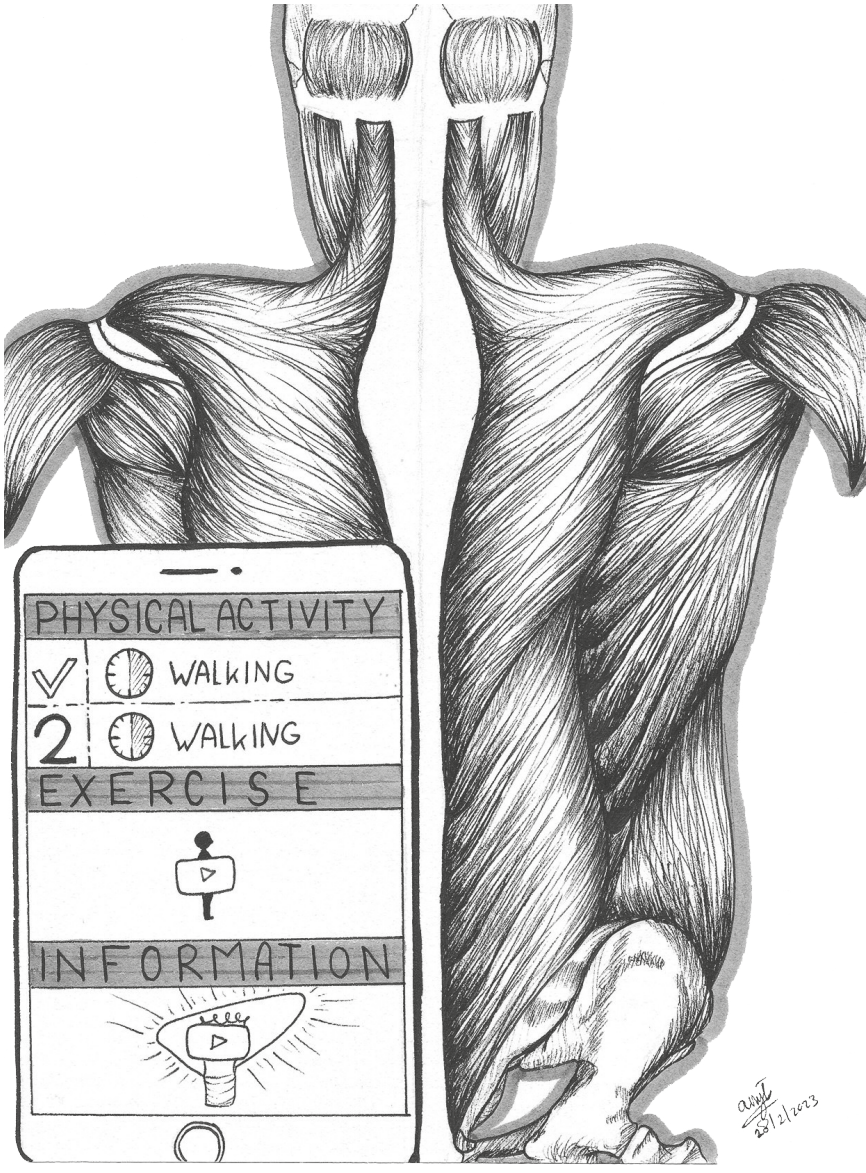
Appendix 1. Print screens of the smartphone application




PHYSICAL ACTIVITY
WALKING
2
WALKING
EXERCISE
INFORMATION

5

Effectiveness and cost-effectiveness of a stratified blended physiotherapy intervention compared to face-to-face physiotherapy in patients with nonspecific low back pain:

A cluster-randomized controlled trial

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Authorship statement

I participated in the development of the design of the study, conducted the study, performed data management, and performed the statistical analyses. I drafted and revised the manuscript and implemented the contribution of the co-authors and external reviewers up to final publication. During the whole process I asked for and implemented input and feedback from the other contributors to this study.

ABSTRACT

Background

Nonspecific low back pain (LBP) is a leading contributor to disability-adjusted life years worldwide, and its socioeconomic burden is enormous. Self-management support tailored to the needs and abilities of individual patients is an important recommendation in clinical guidelines for physiotherapy treatment of patients with LBP and may support cost-effective management of LBP. However, providing adequate individually tailored self-management support is difficult. The integration of online applications in face-to-face care, i.e., blended care, seems to be promising to optimize tailored treatment and enhance patients' self-management and consequently may reduce LBP-related costs.

Objective

To evaluate the long-term effectiveness and cost-effectiveness of stratified blended physiotherapy (e-Exercise LBP) compared to face-to-face physiotherapy in patients with nonspecific LBP.

Methods

An economic evaluation was conducted alongside a prospective, multicenter cluster-randomized controlled trial in 58 primary care physiotherapy practices. Patients with nonspecific LBP were treated with either stratified blended physiotherapy according to the e-Exercise LBP protocol (N=104) or face-to-face physiotherapy (N=104). The content of both interventions is based on the Dutch physiotherapy guidelines for nonspecific LBP. Blended physiotherapy was stratified according to the patients' risk of developing persistent LBP using the STarT Back Screening Tool. The primary clinical outcome was physical functioning (Oswestry Disability Index 2.1a). For the economic evaluation, quality-adjusted life years (QALYs, EQ-5D-5L) and physical functioning were the primary outcomes. Secondary clinical outcomes included fear avoidance beliefs and self-reported adherence. Costs were measured from societal and healthcare perspectives using self-report questionnaires. Effectiveness was estimated using linear mixed models. Seemingly unrelated regression analyses were performed to estimate total cost and effect differences for the economic evaluation.

Results

Neither clinically relevant, nor statistically significant, differences were found between stratified blended physiotherapy and face-to-face physiotherapy in terms of physical functioning (MD: -1.1; 95% CI -3.9 to 1.7) and QALYs (MD: 0.026; 95% CI -0.020 to 0.072) over 12 months. As for the secondary outcomes, fear avoidance beliefs showed a statistically significant improvement in favour of stratified blended physiotherapy. Societal and healthcare costs were higher for stratified blended physiotherapy than for face-to-face physiotherapy, but differences were not statistically significant (societal: €972, 95% CI -1090 to 3264; healthcare: €73, 95% CI -59 to 225). Of the disaggregated

cost categories, only unpaid productivity costs were statistically significantly higher for stratified blended physiotherapy. From both perspectives, a considerable amount of money must be paid per additional QALY or 1-point improvement in physical functioning to reach a relatively low to moderate probability (i.e., 0.23 to 0.81) of stratified blended physiotherapy being cost-effective compared to face-to-face physiotherapy, respectively.

Conclusions
The stratified blended physiotherapy intervention e-Exercise LBP is neither more effective for improving physical functioning, nor more cost-effective from societal or healthcare perspectives when compared to face-to-face physiotherapy for patients with nonspecific LBP.

Trial Registration
ISRCTN 94074203; https://doi.org/10.1186/ISRCTN94074203

Keywords
Economic evaluation; E-health; Nonspecific low back pain; Physiotherapy; Blended care; Mobile phone

INTRODUCTION

Nonspecific low back pain (LBP) is one of the leading causes of disability and disability-adjusted life-years worldwide[1–3]. Most episodes of LBP are short-lasting with few consequences. However, approximately 50% of patients with LBP seen in primary care settings have a trajectory of ongoing or fluctuating low- to moderate-intensity pain, which for some develops into persistent severe LBP[4]. Recurrent episodes of LBP are common. That is, approximately 33% of patients will experience a new episode within one year after recovery[5]. The costs associated with healthcare use and productivity losses from paid work, e.g., due to work absence and reduced productivity while being at work, attributed to LBP are enormous[6]. In 2017, the annual Dutch societal cost of neck pain and LBP was estimated to be 937 million Euros. Healthcare costs, including primary care, secondary care, alternative medicine, and medication expenditures, were estimated to be approximately 878 million Euros[7]. Due to a greater availability of improved healthcare technologies in combination with higher levels of spending on these technologies (higher price per unit of service), population growth and aging, the LBP-related socioeconomic burden is expected to grow even more in the upcoming years[6,8]. This increases the need to identify cost-effective strategies for the management of LBP.

Self-management support tailored to the needs and abilities of individual patients is an important recommendation in clinical guidelines for physiotherapy treatment of patients with LBP[9–13]. In general, this support includes advice, reassurance, and education about the nonspecific nature of LBP and the resumption of normal activities and exercise. For patients with persistent symptoms, personalized and supervised exercise therapy should be considered, possibly supported by a graded activity approach or cognitive behavioural components[14,15]. In addition to a patient-centered and stratified approach, there are indications that patients' adherence to prescribed (home-based) exercises and recommended physical activity behaviour is important for the effectiveness of care[16–19].

Online applications, such as smartphone apps, have the possibility of optimizing personalized face-to-face treatment and enhancing patients' self-management and adherence to prescribed management between and after face-to-face sessions[20–24]. Additionally, a recent meta-analysis of randomized clinical trials concluded that smartphone and web-based self-management programs may be beneficial in improving pain and disability in patients with LBP[25]. Therefore, the integration of online applications into face-to-face care, i.e., blended care[24], seems to be a promising approach in the management of LBP[26].

To investigate whether blended care for patients with nonspecific LBP can positively influence patients' self-management and adherence to prescribed management of LBP and consequently improve patients' physical functioning, we developed and evaluated the stratified blended physiotherapy intervention e-Exercise LBP[27–29]. In the

short-term, i.e., after 3 months, e-Exercise LBP was not more effective than face-to-face physiotherapy in patients with nonspecific LBP in terms of physical functioning. However, patient self-reported adherence was significantly better among patients receiving e-Exercise LBP than among those receiving face-to-face physiotherapy only[29]. We therefore hypothesized that in the long-term, i.e., during 12 months, the stratified blended physiotherapy group patients would have improved self-management and adherence to prescribed LBP management strategies. These improvements could lead to an improvement in physical functioning and other clinical outcomes, which in turn could result in a reduction in societal and/or healthcare costs. Therefore, the present study aimed to evaluate the long-term effectiveness on physical functioning and cost-effectiveness of stratified blended care (e-Exercise LBP) compared to face-to-face physiotherapy in patients with nonspecific LBP.

METHODS

Design overview

An economic evaluation was conducted alongside a prospective, multicenter cluster-randomized controlled trial (RCT). Details on the design and methods of the trial were published previously[28]. The Medical Research Ethics Committee of the University Medical Center Utrecht in the Netherlands approved the study protocol (18-085/D), and the study was registered at the onset of patient enrolment (ISRCTN 94074203). The trial is reported according to the Consolidated Standards of Reporting Trials (CONSORT) statement for cluster randomized trials and the Consolidated Health Economic Evaluation Reporting Standards (CHEERS).

Recruitment

Setting and randomization

A total of 58 Dutch primary care physiotherapy practices with 122 physiotherapists were randomized on the practice level by an independent researcher according to a 1:1 allocation ratio using a computer-generated, a priori created, random sequence table. Half of the practices (n=29) were instructed to treat their patients with nonspecific LBP according to the stratified blended physiotherapy (e-Exercise LBP) protocol. The other half (n=29) treated their patients with face-to-face care following the recommendations of the guidelines for LBP of The Royal Dutch Society for Physiotherapy[30]. Physiotherapists from practices allocated to stratified blended physiotherapy received two 4-hour training sessions about e-Exercise LBP and the study procedures. Physiotherapists from practices allocated to face-to-face physiotherapy received one 4-hour training session in current best evidence practice and the study procedures. Enrolment of patients lasted from June 2018 until December 2019, and follow-up lasted 24 months. This paper evaluates the 12-month effectiveness and cost-effectiveness.

Patients

Patients were eligible if they requested physiotherapy treatment for nonspecific LBP, i.e., pain in the lumbosacral region (sometimes associated with pain radiating to the buttock or leg)[30]; were aged 18 years or older; possessed a smartphone or tablet (iOS or Android operating system) with access to the internet; and had sufficient command of the Dutch language. Physiotherapists informed potentially eligible patients about the study and informed the research team. The research team further informed the patient about the study, verified eligibility, and obtained written informed consent. Patients were excluded if they met any of the following criteria: a specific cause of LBP determined through medical imaging or a medical doctor; serious comorbidities (e.g., malignancy, stroke); and current pregnancy (because of the prevalence of pelvic girdle pain as a specific form of LBP).

Intervention

Experimental: Stratified blended physiotherapy (e-Exercise LBP)

e-Exercise LBP is a stratified blended intervention in which a smartphone application is integrated into face-to-face physiotherapy treatment[27,28]. Both the content of the smartphone application and the face-to-face physiotherapy treatment are based on the recommendations of the guidelines for LBP of The Royal Dutch Society for Physiotherapy[30]. The duration and content of the stratified blended physiotherapy intervention was matched to the patients' risk for developing persistent LBP ('low', 'medium' or 'high') as assessed with the Keele STarT Back Screening Tool[31]. The smartphone application contains video-supported self-management information, video-supported exercises, and a goal-oriented physical activity module. The content of both the face-to-face care and the smartphone application was tailored to the patients' individual needs and progress by the physiotherapists (Table 1). Although physiotherapists were asked to treat according to the stratified blended physiotherapy protocol, they were allowed to deviate from the protocol according to their own clinical judgement. Print screens of the smartphone application are shown in Appendix 1.

Control: Face-to-face physiotherapy

The face-to-face physiotherapy was in line with the LBP guidelines of The Royal Dutch Society for Physiotherapy[30]. The guidelines distinguish three different patient profiles based on the clinical course of recovery (i.e., normal recovery, abnormal recovery without predominant psychosocial factors, and abnormal recovery with predominant psychosocial factors) but do not use a specific tool to stratify care a priori. The content of the face-to-face physiotherapy was the same as that of the stratified blended care intervention, i.e., information, exercises, and recommendations regarding physical activity. However, no recommendations or restrictions were given regarding the number of face-to-face sessions. Physiotherapists were instructed to treat people without using any online applications to assure contrast between the two groups. The exact content of the therapy was left to the discretion of the physiotherapists and their clinical expertise.

Table 1. Overview of the stratified blended physiotherapy intervention (e-Exercise LBP[a])

Mode of delivery	Low-risk profile	Medium-risk profile	High-risk profile
Smartphone application			
- Duration	3 weeks	12 weeks	12 weeks
- Information module	Knowledge-based platform with several LBP self-management information themes (directly available)	12 weekly self-management themes, including assignments	12 weekly self-management themes, including assignments, pain education, and psychosocial risk factors
- Exercise module	3 to 4 home-based exercises tailored to the patient's specific functional limitations	3 to 4 home-based exercises tailored to the patient's specific functional limitations	3 to 4 home-based exercises tailored to the patient's specific functional limitations
- Physical activity module	Physical activity recommendations in accordance with the LBP guidelines of the Royal Dutch Association for Physiotherapy	A 3-day baseline test to determine the current level of physical activity; an 11-week, 3-times per week, goal-oriented training program to maintain or improve the level of physical activity; in patients avoiding physical activity because of LBP, a graded activity functionality can be activated	A 3-day baseline test to determine the current level of physical activity; an 11-week, 3-times per week, goal-oriented training program to maintain or improve the level of physical activity using a graded activity approach
Face-to-face care			
- Sessions	2 sessions	Maximum of 8 sessions	Maximum of 12 sessions
- Content	Reassurance, information about LBP, instruction on self-management options, and the importance of adequate physical activity behaviour	Content similar to low risk, and the following: The physiotherapist can consider providing evidence-based interventions (e.g., passive or active joint mobilization) as recommended by guideline LBP of the Royal Dutch Association for Physiotherapy	Content similar to medium risk, and the following: The physiotherapist addresses patient's specific psychosocial risk factors using a cognitive behavioural approach, and pain education is given

Table 1. Continued

Mode of delivery	Low-risk profile	Medium-risk profile	High-risk profile
Integration of face-to-face care and smartphone application			
- First session	Provide information about LBP and instructions on home-based exercises addressing patient's specific functional limitations using the smartphone application	Provide information about LBP, instructions on home-based exercises addressing patient's specific functional limitations, and instructions on 3-day baseline test using the smartphone application	Provide information about LBP, instructions on home-based exercises addressing patient's specific functional limitations, and instructions on 3-day baseline test using the smartphone application
- Middle sessions	N/A[b]	Evaluation of progress with the smartphone app and optimizing face-to-face care	Evaluation of progress with the smartphone app and optimizing face-to-face care
- Final session	Evaluation of progress with the smartphone application and give recommendations to prevent recurrent episodes of LBP and maintain or improve the physical activity level	Evaluation of progress with smartphone application and optimizing face-to-face care. Evaluate progress with the smartphone application and give recommendations to prevent recurrent episodes of LBP and maintain or improve the physical activity level	Evaluation of progress with smartphone application and optimizing face-to-face care. Evaluate progress with the smartphone application and give recommendations to prevent recurrent episodes of LBP and maintain or improve the physical activity level

[a] LBP = low back pain; [b] N/A = not applicable

Outcome measures

Primary and secondary clinical outcomes were assessed at baseline and at 3 and 12-month follow-ups using online questionnaires and an accelerometer. No financial incentives were offered to complete the measurements. Reminders were sent after seven and fourteen days.

Primary outcome measures

For the effectiveness evaluation, the primary clinical outcome measure was *physical functioning*. Following the internationally accepted "Core Outcome Set" for research on patients with nonspecific LBP[32], physical functioning was assessed with the Oswestry Disability Index (ODI), version 2.1a[33]. A higher ODI score indicates increased functional disability (range: 0-100).

For the economic evaluation, the primary outcomes were *physical functioning* and *health-related quality of life*. Health-related quality of life was assessed using the EuroQol-5D-5L (EQ-5D-5L)[34,35]. This questionnaire comprises five health dimensions (mobility, self-care, usual activities, pain/discomfort and anxiety/depression), all of which can be scored using five severity levels. With this, the instrument differentiates between 3,125 possible health states, which were converted into utility values (range: 0-1) using the Dutch tariff[36]. Quality-adjusted life years (QALYs) were calculated by multiplying the patients' utility values by their time spent in a certain health state using linear interpolation between measurement points[37].

Secondary clinical outcome measures

Secondary clinical outcomes included *average LBP intensity in the last week* measured with an 11-point numeric rating scale (NRS)[32,38]; *mean number of minutes per day spent in moderate to vigorous physical activity (MVPA)* objectively measured using the Activ8 accelerometer (2M Engineering, Valkenswaard, The Netherlands)[39]; *fear avoidance beliefs about physical activity and work* measured using the Fear-Avoidance Beliefs Questionnaire (FABQ)[40]; *pain catastrophizing* measured by the Pain Catastrophizing Scale (PCS)[41]; *self-efficacy* measured using the General Self-efficacy Scale (GSE Scale)[42,43]; *self-management ability* assessed with the Dutch version of the short form Patient Activation Measure (PAM 13-Dutch)[44]; and *patient self-reported adherence to prescribed home exercises* measured with the Exercise Adherence Rating Scale (EARS)[45]. A detailed description of the secondary clinical outcome measures can be found elsewhere[28,29].

Cost outcome measures

Costs included intervention, other healthcare, informal care, absenteeism, presenteeism, and unpaid productivity costs due to nonspecific LBP. Costs were assessed at 3, 6, 9, and 12 months using 3-month retrospective self-reported cost questionnaires. All costs were converted into Euros 2020 using consumer price indices[46]. Discounting of costs was not necessary due to the trial's 12-month follow-up.

Intervention costs were estimated based on the patients' total number of self-reported face-to-face physiotherapy and manual therapy sessions during the first three months of follow-up, valued using Dutch standard costs[47]. Intervention costs also comprised the cost per patient for the development, hosting, and maintenance of the stratified blended physiotherapy intervention. These costs were estimated by dividing the total development, hosting, and maintenance costs (i.e., €28,040) by the expected number of patients with nonspecific LBP who would be eligible for the e-Exercise LBP study during the first 5 years after implementing it broadly (i.e., n=146,309)[48] and an expected implementation rate of 10%. Hence, these costs were €0.19 per patient. Other healthcare costs included the cost of primary and secondary healthcare as well as medication use. Primary and secondary healthcare use were valued using Dutch standard costs[47]. If unavailable, prices according to professional organizations were

used. Both prescribed and over-the-counter medication use were valued using unit prices derived from https://www.medicijnkosten.nl[49]. Informal care (i.e., care by family, friends, and other volunteers) was valued using a Dutch shadow price of €15.14/hour (in Euros 2020)[47]. Paid productivity losses comprised absenteeism (i.e., sickness absence) and presenteeism (i.e., reduced productivity while at work). Absenteeism was measured using a modified version of the IMTA Productivity Cost Questionnaire (iPCQ) and valued in accordance with the "Friction Cost Approach" (FCA) using gender-specific price weights[50,51]. The FCA assumes that costs are limited to the friction period (i.e., period needed to replace a sick worker = 85 days). Presenteeism was measured using the "Productivity and Disease Questionnaire" and valued using gender-specific price weights as well[50–52]. To assess unpaid productivity losses patients were asked to report the number of hours that they were not able to perform volunteer work and domestic and educational activities due to their nonspecific LBP, which were valued using the same Dutch shadow price of €15.14/hour[47].

Baseline measures

Baseline measures included demographic variables and potential confounding variables (i.e., sex, age, body mass index (BMI), presence of comorbidities, educational level, employment status, past LBP surgeries, duration of LBP complaints, the presence of central sensitivity assessed by the Central Sensitization Inventory[53], and the risk of developing persistent LBP assessed by the Keele STarT Back Screening Tool[31,54]).

Data analysis

Statistical analyses were performed according to the intention-to-treat principle. Descriptive statistics were used to explore between-group baseline comparability and to describe patients' general characteristics. Using multivariate imputation by chained equations (MICE) with predictive mean matching, 10 complete datasets were created (loss-of-efficiency <5%)[55]. The imputation model consisted of variables that differed between groups at baseline, variables that were related to the "missingness" of data, variables associated with the outcome, and all available baseline and follow-up costs and clinical outcome measures. Then, each imputed dataset was analysed separately as specified below. Pooled estimates were calculated using Rubin's rules, incorporating both within-imputation variability (i.e., uncertainty about the results from one imputed dataset) and between-imputation variability (i.e., reflecting the uncertainty due to missing information)[55]. Analysis of effectiveness and cost-effectiveness were performed using STATA Corp 13.0.

Analysis of effectiveness

The effectiveness of stratified blended physiotherapy compared to face-to-face physiotherapy for the primary and secondary clinical outcomes was estimated using linear mixed models (LMMs). A two-level structure was used, existing of repeated measurements (level 1), nested within patients (level 2). The necessity of using additional levels in the random effects model to control for the clustering of patients

within physiotherapy practices and individual physiotherapists was checked using log likelihood ratios[56]. Overall mean differences for the complete duration of follow-up, as well as mean differences per time point, were estimated between stratified blended physiotherapy and face-to-face physiotherapy. Regression coefficients with 95% confidence intervals (CIs) were used to signify the differences between stratified blended physiotherapy and face-to-face physiotherapy. Analyses were adjusted for baseline values of clinical outcome measures (e.g., utility score and physical functioning) and variables with a substantial difference at baseline that changed the regression coefficient for the between-group estimate by ≥10% (i.e., duration of LBP complaints).

Analysis of cost-effectiveness

As indicated above, an economic evaluation was performed from both societal and healthcare perspectives. When the societal perspective was applied, all costs were included. When the healthcare perspective was applied, only costs accruing to the formal Dutch healthcare sector were included.

Mean between-group cost differences were calculated for total and disaggregated costs using ordinary least squares (OLS) regression analyses. Seemingly unrelated regression (SUR) analyses were performed to estimate total cost and effect differences (i.e., ΔC and ΔE), while adjusting for baseline values and confounders and taking into account the possible correlation between costs and effects. Variables were considered confounders if they differed considerably at baseline between groups and/or changed the regression coefficient by more than 10%. For effects, the duration of LBP complaints was a confounder. For costs, the confounders were employment status (societal perspective) and the duration of complaints (healthcare perspective). Incremental cost-effectiveness ratios (ICERs) were calculated by dividing the adjusted differences in total costs by the adjusted differences in effects (i.e., ΔC/ΔE). Bias-corrected and accelerated bootstrapping with 5000 replications was used to estimate the uncertainty surrounding the cost differences and ICERs.

Uncertainty surrounding the ICERs was graphically illustrated by plotting bootstrapped cost-effect pairs on cost-effectiveness planes. Cost-effectiveness acceptability curves (CEACs) were constructed to indicate the probability of stratified blended physiotherapy being cost-effective in comparison to face-to-face physiotherapy at different values of willingness-to-pay[37]. In the Netherlands, threshold values for willingness-to-pay of €10,000 to €80,000 per QALY are commonly used for societal perspective analyses[57]. For physical functioning, such threshold values are currently lacking.

Sensitivity analyses

Three sensitivity analyses were performed as part of the economic evaluation. In the first sensitivity analysis, only data from complete cases on the primary clinical outcome and cost outcome measures were included. In a second sensitivity analysis,

absenteeism costs were estimated using the human capital approach (HCA), assuming that productivity losses are generated during the entire duration of absence. In the third sensitivity analysis, the analysis was performed per risk group for developing persistent LBP (low, medium and high) separately, since this proved to be an effect modifier of the between-group differences between stratified blended physiotherapy and face-to-face physiotherapy in the short-term[29].

Sample size

Sample size calculations were based upon the recommendations of Campbell et al. for cluster randomized trials[58]. To detect clinically relevant mean differences between groups at the 12-month follow-up, a difference of >6 points in physical functioning (ODI) and a standard deviation of 14.5 were used[59–61]. In addition, repeated measures of the primary outcome during follow-up were taken into account, and an intraclass correlation coefficient of 0.05 was used. For the repeated measures of physical functioning, a correlation of 0.5 was estimated between baseline and follow-up measurements until the 12-month follow-up[62]. Based on these assumptions (power 80%, α=0.05) and an average cluster size of 5, 165 patients were needed. With an expected dropout rate of 20%, a total of 207 participating patients (n=104 per arm) were needed.

RESULTS

Flow of participants, therapists, and centers through the study

In total, 208 eligible patients participated; 104 were allocated to the stratified blended physiotherapy group and 104 were allocated to the face-to-face physiotherapy group (Figure 1). Complete data on all primary clinical and cost outcome measures were obtained from 171 (82.2%) patients. Four patients (n=2 stratified blended physiotherapy; n=2 face-to-face physiotherapy) were excluded from all analyses since they were diagnosed with specific LBP immediately after inclusion, and hence did not meet the in- and exclusion criteria anymore. At baseline, the stratified blended physiotherapy group consisted of more males, more patients with a low level of education, and more patients with a duration of LBP >12 months than the face-to-face physiotherapy group. No other relevant differences in baseline characteristics were seen between groups (Table 2).

Effectiveness

In the LLM analyses for the primary and secondary clinical outcomes, the log likelihood ratios of the naïve models and the models including a random intercept for both physiotherapy practice and physiotherapist were similar. Physiotherapy practice and physiotherapist were therefore not included as a level in the LMM analyses.

Both interventions were associated with improved clinical outcomes from baseline to 12-months follow-up (within-group differences are presented in Appendix 2). From a clinical perspective, there was neither a clinically relevant, nor a statistically significant adjusted between-group difference over 12 months in the primary outcome of physical functioning (mean difference (MD) -1.1; 95% CI, -3.9 to 1.7). Per time point, adjusted between-group differences in physical functioning were neither clinically relevant, nor statistically significant. For the secondary clinical outcomes, a statistically significant adjusted between-group difference over 12 months, and per time point, was found in favour of stratified blended physiotherapy for fear avoidance beliefs, i.e. Overall MD -4.3; 95% CI, -7.3 to -1.3, 3-month MD -3.9; 95% CI, -7.5 to -0.4, and 12-month MD -4.7; 95% CI, -8.5 to -0.9, respectively. Also, at the 3-month time point, a statistically significant adjusted between-group difference was found in favour of stratified blended physiotherapy for patients' self-reported adherence to prescribed home exercises (MD 0.8; 95% CI, 0.1 to 1.6). Overall differences in secondary clinical outcomes and differences per time point were not considered clinically relevant (Table 3).

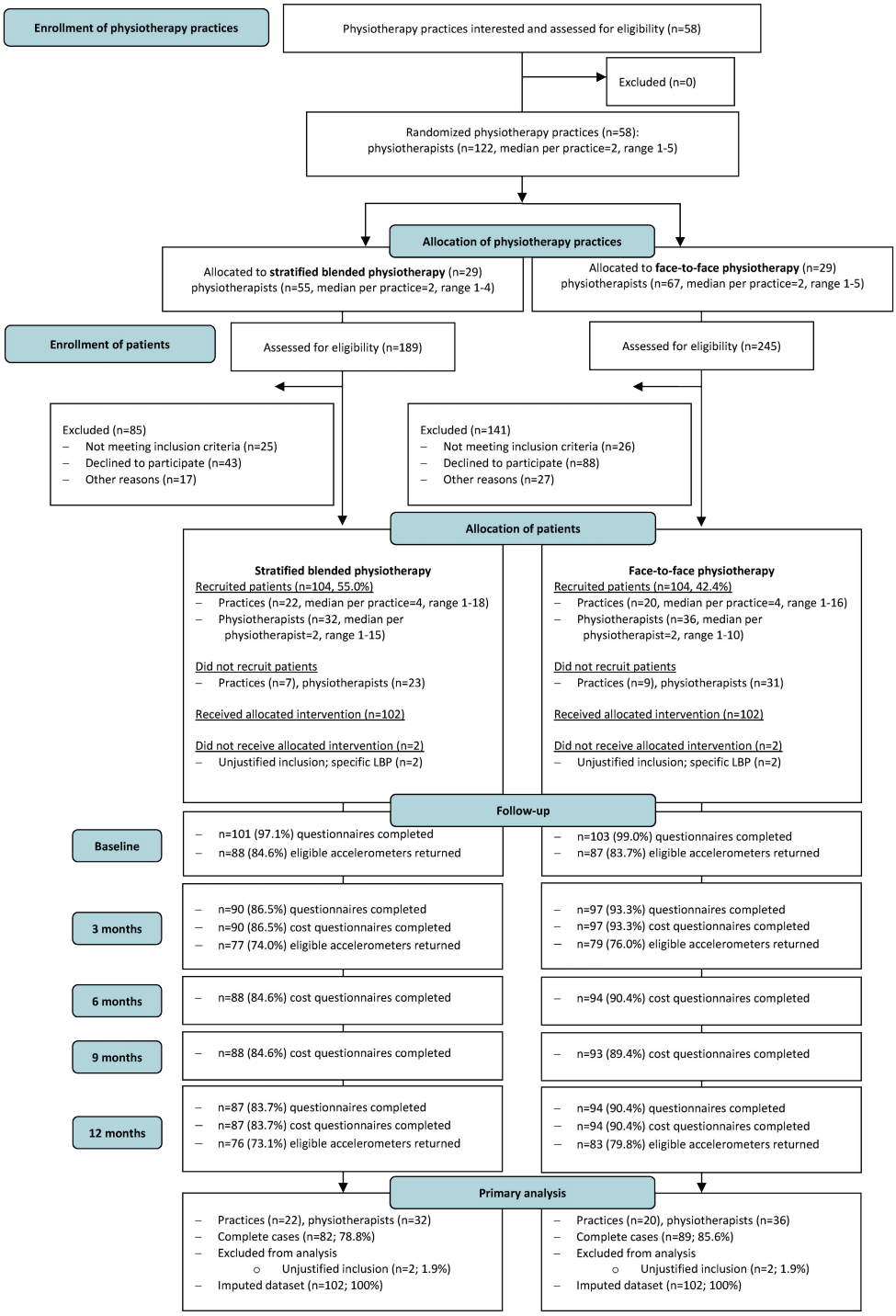

Figure 1. Flow Diagram of the e-Exercise LBP Study

Table 2. Baseline demographic and clinical characteristics of patients from the stratified blended physiotherapy group and face-to-face physiotherapy group

	Stratified blended physiotherapy			Face-to-face physiotherapy		
Characteristic	**All**	**Complete**	**Incomplete**	**All**	**Complete**	**Incomplete**
No. of respondents	104	82	22	104	89	15
Gender, female, n (%)	45 (43.3)	34 (41.5)	11 (50.0)	57 (54.8)	51 (57.3)	6 (40.0)
Age, years, mean (SD)	48.1 (15.1)	50.2 (14.8)	40.4 (13.7)	47.3 (13.6)	48.1 (13.5)	42.5 (13.5)
BMI, kg/m^2, mean (SD)	25.8 (3.8)	26.0 (3.9)	24.9 (3.2)	26.3 (5.1)	26.4 (5.2)	26.0 (4.7)
Presence of comorbidities, yes, n (%)	38 (36.5)	31 (37.8)	7 (31.8)	28 (26.9)	26 (29.2)	2 (13.3)
Employment, yes, n (%)	79 (76.0)	62 (75.6)	17 (77.3)	84 (80.8)	70 (78.7)	14 (93.3)
Past LBP surgery, n (%)						
None	100 (96.2)	79 (96.3)	21 (95.5)	101 (97.1)	87 (97.8)	14 (93.3)
Lumbar fusion	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.0)	0 (0.0)	1 (6.7)
Lumbar discectomy	4 (3.8)	3 (3.7)	1 (4.5)	2 (1.9)	2 (2.2)	0 (0.0)
Educational level, n (%)						
Low	22 (21.2)	15 (18.3)	7 (31.8)	13 (12.5)	12 (13.5)	1 (6.7)
Middle	33 (31.7)	22 (26.8)	11 (50.0)	36 (34.6)	32 (36.0)	4 (26.7)
High	49 (47.1)	45 (54.9)	4 (18.2)	55 (52.9)	45 (50.6)	10 (66.7)
Duration of LBP complaints, n (%)						
0–6 weeks	37 (35.6)	30 (36.6)	7 (31.8)	49 (47.1)	39 (43.8)	10 (66.7)
6–12 weeks	11 (10.6)	7 (8.5)	4 (18.2)	19 (18.3)	18 (20.2)	1 (6.7)
12 weeks – 12 months	9 (8.7)	7 (8.5)	2 (9.0)	9 (8.7)	7 (7.9)	2 (13.3)
> 12 months	47 (45.2)	38 (46.3)	9 (40.9)	27 (26.0)	25 (28.1)	2 (13.3)

Table 2. Continued

Characteristic	Stratified blended physiotherapy			Face-to-face physiotherapy		
	All	Complete	Incomplete	All	Complete	Incomplete
Risk of developing persistent LBP, n (%)						
Low	59 (56.7)	50 (61.0)	9 (40.9)	64 (61.5)	56 (62.9)	8 (53.3)
Medium	35 (33.7)	26 (31.7)	9 (40.9)	37 (35.6)	31 (34.8)	6 (40.0)
High	10 (9.6)	6 (7.3)	4 (18.2)	3 (2.9)	2 (2.3)	1 (6.7)
Central sensitization, score 0-100, mean (SD)	30.9 (13.4)	29.5 (13.3)	37.1 (12.3)	30.2 (12.2)	28.8 (11.4)	39.0 (13.6)
Utility score, score 0-1, mean (SD)	0.731 (0.188)	0.751 (0.152)	0.654 (0.278)	0.752 (0.130)	0.759 (0.131)	0.710 (0.115)
Physical functioning, score 0-100, mean (SD)	19.4 (15.6)	18.7 (14.3)	21.7 (20.0)	20.4 (14.0)	19.9 (14.5)	23.2 (10.8)
Pain intensity, average score 7 days 0-10, mean (SD)	5.6 (2.0)	5.5 (2.0)	6.1 (1.9)	5.4 (2.0)	5.3 (2.0)	5.7 (1.9)
Physical activity, MVPA min/d, mean (SD)	80.3 (36.8)	81.6 (37.3)	73.3 (33.9)	74.8 (40.9)	75.0 (40.7)	73.6 (44.3)
Fear avoidance beliefs, score 0-96, mean (SD)	27.9 (16.0)	24.9 (13.9)	40.8 (18.5)	25.1 (16.2)	24.1 (15.8)	31.5 (17.8)
Pain catastrophizing, score 0-52, mean (SD)	11.1 (9.3)	9.8 (7.9)	16.7 (12.5)	10.2 (8.7)	9.6 (8.7)	13.9 (8.3)
Self-efficacy, score 10-40, mean (SD)	32.1 (4.4)	32.4 (4.4)	31.0 (4.3)	33.1 (3.6)	33.0 (3.8)	33.7 (2.6)
Patient activation, score 0-100, mean (SD)	62.5 (12.4)	63.5 (11.7)	58.6 (14.2)	64.8 (12.6)	65.3 (13.1)	61.4 (8.8)

[a] BMI = Body Mass Index; [b] LBP = Low Back Pain; [c] MVPA = Moderate to Vigorous Physical Activity;
[d] Percentages may not reach 100% due to rounding

Table 3. Adjusted overall between-group differences and adjusted between-group differences per time point for the primary and secondary clinical outcome measures

Outcome	Stratified blended physiotherapy (n=102) Mean (95% CI)	Face-to-face physiotherapy (n=102) Mean (95% CI)	Adjusted between-group difference per time point [a] (n=204) Mean (95% CI)	Adjusted overall between-group difference [a] (n=204) Mean (95% CI)
Physical functioning (ODI, 0-100)				
Baseline	19.4 (16.3 to 22.4)	20.2 (17.5 to 22.9)	-	
3 months	9.7 (6.6 to 12.7)	9.4 (7.0 to 11.9)	-0.6 (-4.3 to 3.2)	
12 months	8.0 (5.3 to 10.6)	8.9 (6.0 to 11.7)	-1.7 (-5.5 to 2.2)	-1.1 (-3.9 to 1.7)
Utility score (EQ-5D-5L, 0-1)				
Baseline	0.729 (0.692 to 0.765)	0.751 (0.725 to 0.776)	-	
3 months	0.847 (0.813 to 0.880)	0.841 (0.806 to 0.876)	0.023 (-0.029 to 0.074)	
12 months	0.851 (0.803 to 0.900)	0.840 (0.791 to 0.889)	0.029 (-0.032 to 0.090)	0.026 (-0.020 to 0.072)
Average pain intensity in past 7 days (NRS, 0-10)				
Baseline	5.7 (5.3 to 6.0)	5.4 (5.0 to 5.8)	-	
3 months	3.2 (2.7 to 3.8)	3.0 (2.5 to 3.4)	0.0 (-0.7 to 0.7)	
12 months	2.4 (1.8 to 2.9)	2.7 (2.2 to 3.2)	-0.6 (-1.3 to 0.0)	-0.3 (-0.9 to 0.2)
Physical activity (Activ8, MVPA min/d)				
Baseline	80.1 (71.5 to 88.7)	74.1 (65.6 to 82.7)	-	
3 months	76.2 (67.0 to 85.3)	69.7 (62.1 to 77.2)	2.5 (-7.5 to 12.6)	
12 months	76.7 (65.8 to 87.7)	70.4 (62.2 to 78.7)	2.4 (-10.6 to 15.3)	2.5 (-6.9 to 11.8)
Fear avoidance beliefs (FABQ, 0-96)				
Baseline	28.1 (24.9 to 31.2)	25.4 (22.2 to 28.5)	-	
3 months	23.3 (20.5 to 26.2)	25.0 (21.6 to 28.4)	-3.9 (-7.5 to -0.4)	
12 months	21.5 (18.1 to 24.9)	24.0 (20.5 to 27.4)	-4.7 (-8.5 to -0.9)	-4.3 (-7.3 to -1.3)
Pain catastrophizing (PCS, 0-52)				
Baseline	11.1 (9.2 to 13.0)	10.3 (8.6 to 12.0)	-	
3 months	9.1 (7.5 to 10.8)	9.3 (7.3 to 11.3)	-0.9 (-2.9 to 1.0)	
12 months	7.9 (6.2 to 9.6)	8.2 (6.6 to 9.9)	-1.1 (-3.1 to 0.9)	-1.0 (-2.6 to 0.6)

Table 3. Continued

Outcome	Stratified blended physiotherapy (n=102) Mean (95% CI)	Face-to-face physiotherapy (n=102) Mean (95% CI)	Adjusted between-group difference per time point [a] (n=204) Mean (95% CI)	Adjusted overall between-group difference [a] (n=204) Mean (95% CI)
Self-efficacy (GSE Scale, 10-40)				
Baseline	32.0 (31.2 to 32.9)	33.1 (32.4 to 33.8)	-	
3 months	31.9 (31.0 to 32.8)	32.6 (31.9 to 33.4)	-0.0 (-1.0 to 1.0)	
12 months	32.6 (31.7 to 33.4)	33.0 (32.2 to 33.9)	0.2 (-0.9 to 1.3)	0.1 (-0.8 to 1.0)
Patient activation (PAM 13-Dutch, 0-100)				
Baseline	62.5 (60.0 to 64.9)	64.7 (62.2 to 67.2)	-	
3 months	61.9 (59.5 to 64.4)	64.5 (61.9 to 67.1)	-1.5 (-4.9 to 2.0)	
12 months	65.6 (62.5 to 68.6)	64.0 (61.2 to 66.9)	2.6 (-1.0 to 6.2)	0.6 (-2.4 to 3.5)
Patient self-reported adherence to prescribed home exercises (EARS, 0-24) [b]				
Baseline	-	-	-	
3 months	11.9 (11.4 to 12.5)	11.1 (10.7 to 11.6)	0.8 (0.1 to 1.6)	
12 months	12.4 (11.8 to 13.1)	12.2 (11.7 to 12.7)	0.2 (-0.5 to 1.0)	0.5 (-0.0 to 1.1)

[a] Adjusted for baseline and duration of LBP complaints (<12 weeks vs. >12 weeks); [b] Patient self-reported adherence to prescribed home exercises could only be measured after the treatment period; [c] ODI = Oswestry Disability Index; [d] NRS = Numeric Rating Scale; [e] MVPA = Moderate to Vigorous Physical Activity; [f] min/d = minutes per day; [g] FABQ = Fear Avoidance Beliefs Questionnaire; [h] PCS = Pain Catastrophizing Scale; [i] GSE = General Self-efficacy Scale; [j] PAM = Patient Activation Measure; [k] EARS = Exercise Adherence Rating Scale

Cost-effectiveness

Resource use and costs

Total societal (FCA) and total healthcare costs were higher in the stratified blended physiotherapy group (societal FCA: €5680 [standard error of the mean (SEM)=1160]; healthcare: €512 [SEM=64]) than in the face-to-face physiotherapy group (societal FCA: €4851 [SEM=701]; healthcare: €439 [SEM=47]). The adjusted between-group differences in total costs were not statistically significant. Most of the disaggregated costs were highest in the stratified blended physiotherapy group. Exceptions included intervention costs and absenteeism costs, which were highest in the face-to-face physiotherapy group. Of all the disaggregated cost differences, only the adjusted difference in unpaid productivity costs was statistically significant (Table 4). A detailed overview of the mean

costs per participant over 12 months in the complete cases only and per risk group for developing persistent LBP is provided in Appendix 3 for both treatment groups.

Effectiveness

The stratified blended physiotherapy group and the face-to-face physiotherapy group gained an average of 0.834 (SEM=0.015) and 0.829 (SEM=0.016) QALYs during the 12-month follow-up, respectively. There was neither a clinically relevant, nor a statistically significant, adjusted between-group difference during the 12-month follow-up period in terms of QALYs (MD 0.026; 95% CI, -0.020 to 0.072) (Table 3).

Societal perspective

The ICER for QALYs was 49,159, indicating that – on average – stratified blended physiotherapy was associated with an additional cost of €49,159 per QALY gained compared with face-to-face physiotherapy (Table 5, Figure 2a). The CEAC indicated that if society is not willing to pay anything per QALY gained, the probability of stratified blended physiotherapy being cost-effective compared to face-to-face physiotherapy is 0.23 (Figure 3a). This probability increased to a maximum of 0.50 at a willingness to pay of €50,000/QALY.

For physical functioning, the ICER was -614. This indicates that stratified blended physiotherapy was – on average – associated with a societal cost of €614 per 1-point improvement on the ODI compared with face-to-face physiotherapy (Table 5, Figure 2b). Please note that a lower ODI score indicates an improved level of physical functioning. The CEAC shows that if decision-makers are not willing to pay anything per 1-point improvement on the ODI, the probability of stratified blended physiotherapy being cost-effective compared to face-to-face physiotherapy was 0.23 (Figure 3b). This probability increased to 0.63 at a willingness to pay of €1,000/point improvement and to 0.79 at a willingness to pay of €10,000/point improvement.

Table 4. Mean costs per participant in the stratified blended physiotherapy and face-to-face physiotherapy groups and the mean cost difference between groups during the 12-month follow-up

Cost category	Cost per participant (€), mean (SEM)		Cost difference (€), Mean (95% CI)	
	Stratified blended physiotherapy (n=102)	Face-to-face physiotherapy (n=102)	Crude (n=204)	Adjusted [c] (n=204)
Healthcare [a]	512 (64)	439 (47)	73 (-60 to 220)	73 (-59 to 225)
Intervention	210 (14)	222 (11)	-12 (-44 to 19)	-13 (-44 to 19)
Primary healthcare excluding intervention	219 (39)	148 (30)	71 (-12 to 154)	72 (-11 to 154)
Secondary healthcare	74 (33)	62 (20)	11 (-43 to 99)	12 (-43 to 102)
Medication	10 (3)	7 (2)	2 (-3 to 9)	2 (-4 to 9)
Informal care	629 (162)	479 (115)	150 (-174 to 484)	143 (-185 to 475)
Absenteeism FCA	773 (370)	646 (283)	127 (-607 to 929)	161 (-557 to 974)
Absenteeism HCA	587 (256)	1344 (967)	-757 (-5182 to 404)	-703 (-4905 to 435)
Presenteeism	2863 (867)	2859 (536)	3 (-1446 to 1532)	131 (-1291 to 1642)
Unpaid Productivity	904 (202)	427 (102)	477 (133 to 892)	464 (122 to 880) *
Societal FCA [b]	5680 (1160)	4851 (701)	830 (-1265 to 3124)	972 (-1090 to 3264)
Societal HCA [b]	5494 (1130)	5549 (1140)	-55 (-3500 to 2297)	108 (-3207 to 2457)

* Statistically significant difference between stratified blended physiotherapy and face-to-face physiotherapy

[a] Healthcare costs are the sum of the primary healthcare costs, secondary healthcare costs, medication costs and intervention costs; [b] Societal costs are the sum of the healthcare costs, informal care costs, absenteeism costs, presenteeism costs and unpaid productivity costs; [c] Adjusted for employment status (yes/no); [d] Costs are expressed in 2020 Euros; [e] FCA = Friction cost approach; [f] HCA = Human capital approach

Healthcare perspective

The ICER for QALYs was 2,239, indicating that stratified blended physiotherapy was – on average – associated with an additional cost of €2,239 per QALY gained compared with face-to-face physiotherapy (Table 5, Figure 2c). The CEAC indicated that if the healthcare system is not willing to pay anything per QALY gained, the probability of stratified blended physiotherapy being cost-effective compared to face-to-face physiotherapy is 0.27 (Figure 3c). This probability gradually increased to a maximum of 0.75 at a willingness to pay of €10,000/QALY.

For physical functioning, the ICER was -28. This indicates that stratified blended physiotherapy was – on average – associated with a healthcare cost of €28 per 1-point improvement on the ODI compared with face-to-face physiotherapy (Table 5, Figure 2d). The CEAC shows that if decision-makers are not willing to pay anything per 1-point improvement on the ODI, the probability of stratified blended physiotherapy being cost-effective compared to face-to-face physiotherapy is 0.27 (Figure 3d). This probability increased to 0.81 at a willingness to pay of €1,000/point improvement and remained the same at a higher willingness to pay.

Sensitivity analysis

The direction and magnitude of the differences in costs and effects between the stratified blended physiotherapy group and the face-to-face physiotherapy group as estimated in the sensitivity analyses were not completely in line with those estimated in the main analysis. In particular, when analysing complete cases only (sensitivity analysis 1), cost differences between the stratified blended physiotherapy group and the face-to-face physiotherapy group were found to be in favour of the stratified blended physiotherapy group, whereas when missing values were imputed (main analysis), these cost differences were in favour of the face-to-face physiotherapy group. This resulted in slightly different CEACs than those obtained in the main analysis. The results of sensitivity analysis 3 showed that the cost difference between the stratified blended physiotherapy group and the face-to-face physiotherapy group increased with a higher risk of developing persistent LBP. That is, for the low-, medium- and high-risk groups, the differences in costs for the societal perspective (QALYs) were €46, €1,124 and €5,225, respectively. In line with the main analysis, however, stratified blended physiotherapy did not seem to be cost-effective in any of the sensitivity analyses (Table 5).

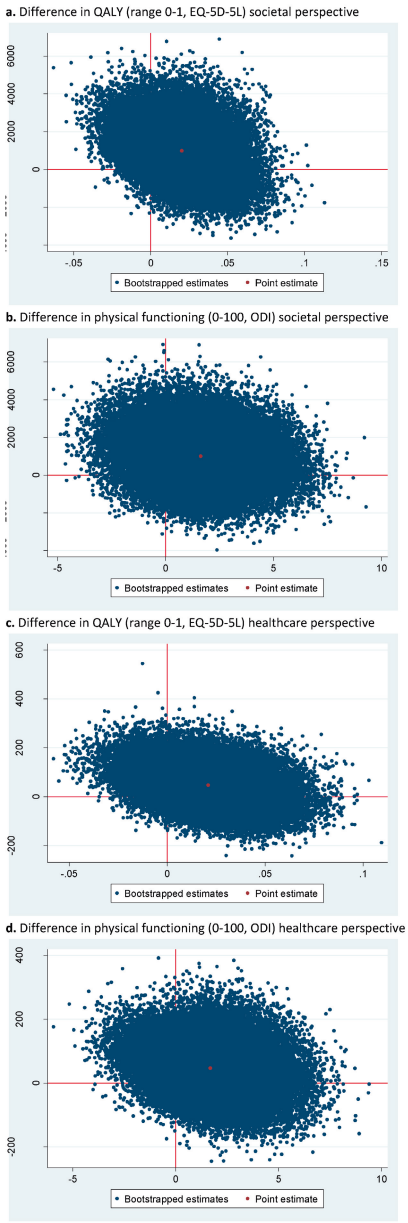

Figure 2. Cost effectiveness planes from the societal and healthcare perspectives.

a. Difference in QALY (range 0-1, EQ-5D-5L) societal perspective.
b. Difference in physical functioning (0-100, ODI) societal perspective.
c. Difference in QALY (range 0-1, EQ-5D-5L) healthcare perspective.
d. Difference in physical functioning (0-100, ODI) healthcare perspective.

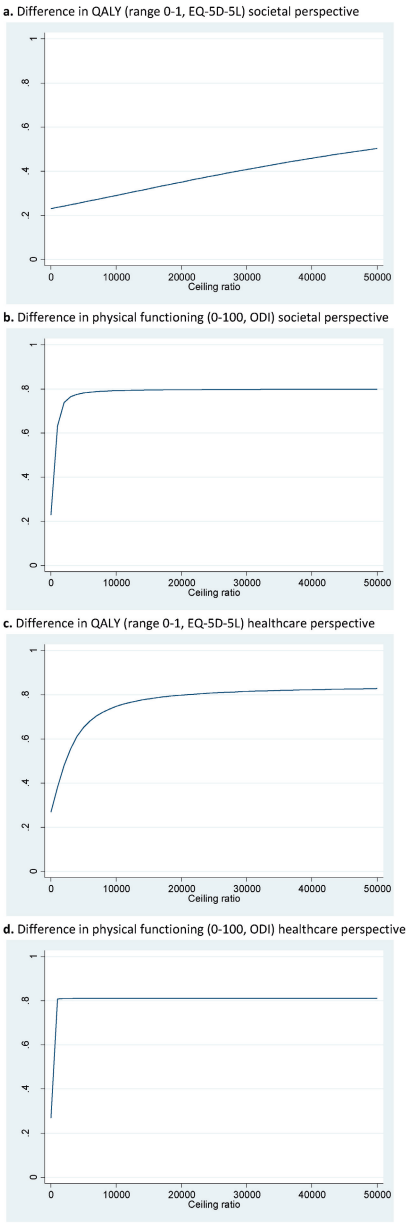

Figure 3. Cost effectiveness acceptability curves from the societal and healthcare perspectives.

a. Difference in QALY (range 0-1, EQ-5D-5L) societal perspective.
b. Difference in physical functioning (0-100, ODI) societal perspective.
c. Difference in QALY (range 0-1, EQ-5D-5L) healthcare perspective.
d. Difference in physical functioning (0-100, ODI) healthcare perspective.

Table 5. Differences in pooled mean costs and effects (95% CI), incremental cost-effectiveness ratios, and the distribution of incremental cost-effect pairs around the quadrants of the cost-effectiveness planes

	n		Outcome	ΔC (95% CI)	ΔE (95% CI)	ICER	Distribution CE-plane (%)			
Analysis	SB PT	F2F PT		€	Points	€/point	NE [a]	SE [b]	SW [c]	NW [d]
Main analysis (imputed dataset)										
Societal perspective	102	102	QALY (0-1)	994 (-1002 to 3320)	0.02 (-0.02 to 0.06)	49159	62.2	22.0	1.0	14.8
	102	102	Physical functioning (ODI, 0-100)	1004 (-1007 to 3306)	-1.63 (-5.43 to 2.16)	-614	60.9	19.4	3.4	16.3
Healthcare perspective	102	102	QALY (0-1)	47 (-81 to 192)	0.02 (-0.02 to 0.06)	2239	59.1	25.6	1.3	13.9
	102	102	Physical functioning (ODI, 0-100)	47 (-81 to 192)	-1.69 (-5.43 to 2.05)	-28	57.6	24.2	2.4	15.8
Sensitivity analysis 1 – Complete case (original dataset)										
Societal perspective	82	89	QALY (0-1)	-385 (-1910 to 1137)	0.02 (-0.00 to 0.04)	-20743	29.6	64.3	2.6	3.5
	82	89	Physical functioning (ODI, 0-100)	-385 (-1915 to 1133)	-2.14 (-4.80 to 0.28)	180	31.0	64.7	1.5	2.8
Healthcare perspective	82	89	QALY (0-1)	-47 (-158 to 84)	0.02 (-0.00 to 0.43)	-2402	21.5	73.9	2.6	2.1
	82	89	Physical functioning (ODI, 0-100)	-47 (-150 to 93)	-2.26 (-4.97 to 0.30)	21	22.8	73.3	2.3	1.6
Sensitivity analysis 2 – Human capital approach (imputed dataset)										
Societal perspective	102	102	QALY (0-1)	136 (-3071 to 2448)	0.02 (-0.02 to 0.06)	6926	41.3	42.1	4.3	12.4
	102	102	Physical functioning (ODI, 0-100)	145 (-3126 to 2455)	-1.57 (-5.34 to 2.21)	-92	42.0	37.9	8.0	12.1

Table 5. Continued

Analysis	n SB PT	n F2F PT	Outcome	ΔC (95% CI) €	ΔE (95% CI) Points	ICER €/point	Distribution CE-plane (%) NE [a]	SE [b]	SW [c]	NW [d]
Sensitivity analysis 3 – Per risk group for developing persistent LBP (imputed dataset)										
Low risk										
Societal perspective	58	62	QALY (0-1)	46 (-2284 to 2492)	0.01 (-0.02 to 0.05)	3498	34.9	44.4	5.3	15.4
	58	62	Physical functioning (ODI, 0-100)	47 (-2239 to 2526)	-0.89 (-4.46 to 2.70)	-53	31.1	37.3	12.3	19.3
Healthcare perspective	58	62	QALY (0-1)	-21 (-165 to 186)	0.01 (-0.02 to 0.05)	-1653	25.1	53.0	7.9	14.1
	58	62	Physical functioning (ODI, 0-100)	-21 (-162 to 193)	-0.84 (-4.38 to 2.71)	25	22.5	45.1	16.2	16.3
Medium risk										
Societal perspective	34	37	QALY (0-1)	1124 (-2357 to 5767)	0.01 (-0.06 to 0.09)	93372	35.9	25.7	8.6	29.8
	34	37	Physical functioning (ODI, 0-100)	1128 (-2370 to 5810)	-2.83 (-10.70 to 5.03)	-398	50.1	26.3	7.6	16.1
Healthcare perspective	34	37	QALY (0-1)	101 (-139 to 348)	0.01 (-0.06 to 0.09)	8485	43.5	17.8	4.6	34.1
	34	37	Physical functioning (ODI, 0-100)	101 (-139 to 345)	-2.83 (-10.63 to 4.98)	-36	55.6	20.4	1.7	22.3

Table 5. Continued

Analysis	n		Outcome	ΔC (95% CI)	ΔE (95% CI)	ICER	Distribution CE-plane (%)			
	SB PT	F2F PT		€	Points	€/point	NE [a]	SE [b]	SW [c]	NW [d]
High risk										
Societal perspective	10	3	QALY (0-1)	5225 (-2183 to 15878)	0.23 (-0.25 to 0.71)	22761	66.1	11.1	0.1	22.7
	10	3	Physical functioning (ODI, 0-100)	5182 (-2610 to 15773)	-12.88 (-31.18 to 5.42)	-402	83.9	11.2	0.1	4.7
Healthcare perspective	10	3	QALY (0-1)	425 (130 to 896)	0.23 (-0.26 to 0.72)	1885	75.3	0.1	0.0	24.5
	10	3	Physical functioning (ODI, 0-100)	425 (125 to 901)	-12.81 (-30.64 to 5.02)	-33	95.1	0.2	0.0	4.7

[a] Refers to the northeast quadrant of the CE plane, indicating that stratified blended physiotherapy is more effective and more costly than face-to-face physiotherapy; [b] Refers to the southeast quadrant of the CE plane, indicating that stratified blended physiotherapy is more effective and less costly than face-to-face physiotherapy; [c] Refers to the southwest quadrant of the CE plane, indicating that stratified blended physiotherapy is less effective and less costly than face-to-face physiotherapy; [d] Refers to the northwest quadrant of the CE plane, indicating that stratified blended physiotherapy is less effective and more costly than face-to-face physiotherapy; [e] Costs are expressed in 2020 Euros; [f] SB PT = Stratified blended physiotherapy; [g] F2F PT = Face-to-face physiotherapy; [h] C = Costs; [i] E = Effects; [j] ICER = Incremental cost-effectiveness ratio; [k] CE = Cost-effectiveness; [l] QALY = Quality-adjusted life year; [m] ODI = Oswestry Disability Index; [n] LBP = Low back pain

DISCUSSION

This study evaluated the long-term effectiveness and cost-effectiveness of the stratified blended physiotherapy intervention e-Exercise LBP in comparison to face-to-face physiotherapy in patients with nonspecific LBP. Both interventions were associated with improved clinical outcomes from baseline to 12-months follow-up, but the study results showed neither a clinically relevant, nor a statistically significant between-group difference in physical functioning. Over 12 months, and for each time point, only fear avoidance beliefs improved significantly more in patients who were allocated to the e-Exercise LBP group. At 3-months, patients who were allocated to the e-Exercise LBP group reported a better adherence to prescribed home exercises. However, the overall between-group difference and the differences in improvement per time point in both fear avoidance beliefs and self-reported adherence to prescribed home exercises were not considered clinically relevant. As for the intervention's cost-effectiveness, from both the societal and healthcare perspectives, a considerable amount of money must be paid per additional QALY or 1-point improvement in physical functioning to reach a relatively low to moderate probability of e-Exercise LBP being cost-effective compared to face-to-face physiotherapy. To illustrate, e-Exercise LBP had a low probability (i.e., 0.29 and 0.60) of cost-effectiveness at the upper and lower bounds of the informal Dutch willingness-to-pay threshold for QALYs (i.e., €10,000 to €80,000 per QALY). For the healthcare perspective and the outcome of physical functioning, willingness-to-pay thresholds are lacking. However, we consider the maximum probability of e-Exercise LBP being cost-effective compared to face-to-face physiotherapy for both outcomes to be moderate at best (i.e., <0.81). Hence, from both societal and healthcare perspectives, e-Exercise LBP does not seem to be cost-effective compared to face-to-face physiotherapy among patients with nonspecific LBP. Between-group differences in costs and effects as estimated in the sensitivity analyses were not completely in line with our main analysis. However, conclusions of the sensitivity analysis confirmed our main analysis.

From a clinical perspective, the results of this study for the primary and secondary clinical outcomes are in line with the short-term results of the e-Exercise LBP study[29] and complement findings from previous systematic reviews of RCTs on the added value of integrating online applications in the treatment of patients with LBP[23,26,63]. Possible explanations for the lack of short-term effectiveness, e.g., the relatively large proportion of patients with a low risk of developing persistent LBP included in the analysis who have a favourable natural prognosis and the fact that blended care is not suitable for all patients, also apply to the findings of this study and have been discussed in detail previously[29]. In general, the selected contrast between the two studied interventions, i.e., the same content delivered either face-to-face or stratified and blended, could be too small and therefore hamper a clear conclusion about the effectiveness of e-Exercise LBP[64]. Given the meaningful and comparable within-group effects in the short term for

both e-Exercise LBP and face-to-face physiotherapy, an equivalence design may have been a better alternative to substantiate the possible added value of e-Exercise LBP.

Although several studies[23,26,65] have assessed the added value of integrating online applications in the treatment of patients with nonspecific LBP, evidence on the cost-effectiveness of such interventions is scarce. Suman et al.[66] studied the cost-effectiveness of a multifaceted eHealth strategy, in which face-to-face care was supported by multiple online components, compared to a digital patient letter for patients with nonspecific LBP in primary care in the Netherlands. The reported mean societal costs and healthcare costs (€8,444 and €1,659 (index year 2016), respectively) and the average number of QALYs gained (0.881) during the 12-month after receiving the intervention are comparable to our findings. The costs and effects of both treatment groups in our study are also comparable to other primary care physiotherapy treatments for patients with nonspecific LBP. In a review by Miyamoto et al.[67] on the cost-effectiveness of exercise therapy in comparison to usual care, the number of gained QALYs during a 12-month follow-up ranged from 0.60 for physiotherapy[68] to 0.78 for exercise therapy[69]. Van de Roer et al.[70] reported a mean societal cost of €4,421 (index year 2004) after 12 months for patients receiving face-to-face physiotherapy in line with the LBP guidelines of The Royal Dutch Society for Physiotherapy[30]. Thus, even though our stratified blended physiotherapy intervention e-Exercise LBP is not more cost-effective when compared to face-to-face physiotherapy, its costs and effects can be considered roughly the same to that of other existing primary care physiotherapy treatments for patients with nonspecific LBP. As a result, e-Exercise LBP can be seen as a valuable alternative for existing primary care physiotherapy treatments. However, the decision about what intervention to administer, reimburse, and/or implement should be based on the preferences of the patient and the decision-maker at hand. This also matches with nowadays ideas of healthcare policymakers on the integration of technology in healthcare[71].

A possible explanation for the lack of effectiveness and cost-effectiveness of e-Exercise LBP might be that, in contrast to our expectations, e-Exercise LBP did not result in a change in patients' self-management and adherence to the prescribed (home) exercises when compared to face-to-face physiotherapy. This is in line with our short-term results[29], and several explanations for this observation are possible. First, the content of the app (i.e., self-management information, integrated fortnightly reminders, and the continuing availability of the app) may have been insufficient to further support patients' self-management behaviour in the home setting. On the other hand, the results of our qualitative study did reveal that patients with chronic LBP (i.e., a duration of LBP of more than 12 weeks at the start of the study) did show adequate self-management behaviour when experiencing a relapse in LBP. In case of a relapse, patients indicated that they first tried to gain control over their new episode of LBP before contacting a healthcare professional. However, patients did indicate that one of the biggest struggles was to maintain adequate health behaviour in the pain-free periods between relapses in LBP[72]. Thus, this could mean

that to facilitate long-term behavioural change in patients' management of LBP, more personalized self-management support during and after treatment is needed.

The comparison to face-to-face physiotherapy in our study might also be an important reason why we were not able to demonstrate better effectiveness and cost-effectiveness of our stratified blended physiotherapy intervention e-Exercise LBP. Despite the reasonably strong evidence that some physiotherapy interventions (compared to minimal or no intervention) for patients with nonspecific LBP are effective, the effect sizes are typically small[2,10,73,74]. Since we wanted to evaluate the advantages of stratified blended physiotherapy in a pragmatic way, we decided to compare it to face-to-face physiotherapy according to the guidelines for LBP of The Royal Dutch Society for Physiotherapy[30]. Since the content of both interventions was based upon the guidelines, the selected between-group contrast in delivery of treatment might have been small beforehand. In addition, given the fact that blended treatment might not be beneficial for all of the patients[24,75], and this suitability was not used as an inclusion criteria, the between-group contrast might have been even smaller than expected. Consequently, a between-group difference in either effects or costs between e-Exercise LBP and face-to-face physiotherapy during 12-months follow-up could not be expected either[64].

A final observation regarding our results is that presenteeism costs contributed substantially to total societal costs (i.e., 50.4% for stratified blended physiotherapy and 58.9% for face-to-face physiotherapy). This finding is in line with previous studies showing that in many chronic conditions, presenteeism makes up the greatest proportion of the overall costs associated with a given chronic condition[76,77]. In addition, presenteeism is a risk factor for future absenteeism and a decrement in self-rated health[78]. The distribution of total costs across the disaggregate cost categories highlights the importance of targeting presenteeism as part of future (blended) and possible cost-effective interventions for patients with nonspecific LBP.

Strengths and limitations

The pragmatic cluster-randomized, controlled trial design with a follow-up period of 12 months is an important strength of this study. Such a design is acknowledged as the best setup for evaluating the effectiveness and cost-effectiveness of interventions in a real-world setting. The pragmatic approach and the involvement of 42 physiotherapy practices and 68 physiotherapists across the Netherlands improves the generalizability of the results to daily physiotherapy practice[37]. A second strength is that the economic evaluation was performed from both societal and healthcare perspectives. In addition to the societal perspective, which is recommended in the Dutch guidelines for economic evaluation, the evaluation of the narrower healthcare perspective enables healthcare decision-makers to first consider the intervention's cost-effectiveness from his or her own perspective and to compare this to its cost-effectiveness from the broader societal perspective. As a result, better informed decisions can be made since local policy is then considered with societal

optimality in mind[79,80]. A final strength is that in addition to QALYs as an outcome measure, physical functioning was used as an outcome measure in the economic evaluation as well. This is important because physical functioning is closely related to the objective of the studied interventions; it is recommended in the core outcome set for research into patients with nonspecific LBP and is probably most relevant to healthcare providers[32].

The present study also had some limitations. An important limitation is that incomplete cases had – on average – higher levels of physical functioning, lower utility scores, and higher aggregate and disaggregate costs than complete cases. This suggests that the result of the complete-case analysis is likely biased to some extent by the self-selection of patients. To address this limitation, multiple imputation, which is considered a highly appropriate method for imputing data that are related to observed data (i.e., missing at random) and simultaneously accounts for uncertainty about the missing data by creating several imputed datasets and pooling their results, was used to handle missing data[55]. In addition, the amount of missing data in this study (i.e., 14% to 21%) was relatively low compared with similar studies[81,82], which further improves the reliability of our multiple imputation results. A second limitation is that stratified blended physiotherapy is still considered a "black box". Although we provided a two-days training for physiotherapists on the integration of the app within face-to-face physiotherapy, we have no insight in the actual fidelity of the intervention, i.e., the degree to which the intervention is delivered as intended. Possibly, low fidelity has contributed to the absence of (cost-)effectiveness of e-Exercise LBP compared to face-to-face physiotherapy. Another limiting factor was the use of retrospective self-report questionnaires administered every 3 months to collect the cost and effect data. Self-report questionnaires are a possible source of "social desirability" and/or "recall bias". However, because of the design, any recall bias or socially desirable answers are likely to have affected both groups equally, and hence, there is a small probability that the between-group differences are incorrect.

CONCLUSIONS

This study shows that the stratified blended physiotherapy intervention e-Exercise LBP is neither more effective in terms of physical functioning, nor more cost-effective from a societal or healthcare perspective when compared to face-to-face physiotherapy for patients with nonspecific LBP. Since clinical outcomes improved in both groups from baseline to 12-months follow-up, and no statistically significant total cost or effect differences were found between the stratified blended physiotherapy intervention e-Exercise LBP and face-to-face physiotherapy, the two interventions seem to be equivalent. As a result, the decision about what intervention should be administered and/or implemented can be based upon the preferences of the patient and the physiotherapist.

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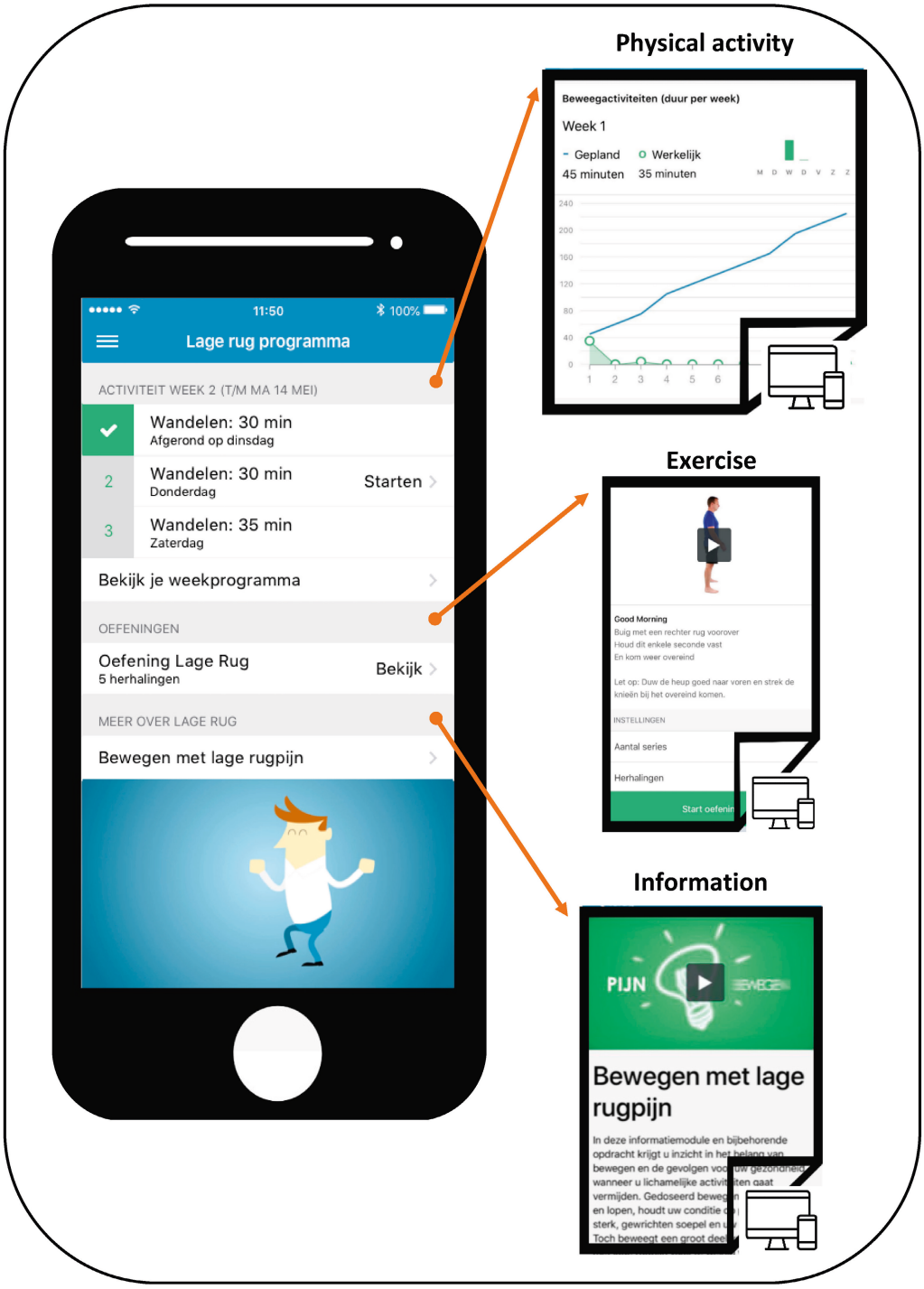
Appendix 1. Print screens of the smartphone application



Appendix 2. Within-group differences in the stratified blended physiotherapy group and the face-to-face physiotherapy group for the primary and secondary clinical outcome measures during the 12-month follow-up

	Stratified blended physiotherapy (n=102)			Face-to-face physiotherapy (n=102)		
	Mean	Within-group difference		Mean	Within-group difference	
Outcome	95% CI	95% CI	*P* value	95% CI	95% CI	*P* value
Physical functioning (ODI, 0-100)						
Baseline	19.4 (16.3 to 22.4)	-	-	20.2 (17.5 to 22.9)	-	-
3 months	9.7 (6.6 to 12.7)	-9.7 (-13.3 to -6.1)	<.001	9.4 (7.0 to 11.9)	-10.7 (-13.7 to -7.8)	<.001
12 months	8.0 (5.3 to 10.6)	-11.4 (-14.9 to -8.0)	<.001	8.9 (6.0 to 11.7)	-11.3 (-14.7 to -8.0)	<.001
Utility score (EQ-5D-5L, 0-1)						
Baseline	0.729 (0.692 to 0.765)	-	-	0.751 (0.725 to 0.776)	-	-
3 months	0.847 (0.813 to 0.880)	0.118 (0.076 to 0.160)	<.001	0.841 (0.806 to 0.876)	0.090 (0.055 to 0.126)	<.001
12 months	0.851 (0.803 to 0.900)	0.123 (0.067 to 0.178)	<.001	0.840 (0.791 to 0.889)	0.089 (0.042 to 0.135)	<.001
Average pain intensity in past 7 days (NRS, 0-10)						
Baseline	5.7 (5.3 to 6.0)	-	-	5.4 (5.0 to 5.8)	-	-
3 months	3.2 (2.7 to 3.8)	-2.4 (-3.0 to -1.9)	<.001	3.0 (2.5 to 3.4)	-2.5 (-3.0 to -1.9)	<.001
12 months	2.4 (1.8 to 2.9)	-3.3 (-3.9 to -2.8)	<.001	2.7 (2.2 to 3.2)	-2.7 (-3.2 to -2.2)	<.001
Physical activity (Activ8, MVPA min/d)						
Baseline	80.1 (71.5 to 88.7)	-	-	74.1 (65.6 to 82.7)	-	-
3 months	76.2 (67.0 to 85.3)	-4.0 (-13.1 to 5.2)	.39	69.7 (62.1 to 77.2)	-4.4 (-11.4 to 2.6)	.22
12 months	76.7 (65.8 to 87.7)	-3.4 (-14.4 to 7.6)	.54	70.4 (62.2 to 78.7)	-3.7 (-11.7 to 4.4)	.37
Fear avoidance beliefs (FABQ, 0-96)						
Baseline	28.1 (24.9 to 31.2)	-	-	25.4 (22.2 to 28.5)	-	-
3 months	23.3 (20.5 to 26.2)	-4.8 (-7.0 to -2.5)	<.001	25.0 (21.6 to 28.4)	-0.3 (-2.5 to 1.8)	.75
12 months	21.5 (18.1 to 24.9)	-6.6 (-10.3 to -2.9)	<.001	24.0 (20.5 to 27.4)	-1.4 (-4.2 to 1.5)	.34

Appendix 2. Continued

	Stratified blended physiotherapy (n=102)			Face-to-face physiotherapy (n=102)		
	Mean	Within-group difference		Mean	Within-group difference	
Outcome	95% CI	95% CI	*P* value	95% CI	95% CI	*P* value
Pain catastrophizing (PCS, 0-52)						
Baseline	11.1 (9.2 to 13.0)	-	-	10.3 (8.6 to 12.0)	-	-
3 months	9.1 (7.5 to 10.8)	-2.0 (-3.5 to -0.4)	.01	9.3 (7.3 to 11.3)	-1.0 (-2.5 to 0.5)	.19
12 months	7.9 (6.2 to 9.6)	-3.2 (-5.1 to -1.3)	.00	8.2 (6.6 to 9.9)	-2.1 (-3.5 to -0.6)	.01
Self-efficacy (GSE Scale, 10-40)						
Baseline	32.0 (31.2 to 32.9)	-	-	33.1 (32.4 to 33.8)	-	-
3 months	31.9 (31.0 to 32.8)	-0.1 (-0.8 to 0.6)	.77	32.6 (31.9 to 33.4)	-0.5 (-1.2 to 0.2)	.20
12 months	32.6 (31.7 to 33.4)	0.5 (-0.4 to 1.4)	.26	33.0 (32.2 to 33.9)	-0.1 (-0.9 to 0.7)	.84
Patient activation (PAM 13-Dutch, 0-100)						
Baseline	62.5 (60.0 to 64.9)	-	-	64.7 (62.2 to 67.2)	-	-
3 months	61.9 (59.5 to 64.4)	-0.5 (-3.0 to 2.0)	.67	64.5 (61.9 to 67.1)	-0.3 (-2.8 to 2.3)	.84
12 months	65.6 (62.5 to 68.6)	3.1 (-0.4 to 6.6)	.08	64.0 (61.2 to 66.9)	-0.7 (-3.4 to 2.0)	.61
Patient self-reported adherence to prescribed home exercises (EARS, 0-24) [a]						
Baseline	-	-	-	-	-	-
3 months	11.9 (11.4 to 12.5)	N/A	N/A	11.1 (10.7 to 11.6)	N/A	N/A
12 months	12.4 (11.8 to 13.1)	N/A	N/A	12.2 (11.7 to 12.7)	N/A	N/A

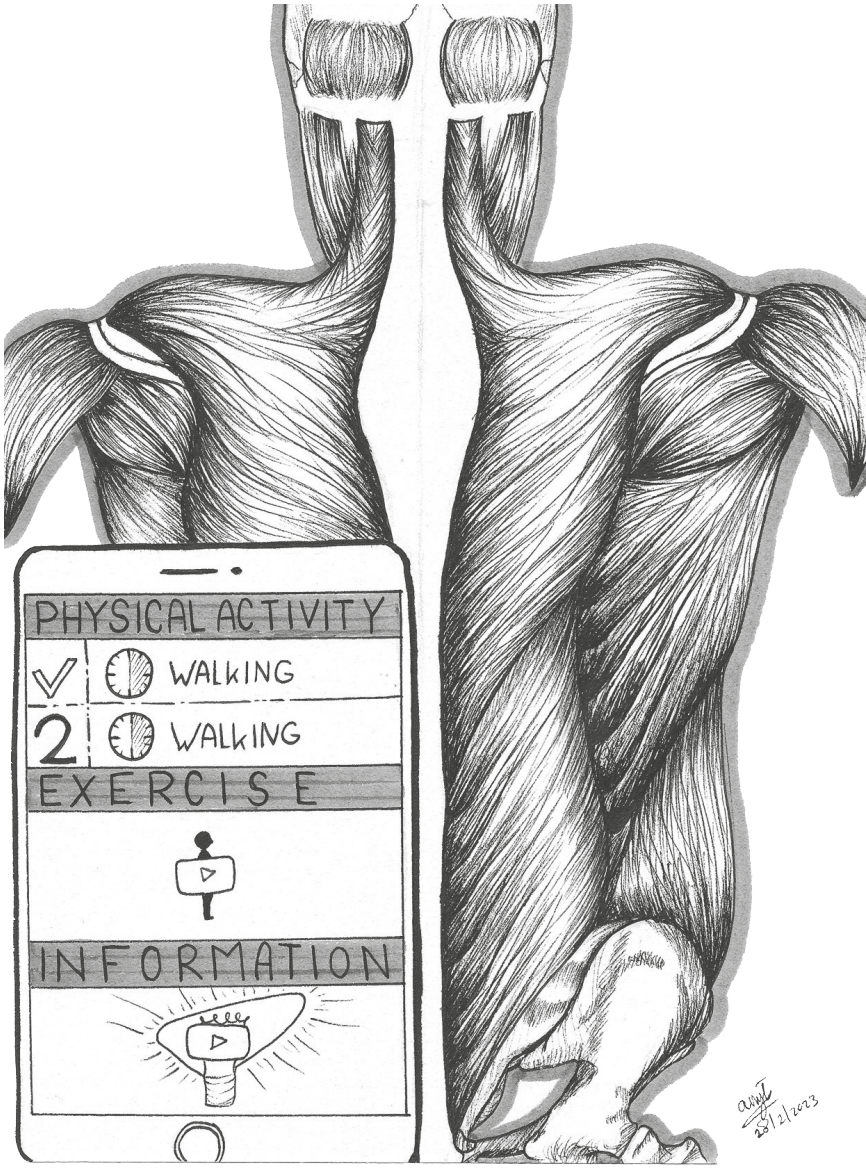
[a] Patient self-reported adherence to prescribed home exercises could only be measured after the treatment period; [b] ODI = Oswestry Disability Index; [c] NRS = Numeric Rating Scale; [d] MVPA = Moderate to Vigorous Physical Activity; [e] min/d = minutes per day; [f] FABQ = Fear Avoidance Beliefs Questionnaire; [g] PCS = Pain Catastrophizing Scale; [h] GSE = General Self-efficacy Scale; [i] PAM = Patient Activation Measure; [j] EARS = Exercise Adherence Rating Scale; [k] N/A = not applicable

Appendix 3. Mean costs per participant in the stratified blended physiotherapy group and the face-to-face physiotherapy group during the 12-month follow-up for complete cases and per risk group for developing persistent low back pain

Complete cases		
Cost category	Cost per participant (€), mean (SEM) [c]	
	Stratified blended physiotherapy (n=82)	Face-to-face physiotherapy (n=89)
Healthcare [a]	370 (54)	384 (40)
Intervention	200 (12)	211 (11)
Primary healthcare excluding intervention	130 (26)	117 (23)
Secondary healthcare	36 (29)	51 (18)
Medication	5 (2)	5 (2)
Informal care	218 (78)	275 (79)
Absenteeism FCA [d]	504 (259)	572 (242)
Absenteeism HCA [e]	542 (290)	1455 (1106)
Presenteeism	1732 (359)	2176 (462)
Unpaid Productivity	403 (97)	300 (72)
Societal FCA [b]	3228 (557)	3708 (560)
Societal HCA [b]	3267 (575)	4590 (1201)

Cost category	Risk of developing persistent low back pain					
	Low Risk		Medium Risk		High Risk	
	Cost per participant (€), mean (SEM) [c]		Cost per participant (€), mean (SEM) [c]		Cost per participant (€), mean (SEM) [c]	
	Stratified blended physiotherapy (n=58)	Face-to-face physiotherapy (n=62)	Stratified blended physiotherapy (n=34)	Face-to-face physiotherapy (n=37)	Stratified blended physiotherapy (n=10)	Face-to-face physiotherapy (n=3)
Healthcare [a]	385 (86)	387 (50)	653 (94)	536 (96)	766 (185)	330 (84)
Intervention	163 (17)	205 (14)	251 (21)	248 (19)	337 (42)	260 (76)
Primary healthcare excluding intervention	150 (42)	118 (29)	304 (74)	205 (64)	334 (132)	48 (12)
Secondary healthcare	66 (47)	59 (28)	85 (43)	72 (33)	80 (105)	0 (0)
Medication	7 (3)	5 (2)	13 (4)	11 (4)	15 (12)	23 (16)
Informal care	322 (152)	249 (92)	987 (318)	747 (247)	1193 (610)	1944 (1161)
Absenteeism FCA [d]	489 (418)	348 (236)	1206 (755)	1197 (636)	949 (756)	0 (0)
Absenteeism HCA [e]	318 (239)	277 (123)	1012 (648)	3241 (2653)	702 (424)	0 (0)
Presenteeism	2096 (729)	2499 (738)	3423 (1691)	3473 (992)	5402 (2798)	2733 (2733)
Unpaid Productivity	369 (166)	225 (102)	1376 (426)	712 (219)	2400 (767)	1090 (555)
Societal FCA [b]	3661 (1102)	3708 (925)	7646 (2356)	6665 (1228)	10711 (3742)	6097 (4170)
Societal HCA [b]	3490 (964)	3637 (867)	7451 (2298)	8709 (2779)	10464 (3747)	6097 (4170)

[a] Healthcare costs are the sum of the primary healthcare costs, secondary healthcare costs, medication costs and intervention costs; [b] Societal costs are the sum of the healthcare costs, informal care costs, absenteeism costs, presenteeism costs and unpaid productivity costs; [c] Costs are expressed in 2020 Euros; [d] FCA = Friction cost approach; [e] HCA = Human capital approach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Characteristics and health outcomes associated with activation for self-management in patients with nonspecific low back pain:

A cross-sectional study

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Authorship statement

I contributed to defining the research question, proposed the methodology and the design, and carried out the data analysis together with an MSc student whom I supervised (Joost van der Heiden). The MSc student wrote the first draft of the manuscript and implemented the contribution of the co-authors up to the first submission of the manuscript. After rejection of the manuscript, I revised the manuscript up to final publication and implemented the comments of the external reviewers (therefore, I am first author). During this whole process I asked for and implemented input and feedback from the other contributors to this study.

ABSTRACT

Background
Research has shown that the course of nonspecific low back pain (LBP) is influenced by, among other factors, patients' self-management abilities. Therefore, clinical guidelines recommend stimulation of self-management. Enhancing patients' self-management potentially can improve patients' health outcomes and reduce future healthcare costs for nonspecific LBP.

Objective
Which characteristics and health outcomes are associated with activation for self-management in patients with nonspecific LBP?

Design
Cross-sectional study.

Methods
Patients with nonspecific LBP applying for primary care physiotherapy were asked to participate. Multivariable linear regression analysis was performed to analyse the multivariable relationship between activation for self-management (Patient Activation Measure, range 0-100) and a range of characteristics, e.g., age, gender, and health outcomes, e.g., self-efficacy, pain catastrophizing.

Results
The median activation for self-management score of the patients with nonspecific LBP (N=208) was 63.10 (IQR=19.30) points. The multivariable linear regression analysis revealed that higher self-efficacy scores (B=0.54), female gender (B=3.64), and a middle educational level compared with a high educational level (B=-5.47) were associated with better activation for self-management in patients with nonspecific LBP. The goodness-of-fit of the model was 17.24% (R^2=0.17).

Conclusions
Patients with better activation for self-management had better self-efficacy, had a higher educational level, and were more often female. This information is a first step in helping physiotherapists to recognise people with a potentially lower degree of activation for self-management, which is important to personalize and individually tailor future self-management interventions more effectively. However, given the explained variance better understanding of the factors that influence this complex construct is warranted.

Keywords
Nonspecific low back pain; Physiotherapy; Self-management; Self-efficacy

INTRODUCTION

Low back pain (LBP) is the leading cause of disability, activity limitation, and work absence worldwide[1]. Approximately 90% of all patients with LBP have nonspecific LBP, meaning there is pain in the lumbosacral region, sometimes with radiating pain to the buttock or leg, without an identifiable pathophysiological cause[2]. Approximately 75-90% of patients with nonspecific LBP recover spontaneously within the first 4-6 weeks[2]. However, approximately 70% of patients with nonspecific LBP will experience recurring episodes within 12 months after recovery[3]. Research has shown that the course of nonspecific LBP is influenced by, among other factors, patients' self-management abilities[4]. Therefore, clinical guidelines in the field of LBP recommend stimulation of self-management[2,5].

Self-management is defined as the ability to manage one's symptoms, treatment, physical and psychological consequences, and lifestyle changes inherent to one's condition[6]. In other words, a person with adequate self-management abilities can make appropriate decisions and take actions to maintain and improve their own health status and will therefore probably have better health outcomes[7]. Enhancing patients' self-management has the potential to both improve patients' health outcomes and reduce future healthcare costs for nonspecific LBP[8].

Self-management is a complex and multifactorial construct. Studies have shown that increased self-efficacy, reduced pain catastrophizing, and reduced fear-avoidance beliefs in patients with chronic nonspecific LBP are mediating factors among self-management, reduced pain and disability, and increased functional outcomes[9]. However, it is unclear how these constructs are precisely related to self-management. It is suggested that theoretical models such as the fear-avoidance model[10] and the social cognitive theory[11] that explain how people might behave, might also be usable to explain how people self-manage[9,12]. However, these models do not explain self-management among patients with nonspecific LBP as such, but merely explain behaviours that are linked to self-management. Therefore, to better understand the construct of self-management in patients with nonspecific LBP, it is important to know which characteristics of patients with nonspecific LBP are associated with better self-management. This information can help to better understand why some patients are better or worse in self-managing nonspecific LBP. The research question of this study is *"Which characteristics and health outcomes are associated with activation for self-management in patients with nonspecific LBP?"*

METHODS

Design

A cross-sectional study was conducted to identify the characteristics and health outcomes that are associated with better activation for self-management in patients with nonspecific LBP. Therefore, a multivariable linear regression analysis was performed using the baseline data from the e-Exercise LBP trial (ISRCTN 94074203)[13]. This study is reported in accordance to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) checklist[14].

Ethics approval

The Medical Ethics Research Committee of the University Medical Centre Utrecht approved this study (18/085D). All patients gave written informed consent before data collection began.

Participants, therapists and centres

Patients with nonspecific LBP, defined as pain in the lumbosacral region with or without radiating pain to the buttock or leg in the absence of an identifiable underlying pathophysiological cause[2], were recruited between July 2018 and December 2019 by 122 physiotherapists at 58 primary care physiotherapy practices in the Netherlands. Patients had to be at least 18 years old, had to have mastery of the Dutch language in speech and writing, and had to provide written informed consent. Patients were excluded if there was a specific cause of LBP determined through medical imaging or a medical doctor, if there were serious comorbidities (e.g., malignancy, stroke), or if the patient was currently pregnant (i.e., because of the prevalence of pelvic girdle pain as a specific form of LBP).

Outcome measure

Patient activation for self-management was assessed with the Dutch version of the short form of the Patient Activation Measure (PAM-13)[15]. The PAM-13 assesses patient self-reported knowledge, skills, and confidence for the self-management of one's health or chronic condition. The PAM-13 is a questionnaire consisting of 13 items that are scored on a 4-point Likert scale, ranging from 'totally disagree' to 'totally agree' , with an additional 'not applicable' option[15]. The PAM-13 scores range from 0 to 100, with a higher score indicating better patient activation for self-management. The PAM-13 makes a distinction among four levels of patient activation assoicated with increasing self-management engagement. Based upon cut-off scores a patient can be divided into level 1 (≤47.0 points), level 2 (47.1-55.1 points), level 3 (55.2-67 points) and level 4 (≥67.1 points)[16]. Level 1 includes the lowest activation score corresponding to a patient with low-self-management engagment. These patients do not take an active role in self-management and thus are considered passive recipients of care[17].

Determinants

Possible determinants of activation for self-management in patients with nonspecific LBP were selected through a comprehensive literature review and included the following characteristics and health-related outcomes: average pain intensity in the past seven days, physical function, fear-avoidance beliefs, pain catastrophizing, self-efficacy, physical activity, age, gender and educational level[9,18–21].

Average pain intensity in the past seven days was measured with an 11-point numeric rating scale (NRS), ranging from 0 ('no pain') to 10 ('worst possible pain')[22]. *Physical functioning* was assessed with the Oswestry Disability Index version 2.1a (ODI), ranging from 0 to 100, with a higher score indicating more functional disability[23]. *Fear-avoidance beliefs* were measured with the Dutch version of the Fear Avoidance Beliefs Questionnaire (FABQ), with a scoring range between 0 and 96 and a higher score indicating more fear-avoidance beliefs[24]. *Pain catastrophizing* was measured with the Pain Catastrophizing Scale (PCS), with a score ranging from 0 to 52 and a higher score indicating more pain catastrophizing[25]. *Self-efficacy* was measured with the General Self-Efficacy (GSE) scale, which has a range from 10 to 40, with a higher score indicating better self-efficacy[26]. *Physical activity* was objectively measured with the Activ8 (2M Engineering, Valkenswaard, The Netherlands)[27]. Patients were instructed to wear the Activ8 on the upper leg (i.e., in a pocket or with a leg strap) for one consecutive week except when sleeping, showering, bathing, or swimming. Activ8 data were eligible if patients had worn the accelerometer for at least three days for 10 hours or more per day. Per patient, the mean time spent in moderate to vigorous physical activity (MVPA) (all activities >3.0 Metabolic Equivalents[28]) in minutes per day was computed by summation and divided by the number of eligible wearing days. Additionally, several demographic characteristics were assessed, namely, *age* (years), *gender* (male/female), *height* (centimeters), *weight* (kilograms), *educational level* (low, middle, high) and *duration of LBP complaints* (1-6, 7-12, 13-52 and >52 weeks).

All determinants, except for physical activity, were self-reported by the patient via an self-reported online questionnaire during a baseline appointment with the researcher. Measurement of physical activity started immediately after obtaining patients' written informed consent.

Data analysis

All analyses were performed using SPSS Statistics version 25.0 (IBM Corp., Armonk (NY), United States of America). Descriptive statistics were calculated to describe patient characteristics and health-related outcomes. Missing value analyses were performed by assuming the missing at random assumption. Multiple imputation was applied using 'Multivariate Imputation by Chained Equations' with Predictive Mean Matching for missing data in all outcomes. A total of 20 imputed datasets were generated, corresponding to the highest missing value percentage[29]. After the

imputation procedure, the data of the imputation sets were pooled to form one dataset for statistical analysis. Statistical power was based on the rule of thumb of 10-20 subjects per variable (n=200), considering the intention to include 10 determinants in the association model[30].

Next, a linear regression was performed to show the univariable association of the determinants with activation for self-management. The analysis was not used as a selection method for candidate variabes[31]. Subsequently, multivariable linear regression analysis was performed to describe the multivariable relationship of the determinants with activation for self-management. The assumptions of linearity, normality of residuals, homoscedasticity and no multicollinearity were checked and approved. A p-value of <0.05 was used to determine if there was a significant association. The explained variance (R^2) of the multivariable model was used to indicate the goodness-of-fit[30].

Finally, to compare the impact of the independent variables in the final model, the relative contributions of the individual model parameters were determined. The relative contributions were determined by multiplying the regression coefficients with a clinically meaningful difference of the independent variables. For the dependent variables gender and educational level, a meaningful difference was a change between groups (from 0 to 1). For the dependent variables age, pain intensity, physical functioning, self-efficacy, pain catastrophizing, fear-avoidance beliefs and physical activity, a meaningful difference was the interquartile range[30].

RESULTS

Response and patient characteristics

In total, 434 patients with nonspecific LBP were approached by the researcher and were asked to participate in this study. A total of 208 of the patients who were willing to participate met the eligibility criteria and were included in this study. The patients were referred by 68 physiotherapists from 42 primary care physiotherapy practices. All patients provided written informed consent.

The mean age of the patients was 47.68 (SD 14.32) years, and a total of 102 (49.0%) patients were female. The mean body mass index (BMI) of the patients was 26.04 (SD 4.49) kg/m2. The median PAM-13 score for activation for self-management was 63.10 (interquartile range (IQR) 19.30) points and the majority of the patients (45.2%) was classified as level 3. An detailed overview of the characteristics and health-related outcomes of the patients is presented in Table 1. In 35 patients (16.8%), there were missing data for one or more variables.

Identifying variables associated with activation for self-management

Results of the univariable lineair regression analyses are shown in Table 2 and of the multivariable lineair regression analysis in Table 3. The multivaribale linear regression analysis revealed that patient activation for self-management was associated with higher self-efficacy scores (B=0.54), female gender (B=3.64), and a middle educational level compared with a high educational level (B=-5.47). A low educational level compared with a high educational level was not significantly associated with patient activation for self-management (P=0.31). Age, pain intensity, physical functioning, physical activity, fear-avoidance beliefs and pain catastrophizing were also not significantly associated with patient activation for self-management. The explained variance (R^2) in patient activation for self-management of the full multivariable lineair model, i.e., goodnesss-of-fit, was 0.17 (i.e., 17.2%).

The relative contribution of the significantly associated independent variables revealed that a meaningful difference in self-efficacy (i.e., IQR=5.75) provided a difference of 3.11 points for the patient activation for self-management score, the difference between women and men provided a difference of 3.64 for the patient activation for self-management score, and the distinction between patients with a high educational level and those with a middle education level provided a difference of -5.47 points for the patient activation for self-management score.

Table 1. Overview of the characteristics and health outcomes of the included patients (N=208)

Characteristic	Value
Age (years), mean (SD)	47.68 (14.32)
Gender, n (%)	
Female	102 (49.0)
Male	106 (51.0)
Height (centimeters), mean (SD)	175.59 (9.84)
Weight (kilograms), mean (SD)	80.42 (15.59)
BMI (kg/m2), mean (SD)	26.05 (4.49)
Marital status, n (%)	
Unmarried	43 (20.7)
Married/living together	142 (68.3)
Widow(-er)	7 (3.4)
Divorced	16 (7.7)
Educational level, n (%)	
Low	35 (16.8)
Medium	69 (33.2)
High	104 (50.0)

Table 1. Continued

Characteristic	Value
Duration of LBP complaints, n (%)	
1-6 weeks	86 (41.4)
7-12 weeks	30 (14.4)
13-52 weeks	18 (8.7)
>52 weeks	74 (35.6)
Activation for self-management (PAM-13), median (IQR)	**63.10 (19.30)**
Level 1 (≤47.0 points), n (%)	16 (7.7)
Level 2 (47.1-55.1 points), n (%)	43 (20.7)
Level 3 (55.2-67 points), n (%)	94 (45.2)
Level 4 (≥67.1 points), n (%)	55 (26.4)
Average pain intensity in the past seven days (NRS), median (IQR)	6.00 (3.00)
Physical activity (MVPA in min/d), median (IQR)	73.49 (38.95)
Physical function (ODI), median (IQR)	18.00 (20.00)
Fear-avoidance beliefs (FABQ), median (IQR)	23.00 (16.50)
Pain catastrophizing (PCS), median (IQR)	8.00 (11.00)
Self-efficacy (GSE), mean (SD)	32.68 (4.11)

SD = Standard Deviation; BMI = body mass index; LBP = Low Back Pain; PAM = Patient Activation Measure; IQR = Interquartile Range; NRS = Numeric Rating Scale; MVPA = Moderate to Vigorous Physical Activity; ODI = Oswestry Disability Index; FABQ = Fear-Avoidance Beliefs Questionnaire; PCS = Pain Catastrophizing Scale; GSE= General Self-Efficacy Scale

Table 2. Lineair regression analyses – univariable associations of the determinants with patient activation for self-management (N=208)

Independent variables	Unstandardized regression coefficients	SE	P-value
Age (years)	-0.05	0.06	0.39*
Gender			
Female vs. male	3.71	1.72	0.03*
Educational level			
Low vs. high	-5.01	2.37	0.04*
Middle vs. high	-7.19	1.89	<0.01*
Pain intensity (NRS)	-0.79	0.43	0.07*
Physical function (ODI)	-0.09	0.06	0.14*
Self-efficacy (GSE)	0.73	0.21	<0.01*
Fear-avoidance beliefs (FABQ)	-0.17	0.05	<0.01*

Table 2. Continued

Independent variables	Unstandardized regression coefficients	SE	P-value
Pain catastrophizing (PCS)	-0.28	0.10	<0.01*
Physical activity (MVPA in min/d)	-0.03	0.03	0.50*

* Characteristics significantly associated with activation for self-management in patients with nonspecific LBP at P-value <0.05.
NRS = Numeric Rating Scale; ODI = Oswestry Disability Index; GSE = General Self-Efficacy Scale; FABQ = Fear-Avoidance Beliefs Questionnaire; PCS = Pain Catastrophizing Scale; MVPA = Moderate to Vigorous Physical Activity

Table 3. Linear regression analyses – multivariable associations of the determinants with patient activation for self-management (N=208)

Independent variables	Unstandardized regression coefficients	SE	P-value	Relative contribution
Intercept	56.97	8.45	-	-
Age (years)	-0.09	0.58	0.13	-2.03
Gender				
Female vs. Male	3.64	1.66	0.03*	3.64
Educational Level				
Low vs. High	-2.42	2.38	0.31	-2.42
Middle vs. High	-5.47	1.87	<0.01*	-5.47
Pain intensity (NRS)	-0.10	0.48	0.83*	-0.30
Physical function (ODI)	<0.01	0.07	0.95*	0.09
Self-efficacy (GSE)	0.54	0.21	<0.01*	3.11
Fear-avoidance beliefs (FABQ)	-0.08	0.06	0.21*	-1.29
Pain catastrophizing (PCS)	-0.17	0.11	0.10*	-1.87
Physical activity (MVPA in min/d)	-0.03	0.02	0.30*	-0.97
Explained variance of the model	**R2 = 0.17**			

* Characteristics significantly associated with activation for self-management in patients with nonspecific LBP at P-value <0.05.
NRS = Numeric Rating Scale; ODI = Oswestry Disability Index; GSE = General Self-Efficacy Scale; FABQ = Fear Avoidance Beliefs Questionnaire; PCS = Pain Catastrophizing Scale; MVPA = Moderate to Vigorous Physical Activity

DISCUSSION

This study aimed to identify characteristics and health-related outcomes associated with patient activation for self-management in the nonspecific LBP population. Among patients with nonspecific LBP, a better self-efficacy, a higher educational level, and the female gender were associated with better activation for self-management. The goodness-of-fit of the mulitvariable lineair regression model explained only 17.2% of the variance in self-management activation, which means that 82.8% remains unexplained.

The activation for self-management score of the patients with nonspecific LBP in this study (median=63.10) is comparable to the activation for self-management scores of patients with a chronic disease or disability. This level indicates that patients are actually taking action, including maintaining lifestyle changes, knowing how to prevent further problems, and handling symptoms on their own[16]. In a Dutch cohort of patients with a chronic disease or disability, the mean score of patient activation for self-management measured with the PAM-13 was 61.3[15]. In another example of a cohort of patients with osteoarthritis in Australia, the mean score of self-management measured with the PAM-13 was 60.5[32]. In addition, the proportion of patients in this study that had a low activation for self-management (PAM-13 level 1-2[16]) is also comparable to the proportion of patients that has a low activation for self-management in other patient populations with a chronic disease or disability[15,32].

Previous studies have described several factors that influence patient activation for self-management. These studies showed that female patients, with a better self-efficacy, less pain catastrophizing, less fear-avoidance beliefs, and a higher educational level had better self-management activation[18,20,33]. Furthermore, a previous study investigated the mean PAM-13 scores for different subgroups in the general population and found that female patients, a relatively younger age, a higher educational level, and a better self-reported health had higher PAM-13 scores[17]. However, all previous studies used univariate analyses. Since patients' self-management is a complex construct, multivariable analyses are essential to understand how self-management is influenced by multiple determinants at the same time. The multivariable linear regression analysis within this study revealed that only better self-efficacy, a higher educational level in comparison with a middle educational level and the female gender were associated with better self-management among patients with nonspecific LBP. Less pain-catastrophizing and less fear-avoidance beliefs were not significantly associated with activation for self-management among patients with nonspecific LBP in the multivariable linear regression analysis. A possible explanation might be the relationship between pain-catastrophizing and fear-avoidance beliefs on the one side, and pain, disability and functional outcomes on the other side. According to the fear-avoidance beliefs model, pain catastrophizing plays an important role in the formation of fear-avoidance beliefs, and those beliefs can consequently influence outcomes like pain or disability, and how this is coped

with by the patient[9,10]. However, how patients actually behave when experiencing pain might not be the same as patients' activation for self-management, i.e., possessing the knowledge, skills, and confidence to manage their health and health care[16].

Although we studied several patient characteristics and health-related outcomes based upon a comprehensive literature review, the goodness-of-fit of our multivariable model only explained 17% of the variance in patient activation for self-management. This is in line with studies of Bos-Touwen et al.[34] and Rockwell et al.[35] in patients with chronic diseases (e.g. chronic heart failure or chronic obstructive pulmonary disease) reporting a low explained variance of 16% and 10.3%, respectively. However, characteristics associated with patient activation for self-management are predominantly different between these studies. In the study of Bos-Touwen et al.[34] age, BMI, educational level, financial distress, physical health status, depression, illness perception and social support were associated with patient activation for self-management. In the study of Rockwell et al.[35] educational level and disease severity were associated with patient activation for self-management. Partly this difference in associated characteristics can be explained trough the available determinants in the e-Exercise LBP study[13]. On the other hand, the different associated characteristics and the low explained variance in these studies highlights that self-management is a complex construct which is not solely influenced by disease and patient characteristics. Other general, non-disease-related characteristics, such as motivation, social support, cognitive abilities, and health literacy, are also recognized as important facilitators or barriers for patient activation for self-management and should therefore be taken into account[36,37]. This is in line with the current narrative on self-management among patients with musculoskeletal pain, which states that self-management is influenced by pain beliefs, emotional and coping responses, social context, and physical and lifestyle factors[38].

Strengths and limitations

To our knowledge, this is the first study that investigated the multivariable relationship between activation for self-management and pain intensity, physical function, fear-avoidance beliefs, pain catastrophizing, self-efficacy, physical activity, age, gender and educational level in patients with nonspecific LBP applying for primary care physiotherapy.

Another strength is the use of the PAM-13 as a generic measure for activation for self-management. The PAM-13 assesses self-reported knowledge, skills and confidence for self-management irrespective of the underlying chronic condition[17]. As a result, found associations can possibly be considered disease transcending which helps in understanding the complexity of activation for self-management in different target populations.

A limitation is that the baseline data of an existing study were used. As a result, the variable selection was limited to the variables that were already included in the

e-Exercise LBP study[13]. Therefore, additional relevant disease-related and non-disease-related characteristics possibly related to self-management in patients with nonspecific LBP, such as motivation, social support, cognitive abilities, and health literacy could not be included in the current analysis[36,37]. In addition, the sample size of the e-Exercise LBP study influenced the number of determinants that could be included in the association model[30].

Another limitation of this study is the use of self-reported online questionnaires to collect the data. Self-reported questionnaires are a possible source of "social desirability" and/or "recall bias" which might have introduced misclasification of patients' activation for self-management. As a result found associations might have been biased.

Finally, due to the cross-sectional design no conclusions can be drawn on the causal relationship between determinants and patient activation for self-management.

Future longitudinal studies are needed to investigate whether the identified determinants for patient activation for self-management are helpful to recognise people with a potentially lower degree of activation for self-management and to identify possible barriers to engage in self-management. However, future studies should also evaluate the importance of other factors, such as motivation, social support, cognitive abilities, and health literacy with regard to patient activtation for self-management. Finally, future studies should focus on unravel the causal relationship between these factors and patient activation for self-management. Understanding these causal relationships might help physiotherapists to better understand the construct of patient activation for self-management and identify patients at risk of inadequate self-management behaviour. As a result treatment can be personalized and individually tailored in a more effective way.

CONCLUSIONS

This study increases the understanding of what determinants are associated with activation for self-management in patients with nonspecific LBP. Patients with better activation for self-management had better self-efficacy, had a higher educational level, and were more often female. This information is a first step in helping physiotherapists to easily recognise people with a potentially lower degree of activation for self-management, which is important to personalize and individually tailor future self-management interventions in a more effective way. However, given the explained variance better understanding of the factors that influence the complex construct of self-management behaviour is warranted.

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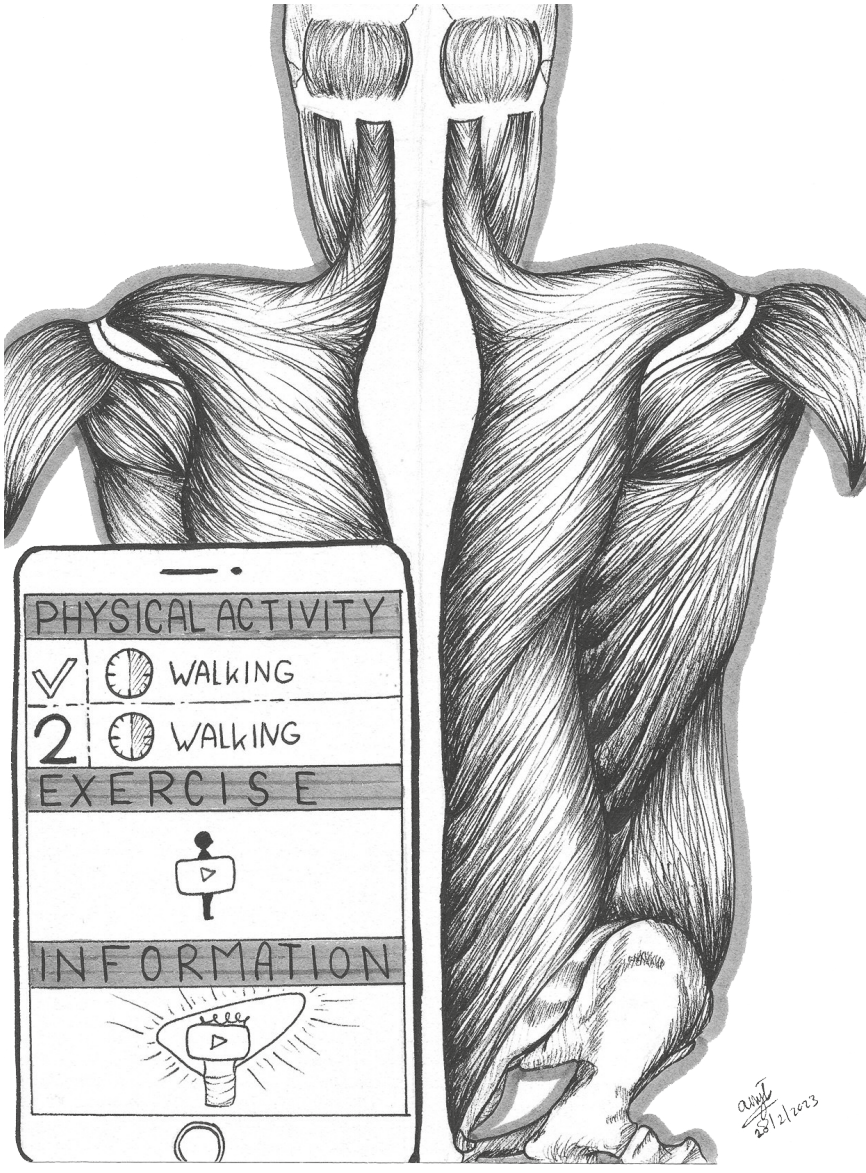
PHYSICAL ACTIVITY
WALKING
2
WALKING
EXERCISE
INFORMATION

7

General discussion

Authorship statement

I had the idea and set-up of the general discussion; I conducted the literature search and wrote the general discussion. During the whole process I asked for and implemented input and feedback from my supervisors. The general discussion represents my opinion and view which may be different from that of my supervisors.

Aim of this thesis

Nonspecific low back pain (LBP) is a leading contributor to the global burden of years lived with disabilities, and this burden is becoming greater due to an increasing and ageing population. The costs of LBP related to healthcare use and paid work productivity loss are enormous and increase the need to identify effective and cost-effective strategies for the management of LBP.

The general aim of this thesis was to evaluate the effectiveness and cost-effectiveness of e-Exercise LBP, a stratified blended physiotherapy intervention, in comparison to face-to-face physiotherapy for patients with nonspecific LBP. The integration of online applications, such as websites and apps, with face-to-face care provided by a physiotherapist, i.e., so-called "blended care", is promising and offers several advantages to optimize the management of patients with nonspecific LBP. The main advantages of blended care are that (1) patients are offered a tool that can support self-management and encourage adherence to prescribed (home) exercises and recommended physical activities anytime and anywhere; and (2) the physiotherapist can monitor individual health behaviour between face-to-face sessions and use this information to coach the patient and to optimize and tailor face-to-face care to the patients' individual needs. Following the promising effects of blended care, we hypothesized that stratified blended physiotherapy supports self-management and adherence to prescribed LBP management strategies. These improvements could lead to an increase in physical functioning and other clinical outcomes, which in turn could result in a reduction in societal and/or healthcare costs. The results of the e-Exercise LBP project were presented in the previous chapters. In this general discussion section, the main findings are reviewed, methodological considerations are discussed, and implications for clinical practice, education, and recommendations for future research are presented.

e-Exercise LBP: An effective and cost-effective alternative to face-to-face care?

Unfortunately, contrary to our expectations, the stratified blended physiotherapy intervention e-Exercise LBP was not more effective than face-to-face physiotherapy in improving physical functioning of patients with nonspecific LBP in both the short and long term **(Chapters 4 and 5**). In the short term, fear-avoidance beliefs and patient self-reported adherence to prescribed home exercises improved significantly in favour of patients who were allocated to stratified blended physiotherapy. In the long term, only fear-avoidance beliefs showed a statistically significant between-group difference in favour of stratified blended physiotherapy. In addition, the economic evaluation (**Chapter 5**) showed that total societal and healthcare costs were not different for our stratified blended physiotherapy intervention e-Exercise LBP when compared to face-to-face physiotherapy. As a result, e-Exercise LBP was not more cost-effective than face-to-face physiotherapy from a societal as well as a healthcare perspective.

Based on the absence of between-group differences in physical functioning and costs, the question arises how these results can be explained. A first important explanation why we were not able to demonstrate effectiveness and cost-effectiveness of our stratified blended physiotherapy intervention e-Exercise LBP might be the comparison to face-to-face physiotherapy. Despite the reasonably strong evidence that some physiotherapy interventions (compared to minimal or no intervention) for patients with nonspecific LBP are effective, the effect sizes are typically small[1–5]. Since we wanted to evaluate the advantages of a stratified blended mode of delivery of physiotherapy in a pragmatic way, we decided to compare it to face-to-face physiotherapy. Since the content of both interventions was based on The Royal Dutch Society for Physiotherapy's guidelines for LBP[6], the between-group contrast was mainly based on the differences in mode of delivery. Given that a blended mode of delivery might not be beneficial for some patients[7], and that patients' suitability for blended care was not an inclusion criterion, the between-group contrast might have turned out smaller than expected a priori. In retrospect, this might clarify the absence of a between-group difference between e-Exercise LBP and face-to-face physiotherapy and emphasize the importance of adequately matching patient characteristics and treatment characteristics, i.e., patients' suitability for blended treatment, in future studies[4].

The study population in the e-Exercise LBP trial might be another important explanation why we were not able to demonstrate the effectiveness and cost-effectiveness of our stratified blended physiotherapy intervention e-Exercise LBP. Since a low risk of developing persistent nonspecific LBP is generally the most common[8], this group was also overrepresented in our pragmatic cluster RCT. For this group, earlier research has shown that a stratified care approach might be non-inferior when compared to usual care[9]. Providing advice as a single intervention is likely to reassure this group of patient with LBP, and many of the patients recover completely within 2 to 3 weeks[10,11]. In line with The Royal Dutch Society for Physiotherapy's LBP guidelines[6] and the e-Exercise protocol[12] (**Chapter 3**), patients in this group only received a few face-to-face sessions. Consequently, our e-Exercise LBP intervention might have resulted in a limited impact on their behaviour and long-term self-management support and between-group differences in clinical outcomes and costs during the 12-month follow-up might not be expected[4,11].

Finally, the heterogeneity of patients with nonspecific LBP might explain why our stratified blended physiotherapy intervention did not result in improved physical functioning when compared to face-to-face physiotherapy[4,13]. Similar to most other RCTs in patients with nonspecific LBP, we compared the physical functioning outcomes between the two groups at different key points in time, i.e., baseline, 3 months and 12 months. This is a comparison between the average change score for the outcomes across all patients in both the e-Exercise LBP group and the face-to-face physiotherapy group. Because of the heterogeneity of the population of patients with nonspecific

LBP, e.g., type or nature of complaints, it can be difficult to evaluate the effect of an intervention because the effects of an intervention can be very diverse and not every patient will respond the same way to treatment. On the other hand, it is also unknown for the time being which factors could cause differential effects of this intervention.

On the other hand, the absence of between-group differences between e-Exercise LBP and face-to-face physiotherapy might be realistic because of several reasons. First, the results from recent studies evaluating a stratified care approach in the treatment of patients with nonspecific LBP suggest that stratified care does not seem to lead to differences in clinical outcomes between patients in the stratified groups and those receiving current practice[14–17]. The Keele STarT Back Screening Tool (SBT)[18] identifies the most important modifiable prognostic risk factors for the development of persistent LBP at a single moment in time to determine the content of the online application. This approach does not take into account the heterogenic causes of nonspecific LBP; not every patient, even within the same subgroup, will experience similar symptoms over time or respond the same way to treatments[19,20]. In other words, since stratification of patients with nonspecific LBP cannot be exhaustive and mutually exclusive, it does not imply prognostic homogeneity or treatment responsiveness[13].

Second, the findings of our e-Exercise LBP study in patients with nonspecific LBP are in accordance with findings from e-Exercise studies in different study populations[21–25]. In addition to patients with nonspecific LBP, e-Exercise was studied in patients with hip and/or knee osteoarthritis[22,23], patients with medically unexplained physical symptoms[24,25], and patients with haemophilic arthropathy[21]. In patients with hip and/or knee osteoarthritis[22,23] and in patients with nonspecific LBP (**Chapter 4 and 5**), no short and long term effects of blended physiotherapy were found. In patients with medically unexplained physical symptoms[25] and in patients with haemophilic arthropathy[21], only short term effects of blended physiotherapy were found. Similar to our findings, the e-Exercise interventions in these studies are associated with improved clinical outcomes, and average within-group changes are comparable to improvements in face-to-face physiotherapy care or routine GP care[23,25]. Concerning cost-effectiveness, these studies showed that e-Exercise cannot be considered cost-effective from a societal or healthcare perspective when compared to face-to-face physiotherapy care in patients with knee and hip osteoarthritis[22] or routine GP care in patients with medically unexplained physical symptoms[24].

Overall, we can conclude that no between-group differences exist between our stratified blended physiotherapy intervention e-Exercise LBP and face-to-face physiotherapy in patients with nonspecific LBP. However, not finding a statistically significant or clinically relevant between-group difference does not mean that e-Exercise LBP cannot be considered a possible treatment option to complement current physiotherapy care in patients with nonspecific LBP which is delivered entirely face-to-face. To make an

informed decision about the use and implementation of e-Exercise LBP in clinical physiotherapy practice, it is essential that besides its effects also other aspects are valued that could determine the additional value of a stratified blended care approach in clinical practice. For this decision, it is important to reflect on the value of a stratified blended care approach from the perspective of the development of the care system, the possible advantages and disadvantages of a stratified blended approach for patients and physiotherapists, and the suitability of both patients and physiotherapists for a stratified blended approach.

Societal relevance of this thesis

Dutch healthcare policy is focused on a transition in healthcare towards adequate insured health care services for everyone in the Netherlands (the Dutch "passende zorg"), that is, ensuring the accessibility and quality of affordable healthcare for all[26,27]. To realize this, the following four principles are essential: (1) healthcare should be value-based care, i.e., cost-effective care; (2) healthcare should be patient-centred; (3) expensive healthcare treatments should be prevented and when possible should be substituted by other forms of care, i.e., eHealth, closer to patients' homes; and finally, (4) healthcare should be focused on health instead of disease[28,29], i.e., stimulate self-management and prevent the development of chronic complaints and more expensive care in the future.

The development and evaluation of e-Exercise LBP in primary care physiotherapy as described in this thesis are in line with the principles of "passende zorg": (1) e-Exercise LBP provides a personalized approach focused on stimulating patients' self-management; (2) e-Exercise LBP focuses on prevention of recurrent episodes of nonspecific LBP, instead of solely curing the current episode; (3) e-Exercise LBP offers a stratified care approach to ensure that both the right content and quantity of physiotherapy care are delivered at the right time; (4) by integrating technology within face-to-face physiotherapy, e-Exercise LBP attempts to increase the effectiveness of physiotherapy in patients with nonspecific LBP; and finally, (5) besides evaluating the effectiveness of e-Exercise LBP in patients with nonspecific LBP, the cost-effectiveness of e-Exercise LBP for both society and the healthcare system are not overlooked. Therefore, the e-Exercise LBP trial is a good example that ties perfectly with the principles of "passende zorg" and provides valuable insights into the possibilities and challenges of similar concepts of care that are in line with these principles.

Stratification of care is not the same as patient-centred care

It is important to realize that online self-management interventions are not a one-size-fits all solution and that matching the appropriate digital content to the individual patient's needs is a challenge[30,31]. An important innovation in our e-Exercise LBP trial is that we used a stratification tool to personalize the e-Exercise LBP app to the individual patient (**Chapter 3**). At the start of our trial, clinical practice guidelines had

adopted and advocated a stratified care approach for several years to improve patient outcomes[2,32–34]. Within this approach, the SBT[18] was a frequently recommended tool to match treatment to the patients' risk of developing persistent LBP, and the original STarT Back trial showed promising results regarding improvements in physical functioning and satisfaction with care among patients with LBP while reducing costs[9,35,36]. Since previous research showed that there was a need to personalize the content of the online part of blended physiotherapy, the SBT seemed to be an appropriate tool to match both online as well as offline treatment to individual needs.

In hindsight, the use of the SBT might not have been the most appropriate tool to personalize the online component of our blended care intervention to individual patients assigned to different prognostic risk groups. As discussed before, the results from recent studies evaluating a stratified care approach in the treatment of patients with nonspecific LBP do not confirm the optimism of the initial trial[14–17]. As a result, a different approach is needed to truly personalize an app to the individual patient's risk factors and development of nonspecific LBP in time. The use of artificial intelligence might be helpful in overcoming this challenge and developing personalized treatment plans based on individual patient data. A good example of the use of artificial intelligence to personalize further treatment based upon the individual patient's development in time is the selfBACK project[37]. This project uses an evidence-based decision support system that uses case-based reasoning (i.e., a technology that utilizes knowledge about previous cases along with data about the current patient case[38]) to tailor advice about the current patient, enabling a patient-centred intervention based on what has and has not been successful in previous cases. The data sources that are used for the case-based reasoning comprise initial patient data, weekly symptom progression and daily physical activity[30]. At 3 months, the selfBACK system as an adjunct to usual care showed a reduction in pain-related disability in patients with LBP when compared to usual care[39]. New methods to personalize treatment to individual patients are promising and need to be further investigated.

Although a stratified care approach might not be beneficial for the individual patient, stratification of our e-Exercise LBP intervention using the SBT[18] might have benefited the physiotherapist. The results of the e-Exercise LBP trial show that the physiotherapist, after specific training, is able to adjust the treatment intensity, i.e., the number of face-to-face sessions, to the patients' risk of developing persistent LBP (**Chapter 4**). This tailoring of treatment intensity possibly helps to prevent low-risk patients from being overtreated and high-risk patients from being undertreated[8].

Suitability for blended physiotherapy

When studying the added value of integrating an app within face-to-face physiotherapy to motivate and stimulate patients to change their attitudes and behaviours[40,41], it is

important that the patients' and physiotherapists' suitability for blended care is not neglected.

Concerning the patients' suitability for blended care, stratified blended physiotherapy might not be the best choice for every patient. Earlier research has shown that it is difficult to determine what works best for each individual patient[30,42] and that patients' suitability is influenced by motivation, safety, equipment, digital skills, and health literacy[7]. In addition, patients' self-management skills, time, and financial resources might also influence the appropriate amount of therapeutic guidance alongside a digital application[7].

During the development phase of e-Exercise LBP the suitability for a blended care approach was discussed with the end-users to ensure that it resonates with a diverse group of potential users[43]. However, during our study we did not take the patient's suitability for blended care into account to determine the optimal personalized blended treatment, nor did we differentiate in the ratio between online and face-to-face care (**Chapter 3**)[12]. As a result, patients might have received stratified blended physiotherapy without being suitable for it, for example, a lack of motivation or digital literacy skills. Consequently, this could have resulted in the suboptimal effectiveness of our stratified blended physiotherapy intervention when compared with face-to-face physiotherapy. The forthcoming results of a study by van Tilburg et al.[44] about a stratified blended approach in patients with neck and/or shoulder complaints could provide more insight into the extent to which patients' suitability for blended care and the online/offline ratio influences the effectiveness of blended physiotherapy in another heterogenic musculoskeletal population.

In addition to patients' suitability for blended care, physiotherapists' suitability for blended care should also be considered, as both might influence the outcome of physiotherapy treatment in a similar way. At the start of the e-Exercise LBP trial, a large number of physiotherapy practices (N=58) and primary care physiotherapists (N=122) were willing to participate in the study. However, at the end of the inclusion period, patients were only included from 42 of the participating physiotherapy practices and 68 of the participating physiotherapists (**Chapters 4 and 5**). In more detail, the majority of patients were included by only a small proportion of the participating physiotherapy practices and physiotherapists, i.e., 50% of the patients were included by approximately 24% of the practices (10/42) and physiotherapists (16/68). During training, it became clear that only a portion of the physiotherapists were positive about the possibilities of the e-Exercise LBP app, its user-friendliness, and its added value in supporting the patients with nonspecific LBP to self-manage their complaints. There were also physiotherapists who were less convinced about the possibilities of the app, experienced difficulty using the software to set up the app and recommended more flexibility in content when using the app. This might have affected whether our stratified

blended intervention was delivered as intended. Since blended care is a new way of delivering treatment, it requires a different way of working by physiotherapists. This different way of working will happen more quickly if the added value of integrating an app within face-to-face physiotherapy is clear.

In our study, we gave the physiotherapists a two-day training focused on the content of the e-Exercise LBP intervention and a booster session after approximately six months. In addition to the training, we provided several individual support sessions to answer questions regarding the use of the e-Exercise LBP intervention. This emphasizes the change required from the participating physiotherapists and the amount of support needed to facilitate a new way of working. Future training should focus more on gaining insight into the added value of blended care and how the online application can be integrated to support patients' self-management[45]. It is important to realize that this requires a behavioural change in the physiotherapist that is influenced by previous education and work experience, and that the need for knowledge, skills and attitude can differ for each[46,47]. To that extent, it might be somewhat naïve to think that a two-day training program is sufficient to develop a new way of working. To illustrate, the clinical training program for physiotherapists to deliver stratified care (IMPaCT Back study) was more intensive and only led to small but significant benefits relative to usual care[36,48]. For this intervention, physiotherapists were trained up to nine days, followed by two hours per month of clinical mentoring for 6 months. Therefore, we suggest that the intensity and type of training for delivering blended physiotherapy is carefully considered and matches the physiotherapist's suitability and required change. A self-test on digital health literacy can possibly be used to determine the content and intensity of training that physiotherapists need[49]. For the form, it is good to realize that multistrategy approaches, e.g., role play, simulation, audit and feedback, can potentially lead to important changes in practice, while educational sessions alone only slightly improve professional practice[50,51].

Presenteeism and cost-effective care for nonspecific LBP from a societal perspective

A final observation regarding the results of our e-Exercise LBP trial is that we might need to target the drivers of presenteeism costs to develop future cost-effective interventions from a societal perspective for patients with nonspecific LBP. Within the transition of healthcare towards "passende zorg", cost-effective care from the societal perspective is essential[26,27]. In our study, the relative contribution of the reported presenteeism costs to the total societal costs was substantial, i.e., 50.4% for stratified blended physiotherapy and 58.9% for face-to-face physiotherapy (**Chapter 5**). This finding is in line with previous studies showing that presenteeism costs are often substantial and in many (chronic) conditions make up the greatest proportion of the overall costs associated with a given (chronic) condition[52–55]. In addition, presenteeism is a risk factor for future absenteeism and a decrement in self-rated health[56]. Therefore, to be able to develop cost-effective interventions from a societal perspective for patients with

nonspecific LBP, the employer and workplace of the patient should not be neglected, e.g., by creating multifaceted interventions that integrate work environment interventions, participatory ergonomics, and self-management interventions for nonspecific LBP[53,57,58].

Methodological considerations

Design

The cluster RCT design is an important strength of the e-Exercise LBP study. Due to the act of randomization, an RCT design is acknowledged as the gold standard for evaluating cause-effect relationships between an intervention and an outcome in a real-life clinical setting. In addition, this design allowed us to investigate the additional value of stratified blended physiotherapy compared to face-to-face physiotherapy. The pragmatic approach and the involvement of 42 physiotherapy practices and 68 physiotherapists across the Netherlands improve the generalizability of the results to daily physiotherapy practice[59]. However, given the small contrast, a noninferiority or equivalence trial might have been a more appropriate design to understand whether e-Exercise LBP has at least as much efficacy as face-to-face physiotherapy for patients with nonspecific LBP, on the premise that, a priori, a stratified blended approach offers other advantages, e.g., reduced burden for the patient, reduced cost, or an increased efficiency of care[60,61]. On the other hand, such a noninferiority or equivalence design would require even more participants to reach sufficient power. To put this into perspective, recruitment of 208 participants for the e-Exercise LBP study in 42 physiotherapy practices by 68 physiotherapists took 18 months, making a noninferiority or equivalence trial almost an unrealistic alternative.

The next step

Our stratified blended physiotherapy intervention e-Exercise LBP is an example of a complex intervention due to the stratified blended care approach and the heterogeneity of the LBP population[62]. Following the evaluation of the proof of concept[63], a cluster RCT design to evaluate the short- and long-term effectiveness and cost-effectiveness of e-Exercise LBP in comparison to face-to-face physiotherapy (**Chapters 4 and 5**) was a logical step to evaluate whether this complex intervention works in clinical physiotherapy practice. However, based upon the results of the evaluation of the effectiveness and cost-effectiveness of the e-Exercise study, integrating an online application within face-to-face care is not that simple, nor cheaper, and requires further development. Therefore, the refinement of our stratified blended intervention e-Exercise LBP and its possible implementation in daily physiotherapy practice need to be considered[62].

Concerning the refinement of the intervention, the heterogeneity of the nonspecific LBP population, the complexity of enhancing patients' self-management behaviour in general and with the use of online applications, and the speed in which technology advances, it is difficult to determine what works best for whom, and in what circumstances. To better

understand how self-management behaviour differs between individuals, and how the integration of online applications can be tailored to positively influence individuals' self-management behaviour, alternative study designs, e.g., n-of-1 studies, might be beneficial to pinpoint swiftly how e-Exercise LBP should be refined[64]. For example, an n-of-1 design can describe behavioural patterns over time and adequately identify the response of the individual patient to the intervention. In addition, such a design with baselines of varying length can distinguish between the effects of treatment and the effects due to change. Finally, an n-of-1 design can monitor the maintenance of long-term behavioural change by integrating follow-up measurements after the completion of treatment.

Concerning the implementation of our stratified blended physiotherapy intervention e-Exercise LBP in daily physiotherapy practice, specific outcomes (e.g., reach or uptake of services), attention to the components of the implementation strategy, and contextual factors that support or hinder the achievement of impacts, are key elements to consider[62]. Given the additional effort required from patients and physiotherapists to use stratified blended physiotherapy in daily practice (e.g., by using additional software to create and tailor the online component to the individual patient), and the required affinity of both patient and physiotherapist with the mode of delivery, it is essential to understand the knowledge, skills and attitudes stakeholders require to adopt such an approach. With this knowledge, tailored implementation strategies to implement stratified blended physiotherapy in daily practice can be developed and future implementation of similar interventions can be enhanced.

Implications for clinical practice

In our opinion, our stratified blended care intervention e-Exercise LBP is neither more effective, nor more cost-effective, than face-to-face physiotherapy care for patients with nonspecific LBP. The results of our e-Exercise LBP trial show that the integration of an app within face-to-face physiotherapy can help to support patients' adherence to prescribed management in the home setting where good management of nonspecific LBP is essential (**Chapters 4 and 5**). To that extent, the integration of an online application can be useful to reveal patients' behaviour regarding the management of their nonspecific LBP and subsequently help a physiotherapist to guide further management. Given the found within-group changes and the between-group differences in both the patients who received stratified blended physiotherapy and the patients who received face-to-face physiotherapy, our stratified blended care intervention e-Exercise LBP seems to be a possible treatment option to complement face-to-face physiotherapy. However, because of the heterogeneity of the nonspecific LBP population, the fact that stratification of care cannot be exhaustive and mutually exclusive, the uncertainty about how blended care should be tailored to enhance a patient's individual self-management behaviour, and the possible additional effort required from both patient and physiotherapist, further refinement is needed before the implementation of

e-Exercise LBP in clinical physiotherapy practice can be considered. In addition, the preferences of both the patient and the physiotherapist can influence the suitability and/or motivation for a blended care approach in clinical practice. It is essential that their willingness and suitability are determined before treatment commences.

Implications for future research

Based on the evaluation of the effectiveness and cost-effectiveness of the stratified blended care intervention e-Exercise LBP in primary care physiotherapy, several suggestions for future research can be made:

- Realize that (online) self-management interventions for patients with nonspecific LBP are not a one-size-fits all solution due to the heterogeneity of the population. As a result, stratification of care for patients with nonspecific LBP cannot be exhaustive and mutually exclusive. The use of artificial intelligence might be helpful to develop personalized treatment plans based on individual patient data.
- Make sure that the patients' and physiotherapists' suitability for blended care are not neglected when studying the added value of future blended interventions. For both patients and physiotherapists, this is a new delivery mode of treatment, and it requires behavioural change. Therefore, to enhance the effectiveness of future blended interventions, the intensity and type of training of involved stakeholders should be carefully considered to ensure that future blended interventions are delivered as intended. In addition, insight into the extent to which patients' and physiotherapists' suitability for blended care and the online/offline ratio influence the effectiveness of blended physiotherapy is needed.
- Investigate the knowledge, skills and attitudes a physiotherapist and physiotherapy practice require to adopt stratified blended physiotherapy in daily practice to develop tailored implementation strategies and to enhance future implementation of similar interventions.
- For the refinement of our e-Exercise LBP intervention, it is essential to understand how self-management behaviour differs between individuals and how the integration of online applications can be tailored to positively influence individuals' self-management behaviour. An n-of-1 study design could be a valuable and swift approach since it is able to describe behavioural patterns over time, identify the response of the individual patient, distinguish between the effects of treatment and the effects due to change, and monitor the maintenance of long-term behavioural change.

Implications for education

Alongside changes in practice, changes in education are needed. Patients with nonspecific LBP, but in a broader sense, all people, are responsible for their own health behaviours, and self-management should be stimulated to prevent the development of chronic complaints and more expensive care in the future. All stakeholders (i.e.,

healthcare professionals, employers and insurance companies) need to facilitate, encourage and support this (secondary) prevention to maintain the accessibility and quality of affordable healthcare for all. However, patients need to be supported to be able to self-manage their health and the possible consequences of their disease. This requires an essential shift in the professional attitude of the healthcare professional. Coaching skills and skills to support self-management and behavioural change in patients are important elements that need to be included in the different curricula of healthcare professionals.

In addition, given that eHealth can provide patient-centred care closer to patients' homes, act as a substitute or preventative measure for expensive healthcare, and the speed at which eHealth is developing, bachelor's degree programmes, e.g., physiotherapy, should incorporate the technology in its programmes. Students can be early adaptors and change future practice; both students and healthcare professionals can benefit from the development of skills to select, understand, investigate and implement eHealth innovations into daily practice[65,66].

CONCLUSION

This general discussion can be seen as a summative evaluation of our stratified blended physiotherapy intervention e-Exercise LBP in patients with nonspecific LBP as part of the Center for eHealth Research Roadmap[40]. This thesis aimed to evaluate the effectiveness and cost-effectiveness of e-Exercise LBP, a stratified blended physiotherapy intervention, in comparison to face-to-face physiotherapy for patients with nonspecific LBP. In conclusion, our stratified blended care intervention e-Exercise LBP cannot be considered more effective, nor more cost-effective, when compared to face-to-face physiotherapy. Further refinement is recommended before deciding whether e-Exercise LBP can be implemented in daily physiotherapy practice as a complement to face-to-face physiotherapy. To optimize its application in primary care physiotherapy, it is important that several important topics are further developed, i.e., tailoring of blended care to enhance individuals' self-management behaviour, the suitability of the intended users, and the knowledge, skills and attitudes stakeholders require to adopt a stratified blended approach in clinical practice. Since the development of such interventions can be considered an iterative process, the focus of the next summative evaluation should focus on the sustainable implementation of a refined version of e-Exercise LBP in daily physiotherapy practice.

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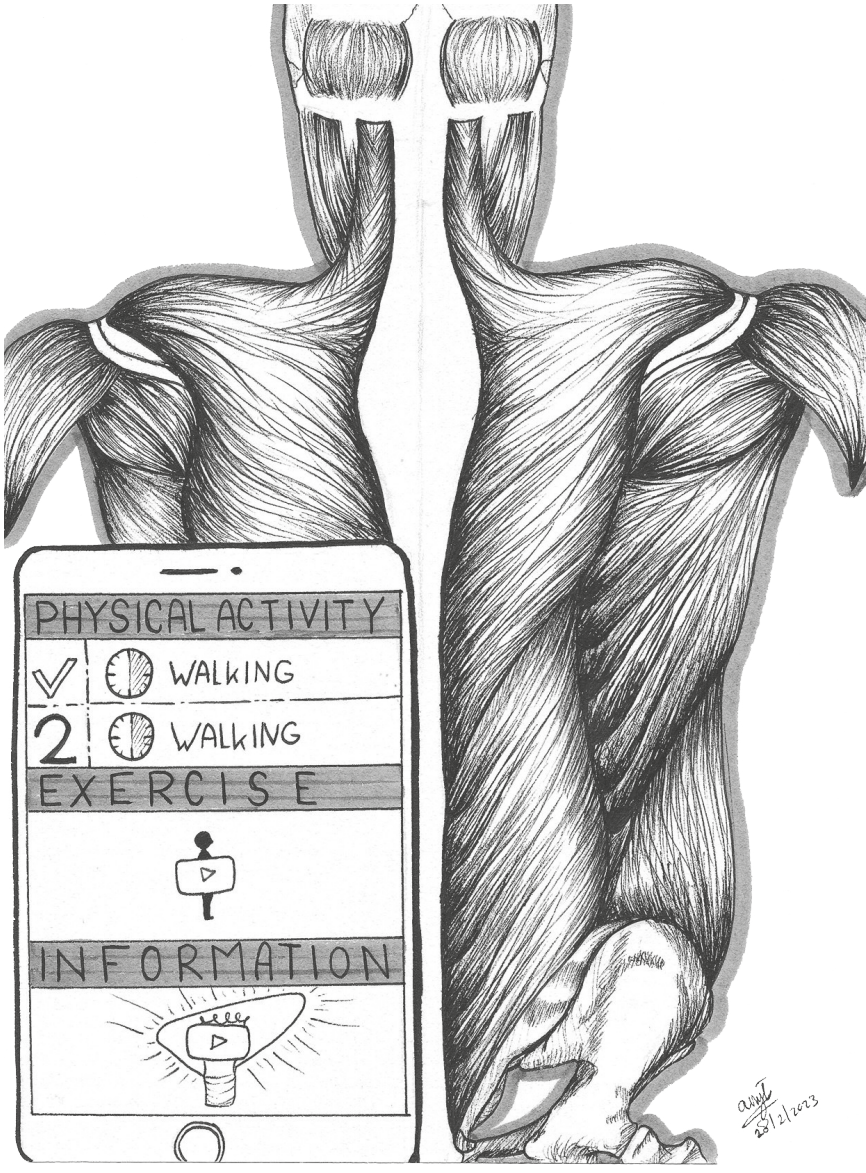
PHYSICAL ACTIVITY
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Summary

Nederlandse samenvatting

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SUMMARY

Nonspecific low back pain is a leading contributor to the global burden of disability-adjusted life years, and this socioeconomic burden is becoming greater due to an increasing and ageing population. The costs of nonspecific low back pain related to healthcare use and productivity loss in the context of paid work are enormous and increase the need to identify effective and cost-effective strategies for the management of nonspecific low back pain.

As described in **Chapter 1**, the integration of online applications, such as websites and apps, into face-to-face care provided by a physiotherapist, i.e., so-called "blended care", is promising and offers several advantages to optimize the management of patients with nonspecific low back pain. The main advantages of blended care are that (1) patients are offered a tool that can support self-management and encourage adherence to prescribed (home) exercises and recommended physical activity behaviour anytime and anywhere; and (2) the physiotherapist can monitor individual health behaviours between face-to-face sessions and use this information to coach the patient and to optimize and tailor face-to-face care to the patients' individual needs.

Despite these benefits, it is important to realize that matching the appropriate blended treatment for the individual patient is reported as a challenge. To resolve this challenge within traditional face-to-face guidance, stratification tools have gained more attention in the past decade. Within a stratified-care approach, the treatment is matched to the patients' risk of developing persistent nonspecific low back pain. It is possible that a stratified-care approach has the same potential for matching the content of blended care interventions to the individual patient as in face-to-face care. Therefore, we developed e-Exercise low back pain, a stratified blended physiotherapy intervention for patients with nonspecific low back pain.

e-Exercise low back pain comprises a smartphone app that is integrated with face-to-face physiotherapy treatment. Both the content of the smartphone app and the face-to-face physiotherapy treatment are based on the low back pain guidelines provided by the Royal Dutch Society for Physiotherapy. The duration and content of the stratified blended physiotherapy intervention are based on the patients' risk of developing persistent nonspecific low back pain as measured using the Keele STarT Back Screening Tool.

The general aim of this thesis was to evaluate the results of the use of e-Exercise low back pain, a stratified blended physiotherapy intervention, in daily physiotherapy practice and to describe its effect on clinical and economic outcome measures.

Chapter 2 presents the results of a systematic review aimed at critically appraising and comparing the measurement properties of all language versions of the Quebec Back Pain Disability Scale (QBPDS). Four databases were searched to find studies concerning the development or evaluation of the measurement properties of the QBPDS in patients with nonspecific low back pain. Assessment of the methodological quality was carried out using the COnsensus-based Standards for the selection of health Measurement INstruments (COSMIN) checklist for both the original language versions of the QBPDS in English and French and all translated versions. The results of the measurement properties were rated based on criteria proposed by Terwee et al. The 27 included articles showed limited-to-moderate evidence of good reliability, validity, and responsiveness of the QBPDS for the different language versions. However, none of the versions had evidence available for all measurement properties. For research and clinical practice, caution is advised when using the QBPDS to measure disability in patients with nonspecific low back pain. Strong evidence is lacking on all measurement properties for each language version of the QBPDS.

Chapter 3 presents the protocol of a prospective, multicentre cluster randomized controlled trial to investigate the short- (3 months) and long-term (12 and 24 months) effectiveness on physical functioning and cost-effectiveness of e-Exercise low back pain in comparison to face-to-face primary care physiotherapy in patients with nonspecific low back pain. Our hypothesis was that e-Exercise low back pain would improve patients' physical functioning by offering a blended stratified-care approach and consequently would positively influence patients' self-management skills and adherence to exercise and physical activity recommendations. In the long term, e-Exercise low back pain could result in an improved handling of recurrent episodes of nonspecific low back pain and a reduction in direct and indirect costs. The aim was to include 208 patients with nonspecific low back pain. The primary outcome was physical functioning at the 12-month follow-up. Secondary outcomes included pain intensity, physical activity, adherence to prescribed (home-based) exercises and recommended physical activity behaviour, self-efficacy, patient activation and health-related quality of life. All measurements were performed at baseline and 3, 12 and 24 months after inclusion. Costs were assessed every 3 months using retrospective self-reported questionnaires. An economic evaluation was performed from the societal and healthcare perspectives and assessed the cost-effectiveness of e-Exercise low back pain compared to usual physiotherapy at 12 and 24 months.

Chapter 4 describes the short-term (3 months) effectiveness of stratified blended physiotherapy (e-Exercise low back pain) on physical functioning in comparison with face-to-face physiotherapy in patients with nonspecific low back pain. Both the stratified blended physiotherapy group and the face-to-face physiotherapy group had clinically relevant and statistically significant improvements in physical functioning; however, there was no statistically significant or clinically relevant between-group

difference. For the secondary outcomes, stratified blended physiotherapy showed statistically significant between-group differences in fear-avoidance beliefs and self-reported adherence. In patients with a high risk of developing persistent low back pain (13/208, 6.3%), stratified blended physiotherapy showed statistically significant between-group differences in physical functioning and several secondary outcomes. Overall, the stratified blended physiotherapy intervention e-Exercise low back pain is not more effective than face-to-face physiotherapy in patients with nonspecific low back pain in improving physical functioning in the short term. For both stratified blended physiotherapy and face-to-face physiotherapy, within-group improvements were clinically relevant.

Chapter 5 reports the findings of the evaluation of the 12-month effectiveness and cost-effectiveness of stratified blended physiotherapy (e-Exercise low back pain) compared to face-to-face physiotherapy in patients with nonspecific low back pain. The economic evaluation was conducted alongside the prospective, multicentre cluster-randomized controlled trial. After 12 months, no clinically relevant or statistically significant differences were found between stratified blended physiotherapy and face-to-face physiotherapy in physical functioning and quality-adjusted life years. For the secondary outcomes, fear avoidance beliefs showed a statistically significant improvement in favour of stratified blended physiotherapy. Societal and healthcare costs were higher for stratified blended physiotherapy than for face-to-face physiotherapy. Adjusted between-group differences in total costs were not statistically significant. Of the disaggregated cost categories, only unpaid productivity costs were statistically significantly higher for stratified blended physiotherapy. From both perspectives, a considerable amount of money must be paid per additional quality-adjusted life year or 1-point improvement in physical functioning to reach a relatively low to moderate probability of stratified blended physiotherapy being cost-effective compared to face-to-face physiotherapy, respectively. Overall, the stratified blended physiotherapy intervention e-Exercise low back pain is neither more effective for improving physical functioning nor more cost-effective from societal or healthcare perspectives when compared to face-to-face physiotherapy for patients with nonspecific low back pain.

Chapter 6 describes the results of a cross-sectional study that aimed to explore the characteristics and health outcomes associated with activation for self-management in patients with nonspecific low back pain. The multivariable linear regression analysis revealed that higher self-efficacy scores, female gender, and a mid-level education compared with a high level of education were associated with better activation for self-management in patients with nonspecific low back pain. The goodness-of-fit of the model was 17.24%. Overall, this study increases the understanding of determinants associated with activation for self-management in patients with nonspecific low back pain. Patients with better activation for self-management had better self-efficacy, had a higher level of education and were more often female. This information is a first step in

helping physiotherapists recognize people with a potentially lower degree of activation for self-management, which is important in tailoring self-management interventions to individuals to increase their effectiveness. However, given the explained variance, a better understanding of the factors that influence this complex construct is warranted.

Chapter 7 presents a general discussion of the entire e-Exercise Low Back Pain project. In this chapter, the main findings are reviewed, methodological considerations are discussed, and implications for clinical practice, education, and recommendations for future research are presented. The research conducted in this thesis showed that e-Exercise low back pain was not more effective, nor more cost-effective, compared to face-to-face physiotherapy in patients with nonspecific low back pain. The results of our e-Exercise low back pain trial show that integrating an app within face-to-face physiotherapy can help to support patients' adherence to prescribed management in the home setting where good management of nonspecific low back pain is essential. From that perspective, the integration of an app within face-to-face physiotherapy can be useful to reveal patients' behaviour regarding the management of their nonspecific low back pain and can subsequently help a physiotherapist guide further management. Given the found within-group changes and the between-group differences in both the patients who received stratified blended physiotherapy and the patients who received face-to-face physiotherapy, our stratified blended care intervention e-Exercise low back pain seems to be a possible treatment option to complement face-to-face physiotherapy. However, because of (1) the heterogeneity of the nonspecific low back pain population, (2) the fact that stratification of care cannot be exhaustive and mutually exclusive, (3) the uncertainty about how blended care should be tailored to enhance a patient's individual self-management behaviour, and (4) the possible additional effort required from both patient and physiotherapist, further refinement is needed before the implementation of e-Exercise low back pain in clinical physiotherapy practice can be considered. In addition, the preferences of both the patient and the physiotherapist can influence the suitability and/or motivation for a blended care approach in clinical practice. It is essential that their willingness and suitability are determined before treatment commences.

For the refinement of our e-Exercise low back pain intervention, future research should focus on understanding how self-management behaviour differs between individuals and how the integration of online applications can be tailored to positively influence individuals' self-management behaviour. The use of artificial intelligence to develop personalized treatment plans based on individual patient data might be helpful to realize this. To enhance the effectiveness of future blended interventions, we suggest to carefully consider the intensity and type of training of involved stakeholders to ensure that future blended interventions are delivered as intended. In addition, insight into the extent to which patients' and physiotherapists' suitability for blended care and the online/offline ratio influence the effectiveness of blended physiotherapy is needed.

To develop tailored implementation strategies and enhance implementation in daily physiotherapy practice, the skills and attitudes a physiotherapist and physiotherapy practice require to adopt stratified blended physiotherapy need to be studied.

In conclusion, our stratified blended care intervention e-Exercise low back pain cannot be considered more effective, nor more cost-effective, when compared to face-to-face physiotherapy. Further refinement is recommended before deciding whether e-Exercise low back pain can be implemented in daily physiotherapy practice as a complement to face-to-face physiotherapy.

NEDERLANDSE SAMENVATTING

Aspecifieke lage rugpijn is een van de belangrijkste oorzaken van beperkingen in het dagelijks leven. De invloed van deze beperkingen, het veelvuldig voorkomen van aspecifieke lage rugpijn, én de toenemende en vergrijzende bevolking zorgen voor een zeer grote maatschappelijke impact. De kosten van aspecifieke lage rugpijn als gevolg van zorggebruik en productiviteitsverlies in betaald werk zijn enorm en versterken de noodzaak om effectieve en kosteneffectieve behandelstrategieën voor aspecifieke lage rugpijn te ontwikkelen.

Zoals beschreven in **hoofdstuk 1**, is het integreren van online toepassingen, zoals websites en apps, binnen het behandeltraject van een fysiotherapeut, i.e., "blended zorg", veelbelovend en biedt deze aanpak verschillende voordelen om de behandeling van patiënten met aspecifieke lage rugpijn te optimaliseren. De belangrijkste voordelen van blended zorg zijn: (1) bij blended zorg krijgen patiënten een digitaal hulpmiddel wat hen altijd en overal kan ondersteunen in het managen van hun aspecifieke lage rugpijn en het naleven van hun voorgeschreven oefeningen en aanbevolen lichaamsbeweging; en (2) bij blended zorg kan de fysiotherapeut tussen de behandelingen door het gezondheidsgedrag van de patiënt monitoren en deze informatie gebruiken om de patiënt te coachen en de face-to-face behandeling te optimaliseren naar de individuele behoeften van de patiënt.

Ondanks de voordelen die blended zorg biedt, is het afstemmen van de optimale inhoud van blended zorg op de individuele patiënt een uitdaging. Binnen de face-to-face behandeling heeft het gebruik van stratificatie-instrumenten als oplossing hiervoor de afgelopen jaren aan aandacht gewonnen. Bij een gestratificeerde zorgbenadering wordt de behandeling van de patiënt afgestemd op het prognostische risico op het ontwikkelen van persisterende aspecifieke lage rugpijn. Mogelijk kan een gestratificeerde zorgbenadering ook van meerwaarde zijn bij het afstemmen van de inhoud van blended zorg op de individuele patiënt. Daarom hebben wij e-Exercise lage rugpijn ontwikkeld, een gestratificeerde blended fysiotherapeutische behandeling voor patiënten met aspecifieke lage rugpijn.

e-Exercise lage rugpijn bestaat uit een smartphone app die geïntegreerd is in de face-to-face behandeling van de fysiotherapeut. De inhoud van de smartphone app en de face-to-face behandeling van de fysiotherapeut zijn beiden gebaseerd op de richtlijnen voor de behandeling van lage rugpijn zoals vastgesteld door het Koninklijk Nederlands Genootschap voor Fysiotherapie. De duur en inhoud van de gestratificeerde blended fysiotherapeutische behandeling zijn gebaseerd op het prognostische risico van de patiënten op het ontwikkelen van persisterende aspecifieke lage rugpijn zoals gemeten met de Keele STarT Back Screening Tool.

Het doel van dit proefschrift is het evalueren van het gebruik van e-Exercise lage rugpijn, een gestratificeerde blended fysiotherapeutische behandeling, in de dagelijkse fysiotherapiepraktijk en het beschrijven van de effecten op klinische en economische uitkomstmaten.

Hoofdstuk 2 presenteert de resultaten van een systematisch literatuuronderzoek gericht op het kritisch beoordelen en vergelijken van de klinimetrische eigenschappen van alle taalversies van de Quebec Back Pain Disability Scale (QBPDS). In vier verschillende databanken werd gezocht naar studies over de ontwikkeling of evaluatie van de klinimetrische eigenschappen van de QBPDS bij patiënten met aspecifieke lage rugpijn. De beoordeling van de methodologische kwaliteit werd uitgevoerd met behulp van de COnsensus-based Standards for the selection of health Measurement INstruments (COSMIN) checklist voor zowel de originele versie van de QBPDS in het Engels en Frans als voor alle vertaalde versies. De resultaten van de klinimetrische eigenschappen werden beoordeeld op basis van criteria voorgesteld door Terwee et al. De 27 geïncludeerde artikelen toonden beperkte tot matige bewijskracht voor een goede betrouwbaarheid, validiteit en responsiviteit van de QBPDS voor de verschillende taalversies. Voor geen enkele van de verschillende taalversies was er echter onderzoek gedaan naar alle klinimetrische eigenschappen. In onderzoek en in de klinische praktijk is daarom voorzichtigheid geboden bij het gebruik van de QBPDS voor het meten van beperkingen in activiteiten bij patiënten met aspecifieke lage rugpijn. Voor alle klinimetrische eigenschappen van de verschillende versies van de QBPDS ontbreekt sterk bewijs.

Hoofdstuk 3 presenteert het protocol van een prospectieve multicenter cluster gerandomiseerde trial naar de korte (3 maanden) en lange termijn (12 en 24 maanden) effectiviteit en de kosteneffectiviteit van e-Exercise lage rugpijn in vergelijking met reguliere face-to-face fysiotherapie bij patiënten met aspecifieke lage rugpijn. Onze hypothese was dat e-Exercise lage rugpijn, in vergelijking met reguliere face-to-face fysiotherapie, het fysieke functioneren van patiënten met aspecifieke lage rugpijn meer zou verbeteren door een blended gestratificeerde aanpak. Daarnaast was de verwachting dat deze blended gestratificeerde aanpak de zelfmanagementvaardigheden en de therapietrouw van patiënten positief zou beïnvloeden. Op de lange termijn zou e-Exercise lage rugpijn, in vergelijking met reguliere face-to-face fysiotherapie, kunnen leiden tot het beter omgaan met terugkerende episoden van aspecifieke lage rugpijn en het verminderen van de directe en indirecte kosten als gevolg van deze rugpijn. Het doel was om 208 patiënten met aspecifieke lage rugpijn aan het onderzoek mee te laten doen. De primaire uitkomst was fysiek functioneren na 12 maanden follow-up. Secundaire uitkomstmaten waren pijnintensiteit, fysieke activiteit, therapietrouw, zelfeffectiviteit, zelfmanagementvaardigheden en gezondheid gerelateerde kwaliteit van leven. Metingen zijn uitgevoerd op baseline en na 3, 12 en 24 maanden. De kosten als gevolg van aspecifieke lage rugpijn werden elke 3 maanden gemeten met

behulp van retrospectieve zelf gerapporteerde kostenvragenlijsten. Na 12 en 24 maanden werd een economische evaluatie uitgevoerd vanuit maatschappelijk en gezondheidszorgperspectief om de kosteneffectiviteit van e-Exercise lage rugpijn in vergelijking met reguliere face-to-face fysiotherapie te bepalen.

Hoofdstuk 4 beschrijft de korte termijn (3 maanden) effectiviteit van gestratificeerde blended fysiotherapie (e-Exercise lage rugpijn) in vergelijking met face-to-face fysiotherapie op het fysiek functioneren van patiënten met aspecifieke lage rugpijn. Na 3 maanden hadden zowel de gestratificeerde blended fysiotherapie groep als de face-to-face fysiotherapie groep een klinisch relevante en statistisch significante verbetering in het fysiek functioneren. Er waren geen statistisch significante of klinisch relevante verschillen tussen de twee groepen. Wat betreft de secundaire uitkomstmaten waren er na 3 maanden significante verbeteringen van pijngerelateerde vrees en zelf gerapporteerde therapietrouw in de gestratificeerde blended fysiotherapie groep ten opzichte van de face-to-face fysiotherapie groep. Bij patiënten met een hoog risico op het ontwikkelen van persisterende lage rugpijn (13/208, 6,3%) zorgde gestratificeerde blended fysiotherapie, ten opzichte van face-to-face fysiotherapie, voor een statistisch significante verbetering van het fysiek functioneren en van verscheidene andere secundaire uitkomstmaten. Over het geheel genomen was de gestratificeerde blended fysiotherapie interventie e-Exercise lage rugpijn niet effectiever dan face-to-face fysiotherapie bij patiënten met aspecifieke lage rugpijn in het verbeteren van het fysiek functioneren op de korte termijn. Voor zowel gestratificeerde blended fysiotherapie als face-to-face fysiotherapie waren de verbeteringen in uitkomstmaten binnen de groep klinisch relevant.

Hoofdstuk 5 beschrijft de bevindingen van de evaluatie van de effectiviteit en kosteneffectiviteit gedurende 12 maanden van gestratificeerde blended fysiotherapie (e-Exercise lage rugpijn) in vergelijking met face-to-face fysiotherapie bij patiënten met aspecifieke lage rugpijn. De economische evaluatie werd uitgevoerd naast de prospectieve multicenter cluster gerandomiseerde trial. Na 12 maanden werden geen klinisch relevante en statistisch significante verschillen gevonden tussen gestratificeerde blended fysiotherapie en face-to-face fysiotherapie in het fysiek functioneren en het aantal levensjaren in goede gezondheid. Voor de secundaire uitkomstmaten was er een statistisch significante verbetering van pijngerelateerde vrees voor de gestratificeerde blended fysiotherapie groep. De maatschappelijke en gezondheidszorg gerelateerde kosten waren hoger voor gestratificeerde blended fysiotherapie in vergelijking met face-to-face fysiotherapie. Gecorrigeerde verschillen tussen de groepen in totale kosten waren niet statistisch significant. Alleen de onbetaalde productiviteitskosten waren statistisch significant hoger voor gestratificeerde blended fysiotherapie vergeleken met face-to-face fysiotherapie. Vanuit zowel het maatschappelijk als het gezondheidszorg perspectief moet een aanzienlijk bedrag betaald worden per extra levensjaar in goede gezondheid, of 1 punt verbetering in het fysiek functioneren, om een relatief kleine kans

te hebben dat gestratificeerde blended fysiotherapie kosteneffectief is in vergelijking met face-to-face fysiotherapie. Over het geheel genomen is de gestratificeerde blended fysiotherapie interventie e-Exercise lage rugpijn niet effectiever in het verbeteren van het fysiek functioneren, noch kosteneffectiever vanuit maatschappelijk of gezondheidszorgperspectief in vergelijking met face-to-face fysiotherapie voor patiënten met aspecifieke lage rugpijn.

Hoofdstuk 6 beschrijft de resultaten van een cross-sectionele studie die tot doel had te onderzoeken welke kenmerken en gezondheidsuitkomsten samenhangen met zelfmanagementvaardigheden bij patiënten met aspecifieke lage rugpijn. Uit de multivariabele lineaire regressieanalyse bleek dat een betere zelfeffectiviteit, het vrouwelijk geslacht en een gemiddeld opleidingsniveau vergeleken met een hoog opleidingsniveau geassocieerd waren met betere zelfmanagementvaardigheden bij patiënten met aspecifieke lage rugpijn. Het model verklaarde 17,24% van de variantie. In het algemeen vergroot deze studie het inzicht in welke determinanten samenhangen met zelfmanagementvaardigheden bij patiënten met aspecifieke lage rugpijn. Patiënten met betere zelfmanagementvaardigheden hadden een betere zelfeffectiviteit, een hoger opleidingsniveau en waren vaker vrouw. Deze informatie is een eerste stap om fysiotherapeuten te helpen mensen met potentieel lagere zelfmanagementvaardigheden te herkennen. Hierdoor kunnen toekomstige zelfmanagementinterventies beter gepersonaliseerd en afgestemd worden op het individu. Echter, gezien de verklaarde variantie is een beter begrip van de factoren die het complexe construct van zelfmanagementvaardigheden beïnvloeden noodzakelijk.

Hoofdstuk 7 bevat een algemene bespreking van het gehele e-Exercise Lage Rugpijn project. In dit hoofdstuk worden de belangrijkste bevindingen en methodologische overwegingen besproken én de implicaties voor de klinische praktijk, het onderwijs en aanbevelingen voor toekomstig onderzoek gepresenteerd. Het in dit proefschrift uitgevoerde onderzoek toonde aan dat e-Exercise lage rugpijn niet effectiever of kosteneffectiever is dan face-to-face fysiotherapie bij patiënten met aspecifieke lage rugpijn. De resultaten van ons onderzoek laten zien dat de integratie van een app in de face-to-face behandeling van de fysiotherapeut kan helpen om de therapietrouw van patiënten in de thuissituatie, waar een goede behandeling van aspecifieke lage rugpijn essentieel is, te ondersteunen. Vanuit dat perspectief kan de integratie van een app in de face-to-face behandeling zinvol zijn en helpen om de wijze waarop patiënten omgaan met hun aspecifieke lage rugpijn zichtbaar te maken. Met deze informatie krijgt de fysiotherapeut handvatten om verdere behandeling vorm te geven. Aangezien de progressie die patiënten maken binnen beide interventiegroepen vergelijkbaar is, en er geen verschillen zijn tussen de interventiegroepen, lijkt onze gestratificeerde blended behandeling e-Exercise lage rugpijn een mogelijke behandeloptie als aanvulling op bestaande face-to-face zorg. Echter, (1) vanwege de heterogeniteit van de populatie met aspecifieke lage rugpijn, (2) het feit dat stratificatie niet 100%

uitputtend en 100% exclusief kan zijn, (3) de onzekerheid over de wijze waarop blended zorg gepersonaliseerd moet worden om het zelfmanagementgedrag van de individuele patiënt te versterken, én, (4) de mogelijk gevraagde extra inspanning van zowel de patiënt als de fysiotherapeut in het gebruik van e-Exercise lage rugpijn, is aanpassing van e-Exercise lage rugpijn noodzakelijk alvorens implementatie in de klinische fysiotherapiepraktijk overwogen kan worden. Tot slot, kan de motivatie en/of de geschiktheid van de patiënt en de fysiotherapeut van invloed zijn op de keuze voor een dergelijke blended behandeling in de klinische praktijk. Het is essentieel dat deze worden vastgesteld alvorens een dergelijke blended behandeling wordt gestart.

Voor de verdere ontwikkeling van e-Exercise lage rugpijn is het belangrijk dat toekomstig onderzoek zich richt op het begrijpen van de verschillen in zelfmanagementgedrag tussen individuen en de wijze waarop blended zorg kan worden personaliseert om het zelfmanagementgedrag van individuen positief te beïnvloeden. Het gebruik van kunstmatige intelligentie zou zinvol kunnen zijn om gepersonaliseerde behandelplannen te ontwikkelen op basis van individuele patiëntgegevens. Om de effectiviteit van blended zorginterventies in de toekomst te vergroten, is het belangrijk om zorgvuldig na te denken over de intensiteit en het type training van de betrokken stakeholders. Adequate scholing van stakeholders draagt bij aan het uitvoeren van de behandeling zoals deze bedoeld is. Daarnaast is inzicht nodig in de mate waarin de geschiktheid van patiënten en fysiotherapeuten voor blended zorg, en de verhouding tussen online en face-to-face zorg, de effectiviteit van blended fysiotherapie kunnen beïnvloeden. Tot slot, om passende implementatie strategieën te creëren en implementatie in de dagelijkse fysiotherapiepraktijk te realiseren, moeten de kennis, vaardigheden en attitudes die een fysiotherapeut en fysiotherapiepraktijk hiervoor nodig hebben onderzocht worden.

Concluderend, onze gestratificeerde blended behandeling e-Exercise lage rugpijn kan in vergelijking met face-to-face fysiotherapie niet als effectiever of kosteneffectiever worden beschouwd. Verdere ontwikkeling van e-Exercise lage rugpijn wordt aanbevolen alvorens implementatie in de dagelijkse fysiotherapiepraktijk als aanvulling op face-to-face fysiotherapie overwogen kan worden.

DANKWOORD

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"*Hora est!*", oftewel "*de tijd is verstreken!*" Het schrijven van dit dankwoord is de bekroning van mijn ontwikkeltraject van de afgelopen vijf jaar welke samengevat is in dit proefschrift.

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Terugkijkend op mijn persoonlijke ontwikkeltraject van de afgelopen jaren herinner ik mij hoogtepunten, maar zeker ook uitdagingen. Ik ben trots op het behalen van mijn opleiding tot epidemioloog. De kennis, inzichten en vaardigheden die ik bij deze opleiding verworven heb, hebben me laten groeien als academicus en hebben zonder meer bijgedragen aan de kwaliteit van mijn proefschrift. Ik heb geleerd dat ik de vaardigheden bezit om een complex (onderzoeks)project van start tot finish vorm te geven, te managen in al zijn facetten en de perspectieven van betrokken stakeholders mee te nemen. Al was het soms ook een uitdaging om alle stakeholders betrokken te houden en de inclusie van participanten te blijven stimuleren. Bijzonder genoeg heeft de COVID-19 periode mij geholpen om een betere werk/privé balans te vinden, om focus aan te brengen in mijn taken als promovendus en om de ruimte te vinden om te groeien in het wetenschappelijk schrijven.

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CURRICULUM VITAE

Tjarco Koppenaal was born on December 21, 1981, in Groningen, the Netherlands. After graduating from secondary school (VWO) in 2000, he studied abroad for a year at Orange Coast Junior College, Costa Mesa, USA, to participate in swimming and study Physical Education. After his return to the Netherlands in 2001, he continued his swimming career at PSV Eindhoven and obtained a propaedeutic exam in Health Sciences at Maastricht University. In 2006, he obtained his Bachelor's degree in Physiotherapy from Fontys Allied Health Professions in Eindhoven. After graduation, he started working as a primary care physiotherapist focused on musculoskeletal complaints at Stichting Gezondheidscentra Eindhoven. Additionally, he started studying Clinical Health Sciences, Physiotherapy Science, at Utrecht University.

After obtaining a Master of Science degree in 2011, he started working as a physiotherapy lecturer at Fontys Allied Health Professions, where he occupied various roles. Unfortunately, in 2012, his activities in primary care physiotherapy ended since they could no longer be combined with his activities at Fontys Allied Health Professions. In 2017, he started his doctoral study, 'e-Exercise Low Back Pain – Stratified blended physiotherapy for patients with nonspecific low back pain,' at University Medical Center Utrecht, which resulted in the present thesis. From 2018 to 2021, he combined his PhD project with participation in a Master of Science programme in Epidemiology.

Currently, Tjarco is the program coordinator for the premaster program in Clinical Health Sciences at Utrecht University/University Medical Center Utrecht. In addition, he continues to work as a lecturer and researcher in the "Bachelor programme Health" at Fontys Allied Health Professions.

PERSONAL & SCIENTIFIC DEVELOPMENT

Personal development

Reflecting on my personal development over the past few years, I remember highlights, but certainly also challenges. I am proud of completing my training as an epidemiologist. The knowledge, insights and skills I acquired in this training have allowed me to grow as an academic and have undoubtedly contributed to the quality of my dissertation. I learned that I possess the skills to shape a complex (research) project from start to finish, manage it in all its facets and take into account the perspectives of involved stakeholders. Although at times it was also a challenge to keep all stakeholders involved and continue to encourage participant inclusion. Extraordinarily, the COVID-19 pandemic helped me find a better work-life balance, helped me to focus on my tasks as a PhD student and helped me to find time to develop my scientific writing skills.

On the other hand, the past few years have also taught me that you do a PhD trajectory mainly for yourself and not to get validation from others. Affinity with the content is an important requirement for me to be successful. This PhD trajectory has taught me to trust myself and get the confirmation from within myself. This confidence in my own abilities facilitates every step of the project and helps me to think in terms of possibilities. I realised that it is essential to "*try*" and (dare) to "*make mistakes*" to keep developing as a person and as an academic. In hindsight, I can say that I would not have wanted to miss this valuable personal development! I have grown as a person and as a professional, and I will take these experiences with me into my future career in which I would love to contribute to the sustainable development of tomorrow's healthcare!

Scientific development

This PhD trajectory has given me the opportunity to discover the role digital technology can play in the development of current and future healthcare. I have learned that the possibilities of digital technology are endless and developments are happening at lightning speed. In my opinion, it is essential that the use of digital technology within healthcare innovations should remain a means and not an end in itself. My PhD trajectory helped me to realize that human-centred design is essential for powerful and sustainable healthcare innovation. By focussing on the human problem, properly examining how the individual can be facilitated in self-management skills, and above all, by developing the innovation in close collaboration with the end users, it is possible to innovate care sustainably. This approach ensures that healthcare innovations are created that fit both the end users and the specific context in which the healthcare innovation needs to be embedded. Digital technology can be of benefit to support end users.

PHD PORTFOLIO

Name of PhD student:	J.T. (Tjarco) Koppenaal
PhD period:	November 1st, 2017 – February 6th, 2023
Name of PhD Supervisors:	C.J.J. (Corelien) Kloek M.F. (Martijn) Pisters R.W.J.G. (Raymond) Ostelo C. (Cindy) Veenhof

PhD Portfolio	Year	Work-load (ECTS)
General courses		
- Academic Writing	2017	2
- Basic course on Regulation and Organization for Clinical Investigators (BROK)	2018	1
- Introduction course PhD program Clinical and Experimental Neuroscience	2018	0.5
- EpidM: Medische Basiskennis	2019	8
- Clinical and Experimental Neurosciene Summerschool	2021	1.6
- Braincenter X-talk	2020-2021	1
PhD training		
- EpidM: Epidemiological research: design and interpretation	2018	4
- EpidM: Principles of epidemiological data-analysis	2018	3
- EpidM: Regression techniques	2019	5
- EpidM: Epidemiology in practice: how to design a study	2019	4
- EpidM: Economic evaluation	2019	2
- EpidM: Longitudinal data analysis	2019	2
- EpidM: Clinimetrics: assessing measurement properties of health measurement instruments	2020	3
- EpidM: Methodological advice	2020	3
- EpidM: Multilevel analysis	2020	2
- EpidM: Clinical Prediction Models	2020	2
- EpidM: Research internship	2021	30
Conferences and presentations		
- 6th Business Community Beweegzorgondernemers (Utrecht, 12 Jun '18) – Oral presentation	2018	0.1
- Meet the Expert Physiotherapy Sciences (Utrecht, 14 Jun '18) – Oral presentation	2018	0.1
- Dag van de Fysiotherapeut (Den Bosch, 08 Dec '18) – Workshop	2018	0.3

PhD Portfolio continued	Year	Work-load (ECTS)
Conferences and presentations		
- World Physiotherapy Congress (Geneva, 10-13 May '19)	2019	0.9
- FysioXperience (Eindhoven, 14 Jun '19) – Workshop	2019	0.9
- Dag van de Fysiotherapeut (Den Bosch, 16 Nov '19)	2019	0.3
- World Physiotherapy Congress (Online, 9-11 Apr '21) – Oral presentation & Poster	2021	0.9
- Seminar Physiotherapy Sciences (Online, 10 May '21) – Oral presentation	2021	0.1
- Seminar Exploring Healthy Behaviour Fontys (Online, 18 May '21) – Oral presentation	2021	0.1
- MSH Research meeting at Hogeschool Utrecht (Online, 14 Sep '21) – Oral presentation	2021	0.1
- 17th International Back & Neck Pain Forum (Online, 11-13 Nov '21) – Oral presentation	2021	0.9
- MSH Research meeting at Amsterdam UMC (Online, 25 Nov '21) – Oral presentation	2021	0.1
- Dag van de Fysiotherapeut (Den Bosch, 21 May '21) – Poster	2022	0.3
Teaching		
- Supervising Bachelor students research internship (21 students)	2018-2022	-
- Lecturer Research methodology and thesis, Fontys Allied Health Professions	2018-2022	-
- Supervising Masters students research internship (2 students)	2019-2022	-
- Lecturer Academic skills, Premaster Klinische GezondheidsWetenschappen, Utrecht University	2020-2022	-
- Program Coordinator Premaster Klinische GezondheidsWetenschappen, Utrecht University	2020-2022	-
List of publications		
- Koppenaal T, Linmans J, Knottnerus JA, Spigt M. Pragmatic vs. explanatory: an adaptation of the PRECIS tool helps to judge the applicability of systematic reviews for daily practice. J Clin Epidemiol. 2011 Oct;64(10):1095-101. doi: 10.1016/j.jclinepi.2010.11.020.		
- Linmans JJ, Viechtbauer W, Koppenaal T, Spigt M, Knottnerus JA. Using electronic medical records analysis to investigate the effectiveness of lifestyle programs in real-world primary care is challenging: a case study in diabetes mellitus. J Clin Epidemiol. 2012 Jul;65(7):785-92. doi: 10.1016/j.jclinepi.2012.01.010.		
- Speksnijder CM, Koppenaal T, Knottnerus JA, Spigt M, Staal JB, Terwee CB. Measurement Properties of the Quebec Back Pain Disability Scale in Patients With Nonspecific Low Back Pain: Systematic Review. Phys Ther. 2016 Nov;96(11):1816-1831. doi: 10.2522/ptj.20140478.		

PhD Portfolio continued

List of publications

- Koppenaal T, Arensman RM, van Dongen JM, Ostelo RWJG, Veenhof C, Kloek CJJ, Pisters MF. Effectiveness and cost-effectiveness of stratified blended physiotherapy in patients with non-specific low back pain: study protocol of a cluster randomized controlled trial. BMC Musculoskelet Disord. 2020 Apr 22;21(1):265. doi: 10.1186/s12891-020-3174-z.
- Arensman RM, Geelen RH, Koppenaal T, Veenhof C, Pisters MF. Measuring exercise adherence in patients with low back pain: development, validity, and reliability of the EXercise Adherence Scale (EXAS). Physiother Theory Pract. 2020 Sep 15:1-10. doi: 10.1080/09593985.2020.1818337.
- Koppenaal T, Pisters MF, Kloek CJ, Arensman RM, Ostelo RW, Veenhof C. The 3-Month Effectiveness of a Stratified Blended Physiotherapy Intervention in Patients With Nonspecific Low Back Pain: Cluster Randomized Controlled Trial. J Med Internet Res. 2022 Feb 25;24(2):e31675. doi: 10.2196/31675.
- Arensman R, Kloek C, Pisters M, Koppenaal T, Ostelo R, Veenhof C. Patient Perspectives on Using a Smartphone App to Support Home-Based Exercise During Physical Therapy Treatment: Qualitative Study. JMIR Hum Factors. 2022 Sep 13;9(3):e35316. doi: 10.2196/35316.
- Achten JPJ, Mooren-van der Meer S, Pisters MF, Veenhof C, Koppenaal T, Kloek CJJ. Self-management behaviour after a physiotherapist guided blended self-management intervention in patients with chronic low back pain: A qualitative study. Musculoskelet Sci Pract. 2022 Oct 19;62:102675. doi: 10.1016/j.msksp.2022.102675.
- Koppenaal T, van Dongen JM, Kloek CJJ, Arensman RM, Veenhof C, Pisters MF, Ostelo RWJG. Effectiveness and cost-effectiveness of a stratified blended physiotherapy intervention compared to face-to-face physiotherapy in patients with nonspecific low back pain: a cluster-randomized controlled trial. Submitted to Journal of Medical Internet Research. 2022.
- Koppenaal T, van der Heiden J, Kloek CJJ, Arensman RM, Ostelo RWJG, Veenhof C, Pisters MF. Characteristics and health outcomes associated with activation for self-management in patients with non-specific low back pain: a cross-sectional study. Submitted to Musculoskeletal Science and Practice. 2022.
- Arensman RM, Heymans MW, Kloek CJJ, Ostelo RWJG, Veenhof C, Koppenaal T, Pisters MF. Trajectories of adherence to home-based exercise recommendations among people with low back pain: a longitudinal analysis. Submitted to Physical Therapy & Rehabilitation Journal. 2022.


e-Exercise