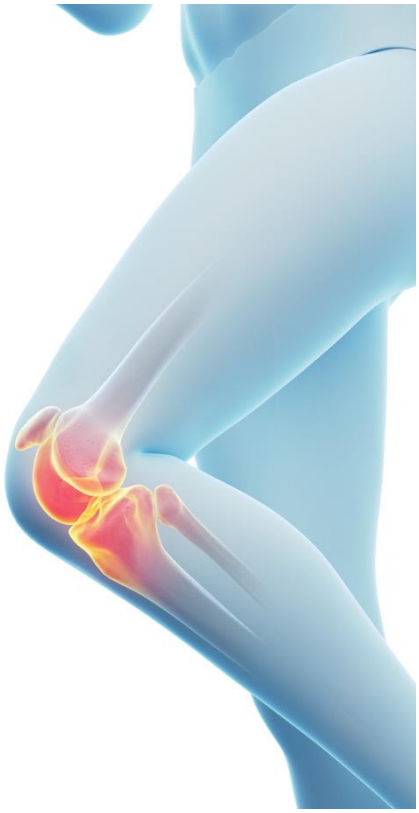
Individual App-guided Exercise Therapy in Patients with Anterior Knee Pain and/or Knee Osteoarthritis

Der Fakultät für Medizin und Gesundheitswissenschaften



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List of Abbreviations

ANCOVA	Analysis of covariance
ADL	Activities of daily life
BfArM	Bundesinstitut für Arzneimittel und Medizinprodukte
CG	Control Group
DRKS	Deutsches Register klinischer Studien
DiGA	Digitale Gesundheitsanwendung
DVG	Digitale Versorgungsgesetz
GDPR	General Data Protection Regulation
IG	Intervention Group
KOOS	Knee Injury and Osteoarthitis Outcome Score
MCS	Mental Component Score
NRS	Numeric Rating Scale
OA	Osteoarthritis
PCS	Physical Component Score
PFPS	Patellofemoral Pain Syndrom
QoL	Quality of Life
RH	Research Hypothesis
ROM	Range of motion
SD	Standard deviation
SF-12	Short Form Health Survey 12
VAS	Visual analog scale

1. Abstract

This study investigated the effects of an app-guided, individually tailored exercise program compared to a conventional paper-based exercise plan for patients with anterior knee pain caused by Patellofemoral Pain Syndrome (PFPS) and knee osteoarthritis (OA). The study included 48 participants, divided into a control group (CG) and an intervention group (IG).

The randomized controlled trial assessed pain levels, knee function, quality of life, adherence to therapy, and time-to-treatment. It also investigated patient acceptance of the digital treatment approach. The study's primary endpoint was to determine if the app-guided exercise therapy results in a difference in pain levels between the IG and CG after eight weeks.

The study initially aimed to include 130 patients but was downscaled due to the COVID-19 pandemic, including 48 patients (26 in IG and 22 in CG). Inclusion criteria include age between 18 and 75, anterior knee pain for at least 2 weeks, and access to a mobile device.

The study found no statistically significant differences in pain, function, and quality of life between the CG and IG, despite both groups showing improvements over the study's duration. This suggests that while both exercise programs had positive effects and that the app-based approach did not lead to significantly better outcomes.

The IG demonstrated a higher adherence to the exercise therapy compared to the CG. This indicates that the app may offer a more convenient and accessible method for patients to engage in exercise therapy. However, the increased adherence did not translate into significantly better outcomes in this study. Patients in the IG reported a positive experience with the Herodikos® app, indicating its acceptance as a valuable supplement to conventional therapy. This suggests that patients are open to using digital tools for their treatment.

The study had several limitations, including a small sample size, potential biases due to the lack of blinding, and challenges in recruitment due to external factors like the COVID-19 pandemic.

To build on these findings, the study recommends conducting research with larger sample sizes, longer follow-up periods, and the inclusion of placebo-controlled arms. Additionally, exploring the impact of patients' digital literacy and technology acceptance on app-based interventions could inform the design of future digital solutions.

In conclusion, while this study provided valuable insights into the potential benefits of app-guided exercise programs for patients with anterior knee pain, further research is needed to fully understand the impact of digital interventions on pain, function, and quality of life in this population.

2. Zusammenfassung

Diese Studie untersuchte die Auswirkungen eines App-basierten, individuell zugeschnittenen Übungsprogramms im Vergleich zu einem konventionellen, papierbasierten Übungsplan für Patienten mit vorderem Knieschmerz, die durch das Patellofemorale Schmerzsyndrom (PFPS) und Kniearthrose (OA) verursacht werden. Die Studie umfasste 48 Teilnehmer, die in eine Kontrollgruppe (CG) und eine Interventionsgruppe (IG) unterteilt waren.

In der randomisierten, kontrollierten Studie wurden die Schmerzwerte, die Kniefunktion, die Lebensqualität, die Therapietreue und die Zeit bis zum Behandlungsbeginn analysiert. Außerdem wurde die Akzeptanz des digitalen Behandlungsansatzes durch die Patienten untersucht. Der primäre Endpunkt der Studie bestand darin, festzustellen, ob die App-geführte Bewegungstherapie nach acht Wochen zu einem Unterschied in den Schmerzwerten zwischen IG und CG führt.

Ursprünglich sollten 130 Patienten rekrutiert werden, doch aufgrund der Corona-Pandemie wurden nur 48 Patienten (26 in IG und 22 in CG) in die Studie aufgenommen. Zu den Einschlusskriterien gehörten ein Alter zwischen 18 und 75 Jahren, vorderer Knieschmerz seit mindestens zwei Wochen und Zugang zu einem mobilen Gerät.

Die Studie ergab keine statistisch signifikanten Unterschiede in Bezug auf Schmerzen, Funktion und Lebensqualität zwischen CG und IG, obwohl beide Gruppen während der Studiendauer Verbesserungen aufwiesen. Dies deutet darauf hin, dass zwar beide Übungsprogramme positive Auswirkungen hatten, der App-basierte Ansatz jedoch nicht zu signifikant besseren Ergebnissen führte. Die IG zeigte im Vergleich zur CG eine höhere Therapietreue. Dies lässt schließen, dass die App für die Patienten eine bequemere und leichter zugängliche Methode zur Teilnahme an der Bewegungstherapie darstellen könnte. Die höhere Therapietreue schlug sich in dieser Studie jedoch nicht in signifikant besseren Behandlungsergebnissen nieder.

Die Patienten der IG berichteten über positive Erfahrungen mit der Herodikos® -App, was darauf hindeutet, dass sie als wertvolle Ergänzung zur herkömmlichen Therapie akzeptiert wird und dass die Patienten der Nutzung digitaler Hilfsmittel für ihre Behandlung offen gegenüberstehen.

Die Studie wies mehrere Limitationen auf, darunter eine geringe Stichprobengröße, potenzielle Verzerrungen aufgrund der fehlenden Verblindung und Schwierigkeiten bei der Rekrutierung aufgrund externer Faktoren wie der Corona-Pandemie.

Um auf diesen Ergebnissen aufzubauen, empfiehlt die Studie die Durchführung von Untersuchungen mit größeren Stichproben, längeren Nachbeobachtungszeiträumen und die Einbeziehung von Placebo-kontrollierten Armen. Darüber hinaus könnte die Untersuchung der Auswirkungen der digitalen

Kompetenz und der Technologieakzeptanz der Patienten auf App-basierte Interventionen Aufschluss über die Gestaltung künftiger digitaler Lösungen geben.

Zusammenfassend lässt sich sagen, dass diese Studie zwar wertvolle Einblicke in den potenziellen Nutzen von App-geführten Übungsprogrammen für Patienten mit vorderen Knieschmerzen lieferte, jedoch weitere Forschung erforderlich ist, um die Auswirkungen digitaler Interventionen auf Schmerzen, Funktion und Lebensqualität in dieser Bevölkerungsgruppe vollständig zu verstehen.

3. Introduction

3.1. Background

Patellofemoral Pain Syndrome (PFPS) is an umbrella term used to describe non-specific anterior knee pain resulting from mechanical dysfunction between the patella and the femur (Saltychev et al. 2018). It is the most common source of anterior knee pain among physically active individuals. Patients often complain about retropatellar (i.e. behind the kneecap) or peripatellar (i.e. around the kneecap) pain, especially while loading the knee, for example, in jumping, climbing /descending stairs or hills, squatting, and running. While there is some debate as to what exactly causes the pain in PFPS, a variety of factors have been implicated to be risk factors for developing PFPS. Amongst these patellar maltracking, foot overpronation, lower quarter muscular weaknesses, and muscular inflexibilities are frequently reported (Pappas and Wong-Tom 2012; Waryasz and McDermott 2008). The optimal management strategy would include finding the individual underlying factors and addressing them directly with an individually tailored therapy program (Barton et al. 2015).

However, currently therapy tends to be very heterogenous. In most cases the underlying causes are not evaluated, and therapy is rather chosen according to the symptoms. It includes the prescription of pain medication, rest, physio therapy, taping (Logan et al. 2017), and in some cases the prescription of knee orthoses (straps, braces) which are supposed to lift the patella mechanically (Smith et al. 2015) .

Another common disorder that regularly causes knee pain – especially in individuals aged 60+ years – is knee osteoarthritis (OA). In general, OA is a progressive degenerative joint disorder, which's pathogenesis is multifactorial. Risk factors for the development of OA include genetic predisposition, obesity, trauma, and high workload due to unfavorable lifestyle conditions to mention a few (REF). These factors can lead to cartilage extracellular matrix changes, subsequently leading to loss of cartilage (Stöve, Steubesand 2018). Finally, the entire joint including the subchondral bone, synovial tissue and periarticular structures such as muscles, ligaments and tendons are affected (Primorac et al. 2020). The knee is one of the most frequently affected joints (Vina and Kwoh 2018) with a reported prevalence of about 20% amongst 18-79-year-olds (Scheidt-Nave et al. 2012).

Regarding knee OA management, current guidelines recommend patient education about the disease, adequate medications, and the adoption of joint-preserving behaviors (e.g., weight loss in overweight or obese individuals). In addition, exercising is considered a key element of conservative, non-pharmacological OA management (Stöve, Steubesand 2018). It is thought to be particularly helpful in

reducing pain and maximizing joint mobility, as well as building muscle strength and improving neuromotor control of the affected joint (Fransen et al. 2015).

The effects of exercise therapy are transient and last until 2-6 months after therapy termination. (Fransen et al. 2015). However, such therapeutic management should be tailored to the individual patient's situation and consider the patient-individual anatomical conditions such as leg axis and accompanying pathologies (Vannini et al. 2016) as well as biological, psychological, and social aspects (Pourbordbari et al. 2022).

When it comes to individualizing therapeutic management both basic clinical knee tests such as range of motion (ROM) assessment, capsular-ligamentous stability testing and resistance tests as well as more specific clinical tests can be helpful to qualitatively examine knee malalignment and to select appropriate correctional exercises for the patient (Rabelo and Lucareli 2018). Once the training program has been established, the patient is encouraged to conduct the exercises regularly and precisely (Skou and Roos 2019). To follow a structured approach to the previously mentioned pathway within practical routines, a guiding system for example, provided via smart app may be helpful.

In Germany the Digitale-Versorgung-Gesetz (DVG) was passed in 2019 (Stern et al. 2022). It regulates that "Digitale Gesundheitsanwendungen" (DiGAs) can be prescribed by physicians and psychotherapists. DiGAs are software-based tools or apps designed to support healthcare professionals and patients in the management of health and wellness. DiGAs have the potential to enhance patient engagement, promote preventive care, and facilitate more efficient and personalized healthcare delivery (Stern et al. 2022). Since 2019, 46 DiGAs have been added to the official register published by the Bundesinstitut für Arzneimittel und Medizinprodukte (BFARM). Three of them are addressing knee pain: Mawendo® (addressing patella disorders), re.flex® (addressing knee OA) and companion patella powered by medi® (addressing patella disorders and tendinitis of the patellar tendon). All of them are licensed temporally, since no evidence for their effectiveness has yet been published (BFARM 2023).

Another app licensed as medical app for the management of musculoskeletal disorder-related knee pain is the Herodikos® app. The Herodikos® app is an innovative measure to guide the medical professional through both a structured diagnostic process and the subsequent design of specifically tailored exercise programs. However, whether an individual exercise program guided via the Herodikos® app is as efficient or may be even superior to a standardized exercise program in the same patient population has yet to be evaluated.

Therefore, this study aims to evaluate the possible benefits of individual exercise presented on a digital app and a standard training regimen presented on paper considering patients' pain levels, quality of life and subjective knee function. Another focus was laid on adherence and time-to-treatment. This part of the study is referred to as outcome evaluation, whereas in the other part of the study – the process evaluation, we aimed to find out, whether the intervention is given a favorable reception by the patients.

4. Methods

4.1. Research Questions and Hypotheses

First, this study asks about the effect of exercise therapy on PFPS and OA patients' anterior knee pain levels in the short-term.

We chose a duration of 8 weeks for the intervention based on current research. For knee OA exercise significantly reduces pain and improves function, performance as compared with usual care at 8 weeks. The effects are maximally around 2 months and thereafter slowly diminish (Goh et al. 2019). For PFPS, 4 studies included in a review also showed significant effects at 8 weeks (Saltychev et al. 2018).

However, no study to date has examined the influence of using the Herodikos® app versus an exercise program delivered via a paper-based leaflet.

Several publications examined the effectiveness of exercise therapy in general, though. systematic review indicates that technology-based exercise interventions have good adherence.

Baldon et al. (2014) found positive effects on pain for PFPS while Goh et al (2019) found positive effects on pain for knee OA. Similarly, Smittenaar et al. (2017) and van der Heijden et al. (2015) found improved functional levels after exercising across various timespans. Brosseau found positive effects on quality of life in a review on 26 similar interventions (Brosseau et al. 2017). Other studies examined the effectiveness of digitally guided exercise therapy. Schäfer describes a positive effect on pain, function and QoL for a eHealth supported exercise interventions (Schäfer et al. 2018).

Therefore, our first hypothesis suggests that the IG will show significantly greater improvements following the individually tailored exercise protocol regarding the self-reported clinical outcomes pain, function and QoL after 2,4, and 8 weeks compared to the CG.

In general, in exercise therapy, adherence is a key to success (Garber et al. 2011). A systematic review indicates that technology-based exercise interventions have high adherence, which means that they conduct 91% of the scheduled workouts over the course of 4-12 weeks (Valenzuela et al. 2018).

Another study found out that digital interventions which offer content covering different modalities and feature direct interaction between user and developer tend to reach higher adherence rates (Kernebeck et al. 2021).

To cover these items, the Herodikos® app features individualized push messages to remind the patient to exercise. Users can contact the developers within the app. Furthermore, the content includes mobility and strength training, mental health components and additional informational sections.

That is why we suggest that the intervention group performs more workouts and keeps on working out longer than the control group (Research Hypothesis 4; RH4).

Bossen et al. (2013) and Kernebeck et al. (2021) found out that usability and multimodal content in digital health products affect the acceptance and adherence positively. To evaluate these factors for the Herodikos® app, we designed a questionnaire which asks about the subjective contentment with the app addressing usability, design, and medical content. We expected the patients to accept the intervention, which means that at least 6 of the 8 questions in the questionnaire are answered positively (Research Hypothesis 5; RH5).

4.2. Research Design and Setting

This pilot study incorporated a randomized controlled trial in a cohort of adult patients diagnosed with anterior knee pain due to PFPS or OA. The study was conducted between May 2021 and October 2022 at a University Hospital for Orthopedics and Trauma Surgery's outpatient clinic, a privately owned general practitioner's outpatient clinic, and an outpatient physical therapy clinic in north-western Germany.

The patient flow over the course of eight weeks is sketched in Figure 1.

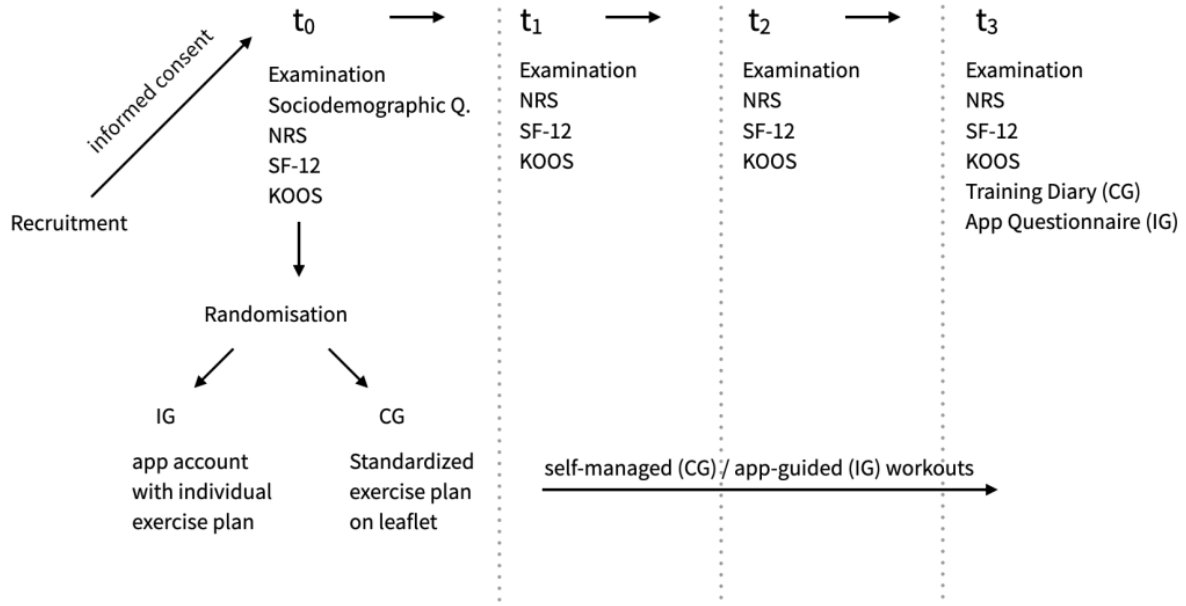

Figure 1: Patient flow during the study

t0 = baseline measurements, t1 = measurements after 2 weeks, t2 = measurements after 4 weeks, t3= measurements after 8 weeks, NRS= Numeric rating scale SF-12= Short-Form 12.

4.3. Sampling and subjects

4.3.1. Sample size

An a priori sample size calculation was performed based on data from a similar study conducted by Baldon et al. (2014). They compared the effects of functional stabilization training vs. standard training

(quadriceps strengthening) in a cohort of patients with PFPS. These authors reported an effect size of -21.0 points reflecting the raw mean difference between the change in pain levels in an intervention versus a control group assessed with a 100-cm visual analog scale (VAS) (Baldon et al. 2014). Previous research established the minimal differences pain scale measures should achieve for patients to experience a clinical benefit. This so-called minimal clinically significant difference is a change of 20 points on a VAS and 2 points on a numeric rating scale (NRS), respectively. Based on these findings, the current study's primary endpoint was a minimum 20-point difference in pain levels between the intervention and the control group eight weeks after using the Herodikos® app. Based on this 20-point group difference, a Mann-Whitney-U-Test, a desired power of 90%, and alpha .05, a total sample of 108 subjects was needed to find significance regarding the effect of app-guided exercise therapy. Taking a drop-out rate of 20% into account, we planned to include 130 patients (65 per group) in the study.

However, during the current study, the Covid -19 pandemic hit, and recruitment was limited due to official measures and restrictions affecting outpatient health care. Research shows, that especially small research projects – such as the current one – were impacted profoundly during the Covid-19 pandemic (Bansal et al. 2022). Approximately 18 months into the trial, it became clear that it would be impossible to enroll the number of subjects identified in our a priori sample size calculation within a reasonable period. However, in order not to simply abandon the study but at least to make use of the data from all the patients who had already invested their time and effort in the study, it was decided to reduce the evaluation to an exploratory pilot RCT involving all 48 participants who were at that time enrolled in either IG (n=26) or CG (n=22).

4.3.2. Inclusion and exclusion criteria

To participate in the current study, subjects had to fulfill the following criteria: (1) age between 18 to 75 years; (2) presence of anterior knee pain and/or painful knee OA for at least 2 weeks and up to 6 months before enrollment; (3) anterior knee pain level of at least NRS 4/10 at the time of recruitment; (4) having unlimited access to a mobile device (smartphone, tablet, etc.); (4) have basic knowledge about how to use a web app. The following criteria precluded subject study enrollment: (1) Inability to sufficiently understand, read, and/or write German; (2) lower limb surgery on the affected side during the past 12 months.

4.3.3. Recruitment

Eligible patients were recruited between May 2021 and October 2022 at a University Hospital for Orthopedics and Trauma Surgery's outpatient clinic, a privately owned general practitioner's

outpatient clinic, and an outpatient physical therapy clinic in Germany. Due to the measures implemented to combat the Covid 19 pandemic which were active until May 2023, recruitment proved to be much more challenging than anticipated. Lockdowns and additional hygienic measurements limited the availability of examination rooms in the outpatient centers. Therefore, it was less convenient for subjects to participate since available appointments were limited and there was an evident risk of catching an infection. Some patients who were interested in enrolling cancelled because they were tested positive with Covid 19. Oftentimes it was impossible to encourage them to reconsider participation afterwards.

Consequently, various steps were taken to inform potentially eligible patients about the study beyond the recruiting institutions and encourage their participation. These measures comprised of newspaper articles in the local press, presentation of the study in local running clubs, attachments in the sports department of the University of Oldenburg, as well as in local fitness centers, outpatient physiotherapy clinics, and medical practices.

4.4. Variables and evaluation measures

To address the study aims and hypotheses participants had to fill in a questionnaire at the beginning of the intervention (T0) as well as 2 weeks (t1), 4 weeks (t2) and eight weeks (t3 after the beginning of the intervention. The questionnaire included a self-designed socioeconomic questionnaire, a self-designed pain questionnaire, the Knee Osteoarthritis Outcome Scale (KOOS) and the Short Form-12 (SF-12).

The socioeconomic questionnaire was designed by the investigator and included questions addressing age, sex, living situation, education, and activity level as well as questions addressing the current knee pain (side of the leg and duration of pain). The information was used to evaluate correlations.

The Pain Questionnaire contained five questions regarding subjects' pain levels. Subjects were asked to indicate their pain levels on a numeric rating scale (NRS) ranging from 0 (= no pain) to 10 (= worst imaginable pain). The first question asked about subjects' current level of knee pain. While the second question centered around the worst pain subjects experienced within the last two weeks, the third question asked to indicate the least pain experienced within the last two weeks. The fourth questions evaluated subjects' pain frequency. Finally, question 5a-g asked for details in terms of specific situations or movements that exacerbate their knee pain. The NRS is a simple and efficient method for individuals to express the intensity of their knee pain (Alghadir et al. 2018). It showed the most sensitivity and stability compared to Visual Analogue Scale, Face-Pain Scale and Verbal Rating Scale (Euasobhon et al. 2022).

The KOOS is a disease-specific tool consisting of 5 different subscales: (1) Pain; (2) Symptoms; (3) ADL; (4) KOOS Sport/Recreation, (5) Quality of life (QoL) (Roos and Lohmander 2003).
Scoring is done on a 5-point Likert scale ranging from 0-4, with higher numbers indicating greater difficulty. For each subscale, a normalized score is calculated on a 0-100 scale, with zero representing extreme knee symptoms and 100 representing no knee symptoms (Collins et al. 2016). The KOOS in general has been shown to have good psychometric properties (Collins et al. 2016). It has been translated into German and showed good reliability and validity (Neuhaus et al. 2023).
Patients' health-related QoL was evaluated via the generic SF-12® Health Survey (SF-12) (Ware, Kosinski, & Keller, 1996). The SF-12 consists of a subset of 12 items from the SF-36® Health Survey (SF-36) (Ware & Sherbourne, 1992; Ware, Snow, Kosinski, & Gandek, 1993). It is divided into eight domains namely Physical Function, Physical Role Function, Physical Pain, General Health Perception, Vitality, Social Function, Emotional Role Function, and Mental/Psychological Health (Turner-Bowker and Hogue 2014). The eight subscales are grouped into two summary measures: The Physical Component Summary (PCS) and the Mental Component Summary (MCS).
The PCS score reflects the person's physical health status, while the MCS score reflects their mental health status. To process the SF-12, we used the standard scoring algorithm provided by the company which owns the copyright of the survey (Hogrefe). This algorithm takes into account the weighted responses to the 12 items and calculates the two summary scores, which are then normalized to have a mean of 50 and a standard deviation of 10 in the general population (Stieglitz 1999).
The SF-12 has been shown to have good psychometric properties (Gandhi et al. 2001). The German version of the SF-12 has been shown to reflect core components of health-related QoL "within a biopsychosocial framework aiming at predicting satisfaction with life"(Drixler et al. 2020).

Additionally, at t3 the IG was given a questionnaire which covered the usability, interface and design of the app used for guidance through the individual exercise program. Patients were asked to score 8 items from 1-10 with 1 = not at all up to 10 = I totally agree. The questionnaire was designed by the investigator and consists of eight questions. The design of the questions is based on the Net Promoter Score. The Net Promoter Score is a widely used metric in the business world to gauge customer satisfaction. The NPS survey typically consists of a single question: "On a scale of 0 to 10, how likely are you to recommend the product to a friend or colleague?" Based on their responses, subjects are segmented into three categories:
1. Promoters (score 9-10): These are highly satisfied customers who are likely to promote the product.

2. Passives (score 7-8): These customers are satisfied but not enthusiastic enough to actively promote the product.
3. Detractors (score 0-6): Detractors are unsatisfied customers who may voice their negative experiences (Farris et al. 2017).

All questionnaires handed out to the subjects can be found in Appendix

4.5. The App

A project team attached to the Founding and Innovation Center of Carl von Ossietzky University Oldenburg has developed the Herodikos® app. The team was financed by the European Union`s Exist grant and specially designed the app to fulfill the studies requirements. The investigator was part of that project team.

The Herodikos® app consists of two apps – one for the consultant, and a basic one for the patient. The app serves as information and administration tool for the consultant who provides the individual exercise plans. The app guides the consultant through a movement analysis by offering possible items in form of a questionnaire. The results are saved and linked to the 9-digit patient code.

The patient's app version allows to open their individual exercise plan after entering the 9-digit-code and guides through the workouts with videos and audio-commentaries. Furthermore, it offers a graphic presentation of the exercise's goals and progress.

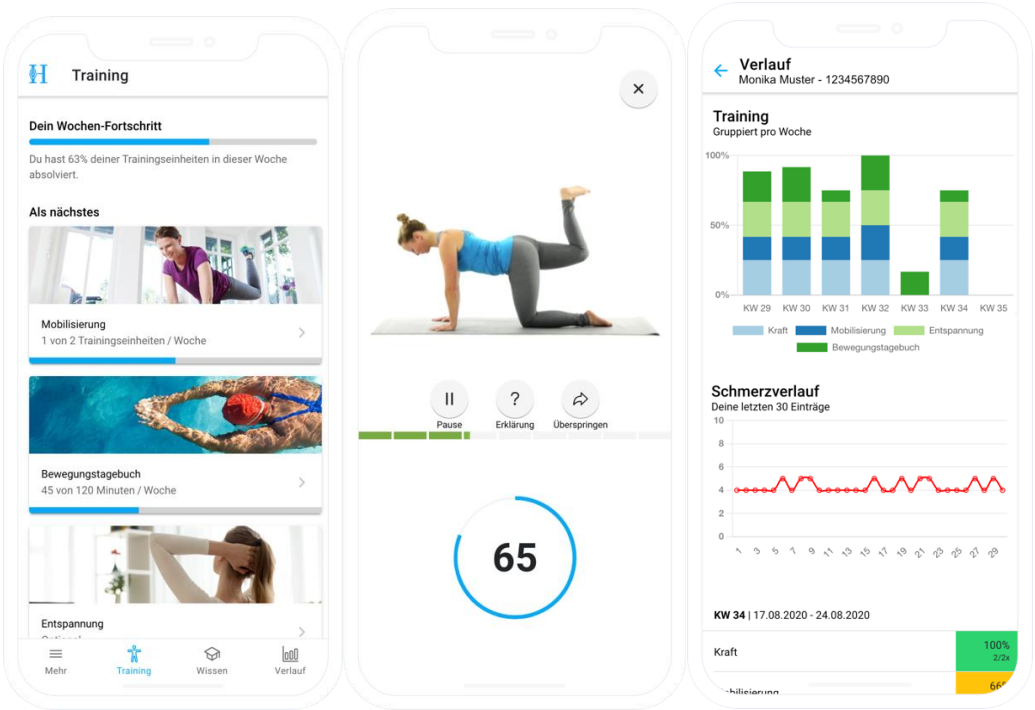

Figure 2: Screenshots of the Herodikos® patient app

The app is a certified class 1 Medical Device. The app provider Herodikos GmbH follows all guidelines in the General Data Protection Regulation (GDPR, German: DSGVO). It does not save any personal data except that every user must register with an E-Mail address and password. The process must be executed in that way to ensure the conformity with the GDPR. The GDPR demands that user accounts must be deleted if the user wants to. To link the user to the 9-digit code and offer an opt-out option, it is inevitable to save the E-Mail address.

4.6. Measurement procedures

All patient appointments were conducted by the primary investigator (i.e. the doctoral candidate ES). The first visit, the recruitment visit (baseline, t0), took place in the above-mentioned participating health-care facilities. Patients that matched the inclusion criteria - confirmed by their consultant – were introduced to the study, given the information letter and signed the written informed consent form (Appendix B). Following, subjects received the questionnaire and were asked to fill these in. Next, patients were examined by the responsible investigator following a standardized examination process. All examination results were documented on the standardized knee examination sheet of the Berufsgenossenschaft ("Ergänzungsbericht Knie", Appendix B). Following the examination, patients were randomized into either the IG or the CG. The randomization process was done electronically and by a third investigator (GHS) who was not aware of the respective patient's examination results. Patients who have been randomized into the CG then received a leaflet with a standard exercise program for 6 weeks. Each exercise was explained and showed to the patient. Moreover, the patient had sufficient time to practice each exercise and ask questions. Patients were asked to perform the standard exercise program over a course of 8 weeks and document each training session in the standardized training diary.

Patients who have been randomized into the IG subsequently underwent an additional app-guided functional examination, which consisted of the following seven items illustrated with screenshots from the App.

1. Qualitative knee alignment (Genu varus, neutral or Genu valgus)

The Mikulicz-Line is an imaginary line from the center of the femoral head, through the middle of the knee joint to the center of the ankle. The Mikulicz-Line was marked with a Tape stripe which was attached at the estimated location of the center of the femoral head and stretched to the center of the ankle. If the middle of the knee joint was located laterally of the Mickulicz-Line, it was defined as Genu varus, if it was located medially of the line, it was defined as Genu valgus. Neutral was defined as all three points being on one straight line (Schünke, Schulte, Schumacher, Voll, Wesker 2004).

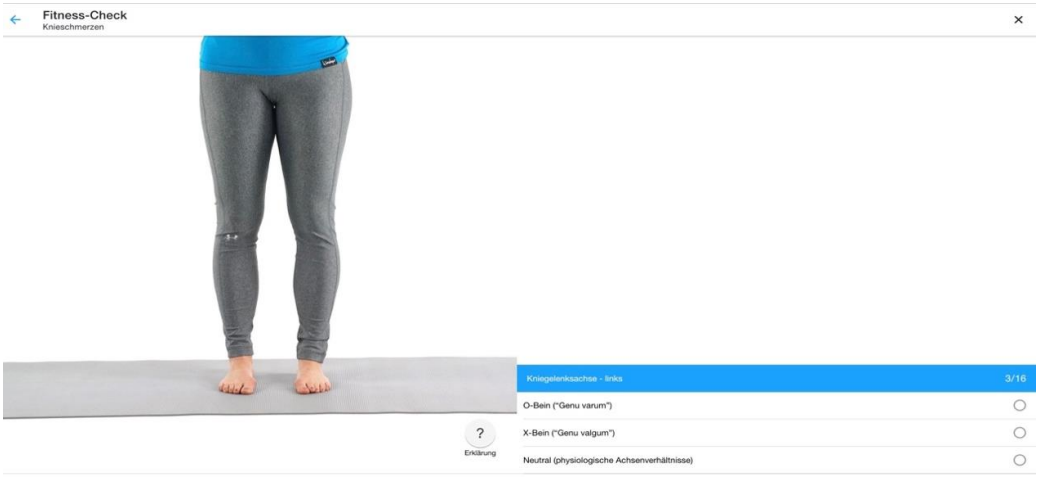

Figure 3: Qualitative knee alignment (Herodikos® Web App).

2. Free one-legged stand (<30 sec., 30-60 sec. or >60 sec.)

The patient was asked to stand on one foot and bend the other leg in 90° in the knee. Both knees were supposed to stay parallel, the arms were allowed to reach out horizontally. The timer integrated in the app was used to keep the time during which the position could be held correctly.

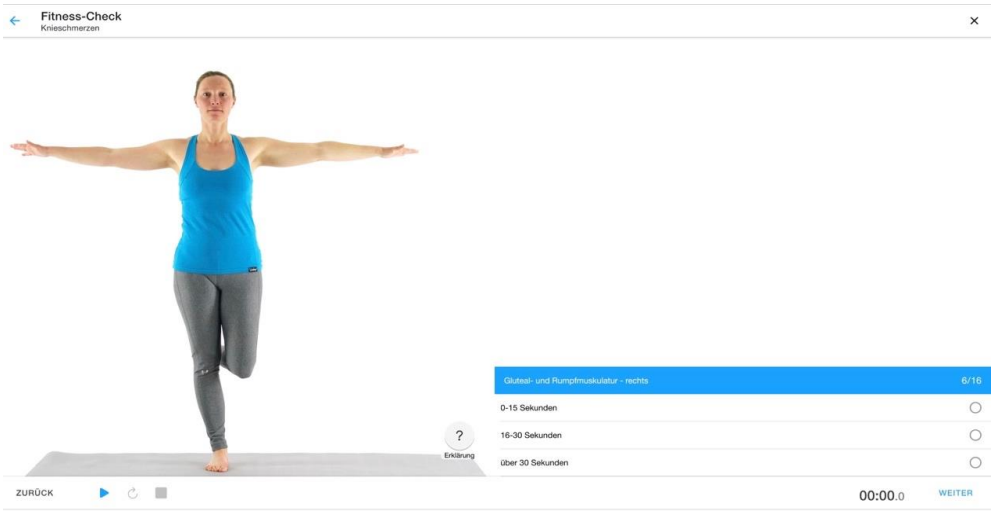

Figure 4: Free one-legged stand (Herodikos® Web App).

3. Thomas-Test on floor for hip flexor mobility (lower limb on the floor, distance between lower limb and floor < 2cm or distance between lower limb and floor >2cm)

The patient was asked to lie flat on the back. If the right leg was to be tested, the patient had to bend the left knee and pull the bent knee as close to the torso as possible. The distance between the mid-thigh of the stretched-out leg and the floor was measured in the end-range position using a commercially available tape measure. The distance was measured three times to calculate the mean.

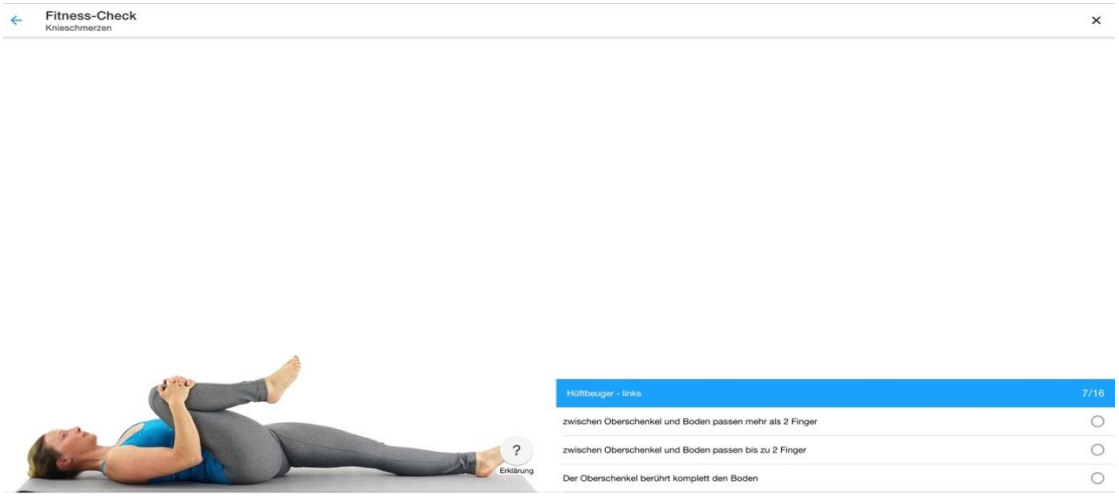

Figure 5: Thomas-Test on floor for hip flexor mobility (Herodikos® Web App).

4. Straight leg raise (angle between ground and leg >90°, 70-90° or <70°)

The supine-lying patient was asked to lift one lower extremity as high as possible with the knee stretched out. The angle between the floor and the leg will were measured using a goniometer. The angle was measured three times and the mean of all three measurements during data analyses.

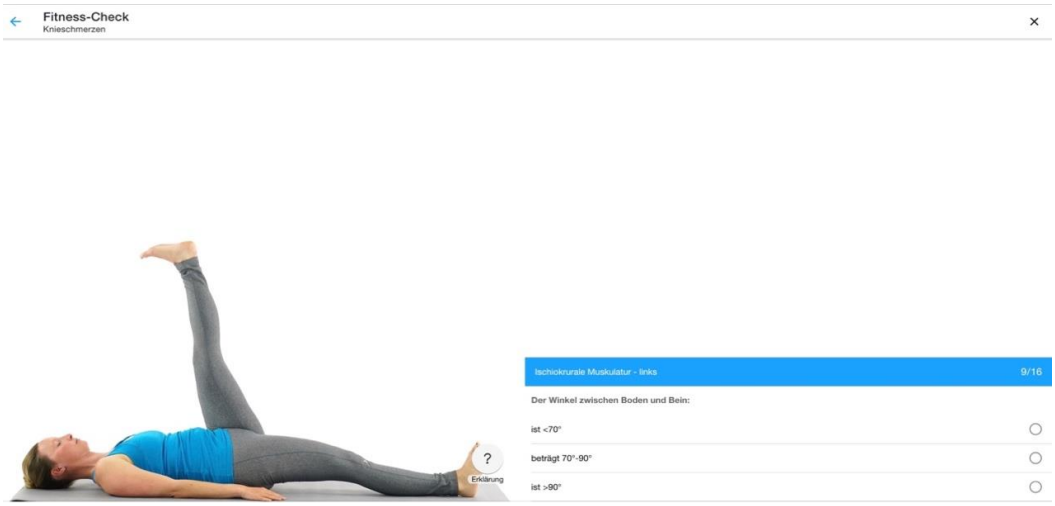

Figure 6: Straight leg raise (Herodikos® Web App).

5. Quadriceps mobility test (heel touches buttock, <5cm distance between heel and buttock or >5cm distance between heel and buttock)

The patient was asked to lie prone and bend the knee of the test-side lower limb. If possible, the hands were allowed to grab the ankle and pull the heel towards the buttock. The investigator then measured the distance between the heel and the buttock with a commercially available tape measure. The distance was measured three times to calculate the mean.

In case there was a movement restriction due to massive tissue at the back of the leg, the test was counted as >5cm distance.

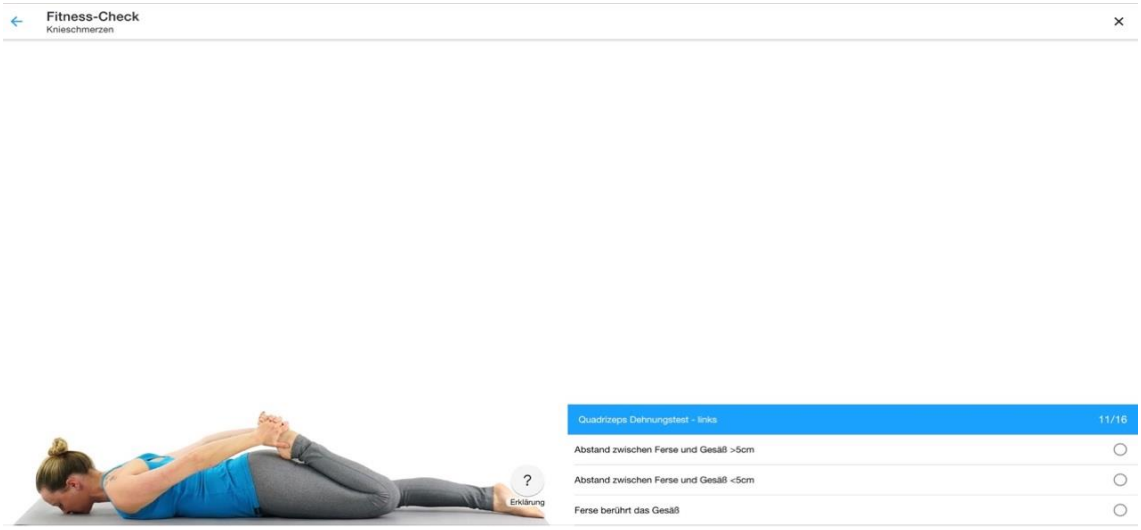

Figure 7: Quadriceps mobility test (Herodikos® Web App).

6. Heel Lift (0-5, 6-10 or >10 repetitions)

The patient was asked to stand on both feet, lift the heels as high as possible and subsequently lower them to the ground without totally touching the ground. It was allowed to put a hand on a wall to keep the balance. The investigator counted the correctly performed repetitions. A repetition was considered incorrect if the ankle didn't stay neutral but drew aside to medial or lateral or if the heel was put on the ground. The patient was allowed to conduct 15 repetitions in total.

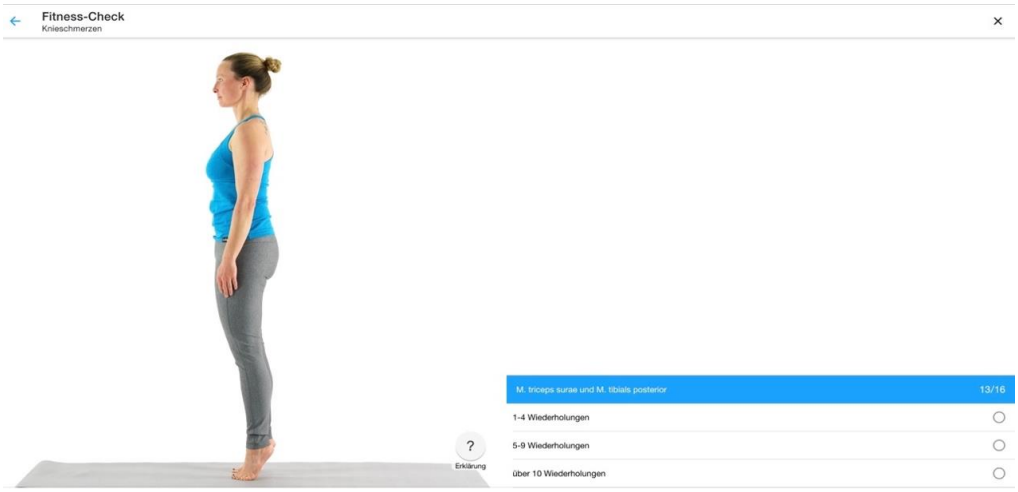

Figure 8: Heel Lift (Herodikos® Web App).

7. Wall Sit (0-15 sec., 16-30 sec. or > 30sec.)

The patient was asked to lean against a wall, feet shoulder width apart and about 30 centimeters from the wall. Then, he or she was instructed to slowly slide the back down the wall until the thighs were parallel to the ground. The feet had to be adjusted so the knees were directly above the ankles (rather

than over the toes). The back had to be flat against the wall. The timer integrated in the app can was used to keep the time during which the position was held correctly.

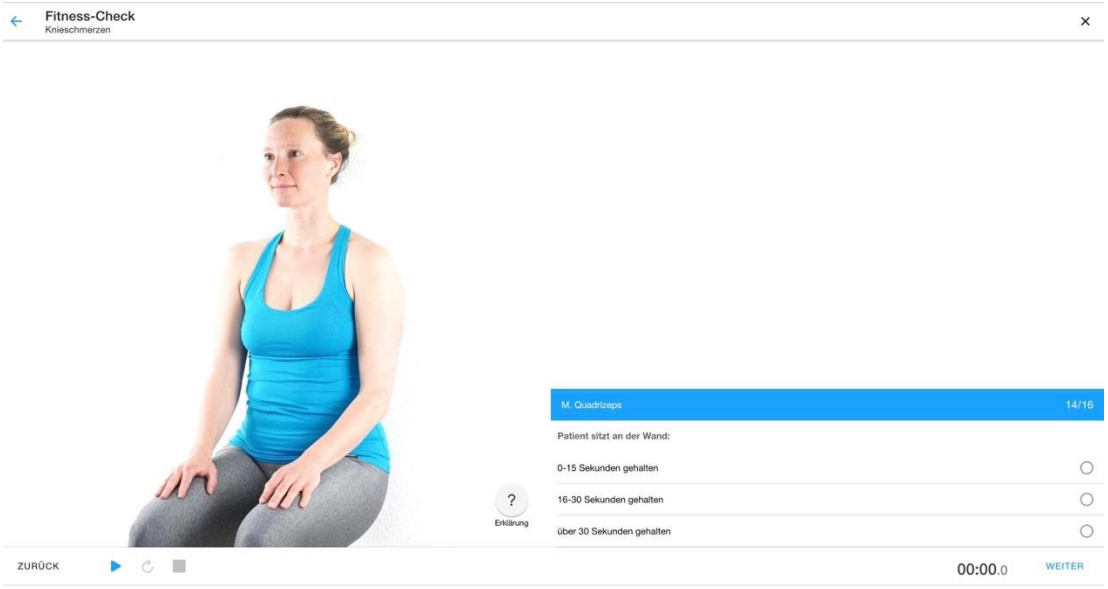

Figure 9: Wall Sit Herodikos® Web App)

This app-guided examination was mandatory to establish the individual exercise programs. Once all mentioned test items were performed, the IG patients received an individual exercise program, based on the test results and tailored by the responsible investigator.

The exercises were provided by the investigator from a pool of evidence-based exercises (please refer to section 4.5 Exercise Therapy for IG/CG for more detailed information). For instance, if the quadriceps strength test (here: wall sit) showed a lack of strength, evidence-based strength exercises for the quadriceps such as squats were integrated into the workout plan. Once the individual training program has been set up, the patient was introduced to the app and explained how to access the exercise plan.

The responsible investigator led the patient through the corrective exercises on paper (CG) or explained the app and the corrective exercises (IG) during the first appointment. After that, patients were asked to independently exercise at home according to the standard or individual workout plan, respectively, over the course of eight weeks.

The exercise regimen of the IG was monitored using the dedicated mobile app, while the CG participants were required to maintain a training diary. The primary objective was to achieve a workout frequency of four times per week – as preset in the standard training protocol by Biesenbach (2014).

The extent to which this goal was met was expressed as a percentage. For instance, if a participant completed the full workout twice a week, they would attain a score of 50%. Similarly, if a patient exercised four times a week but only completed half of the prescribed exercises during each session, their score would also be 50%. That is the designated display mode in the app was chosen by the developers, based on usability and interface experience standards. The data of the CG was adjusted to be comparable.

All patients, CG and IG, returned for follow up measurements after 4 weeks (t2) and 8 weeks (t3). All patients received the same questionnaires during these follow-up appointments and underwent the same examination process. At t1 (after 2 weeks) the patients were asked to answer the same questionnaires as at t2. Additionally, a questionnaire considering the perceived usefulness, usability and design of the app was handed out to the IG at t3 as described previously.

4.7. Exercise therapy for Intervention Group and Control Group

Intervention group

For the IG, the app offered a library of several corrective exercises from which the investigator could choose the exercises correlated to the outcomes of the app guided functional examination. To support the process, the built-in AI-algorithm of the app suggested an exercise plan based on the previous examination's results, which were documented in the app during the examination process. The exercises were distributed in two categories – strength and mobilization. The investigator instructed the subject how to perform the exercises and supervised the first performance.

If the patient was not able perform an exercise correctly, the investigator deleted this exercise and substituted it by an alternative exercise from the same category.

The structure of the exercise therapy was built according to publications of Buitrago et al., Kleinöder and Biesenbach.

The actual training was built like a circle training (Biesenbach 2014). The exercises were lined up one after the other with 40 seconds exercise time (Buitrago et al. 2012) and a 20 second rest period (Kleinöder 2016). The investigator was able to add rounds or sets to the exercise plan. The weekly goal was to conduct the strength and mobilization workout twice each with a total of four weekly workouts, analogous to the workout frequency in the CG (Sebastian Buitrago et al. 2014; Biesenbach 2014).

After the entire plan was set, the app delivered a 9-digit code, which was handed to the patient on a flyer provided by the app company which also included information on how to download and install the app and how to register.

Once registered (registration required a name and an Email address) the patient had to type the code into their own version of the app to access the personalized workout plan. This approach led to different, thus individualized exercise programs for each participant.

We aimed to compare patients with different exercise programs on purpose since it is important to differentiate whether the personalization of corrective exercises is superior to handing out a standard one-exercise-fits-all plan for knee pain in general without considering the different underlying causes (Skou and Roos 2019).

Control group

As previously outlined, CG patients received a standard training protocol on paper and were asked to exercise four times a week at home and to document each session in an exercise diary. The CG exercises were explained and illustrated by photographs on the handout. Exercises could not be replaced or adjusted. All patients in the control group received the same exercises. The standard training protocol was based on the exercise plan for functional exercises for patients with PFPS from Biesenbach (2014). The **training protocol for the CG** can be found in Appendix C.

4.8. Ethical considerations / Ethical vote

The study was conducted in agreement with the World Medical Association Declaration of Helsinki (2013). In accordance with these ethical principles the responsible institutional review board of the School of Medicine, Carl von Ossietzky University Oldenburg was informed about the study and asked for a written approval. The review board declared their consent in March 2021. The corresponding document (Ethikvotum) can be found in Appendix E. All subjects gave their written informed consent for study participation. The study was registered in the German Clinical Trials Register (DRKS) under the registration number DRKS00025309.

5. Data reduction and statistical analysis

Data reduction and analyses were performed using the software packages R (Version 4.2.3, © The R project) and Jamovi (Version 2.3.26, ©The Jamovi Project).
Descriptive statistics reporting the mean, standard deviation, median and range were used to describe sample characteristics (e.g., sex, age, socioeconomic data, duration of knee pain).
Inferential statistics used non-parametric tests for the following reasons. First, several of our datasets violated the assumptions of normality, precluding the use of parametric tests (Gibbons and Chakraborti 2014). By employing non-parametric tests, we mitigated the risk of obtaining misleading conclusions due to distributional mismatches. Second, non-parametric tests are valuable when working with small sample sizes as in the case of the current study.

Several ANCOVAs for the difference between t0 and t3 including the covariate t0 for the SF-12 PCS and SF-12 MCS, the four values of the pain questionnaire, and for all dimensions of the KOOS. The resulting F value was used to test the null hypothesis which states that group means are equal, while controlling for the effects of the covariate. The accompanying Pr refers to the probability value and indicates the probability of observing the results if the null hypothesis were true (Kim et al. 2006). Hence, if the Pr-value was less than the significance level (i.e., .05), this indicated statistical significance meaning there was a significant between-group difference.

For each variable, we conducted a within-group analysis. Therefore, we conducted Friedman-Tests and pairwise comparisons according to the Durbin-Conover method. The Durbin-Conover method employs a stepwise procedure to compare each measurement against all others, calculating a test statistic and p-value for each pairwise comparison (Richardson and Machan 2021).
To compare the IG vs. CG, we looked at all variables and times separately but also at the differences between the measurements. Mann-Whitney-U-tests were conducted. The level of significance was pre-set at α=.05.

6. Results

6.1. Descriptive Statistics

As already mentioned, we were not able to recruit the initially calculated sample size due to reasons associated with the Covid-19 pandemic. It was decided to reduce the evaluation to an exploratory pilot RCT involving all 48 participants who were enrolled at that time. Of these, 22 subjects were randomized into the CG (46%), and 26 (54%) subjects into the IG. Four subjects (all initially randomized to IG) dropped out after the first appointment and one subject (initially randomized to CG) after the second due to personal reasons. Consequently, 21 complete data sets from the CG and 22 complete data sets from the IG were available for the final analysis.

6.1.1. Demographic Descriptive Statistics

Overall, 52% (25 individuals) were identified as male, while 48% (23 individuals) were identified as female. Among the female participants, 14 were randomized into the IG, where three of them dropped out during the study, nine were randomized into the CG. Among the male participants, two dropped out, with one belonging to the IG and the other to the CG. The total amount of male individuals in the IG was 12. The samples (male and female) mean age was 49.8 years (18-75 years).

Regarding the age distribution there were no significant differences between the IG and CG at baseline. Further demographic statistics are displayed in Table 1.

Table 1: Demographic sample description

Variable	Number of patients (%)		
Living situation	CG, n=22	IG, n=26	Overall, n=48
Living alone	8 (36%)	3 (12%)	11 (23%)
Living with partner and children	10 (45%)	11 (42%)	21 (44%)
Living with children	3 (14%)	11 (42%)	14 (29%)
Other	0 (0%)	1 (3.8%)	1 (2%)
Unknown	1 (4%)	0 (0%)	1 (2%)
Education level			
Low	3 (14%)	2 (8%)	5 (11%)
Medium	7 (33%)	10 (38%)	17 (36%)
High	10 (57%)	14 (54%)	24 (50%)
Other	1 (4%)	0 (0%)	1 (2%)
Unknown	1 (4%)	0 (0%)	1 (2%)

IESCD= International Standard Classification of Education (ISCED); IG= Intervention Group; CG= Control Group; Low = IESCD-Level 0-2B; Medium = IESCD-Level 2A; High = IESCD-Level 3A and more

6.1.2. Diagnosis

Almost one third of the entire study population suffered from pain in both knees (34%). Patients with either knee OA or PFPS or both diagnoses were eligible for the study. A history of officially diagnosed and MRI-verified “meniscal pathology” was also documented. The diagnosis PFPS was reported in 21 subjects, while knee OA was present in 16 subjects. Eleven subjects presented with PFPS or OA, respectively in combination with meniscal pathologies (Table 2).

Table 2: Distribution of diagnoses

Diagnosis	CG n=22	IG n=26	Overall n=48
Knee OA	10 (45%)	6 (23%)	16 (33%)
Knee OA + PFPS	1 (4.5%)	3 (11.5%)	4 (8.3%)
Knee OA + PFPS + Meniscal pathology	1 (4.5%)	1 (3.8%)	2 (4.2%)
Knee OA + Meniscal pathology	0 (0%)	1 (3.8%)	1 (2.1%)
PFPS	9 (41%)	12 (46%)	21 (44%)
PFPS + Meniscal pathology	1 (4.5%)	3 (12%)	4 (8.3%)

(PFPS= Patellofemoral Pain Syndrome; OA= Osteoarthritis; IG= Intervention Group; CG= Control Group)

No differences were found between the IG and CG regarding diagnosis at baseline (p≥ .716; Chi-square).

Most patients (34 individuals, 72%) had been experiencing the knee pain for more than three months. Two patients (4.3%) reported acute pain lasting less than two weeks, while six patients (13%) reported pain persisting for two to four weeks. Additionally, five patients (10.6%) reported suffering from their knee pain for more than four weeks but less than three months. No statistically significant differences between the IG and CG were found regarding the distribution of knee pain duration at baseline (p≥ .461, Chi-Square).

6.1.3. Physical Activity

Overall, 67% reported being physically active (58%IG/77%CG), while the remaining 33% indicated they were not physically active (42%IG/23%CG). No statistically significant differences were found between the IG and CG regarding the association between physical activity status and group assignment. (p= .152, Chi-Square).

6.1.4. Duration of knee pain

Participants were asked about the duration from the onset of their knee pain until first being diagnosed by a physician.

Owing to substantial heterogeneity, participants' responses were categorized into four groups.

- Group 1: individuals who were diagnosed <2 weeks after pain onset.

- Group 2: individuals who were diagnosed between 2-6 weeks after pain onset.
- Group 3: individuals who were diagnosed >6 weeks and <12 months after pain onset.
- Group 4: individuals who were diagnosed >12 months after pain onset.

Patient classification regarding the time from pain onset until being diagnosed is shown in Table 3. There were no statistically significant differences between the IG and CG regarding time to treatment ($p \geq .562$, Chi-Square).

Table 3: Distribution of the duration of knee pain

Time to Treatment	Group		
	IG	CG	Overall
Group 1	9	5	14
Group 2	1	3	4
Group 3	6	4	10
Group 4	10	10	20
Overall	26	22	48

Group 1= individuals who were diagnosed <2 weeks after pain onset; Group 2= individuals who were diagnosed between 2-6 weeks after pain onset; Group 3= individuals who were diagnosed >6 weeks and <12 months after pain onset; Group 4= individuals who were diagnosed >12 months after pain

6.2. Within-group and between-groups analyses

6.2.1. Pain

The following aspects of pain were assessed by patient self-report on a NRS ranging from 0 (= no pain) to 10 (= worst imaginable pain) as previously described:

- Current knee pain
- Worst knee pain within the last two weeks
- Least knee pain within the last two weeks
- Frequency of knee pain.

Current pain

Within the IG, the Friedman test revealed statistically significant differences (<.001) for self-reported current pain. Post-hoc pairwise comparisons (Durbin-Conover) revealed that current pain decreased at all time points compared to the previous assessment except for t2 compared to t1. (Table 4).

Table 4: Pairwise comparisons for item “current pain” for IG

Pairwise Comparisons (Durbin-Conover)				
			Statistics	p
Current pain at baseline	vs.	Current Pain after two weeks	4.3	<.001
Current pain at baseline	vs.	Current Pain after four weeks	5.4	<.001
Current pain at baseline	vs.	Current Pain after eight weeks	7.5	< .001
Current Pain after two weeks	vs.	Current Pain after four weeks	1.1	0.276
Current Pain after two weeks	vs.	Current Pain after eight weeks	3.2	0.002
Current Pain after four weeks	vs.	Current Pain after eight weeks	2.1	0.041

Similarly, within the CG, the Friedman test revealed statistically significant differences (p=.047) for self-reported current pain. Post-hoc pairwise comparisons (Durbin-Conover) revealed those differences were located between t0-t2 and t0-t3, indicating that current pain at t2 was lower than at t0 and current pain at t3 was lower than at t0.

Table 5: Pairwise comparisons for item “current pain” for CG

Pairwise Comparisons (Durbin-Conover) Control Group				
			Statistics	p
Current pain at baseline	vs.	Current Pain after two weeks	0.5	0.595
Current pain at baseline	vs.	Current Pain after four weeks	2.3	**0.026**
Current pain at baseline	vs.	Current Pain after eight weeks	2.3	**0.022**
Current Pain after two weeks	vs.	Current Pain after four weeks	1.7	0.085
Current Pain after two weeks	vs.	Current Pain after eight weeks	1.8	0.072
Current Pain after four weeks	vs.	Current Pain after eight weeks	0.1	0.939

Between-group analysis for current pain showed no statistically significant differences between the IG and CG at any time (p>.05; Mann-Whitney-U test). (Table 1; Appendix D)

Worst pain in last two weeks

Within the IG, the Friedman test showed statistically significant differences for self-reported worst pain within the last two weeks (p <.001). Post-hoc pairwise comparisons (Durbin-Conover) revealed these significant differences were located between baseline (t0) and each of the following t1, t2 and t3 (Table 6), indicating that pain decreased between baseline and t1, t2 and t3

Table 6: Pairwise Comparisons for item “worst pain” for the Intervention Group

Pairwise Comparisons (Durbin-Conover)				
			Statistics	p
WP at baseline	-	WP after two weeks	3.55	< .001
WP at baseline	-	WP after four weeks	3.31	0.002
WP at baseline	-	WP after eight weeks	5.13	< .001
WP after two weeks	-	WP after four weeks	0.24	0.814
WP after two weeks	-	WP after eight weeks	1.58	0.120
WP after four weeks	-	WP after eight weeks	1.81	0.075

WP= Worst pain in the last two weeks

Within the CG, the Friedman test revealed no statistically significant differences (p =.118) for self-reported worst pain within the last two weeks at any measurement time point (Table 2; Appendix D). In addition, between-group analyses for self-reported worst pain within the last two weeks showed no statistically significant differences between the IG and CG at any time (p>.05; Mann-Whitney-U test; Table 3; Appendix D).

Least pain in last two weeks

Within the IG, the Friedman test showed statistically significant differences for self-reported least pain in the last two weeks (p = .009). Post-hoc pairwise comparisons (Durbin-Conover) revealed these significant differences were located between baseline (t0) and each of the following t2 and t3 (Table 7).

Table 7 : Pairwise Comparisons for item “least pain” for the Intervention Group

Pairwise Comparisons (Durbin-Conover) Intervention Group				
			Statistics	**p**
LP at baseline	vs.	LP after two weeks	1.36	0.181
LP at baseline	vs.	LP after four weeks	3.16	**0.003**
LP at baseline	vs.	LP after eight weeks	3.07	**0.003**
LP after two weeks	vs.	LP after four weeks	1.81	0.076
LP after two weeks	vs.	LP after eight weeks	1.72	0.092
LP after four weeks	vs.	LP after eight weeks	0.09	0.928

LP = Least pain; Bold = significant p-value

Within the CG, the Friedman test revealed no statistically significant differences (p =.087) for self-reported least pain within the last two weeks (Table 4; Appendix D).

Similarly, between-group analysis for self-reported least pain within the last two weeks showed no statistically significant differences between the IG and CG at any time (p>.05; Mann-Whitney-U test; Table 5; Appendix D).

Pain Frequency

Regarding self-reported pain frequency during the last week before the respective measurement time point, the analysis revealed statistically significant differences within the IG (p=.038; Chi-Square).

In the CG, there were no statistically significant differences in self-reported pain frequency at any measurement timepoint (p=.540; Chi-Square).

Table 8: Frequency of pain

	Baseline		After two weeks		After four weeks		After eight weeks	
Pain Frequency	IG	CG	IG	CG	IG	CG	IG	CG
up to twice a week	2.1 %	4.2 %	7.9 %	10.5 %	14.0 %	14.0 %	18.6%	14.0 %
two to four times a week	16.7 %	16.7 %	26.3 %	21.1 %	14.0 %	18.6%	18.6%	20.9%
daily	35.4 %	25.0 %	18.4 %	15.8 %	23.3%	16.3%	14.0 %	14.0 %

IG = Intervention Group; CG = Control Group

Compared to baseline when 35,4% of the subjects in the IG reported daily pain, after eight weeks only 14% of the subjects in the IG reported daily pain.

Between-group analysis showed no statistically significant differences between self-reported pain frequency in the IG versus the CG one week before the respective measurement timepoints (Table 6; Appendix D).

Furthermore, additional details regarding specific situations or movements that may exacerbate each patient's knee pain were evaluated. These detailed questions were answered inconsistently or not at all by most subjects. Subsequently, we were not able to evaluate these additional questions.

6.2.2. Self-reported knee Function assessed via Knee Injury and Osteoarthritis Outcome Score

The Friedman test revealed statistically significant differences for self-reported knee function in the IG (all KOOS subscales p<.01). Such were found for the subscale *Pain* (p<.001), *Symptoms* (p=.001), *ADL* (p<.001), *Sports and Recreation* (p= .005), and *QoL* (p<.001). Post-hoc testing revealed the specific measurement time points at which those significant differences occurred (Table 9).

For the CG, the Friedman test revealed statistically significant differences for the same measure only in the KOOS-subscales *Pain* (p=.005) and *QoL* (p=.011). Post-hoc testing revealed the specific measurement time points at which these significant differences were located (Table 9).

Table 9: Friedman Test and Pairwise comparisons

Friedman Tests and Pairwise comparisons for all measurements and subdivisions								
		Friedman	Post hoc tests (Pairwise comparisons)					
		P	P (t0; t1)	p (t0; t2)	p (t0; t3)	p (t1; t2)	p (t1; t3)	p (t2; t3)
Pain	IG	<.001	0.046	< .001	< .001	0.020	< .001	0.031
	CG	0.005	ns	0.002	< .001	ns	ns	ns
Symptoms	IG	0.001	ns	< .001	< .001	0.021	0.012	ns
	CG	ns	ns	ns	ns	ns	ns	ns
ADL	IG	<.001	ns	0.024	< .001	ns	< .001	0.008
	CG	ns	ns	ns	ns	ns	ns	ns
Sport.Rec	IG	0.005	ns	0.007	< .001	ns	0.031	ns
	CG	ns	ns	ns	ns	ns	ns	ns
QOL	IG	<.001	ns	ns	< .001	ns	< .001	.013
	CG	0.011	ns	0.021	0.001	ns	0.021	ns

IG= Intervention Group; CG= Control Group; t0= baseline; t1= after two weeks; t2= after four weeks; t3= after eight weeks; ns= not significant

Between-group analysis revealed statistically significant differences (p=.038) for self-reported knee function between the IG versus the CG for the KOOS-subscale *Pain.* At t2 values for self-reported *pain* were significantly higher in the IG (mean 75,3) compared to the CG (mean 66,4) (p=.038; Mann-Whitney-U; Table 10).

Table 10: Between-Group analysis (Mann-Whitney-U)

		p	Effect size
KOOS.Pain at baseline	Mann-Whitney U	0.309	0.08
KOOS.Pain after two weeks	Mann-Whitney U	0.126	0.22
KOOS.Pain after four weeks	Mann-Whitney U	**0.038**	0.32
KOOS.Pain after eight weeks	Mann-Whitney U	0.055	0.28

Bold = significant p-value

Furthermore, between-group analysis revealed statistically significant differences for self-reported knee function between the IG versus the CG for the difference between t2 vs. baseline (p= .012), t3 vs. baseline (p=.044) and t1 vs. t2 (p= .044) for the KOOS-subscale *Symptoms* (Table 11) in favor of the IG.

Table 11: Between-Group-Analysis (Mann-Whitney-U)

		p	Effect size
Symptoms_t0-t1	Mann-Whitney U	0.461	0.14
Symptoms_t0-t2	Mann-Whitney U	**0.012**	0.46
Symptoms_t0-t3	Mann-Whitney U	**0.045**	0.37
Symptoms_t1-t2	Mann-Whitney U	**0.044**	0.38
Symptoms_t1-t3	Mann-Whitney U	0.233	0.23
Symptoms_t2-t3	Mann-Whitney U	0.862	0.03

t0= baseline; t1= after four weeks; t2= after four weeks; t3= after eight weeks; Bold = significant p-value

No statistically significant between-group differences were found for the KOOS subdivisions *Sport and Recreation*, *ADL* and *QOL*(p>.05)

6.2.3. Quality of life

The SF-12 consists of eight subscales that are grouped into two summary measures: the *Physical Component Summary* (PCS) and the *Mental Component Summary* (MCS).

Physical Component Score

Within the IG, the Friedman test revealed statistically significant differences for the physical component score of the SF-12 (p=.032). Post-hoc testing revealed the specific measurement time points at which those significant differences occurred (Table 12).

Within the CG, Friedman test revealed statistically significant differences (p= .012). Post-hoc testing revealed the specific measurement time points at which these significant differences were located (Table 12).

Table 12: Physical Component Score of SF-12

Friedman Test and pairwise comparisons for all measurements								
		Friedman	p (t0; t1)	p (t0; t2)	p (t0; t3)	p (t1; t2)	p (t1; t3)	p (t2; t3)
PCS	IG	0.032	ns	ns	0.004	ns	0.037	ns
	CG	0.012	ns	ns	0.002	ns	0.006	ns

IG= Intervention Group; CG= Control Group; t0= baseline; t1= after two weeks; t2= after four weeks; t3= after eight weeks; ns= not significant

Between-group analysis showed no statistically significant differences between PCS in the IG versus the CG (Table 7; Appendix D).

Mental Component Score

Within the IG an CG, Friedman test revealed no statistically significant differences ($p>.05$) and between-group analysis also showed no statistically significant differences between MCS in the IG versus the CG (Tables 8-10; Appendix D).

6.2.4. Workout frequency

Figure 11 shows the adherence to therapy measured in the percentage of workouts done and illustrates the significant difference in adherence in weeks 1-4 and week 6-8. The corresponding p-values can be witnessed in Table 13.

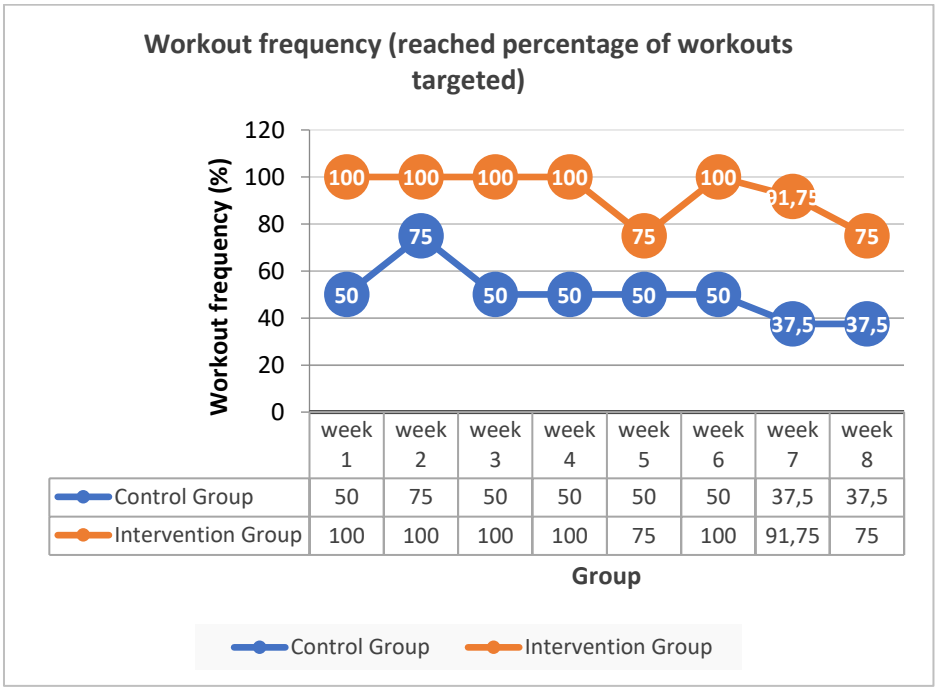

Figure 10: Workout frequency

Table 13: Workout frequency (Mann-Whitney-U)

Workout frequency		
Timepoint		p
week 1	Mann-Whitney U	**0.031**
week 2	Mann-Whitney U	**0.009**
week 3	Mann-Whitney U	**<0.001**
week 4	Mann-Whitney U	**0.006**
week 5	Mann-Whitney U	0.091
week 6	Mann-Whitney U	**<0.001**
week 7	Mann-Whitney U	**<0.001**
week 8	Mann-Whitney U	**0.008**

Bold = significant p-value

6.3. Analysis of the app questionnaire of the IG

At t3 the IG was given a questionnaire which covered the usability, interface and design of the app used for guidance through the individual exercise program. Patients were asked to score 8 items from 1-10 with 1 = not at all up to 10 = I totally agree. The distribution of the answers is displayed in table 12.

Table 14: App Questionnaire

Question		Score												
		Distractors						Sum	Passives		Sum	Promoters		Sum
		1 (not at all)	2	3	4	5	6		7	8		9	10 (totally agree)	
How helpful did you find the app?	frequency of occurrence			1				1		1	1	8	12	20
	% of overall IG subjects			4.5				4.5		4.5	4.5	36	55	91
What did you think of the design and the menu navigation of the app?	Frequency of occurrence				1			1	1	3	4	9	8	17
	% of overall IG subjects				4.5			4.5	5	14	19	41	36	77
How understandable did you find the explanations of the exercises?	frequency of occurrence									2	2	3	17	20
	% of overall IG subjects									9.1	9.1	14	77	91
How well did you get on with using the app?	frequency of occurrence	1		1				2		1	1	4	15	19
	% of overall IG subjects	4.5		4.5				9		4.5	4.5	18.2	68	86
Do you think the app is a useful supplement to therapy?	frequency of occurrence			1				1				7	14	21
	% of overall IG subjects			4.5				4.5				32	64	96
How likely are you to recommend the app?	frequency of occurrence									1	1	8	13	21
	% of overall IG subjects									4.5	4.5	36	59	95
How did you like the Herodikos® app?	frequency of occurrence									2	2	7	13	20
	% of overall IG subjects									9.1	9,1	32	59	91
Would you use the app again if you had similar complaints?	frequency of occurrence				1			1		1	1	4	16	20
	% of overall IG subjects				4.5			4.5		4.5	4.5	18.2	73	91

6.4. Analysis of Covariant Factors

The ACOVA analysis revealed that the KOOS subscale “Symptoms” was the only statistically significant variable (p= .041; Table 15).

Table 15: Analysis of covariant Factors

Variable	Df	Sum square	Mean Square	F value	Pr (>F)
SF-12 Physical Component score	1	15.32	15.32	0.08	0.78
SF-12 Mental Component Score	1	484.28	484.28	2.57	0.116
Current average Pain	1	73.59	73.59	0.39	0.536
Worst pain in last 2 weeks	1	73.59	73.59	0.39	0.536
Least pain in last 2 Weeks	1	0.10	0.10	0.01	0.981
Frequency of pain in last week	1	16.22	16.22	0.11	0.744
KOOS Score Pain	1	658.05	658.06	3.95	0.053
KOOS Score Symptoms	1	788.64	788.64	4.41	0.041
KOOS Score Activities of daily life	1	361.5	361.50	2.39	0.129
KOOS Score Sports and recreational activities	1	477.07	477.07	3.04	0.088
KOOS Score Quality of life	1	290.43	290.43	1.88	0.177

SF-12= Short Form Health Survey 12; KOOS= Knee Osteoarthritis Outcome Score; Df= Degrees of freedom; Sum square= sum of squared deviations from the mean; F= ratio of between-group- and within-group variance Pr (>F) = p-value associated with F-statistic

7. Discussion

This study aimed to evaluate the possible benefits of individual exercise presented via a digital app compared to a standard training regimen presented on paper considering anterior knee pain patients' pain levels, QoL and subjective knee function. Another focus was laid on the adherence to exercise therapy and the acceptance of the digital treatment approach.

Therefore, this randomized controlled pilot study enrolled subjects with anterior knee pain due to PFPS or OA. Subjects randomized into the IG were given a tailored exercise program via the app Herodikos®. In contrast, subjects randomized into the CG received a conventional (i.e., non-tailored) exercise plan, disseminated in a paper-based format.

Statistically significant improvements in self-reported knee pain and function as well as the physical component of quality of life were witnessed within both groups.

In contrast, comparisons of knee pain and function as well as quality of life between the IG versus the CG showed no statistically significant differences over time except for the KOOS-subscale *Pain* after 4 weeks of the intervention and for the KOOS-subscale *Symptoms* for the difference between after four weeks and baseline, for the difference between after eight weeks and baseline and for the difference between after two weeks and after four weeks.

Regarding therapy adherence, this pilot study's findings indicate that utilizing a tailored exercise program delivered through a digital app is more beneficial compared to a non-tailored exercise program delivered through a leaflet. In addition, the IG subjects reported favorable attitudes specifically towards the Herodikos® App and its usability.

Previous studies that focused on PFPS or knee OA compare exercise therapy with other treatment modalities (e.g., bracing, taping, osteopathic interventions) or compare different exercise regimens (e.g. open- vs. closed-chain exercises or functional stabilization training vs. standard training) (Brosseau et al. 2017; van der Heijden et al. 2015). Studies that evaluate digitally supported knee OA therapy are currently still rare (de Vries et al. 2017; Schäfer et al. 2018), and only two recent studies evaluate the DiGAs Mawendo® and Companion patella powered by medi® in a PFPS cohort (BFARM 2023). However, another potentially useful digital app for knee pain patients (i.e., the Herodikos® App) has not yet been investigated for its usefulness and patient acceptance. An advantage of the Herodikos® app compared to the aforementioned DiGAs may be the build-in functional assessment which can be used by the health-care professional (e.g., medical doctor or physical therapist) to tailor exercise programs to the specific patient's needs. The app generates an exercise plan based on the results of the assessment which can be adjusted manually by the health-care professional. Moreover, the app offers motivational tools such as push messages and allows communication between the

patient and their health-care professional. Additionally, it offers a broad selection of content such as scientific information displayed in easy understandable short texts and video guided relaxation trainings such as progressive muscle relaxation.

Research Hypothesis 1 - discussion

Our RH1 suggested, the IG would show significantly higher changes in pain levels compared to the CG after two, four and eight weeks. This hypothesis was, however, not met as both the IG and the CG improved significantly with regard to knee pain with no statistically differences between both groups. These study's findings are in line with previous investigations (Kloek et al. 2018, Umapathy et al 2015). Kloek et al. (2018) compared a blended intervention program (i.e., physical therapy accompanied by an online program) for knee and hip OA patients versus physical therapy alone. Similarly, Umapathy et al (2015) compared standard care for hip and/or knee OA patients with a digital intervention which provided tailored information to the patients. These authors report improved pain levels in both groups with no difference between the two groups.

In those as well as in our study, subjects had multiple personal appointments at the study centers (Kloek et al. 2018; Umapathy et al. 2015).

The intensive personal care might have influenced the self-reported results of the study. Both groups might have answered more positively to please the investigator. Or another option is that the personal care itself is the factor which causes the improvement. A qualitative review says that therapeutic relationship and person-centered care improves the patient's self-confidence which leads to less pain (Cheung and Soundy 2021).

Maybe, increased movement is the crucial factor, no matter which exercises are selected, or which modality is used to display the exercise plan. However, in a publication by Baldon et al (2014) a group with functional stabilization training had less pain than a standard training group after a 3-months follow-up (n=31, PFPS) and Schäfer also found that eHealth-supported exercises for subjects with OA resulted in less pain compared with other interventions (Schäfer et al. 2018).

With the results of our study, we cannot distinguish the impact of intensive personal care and we cannot distinguish between the two different exercise regimens.

Research Hypothesis 2 - discussion

Our RH2 suggested that the intervention group would show significantly higher changes in function compared to the CG and eight weeks. However, like RH1, this second hypothesis was also not met.

While the within-group analyses showed significant improvements for both groups during the study, there were no significant between-groups differences.

Contrary to our results, Mecklenburg et al. (2018) reported significant differences for knee pain in OA patients regarding the KOOS subscales pain and function. Participants in the IG were enrolled in the Hinge Health digital care program for chronic knee pain. This is a remotely delivered, home-based 12-week intervention that includes sensor-guided exercise therapy, education, cognitive behavioral therapy, weight loss, and psychosocial support through a personal coach and team-based interactions (Mecklenburg et al. 2018). The control group received three education pieces regarding self-care for chronic knee pain.

There is a chance that sensor-guided exercises are executed with better quality than exercises without sensor devices and thus improve functionality to a higher degree.

However, selected authors criticize that difference between CG and IG which the Hinge Health study showed in the intent-to-treat analyses in the KOOS subdivision *Pain* did not reach the minimum clinically important difference which was stated at 12 points according to Devji (McHugh et al. 2022; Devji et al. 2017).

Research Hypothesis 3 - discussion

Our RH3, which suggests that the IG would show significantly higher improvement of QoL measured with the SF-12 compared to the CG after two, four, and eight weeks of exercising was not met - analogous to RH 1 and RH2. Only the results of the *SF-12-PCS*-subdivision improved within both groups but no significant between-groups differences were found. While the current study's findings did not suggest any improvement in the *SF-12*-MCS subscale after four weeks, the observational study by Lee et al. (2016) conducted over the course of four weeks, suggest the exact opposite. These authors found that the *SF-12-PCS*-subscale scores of the 33 investigated subjects did not improve while the *SF-12-MCS*-subscale scores did. These different outcomes could be caused by different study durations (four vs. eight weeks). Subjects might be more enthusiastic about an intervention at the beginning – resulting in a better mental health score and 4 weeks might be too short to see improvements of the physical component. A systematic review and meta-analysis on exercise therapy for knee and hip OA also sees a significant improvement of QoL at or near 8 weeks for all groups. That matches our findings for the PCS (Goh et al. 2019).

Research Hypothesis 4- discussion

Our RH4 suggested that the IG would perform more workouts and keep on working out for longer periods of time than the CG. This hypothesis was confirmed by the study findings. After eight weeks

the adherence in the IG (75%) was significantly greater versus the CG's adherence (37,5%) suggesting that using the Herodikos® app increased patients' motivation to do their exercise. These results are similar to the results of a study conducted with hip and/or knee OA patients with an adherence to the online component of a blended intervention of 81% over eight weeks (de Vries et al. 2017). Still, the comparability is limited since the study didn't include a CG. Another study investigating a digital only intervention for patients with knee and/or hip OA reports an adherence of 48% only (Bossen et al. 2013). In a larger scale study including 10,264 subjects with knee (n=3796) or low back pain (n= 6468), 73% of subjects completed a 12-week digital care program (Bailey et al. 2020). The authors report that the number of digital therapy sessions and coaching interactions were positively associated with improvement in pain (Bailey et al. 2020). This contrasts with the current study's findings, but the study was observational and did not include a control group. Although, in our study, the IG showed a significantly higher adherence, we were not able to witness differences in the clinical outcomes, namely knee pain, function and QoL. If we take a closer look at the workout sessions, CG subjects only conducted almost 50% of the workout sessions of the IG.

For exercise therapy, it is difficult and complex to exactly measure the minimum effective dose for improving pain, function and QoL (Wasfy and Baggish 2016). The American Society of Pain and Neuroscience states that the amount of exercise should be at least three times per week over a four-week period to relieve pain and reduce disability in patients with knee OA and PFPS (Hunter et al. 2022). We aimed at four sessions over an eight-week period. Maybe the CG experienced significant results because they still reached the minimum effective dose even if they trained less than the IG.

Research Hypothesis 5 - discussion

The a-priory formulated RH 5 suggested that patients would accept the intervention, which means that at least 6 of the 8 questions in the app questionnaire were answered positively. This hypothesis would be confirmed, as overall 90% (7,2 questions out of 8) of the questions were answered positively. In a qualitative study in which 19 OA-subjects who were purposefully selected, including both sexes, different ages, OA severity and physical function, were interviewed about their experiences of a digital management program for hip and knee OA revealed that the web/app-based education and exercise was experienced as a valid alternative to traditional treatment (Cronström et al. 2019). Easy access, exercising at one's own convenience, but also follow-up and the access to support by a physical therapist within the digital solution were mentioned as the most important features (Cronström et al. 2019). All of these features are supported by the Herodikos® app- resulting in high acceptance rates.

In the current study, the mean age of the participants was 49 (range 18-75 years). The acceptance might have been lower, if participants had been older since digital affinity declines with age (Friemel 2016, van Kessel et al. 2023). A review from Valenzuela et al (2018) with a mean cohort age range of 67-86 years particularly examined acceptability and adherence to technology-based exercise interventions amongst older people. These authors suggest that adherence was higher for technology-based interventions versus traditional interventions (exercise training including balance and strength training) independent of study site, level of supervision, and delivery mode (Valenzuela et al. 2018) . Another study focusing on the acceptance of health apps amongst seniors stated that the subject's smartphone use and the breadth of mobile phone features used were significant factors, while the significance of seniors' personal characteristics and socio-economic conditions varied (Petrovčič, Peek, and Dolničar 2019). These findings are supported by a study which compared *Generation Z* with the *Baby Boomers* (Kim et al. 2022). *These authors suggest* that there is a relationship between the intention to use digital therapeutics and digital literacy (Kim et al. 2022). It is possible that subjects who were interested in participating in the study were already experienced in dealing with digital technologies. That might have influenced the acceptance.

The results of a survey with over 700 German participants indicate that, rather than by practical factors such as usefulness, Health app acceptance is influenced by emotional factors like hedonic motivation and partly by habit, social influence, and trust (Schomakers et al. 2022). The study setting with personal appointments might have had some kind of social influence on the subjects and therefore might have influenced the acceptance. Unfortunately, the subjects were not asked whether using the Herodikos® app was fun and whether they trust the app developers, but that might be useful for future studies.

8. Study Limitations, Delimitations and Further Research

Despite the valuable insights gained from this study, several limitations need to be acknowledged, which may impact the interpretation and generalizability of the findings.

First, the responsible investigator had a potential conflict of interest as she was part of the Herodikos® App developer team and still is a shareholder of the Herodikos GmbH. However, for financial and practicable reasons, it was not possible to find another clinician to examine the patients enrolled in this study. Consequently, the responsible investigator (ES) was in charge for all steps of this study. Moreover, she was not blinded to subjects' group allocation, creating possible bias. Yet, the investigator initially examined the subjects without knowledge about to which of the two groups the respective subject will be allocated after this baseline examination/measurements where the

randomization process was executed by another, thus independent person. Furthermore, the responsible investigator sticked fully to the predefined examination form, used objective measures (e.g. goniometer) and repeated each measurements multiple times (e.g. ROM measures) to calculate a mean value for further analyses whenever possible to avoid biases on the clinician's side to the best possible way. In addition, research suggests the possibility of response bias in study participants (Grimes and Schulz 2002). To avoid such bias, subjects were not informed about that fact that the used app was developed by the study investigator.

A second limitation is that different measures during the recruitment process might have led to different motives as to why patients enrolled. Some were motivated by their physicians or physio therapists, others enrolled self-motivated by responding to a post or notice or even by word-of-mouth. Activity-related studies usually appeal to people who generally enjoy exercise (Sherwood and Jeffery 2000). Moreover, after having difficulties in recruiting patients, the study was advertised predominantly in sport shops, running clubs etc. what might have led to a selection bias. The high number of physically active persons is indeed not representative for the majority of the German population. Around 75% of adult men and 80% of adult woman in Germany do not meet the given recommendations of aerobic physical activity in combination with muscle strengthening made by the WHO (Finger et al. 2017) but 67% of the study subjects report that they meet the recommendations. In retrospect, a broader advertisement strategy may have served the study better regarding recruiting a more heterogeneous sample. However, PFPS is a typically running-related disorder, which is why we chose to follow the explained advertisement strategy. Furthermore, for similar reasons, the patients who enrolled might be particularly digitally savvy because the title of the study includes the fact that it is an app-based intervention. This is another reason why a transfer of the results to the general population should be evaluated critically.

Third, the study relied primarily on self-reported measures, including self-reported pain levels, function, and QoL. While the subjective patient view is generally seen as a highly important outcome (REF), self-reported measures are susceptible to individual biases, recall errors and subjective interpretation, potentially affecting the accuracy of the results (Prince et al. 2020; Furbish, Anderson, and Field-Fote 2022; Wunsch et al. 2021).However, the selection of used measurement tools used for the current study was based on previous investigations that evaluated similar outcomes (Smittenaar et al. 2017; Kloek et al. 2018; Bailey et al. 2020; Mecklenburg et al. 2018). Research suggests, that in order to be able to compare various outcomes across different studies, the same measurement tools should be used whenever possible (REF). The NRS, for example, is as commonly used tool to assess

subjects' pain. Moreover, the KOOS and the SF-12 are two well established, commonly used valid and reliable patient-reported outcome measures to evaluate subjective functioning and QoL, respectively. In addition, in order to standardize the examination as good as possible, the "Untersuchungsbogen Knie" published by the German Berufsgenossenschaft was followed. The documentation form includes a common knee joint examination, ligament, and meniscus tests and three circumference measurements, where all examinations were executed by the same investigator to add to the consistency of the examination procedure. The IG underwent an additional functional assessment which is predefined in the Herodikos® app. The functional assessment was designed by the app's medical team based on common examination techniques. The investigator went through the assessments with the subjects and documented the results in the app. The app used the results to generate an exercise plan which was adjusted manually by the investigator. We didn't repeat the functional assessment at another timepoint. It might have been better to conduct the functional assessment provided by the app with both groups and to repeat it after 8 weeks in order to gain a better understanding of functionality and to reduce bias amongst the CG.

Fourth, n= 48 is a relatively small sample size. The randomization in two groups further reduced the group sizes. The limited sample size might have reduced the statistical power to detect significant differences, potentially leading to type II errors. Originally, a pilot study with 40 patients was supposed to be followed by the main study with 120 patients– both designed as a randomized controlled trial (RCT) in a cohort of adult patients diagnosed with anterior knee pain or painful knee OA. The intention was to test the planned study procedures in advance to the larger-scale RCT and modify planned operations in accordance with the current COVID safety measures where necessary in a pilot study setting. The number of 40 was chosen for the pilot study in accordance with a similar study (Lee, Lee, and So 2016). The plan was that, if during the pilot study turned out that all processes can be performed for the main study as initially planned, the data sets of these pilot patients would have been included in the main study. However, since recruitment in times of the Covid-19 pandemic was more challenging than expected, the pilot study included 48 patients after a recruitment period of 1,5 years and was not followed by a main study with a bigger number of patients. Hence, the transferability of the results to the general population of patients with anterior knee pain is limited. The results observed can merely indicate a tendency. It is pointed out that the study as a pilot project is merely exploratory in nature and should be viewed as the basis for further research. Anyhow, Kloek investigated a digital intervention for OA patients and compared it with usual physiotherapy. Despite the fact that they included a total of 208 subjects, they didn't find any significant differences (Kloek et al. 2018).

Fifth, the existence of a placebo effect must be discussed. Placebo is defined as a substance without medical effects taken by control group of patients in the study, in order to eliminate effects of the process of taking substance (Požgain et al. 2014). Colloca and Miller (2011) propose that the placebo effect is a learned response, whereby various types of cues (verbal, conditioned, and social) trigger expectancies that generate placebo effects via the central nervous system. Nocebo is defined as a substance without medical effects but which worsens the health status of the person taking it by the negative beliefs and expectations of the patient (Colloca and Miller 2011). Although the definitions aim at substances, it is commonly adapted for other interventions such as surgeries or exercise (Colagiuri et al. 2015).

As soon as the functional assessment with the app started, the subject knew that they were randomized into the IG. Since the subjects in the CG did not experience the functional assessment but were introduced to the paper-based training plan, they knew that they were randomized into the CG, and they knew that they performed standard instead of tailored exercises. That might have formed negative beliefs about the efficacy of the exercises performed and thus may have influenced the results of the study.

The subjects randomized into the CG might have been demotivated by the fact that they did not receive the tailored exercise program and therefore might have been less adherent.

To distinguish between the effects of a tailored exercise program vs. standard exercise program it would probably have been better to blind the subjects by making them all go through the functional assessment provided by the app and giving the CG a placebo app with the standard training plan. Then, we would have been able to make a final statement about whether the observed intervention effect is due to the individually tailored or standard exercise program. Another option would have been not to use a standard training plan but to use exercises which are likely to have no effect on the stabilization of the knee and on the knee pain in general. In a study focusing on sport-related concussions in adolescents, aerobic exercise was compared with placebo stretching (Leddy et al. 2021). The results showed a significant effect of the exercise vs. placebo exercise. Anyhow, with that design, we couldn't have evaluated possible advantages of an app-based intervention compared to a paper-based intervention.

To explicitly evaluate the measure of exercise presentation, it would have been better to either tailor the exercise programs for both groups or use the same standard program for both groups. In that case, it would have been a straight app versus paper study design.

Finally, the study evaluated the specific Herodikos® App as a digital solution for exercise guidance. The findings may not be directly transferable to other apps or digital platforms with varying designs, functionalities, and usability.

While this study provided valuable insights into the effects of an app-guided exercise program for patients with anterior knee pain, several opportunities for further research can be explored to enhance our understanding and address the limitations inherent in the current study.

Those include conducting studies with longer follow-up periods, such as six months to one year to assess the sustainability of improvements gained from app-guided exercise programs. This would provide a more comprehensive understanding of the long-term effects on pain reduction, functional enhancement, and quality of life. Incorporating placebo-controlled arms in studies would be another option which could help disentangle the specific effects of app-guided exercise programs from potential placebo effects. By comparing the app-based intervention to a placebo app, researchers could better attribute observed outcomes to the intervention itself. Integrating objective measures such as biomechanical analyses, muscle strength assessments, or imaging techniques (e.g., MRI, ultrasound) could provide a more comprehensive understanding of the physiological changes accompanying pain reduction and functional improvement. Objective measures could strengthen the validity of outcomes beyond self-report. Research exploring the impact of patients' digital literacy, technology acceptance, and attitudes toward app-based interventions can inform the design and implementation of digital solutions. Understanding barriers and facilitators to app usage can help tailor interventions to different user profiles. Further research could also focus on refining the algorithms used in app-guided exercise programs to enhance the personalization of exercise plans. This involves considering individual differences in baseline characteristics and functional limitations to optimize the program's effectiveness. A larger sample size might also lead to more distinguished results. Multi-center studies might be a solution to the challenge of recruitment.

9. Conclusion

The results revealed that there were no statistically significant differences in pain, function, and quality of life between the CG and IG, despite observable improvements within both groups over the course of the study. The IG showed a higher adherence to the exercise therapy than the CG. This suggests that the app may be a more convenient and accessible way for patients to receive exercise therapy. However, the adherence was not high enough to significantly impact the outcomes of the study.

Patients in the IG reported a positive experience with the app, indicating its acceptance as a useful supplement to conventional therapy.

While this study provided insights into the potential benefits of app-guided exercise programs for anterior knee pain patients, further research with larger sample sizes and longer study durations is warranted to fully explore the impact of digital interventions on pain, function, and quality of life in this population.

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12. Conflict of Interest Declaration

Eva Schobert
Shareholder of the Herodikos GmbH
07.09.2023

I, Eva Schobert, declare the following potential conflicts of interest related to the research presented in this dissertation, titled "Individual App-guided Exercise Therapy in Patients with Anterior Knee Pain and/or Knee Osteoarthritis".
As a shareholder, I have financial interests in the Herodikos GmbH. Currently, I'm not employed at Herodikos GmbH but until April 2023 my role within the organization was CEO.
In the interest of full transparency and to maintain the integrity of the research, I affirm that the research and its findings have not been unduly influenced by any conflicting interests.

13. Declarations

Hiermit erkläre ich eidesstattlich, dass ich die Dissertation selbständig und ohne fremde unzulässige Hilfe erbracht habe, das heißt ohne Benutzung anderer als der angegebenen Hilfsmittel angefertigt und die aus fremden Quellen direkt oder indirekt übernommenen Gedanken als solche kenntlich gemacht habe.

Hiermit erkläre ich eidesstattlich, dass der Inhalt der Dissertation nicht schon überwiegend für eine eigene Bachelor-, Master-, Diplom- oder ähnliche Prüfungsleistung verwendet wurde.

Hiermit erkläre ich eidesstattlich, dass die Regelungen zu guter wissenschaftlicher Praxis an der Carl von Ossietzky Universität Oldenburg befolgt worden sind.

Hiermit erkläre ich eidesstattlich, dass im Zusammenhang mit dem Promotionsvorhaben keine Vermittlungs- oder Beratungsdienste (Promotionsberatung) in Anspruch genommen worden sind.

14. Appendix

Appendix A - Questionnaires

1. Socioeconomic Data

Allgemeine Daten

Die folgenden Fragen beziehen sich auf Ihre Lebenssituation und Ausbildung. Bitte füllen Sie die zutreffende Antwort aus oder markieren Sie die Antwort die am besten auf Sie zutrifft.

1. Wie alt sind Sie? .....Jahre

2. Geschlecht ○ männlich ○ weiblich

3. Wie ist Ihre Lebenssituation?
   - ○ alleine
   - ○ mit Partner/in
   - ○ mit Partner/in und Kindern
   - ○ mit Kindern
   - ○ Ansonsten, nämlich_____

4. Was ist der höchste von Ihnen erworbene Abschluss?
   - ○ Hauptschulabschluss (Volksschule)
   - ○ Realschulabschluss (mittlere Reife)
   - ○ Gymnasium (allg. oder fachgebundene Hochschulreife/Abitur)
   - ○ Fachhochschulabschluss
   - ○ Universitätsabschluss (Diplom, Magister, Staatsexamen, Bachelor/Master)
   - ○ Promotion/Habilitation
   - ○ Ansonsten, nämlich _____

5. Welches Knie ist betroffen? ○ Rechts ○ Links ○ Beide

2. Pain Questionnaire

Schmerzstärke

Frage 1:
Auf einer Skala von 0-10, wie hoch ist Ihre **aktuelle** Schmerzstärke?
(0 = kein Schmerz, 10 = stärkster vorstellbarer Schmerz)

_____
Frage 2:
Auf einer Skala von 0-10, wie hoch war die schlimmste Schmerzstärke **innerhalb der letzten 2 Wochen**?
(0 = kein Schmerz, 10 = stärkster vorstellbarer Schmerz)

_____
Frage 3:
Auf einer Skala von 0-10, wie hoch waren die geringsten Schmerzen **innerhalb der letzten 2 Wochen**?
(0 = kein Schmerz, 10 = stärkster vorstellbarer Schmerz)

_____
Frage 4:
Wie häufig hatten Sie in der letzten Woche Knieschmerzen

- 0-2x
- 2-4x
- täglich

Frage 5:
Wann traten die Knieschmerzen **innerhalb der letzten Woche** auf (Mehrfachnennungen möglich)?
Geben Sie bitte für jede Antwort die durchschnittliche Schmerzstärke von 0 (= kein Schmerz) bis 10 (= stärkster vorstellbarer Schmerz) mit an.

- Nur bei Belastung, durchschnittliche Schmerzstärke dabei ____
- Nur bei Ruhe, durchschnittliche Schmerzstärke dabei ___
- In Ruhe und bei Belastung, durchschnittliche Schmerzstärke dabei ___
- Nur beim Treppe hochgehen, durchschnittliche Schmerzstärke dabei ___
- Nur beim Treppe runtergehen, durchschnittliche Schmerzstärke dabei ___
- Beim Treppe Hoch und Runtersteigen, durchschnittliche Schmerzstärke dabei ___
- Nur beim Joggen, durchschnittliche Schmerzstärke dabei ___

3. KOOS-Score

Kessler S. et al. Der Knee Injury and Osteoarthritis Outcome Score - ein Funktionsfragebogen zur Outcome-Messung in der Knieendoprothetik Z Orthop 2003; 141:277-282

„KOOS“ KNIEFRAGEBOGEN

Datum:_____/_____/_____Geburtsdatum:_____/_____/_____

Patienten Nr: _____

ANLEITUNG: Dieser Ankreuzbogen befragt Sie, welchen Eindruck Sie von Ihrem Knie haben. Die dadurch gewonnene Information wird uns helfen zu überwachen, wie es Ihnen mit Ihrem Knie geht und wie gut Sie in der Lage sind, Ihre üblichen Aktivitäten zu verrichten.
Beantworten Sie bitte jede Frage durch ankreuzen des zugehörigen Kästchens. Bitte nur ein Kästchen pro Frage ankreuzen. Wenn Sie sich unsicher sind, wie Sie die Frage beantworten sollen, wählen Sie die Antwort aus, die Ihnen am zutreffendsten erscheint.

Symptome

Diese Fragen beziehen sich auf Beschwerden von Seiten Ihres Kniegelenkes in der **vergangenen Woche**.

S1. Haben Sie Schwellungen an Ihrem Knie?
niemals selten manchmal oft immer

☐ ☐ ☐ ☐ ☐

S2. Fühlen Sie manchmal ein Mahlen, hören Sie manchmal ein Klicken oder irgendein Geräusch, wenn Sie Ihr Knie bewegen?
niemals selten manchmal oft immer

☐ ☐ ☐ ☐ ☐

S3. Bleibt Ihr Knie manchmal hängen, oder blockiert es, wenn Sie es bewegen?
niemals selten manchmal oft immer

☐ ☐ ☐ ☐ ☐

S4. Können Sie Ihr Knie ganz ausstrecken?
immer oft manchmal selten nie

☐ ☐ ☐ ☐ ☐

S5. Können Sie Ihr Knie ganz beugen?
immer oft manchmal selten nie

☐ ☐ ☐ ☐ ☐

Steifigkeit

Die nachfolgenden Fragen betreffen die Steifigkeit Ihres Kniegelenkes während der **letzten Woche**. Unter Steifigkeit versteht man ein Gefühl der Einschränkung oder Verlangsamung der Fähigkeit Ihr Kniegelenk zu bewegen.
Für jede der nachfolgenden Aktivitäten sollen Sie das Ausmaß der Schwierigkeiten angeben, welche Sie durch Ihr Kniegelenk innerhalb der letzten Woche erfahren haben.

S6. Wie stark ist Ihre Kniesteifigkeit morgens direkt nach dem Aufstehen?
keine schwach mäßig stark sehr stark

☐ ☐ ☐ ☐ ☐

S7. Wie stark ist Ihre Kniesteifigkeit nach dem Sie saßen, lagen, oder sich ausruhten im **Verlauf des Tages**?

keine schwach mäßig stark sehr stark

Schmerzen

P1. Wie oft tut Ihnen Ihr Knie weh?

niemals monatlich wöchentlich täglich immer

Wie ausgeprägt waren Ihre Schmerzen in der **vergangenen Woche** als Sie z.B:

P2. sich im Knie drehten?

keine schwach mäßig stark sehr stark

P3. Ihr Knie ganz ausstreckten?

keine schwach mäßig stark sehr stark

P4. Ihr Knie ganz beugten?

keine schwach mäßig stark sehr stark

P5. auf ebenem Boden gingen?

keine schwach mäßig stark sehr stark

P6. Treppen herauf oder heruntergingen?

keine schwach mäßig stark sehr stark

P7. nachts im Bett lagen?

keine schwach mäßig stark sehr stark

P8. saßen oder lagen, z.B. auf der Couch?

keine schwach mäßig stark sehr stark

P9. aufrecht standen?

keine schwach mäßig stark sehr stark

Aktivitäten des täglichen Lebens

Die nachfolgenden Fragen beziehen sich auf Ihre körperliche Leistungsfähigkeit. Hierunter verstehen wir Ihre Fähigkeit sich selbständig zu bewegen bzw. sich selbst zu versorgen.

Für jede der nachfolgenden Aktivitäten sollen Sie das Ausmaß der Schwierigkeiten angeben, welche Sie durch Ihr Kniegelenk innerhalb der **letzten Woche** erfahren haben.

Welche Schwierigkeiten hatten Sie **letzte Woche** als Sie z.B.:

A1. Treppen herunterstiegen?

keine wenig einige große sehr große

A2. Treppen heraufstiegen?

keine wenig einige große sehr große

A3. vom Sitzen aufstanden?
keine wenig einige große sehr große

Welche Schwierigkeiten hatten Sie **letzte Woche** als Sie z.B.:

A4. standen?
keine wenig einige große sehr große

A5. sich bückten um z.B. etwas vom Boden aufzuheben?
keine wenig einige große sehr große

A6. auf ebenen Boden gingen?
keine wenig einige große sehr große

A7. ins Auto ein- oder ausstiegen?
keine wenig einige große sehr große

A8. einkaufen gingen?

keine wenig einige große sehr große

A9. Strümpfe/Socken anzogen?
keine wenig einige große sehr große

A10. vom Bett aufstanden?
keine wenig einige große sehr große

A11. Strümpfe/Socken auszogen?
keine wenig einige große sehr große

A12. im Bett lagen und sich drehten, ohne das Knie dabei zu beugen?
keine wenig einige große sehr große

A13. in oder aus der Badewanne kamen?
keine wenig einige große sehr große

A14. saßen?
keine wenig einige große sehr große

A15. sich auf die Toilette setzten oder aufstanden?
keine wenig einige große sehr große

A16. schwere Hausarbeit verrichteten (schrubben, Garten umgraben, ...)?
keine wenig einige große sehr große

A17. leichte Hausarbeit verrichteten (Staub wischen, kochen, ...)?
keine wenig einige große sehr große

Sport und Freizeit

Die nachfolgenden Fragen beziehen sich auf Ihre körperliche Belastbarkeit im Rahmen eher sportlicher Aktivitäten. Für jede der nachfolgenden Aktivitäten sollen Sie das Ausmaß der Schwierigkeiten angeben, welche Sie durch Ihr Kniegelenk innerhalb der **letzten Woche** erfahren haben.

Hatten Sie Schwierigkeiten **letzte Woche** als Sie z.B.:

SP1. in die Hocke gingen?

keine wenig einige große sehr große

SP2. rannten?

keine wenig einige große sehr große

SP3. hüpften?

keine wenig einige große sehr große

SP4. sich auf Ihrem kranken Knie umdrehten?

keine wenig einige große sehr große

SP5. sich hinknieten?

keine wenig einige große sehr große

Beeinflussung der Lebensqualität durch das betroffene Knie

Q1. Wie oft spüren Sie Ihr erkranktes Knie?

nie monatlich wöchentlich täglich immer

Q2. Haben Sie Ihre Lebensweise verändert um eventuell Ihrem Knie schadende Tätigkeiten zu vermeiden?

nicht wenig etwas stark vollständig

Q3. Wie sehr macht es Ihnen zu schaffen, dass Ihr Knie nicht stabil ist?

gar nicht wenig einiges schlimm sehr schlimm

Q4. Wie würden Sie insgesamt die Schwierigkeiten bewerten die Sie durch das Knie haben?

keine wenig etwas große sehr große

Vielen Dank für die Beantwortung aller Fragen dieses Fragebogens

4. Short-Form 12

In diesem Fragebogen geht es um die Beurteilung Ihres Gesundheitszustandes. Der Bogen ermöglicht es, im Zeitverlauf nachzuvollziehen, wie Sie sich fühlen und wie Sie in Ihrem Alltag zurechtkommen. (Mit freundlicher Genehmigung der Hogrefe Verlag GmbH & Co.KG)

*Bitte beantworten Sie **jede Frage**, indem Sie bei den Antwortmöglichkeiten die Zahl ankreuzen, die am besten auf Sie zutrifft!*
1. Wie würden Sie ihren Gesundheitszustand im Allgemeinen beschreiben?

(1) Ausgezeichnet
(2) Sehr gut
(3) Gut
(4) Weniger gut
(5) Schlecht

2. Im Folgenden sind einige Tätigkeiten beschrieben, die Sie vielleicht an einem normalen Tag ausüben. Sind Sie durch ihren **derzeitigen** Gesundheitszustand bei diesen Tätigkeiten eingeschränkt? Wenn ja, wie stark?

	Ja, stark eingeschränkt	**Ja, etwas eingeschränkt**	**Nein, überhaupt nicht eingeschränkt**
mittelschwere Tätigkeiten, z. B. einen Tisch verschieben, staubsaugen, kegeln, Golf spielen	1	2	3
mehrere Treppenabsätze steigen	1	2	3

3. Hatten Sie **in den vergangenen 4 Wochen** aufgrund ihrer **körperlichen Gesundheit** irgendwelche Schwierigkeiten bei der Arbeit oder anderen alltäglichen Tätigkeiten im Beruf bzw. zu Hause?

	Ja	**Nein**
Ich habe **weniger geschafft** als ich wollte	1	2
Ich konnte **nur bestimmte Dinge** tun	1	2

4. Hatten Sie **in den vergangenen 4 Wochen** aufgrund **seelischer Probleme** irgendwelche Schwierigkeiten bei der Arbeit oder anderen alltäglichen Tätigkeiten im Beruf bzw. zu Hause (z. B. weil Sie sich niedergeschlagen oder ängstlich fühlten)?

	Ja	**Nein**
Ich habe **weniger geschafft** als ich wollte	1	2
Ich konnte **nicht so sorgfältig** wie üblich arbeiten	1	2

5. Inwieweit haben die Schmerzen Sie **in den vergangenen 4 Wochen** bei der Ausübung Ihrer Alltagsaktivitäten zu Hause oder im Beruf behindert?
(1) Überhaupt nicht
(2) Ein bisschen
(3) Mäßig
(4) Ziemlich
(5) Sehr

6. In diesen Fragen geht es darum, wie Sie sich fühlen und wie es Ihnen in den **vergangenen 4 Wochen** gegangen ist. (Bitte kreuzen Sie in jeder Zeile die Zahl an, die Ihrem Befinden am ehesten entspricht).

Ihrem Befinden am ehesten entspricht). **Wie oft waren Sie in den vergangenen 4 Wochen…**	**Immer**	**Meistens**	**Ziemlich oft**	**Manch-mal**	**Selten**	**Nie**
…ruhig und gelassen?	1	2	3	4	5	6
…voller Energie?	1	2	3	4	5	6
…entmutigt und traurig?	1	2	3	4	5	6

7. Wie häufig haben Ihre körperliche Gesundheit oder seelischen Probleme **in den vergangenen 4 Wochen** ihre Kontakte zu anderen Menschen (Besuche bei Freunden, Verwandten, usw.) beeinträchtigt?
(1) Immer
(2) Meistens
(3) Manchmal
(4) Selten
(5) Nie

5. App-Questionnaire

Fragebogen zur Nutzung der App Herodikos

Dieser Fragebogen wird anonym ausgewertet und die Beantwortung – auch hinsichtlich einzelner Fragen – ist freiwillig.

1. Wie hilfreich fanden Sie die App?

nicht hilfreich					sehr hilfreich				
1	2	3	4	5	6	7	8	9	10

2. Wie fanden Sie das Design und die Menüführung der App?

hat mir nicht gefallen					hat mir gut gefallen				
1	2	3	4	5	6	7	8	9	10

Was könnte verbessert werden?

_____

3. Wie verständlich fanden Sie die Erklärungen der Übungen?

habe ich gut verstanden					habe ich nicht verstanden				
1	2	3	4	5	6	7	8	9	10

4. Wie gut sind Sie mit der Bedienung der App zurechtgekommen?

ich fand die Bedienung sehr komplex					ich fand die Bedienung einfach				
1	2	3	4	5	6	7	8	9	10

5. Halten Sie die App für eine sinnvolle Therapieergänzung?

nicht sinnvoll					sehr sinnvoll				
1	2	3	4	5	6	7	8	9	10

6. Wie wahrscheinlich ist es, dass Sie die App weiterempfehlen?

unwahrscheinlich					sehr wahrscheinlich				
1	2	3	4	5	6	7	8	9	10

7. Wie hat Ihnen die Herodikos App gefallen?

Hat mir nicht gut gefallen					Hat mir gut gefallen				
1	2	3	4	5	6	7	8	9	10

Was können wir an der App verbessern?

_____

8. Würden Sie die App bei ähnlichen Beschwerden wieder nutzen?

würde ich nicht mehr nutzen					würde ich wieder nutzen				
1	2	3	4	5	6	7	8	9	10

Vielen Dank für Ihre Angaben!

Appendix B

1. Ergänzungsbericht Knie

Name, Vorname:

geb.:

Unfalltag:

Anlage zum D-Bericht Nr.: **oder Anlage zum Verlaufsbericht vom:**

Ergänzungsbericht - Knie -

Rechts ☐ **Links** ☐

Nur bei Verdacht auf Kniebinnenschaden, ggf. auch im Behandlungsverlauf.

1 **Unfallhergang, sofern nicht im D-Bericht beschrieben:**
Möglichst wörtliche Wiedergabe der Schilderung. Unklare Angaben (z. B. Um- oder Einknicken) bitte erläutern.

1.1	Kam es zu einer direkten Gewalteinwirkung, ggf. wie?	☐ Nein ☐ Ja:
1.2	Kam es zu einer indirekten Gewalteinwirkung, ggf. wie?	☐ Nein ☐ Ja:
1.3	War einer der Gelenkpartner im Rahmen des Unfallgeschehens fixiert, ggf. welcher und wodurch?	☐ Nein ☐ Ja:
2	**Verhalten nach dem Ereignis:**	
2.1	Als Unfall dem Arbeitgeber/der Arbeitgeberin gemeldet	☐ Nein ☐ Ja, am
2.2	Zeitpunkt der Arbeitseinstellung	☐ Sofort ☐ Später, am
2.3	Noch selbstständig gehfähig	☐ Nein ☐ Ja
3	**Beschwerden:**	☐ Sofort ☐ Später, am Welche:
4	**Frühere Behandlungsbedürftigkeit, weitere Erkrankungen oder Verletzungen:**	☐ Nein ☐ Ja, welche?
4.1	An dem geschädigten Knie	
4.2	An dem betroffenen Bein	
4.3	An anderen Gelenken (auch Gegenseite)	
4.4	Allgemeinerkrankungen, die auf die Beschwerden Einfluss gehabt haben können	
5	**Sportliche Betätigung:** (Auch gelegentliche Freizeit-Sporttätigkeit erfragen) Ggf. welche und wie lange?	☐ Nein ☐ Ja, welche?
6	**Berufliche Betätigung:**	
6.1	Kniebelastende Tätigkeit, ggf. wodurch und wie lange?	☐ Nein ☐ Ja, wodurch und wie lange?
7	**Befund:**	
7.1	Äußere Verletzungszeichen (Hautdruckmarken, Hautabschürfungen, Wunden)	☐ Nein ☐ Ja, wo?
7.2	Blutergussverfärbung	☐ Nein ☐ Ja, ☐ frisch ☐ älter ☐ abklingend
7.3	Weichteilschwellung	☐ Nein ☐ Ja, wo?
7.4	Kapselverdickung	☐ Nein ☐ Ja, wo?
7.5	Schleimbeutelbeteiligung, ggf. wo und welcher Art?	☐ Nein ☐ Ja, wo und welcher Art?

7.6	Grobe Prüfung der Hautwärme	☐ Normal	☐ Erhöht			
7.7	Druckempfindlichkeit	☐ Nein	☐ Ja, wo?			
7.8	Bandapparat:			Gelockert:		
	Innenbandführung	☐ Normal	☐ Gering	☐ Mittel	☐ Stark	
	Außenbandführung	☐ Normal	☐ Gering	☐ Mittel	☐ Stark	
	Schubladenzeichen	☐ Normal	☐ 3-5 mm	☐ 6-10 mm	☐ > 10 mm	
	Schublade	☐ Vordere	☐ Hintere	☐ Nicht prüfbar, weil		
	Ergebnisse weiterer klinischer Tests zur Bandinstabilität					
	Bandführung der Gegenseite	☐ Normal	☐ Verändert, wie?			
7.9	Zeichen für Meniskusbeteiligung	☐ Nein	☐ Ja, welche?			
7.10	Gelenkgeräusche:		**Rechts:**		**Links:**	
	Knirschen/Knacken/Reiben	☐ Nein	☐ Ja:		☐ Nein	☐ Ja:
				☐ Bds. gleich stark		
7.11	Bewegungsmaße – Kniegelenk					
	Streckung/Beugung (Abb.)					
7.12	Umfangmaße:					
	Oberschenkel 20 cm oberhalb inn. Kniegelenkspalt	cm:			cm:	
	Oberschenkel 10 cm oberhalb inn. Kniegelenkspalt	cm:			cm:	
	Kniescheibenmitte	cm:			cm:	
7.13	Gelenkerguss:	☐ Nein	☐ Ja			
	Punktion	☐ Nein	☐ Ja, Menge:	ml		
	Beschaffenheit des Punktats					
	Bakteriologisch-mikroskopische Untersuchung veranlasst	☐ Nein	☐ Ja (Ergebnis nachliefern)			
7.14	Laborchemische Entzündungsparameter (z. B. CRP)	☐ Nein	☐ Ja, Ergebnis:	(ggf. nachliefern)		

8	**Bildgebende Diagnostik, soweit nicht im D-Arztbericht beschrieben** (Nicht nur knöcherne Verletzungszeichen, sondern auch krankhafte Veränderungen oder Anomalien beschreiben)**:**
9	**Diagnose:**
10	**Behandlung bzw. Behandlungsvorschläge:**
11	Sind zur Klärung der Diagnose oder des ursächlichen Zusammenhanges noch weitere Maßnahmen erforderlich (z. B. Kernspintomografie, weitere Laborleistungen)? ☐ Nein ☐ Ja, welche?
12	**Welche Unterlagen sind noch zu beschaffen?**

Datenschutz:
Ich habe die Hinweise nach § 201 SGB VII gegeben.

Datum Name und Anschrift der Durchgangsärztin/des Durchgangsarztes

2. Informed consent

CARL VON OSSIETZKY UNIVERSITÄT OLDENBURG – 26111 OLDENBURG

Sehr geehrte/r Patient/in,

Sie haben sich im Pius-Hospital Oldenburg, der allgemeinmedizinischen Praxis Heiser-Kügler, der Praxis Theraktiv oder bei PhysiOLine gemeldet, weil Sie unter Knieschmerzen leiden. Die vorgenannten Praxen haben sich dazu bereit erklärt, die Universitätsklinik für Orthopädie und Unfallchirurgie im Pius-Hospital Oldenburg in der wissenschaftlichen Forschung zu unterstützen, mit dem Ziel, die Qualität in der orthopädischen Versorgung zu gewährleisten bzw. weiter zu verbessern. Unter der Leitung von Klinikdirektor Prof. Dr. med. habil. Lazovic führen wir eine Studie durch, in der untersucht wird, ob ein individuelles Bewegungstherapieprogramm bei vorderem Knieschmerz effektiver ist als ein Standard-Bewegungstherapieprogramm.

Die Studie hat den Titel:

Individuelle, App-gestützte Trainingstherapie bei Patienten mit vorderem Knieschmerz und schmerzhafter Gonarthrose

Mit diesem Brief möchten wir Sie herzlich einladen, an der o.g. Studie teilzunehmen. Um ein aussagekräftiges Ergebnis zu erzielen, benötigen wir die Unterstützung von mindestens 120 Patient/innen.

Vorderer Knieschmerz – auch femoropatellares Schmerzsyndrom genannt – und Kniegelenksarthrose sind die häufigsten Ursachen von Kniebeschwerden bei aktiven Personen.

Es gibt viele verschiedene Therapieansätze, aber bisher ist für keine Methode ein herausragender Nutzen belegt. Es ist jedoch nachgewiesen, dass Trainingstherapie sinnvoll ist und zu einer Besserung der Symptomatik führt.

In dieser Studie möchten wir einen Schritt weiter gehen. Wir wollen herausfinden, ob individualisierte Trainingstherapie effektiver ist als eine standardisierte Trainingstherapie. Dazu werden die Teilnehmer/innen der Studie zufällig in zwei Gruppen aufgeteilt. Eine Gruppe, die sog. Kontrollgruppe, erhält ein festgelegtes Standard-Trainingsprogramm in Papierform mit Bildern und ausführlichen Übungserklärungen. Die Teilnehmer dieser Gruppe müssen jedes Training in einem Bewegungstagebuch dokumentieren.

In der anderen Gruppe, der sog. Interventionsgruppe, wird für jede/n Patient/in ein individuelles Trainingsprogramm erstellt, das anschließend mit Hilfe einer App abgerufen und durchgeführt werden kann. In der App gibt es Videos und entsprechende Erklärungen für jede einzelne Übung. Über die Nutzung der App wird automatisch dokumentiert, wie häufig das Programm absolviert wurde.

Unabhängig von der späteren Gruppenzuordnung wird jede/r Patient/in zu Beginn der Studie ausführlich von einer Ärztin körperlich untersucht und gebeten, mehrere Fragebögen auszufüllen. Dies nimmt insgesamt ca. 1h

Ihrer Zeit in Anspruch. Anschließend erfolgt die zufällige Zuordnung zu einer der beiden Gruppen – Kontrollgruppe oder Interventionsgruppe. Sie wissen also vorher nicht, ob Sie die App bekommen oder nicht. Wenn Sie in der Interventionsgruppe sind, müssen Sie sich mit E-Mail-Adresse und Passwort in der App registrieren. Die Bereitschaft dazu ist Voraussetzung für die Studienteilnahme.

Sobald die Gruppenzugehörigkeit festgelegt wurde, werden für die Teilnehmer der Kontrollgruppe einmal alle Übungen aus dem Standardtherapieprogramm durchgesprochen und deren Ausführung erklärt; für die Teilnehmer der Interventionsgruppe wird ein individuelles Trainingsprogramm erstellt und entsprechend besprochen.

Anschließend führen alle Teilnehmer ihr jeweiliges Training selbständig zu Hause durch. Nach 2 und 4 Wochen erfolgt jeweils eine ca. einstündige Nachuntersuchung. Hierin werden Sie dann erneut ärztlich untersucht sowie gebeten, die gleichen Fragebögen wie zu Beginn der Studie nochmals aus. Nach 8 Wochen erfolgt die Abschlussuntersuchung die dem gleichen Ablauf folgt. Die Teilnehmer, die der Interventionsgruppe zugeordnet waren, werden zudem nach ihrer Zufriedenheit mit der App befragt. Es kann eventuell vorkommen, dass wir Sie nach 4 Monaten erneut kontaktieren und zu ihrem medizinischen Verlauf befragen.

Wie bereits erwähnt, erfolgt die Zuordnung zu den zwei Vergleichsgruppen zufällig und erst im Anschluss an die erste ärztliche Untersuchung. Das bedeutet, wenn Sie sich dazu entschließen, an der Studie teilzunehmen, wissen Sie noch nicht, welcher Gruppe Sie zugeordnet werden. Um Teilnehmern der Kontrollgruppe das individualisierte Training nicht vorzuenthalten, bieten wir diesen Teilnehmern an, dass sie nach Beendigung des Studienzeitraumes – also nach 8 Wochen – ebenfalls ein für sie individuell erstelltes Trainingsprogramm und einen entsprechenden App-Zugang für 8 Wochen nutzen können.

Bei einer Teilnahme bitten wir Sie, vorab zu bedenken, dass insgesamt 4 Untersuchungstermine mit einer Dauer von je ca. 1h auf Sie zukommen werden.

Die Fragebögen sowie alle anderen Studienergebnisse werden von uns vertraulich behandelt. Die Auswertung Ihrer Daten aus der ärztlichen Untersuchung sowie den Fragebögen erfolgt pseudomymisiert in der Universitätsklinik für Orthopädie und Unfallchirurgie im Pius-Hospital Oldenburg unter Verwendung einer Nummer und ohne Angaben Ihres Namens. Es existiert eine Codierliste, die Ihren Namen mit der Ihnen zugewiesenen Nummer verbindet. Die Codierliste wird getrennt von den anderen Daten aufbewahrt und ist nur den Projektmitarbeiter/innen zugänglich, d.h. nur diese können die erhobenen Daten falls nötig mit Ihrem Namen in Verbindung bringen.

Die Teilnehmer die Interventionsgruppe (App-basiertes, individualisiertes Training) zugeordnet werden, müssen sich allerdings mit einer E-Mail-Adresse und einem Passwort registrieren, damit der Account zugeordnet und somit nach Beendigung der Datenaufnahme und nach erfolgter Zustimmung gelöscht werden kann.

Nach Abschluss der Datenaufnahme und Datenauswertung wird auch die Codierliste gelöscht. Ab diesem Zeitpunkt sind die Daten vollständig anonymisiert, d.h. es ist dann niemandem mehr möglich, die erhobenen Daten mit Ihrem Namen in Verbindung zu bringen. Die innerhalb dieser Studie erhobenen Daten werden ausschließlich für Forschungszwecke verwendet und in anonymisierter Form 10 Jahre gespeichert.

Die Teilnahme an der Studie ist freiwillig. Durch Nicht-Teilnahme entsteht Ihnen kein Nachteil bei Ihrer Behandlung. Wenn Sie an der Studie teilnehmen möchten, unterschreiben Sie bitte die beiliegende Einwilligungserklärung und geben diese zusammen mit dem vollständig ausgefüllten Fragebogen an die zuständige Doktorandin noch vor Ort zurück.

Entscheiden Sie sich für eine Teilnahme, haben Sie trotzdem jederzeit das Recht, Ihre Zustimmung schriftlich und/oder mündlich zu widerrufen, ohne dass Ihnen dadurch Nachteile entstehen. Bei Rücktritt von der Studie kann auf Wunsch bereits gewonnenes Datenmaterial vernichtet werden. Wenn allerdings die Codierliste bereits gelöscht wurde, kann Ihr Datensatz nicht mehr identifiziert und somit auch nicht mehr gelöscht werden. Ihre Daten sind dann anonymisiert.

Sollten Sie Fragen zu unserer Untersuchung haben oder die Studie betreffende Unklarheiten bestehen, zögern Sie bitte nicht, mit uns persönlich, über E-Mail oder telefonisch Kontakt aufzunehmen.

Freiwilligkeit und Anonymität

Die Teilnahme ist für Sie freiwillig. Sie wird nur mit Ihrer schriftlichen Einwilligung stattfinden. Sie können jederzeit und ohne Angabe von Gründen die Teilnahme an dieser Studie beenden, ohne dass Ihnen daraus Nachteile entstehen. Die im Rahmen dieser Studien erhobenen, oben beschriebenen Daten und persönlichen Mitteilungen werden vertraulich behandelt. Alle involvierten Ärzte, und wissenschaftlichen Mitarbeiter unterliegen der ärztlichen Schweigepflicht und/oder haben eine Vertraulichkeitsvereinbarung unterzeichnet.

Dauer der Studie

Die Daten für das Vorhaben werden ab dem 15.04.2021 erhoben. Die Laufzeit beträgt 2 Jahre.

Ansprechpartnerin für Patienten:

Eva Schobert

eva.schobert@uni-oldenburg.de

0151-46176946

- Ich bin einverstanden, dass meine Daten zu Forschungszwecken verwendet werden.

- Ich bin damit einverstanden, für Nachuntersuchungen im Zusammenhang mit diesem Projekt zu einem späteren Zeitpunkt nochmals kontaktiert zu werden.

- Ich erkläre hiermit meine freiwillige Teilnahme an der o.g. Studie.

X_____	X_____	X_____
Ort, Datum	Unterschrift Teilnehmer/in	Name Teilnehmer/in in Druckschrift
X_____	X_____	X_____

Vielen herzlichen Dank für Ihre Mitarbeit an dieser Studie.

Mit freundlichen Grüßen,

_____	_____
Eva Schobert	Prof. Dr. med. Djordje Lazovic

Datenschutzhinweis

Rechtsgrundlage

Die Rechtsgrundlage für die Erhebung Sie betreffenden personenbezogener Daten ist die Einwilligung gem. Art. 6 Abs. 1 lit. a DSGVO/ Einwilligung Art. 9 Abs. 2 lit. A DSGVO

Kategorien personenbezogener Daten

Von der Datenverarbeitung sind folgende personenbezogene Daten umfasst:

Allgemeine Kategorien personenbezogener Daten:

☒ Kontaktdaten (Name, Anschrift, E-Mail-Adresse, Telefonnummern)

☒ demografische Daten (siehe Anhang sozioökonomischer Fragebogen)

Besondere Kategorien personenbezogener Daten:

☒ Gesundheitsdaten (Untersuchungsergebnisse, Schmerzstärke)

Einwilligung zur Datenverarbeitung und Studienteilnahme

Mit der beschriebenen Erhebung und Verarbeitung meiner Daten im Rahmen der Studie

Individuelle, App-gestützte Trainingstherapie bei Patienten mit vorderem Knieschmerz und schmerzhafter Gonarthrose

bin ich einverstanden.

Die Aufzeichnung dieser Daten erfolgt pseudonymisiert in der Universitätsklinik für Orthopädie und Unfallchirurgie im Pius-Hospital Oldenburg, in der allgemeinmedizinischen Praxis Heiser-Kügler, in der Praxis Theraktiv oder bei PhysiOLine unter Verwendung einer Nummer ohne Angabe meines Namens. Die Auswertung der Daten erfolgt in der Universitätsklinik für Orthopädie und Unfallchirurgie im Pius-Hospital Oldenburg. Dort existiert eine Codierliste, die meinen Namen mit dieser Nummer verbindet. Sollte ich in die Interventions-gruppe kommen, muss ich mich zusätzlich in der Herodikos-App mit meiner E-Mail-Adresse und einem Passwort registrieren. Mein Account wird mit der Pseudonymisierungsnummer verknüpft. Die Codierliste wird getrennt von den anderen Daten aufbewahrt und ist nur den Projektmitarbeiter/ innen zugänglich, d.h. nur sie können die erhobenen Daten mit meinem Namen in Verbindung bringen. Nach Abschluss der Datenaufnahme und Datenauswertung werden die Codierliste sowie alle App-Accounts vollständig gelöscht. Ab diesem Zeit-punkt sind die Daten anonymisiert, d.h. es ist niemandem mehr möglich, die erhobenen Daten mit meinem Namen in Verbindung zu bringen.

Mir ist bekannt, dass ich mein Einverständnis zur Aufbewahrung bzw. Speicherung meiner Daten schriftlich oder mündlich widerrufen kann, ohne dass mir daraus Nachteile entstehen. Ich bin darüber informiert worden, dass ich jederzeit das Recht auf Auskunft (einschließlich unentgeltlicher Überlassung einer Kopie) über die im Rahmen dieser Studie erhobenen personenbezogenen Daten habe und ggf. deren Berichtigung und/oder Löschung verlangen darf. Zudem kann ich die Löschung aller meiner weiteren, im Zusammenhang mit dieser Studie stehenden Daten verlangen (z.B. Löschung des App-Accounts inkl. aller dort hinterlegten Daten). Mir ist bewusst, dass mein Datensatz nicht mehr identifiziert und somit auch nicht mehr gelöscht werden kann, sobald die o.g. Codierliste und mein App-Account gelöscht sind. Meine Daten sind dann anonymisiert.

Dauer der Verarbeitung

Nach Auswertung aller Daten und Abschluss der Studie, spätestens jedoch nach Wegfall des Forschungszwecks, werden Ihre Daten schnellstmöglich – **insbesondere bevor eine Veröffentlichung zu wissenschaftlichen Zwecken** (z.B. Fachartikel, Tagungsbeiträge, wissenschaftliche Datenbanken [Open Data Repositories]) **stattfindet** – anonymisiert. Hierzu ist die Verantwortliche nach § 13 Absatz 2 Satz 1 Niedersächsisches Datenschutzgesetz (NDSG) verpflichtet. Anonymisierung bedeutet, dass niemand mehr Ihre Daten Ihrer Person zuordnen kann. Ihre Daten sind dann nicht mehr „personenbezogen“ im Sinne der datenschutzrechtlichen Rechtsvorschriften.

Kontaktdaten der Verantwortlichen und des Datenschutzbeauftragten

Verantwortliche Stelle

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Weitere/r Verantwortliche/r

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Dortige/r Datenschutzbeauftragte/r

Hr. Kabir
z.kabir@sco-consult.de

Ansprechpartnerin

Zur Kontaktaufnahme, insbesondere zur Wahrnehmung Ihrer Betroffenenrechte, wenden Sie sich bitte an:

Frau Eva Schobert (e-Mail: eva.schobert@uol.de; Telefon: 0151-46176946)

Rechte als Betroffener

- Sie haben ein **Recht auf Auskunft** über die Sie betreffenden personenbezogenen Daten (Art. 15 DSGVO).
- Sie können unverzüglich von dem Verantwortlichen **Berichtigung** Sie betreffender unrichtiger oder **Vervollständigung** unvollständiger personenbezogener Daten verlangen (Art. 16 DSGVO).
- Sie sind hiermit darüber informiert worden, dass Sie jederzeit eine **Löschung** der Sie betreffenden personenbezogenen Daten verlangen können (Art. 17 DSGVO).
- Sie können die **Einschränkung der Verarbeitung** verlangen, soweit die gesetzlichen Voraussetzungen vorliegen (Art. 18 DSGVO).
- Sie haben das Recht, die Sie betreffenden personenbezogenen Daten, **in einem strukturierten, gängigen und maschinenlesbaren Format zu erhalten** und diese Daten einem anderen Verantwortlichen zu übermitteln (Art. 20 DSGVO).
- Sie können jederzeit gegen die Verarbeitung Sie betreffender personenbezogener Daten **Widerspruch einlegen**, die aufgrund von Artikel 6 Abs. 1 lit. e oder f DSGVO erfolgt (Art. 21 DSGVO).
- Sie können die erteilte **Einwilligung jederzeit mit Wirkung für die Zukunft widerrufen,** ohne, dass die Rechtmäßigkeit der aufgrund der Einwilligung bis zum Widerruf erfolgten Verarbeitung berührt wird (Art. 7 Abs. 3 DSGVO)

Bereitstellung der Daten und Folgen der Nichtbereitstellung

Die Bereitstellung der Sie betreffenden personenbezogenen Daten ist weder vertraglich noch gesetzlich vorgeschrieben. Sie sind nicht dazu verpflichtet, Sie betreffende personenbezogene Daten bereitzustellen. Die Nichtbereitstellung hätte zur Folge, dass *sie nicht weiter an der Studie teilnehmen können.*

Beschwerderecht bei einer Aufsichtsbehörde

Falls Sie der Ansicht sind, dass die Verarbeitung Ihrer personenbezogenen Daten gegen Datenschutzvorschriften verstößt, wenden Sie sich bitte an den Datenschutzbeauftragten der Verantwortlichen (s.o.). Unabhängig hiervon haben Sie ein Recht auf **Beschwerde** bei der zuständigen Aufsichtsbehörde. Die zuständige Aufsichtsbehörde ist:

Die Landesbeauftragte für den Datenschutz Niedersachsen
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30159 Hannover

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Email: poststelle@lfd.niedersachsen.de

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Appendix C - Training protocol for control group

Trainingsplan Kontrollgruppe: (E=Einheiten, Whlg= Wiederholungen, P=Pause zwischen Sätzen)

WOCHE	ÜBUNG NR.	REIZDAUER (4 E/WOCHE)
1-2	**Übung 1: Ausfallschritt mit Hilfestellung**	3x8 Whlg./Bein, 1 Min. P
	Übung 2: Kniebeuge	3x 8 Whlg., 5x 30 Sek. unten halten, 1 Min. P
	Übung 3: Stufensteigen abwärts frontal	3x8 Whlg./Bein
	Übung 4: Stufensteigen abwärts seitlich	3x8 Whlg./Bein
3-4	**Übung 2c: Ausfallschritt mit Knie Hochziehen**	3x8 Whlg./Bein
	Übung 2d: Ausfallschritt mit Rotation	3x8 Whlg./Bein
	Übung 3: Stufensteigen abwärts frontal	3x12 Whlg./Bein
	Übung 4: Stufensteigen abwärts seitlich	3x12 Whlg./Bein
	Übung 5: Kniebeuge isometrisch plus instabiler Untergrund	3x30 Sek., 1 Min. P
5-6	**Übung 6: Stufensteigen abwärts frontal mit Gewicht**	3x8 Whlg./Bein
	Übung 7: Ausfallschritt – Balance	3x8 Whlg./Bein
	Übung 8: Ausfallschritt-Rumpfrotation mit Gewicht	3x8 Whlg./Bein
	Übung 9: Stufensteigen aufwärts mit/ohne Gewicht bis in den Einbeinstand:	3x8 Whlg./Bein

Übung 1: Ausfallschritt mit Hilfestellung
(Alternative: Übung 2 ab)


Ziel: Die optimale Bewegung in den Ausfallschritt mit Hilfestellung (z.B. durch einen Stuhl) zu erarbeiten.

Schritt 1: Stelle dich neben einen Stuhl und stütze dich mit der rechten (bzw. linken) Hand an der Stuhllehne ab. Die andere Hand kann in die Hüfte gestützt werden.
Schritt 2: Stelle einen Fuß nach hinten und senke das Knie nach unten ab. Verteile das Gewicht gleichmäßig auf beide Beine.
Schritt 3: Beuge das vordere Bein bis zu einem Winkel von maximal 90° im Kniegelenk. Dabei hebt sich die Ferse vom hinteren Bein vom Boden ab. Der Rumpf sollte sich dabei senkrecht nach unten bewegen.
Schritt 3: Überprüfe, dass die Kniescheibe des vorderen Beines sich in der Endposition über oder hinter dem Vorfuß befindet und nicht weiter vorne ist als der Fuß.

Übung 2: Kniebeuge

Ziel: Eine saubere Kniebeuge mit Hilfestellung (z.B. durch einen Stuhl) zu erarbeiten.

Schritt 1: Stelle dich hinter einen Stuhl und stütze dich mit deinen Händen auf der Rückenlehne ab.
Schritt 2: Beuge dann langsam beide Knie und senke den Po ab.
Schritt 3: Überprüfe, dass der Rücken gerade und beide Fußsohlen auf dem Boden sind.

Übung 2a/b: Freier Ausfallschritt

Ziel: Die optimale Bewegung in den Ausfallschritt ohne Hilfestellung zu erarbeiten.

Schritt 1: Stelle dich in den Ausfallschritt.
Schritt 2: Lege dabei die Hände in die Taille. **(2a)**
Schritt 3: Senke den Rumpf senkrecht ab, indem du die Knie um 60-90° beugst. **(2b)**
Schritt 4: Überprüfe, dass die Kniescheibe sich über/hinter dem Vorfuß befindet und nicht weiter vorne ist als der Fuß.

Übung 2c: Ausfallschritt mit Knie Hochziehen

Ziel: Aus dem Ausfallschritt in den Einbeinstand kommen

Schritt 1: Komme in den freien Ausfallschritt (Übung **2b**).
Schritt 2: Richte dich aus dem Ausfallschritt auf, indem du dich mit der hinteren Ferse abdrückst uns das Bein nach vorne-oben anhebst, sodass dieses in Hüfte und Knie jeweils um 90% gebeugt ist.
Schritt 3: Halte diesen stabilen Einbeinstand für ca. 3 Sekunden und kehre zurück in den Ausfallschritt.

Übung 2d: Ausfallschritt mit Rotation


Schritt 1: Stelle dich in den Ausfallschritt.
Schritt 2: Lege dabei die Hände in die Taille. **(2a)**
Schritt 3: Drehe den Rumpf mit ausgebreiteten Armen zum hinteren Bein und senke den Rumpf gleichzeitig senkrecht ab, indem du die Knie um 60-90° beugst.
Schritt 4: Überprüfe, dass die Beine stabil sind und die Kniescheibe sich über/hinter dem Vorfuß befindet und nicht weiter vorne ist als der Fuß.

Übung 3: Stufensteigen abwärts frontal


Ziel: Stabilität beim Stufensteigen abwärts erreichen.

Schritt 1: Stelle dich auf eine Treppenstufe oder einen Stepper.
Schritt 2: Stemme die Arme in die Hüften.
Schritt 3: Stelle den Fuß des Standbeines an die Vorderkante der Stufe, und beuge das Knie so weit, dass die Ferse des Übungsbeines die Vorderkante berührt
Schritt 4: Beuge das Standbein soweit, dass die Ferse des anderen Beines den Boden berührt und drücke dich wieder nach oben in die Ausgangsposition.

Übung 4: Stufensteigen abwärts seitlich

Ziel: Den seitlichen Abwärtsschritt von einer Stufe zu erlernen.

Schritt 1: Stelle dich seitwärts auf eine Stufe/Stepper.
Schritt 2: Strecke das rechte (bzw. linke) Bein zur Seite und leicht nach vorne hin zum Boden (Spielbein) und beuge dabei das andere Bein (Standbein).
Schritt 3: Berühre mit dem Spielbein kurz den Boden und bringe es dann zurück zur Ausgangsposition.

Übung 5: Kniebeuge isometrisch plus instabiler Untergrund



Ziel: Eine gleichmäßige Spannung in der Oberschenkelmuskulatur auf einem instabilen Untergrund halten.

Schritt 1: Stelle dich frei auf eine Wackelmatte/Wackelkissen/Kissen.
Schritt 2: Gehe in die Kniebeuge von 60-80°.
Schritt 3: Halte die Balance.
Schritt 4: Belaste die Beine wechselseitig mehr.

Übung 6: Stufensteigen abwärts frontal mit Gewicht


Ziel: Stabilität beim Stufensteigen abwärts erreichen.

Schritt 1: Stelle dich auf eine Treppenstufe oder einen Stepper. Halte ein Gewicht oder einen Ball mit beiden Händen und strecke diese waagerecht nach vorne vom Körper weg, etwas unter Schulterhöhe mit leicht gebeugten Ellenbogen.

Schritt 2: Stemme die Arme in die Hüften.
Schritt 3: Stelle den Fuß des Standbeines an die Vorderkante der Stufe, und beuge das Knie so weit, dass die Ferse des Übungsbeines die Vorderkante berührt
Schritt 4: Beuge das Standbein soweit, dass die Ferse des anderen Beines den Boden berührt und drücke dich wieder nach oben in die Ausgangsposition.

Übung 7: Ausfallschritt – Balance

Ziel: Den Ausfallschritt auf einem instabilen Untergrund für das vordere Bein halten.

Übung 5a:
Schritt 1: Lege eine Wackelmatte/Wackelkissen/Kissen vor dich.
Schritt 2: Stelle dich in den Ausfallschritt (wie Übung **2b**), stelle dabei das vordere Bein auf die Wackelmatte/Wackelkissen/Kissen und nutze die Arme zur Unterstützung.
Schritt 3: Lege die Hände auf den vorderen Oberschenkel zur Balancekontrolle und überprüfe die Anspannung der Oberschenkelmuskulatur.

Übung 5b:
Schritt 1: Wiederhole 5a und stütze dabei die Hände in die Hüften, ggf. kann die Wackelmatte oder -kissen zuvor umgedreht werden.

Übung 8: Ausfallschritt-Rumpfrotation mit Gewicht

Ziel: Ausfallschritt mit Rumpfrotation und Gewichtsbelastung erarbeiten.

Schritt 1: Halte ein Gewicht oder einen Ball mit beiden Händen und strecke diese waagerecht nach vorne vom Körper weg, etwas unter Schulterhöhe mit leicht gebeugten Ellenbogen.
Schritt 2: Wiederhole den Ausfallschritt mit Rumpfrotation (Übung **2d**)
Schritt 3: Drehe den Rumpf mit dem vom Körper weg gestreckten Gewicht oder Ball zum hinteren Bein.
Schritt 4: Überprüfe, dass die Beine stabil sind und die Kniescheibe des vorderen Beines sich über/hinter dem Vorfuß befindet.

Übung 9: Stufensteigen aufwärts mit/ohne Gewicht bis in den Einbeinstand:

Ziel: Stabilität beim Stufensteigen mit Gewichtsbelastung erreichen.

Schritt 1: Stelle dich vor eine Stufe oder einen Stepper. Halte ein Gewicht oder einen Ball mit beiden Händen und strecke diese waagerecht nach vorne vom Körper weg, etwas unter Schulterhöhe mit leicht gebeugten Ellenbogen.
Schritt 2: Gehe in einen Ausfallschritt (wie Übung **2b**), das vordere Bein ist auf der Stufe.
Schritt 3: Drücke dich nun mit dem hinteren Bein vom Boden ab und ziehe das Knie nach vorne-oben, wie in Übung **2c** (Hüfte und Knie um jeweils 90° gebeugt)

Allgemeine Anmerkungen:

- Gewicht: Hantel, Gewichtsscheibe oder **gefüllte Flasche**
- Instabile Unterlage: Wackelkissen, Bosu-Ball, Wackelbrett oder **dickes Kissen**
- Stufe: die meisten Treppenstufen sind 20cm hoch

Appendix D - Statistics

Table 1: Between-group analysis for item „current pain“

Between-group analysis “Current pain”			
		p	**Effect size**
Current pain at baseline	Mann-Whitney U	0.619	0.09
Current Pain after two weeks	Mann-Whitney U	0.183	0.25
Current Pain after four weeks	Mann-Whitney U	0.500	0.12
Current Pain after eight weeks	Mann-Whitney U	0.295	0.1
Difference Current pain at baseline – Current pain at t1	Mann-Whitney U	0.101	0.3111
Difference Current pain at baseline – Current pain at t2	Mann-Whitney U	0.294	0.1950
Difference Current pain at baseline – Current pain at t3	Mann-Whitney U	0.140	0.2690
Difference Current pain at t1 – Current pain at t2	Mann-Whitney U	0.353	0.1790
Difference Current pain at t1 – Current pain at t3	Mann-Whitney U	0.697	0.0760
Difference Current pain at t2 – Current pain at -t3	Mann-Whitney U	0.607	0.0929

t0= baseline; t1= after two weeks; t2= after four weeks; t3= after eight weeks

Table 2: Pairwise comparisons for item „Worst pain“ for control group

Pairwise Comparisons (Durbin-Conover)				
			Statistik	**p**
WP at baseline	-	WP after two weeks	0.99	0.324
WP at baseline	-	WP after four weeks	2.81	0.023
WP at baseline	-	WP after eight weeks	1.77	0.081
WP after two weeks	-	WP after four weeks	1.35	0.182
WP after two weeks	-	WP after eight weeks	0.78	0.437
WP after four weeks	-	WP after eight weeks	0.57	0.572

WP= Worst pain in the last two weeks

Table 3: Between-group analysis for item „worst pain“

Between-group analysis "worst pain"			
		p	**Effect size**
Worst pain at baseline	Mann-Whitney U	0.702	0.07
Worst Pain after two weeks	Mann-Whitney U	0.148	0.28
Worst Pain after four weeks	Mann-Whitney U	0.185	0.24
Worst Pain after eight weeks	Mann-Whitney U	0.019	0.42
Difference Worst pain at baseline – Worst pain at t1	Mann-Whitney U	0.390	0.16
Difference Worst pain at baseline – Worst pain at t2	Mann-Whitney U	0.410	0.15
Difference Worst pain at baseline – Worst pain at t3	Mann-Whitney U	0.108	0.29
Difference Worst pain at t1 – Worst pain at t2	Mann-Whitney U	0.392	0.16
Difference Worst pain at t1 – Worst pain at t3	Mann-Whitney U	0.818	0.05
Difference Worst pain at t2 – Worst pain at -t3	Mann-Whitney U	0.192	0.23

t0= baseline; t1= after two weeks; t2= after four weeks; t3= after eight weeks

Table 4: Friedman test for item „least pain“ for control group

Friedman test for item „least pain" for control group					
X^2		**df**		**p**	
6,56		3		0.087	

df= degrees of freedom

Table 5: Between-group analysis for item „least pain“

Between-group analysis "least pain"

		p	Effect size
Least pain at baseline	Mann-Whitney U	0.417	0.14
Least Pain after two weeks	Mann-Whitney U	0.841	0.04
Least Pain after four weeks	Mann-Whitney U	0.364	0.16
Least Pain after eight weeks	Mann-Whitney U	0.627	0.08
Difference Least pain at baseline – Least pain at t1	Mann-Whitney U	0.639	0.09
Difference Least pain at baseline – Least pain at t2	Mann-Whitney U	0.739	0.06
Difference Least pain at baseline – Worst pain at t3	Mann-Whitney U	0.979	0.01
Difference Least pain at t1 – Least pain at t2	Mann-Whitney U	0.726	0.06
Difference Least pain at t1 – Least pain at t3	Mann-Whitney U	0.864	0.03
Difference Least pain at t2 – Least pain at -t3	Mann-Whitney U	0.861	0.03

t0= baseline; t1= after two weeks; t2= after four weeks; t3= after eight weeks

Table 6: Between-group analysis for item „Pain frequency“

Between-group-Analysis for Pain Frequency			
		p	**Effect size**
Pain frequency at baseline	Mann-Whitney U	0.407	0.12
Pain frequency after two weeks	Mann-Whitney U	0.739	0.06
Pain frequency after four weeks	Mann-Whitney U	0.578	0.09
Pain frequency after eight weeks	Mann-Whitney U	0.708	0.06

Table 7: Between-group analysis for „Physical component score“

Between-group analysis “Physical Component Score”			
		p	**Effect size**
PCS at baseline	Mann-Whitney U	0.428	0.14
PCS after two weeks	Mann-Whitney U	0.796	0.06
PCS after four weeks	Mann-Whitney U	0.747	0.06
PCS after eight weeks	Mann-Whitney U	0.657	0.08
Difference PCS at baseline – PCS at t1	Mann-Whitney U	0.238	0.15
Difference PCS at baseline – PCS at t2	Mann-Whitney U	0.378	0.07
Difference PCS at baseline - PCS at t3	Mann-Whitney U	0.279	0.11
Difference PCS at t1 – PCS at t2	Mann-Whitney U	0.170	0.20
Difference PCS at t1 – PCS at t3	Mann-Whitney U	0.231	0.16
Difference PCS at t2 – PCS at -t3	Mann-Whitney U	0.386	0.06

Table 8: Friedman Test for Mental Component Score for Intervention Group

Friedman for MCS for Intervention Group		
X^2	**df**	**p**
2,75	3	0.433

df= degrees of freedom

Table 9: Friedman Test for Mental Component Score for Control Group

Friedman for MCS for Control Group		
X^2	**df**	**p**
0.761	3	0.859

df= degrees of freedom

Table 10: Between-group analysis for Mental component score

Between-group analysis "Mental Component Score"			
		p	**Effect size**
MCS at baseline	Mann-Whitney U	0.347	0.17
MCS after two weeks	Mann-Whitney U	0.849	0.04
MCS after four weeks	Mann-Whitney U	0.639	0.09
MCS after eight weeks	Mann-Whitney U	0.855	0.04
Difference MCS at baseline – MCS at t1	Mann-Whitney U	0.850	0.21
Difference MCS at baseline – MCS at t2	Mann-Whitney U	0.514	0.01
Difference MCS at baseline - MCS at t3	Mann-Whitney U	0.920	0.26
Difference MCS at t1 – MCS at t2	Mann-Whitney U	0.555	0.03
Difference MCS at t1 – MCS at t3	Mann-Whitney U	0.545	0.02
Difference MCS at t2 – MCS at -t3	Mann-Whitney U	0.749	0.13

Appendix E - Ethical vote

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OLDENBURG, 23.03.2021

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Titel: Individual App-guided Exercise Therapy in Patients with Anterior Knee Pain and Knee Osteoarthritis

Antragsteller: Prof. Dr. Djordje Lazovic
Eva Schobert

Unser Zeichen: 2021-043

Beratung gem. §§15 BO ÄKN, 23b MPG

Sehr geehrter Herr Prof. Lazovic,

Ihr Antrag vom 22.02.2021 hat der medizinischen Ethikkommission in ihrer Sitzung am 17.03.2021 zur Beratung vorgelegen.

Die medizinische Ethikkommission hat keine rechtlichen oder ethischen Bedenken gegen die Durchführung der o. g. Studie.

Hinweis:

- Bitte versionieren und datieren Sie die überarbeitete Patienteninformation neu.

Bitte beachten Sie noch folgende Punkte:

- Die Ethikkommission erwartet, dass ihr ohne Aufforderung ein Abschlussbericht mit dem beigelegten **Formular B** übermittelt wird.
- Unabhängig davon ist die Ethikkommission unaufgefordert und zeitnah über alle Änderungen am Prüfplan, sowie den in diesem Antrag vorgelegten Dokumenten unaufgefordert und unverzüglich zu unterrichten. Ihr sind unaufgefordert alle schweren

unerwünschten Ereignisse mitzuteilen, soweit sie im Zuständigkeitsbereich der Ethikkommission aufgetreten sind.
- Die ethische medizinische und juristische Verantwortung des Studienleiters und des an der Studie beteiligten medizinischen und wissenschaftlichen Personal bleibt entsprechend der Beratungsfunktion der medizinischen Ethikkommission durch diese Stellungnahme unberührt.
- Die Ethikkommission kann dieses Votum jederzeit zurückziehen oder ändern. Dies wird dem Antragsteller mitgeteilt.
- Bitte machen Sie dieses Votum und die der Begutachtung zugrundeliegenden Dokumente allen beteiligten Ärztinnen und Ärzten und Wissenschaftlerinnen und Wissenschaftlern zugänglich.

An der Beratung und Beschlussfassung haben keine Kommissionsmitglieder teilgenommen, die selbst an dem Forschungsvorhaben mitwirken oder deren Interessen davon berührt werden.

Wir bitten um Mitteilung der teilnehmenden Ärztinnen und Ärzte im Zuständigkeitsbereich der Universität Oldenburg, sobald diese bekannt sind bzw. sofern im Verlauf weitere Ärztinnen und Ärzte hinzukommen.

Wir möchten darauf hinweisen, dass die Stellungnahme der medizinischen Ethikkommission und die studienrelevante Korrespondenz an alle teilnehmenden Ärztinnen und Ärzte weiterzuleiten ist.

Bitte informieren Sie die Ethikkommission unter Nutzung des beigefügten Formulars A über den Beginn der Rekrutierung an Ihrem Studienzentrum.

Wir wünschen Ihnen bei der Durchführung Ihrer Studie viel Erfolg.

Mit freundlichen Grüßen

Prof. Frank Griesinger
Vorsitzender der medizinischen Ethikkommission

Eingereichte Unterlagen:

- E-Mail vom 23.02.2021
- Anschreiben vom 22.02.2021
- Synopse vom 22.02.2021
- Studienprotokoll V.1 vom 24.02.2021
- Formaler Antrag V1 vom 24.02.2021
- Liste der eingesetzten Medizinprodukte vom 22.01.2021
- Kostenübernahmeerklärung vom 22.02.2021
- Antrag Studienzentrum vom 22.02.2021
- Zustimmung des Klinikdirektors der Orthopädie und Unfallchirurgie des Pius-Hospitals vom 22.02.2021
- Erklärung von Interessenskonflikten vom 22.01.2021
- Patienteninformation und Einwilligung V1
- Datenerhebungsbogen
- Patientenfragebogen V1
- Biometrisches Gutachten zur Studie vom 31.07.2019
- Einverständniserklärung zur Patientenrekrutierung in der Praxis Cornelia Heiser-Kügler vom 19.02.2021
- Einverständniserklärung Theraktiv Oldenburg zur Patientenrekrutierung vom 22.02.2021
- Einverständniserklärung PhysioLine
- Handbuch Patientenversion V1.1
- Zweckbestimmung Lebenslauf von Eva Schobert vom 21.02.2021
- Risk Management vom 13.05.2020
- Sozioökonomische Daten
- Fragebogen zur Zufriedenheit
- Trainingsplan: Kontrollgruppe
- Überarbeitete Patienteninformation, eingereicht am 18.03.2021

Mitglieder der Medizinischen Ethikkommission der Carl von Ossietzky Universität Oldenburg

Die Namen der an der Abstimmung zu diesem Forschungsvorhaben beteiligten Kommissionsmitglieder sind hervorgehoben:

Prof. Dr. Frank Griesinger (Vorsitzender), Dr. jur. Hans Oehlers (stv. Vorsitzender), **Carola Alvarez Castillo**, Dr. jur. Marco Bartsch, PD Dr. Dalibor Bockelmann, Dr. Michael Buschermöhle, Prof. Dr. Michael Freitag, Dr. Thilo Gronow, Dr. Martin Groß, **Dr. Jörg Hennefründ**, **Prof. René Hurlemann**, **Hendrik Huscher**, Dr. Kathrin Janitzky, **PD Dr. Alexander Kluge**, Dr. Kristina Kolbow, **PD Dr. Claus Lüers**, Andrea Mahnken, **PD** Dr. Christian Mathys, PD Dr. Bernd Metzner, Dr. Sven Meyer, Prof. Dr. Hermann Müller, PD Dr. Oliver Pieske, Prof. Dr. Michael Reinhardt, Josef Roß, Dr. Dirk Scheele, Prof. **Dr. Mark Schweda**, Dr. Kay C. Willborn, Prof. Dr. Karsten Witt