Title: The Effectiveness of an Internet-Based Cognitive Behavioural Therapy and Exercise in Chronic Knee Patients with Psychological Distress: Study Protocol

Authors: Amal Alaradi[1], MSc. Yusuf Alkhabaz, Phd[2].

[1]Physiotherapy Department, National Bank of Bahrain-Arad Health Center, Primary Healthcare Centers, Manama, Bahrain

[2]Department of Physiotherapy, College of Health and Sport Sciences, University of Bahrain, Manama, Bahrain

Correspondence: Amal Alaradi, National Bank of Bahrain-Arad Health Center, Physiotherapy Department, Primary Healthcare Centers, Manama, Bahrain, Phone: + 973 363 663 00,
✉**to.alaradi@gmail.com**

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Aim/Objectives :

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To investigate the effects of combining iCBT interventions with a standardized exercise program in chronic knee pain patients with psychological distress compared to a control group.

Objectives:
1. To measure the effect of combined iCBT interventions with a standardized exercise program on pain and function in individuals with chronic knee pain at 8 weeks.
2. To measure the effect of combined iCBT interventions with a standardized exercise program on depression, psychological distress, physical function, quality of life, pain catastrophizing and quadriceps muscle strength in individuals with chronic knee pain at 8 weeks.
3. To measure the effects of combined iCBT interventions with a standardized exercise program on pain and function in individuals with chronic knee pain compared to a control group at 8 weeks.
4. To examine the correlations between subjective and objective outcome measures in chronic knee pain patients.

Research method :

a. Study Design
This is a 2-arm randomized controlled trial of 8 weeks of intervention involving 8 sessions of standardized exercise program and either concomitant iCBT and educational sessions or educational sessions only. Measurements will be taken at baseline and 8 weeks immediately following the intervention. The study will be conducted in National Bank of Bahrain Health Center (NBB HC).

b. Participants
Participants will be recruited from NBB HC patients who will be referred to the physiotherapy department for knee pain. Health centers physicians will be informed about the study so that they can advise or refer eligible participants. Furthermore, the I-Seha database in the ministry of health will be searched for eligible participants who were diagnosed previously with one of the following diagnoses: osteoarthritis/ pain in joint/ pain in limb/ disorder of patella.

- **Inclusion criteria:**

1. Age ≥ 45 years
2. Depression level of at least 2 out 6 on the Patient Health Questionnaire (PHQ-2)
3. Psychological distress level (K-6) of at least 7 out of 24
4. Knee pain for more than 3 months and for most days of the previous month
5. A minimum average knee pain intensity of 4 on an 11-point numeric rating scale in the previous week
6. Mild to moderate difficulty with physical activities on Knee Injury and Osteoarthritis Outcome Score Physical Function Short Form (KOOS-PS)
7. Has a smartphone with internet access.

Determination of the depression and psychological distress levels were based on the mean levels of each variable in the high health care utilizer's group from Lentz et al. (2019) study. These two specific variables were chosen as these were improved after CBT interventions

(Bennell, Ahamed, et al., 2016; Lentz et al., 2019).

- **Exclusion criteria:**

1. Knee surgery including arthroscopy within the past 6 months
2. Awaiting or planning any back or lower limb surgery within the next 12 months
3. Current or past (within 3 months) oral or intra-articular corticosteroid use
4. Current long-term use of analgesics or drugs that cause analgesic effects such as the drugs used for epilepsy and bipolar disorders
5. Systemic arthritic conditions such as rheumatoid arthritis
6. Physiotherapy, chiropractic or acupuncture treatment or exercises specifically for the knee within the past 6 months
7. Walking >30 min continuously daily or participating in a regular (more than twice a week) exercise program
8. Past participation in a CBT program
9. Inability to walk unaided as this is necessary for some of the physical testings
10. Grade IV on Kellgren and Lawrence grading system for Osteoarthritis classification
11. Medical condition precluding safe exercise such as uncontrolled hypertension or heart condition
12. Major joint pain (e.g. back, hip or ankle) to a greater extent than the knee pain that could limit the ability to exercise
13. Self-reported psychiatric history such as schizophrenia, epilepsy and bipolar disorders
14. Self-reported diagnosis of current clinical depression
15. Neurological condition such as Parkinson's disease, Multiple sclerosis or stroke
16. Inadequate written and spoken Arabic
17. Unable to comply with the protocol such as the inability to attend therapy sessions or attend assessment appointments at the health center.

- **Sample Size**

Convenient sampling has been used for this study based on the time and resources limit for this study. A number of twenty participants were assigned in each group.

c. Study Procedure

Eligible patients will be randomly allocated to either the study group or the control group (1:1). Initial assessments by self-reported questionnaires will be done at baseline. Initial assessment of knee joint will be done as well as the objective outcome measures that include: Isometric muscle strength of quadriceps using a hand-held dynamometer, functional tests (40mFPWT/ 30s CST/ 9 SST). The total time for completion of the three tasks will be approximately 25 min (Rejeski et al., 1995). Then the participant will be prescribed strengthening exercises under the supervision of the researcher and to follow at home, 3-4 times per week. Depending on the participant's allocation, the participant will be provided with a link to access online material of pre-recorded sessions of CBT or educational material about knee pain, healthy diet and other general information. In addition to their access to iCBT sessions, the study group will be able to access the same educational material that is accessed by the control group. On the 2nd -8th session, the physiotherapist will follow up on the exercises and progress as needed and will respond to any questions or doubts the participant has regarding the online sessions.

In the 8th session, self-reported questionnaires will be undertaken again as well as the objective outcome measures. All self-reported questionnaires will be completed through a survey administration application (Google or Microsoft forms) except for the questionnaires required for eligibility i.e. PHQ-2, K6 and KOOS-PS. All participants will provide written informed consent prior to their enrolment.

d. Interventions

1. Standardized Exercise Program (common to both groups)

Participants will attend the clinic for 8 supervised physiotherapy sessions designed to strengthen lower limb muscles. Eight sessions were chosen as this number should be able to achieve improvements in pain and function (Fransen et al., 2015).

The exercise program will be adopted from Bennell et al. (2012) study as it proved its effectiveness in improving pain and function. The program will comprise of a minimum of 4 and a maximum of 6 individualized lower limb exercises to be performed 3-4 times per week. All exercise programs will include at least 3 knee extensor strengthening exercises, and at least 1 hip abductor strengthening exercise selected from a pre-determined list (Table 1). The remaining optional 1 or 2 exercises can be chosen from other exercises on the list or be any exercise of the researcher's choice, in order to address an impairment or functional deficit related to the participant's knee problem. Examples include functional drill or dynamic balance exercise(s), muscle stretch(es) or other lower limb muscle strengthening. The researcher will select exercises and prescribe dosages for each exercise based on the assessment findings, including muscle strength, the participant's pain and their perceived level of effort during the performance of the exercise. Participants might be asked to have elastic bands and/or ankle cuff weights for the execution of the exercises if required. Participants will be asked to follow exercises at home 3-4 times/week.

A brief assessment will be performed by the researcher at each physiotherapy session in order to ascertain any adverse effects (if any) that may have occurred with home exercises and to check the quality and form of exercise performance. Progression of exercises is an essential component of the program and the findings from the assessment will help guide the researcher's decisions regarding progression. Progression will be provided by varying the exercises including the type of exercise as well as the number of repetitions, load or degree of difficulty within an exercise. In order to gain strength, the level of effort experienced during each strengthening exercise will be self-rated as at least 5 out of 10 (hard) on a modified Borg Rating of Perceived Exertion (RPE) CR10 scale designed specifically for strengthening exercise (Appendix 1)(Day et al., 2004). In addition, the resistance prescribed will aim to approximate a 10-repetition maximum level. Participants will be provided with exercises handouts and log sheets (Appendices 2 and 3).

The researcher will also discuss the disease-specific and general health benefits of increased levels of general physical activity, including both incidental physical and whole-body exercise.

Risk Factor

Some discomfort is expected during the strengthening exercise sessions and whole-body physical activity, however, the pain should subside to usual levels by the next day with no increase in swelling following the exercise session. Participants will be taught how to determine whether pain levels during and for a short time after the exercises are acceptable. If a specific exercise is aggravating the participant's pain, then the researcher will reduce the resistance, dosage and/or level of challenge within the exercise until the pain flare settles. Progression will be partially based on the absence of significant pain (2-3 out of 10) during exercises (Crossley et al., 2019).

2. Educational Material (common to both groups)

Participants will receive a specific link to access online educational material about chronic knee pain. This will be 5 sessions, with each lasting for 10-15 minutes, and will comprise of general information about the following: healthy eating, water intake, physical activity, emotions and proper footwear. Participants are encouraged to access the education material at their own leisure and pace.

3. Internet-Based Cognitive Behavioural Therapy (study group only)

In addition to their access to the educational material, participants in this group will receive a link to access pre-recorded online sessions of CBT. The content of sessions will be adopted from the painCOACH program that was effectively used in an RCT for the effects of adding and iCBT to an exercise program in persistent hip pain patients (Bennell et al., 2015). The iCBT translated key therapeutic components of face-to-face PCST (keefe et al., 2002). The program proved its effectiveness in improving pain and function in patients with arthritis (Bennell et al., 2018; Rini et al., 2015).

The link will contain eight 35- to 45-minute sessions, designed to be completed weekly, each will provide an explanation of a cognitive or behavioural pain coping skill. Session 1 will provide an overview, including a therapeutic rationale of CBT, followed by training in progressive muscle relaxation. Sessions 2 through 7 will teach brief relaxation skills, activity-rest cycling, pleasant activity scheduling, cognitive restructuring, pleasant imagery, and problem-solving. Session 8 will consolidate learning and teaches strategies for long-term skill use. Each session has to be completed within the same week where the physiotherapy session is given. Participants will be asked to practice and actively use each new skill they learn, and skills practice will be reviewed in subsequent sessions. Participants will have the opportunity to ask questions when they attend the physiotherapy exercise session. Companion worksheets and practice logs will be provided.

e. Outcome Measures

1. Primary Outcome Measures

- The Single-Item Numerical Rating Scale (NRS)

Participants will be asked to rate their average knee pain in the past week on a scale from 0 to 10, with '0' meaning 'No pain' and '10' meaning 'Pain as bad as you can imagine'(Dworkin et al., 2005). This is a reliable tool that was recommended by the Veterans health administration workgroup as one of the core outcome measures for chronic musculoskeletal conditions (Kroenke et al., 2019).

- 40-m Fast-Paced Walk Test (40-m FPWT)

A participant will be instructed to walk as quickly but as safely as possible to a mark 10 m away, return, and repeat for a total distance of 40 m. Regular walking aid is allowed and recorded. Time of one trial, with turn time excluded, is recorded and expressed as speed m/s by dividing distance (40 m) by time (s) (Dobson et al., 2013).

- Step Test (ST)

This test will be performed while the participant maintained balance on the study limb, then the contralateral foot will be stepped on and off a 15-cm step as many times as possible within 15 seconds. The count of the number of times the participant could step the foot up and return it to the floor over a 15-s interval will be recorded. The test will be performed with no hand

support allowed (Hatfield et al., 2016; Hinman et al., 2002). For participants with unilateral knee OA, the test will be performed while standing on the affected side. For participants with bilateral knee OA, the most symptomatic limb was considered the osteoarthritic limb for the purpose of this study.

- **30 seconds Chair Stand Test (30s CTS test)**

From the sitting position in the middle of seat with feet shoulder-width apart, flat on the floor, arms crossed at chest, a participant will stand completely up, then sit completely back down, repeatedly for 30 s. the chair should be against a wall. Count the total number of complete chair stands (up and down represents one stand) of one trial. If a full stand is completed at 30 s then this is counted in the total. The same chair is needed for re-testing (Dobson et al., 2013).

2. Secondary Outcome Measures

- **Patient Health Questionnaire (PHQ-9)**

This is a 9-item scale for depression screening in primary care (Kroenke, 2012). Its Arabic version is a valid and reliable tool to screen for depression (AlHadi et al., 2017). It will be given by paper at baseline and then online forms will be used.

- **Psychological Distress (Kessler 6)**

This is a 6-item self-report questionnaire that measures psychological distress based on anxiety and depressive symptoms in the patient's most recent 4-week period (Kessler et al., 2002). The translated version of the K6 scale is a valid and reliable measurement of psychological distress (Easton et al., 2017). It will be given by paper at baseline and then online forms will be used.

- **Knee Injury and Osteoarthritis Outcome Score Physical Function Short Form (KOOS- PS)**

This is a 7-item measure of physical function derived from the items of the Function, daily living and Function, sports and recreational activity subscales of the KOOS. The Arabic language version of the KOOS-PS was found to be valid and reliable enough to measure the physical function in knee OA patients (Torad et al., 2015). It will be administered through an online survey.

- **Health-Related Quality of Life-Short Form-12 (SF-12)**

This is a questionnaire consisting of twelve questions that measure eight health domains to assess physical and mental health-related quality of life (Huo et al., 2018). The reliability and validity of this questionnaire are questionable, yet it will be used in this study as it was the only short form with free access that was found (Al Sayah et al., 2013). It will be administered through an online survey.

- **Maximum Isometric Muscle Strength**

Assessing quadriceps muscle strength can indicate the individual's mobility and pain and hence it will be assessed in this study (Luc-Harkey et al., 2018). Maximal voluntary isometric quadriceps muscle strength will be assessed using a hand-held dynamometer as described by Luc-Harkey et al (2018) (Figure 4). To do the test, a participant will be seated on an examination table with their knees flexed to 60° and their feet off the ground. The hand-held dynamometer will be positioned on the anterior aspect of the distal tibia, just superior to the malleoli. An inelastic strap will be secured around the treatment table under the participant and will be used to maintain the position of the hand-held dynamometer and the knee angle during each testing trial. The participant will grasp the examination table with his/her hands for stabilization, and the participant will be instructed to extend his/her knee "as hard as possible" into the hand-

held dynamometer. The participant will continue to exert force into the hand-held dynamometer for 4 s, and the maximum force across the trial will be recorded. Three testing trials will be completed, and the average force (Newtons [N]) across the three trials will be normalized to body mass (N/kg) (Luc-Harkey et al., 2018).

f. Data Collection

Data collection points will be done at 0 and 8 weeks. In addition to the outcome measures, descriptive data will be collected at baseline by an online questionnaire. Descriptive data to be collected are age, gender, employment status, marital status, body mass index (BMI), duration of knee symptoms, previous treatments, medical history, and medications.

g. Ethical Considerations

- Ethical Approval

This research was approved by 1. The Scientific Research and Publication Committee, College of Health and Sport Sciences (CHSS), University of Bahrain (CHSS SRPC Recommendation No: 6/2020-21 dt. Feb 23, 2021) 2. Research Technical Support Team, Office of Assistant Undersecretary for Researces and Services, Ministry of Health, Kingdom of Bahrain, Project ID: 498 dt. Apr 8, 2021.

- Human Participants

Participants will take part in the study voluntarily after receiving sufficient information and after signing a consent sheet. Moreover, participants will have the right to withdraw from the study at any stage if they wish to do so without prejudice.

- Personal Data

Personal information of participants will be dealt with confidentiality and will not be shared with anyone. Research information will be kept safely in a USB flash drive. Only research personnel will have access to the files. After completion of this study, the personal and contact details of participants will be erased while the dataset will be retained and might be used for further researches done by the UOB or the MOH in the kingdom of Bahrain.

- Anonymity of Participants

The anonymity of participants will be ensured by assigning each participant a code number to enter and to analyse the primary data collected from questionnaires or physical assessments. Participant's face or identity will not be revealed if photographs or video recordings were taken.

- Conflict of Interest

The researcher declares that she has no conflict of interest.

h. Data Analysis

Main comparative analyses between groups will be performed using intention-to-treat. This analysis will include all participants who have missing data and those who do not fully adhere to the protocol. Demographic characteristics, as well as baseline scores on primary and secondary outcome measures, will be inspected to assess baseline comparability of treatment groups. These variables will also be examined for those participants who withdraw from the study and those who remain. Descriptive statistics will be presented for each group as the mean change (standard deviation, 95% confidence intervals) in the outcomes from baseline to each time-

point. For continuous outcomes differences in mean change will be compared between groups using linear regression random effects modelling adjusted for baseline values of the outcome. Proportional odds models will compare improvement between groups based on perceived ratings of change as well as the proportion in each group who attain the minimum clinical important difference (MCID) for pain and function. The MCID to be detected in chronic musculoskeletal trials is a change in pain of 1 unit (out of 10) (Salaffi et al., 2004). The MCID to be detected in the 30sCST and 40mFPWT are 2.0 and 0.19 respectively (Dobson et al., 2013).

- **Limitations**

This study has limitations. First, the study will be conducted with one researcher which exposes it to a risk of bias, but this risk will be minimized by blinding participants to hypotheses. Second, the determined sample size might not be reached within the study's time frame and this might affect the effect size between both groups leading to no significant results between the group. Second, some of the Arabic translated questionnaires have low reliability and/ or low validity levels, thus limiting the generalizability of their results.

Expected outcomes:

Chronic knee pain is a debilitating condition that can affect the physical and mental health of individuals consequently compromising their quality of life. It is of great importance to address the intercorrelated physical and mental health consequences of chronic pain as this is reflected in one's wellbeing. General guidelines recommend education and exercises as core treatments. Furthermore, recommendations to incorporate CBT programs in the management of chronic knee pain are growing. Such programs are time and cost-consuming interventions. Novel methods of CBT delivery have been investigated and done with different methodologies. Many studies have been done combining exercises with an internet-based CBT. Due to the delivery mode (internet or application-based) of these studies, objective outcome measures were missed, thereby compromising the confidence in the results of these studies. In order to improve the quality of evidence, it is important to incorporate subjective and objective outcome measures. This study aims to remedy the shortcoming of missing objective outcome measures through combining a supervised face-to-face exercise program with an iCBT. In turn, this will enhance the delivery of comprehensive cost- and time-effective interventions for patients and will ensure patients' availability for objective outcome measures. Moreover, this study aims to study the effects of the combined program in patients who have certain levels of depression and psychological distress. The effectiveness of combined iCBT interventions and exercises in this specific group of individuals has not been addressed in the literature. Conducting this research will help in identifying individuals who will benefit the most of such programs and might reframe the criteria for patients to be included in these programs as they benefit the most from it.

Conducting such research will have a great impact on individuals' lives and hence on society. To begin with, this study will ensure that evidence-based practice is delivered for Arabic speaking patients suffering from chronic knee pain. Additionally, Providing a comprehensive non-pharmacological intervention for chronic knee pain has many advantages. First, reducing the chronicity of knee pain will reduce the high utilization of health care services. Second, it will reduce patients' dependency on pharmacological intervention, thus will cut a lot of its costs. Third, it can be incorporated as a program for patients waiting for surgery or even -in selected cases- can work as an alternative for surgical interventions. Fourth, reducing the chronicity of knee pain is reflected positively on individuals' physical function, therefore reducing the burden of physical disability. Improved physical function reduces the risk of diseases where reduced mobility is considered one of its highest risk factors, such as the most common non-

communicable diseases (NCD) of hypertension, diabetes and high cholesterol levels. NCDs are considered a health burden that cost much of the health budget. Reducing the burden of NCD through such programs will reduce its costs that can be utilized in other health areas.

It is expected that there will be a significant difference between both group of the study for the primary outcome measures (pain and function) and for most of the secondary outcome measures. Moreover, it is expected to find a significant difference between the intervention and control group in favour of the intervention group.

It is expected also, to find correlation between patients' subjective outcome measures and objective outcome measures in line with what's available in the literature.