The effectiveness of group CBT and exercise in management of Depression: Protocol for a three-arm randomized controlled pilot trial

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ABSTRACT

Introduction: There is strong evidence in scientific literature indicating the effectiveness of Cognitive-Behavior Therapy (CBT) in the management of Major Depressive Disorder (MDD) and some clinical trials indicating physical exercise is also an effective treatment for the disorder. However, few studies have evaluated the effect of group CBT or physical exercise in the management of MDD compared to wait-listing to receive usual treatment of MDD. This study will evaluate and compare the effectiveness of: 1) group CBT plus wait-listing to receive treatment as usual (TAU); versus 2) group physical exercise plus wait-listing to receive TAU; versus 3) only wait-listing to receive TAU in management of MDD. The investigators hypothesize that participants with MDD assigned to the group CBT or group exercise (plus wait-listed to receive TAU) arms of the study will achieve superior outcomes compared to participants only wait-listed to receive TAU.

Methods and analysis: This is a prospective rater-blinded randomized controlled trial assessing the benefits for participants with MDD. 120 patients with MDD referred to Addiction and Mental Health (AMH) clinics in Edmonton Zone who are informed about the study and consent to participate will be randomly assigned to one of the three arms of the study: 1) 40 participants wait-listed to receive TAU will also receive weekly sessions of group CBT for 14 weeks; 2) 40 participants wait-listed to receive TAU will also receive group exercise 3 times a week for 14 weeks; and 3) 40 participants will only be wait-listed to receive TAU. All participants will be assessed at baseline, 7 and 14 weeks. Their assessments will cover primary outcomes including functional variables (recovery, quality of life, employment) and symptom variables (changes in depressive symptoms scores). Secondary client outcomes will be service variables (e.g. patient satisfaction with the service). The data will be analyzed using repeated measures and effect size analyses, and correlational analyses will be completed between measures at each time point.

Ethics and dissemination: The study will be conducted in accordance with the Declaration of Helsinki (Hong Kong Amendment) and Good Clinical Practice (Canadian Guidelines). Written informed consent will be obtained from each subject. The study has received ethical clearance from Health Ethics Research Board of the University of Alberta (Ref. # Pro 00080975) and operational approval from our provincial health authority (AHS # 43638). The study will also be registered with clinicaltrials.gov. The results will be disseminated at several levels, including patients, practitioners, academics/researchers, and healthcare organizations.

INTRODUCTION

Background and rationale

Depressive disorders are a major public health problem. For example, the global prevalence of depressive disorders is over 4%, and depression is the single largest contributor to non-fatal health loss. There is a need to identify interventions that are relatively cost-efficient, scalable, and can be offered to many people. Treatment for depressive disorders typically includes anti-depressant medication and/or counselling and psychotherapy.

Exercise as a form of treatment for depressive disorders, especially of mild-to-moderate severity, has evidence of benefit. In fact, the magnitude of the effect of exercise as a treatment for depression is reported to be comparable to conventional treatment. An umbrella review of systematic reviews and meta-analyses of the use of exercise to treat depressive symptoms in older adults, for example, concluded that "exercise is safe and efficacious in reducing depressive symptoms in older people" and exercise "should be considered as a core intervention in the multidisciplinary treatment of older adults experiencing depression". A meta-analysis adjusting for publication bias, concluded that "exercise has a large and significant antidepressant effect in people with depression". The mechanisms by which exercise decreases depressive symptoms may include biological mechanisms, such as anti-inflammatory effects or increasing neurotransmitter levels implicated in depression. Other mechanisms may include increasing self-efficacy or enhancing social interaction.

Despite this strong evidence base, few studies have incorporated multiple treatment conditions in a randomized controlled trial design, and few studies appear to have assessed the effect of group CBT. A randomized clinical trial that assigned 54 mild to moderately depressed patients to a combined CBT plus exercise condition vs. a CBT only condition found superior outcomes in suicidal ideation, depression, and activities of daily living in the combined compared to CBT only group. However, few studies could be found that compared group CBT, group exercise, and wait-listing for treatment as usual conditions. This is important in further delineating the effective components of treatment for mild to moderate depression, and results have implications for service delivery and clinical recommendations in the treatment of depression within healthcare organizations in Alberta and beyond. Specifically, patients with MDD referred to Addiction and Mental Health Clinics in Edmonton Zone may wait for weeks before receiving individual treatment. Thus, if found to be effective, group treatment conditions examined in this study may serve as an expedient treatment avenue to decrease wait-list times for patients with MDD.

Aim and Objectives

The aim of the project is to conduct a three-arm randomized controlled pilot trial to evaluate the feasibility and initial efficacy of group CBT or group exercise on depression symptom scores and quality of life measures in patients with MDD. The client outcomes will be organized according to: functional variables (quality of life, employment), symptom variables (change in depressive symptoms scores), and service variables (e.g. patient compliance and retention in treatment and patient satisfaction).

Given the aim, the objectives of the project are to compare mean changes in recovery, functional outcomes, clinical symptoms, and service satisfaction variables after seven and fourteen weeks for participants in each of the three arms of the study: 1) those receiving group CBT plus wait-listed to receive TAU; 2) those receiving scheduled exercise plus wait-listed to receive TAU; and 3) those only wait-listed to receive TAU.

Hypothesis

The investigators hypothesize that participants enrolled in the group CBT or group exercise conditions while wait-listed to receive TAU will achieve statistically superior outcomes compared to participants only wait-listed to receive TAU on each outcome measure used. In turn, participants enrolled in group CBT plus TAU will have comparable outcomes to those enrolled in the group exercise plus TAU arm of the study.

MATERIALS AND METHODS

Overview of study design, timeline and participant selection

This study will be a longitudinal, prospective, parallel design, three-arm, rater-blinded randomized clinical trial with a recruitment period of six months and an observation period of 14 weeks for each participant. The study will be executed according to the timelines specified in the Gantt chart in Table1.

The research will be carried out in a municipal recreational centre as well as Addiction and Mental Health clinics in Edmonton, a large, socio-demographically diverse city in Western Canada. Potential participants will be recruited from the Addiction and Mental Health Intake Clinic in Edmonton. Patients with depression at intake assessment who are presumed to meet the inclusion criteria of the study will be invited to enroll in this study.

To confirm the diagnosis of MDD using the DSM 5 criteria, potential participants will be sent to the "Mood and Anxiety clinic" or "Urgent Clinics" in Edmonton where they will be assessed by one of a group of psychiatrists or psychiatry residents who are independent from the study team. The psychiatrist or resident may or may not initiate, continue or adjust pharmacotherapy. The diagnosis will be communicated to the study coordinator and clinic nurse. The participants with MDD will be informed of their eligibility to participate in the study and will be considered for randomization after providing informed consent whereas patients with other diagnoses will be informed of their exclusion from the study and will be directed to receive an appropriate treatment for their condition.

After diagnostic confirmation by a psychiatrist, a clinic nurse who is trained in study procedures will provide the potential participants with an information leaflet about the study and answer any related questions they may have. All potential participants who agree to take part in the study will provide written informed consent prior the completion of baseline assessment measures and randomization.

Patients who are 18 to 65 years of age, have been referred by a primary care provider or self-referred to the addiction and mental health intake service in Edmonton, have received a diagnosis of MDD from a consultant psychiatrist based on DSM 5 criteria, and have provided written informed consent will be included in the study. Patients will be ineligible if they do not meet the above inclusion criteria, have not provided informed consent, or have a diagnosis of Bipolar Disorder, Schizophrenia or Schizoaffective Disorder.

At baseline, demographic and contact information will be collected. The participants' name and contact information will also be collected but only used for future communication or for arrangement of treatment, assessment and follow-up sessions.

Participant's Medical Record will also be reviewed to gather information about the participant's use of health services 3 months prior to enrollment in the study and 3 months after study completion to compare pre-post service utilization and determine if participation in the

intervention group impacts the clients' use of other health services in the short term. This same data can also be used for any economic analyses (i.e., cost-effectiveness) that will be conducted.

All the data will be stored for a minimum of 7 years prior to destruction as per the research ethics board requirements, and research ethics board requirements pertaining to collection and storage of information will be followed.

Table 1: Gantt chart for group CBT and exercise project

		Year 1				Year 2	
		Start Date-End Date				Start Date-End Date	
Milestone No.	Milestones	Q1	Q2	Q3	Q4	Q1	Q2
Milestone 1: Setting up of infrastructure for group CBT and gymnasium							
1.1	Assembling of group CBT facilitators and setting of gymnasium in the community						
Milestone 2: The recruitment of study participants							
2.1	Recruitment, baseline assessment, randomization						
2.2	Assignment into one of the three arms of the study						
2.3	Delivery of group CBT or scheduled exercises or wait-listing for usual treatment						
Milestone 3: Follow-up assessment of study participants							
3.1	Follow-up assessments of individual study participants (Excluding satisfaction surveys)						
3.2	Follow-up satisfaction survey of participants all groups						
Milestone 4: Data compilation, analysis and preparation of reports, publications and presentations							
4.1	Data compilation						
4.2	Data Analysis						
4.3	Preparation of reports, publications and presentations						

Interventions

Participants enrolled in the group CBT plus TAU condition will be wait-listed to receive TAU and will receive a 2-hour session of group CBT every week for 14 weeks. Participants enrolled in the group exercise plus TAU arm of the study will be wait-listed for TAU and will receive 50 minutes of scheduled and facilitated exercises three times a week for 14 weeks. Participants in the TAU only arm of the study will be wait-listed to receive individual therapy or counselling from a therapist as per current standard protocol for managing patients with MDD at our centre. All above participants may or may not receive pharmacotherapy as prescribed by a psychiatrist who is independent from the study team.

Group CBT: The group CBT will be offered in Addiction and Mental Health Clinics of Edmonton at 3 sites: 108 St. Building, Hope and Wellness Centre, and College Plaza. All therapists will use a manualized CBT protocol with the same handouts and schedule developed based on the

book “Mind Over Mood”. It will be provided to a group of maximum 10 participants. Each session will be 2 hours long and will be provided by certified therapists with special training to deliver group CBT. The structure of the session will be agenda setting, check-in, review of homework, new concepts/skills, homework assignment, and feedback.

Group exercise: For scheduled group exercise, the research team will follow the current recommendations based on a literature review for the use of exercise for the treatment of depression, as well as Canadian Physical Activity Guide recommendations. Scheduled group exercises incorporate the following parameters:

Type – aerobic or strength training exercises

Dose – 3 times per week

Intensity- moderate [participant self-rated physical activity of a 5 or 6 on the Borg Perceived Exertion (BPE) scale of 10, relative to the individual’s personal capacity].

Time – 50 minutes per session with 3 sessions per week (150 minutes/week).

Duration – 14 weeks

Other - with supervision: Physical exercise sessions will be run by CanFit Pro or AFLCA certified Recreational Therapists who will assess safety of patients' involvement in physical activity using "Par-Q & You" questionnaire before initiation of the study and address any physical problems to minimize the risk of any adverse events happening during sessions. This form is a screening tool to determine safe participation in exercise. Participants identified as potentially at risk with physical activity will require clearance to participate by his/her medical doctor.

Participants will have an opportunity to choose from a variety of physical activities in order to facilitate a meaningful physical activity experience which is important for long term maintenance (Hargreaves et. al, 2017). Participants will have the opportunity to engage in three of the following fitness programs per week for fourteen weeks: Monday: Individual fitness for 50 minutes; Tuesday: Group exercise or individual fitness for 50 minutes; Wednesday: Aqua/swimming for 50 minutes; Thursday: Walking track and group exercise for 50 minutes; Friday: Pole walking or hiking according the season for 50 minutes

All participants must consent to participate in the study facilitated exercise groups to be considered in the study because supervision and guidance is required for safety and ensuring consistent results. During the trial they are encouraged to participate in the exercise options offered. If the participant engages in the exercise independently it will not be counted as one of their sessions. Once the trial is completed they will be supported to continue exercise options in the community. Participants will be provided with fitness passes and equipment as needed. It will be explained to the participant that although the expense of the equipment is subsidized by the study team to facilitate their participation, they do not have to participate because of this supportive act. They may keep the equipment should they decide to withdraw from the study at any point.

For each session, two Recreation Therapists will provide programming to a maximum of 20 participants. During the sessions the Recreation Therapists will provide participants with information regarding health, wellness, fitness training, and understanding exertion levels within exercise. Participants will be encouraged to participate at a moderate level of perceived exertion for the best results (5-6 on a 10-point scale). While engaging in the exercise programs the participants will be self-reporting intensity using a rating of perceived exertion scale to the facilitators. Each participant must attend at least 75% of programs (32 session out of 42 sessions) during the 14-week period to be considered as having completed the program and for data analysis purposes.

Sample Size

As this is a pilot study, the research will utilize data that can be elicited from participants who can be enrolled within existing operational resources and time frames. The study will therefore be limited to a sample size of 120, with about 40 patients recruited into each arm of the study.

Outcome Measures:

Outcome measures are detailed in Table 2. Primary outcomes include functional variables (quality of life, recovery, level of physical activity) and symptom variables (changes in depressive symptoms scores). Secondary client outcomes include service variables (e.g. satisfaction, health utilization).

Table 2 Outcome Measures

	Construct	Tool	Rater	Approximate Time Required	Time Points Assessed				
					At Enrollment	At Baseline	7 weeks	14 weeks	3 months after completion
Symptom Variables	Depressive symptoms	Beck Depression Inventory (BDI)	Client	5 min		X	X	X	
Functional variables	Quality of Life	WHOQOL-BREF (World Health Organization Quality of Life Brief instrument)	Client	10 min		X	X	X	
	Recovery	Recovery Assessment Scale (RAS)	Client	5 min		X	X	X	
	Physical Activity	International Physical Activity Questionnaire	Client	5 min		X	X	X	
Service variables	Patient Satisfaction with Service	Addiction and Mental Health Client Experience Survey	Client	5 min			X	X	
	Health Utilization	Data extraction	Research Team	-	X				X
			Total Time	Client		~25 min	~30 min	~30 min	

Randomization and Blinding

Randomization will be enacted via randomly generated codes. Each study participant will receive a randomization code. Because it will not be possible for participants to be blinded, treatment allocation will be made explicit to them as soon as randomization is concluded. Outcome assessors will be blinded to treatment group allocation by not involving them in discussions about study participants and not granting them access to the database that contains the randomization code. In addition, study participants will self-complete all outcome assessments with the assessor facilitating procedural aspects if needed. Moreover, these assessors will not be involved in data analysis. After data collection is complete all data will undergo a blind review for the purposes of finalizing the planned analysis.

Follow-up Assessment

At 7 and 14 weeks, a blinded researcher will contact all study participants and assist them in the completion of a range of assessment tools related to the primary and secondary outcome measures. The participants who are wait-listed to receive TAU will be assessed at 7 and 14 weeks from the time they are added to the wait-list even if they are not receiving any treatment at the time of assessment.

Statistical Methods

The primary goal of the statistical analysis will be to produce summary descriptive statistics for the longitudinal data, which will provide estimates for future sample size calculations and enable calculation of effect size. The data will be analyzed using repeated measures and effect size analyses, and correlational analyses will be completed between measures at each time point. The results of this study will guide the design for a future, more highly powered, study.

Patient and public involvement

The study was designed and finalized based on feedback from patient representatives. This randomized trial also offers patients the opportunity to provide feedback via the patient satisfaction survey.

ETHICS AND DISSEMINATION

The study will be conducted in accordance with the Declaration of Helsinki (Hong Kong Amendment) and Good Clinical Practice (Canadian Guidelines). Written informed consent will be obtained from each participant. The study has received ethical clearance from Health Ethics Research Board of the University of Alberta (Ref. # Pro 00080975) and operational approval from the regional health authority (AHS # 43638). The results will be disseminated at several levels, including patients, practitioners, academics/researchers, and healthcare organizations.

The investigators team will plan an organizational engagement strategy to advance discussions about feasibility and effectiveness prior to the conclusion of the trial. This will help ensure the findings are a relevant part of decision-making processes in a way that is aligned with study findings as they emerge. This may facilitate planning of a larger study that is endorsed at both leadership and operational levels, so that the potential benefits of the interventions can reach patients in a more timely fashion.

DISCUSSION

The results of the study will provide important information about the effectiveness of group CBT and/or group exercise in treatment of MDD. This will augment the literature in this area, and also provide practical benefits in examining if benefit can be derived from group treatment modalities. Currently, patients with MDD referred to Addiction and Mental Health Clinics in Edmonton Zone may wait for weeks before receiving care from a health care professional in a one-to-one setting. Long wait may negatively impact patients' well-being, personal and occupational function as well as their satisfaction with care, and a group-based treatment may serve as an alternative for patients with MDD that can be more expediently accessed.

The results of the pilot trial may inform the implementation of a multi-center clinical trial and provide useful information for administrators and clinicians who are interested in incorporating these interventions into existing care. The investigators expect that the pilot findings will inform and support administrative decision-making with respect to further scaling and studying the intervention within the province of Alberta and beyond.

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