Targeting Physical Health in Schizophrenia: Physical Activity Can Enhance Life Randomized Control Trial

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Clinical Protocol

Targeting Physical Health in Schizophrenia: Physical Activity Can Enhance life (PACE-Life) Randomized Controlled Trial (RCT)

Version 2.0

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ABBREVIATIONS AND DEFINITIONS OF TERMS

Abbreviation	Definition
6MWT	6-minute walk test
ACSM	American College of Sports Medicine
AE	Adverse Event
BMI	Body Mass Index
BPNES	Basic Psychological Needs in Exercise Scale
BREQ-2	Behavioral Regulation in Exercise Questionnaire-2
CRF	Cardiorespiratory fitness
CSQ-8	Client Satisfaction Questionnaire
CVD	Cardiovascular Disease
DSC	Data Safety Committee
DSM-V SCID	Structured Clinical Interview for DSM disorders
FDA	Food and Drug Administration
HRR	Heart Rate Reserve
IPAQ	Short Form International Physical Activity Questionnaire
NCPRC	North Carolina Psychiatric Research Center
OPTMH	Organization of Physical Therapy in Mental Health
PA	Physical Activity
Pace-Life	Targeting Physical Health in Schizophrenia: Physical Activity Can Enhance life
PACES	Physical Activity Enjoyment Scale
PAGEQ	Physical Activity Group Environment Questionnaire
PANSS	Positive and Negative Syndrome Scale PANSS
PAR-Q	Physical Activity Readiness Questionnaire

RCT	Randomized Control Trial
RHR	Resting Heart Rate
SAE	Serious Adverse Event
SDT	Self-determination Theory
SSD	Schizophrenia Spectrum Disorder
STEP	Schizophrenia Treatment and Evaluation Program
WAI-SR	Working Alliance Inventory (Group) – Short Form Revised
WASI	Wechsler Abbreviated Scale of Intelligence
WRAT	Wide Range Achievement Test

PROTOCOL SYNOPSIS

Study Title	Targeting Physical Health in Schizophrenia: Physical Activity Can Enhance life (PACE-Life)
Funder	National Institutes of Mental Health
Clinical Phase	Phase II
Study Rationale	The purpose of the PACE-Life trial is to develop and test the feasibility of an exercise intervention that combines group walking, activity tracking, and heart rate monitoring, and determine the effectiveness of this intervention on the physical and mental health for individuals with schizophrenia spectrum disorders.
Study Objective(s)	1. Feasibility- Can PACE-life be delivered within this treatment setting? 2. Tolerability- How well is PACE-life accepted by the subjects? 3. Intervention adherence 4. Evaluation of PACE-life
Test Article(s) *(If Applicable)*	Fitbits Charge 3 devices, worn on the wrist, will be utilized to track daily steps, minutes spent walking, and monitor HR throughout exercise sessions. These devices will also be used to facilitate the individualized/home-based component and goal-setting.
Study Design	This is a two arm (fitbit only vs. fitbit + exercise intervention group), randomized controlled trial with 56 subjects (multiple groups occurring consecutively ranging from 13-18 participants).
Subject Population key criteria for Inclusion and Exclusion:	<u>Inclusion Criteria</u> 1. DSM-V diagnosis of a SSD (Schizophrenia, Schizoaffective Disorder, Brief Psychotic Disorder, Schizophreniform Disorder, and Unspecified Schizophrenia Spectrum and Other Psychotic Disorder) 2. Between the ages of 18-65, both genders, and any ancestry; 3. IQ>70 and/or reading level at, or above the 4th grade. IQ will be assessed using the Wechsler Abbreviated Scale of Intelligence (WASI) and the Wide Range Achievement Test (WRAT). 4. No hospitalizations for psychiatric reasons in the last 3 months 5. Clinically stable (no psychiatric medication changes within the past month) 6. Are not already engaging in consistent moderate-intensity exercise (cutoff = 60 min/week for the past 6 months);

	7. Present with no contra-indication to engage in regular moderate intensity exercise based on the American College of Sports Medicine guidelines. (If an individual answers yes to one item on the of the Physical Activity Readiness Questionnaire (PAR-Q), she/he will be asked to get clearance from a physician prior to participating in the study) 8. Willing and able to provide informed consent. <u>Exclusion Criteria</u> 1. Pregnant women will be excluded because pregnancy alters autonomic and immune responsiveness, increase weight gain, and can influence heart rate.
Number Of Subjects	56 individuals with schizophrenia spectrum disorders
Study Duration	Each subject's participation will last 5 months, 4 months of intervention and a 1 month follow-up
Study Phases **Screening** **Study Treatment** **Follow-Up**	<u>Pre- Screening</u>- Will be completed prior to the first in-person visit via a telephone screen for study eligibility. <u>Screening</u>- Subjects who are deemed eligible will be brought on site, or virtually via HIPAA-compliant Zoom video call, to obtain consent and complete the screening assessments (Demographics, WASI/WRAT, a licensed physician will complete a medical history and physical exam, PAR-Q. <u>Baseline, Mid-point, Post-test, and 1-Month Follow-up</u>- Subjects will complete the Demographics, Minutes Spent Walking, the Positive and Negative Syndrome Scale (PANSS), the Short Form International Physical Activity Questionnaire (IPAQ), Steps/day, Cardiorespiratory fitness (CRF)- CRF will be measured using the 6-minute walk test (6MWT), Chair-Rise Task, 2-minute Step Test, Self-determination Basic Needs, the Basic Psychological Need Scale-in General, the Basic Psychological Needs in Exercise Scale (BPNES), Resting Systolic/Diastolic Blood Pressure and resting heart rate (RHR), autonomous motivation will be measured with the Behavioral Regulation in Exercise Questionnaire-2 (BREQ-2), enjoyment of walking will be measured with the Physical Activity Enjoyment Scale (PACES), the UCLA Loneliness Scale, Weight, BMI, and Waist/hip Circumference: study intervention/experimental treatment. CRF will also be calculated using an equation by Jackson, A. S., et al. 1990 (119) that includes recent weight and height for the calculation of BMI, gender, self-reported physical activity level, and age.

	At the baseline assessment, subjects will be provided with a Fitbit wristband and instructed how to use it. At the conclusion of the trial, investigators will administer a brief questionnaire to the subjects regarding satisfaction and acceptability. Study Treatment- Walking groups will occur twice per week for 30 minutes. The intensity of both group walks and home-based walks will increase throughout this intervention in a stepwise fashion to create an exercise dose response to maximize impact on CRF. During the COVID-19 pandemic, participants will participate in group walks via Zoom video meetings twice per week, starting at 15-minute sessions and progressing to 30-minute sessions, where group leaders will lead participants through exercise sessions.
Efficacy Evaluations	Primary outcome- 6MWT will be used to measure CRF during which individuals will be asked to walk continuously for six minutes on a flat, indoor surface around cones (separated by 100ft). Supplemental CRF measures will also be used. CRF will be calculated using an equation by Jackson, A. S., et al. 1990 that includes recent weight and height for the calculation of BMI, gender, self-reported physical activity level, and age. Finally, participants will complete the Chair-Rise Task, and the 2-minute Step Test to measure CRF. Secondary outcomes- Psychological- UCLA Loneliness Scale will be used to assess subjective feelings of loneliness. The PANSS will be utilized to assess psychiatric symptoms. Secondary outcomes- Biological- We will measure weight, BMI, and waist circumference at all in-person assessments. We will examine these characteristics to determine if they changed as a result of increasing exercise. Resting Systolic/Diastolic Blood Pressure and RHR will also be assessed following standardized procedures.
Safety Evaluations	A safety plan for the walking groups will be developed prior to the initiation of the study with Drs. Battaglini and Jarskog, as well as the study clinicians.
Statistical And Analytic Plan	Analyses will primarily be descriptive in nature. We will calculate means, standard deviations, and within-group effect sizes of the primary outcome (CRF) and secondary outcomes (loneliness, symptoms, weight, BMI, waist circumference, resting heart rate, and blood pressure). Additionally, we will examine means, standard deviations, and within-group effect sizes of intermediate targets (self-determination basic needs and autonomous motivation) and proximal outcomes (minutes spent walking and daily steps).

DATA AND SAFETY MONITORING PLAN	Dr. Jarskog will function as the Project Medical Officer. An independent physician will serve as the Medical Monitor (Dr. Karen Graham, from the Department of Psychiatry).

1 BACKGROUND AND RATIONALE

Individuals with schizophrenia spectrum disorders (SSDs) have a life expectancy up to 25 years shorter than individuals in the general population primarily due to elevated levels of chronic physical and medical illnesses (1-4). Premature mortality in this population may be explained by high levels of six known modifiable risk factors for mortality: high blood pressure, smoking, raised glucose, physical inactivity, obesity, and high cholesterol (5-7), with physical inactivity and smoking being the strongest contributors to this risk (8, 9). Specifically, cardiorespiratory fitness (CRF) impacts not only cardiovascular mortality but also all-cause mortality (10-13), including in individuals with SSDs. Thus, physical inactivity contributes to significantly elevated rates of chronic medical diseases, especially cardiovascular disease (CVD) in individuals with SSDs (1, 5, 6, 14, 15). Further, despite reductions in mortality from CVD in the general population over the past 20 years, rates in people with SSDs have remained high (16, 17). Indeed, sedentary behavior and poor CRF among individuals with SSDs relative to the general population (13, 18-21) are likely major contributors to the premature mortality in this at-risk population. As a result, the potential benefits of interventions that increase physical activity (PA) in this population are substantial and could have a meaningful impact on public health.

Studies examining the effects of exercise on physical and mental health in individuals with SSDs have yielded encouraging results (22-24). Indeed, well-designed multi-component interventions that target exercise and diet, such as the ACHIEVE trial and the In SHAPE program, led to weight-loss and improved fitness in individuals with serious mental illness (25-27). However, these findings are tempered by questions of long-term accessibility and sustainability. Specifically, the In SHAPE program involved individual meetings with a trainer and continued access to a gym, perks that are inaccessible to most individuals with SSDs after study completion (26, 28-33). While a strength of the ACHIEVE trial was housing it in psychiatric rehabilitation settings, not all people with SSDs have access to such programs. In addition, attendance at the intervention sessions waned after the first 6 months of the study, which the authors attributed to hospitalizations and social issues (19) (p. 1601); however, decreasing subject motivation may have also played a role.

Prior work has been largely unsuccessful in overcoming the many barriers faced by individuals with SSDs. Specifically, exercise participation is hampered by lack of access and cost (e.g. personal trainers), biological factors such as physical health problems, social variables such as loneliness and limited social support, and self-regulatory problems (e.g., forgetting to exercise, being overwhelmed) (34-43). And, most interventions fail to address motivation, a critical factor for initiating and sustaining exercise, particularly for people with SSDs (44). Ironically, even work that has directly targeted motivation in this population (45) observed difficulties in promoting long-term adoption and sustained exercise after the program ends (46). These findings speak to the need for additional strategies to sustain motivation and ensure the effective translation of motivation into action. Thus, interventions aimed at this population should be designed and delivered in ways that address the substantial barriers to exercise, so as to promote the adoption and long-term maintenance of physical activity (47, 48).

Given the importance of motivation and translating intentions to actions, our treatment model is rooted in both self-determination theory (SDT) (49, 50) and implementation intentions (i.e., if-then plans) (51). SDT is a prominent theory of motivation which is highly suited for exercise interventions (52). SDT posits that the fulfillment of three basic psychological needs: autonomy, relatedness, and competence facilitates autonomous motivation (i.e. motivation due to one's own choice rather than as a result of external factors) (50). Autonomous motivation, in turn, is associated with levels of exercise participation in the general population (52, 53) and in people with SSDs (54).

If-then plans have the structure if (opportunity/obstacle)-then I will (response) and engender associations that mimic the effects of habits (55). If-then plans create mental links between good opportunities to act and responses that move the person towards their exercise goal (e.g., If I have to go shopping for 1-2 items, then I will walk rather than drive to the store!") or between obstacles to exercise and responses that will be effective in overcoming those obstacles (e.g., "If I am tempted not to exercise, then I remind myself how proud I feel at the end of the session!"). Two separate meta-analyses revealed that if-then plans were highly effective in increasing physical activity [ES = .31 and.38] (56, 57)] and led to sustained behavior change one year (58-61) and two years (62, 63) post-treatment. If-then plans have also demonstrated effectiveness among samples with psychiatric and clinical diagnoses (64) including people with SSDs (65). Importantly, autonomous motivation and if-then plans are known to combine synergistically, and engender better outcomes compared to the use of either strategy on its own (66, 67).

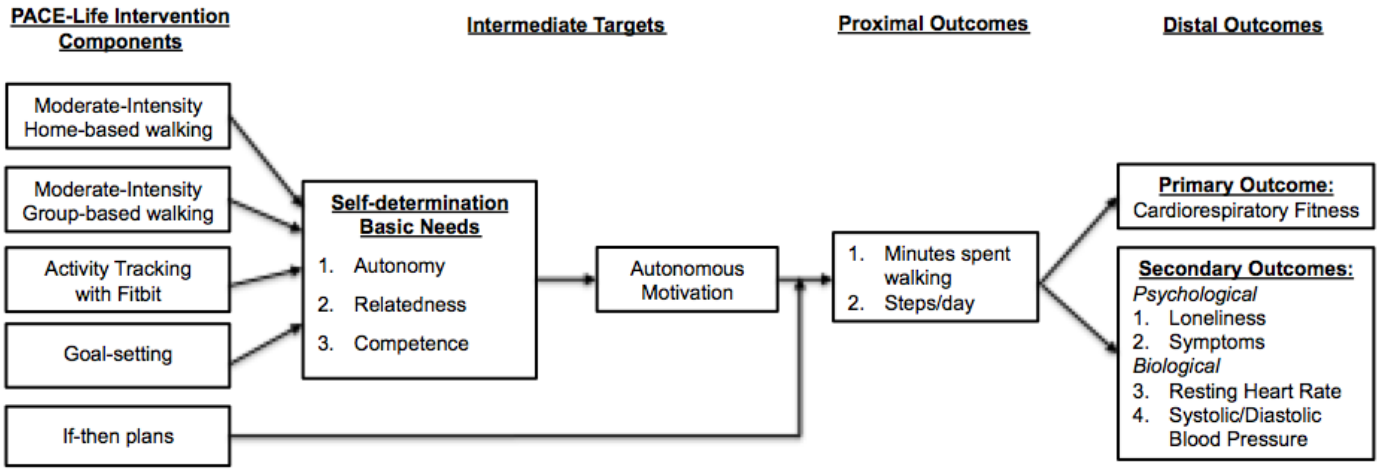
In addition to considering motivation and intention translation, we also sought to develop an exercise intervention that involves minimal staff resources, that is free and easy to access, and has the potential for long-term sustainability. Thus, we chose an intervention that requires no equipment or special training, and can be done anywhere: Walking (68, 69). Research has shown that walking leads to improved physical health, well-being, and weight loss (70-73). Furthermore, walking without dietary change has been shown to improve CRF (10, 74, 75), and reduce the risk of all-cause mortality (76), premature death (77), and the rate of cardiovascular disease (78) in the general population. Dose-response analyses have determined that the strongest health benefit accrues within the first 120 minutes per week of walking, further highlighting the potential impact of increasing PA among sedentary individuals (76). Moreover, given the widely accepted PA recommendations set forth by the American College of Sports Medicine (ACSM) (79) and by the International Organization of Physical Therapy in Mental Health (IOPTMH) (42), walking at a moderate-intensity level should be prioritized (See section C.3. for more details).

A valuable way to facilitate the initial engagement of exercise and address the barriers of social isolation in individuals with SSDs is through group-based interventions, as they promote social interaction, camaraderie, and social support (36-39, 80). Group-based interventions also impact motivation by offering the opportunity to develop friendships centered around a common goal, thus satisfying relatedness and competence needs and promoting self-efficacy (35). Walking programs in the general population that promote social support also led to greater maintenance of behavior change (81, 82). Therefore, social support (and reduction of loneliness) may play a critical role in helping individuals with SSDs initiate and adhere to exercise programs (35).

A critical component of goal setting and attainment is being able to monitor progress, which can be achieved via physical activity tracking devices. Pedometer use leads to an increase in PA – they are considered acceptable and are highly useful for setting PA goals (83-85), which helps to facilitate changes in exercise behavior (86). In fact, pedometers are the most cost-effective means of increasing PA in the general population (87). In a systematic review of 26 studies, pedometer use resulted in significant increases in PA (26.9% over baseline) (70). With recent advances in sensor and Bluetooth technologies, new physical activity monitors have emerged and are currently commercially available (e.g., Fitbit), which also allow the measuring of walking intensity (e.g., through heart rate; See Section C.3.).

Figure 1

Proposed Model



The model above illustrates how our proposed intervention, (PACE-Life) will lead to increased exercise and improved outcomes. Specifically, PACE-Life includes five primary components: home-based walking, group-based walking, activity tracking, goal-setting, and if-then plans, four of which impact the SDT basic needs and one of which enhances autonomous motivation. Specifically, homebased walking targets autonomy needs (as individuals can do this independently), group-based walking targets relatedness needs, and activity tracking and goal setting target competence needs. Satisfaction of each of the SDT needs leads to the intermediate target of increased autonomous motivation. PACE-Life subjects also form if-then plans which serve to enhance the impact of autonomous motivation (66, 67) and promote actual exercise behavior (56, 57). Engaging these intermediate targets in turn engenders the proximal outcomes of greater exercise participation (as measured by minutes spent walking per week and steps/day). Finally, increased exercise should lead to the improved primary outcome of CRF as well as improved secondary outcomes of loneliness, symptoms, resting heart rate, and systolic/diastolic blood pressure.

The proposed research is highly innovative in at least three respects. First, the simplicity and practicality of PACE-life is a key innovation. As noted above, most previous interventions for individuals with SSDs required gym equipment (e.g., treadmills) as well as professional supervision to engage in exercise, thus limiting both sustainability and scalability (22-24, 26). The field demands pragmatic interventions that are low in resource costs and can be rapidly translated into clinical practice (48, 88). Our walking intervention is both cost-effective and highly accessible given that the group-based portion will be implemented in the vicinity of the outpatient clinic and the home-based portion will be completed at locations selected by subjects (e.g., outdoors on residential streets or indoors at malls during inclement weather). Additionally, the COVID-19 pandemic has provided subjects an opportunity to participate in a virtual walking intervention. Though, technological inequities may serve as a barrier to overall feasibility outside of this intervention, providing subjects with technology (e.g., tablets and data plans) has further improved potential feasibility and scalability.

Second, the focus on cardiorespiratory fitness (CRF) is novel. Although CRF has long been identified as a significant predictor of health, it has only recently received attention in exercise intervention research among individuals with SSDs. A meta-analysis on the effects of exercise on CRF in individuals with SSDs (12) revealed only 3 published randomized controlled trials that examined this health indicator (32, 89, 90). Vancampfort and colleagues (13) concluded that despite the few available studies on CRF in schizophrenia,

improvements in this domain are possible and may provide a "novel and valid exercise target that could lead to reductions in premature mortality in people with schizophrenia" (p. 456). In addition, we will measure CRF in a cost-effective and feasible manner without the need for expensive equipment, further displaying our commitment to scalability and sustainability.

Third, the present research is conceptually innovative in targeting both motivation to exercise, and the effective translation of motivation into action. Previous interventions that focused merely on generating strong intentions to exercise have had little success (91) because the quality of motivation supporting these intentions was not addressed (92). PACE-Life is deliberately designed to engender high-quality (i.e., autonomous) motivation. However, even high-quality motivation may not equip people to deal effectively with problems that are inevitably encountered as they strive to exercise. These problems include failing to get started, becoming derailed by unwanted influences (e.g., distractions), and coping badly with unforeseen obstacles and lapses (51). If-then plans are an effective tool for dealing with each of these problems experienced by new exercisers (61, 93-95) and synergize the impact of autonomous motivation, helping to turn that motivation into action.

2 RESEARCH DESIGN AND METHODS

2.1 OVERVIEW

The project will consist of three primary phases: manual development, an open trial, and a small-scale RCT (See Table 1; Table 2 indicates updated project time based on the COVID-19 pandemic). These three phases will be iterative such that we will obtain and incorporate end-user feedback from clients and clinicians. Feedback from users will inform both the open trial and subsequently, the RCT.

Table 1 : Project Timeline

	Year 1												Year 2												Year 3											
Month	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	32	33	34	45	36
Manual Development																																				
Training of Clinical Staff																																				
Recruitment: Open Trial																																				
Open Trial																																				
Feedback & Manual Revisions																																				
Recruitment: RCT																																				
RCT: Cohorts 1, 2																																				
Recruitment: RCT																																				
RCT: Cohorts 3, 4																																				
Data Analysis & Manuscript Prep																																				

Table 2: Project Timeline (COVID-19 Updated)

	Year 1												Year 2												Year 3												Year 4: No Cost Extension											
Month	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	32	33	34	35	36	37	38	39	40	41	42	43	44	45	46	47	48
Manual Development																																																	
Training of Clinical Staff																																																
Recruitment: Open Trial																																																
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Recruitment: RCT																																																
RCT: Cohorts 3, 4																																																
Data Analysis & Manuscript Prep																																																

Rationale for clinic-based/home-based rather than a gym-based exercise intervention. We propose to provide PACE-life through a mental health clinic as individuals with SSDs usually have frequent contact with their providers. Furthermore, interventions that don't require additional equipment or supervision by an exercise trainer have greater potential for integration into healthcare services for individuals with SSDs. Our rationale for a clinic-based versus a gym-based exercise program is also based upon recommendations for integrated medical care (104) as well as integrated physical activity within mental health services for this population (105). In addition to clinic-based sessions, we will include home-based sessions, which can be completed at any location and time of the subjects' choosing to improve self-management and facilitate long-term exercise adoption. The term, "home-based," means only that individuals will be engaging in this component independently and do not need to attend a select location or require additional equipment. We will work with subjects to identify convenient walking routes using websites and apps (e.g. map my walk). Therefore, our intervention will include both clinic-based sessions and instructions for home-based sessions to prioritize feasibility and sustainability. Moreover, given the disruption of the COVID-19 pandemic, we've re-designed our study to have feasibility in a virtual format. Subjects can participate in the study from their homes, as we provide them with technology (e.g., tablets and data plans) necessary for participating in virtual exercise sessions. Exercise sessions include dynamic, stationary exercises that model walking movements, to best match movements performed in outdoor walking sessions. These obstacles have provided the research team with an opportunity to learn about the sustainability and scalability of home-based virtual interventions, in addition to clinic-based interventions.

Rationale for moderate-intensity walking as exercise modality. Walking is the primary form of exercise in PACE-life given its accessibility and association with meaningful fitness and health outcomes. PACE-life will combine walking groups and Fitbit with heart rate monitoring to encourage moderate-intensity walking in individuals with SSDs. The goal of PACE-life is to facilitate engagement in 150 min/week of moderate- intensity walking spread throughout the week, which is consistent with recommended fitness guidelines set forth by the ACSM (79) and by the IOPTMH (42). To achieve this goal, we will employ a stepwise approach of exercise participation to provide individual tailoring and reduce the likelihood of dropouts (103). Specific details and rationale of this approach are discussed below:

Overview and rationale of stepwise approach. Stepwise approaches to exercise participation are often recommended for use with sedentary populations to reduce the risk of injury and dropouts (32, 103). Typically, these interventions will begin at low intensity and low frequency, and as individuals become more physically active, the intensity and frequency increase. This strategy is especially relevant to individuals with SSDs as they are quite sedentary and have little experience with consistent participation in exercise. Furthermore, individuals need to engage in moderate-intensity exercise, defined as exercising within 60-70% of heart rate reserve (HRR), in order to achieve meaningful changes in CRF (103). In sedentary individuals, moderate to high intensity exercise may not be achievable immediately in the first weeks of the program and starting physically deconditioned individuals in a program that is too intense can be physically dangerous and lead to significant dropouts (103, 106). As a result, a step-wise approach that begins at a lower-intensity and increases to moderate intensity is more appropriate and has been successfully implemented in SSDs (32, 89). For the present study, low and moderate intensity exercise will be operationalized by HRR (103, 106) where Low-intensity Exercise = 50-60% of HRR and Moderate-intensity exercise = 60-70% of HRR.

We (Battaglini, PI) demonstrated the potential benefits of a step-wise exercise program in African-American breast cancer survivors that began at a low intensity and later progressed to moderate intensity (107). The results showed a high completion rate (76%) and adherence to walking goals (70%).

2.2 SUBJECTS

Based on the grave health concerns, physical inactivity, and growing urgent calls for action in individuals with psychotic disorders (116, 117), 56 study subjects will be recruited from various clinics in the Durham, Carrboro, Chapel Hill, and Raleigh area including, the UNC Schizophrenia Treatment and Evaluation Program (STEP) clinic in Raleigh and Carrboro, the Outreach and Support Intervention Services (OASIS) program in Chapel Hill, Carolina Behavioral Care, Club Nova, and Threshold. All subjects will have a primary diagnosis of a schizophrenia spectrum disorder. To obtain an estimate of IQ and to rule out any individuals with possible mental retardation, we will administer the WASI, which is comprised of Matrix Reasoning, Vocabulary, Similarities, and the Block Design subtests. During the COVID-19 pandemic, we will also administer the WRAT to test the reading level of participants. Additional demographic and clinical information that will be collected as self-report for possible use as covariates includes: 1) demographics: age, sex, ancestry, education, parent education; 2) health: smoking, substance use, current medications, duration of outpatient treatment, diet, physical activity, height, weight, BMI, and waist and hip circumference.

2.2.1 INCLUSION CRITERIA

1. DSM-V diagnosis of a Schizophrenia Spectrum Disorder (Schizophrenia, Schizoaffective Disorder, Brief Psychotic Disorder, Schizophreniform Disorder, and Unspecified Schizophrenia Spectrum and Other Psychotic Disorder)
2. Age 18 or above, both genders, and any ancestry
3. IQ>70; Reading Level > 4^{th} Grade
4. No hospitalizations in the last 3 months
5. Clinically stable (no medication changes within the past month)
6. Are not already engaging in consistent moderate-intensity exercise (cutoff = 60 min/week for the past 6 months)
7. Present with no contra-indication to engage in regular moderate intensity exercise based on the ACSM guidelines (118). If individuals answer yes to one or more items on the of the PAR-Q, a questionnaire that assesses cardiovascular risk factors, she/he will require further evaluation by a physician prior to participating in the study
8. Willing and able to provide informed consent.

2.2.2 EXCLUSION CRITERIA

1. Pregnant women will be excluded because pregnancy alters autonomic and immune responsiveness, increase weight gain, and can influence heart rate.

3 ASSESSMENT OF DATA

At this stage of treatment development, specific outcomes include:

1. Feasibility (Can PACE-life be delivered within this treatment setting?)
    - Will determine if recruitment procedures yield the target number of subjects in 3 months
    - Will determine feasibility of assessments based on subject compliance rates
2. Tolerability (How well is PACE-life accepted by the subjects?)

- Will be evaluated by examining subject attendance to groups, adherence to homebased component of program, Fitbit usage, and dropout rates.

3. Intervention adherence
4. Evaluation of PACE-life. We will evaluate feasibility in two ways. First, we will determine if recruitment procedures yield the target number of subjects in 3 months. Second, we will determine feasibility of assessments based on subject compliance rates. The tolerability of PACE-life will be evaluated by examining subject attendance to groups, adherence to homebased component of program, Fitbit usage, and dropout rates.

3.1 OUTCOMES

The central hypothesis is that an intervention that increases physical activity as measured by minutes spent walking (at the prescribed intensity) and steps/day will result in improved health and lowered risk for premature mortality as evidenced by superior CRF (primary outcome), and on a variety of secondary outcomes (e.g. blood pressure). Guided by strong preliminary data and grounded in SDT, this hypothesis will be tested via three specific aims:

1. To develop a manual-based walking intervention for individuals with SSDs: PACE-Life. The manual will include guidelines for goal setting and translating intentions into behaviors (i.e., "if-then" plans), instructions for the group-based walking activity and home-based walking activity (which includes Fitbits), and increasing exercise intensity in a step-wise manner.
2. To examine the feasibility of implementing PACE-life at a community mental health clinic, and in a home-based virtual capacity, in a randomized controlled trial of 56 individuals with SSDs.
3. We will also examine the impact of PACE-life on intermediate targets (autonomous motivation and SDT needs), proximal outcomes (minutes spent walking and steps/day), the primary outcome of CRF, and secondary outcomes.

We hypothesize that PACE-life will be associated with:

- Improved proximal and primary outcomes including greater minutes/week spent walking and steps/day and increased CRF at mid-treatment (3 months), post-test (6 months), and one-month follow-up;
- Decreases in secondary outcomes including loneliness, SSD symptoms, resting heart rate, and blood pressure at mid-point, post-test, and one-month follow-up.
- Higher levels of theoretically-relevant, intermediate targets (autonomous motivation and SDT needs) at mid-treatment, post-test, and one-month follow-up.

4 STUDY DESIGN

During this phase of the trial, 56 subjects will be assigned to the fitbit only group (control) or the PACE-Life walking group (intervention). The exercise intervention, PACE-Life, will last for 16 weeks and includes both group walks and independent walks (done at a location of the subject's choosing). Subjects will be asked to complete a total of 5 in-person, or virtual assessments at screening, baseline, mid-point, post-test, and 1-month follow-up.

4.1 INTERVENTION

Groups will occur twice per week, starting at 15-minute walking sessions, and increasing to 30 minutes sessions over the course of the intervention. The intensity, of both group walks and home-based walks will increase throughout this intervention in a stepwise fashion to create an exercise dose response to maximize impact on CRF. The rationale for this plan hinges on both the importance of maintaining cohesion and social interaction as well as the practicality concerns regarding sustainability. Furthermore, we tested a 2x/week group schedule in the pilot with high attendance rates and feedback (overall attendance: 84%). The overviews of in-person and virtual formats are given below:

Weeks	# of Clinic-based Group Sessions	Duration of Group Sessions	# of Home-based Sessions	Duration of Home-based Sessions	Intensity
1-3	2	30 Minutes	0	30 Minutes	50-60% of HRR
4-6	2	30 Minutes	0	30 Minutes	50-65% of HRR
7-9	2	30 Minutes	1	30 Minutes	60-65% of HRR
10-12	2	30 Minutes	1	30 Minutes	65-70% of HRR
13-15	2	30 Minutes	2	30 Minutes	65-70% of HRR
16-18	2	30 Minutes	2	30 Minutes	65-70% of HRR
19-21	2	30 Minutes	3	30 Minutes	70% of HRR
22-24	2	30 Minutes	3	30 Minutes	70% of HRR

Week	# of Virtual Group Sessions	Links to Virtual Group Sessions	Duration of Virtual Group Sessions	# of Independent Walks	Duration of Independent Sessions	Intensity	R Pe Ex (
1	2	1st group: https://www.youtube.com/watch?v=cvrcgZ25MWw 2nd group: https://www.youtube.com/watch?v=iBAjNQODSVo	15 minutes	0	15 minutes	50-60% of HRR	
2	2	1st group: https://www.youtube.com/watch?v=tW9IY48x1bc 2nd group: https://www.youtube.com/watch?v=u08lo0bESJc	15 minutes	0	15 minutes	50-60% of HRR	
3	2	1st group: https://www.youtube.com/watch?v=wQrV75N2BrI 2nd group: https://www.youtube.com/watch?v=-SSYX8sIOmM	20 minutes	1	20 minutes	50-65% of HRR	
4	2	1st group: https://www.youtube.com/watch?v=kqaNUjTR70A 2nd group: https://www.youtube.com/watch?v=m9yI2LGZRE0	20 minutes	1	20 minutes	50-65% of HRR	
5	2	1st group: https://www.youtube.com/watch?v=kqaNUjTR70A 2nd group: https://www.youtube.com/watch?v=UhpOl71brYI	20 minutes	1	20 minutes	60-65% of HRR	
6	2	1st group: https://www.youtube.com/watch?v=UXS_fFeGAlc 2nd group: https://www.youtube.com/watch?v=0KPpICARPGQ	20 minutes	1	20 minutes	60-65% of HRR	
7	2	1st group: https://www.youtube.com/watch?v=_UabUNrjSE4 2nd group: https://www.youtube.com/watch?v=GfiL9jPXMFE	25 minutes	2	25 minutes	60-65% of HRR	

8	2	1st group: https://www.youtube.com/watch?v=v4YyCdTf9BM 2nd group: https://www.youtube.com/watch?v=RImvimPo5u0	25 minutes	2	25 minutes	60-65% of HRR	
9	2	1st group: https://www.youtube.com/watch?v=hXhudyDRX8M 2nd group: https://www.youtube.com/watch?v=baO6jTGmNFs	25 minutes	2	25 minutes	60-65% of HRR	
10	2	1st group: https://www.youtube.com/watch?v=RP0Q8geTcJc 2nd group: https://www.youtube.com/watch?v=vUQXg5V7y2Q	30 minutes	2	30 minutes	60-65% of HRR	
11	2	1st group: https://www.youtube.com/watch?v=enYITYwvPAQ 2nd group: https://www.youtube.com/watch?v=jf1Q8nep6JU	30 minutes	2	30 minutes	60-65% of HRR	
12	2	1st group: https://www.youtube.com/watch?v=p2ggHwtb-Zg 2nd group: https://www.youtube.com/watch?v=R3AUw3-jtEo	30 minutes	2	30 minutes	60-65% of HRR	
13	2	1st group: https://www.youtube.com/watch?v=l5uilZNoaAU 2nd group: https://www.youtube.com/watch?v=HSoDitXs35w	30 minutes	3	30 minutes	65-70% of HRR	
14	2	1st group: https://www.youtube.com/watch?v=kp67VFhbpsQ 2nd group: https://www.youtube.com/watch?v=uUki7XMG0iA	30 minutes	3	30 minutes	65-70% of HRR	
15	2	1stgroup: https://www.youtube.com/watch?v=enYITYwvPAQ&list 2nd group: https://www.youtube.com/watch?v=RP0Q8geTcJc	30 minutes	3	30 minutes	65-70% of HRR	
16	2	1st group: https://www.youtube.com/watch?v=p2ggHwtb- 2nd group: https://www.youtube.com/watch?v=wwn3YJyOzdY	30 minutes	3	30 minutes	65-70% of HRR	

PACE-life will be integrated into the STEP outpatient clinics in Raleigh, NC and Carrboro, NC. The group walks will occur in the surrounding area around the clinics on sidewalks, bike trails, and residential streets. Goal setting groups and all assessments will take place in a conference room at the clinic. Virtual walking sessions will take place on the UNC HIPAA and Security-compliant Zoom video calls and can be completed at subjects' homes.

4.1.1 GOAL-SETTING

Goal-setting will include setting goals for the upcoming week in terms of number of steps as well as how many intensity walks (at specified heart rate) that individuals plan to complete. Goal-setting materials draw upon SMART (specific, measurable, achievable, relevant, and time-based) principles as well as implementation intentions (i.e., if-then plans) and mental contrasting. Specifically, subjects will be asked to imagine what the best thing would be about walking/exercise more and then identify the biggest barriers. They will then be encouraged to create if-then plans about how to manage barriers to exercising more. This procedure has been extensively examined in social psychology research and has been shown to be successful in helping individuals increase their exercise (93). Goal-setting groups will be audiotaped and subsequently coded for fidelity to the protocol.

4.1.2 FITBITS

All subjects will be provided with a Fitbit that is labeled with a subject number. All Fitbits are paired to a Fitbit account with the username (pacelifeIDnumber@gmail.com) and password (pacelife; or

PacelifeIDnumber!). Data from Fitbit devices can be synced to the corresponding account and accessed through Fitbit.com. Subjects will be provided information about their accounts should they want to look at the data but will be asked not to change any of the settings as we will be using data for tracking steps/day and minutes spent walking. No identifying information will be inputted in the Fitbit.com account for subjects.

4.1.3 Tablets & Data Plans

All subjects assigned to the PACE-Life group will be given a tablet labeled with their subject number. If subjcets do not own a smartphone or personal computer, they may use the tablet for syncing their Fitbit devices. . The tablets will also be used to join virtual walking sessions. Subjects will be provided information about their devices but will be asked not to change any of the settings (or download new apps). No identifying information will be inputted in the subjects' tablet. Additionally, subjects who do not have reliable wifi in their homes, will be given a monthly data plan to ensure proper connectivity throughout the study.

4.2 STUDY PROCEDURES AND MEASUREMENTS

4.2.1 SCREENING VISIT

The following measures will be examined at screening:

- Demographics- We will collect information on age, sex, ancestry, education, parent education, smoking, substance use, current medications, duration of outpatient treatment, and diet.
- Intelligence- In adherence with our inclusion criteria that subjects must have an IQ greater than 70, the Wechsler Abbreviated Scale of Intelligence (WASI) will be administered. Subjects participating during the COVID-19 pandemic must have a reading level above the 4th grade, the Wide Range Achievement Test (WRAT) will be administered.
- Medical History- A licensed physician will complete the Medical History and Physical Exam Form. They will also complete a 10 minute physical to ensure health. Subjects participating during the COVID-19 pandemic will receive medical clearance from a General Practitioner (GP). Medical Clearance forms will be sent to and received from providers through the EPIC system.
- Current Physical Activity- In order to ensure that subjects are healthy enough to begin the walking program, subjects will complete the Physical Activity Readiness Questionnaire (PAR-Q).
- Diagnosis-The Mini International Neuropsychiatric Interview (MINI) will be utilized to assess symptoms. The MINI is a semi-structured interview that assesses for DSM diagnoses. The MINI will be used to verify that subjects have a schizophrenia spectrum diagnosis before they are enrolled in the study. Raters will be trained to conduct the MINI to a gold standard of reliability (i.e., intraclass correlation > .80).

4.2.2 BASELINE, MID-POINT, POST-TEST, 1 MONTH FOLLOW-UP

The following measures will be examined at the baseline, mid-point, post-test, and 1 month follow-up study visits:

- Demographics- We will collect information on age, sex, ancestry, education, parent education, smoking, substance use, current medications, duration of outpatient treatment, and diet.
- Minutes Spent Walking- We will utilize data recorded from Fitbits to assess minutes spent walking (by syncing Fitbits to corresponding Fitbit.com accounts and loading deidentified data onto study laptops).

- The Short Form International Physical Activity Questionnaire (IPAQ), a valid self-report measure, to assess changes in physical activity. The IPAQ Short Form is a four-item scale that assesses frequency and duration of walking, moderate-intensity exercise, vigorous-activity exercise, and sitting.
- Steps/day. We will also collect daily step numbers using Fitbit data downloaded onto study laptops from Fitbit.com at group sessions.
- Cardiorespiratory fitness (CRF)- CRF will be measured using the 6-minute walk test (6MWT) during which individuals are asked to walk continuously for six minutes on a flat, indoor surface around cones (separated by 100ft) and the primary outcome is the total distance walked. The 6MWT is recommended for use with sedentary individuals and to evaluate the impact of an exercise intervention. Moreover, the 6MWT has been successfully administered to individuals with SSDs, including those in our pilot trial. As a result, we plan to utilize the 6MWT as our primary measure of CRF. Supplemental CRF measures will also be used. CRF will be calculated using an equation by Jackson, A. S., et al. 1990 (119) that includes recent weight and height for the calculation of BMI, gender, self-reported physical activity level, and age. Finally, participants will complete a Chair-Rise Task, where subjects will sit and stand from a chair for 30 seconds, and the 2-minute Step Test, where subjects will walk in place with their knees raising to hip-height, to measure CRF.
- Self-determination Basic Needs. The self-determination basic needs of autonomy, relatedness, and competence will be measured with two scales. The Basic Psychological Need Scale-in General is a self-report measure that assesses general satisfaction with autonomy, relatedness, and competence. Three subscale scores are produced. The Basic Psychological Needs in Exercise Scale (BPNES) is self-report scale that measures the extent to which basic needs are satisfied through exercise.
- Symptoms- the Positive and Negative Syndrome Scale (PANSS) will be utilized to assess symptoms specifically present in schizophrenia spectrum disorders. The PANSS is a semi-structured interview assessing positive symptoms, negative symptoms, and general psychopathology symptoms. Raters will be trained to conduct the PANSS to a gold standard of reliability (i.e., intraclass correlation > .80)
- Resting Systolic/Diastolic Blood Pressure and RHR will be assessed following standardized procedures at the STEP clinic. Individuals with SSDs will be placed in a sitting position in a quiet room, with lights dimmed, and will be asked to remain quiet and relaxed with their eyes closed while avoiding movement for approximately 10 minutes. After 10 minutes, research team members will assess their RHR via palpation for 1 minute. Following the assessment of RHR, resting BP will be assessed using an automated blood pressure device following the manufacture standard procedures. Given the high rates of hypertension in this population, the assessments of blood pressure changes throughout this exercise intervention are significant indicators of potential benefits of exercise on improvements in physical health. Further, given the sedentary lifestyle of many individuals with SSD, changes in RHR upon the initiation of exercise is a valuable indicator of fitness and physical health. Due to COVID-19, all subjects completing virtual study visits will have these measures assessed at their homes, on UNC-CH campus (Fetzer Hall), or at the Wake STEP Clinic in Raleigh, NC.

- Autonomous Motivation- Given the available research indicating that autonomous motivation is related to negative symptoms and subsequent engagement, maintenance, and adoption of exercise in individuals with SSDs, we will measure this construct with The Behavioral Regulation in Exercise Questionnaire-2 (BREQ-2).
- Enjoyment of Walking- Given that enjoyment of the walking program can impact adherence to the treatment, we will measure this construct with the Physical Activity Enjoyment Scale (PACES).
- Planned Behavior- Available research has shown that intentions, self-efficacy, attitudes and norms are correlated to adherence in exercise. All items are derived from established measures of theory of planned behavior variables (e.g., Conner & Sparks, 2015). Responses are all on 7-point scales. The order of items would be randomized.
- Loneliness: The UCLA Loneliness Scale is a brief self-report measure that will be used to assess this construct.
- Weight, BMI, and Waist/hip Circumference- We will measure weight, BMI, and waist/hip circumference at all assessments using the scale and measuring tape located at the STEP clinic.
- Exit Surveys on PACE-life- At the conclusion of the open trial, we will administer a brief questionnaire to the subjects regarding satisfaction and acceptability that will have both forced choice and open-ended questions (End of Study Survey & CSQ-8).

5 STATISTICAL ANALYSES

5.1 DATA ANALYTIC PLAN

Feasibility will be defined by our ability to meet our recruitment targets (56 people), frequency of engagement in the intervention by participants (group attendance and activity tracking/home-based adherence), and feedback on the intervention from participants. Feedback from participants will be incorporated into modifying the manual for the RCT and/or future interventions.

Analyses of intermediate and primary outcomes will primarily be descriptive in nature. We will calculate means, standard deviations, and within-group effect sizes of intermediate targets (SDT needs and autonomous motivation), proximal outcomes, including minutes spent walking, and steps/day, the primary outcome of CRF, and the secondary outcomes including RHR, blood pressure, loneliness, and symptoms. Further, we will calculate the percentage of the sample meeting the threshold for clinically significant changes in our outcomes of 6MWT, steps/day, and minutes spent walking to determine whether these changes are clinically meaningful. Finally, we will explore the relationship between baseline IQ, treatment adherence and outcome improvement so as to determine if cognitive functioning is associated with treatment response.

5.2 POWER ANALYSIS

Power was estimated using Optimal Design Software. Assuming n=56 (28 per group), alpha=05, and the covariate accounted for 50% of variance, the proposed study has reasonable power to detect an effect size of .50 or larger in comparison of the groups at the end of treatment or follow-up and of .75 or larger in comparisons of the size of change over time. Thus, this study has good power to detect the types of differences detected in pilot study (ES of .50-1.03 in steps, .33-.40 in six-minute walk test, .54-.83 for BP and .52-1.09 for symptoms).

5.3 DATA MANAGEMENT

All data will be entered by trained research assistants using REDCap software. Double data entry will be required for information not directly entered by the participants. Double data entry will also be entered by trained research assistants using REDCap software. All data analysis will be conducted by statistician, Oscar Gonzalez.

6 RISKS AND BENEFITS

There are some risks associated with the proposed research. First, collection of the clinical information may be associated with anxiety or embarrassment due to revealing personal information. Second, there is the risk that confidential personal information could be disclosed to others outside of the research staff. Third, there is risk in participating in the 6-minute walk test, Chair-Rise task, and 2-minute Step Test as a measure of cardiorespiratory fitness (CRF). Finally, there is risk associated with participating in the walking groups, such as ankle, leg, and back injuries, and cardiovascular distress.

6.1 Monitoring Risks

To address subject anxiety or embarrassment due to revealing person information, we have trained research staff who are experienced in working with individuals with schizophrenia spectrum disorders. They have been trained to put subjects at ease, let them take their time, and to conduct interviews in private rooms.

To address the issue of accidental disclosure of personal information to others outside of the research staff, we will obtain a NIH Certificate of Confidentiality for the study. In addition, identifying research subjects by study number on all research documents minimizes the risk of breach of confidentiality. Study documents that must contain personal information, including the informed consent document, and the document that links study ID number to personal identifying information (necessary due to the longitudinal nature of the open trial and RCT) are kept in locked filing cabinets in locked rooms. Research data will be kept on password-protected drives, and our computer systems are HIPAA compliant. All study staff participate in annual human subject training that includes education about responsibilities to minimize risk that confidentiality may be breached.

To address the potential health risk associated with participation in the walking groups as well as the 6-minute-walk-test, chair-rise task, and 2-minute step test, all subjects will obtain medical clearance from their general practitioner, or have a medical history and physical examination performed by Dr. Jarskog as part of the Screening procedures. Dr. Jarskog and/or a trained research assistant will also administer the PAR-Q, a widely used questionnaire to assess cardiovascular risk factors in advance of exercise initiation. For any subject who answers “yes” to one or more items on the PAR-Q, Dr. Jarskog and/or a trained research assistant will contact their PCP to discuss appropriateness for the subject to participate and help facilitate further evaluation as needed. In addition, the research staff will be trained by one of the PIs, Claudio Battaglini, an exercise physiologist, on the 6-minute-walk-test, chair-rise task, and 2-minute step test procedures. Further, if an individual shows any distress during this assessment, she or he will be instructed to stop the assessment and the research staff will contact Dr. Battaglini and Dr. Jarskog.

To address the issue of physical injury or cardiovascular distress during the walking groups, the study clinicians will be trained by Dr. Battaglini on potential cardiovascular warning signs, and appropriate responses to any reported symptoms. Further, a safety plan for the walking groups will be developed prior to the initiation of the study with Drs. Battaglini and Jarskog, as well as the study clinicians. The walking groups will be conducted on level terrain, to minimize any potential leg, ankle or back injuries. Finally, it should be emphasized that this project is testing the impact of moderate-intensity walking, a less physically demanding and inherently safer activity when compared to other more rigorous activities that could pose greater cardiovascular and joint-related risks.

Should any subject experience any problems during the study, our research team has trained staff that will be able to provide immediate care on-site. Subjects will be referred for additional care to the appropriate

providers on campus, such as Campus Health Services or the UNC Hospitals Emergency Department, if necessary.

6.2 NON-SIGNIFICANT RISK DOCUMENTATION

Pregnant women will be excluded because pregnancy alters autonomic and immune responsiveness, increase weight gain, and can influence heart rate.

6.3 POTENTIAL BENEFITS OF THE RESEARCH TO SUBJECTS AND OTHERS

The subjects who participate in the walking groups (in the open trial and RCT) may have a significant benefit on their cardiorespiratory fitness, which could have a subsequent impact on their overall physical and mental health. This study will provide currently unavailable information about the potential feasibility and effectiveness of a scalable and accessible exercise intervention for individuals with schizophrenia spectrum disorders. The risks of the study are minimal and reasonable in light of the knowledge gained.

6.4 CONFIDENTIALITY OF DATA

Risks regarding confidentiality will be minimized by using code numbers instead of names on study data. The code and the data will be stored in separate locked files at Davie or Howell Hall on UNC's campus. Similar subject records are scrutinized regularly and our procedure will add an extra level of protection because the research case numbers will be different from subject numbers (random numbers not associated with date of birth) and the code will be unavailable to anyone outside of the research team. Audio recordings of weekly group sessions will be saved on our secure lab server and on OneDrive so that offsite investigators may review and provide feedback to the clinicians conducting the sessions.

Identifiable data will only be shared with the clinicians of subjects in the study with the permission of the subjects (obtained during informed consent). Clinicians will be contacted if issues arise related to safety during the trial. As part of the informed consent process, all subjects will provide the name and contact info of a clinician that we may contact if we become concerned about their safety (e.g., physical and/or mental health) during the course of the trial. We will not be sharing any confidential information with anybody outside of these clinicians.

Identifiable data will be maintained for 5 years following study completion. At that point, hard copies of identifiable data including consent forms and contact information will be shredded. Electronic data will be de-identified upon entry, with the exception of the subjects' birth dates for the purposes of calculating their exact age.

7 DATA SAFETY AND MONITORING PLAN

7.1 ADVERSE EVENTS

Dr. Jarskog (Co-I) will function as the Project Medical Officer and will be available on pager and cell phone to all co-investigators to discuss any safety issue that emerges over the course of the study. All adverse events (AEs) occurring during the course of the study will be documented and reported to Dr. Jarskog. All Serious Adverse Events (SAEs) will also be reported to the IRB and NIMH. The occurrence of AEs will be assessed during the study and the investigators will follow all AEs to the point of satisfactory resolution. An independent physician will serve as Medical Monitor (Dr. Karen Graham, from the Department of Psychiatry). AEs will be tracked over the course of the study and will be reported at the midpoint and endpoint of each walking group cohort to the DSC. All SAEs will be reported to the DSC within 24 hours of learning of the event.

7.2 SERIOUS ADVERSE EVENTS

AEs will be assessed to determine if they meet criteria for a SAE. SAEs, as defined by the FDA, will be systematically evaluated at each clinic visit. Any SAE will be reported to the IRB and NIMH. The initial SAE report will be followed by submission of a completed SAE report to each institution. In the event that a subject either withdraws from the study or the investigator decides to discontinue a subject due to SAE, the subject will have appropriate follow-up and/or stabilization. Follow-up will continue until the problem requiring hospitalization has resolved or stabilized with no further change expected, is clearly unrelated to study procedures, or results in death. Outcome of SAEs will be periodically reported to NIMH. A summary of the SAEs that occurred during the previous year will be included in the annual progress report to NIMH.

The trial period is defined from the time that the informed consent document is signed until 30 days after the last study visit. All serious AE's occurring during the trial period (including death due to any cause) or within 30 days after the last study visit will be communicated within 1 day of the investigator becoming aware of the event to designated personnel, using the telephone or fax numbers provided in the Study Reference Manual. Any fatal or life-threatening AE's will be reported immediately, but no longer than 1 day from the time the investigator becomes aware of the event. A causality assessment will be provided for all SAEs. Critical follow-up information on SAEs will be provided as soon as it is available, but no longer than 1 day from the time the investigator became aware of the information. Other essential, but not critical, information may be reported within the following 5 days. An SAE, as defined by the FDA for use in clinical trials https://www.fda.gov/safety/medwatch/howtoreport/ucm053087.htm), is an adverse event that satisfies any of the following criteria:

- Results in death.
- Is immediately life-threatening, including potentially life threatening suicidal behavior or suicidal behavior that results in hospitalization.
- Requires inpatient hospitalization or prolongation of existing hospitalization.
- Results in persistent or significant disability or incapacity.
- Is a congenital abnormality or birth defect.
- Is an important medical event that may jeopardize the subject or may require medical intervention to prevent one of the outcomes listed above. Examples would include allergic bronchospasm that requires treatment in an emergency department, or a seizure that does not result in hospitalization.

The causality of SAEs (i.e., their degree of relatedness to study treatment) will be assessed by the investigators.

7.3 DEATH

All deaths occurring within the trial period or within 30 days after the last day that the study intervention is administered will be reported within 1 day of the investigator becoming aware of the event. If an autopsy has been performed, results of the autopsy will be obtained and forwarded along with any available toxicology reports.

7.4 PREGNANCY

Pregnancy is an exclusion criterion and women who can become pregnant should use adequate methods of birth control as outlined in the inclusion criteria. Should a pregnancy occur it must be reported in accordance with the procedures described below. Pregnancy in itself is not regarded as an AE unless there is a suspicion that an intervention may have interfered with the effectiveness of a contraceptive medication. However, the outcome of all pregnancies (spontaneous miscarriage, elective termination, normal birth or congenital abnormality) must be followed up and documented even if the subject was discontinued from the study. The Adverse Events/Side Affects form will be used for this purpose. All reports of congenital abnormalities/birth defects are SAE's. Spontaneous miscarriages should also be reported and handled as SAE's. All other outcomes of pregnancy must be reported on the Adverse Events/Side Effects form.

8 RECRUITMENT STRATEGY

Subjects will be recruited from various clinics in Durham, Carrboro, Chapel Hill, and Raleigh, North Carolina. Clinics and sites include the UNC Schizophrenia Treatment and Evaluation Program (STEP) clinics in Raleigh and Carrboro, the Outreach and Support Intervention Services (OASIS) program in Chapel Hill, Carolina Behavioral Care, Club Nova, and Threshold.. STEP, in particular, provides services to approximately 435 clients annually; 76% at STEP meet criteria for schizophrenia spectrum disorders (SSD). Clients will be approached about the study in a manner similar to what would happen in the real world outside of a research study. Specifically, psychiatrists, clinicians, and nurses will provide information to clients during appointments, groups, and in the clinic waiting area of a potential new exercise group. If the client is interested, then the research assistant will be notified to get in contact with the interested client. IRB approved flyers will also be posted at STEP.

We will supplement recruitment at STEP Wake, as needed, with assistance from the North Carolina Psychiatric Research Center (NCPRC) and STEP-Chapel Hill. Jarskog (Co-I) is the research director of the NCPRC. The NCPRC is co-located with the STEP clinic in Raleigh and has dedicated staff and space dedicated to outpatient research. The NCPRC is an outpatient research facility that is integrated into the UNC STEP Clinic of Wake County. The mission of the NCPRC is to study the pathophysiology of and advance treatments for schizophrenia and related disorders. Research conducted at the NCPRC is currently funded by the NIMH, NIDDK, foundations that support mental health research, and selective collaborations with the pharmaceutical industry. The NCPRC fosters active collaborative research both within and across departments at UNC-Chapel Hill and with other academic institutions. It also serves as a core facility where other investigators at UNC-Chapel Hill can conduct mental health-related research. STEP-Chapel Hill has 944 active clients. Over 75% have a psychotic disorder and approximately 56% are female. Finally, we will recruit individuals who have agreed to be contacted about future studies while they were subjects in past research studies conducted by Penn (~300 individuals with SSDs).

9 CONSENT PROCESS

Research staff will obtain informed consent directly from each subject. Staff obtaining the consent will provide the subject with a written document explaining the testing procedures and risks, and will answer any questions. We have several procedures in place to ensure that prospective participants fully understand the procedures, risks, and protections of the study. First, the consent form is written in easy to understand language. Second, the researcher reads the form to and with the potential subject, and invites questions after each section of the form. Third, the researcher asks the subject a series of questions about the study, such as

what they are to do if they no longer want to participate, or what they would do if they experience any stress during the protocol (this is to be used as comprehension check before signing). Potential subjects also had the option of providing informed consent verbally, to limit their exposure to the COVID-19 virus. In the virtual setting, subjects were provided an electronic copy of the consent form and followed along while the researcher reads the form to and with the potential subject, inviting questions after each section of the form. The same comprehension checks were used in the virtual setting.

10 REFERENCES

1. Brown S, Barraclough, B., & Inskip, H. . Causes of the excess mortality of schizophrenia. The British Journal of Psychiatry. 2000;177(3):212-7.
2. Laursen TM. Life expectancy among persons with schizophrenia or bipolar affective disorder. Schizophr Res. 2011;131(1):101-4.
3. Laursen TM, Munk-Olsen, T., & Vestergaard, M. . Life expectancy and cardiovascular mortality in persons with schizophrenia. Current Opinion in Psychiatry. 2012;25(2):83-8.
4. Hjorthøj C, Stürup, A. E., McGrath, J. J., & Nordentoft, M. Years of potential life lost and life expectancy in schizophrenia: A systematic review and meta-analysis. The lancet Psychiatry. 2017;4(4):295-301.
5. Connolly M, & Kelly, C. . Lifestyle and physical health in schizophrenia. Advances in Psychiatric Treatment. 2005;11(2):125-32.
6. Glover CM, Ferron, J.C., & Whitley, R. . Barriers to exercise among people with severe mental illness. Psychiatric Rehabilitation Journal. 2013;36(1):45-7.
7. Organization WH. Global health risks: Mortality and burden of disease attributable to selected major risks 2009.
8. Blair SN. Physical inactivity: The biggest public health problem of the 21st century. Br J Sports Med. 2009;43(1):1-2.
9. Wildgust HJ, & Beary, M. . Review: Are there modifiable risk factors which will reduce the excess mortality in schizophrenia?. Journal of Psychopharmacology. 2010;24(4 suppl):37-50.
10. Kodama S. SK, Tanaka S., Maki M., Yachi Y., Asumi M., ..., Sone, H. Cardiorespiratory fitness as a quantitative predictor of all cause mortality and cardiovascular events in healthy men and women: A meta-analysis. J Am Med Assoc. 2009;301(19):2024-35.
11. Myers J, Prakash, M., Froelicher, V., Do D., Partington S., & Atwood J. E. Exercise capacity and mortality among men referred for exercise testing. N Engl J Med. 2002;346:793-801.
12. Vancampfort D, Rosenbaum, S., Probst, M., Soundy, A., Mitchell, A. J., De Hert, M., & Stubbs, B. . Promotion of cardiorespiratory fitness in schizophrenia: A clinical overview and meta- analysis. Acta Psychiatr Scand. 2015;132(2):131-43.
13. Vancampfort D, Rosenbaum, S., Ward, P. B., & Stubbs, B. Exercise improves cardiorespiratory fitness in people with schizophrenia: A systematic review and meta-analysis. Schizophr Res. 2015;169(1-3):453-7.
14. Goff DC, Cather, C., Evins, A. E., Henderson, D. C., Freudenreich, O., Copeland, P. M., ... & Sacks, F.M. . Medical morbidity and mortality in schizophrenia: Guidelines for psychiatrists. The Journal of Clinical Psychiatry. 2005;66(2):183-94.
15. Vancampfort D, Firth, J., Schuch, F.B., Rosenbaum, S., Mugisha, J., Hallgren, M., Probst, M., Ward, P.B., Gaughran, F., De Hert, M., Carvalho, A.F., & Stubbs, B. Sedentary behavior and physical activity levels in people with schizophrenia, bipolar disorder and major depressive disorder: A global systematic review and meta-analysis. World Psychiatry. 2017;16(3):308-15.
16. Lawrence D, Kisely, S., & Pais, J. . The epidemiology of excess mortality in people with mental illness. Canadian Journal of Psychiatry. 2010;55(12):752-60.
17. Correll CU, Solmi, M., Veronese, N., Bortolato, B., Rosson, S., Santonastaso, P., ... & Pigato, G. . Prevalence, incidence and mortality from cardiovascular disease in patients with pooled and

specific severe mental illness: A large-scale meta-analysis of 3,211,768 patients and 113,383,368 controls. World Psychiatry. 2017;16(2):163-80.
18. Ozbulut O, Genc, A., Bagcioglu, E., Coskun, K. S., Acar, T., Alkoc, O. A., ... & Ucok, K. . Evaluation of physical fitness parameters in patients with schizophrenia. Psychiatry Res. 2013;210(3):806-11.
19. Vancampfort D, Rosenbaum, S., Schuch, F., Ward, P. B., Richards, J., Mugisha, J., ... & Stubbs, B. . Cardiorespiratory fitness in severe mental illness: A systematic review and meta-analysis. Sports Med. 2017;47(2):343-52.
20. Stubbs B, Williams, J., Gaughran, F., & Craig, T. . How sedentary are people with psychosis? A systematic review and meta-analysis. Schizophr Res. 2016;171(1):103-9.
21. Stubbs B, Gardner-Sood, P., Smith, S., Ismail, K., Greenwood, K., Farmer, R., & Gaughran, F. Sedentary behaviour is associated with elevated C-reactive protein levels in people with psychosis. . Schizophr Res. 2015;168(1):461-4.
22. Dauwan M, Begemann, M. J., Heringa, S. M., & Sommer, I. E. . Exercise improves clinical symptoms, quality of life, global functioning, and depression in schizophrenia: A systematic review and metaanalysis. Schizophr Bull. 2015;sbv164:1-12.
23. Firth J, Cotter, J., Elliott, R., French, P., & Yung, A. R. A systematic review and meta-analysis of exercise interventions in schizophrenia patient. Psychol Med. 2015;45(7):1343-61.
24. Rosenbaum S, Tiedemann, A., Sherrington, C., Curtis, J., & Ward, P. B. . Physical activity interventions for people with mental illness: A systematic review and meta-analysis. . The Journal of Clinical Psychiatry. 2014;75(9):964-74.
25. Daumit GL, Dickerson, F. B., Wang, N. Y., Dalcin, A., Jerome, G. J., Anderson, C. A., ... & Oefinger, M.. A behavioral weight-loss intervention in persons with serious mental illness. N Engl J Med. 2013;368(17):1594-602.
26. Bartels SJ, Pratt, S. I., Aschbrenner, K. A., Barre, L. K., Jue, K., Wolfe, R. S., ... & Naslund, J. A. . Clinically significant improved fitness and weight loss among overweight persons with serious mental illness. Psychiatr Serv. 2013;64(8):729-36.
27. Bartels SJ, Pratt, S. I., Aschbrenner, K. A., Barre, L. K., Naslund, J. A., Wolfe, R., ... & Feldman, J. Pragmatic replication trial of health promotion coaching for obesity in serious mental illness and maintenance of outcomes. Am J Psychiatry. 2015;172(4):344-52.
28. Acil AA, Dogan, S., Dogan, O. The effects of physical exercises to mental state and quality of life in patients with schizophrenia. J Psychiatr Ment Health Nurs. 2008;15(10):808-15.
29. Beebe LH, Tian, L., Morris, N., Goodwin, A., Allen, S. S., & Kuldau, J. . Effects of exercise on mental and physical health parameters of persons with schizophrenia. Issues Ment Health Nurs. 2005;26(6):661-76.
30. Marzolini S, Jensen, B., & Melville, P. . Feasibility and effects of a group-based resistance and aerobic exercise program for individuals with severe schizophrenia: A multidisciplinary approach. Mental Health and Physical Activity. 2009;2(1):29-36.
31. Pelham TW, Campagna, P. D., Ritvo, P. G., & Birnie, W. A. . The effects of exercise therapy on clients in a psychiatric rehabilitation program. Psychosocial Rehabilitation Journal. 1993;16(4):75-84.
32. Scheewe TW, Takken, T., Kahn, R. S., Cahn, W., & Backx, F. J. . Effects of exercise therapy on cardiorespiratory fitness in patients with schizophrenia. Med Sci Sports Exerc. 2012;44(10):1834-42.

33. Skrinar GS, Huxley, N. A., Hutchinson, D. S., Menninger, E., & Glew, P. . The role of a fitness intervention on people with serious psychiatric disabilitie. Psychiatric Rehabilitation Journal. 2005;29(2):122-7.
34. Browne J, Mihas, P., & Penn, D. L. . Focus on exercise: Client and clinician perspectives on exercise in individuals with serious mental illness. Community Ment Health J. 2015:1-8.
35. Gross J, Vancampfort, D., Stubbs, B., Gorczynski, P., & Soundy, A. A narrative synthesis investigating the use and value of social support to promote physical activity among individuals with schizophrenia. Disabil Rehabil. 2016;38(2):123-50.
36. Johnstone R, Nicol, K., Donaghy, M., & Lawrie, S. . Barriers to uptake of physical activity in community based patients with schizophrenia. Journal of Mental Health. 2009;18(6):523-32.
37. Leutwyler H, Hubbard, E. M., Slater, M., & Jeste, D. V. . "It's good for me": Physical activity in older adults with schizophrenia. Community Ment Health J. 2014;50(1):75-80.
38. Rastad C, Martin, C., & Åsenlöf, P. Barriers, benefits, and strategies for physical activity in patients with schizophrenia. Phys Ther. 2014;94(10):1467-79.
39. Bassilios B, Judd, F., & Pattison, P. . Why don't people diagnosed with schizophrenia spectrum disorders (SSDs) get enough exercise?. Australasian Psychiatry. 2013;22(1):71-7.
40. McDevitt J, Snyder, M., Miller, A., & Wilbur, J. Perceptions of barriers and benefits to physical activity among outpatients in psychiatric rehabilitation. J Nurs Scholarsh. 2006;38(1):50-5.
41. Ussher M, Stanbury, L., Cheeseman, V., & Faulkner, G. . Physical activity preferences and perceived barriers to activity among persons with severe mental illness in the United Kingdo. Psychiatr Serv. 2007;58(3):405-8.
42. Vancampfort D, De Hert, M., Skjerven, L. H., Gyllensten, A. L., Parker, A., Mulders, N., ... & Probst, M. International Organization of Physical Therapy in Mental Health consensus on physical activity within multidisciplinary rehabilitation programmes for minimising cardio-metabolic risk in patients with schizophrenia. Disabil Rehabil. 2012;34(1):1-12.
43. Firth J, Rosenbaum, S., Stubbs, B., Gorczynski, P., Yung, A. R., & Vancampfort, D. . Motivating factors and barriers towards exercise in severe mental illness: a systematic review and meta-analysis. Psychol Med. 2016;46(14):2869-81.
44. Farholm A, & Sørensen, M. . Motivation for physical activity and exercise in severe mental illness: A systematic review of intervention studies. Int J Ment Health Nurs. 2016;25(3):194-205.
45. Beebe LH, Smith, K., Burk, R., McIntyre, K., Dessieux, O., Tavakoli, A., ... & Velligan, D. . Effect of a motivational intervention on exercise behavior in persons with schizohprenia spectrum disorders. Community Ment Health J. 2011;47(6):628-36.
46. Beebe LH, Smith, K. D., Roman, M. W., Burk, R. C., McIntyre, K., Dessieux, O. L., ... & Tennison, C. . A pilot study describing physical activity in persons with schizophrenia spectrum disorders (SSDS) after an exercise program. Issues Ment Health Nurs. 2013;34(4):214-9.
47. Daumit GL, Goldberg RW, Anthony C, Dickerson F, Brown CH, Kreyenbuhl J, Wohlheiter K, Dixon LB. Physical activity patterns in adults with severe mental illness. J Nerv Ment Dis. 2005;193(10):641-6. PubMed PMID: 16208158.
48. Vancampfort D, Stubbs, B., Ward, P. B., Teasdale, S., & Rosenbaum, S. . Integrating physical activity as medicine in the care of people with severe mental illness. Aust N Z J Psychiatry. 2015;49(8):681-2.

49. Deci EL, & Ryan, R. M. . A macrotheory of human motivation, development, and health. . Can Psychol Rev. 2008;49(2):182.
50. Ryan RM, & Deci, E. L. Self-determination theory and the facilitation of intrinsic motivation, social development, and well-being. American Psychologist. 2000;55(1):68-78.
51. Gollwitzer PM, & Sheeran, P. (2006). Implementation intentions and goal achievement: A metaanalysis of effects and processes. Advances in experimental social psychology, 38, 69-119. Implementation intentions and goal achievement: A meta- analysis of effects and processes. Adv Exp Soc Psychol. 2006;38:69-119.
52. Teixeira PJ, Carraça, E. V., Markland, D., Silva, M. N., & Ryan, R. M. . Exercise, physical activity, and self-determination theory: A systematic review. . Int J Behav Nutr Phys Act. 2012;9(1):78.
53. Ng JY, Ntoumanis, N., Thøgersen-Ntoumani, C., Deci, E. L., Ryan, R. M., Duda, J. L., & Williams, G. C. Self-determination theory applied to health contexts a meta-analysis. Perspect Psychol Sci. 2012;7(4):325-40.
54. Vancampfort D, De Hert, M., Vansteenkiste, M., De Herdt, A., Scheewe, T. W., Soundy, A., ... & Probst, M. . The importance of self-determined motivation towards physical activity in patients with schizophrenia. Psychiatry Research. 2013;210(3):812-8.
55. Aarts H, & Dijksterhuis, A. . Habits as knowledge structures: Automaticity in goal-directed behavior. J Pers Soc Psychol. 2000;78(1):53.
56. Carraro N, & Gaudreau, P. . Spontaneous and experimentally induced action planning and coping planning for physical activity: A meta-analysis. Psychol Sport Exerc. 2013;14(2):228-48.
57. Bélanger-Gravel A, Godin, G., & Amireault, S. . A meta-analytic review of the effect of implementation intentions on physical activity. Health Psychol Rev. 2013;7(1):23-54.
58. Sudeck G, & Höner, O. . Volitional interventions within cardiac exercise therapy (VIN- CET): Longterm effects on physical activity and health- related quality of life. Applied Psychology: Health and Well- Being. 2011;3(2):151-71.
59. Fuchs R, Göhner, W., & Seelig, H. Long-term effects of a standardized group intervention on physical exercise and health: The MoVo concept. Br J Health Psychol. 2009.
60. Godin G, Germain, M. Conner, M., Delage, G., & Sheeran, P. . Promoting the return of lapsed donors: A 7-arm randomized controlled trial of the question-behavior effect. Health Psychol. 2014;33:646-55.
61. Marquardt MK, Oettingen, G., Gollwitzer, P. M., Sheeran, P., & Liepert, J. . Mental contrasting with implementation intentions (MCII) improves physical activity and weight loss among stroke survivors over one year. Rehabil Psychol. in press.
62. Conner M, & Higgins, A. R. . Long-term effects of implementation intentions on prevention of smoking uptake among adolescents: A cluster randomized controlled trial. Health Psychol. 2010;29(5):529.
63. Martin J, Sheeran, P., Slade, P., Wright, A., & Dibble, T. . Durable effects of implementation intentions: Reduced rates of confirmed pregnancy at two years. Health Psychol. 2011;30:368-73.
64. Toli A, Webb, T. L., & Hardy, G. E. . Does forming implementation intentions help people with mental health problems to achieve goals? A meta- analysis of experimental studies with clinical and analogue samples. Br J Clin Psychol. 2016;55(1):69-90.
65. Brandstätter V, Lengfelder, A., & Gollwitzer, P. M. Implementation intentions and efficient action initiation. J Pers Soc Psychol. 2001;81(5):946-60.

66. Koestner R, Otis, N., Powers, T. A., Pelletier, L., & Gagnon, H. . Autonomous motivation, controlled motivation, and goal progress. J Pers. 2008;76(5):1201-30.
67. Koestner R, Lekes, N., Powers, T. A., & Chicoine, E. . Attaining personal goals: Self-concordance plus implementation intentions equals success. J Pers Soc Psychol. 2002;83(1):231-44.
68. Subramaniapillai M, Arbour-Nicitopoulos, K., Duncan, M., McIntyre, R. S., Mansur, R. B., Remington, G., & Faulkner, G. (2016). BMC research notes, 9(1), 340. Physical activity preferences of individuals diagnosed with schizophrenia or bipolar disorder. BMC Res Notes. 2016;9(1):1-9.
69. Morris JN, & Hardman, A. E. . Walking to health. Sports Med. 1997;23(5):306-32.
70. Bravata DM, Smith-Spangler, C., Sundaram, V., Gienger, A. L., Lin, N., Lewis, R., ... & Sirard, J. R. . Using pedometers to increase physical activity and improve health. J Am Med Assoc. 2007;298(19):2296-304.
71. Ogilvie D, Foster, C. E., Rothnie, H., Cavill, N., Hamilton, V., Fitzsimons, C. F., & Mutrie, N. . Interventions to promote walking: Systematic review. Br Med J. 2007;334:1204-13.
72. Richardson CR, Newton, T. L., Abraham, J. J., Sen, A., Jimbo, M., & Swartz, A. M. . A meta-analysis of pedometer-based walking interventions and weight loss. The Annals of Family Medicine. 008;6(1):69-77.
73. Soundy A, Muhamed, A., Stubbs, B., Probst, M., & Vancampfort, D. . The benefits of walking for individuals with schizophrenia spectrum disorders: A systematic review. International Journal of Therapy and Rehabilitation. 2014;21(9):410-20.
74. Dunn AL, Marcus, B. H., Kampert, J. B., Garcia, M. E., Kohl III, H. W., & Blair, S. N. . Comparison of lifestyle and structured interventions to increase physical activity and cardiorespiratory fitness: A randomized trial. J Am Med Assoc. 1999;281(4):327-34.
75. Macko RF, Ivey, F. M., Forrester, L. W., Hanley, D., Sorkin, J. D., Katzel, L. I., ... & Goldberg, A. P. . Treadmill exercise rehabilitation improves ambulatory function and cardiovascular fitness in patients with chronic stroke: A randomized, controlled trial. Stroke. 2005;36(10):2206-11.
76. Kelly P, Kahlmeier, S., Götschi, T., Orsini, N., Richards, J., Roberts, N., ... & Foster, C. . Systematic review and meta-analysis of reduction in all-cause mortality from walking and cycling and shape of dose response relationship. International Journal of Behavioral Nutrition and Physical Activity. 2014;11:1-15.
77. Nelson ME, Rejeski, W. J., Blair, S. N., Duncan, P. W., Judge, J. O., King, A. C., ... & Castaneda-Sceppa, C. Physical activity and public health in older adults: Recommendation from the American College of Sports Medicine and the American Heart Association. Circulation. 2007;116(9):1094.
78. Manson JE, Greenland, P., LaCroix, A. Z., Stefanick, M. L., Mouton, C. P., Oberman, A., ... & , Siscovick DS. Walking compared with vigorous exercise for the prevention of cardiovascular events in women. N Engl J Med. 2002;347(10):716-25.
79. Haskell WL, Lee, I. M., Pate, R. R., Powell, K. E., Blair, S. N., Franklin, B. A., ... & Bauman, A. . Physical activity and public health: Updated recommendation for adults from the American College of Sports Medicine and the American Heart Association. Circulation. 2007;116(9):1081.
80. Perese EF, & Wolf, M. . Combating loneliness among persons with severe mental illness: Social network interventions' characteristics, effectiveness, and applicability. Issues Ment Health Nurs. 2005;36(6):591-609.

81. Kassavou A, Turner, A., & French, D. P. Do interventions to promote walking in groups increase physical activity? A meta-analysis. International Journal of Behavioral Nutrition and Physical Activity. 2013;10(18):1-12.
82. Mason OJ, & Holt, R. Mental health and physical activity interventions: A review of the qualitative literature. Journal of Mental Health. 2012;21(3):274-84.
83. Lauzon N, Chan CB, Myers AM, Tudor-Locke C. Participant experiences in a workplace pedometer based physical activity program. Journal of physical activity & health. 2008;5(5):675-87. PubMed PMID: 18820340.
84. Heesch KC, Dinger MK, McClary KR, Rice KR. Experiences of women in a minimal contact pedometer based intervention: a qualitative study. Women & health. 2005;41(2):97-116. doi: 10.1300/J013v41n02_07. PubMed PMID: 16219590.
85. Tudor-Locke C MA, Rodger NW. Formative evaluation of the First Step Programm: a practical intervention to increase daily physical activity. Can J Diab Care 2000;47(1):23-8.
86. Tudor-Locke C, Lutes L. Why do pedometers work?: a reflection upon the factors related to successfully increasing physical activity. Sports Med. 2009;39(12):981-93. Epub 2009/11/12. doi: 10.2165/11319600-000000000-00000. PubMed PMID: 19902981.
87. Cobiac LJ, Vos T, Barendregt JJ. Cost-effectiveness of interventions to promote physical activity: a modelling study. PLoS medicine. 2009;6(7):e1000110. doi: 10.1371/journal.pmed.1000110. PubMed PMID: 19597537; PMCID: 2700960.
88. Rosenbaum S, Tiedemann, A., Stanton, R., Parker, A., Waterreus, A., Curtis, J., & Ward, P. B. . Implementing evidence-based physical activity interventions for people with mental illness: an Australian perspective. 24. 2016;1(49-54).
89. Kimhy D, Vakhrusheva, J., Bartels, M. N., Armstrong, H. F., Ballon, J. S., Khan, S., ... & , Castrén E. The impact of aerobic exercise on brain-derived neurotrophic factor and neurocognition in individuals with schizophrenia: A single-blind, randomized clinical trial. Schizophr Bull. 2015;41(4):859-68.
90. Pajonk FG, Wobrock, T., Gruber, O., Scherk, H., Berner, D., Kaizl, I., ... & Backens, M. . Hippocampal plasticity in response to exercise in schizophrenia. Arch Gen Psychiatry. 2010;67(2):133-43.
91. Rhodes RE, & Dickau, L. (2012). Health Psychology, 31(6), 724–727. Experimental evidence for the intention–behavior relationship in the physical activity domain: A meta-analysis. Health Psychol. 2012;31(6):724-7.
92. Sheeran P, & Webb, T. L. . The intention–behavior gap. Soc Personal Psychol Compass. 2016;10(9):503-18.
93. Armitage CJ, & Arden, M. A. . A volitional help sheet to increase physical activity in people with low socioeconomic status: A randomized exploratory trial. Psychology and Health. 2010;25(10):1129-45.
94. Epton T, & Armitage, C. J. . Does situation-specificity affect the operation of implementation intentions? Behav Ther. 2017:1-31.
95. Latimer AE, Martin Ginis, K.A., & Arbour, K.P. . The efficacy of an implementation intention intervention for promoting physical activity among individuals with spinal cord injury: A randomized controlled trial. Rehabil Psychol. 2006;51(4):273-80.
103. Garber CE, Blissmer, B., Deschenes, M. R., Franklin, B. A., Lamonte, M. J., Lee, I. M., ... & Swain, D. P. American College of Sports Medicine position stand. Quantity and quality of exercise for

developing and maintaining cardiorespiratory, musculoskeletal, and neuromotor fitness in apparently healthy adults: Guidance for prescribing exercise. Med Sci Sports Exerc. 2011;43(7):1334-59.

104. Druss BG, Rohrbaugh, R. M., Levinson, C. M., & Rosenheck, R. A. Integrated medical care for patients with serious psychiatric illness: A randomized trial. Arch Gen Psychiatry. 2001;58(9):861-8.
105. Richardson CR, Faulkner, G., McDevitt, J., Skrinar, G. S., Hutchinson, D. S., & Piette, J. D. . Integrating physical activity into mental health services for persons with serious mental illness. Psychiatr Serv. 2005;56(3):324-33.
106. Pollock ML, Gaesser, G. A., Butcher, J. D., Després, J. P., Dishman, R. K., Franklin, B. A., & , Garber CE. ACSM position stand: The recommended quantity and quality of exercise for developing and maintaining cardiorespiratory and muscular fitness, and flexibility in healthy adults. Medicine and Science in Sports & Exercise. 1998;30(6):975-91.
107. Spector D, & Battaglini, C. . The feasibility of delivering a home-based motivational exercise program to African-American breast cancer survivor. Journal of Health Disparities Research and Practice. 2015;8(1):128-40.
116. Shiers D, Bradshaw, T. & Campion, J. . Health inequalities and psychosis: Time for action. The British Journal of Psychiatry. 2015;207(6):471-3.
117. Stewart R. Mental disorders and mortality: So many publications, so little change. Acta PsychiatrScand. 2015;132(5):410-1.
118. American College of Sports Medicine & Pescatello LS. ACSM's guidelines for exercise testing and prescription: Wolters Kluwer/Lippincott Williams & Wilkins Health; 2014.
119. JACKSON, A. S., BLAIR, S. N., MAHAR, M. T., WIER, L. T., ROSS, R. M., & STUTEVILLE, J. E. Prediction of functional aerobic capacity without exercise testing. Medicine & Science in Sports & Exercise, 1990;*22*(6), 863.