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Evaluating the clinical implementation of structured exercise: A randomized controlled trial among non-insulin dependent type II diabetics

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A B S T R A C T

Background: The American Diabetes Association (ADA) currently recommends 150 min of moderate-intensity aerobic exercise per week and resistance exercise at least twice per week in individuals with type 2 diabetes (T2DM) to improve overall health [1]. However, approximately 38% of patients with T2DM do not exercise at recommended levels and 31% do not exercise at all [2]. The efficacy of structured exercise interventions has been proven effective in reducing glycosylated hemoglobin A1c (HbA1c) levels in patients, but practical approaches are needed to translate these findings into the clinical setting [3–7].

Objective: The Initiate and Maintain Physical Activity in Clinics (IMPACT) Study aims to compare structured group exercise within the clinic to usual care in T2DM patients. The main purpose of the study is to determine the optimal and feasible level and weekly frequency of structured contact in a clinical setting needed to initiate and maintain physical activity recommendations long-term.

Study design: IMPACT is a longitudinal, randomized-controlled study designed to track study participants over 30 months. Once study participants have met eligibility and enrollment criteria, they are randomized and enrolled into one of three arms: 1× per week exercise, 3× per week exercise, or the usual care control group. After randomization, participants begin Phase 1: Initiate lasting 6 months. Over the course of Phase 1, participants in the exercise groups will attend instructor led group training at a Stanford approved physical fitness facility. At the end of 6 months, participants enter Phase 2: Maintain lasting 24 months. Over the course of Phase 2, participants in all three arms will attend periodic follow-up visits for clinical measurements and survey administration for their final two years of participation. These findings will enable the clinical implementation of a structured exercise regimen designed to specifically address the aerobic and resistance training recommendations for patients with T2DM.

1. Background

In 2017, the CDC released a statistics report detailing the estimated prevalence and incidence rate of T2DM in the US as well as its costs [8]. There are currently 23.1 million people in the US that are diagnosed with T2DM, and an estimated 7.2 million people are thought to be undiagnosed [8]. According to the current American Diabetes Association (ADA) guidelines, individuals with T2DM should engage in at least 150 min of moderate-intensity aerobic activity per week and resistance exercise at least 2 times per week [1]. Despite ADA physical activity recommendations, approximately 38% of T2DM patients do not exercise at recommended levels and 31% do not exercise at all [2]. Research has shown that physical activity is beneficial in T2DM management with improved glycemic control achieved in patients who followed a structured exercise program in a research setting [4,5,13,16–18]. Given the known benefits of dietary changes in T2DM, nutrition referrals are common in current clinical practice. However, despite the similarly known benefits of exercise [3–7], physical activity referrals are not readily available in the clinical setting.

1.1. Nutritional counseling and cardiac rehabilitation as models for physical activity in clinical practice

The efficacy of nutrition counseling for T2DM was first recognized in clinical trials [9] with its effectiveness later proven in translational clinical trials [10,11]. In December 1999, the Institute of Medicine released a report [12] confirming the clinical- and cost-effectiveness of nutrition counseling for T2DM. The report estimated short-term cost

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savings of $132 to $330 million for those with diabetes [12]. According to a randomized controlled study, after 6 months of beginning nutrition care, 63% of participants achieved or maintained a successful glycemic outcome [27]. As a result, nutrition counseling became a covered Medicare benefit, and all major insurers followed this reimbursement practice. In 2002, the ADA recommended that specialized nutrition services be offered in addition to routine physician office visit counseling. As a result, for over a decade, nutrition counseling has been successfully institutionalized within the healthcare environment [13]. Similarly, cardiac rehabilitation, which includes physician prescribed exercise training, is integral to the comprehensive care of patients with cardiovascular disease [14] and is a covered Medicare practice [15]. Though physical activity is similarly beneficial for T2DM patients, structured exercise programs have not been developed to assist physicians and patients in a clinical setting.

1.2. Merits of structured physical activity regimens

The efficacy of physical activity in T2DM patients is well known. Structured exercise has been shown to improve glycemic control [4,5,13,16–18] and reduce the risk of cardiovascular disease [19,20]. In a 1997 study by Eriksson et al., circuit exercise led to significant improvement in glycemic control by reducing HbA1c levels from 8.8%–8.2% [17]. While the value of aerobic exercises has been acknowledged [13], resistance training may be particularly helpful for T2DM patients [21,22], as improved muscle function and growth may increase muscle glucose storage, alter insulin sensitivity via the expression of the GLUT-4 transporter, and thereby improve glycemic control [23–25]. The combination of both aerobic and resistance training exercise has been found to provide the greatest reduction in HbA1c levels in T2DM patients, compared to either aerobic or resistance training alone.

Advice alone for physical activity has been shown to be ineffective, and despite strong support for structured exercise programs and physical activity, structured exercise programs for patients with T2DM are not currently available in clinical settings. Therefore, doctors and patients are left to rely on only physical activity advice [3]. A recent meta-analysis of randomized controlled trials (RCTs) demonstrated that highly structured physical activity training regimens were effective in reducing glycosylated hemoglobin A1c (HbA1c) levels in individuals with T2DM, while physical activity advice alone had no effect on HbA1c [3]. Of the 23 RCTs which tested structured training programs, most consisted of at least three structured sessions per week, and ranged in length from 3 to 12 months. While the efficacy of such intensive physical activity interventions among individuals with T2DM in a highly structured research setting has been proven, practical approaches to translate and extend these findings into the clinical setting are needed. Less intensive approaches, such as physical activity advice delivered by physicians, have been tested in clinical settings, and have not been effective in increasing physical activity [26]. Furthermore, previous research examining physical activity counseling within the clinical setting has shown that physician counseling for physical activity occurs at < 30% of ambulatory care visits [16]. The Activity Counseling Trial (ACT) found that physician advice and written educational materials did not increase physical activity in patients compared to baseline [26]. Thus, translational studies are needed to test innovative and practical adaptations of evidence-based interventions in order to integrate physical activity as a part of standard clinical practice.

1.3. Rationale of study

The goal of IMPACT is to translate efficacious structured physical activity interventions to the clinical setting. There are 3 goals of the IMPACT study: [1] Clinical Effectiveness, [2] Patient-Centered Outcomes, and [3] Cost-Effectiveness. The clinical effectiveness will be tested by measuring if there are absolute changes in HbA1c in the combined exercise groups. The process measures that the study will implement to achieve this objective are the changes in physical fitness and physical activity. The study also has the intention of addressing patient-centered outcomes through the administration of surveys to measure self-reported satisfaction and quality of life. The cost-effectiveness assessment will be based on clinical outcomes and quality of life. With all three aims, the IMPACT study will assess the potential to translate efficacious structured physical activity interventions to the clinical setting.

2. Study population

The study will include adults aged 18–80 years who are diagnosed with T2DM and are not currently taking insulin. Potential participants are being recruited in the San Francisco Bay Area and are of any gender and racial or ethnic background. The anticipated study population is 345 enrolled participants. As a three-arm randomized study, this will allow for a total of 115 participants per study arm. Exclusion criteria include insulin dependency, participation in other clinical trials that may interfere with study compliance, current cancer treatment, and other health conditions that may render the participant unable to exercise safely. A complete list of both inclusion and exclusion criteria are provided in Table 1.

3. Methods

3.1. Recruitment

IMPACT utilizes four primary methods to identify and recruit potential participants to the study. These methods include calling Stanford patients identified via electronic medical records (EMR), in-clinic recruitment, community outreach, and media outreach and advertising.

3.1.1. Method 1: Calling/health record eligibility

Prospective participants may be identified via Stanford's electronic medical record. Once a patient has been identified as a prospective study participant, the study team obtains approval for contacting the patient. Upon approval, the study team contacts the prospective patients via telephone to explain the purpose of the study and invite interested participants to proceed with the screening process. Additionally, the study will use the Stanford Research Registry to

Table 1
Inclusion and Exclusion Criteria.

Inclusion criteria	• Age 18–80 • Diagnosed with Type II Diabetes Mellitus (T2DM) • HbA1c result between 6.5% and 13.0% • Has ability to communicate with study staff in English, sign informed consent, and accept randomization • Free of intervening events (ie. a sick spouse) • Willing to exercise at a Stanford approved physical fitness facility up to three times a week for six months • Willing to attend all study visits
Exclusion criteria	• Insulin-dependent • Any serious medical condition which would prevent long-term participation or which would contraindicate physical activity • Age < 18 years or > 80 years • Currently meeting exercise guidelines • Current atrial fibrillation • Active treatment for cancer • Pregnancy • BMI > 70 kg/m2 • Cognitive inability as judged by the interviewer • Plans to leave the community within five years • Language barrier (cannot speak, read or write English proficiently)