

A 12-Week Pilot Exercise Program for Inactive Adults With Celiac Disease: Study Protocol

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Abstract

Background: Individuals with celiac disease must follow a strict gluten-free diet (GFD) in order to avoid negative short- and long-term health consequences. Unfortunately, many people with celiac disease report poor quality of life (QoL) despite following a strict GFD, and up to 30% still report negative symptoms (eg, gastrointestinal upset).

Purpose: The purpose of the MOVE-C (understanding the relationship between the Microbiome, Vitality, and Exercise in Celiac disease) pilot study is to explore the effects of a 12-week supervised progressive high-intensity interval training (HIIT) and lifestyle intervention on physiological, behavioral, and psychosocial outcomes among inactive adults with celiac disease.

Methods/Design: Sixty inactive adults diagnosed with celiac disease will be randomized to HIIT+ or waitlist control (WLC). Participants in the HIIT+ will engage in a 12-week HIIT + lifestyle education program. HIIT sessions will be comprised of 2 workouts per week, working up to 14 × 30-second intervals at 90% maximal heart rate (HRmax) followed by 2 minutes recovery at 50% HRmax. The 6 biweekly lifestyle sessions will involve education on the promotion of a whole foods GFD, sleep hygiene, psychosocial coping skills (eg, self-compassion), and self-regulatory skills to master changes in behaviors. Assessments will occur at pre and post 12-week intervention and 3-month follow-up. WLC participants will be offered a 12-week HIIT program + online lifestyle education sessions after completing the final assessment. The primary outcomes are QoL and gut microbiota composition assessed with 16S rRNA sequencing. The secondary outcomes are markers of metabolic syndrome (waist circumference, fasting glucose, serum lipids, blood pressure, and body composition), gastrointestinal symptoms, sleep quality, adherence to a GFD, exercise behavior, self-regulatory efficacy, and self-compassion. It is hypothesized that participants in the HIIT+ will experience improvements in all outcomes when compared to those in the WLC. These improvements are expected to be maintained at the 3-month follow-up.

Discussion: The findings from this study will advance the knowledge regarding the effects of HIIT and lifestyle education on key outcomes for an at-risk chronic disease population. Furthermore, the findings can be used to inform future programs to improve fitness and physical and mental health outcomes for people with celiac disease.

Keywords

high-intensity interval training, celiac disease, lifestyle education, quality of life, microbiota, protocol

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Introduction

Celiac disease is a chronic autoimmune condition that affects 1 in 133 people in North America.¹ The incidence of celiac disease has increased 4 to 5 fold over the past 50 years.¹ Strict adherence to a gluten-free diet (GFD) is currently the only treatment for preventing both short- and long-term consequences from celiac disease (eg, infertility, intestinal cancers, osteoporosis).² However,

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1 year after starting a GFD, people with celiac disease are significantly more likely to be diagnosed with metabolic syndrome.³ In addition, despite following a GFD, individuals with celiac disease often have altered gut microbiota,⁴ report high treatment burden (comparable to those with end-stage renal disease),⁵ up to 30% still report negative symptoms (eg, gastrointestinal upset)⁶ and sleep disturbances⁷. As such, enhanced strategies are needed to improve the physical outcomes and psychological well-being of this chronic disease population.

Engagement in regular physical activity is associated with a range of physical and psychological benefits among chronic disease populations.⁸ Many individuals with chronic diseases experience a beneficial dose–response relationship with physical activity, whereby starting to do regular movement leads to physical and mental health benefits.⁹ Indeed, it is recommended that patients aim to accumulate 150 minutes of moderate intensity physical activity every week as a first step in the prevention and/or management of lifestyle related chronic diseases.^{9,10} Unfortunately, preliminary research reveals that rates of physical activity among women living with celiac disease are dismal, with over 50% engaging in only low levels of physical activity based on the International Physical Activity Questionnaire.^{11,12} Thus, similar to the general population, women with celiac disease are also not meeting physical activity guidelines.^{11,13,14}

There are numerous types of physical activity that can be engaged in for health benefits, including resistance training or functional movement, fine tuning the frequency, intensity, time, and type (FITT) prescription within a format of lower intensity continuous or higher intensity interval training depending on the needs of the target population. Given that the majority of adults do not currently achieve the recommended levels of physical activity for health benefits, opportunities that encourage regular movement and provide health benefits for inactive adults with celiac disease require further investigation. Exercise is a specific type of physical activity that involves intentional repetitive movement that is planned and structured. High-intensity interval training (HIIT) has been found to be a safe and appropriate type of exercise for those with lifestyle-induced chronic diseases, including type 2 diabetes, atherosclerotic cardiovascular disease, and metabolic syndrome.^{15,16} HIIT involves repeated bouts of high intensity effort followed by varied recovery times and can be easily modified for people of all fitness levels and special conditions.¹⁷ For example, Jung et al.¹⁸ explored adherence to independent sessions of HIIT compared to moderate-intensity continuous training (MICT) among people with prediabetes. After an initial 12-day training period, compared to those in MICT, participants randomized to HIIT engaged in significantly more independent exercise and completed more exercise at a higher

intensity over a 4-week follow-up period. Findings from this study provide preliminary evidence that HIIT can be an efficacious alternative to MICT among a chronic disease population.

Setting participants up for success, such that they can engage in regular independent exercise *after* a program comes to completion, is a primary goal of exercise interventions for chronic disease populations. Quality of life (QoL) is often one of the key outcomes of exercise interventions, as improving physical and psychological well-being suggests effective management of the disease. Although patients often report improvements in QoL when following a GFD,¹⁹ this is not always the case⁷. Fortunately, engagement in regular exercise leads to numerous physical and psychological health benefits and improved QoL in healthy and chronic disease populations.⁹ As such, an exercise regime that patients engage in independently will maximize the chances of optimizing QoL among previously inactive adults with celiac disease. Over the past decade, findings from studies examining the effects of different exercise protocols in clinical populations indicate that HIIT leads to greater or similar improvements in QoL when compared to MICT.^{20–22}

In addition to the benefits of improved exercise adherence and QoL, Denou et al.²³ found that compared to consumption of a high fat diet and no exercise, mice fed a high-fat diet and engaged in HIIT experienced improvements in the alpha diversity and ratio of Bacteroidetes to Firmicutes in the distal and fecal microbiota. Given that people with celiac disease are likely to have altered gut microbiota (ie, higher amount of potentially pathogenic bacteria and lower amounts of beneficial bacteria),⁴ strategies to promote a healthy balance of bacteria in the gut are warranted. Building on the preliminary research that revealed exercise (HIIT and MICT) has independent effects from diet on gut microbiota in healthy and mice with diabetes²⁴ and obesity,²³ it is possible that engagement in regular exercise may lead to improvements in the balance of gut microbiota in adults with celiac disease. Furthermore, as dysbiosis of the gut microbiota is related to the occurrence of negative symptoms, improvements in the composition of gut bacteria may lead to reductions in gastrointestinal symptoms.⁴ Thus, getting previously inactive adults with celiac disease to engage in regular exercise may lead to improvements in not only the composition of the gut microbiota but also in gastrointestinal symptoms experienced.

Although there has been considerable debate in the literature regarding the acceptability and enjoyability of HIIT,²⁵ findings from a recent scoping review of the literature on the psychological responses to interval exercise reveal that enjoyment of and preferences for interval training are greater than or equal to that of continuous exercise.²⁶ Participants report positive social cognitions

(eg, self-efficacy, intentions) in regards to interval training,²⁶ and physiological benefits that are equal to or greater than those for continuous exercise including improved metabolic health (ie, insulin sensitivity and glucose control), cardiovascular health, aerobic fitness,²⁷ and sleep quality.²⁸ Given that people with celiac disease are likely to be insufficiently active, have increased rates of metabolic syndrome, altered gut microbiota, and often report reduced QoL and sleep disturbances, increasing exercise among this population could be particularly beneficial to improve both psychological and physical outcomes.

Group-Mediated Behavior Change

Changing exercise behavior among chronic disease populations can be difficult; however, the group-mediated cognitive-behavioral (GMCB) approach has demonstrated success in a variety of populations (eg, CVD, elderly adults, youth with obesity, postnatal women).²⁹ GMCB interventions teach participants how to self-monitor daily activity, set goals, and brainstorm ways to overcome barriers to regular physical activity.³⁰ To prevent dependence on the group, self-regulation becomes a greater emphasis over the course of the GMCB sessions.³⁰ Previous GMCB interventions have led to greater improvements in frequency of physical activity,^{30,31} long-term adherence,^{31,32} fitness,³¹ self-efficacy for mobility,³¹ and barrier self-efficacy,³⁰ as compared to those in control groups. Rejeski et al.³¹ concluded that improvements in the GMCB groups may be because participants are given the self-regulatory skills needed to exercise on their own and are encouraged to engage in regular physical activities they find enjoyable. Given the potential barriers to engaging in regular exercise, a GMCB approach thus should be considered as an integral component of an exercise intervention to help inactive adults with celiac disease become and remain physically active.

The MOVE-C Study

This study is an innovative examination of the effects of exercise on physiological, behavioral, and patient-reported outcomes among inactive adults with celiac disease. Specifically, we will explore the effects of a 12-week HIIT and lifestyle intervention on the primary outcomes of QoL and gut microbiota composition, and secondary outcomes of gastrointestinal symptoms, sleep quality, adherence to a GFD, exercise behavior, social cognitions (self-regulatory efficacy + self-compassion), and markers of metabolic syndrome (waist circumference, fasting glucose, serum lipids, and blood pressure). It is hypothesized that participants in HIIT+ will experience improvements in all outcomes when compared to those

in the WLC. These improvements are expected to be maintained at the 3-month follow-up.

Methods

Design

The MOVE-C (*MicrobiOme, Vitality, and Exercise in Celiac disease*) study is a 2-arm parallel, randomized controlled registered trial (ClinicalTrials.gov number NCT03520244). This is a 12-week intervention study on the effects of HIIT exercise and lifestyle intervention on 60 inactive adults with celiac disease. Participants will be randomized to a HIIT plus GMCB lifestyle intervention (HIIT+ condition) or waitlist control (WLC condition). Randomization will occur via a computer-generated random numbers table. The MOVE-C study coordinator will be responsible for enrolling participants and group assignment. The testers are Certified Exercise Physiologists and will be blinded to group assignment. Assessments will be conducted pre-intervention, immediately post-intervention, and 3 months post-intervention. The University of Calgary Behavioural Research Ethics Board has approved this study (REB16-1774).

Participants

Adults diagnosed (through blood test and/or biopsy) with celiac disease will be recruited to participate in this study via local gastrointestinal physician referrals, posters in public centers, social media, news advertisement, and word of mouth. Individuals will be eligible to participate if they are over 18 years old, formally diagnosed with celiac disease, not currently active as per Canada's Physical Activity Guidelines, live in the Calgary area and can attend exercise sessions at the university 2 times per week for 12 weeks, and are fluent in English. Individuals will be excluded if they are not medically fit to participate in HIIT. See Figure 1 for participant flow through the MOVE-C study.

General Procedure

Participants will be contacted via e-mail by a research assistant to review the study protocol, confirm eligibility, provide consent, and receive medical clearance by completing the Physical Activity Readiness Questionnaire (PAR-Q). All PAR-Qs will be reviewed by a Certified Exercise Physiologist. Any medical concerns impacting the participants' ability to participate in HIIT will require completion of a Physical Activity Readiness Medical Examination (PARMed-X) and physician clearance. Any questions or concerns about the study will be addressed at this time.

Pretesting: Body Composition, Fitness, Gut Microbiota, Psychosocial, Dietary Adherence, and Blood Measures

Baseline testing will be completed over a 2-week time period. Participants will be invited for their first 1-hour appointment with a Certified Exercise Physiologist at the University of Calgary, Thrive Lab. They will perform a physical assessment measuring blood pressure, resting heart rate (HR), body mass index, waist to hip ratio, sit and reach, shoulder flexibility, and a submaximal cycle test. A dual-energy x-ray absorptiometry (DXA) scan (Hologic QDR 4500; Hologic, Inc, Bedford, MA) will also be completed at this time.

In addition, participants will be provided with a 3-day diet record and food scale to record their entire food and beverage intake on 2-week days and 1-weekend day. A stool collection kit and instructions will be packaged to take home and return with the food log within the 2-week testing period. Participants will be instructed to collect the stool sample into a sterile conical tube and then store it in a biohazard bag in their home freezer until they deliver it on ice to the investigators. Samples will be stored at -80°C until analyzed. A preordered blood requisition will be taken by participants to a lab of their choice to complete the fasted blood draw and testing. Calgary Lab Services will measure serum lipids and fasting glucose, and provide the results to the investigators via mail and/or fax. Finally, participants will complete an online questionnaire.

Upon completion of the 1-hour assessment, participants will meet with a research assistant to be randomized to the HIIT+ or WLC group. Participants will then receive their schedule to participate in the respective arm of the study.

Post-testing: Body Composition, Fitness, Gut Microbiota, Psychosocial, Dietary Adherence, and Blood Measures

Post-testing will occur after completion of the 12-week exercise intervention. All participants will be invited for their second 1-hour appointment at the Thrive Lab. Participants will perform the same physical assessment with a Certified Exercise Physiologist and have another DXA scan at this time. Participants will also be asked to complete a second 3-day dietary food log and stool sample to be returned to the university, provide a blood sample, and respond to an online questionnaire.

Three-Month Post-testing: Body Composition, Fitness, Gut Microbiota, Psychosocial, Dietary Adherence, and Blood Measures

Three-month post-testing will be conducted 3 months after the end of the 12-week program. All participants

will be invited for the third and final 1-hour appointment at the Thrive Lab. Participants will perform the same physical assessment with a Certified Exercise Physiologist and have another DXA scan. Participants will also be asked to complete a third 3-day diet record and stool sample to be returned to the university, provide a blood sample, and will also respond to the online questionnaire. Participants in the HIIT+ group will be finished the study and the WLC group will be offered the 12-week exercise intervention. See Table 1 for a list of assessments completed at each time point.

Sample Size and Statistical Analyses

At the time of study design, there were no available exercise intervention studies upon which to base our gut microbiota sample size calculation. Therefore, we used data from our previous work with a dietary intervention in adults to estimate sample size.³³ *Bifidobacterium* was selected as the bacterium of choice based on previous work in which we showed an increase in *Bifidobacterium* in response to exercise in mice.²⁴ It was determined that $n=25$ per group would detect a difference of 8.5% relative abundance, assuming a standard deviation of 10.6% with 80% power at a significance level of 0.05. Assuming a dropout rate similar to our previous lifestyle intervention studies of approximately 20%, we will aim to recruit an additional 5 participants ($n=30$ per group).

Data will be collected at 3 time points—baseline, post-intervention, and 3 months post-intervention. Specifically, a generalized estimating equation (GEE; ie, GEE under GENLIN procedure in SPSS v.24) will be used to examine between group changes in the outcome variables over time. GEE will be utilized as this type of analysis is appropriate for longitudinal data in which the responses are correlated across time points. α was set at .05, as such, any computed *P* values of less than .05 were considered statistically significant.

MOVE-C Intervention

HIIT exercise sessions. The 12-week HIIT program will entail two 60-minute structured group exercise sessions per week. Participants will begin with 20- to 30-minute sessions and progress to 40- to 60-minute sessions over the course of 12 weeks. As participants will not be meeting the recommended guidelines for weekly physical activity (150 min of moderate intensity or greater),³⁴ workouts will be progressive in nature. In addition, an initial conditioning phase will be integrated into the 12-week program. The initial conditioning phase will be included to ensure that each participant had an appropriate base level of fitness before the introduction of higher intensity exercise. Establishing a foundational level of fitness prior to a HIIT program reduces the risk

Table 1. Summary of Group-Mediated Cognitive-Behavioral-Based Holistic Education Session Content.

Week	Session Content	Topics Discussed
1	Introduction to evidence-based holistic approaches to celiac disease management	<ul style="list-style-type: none"> • General introduction to the holistic education sessions • Role of exercise in management of celiac disease • Introduction to self-regulation • Self-monitoring and goal setting
2	Mindset matters: role of self-compassion in celiac disease management	<ul style="list-style-type: none"> • Importance of coping strategies • Introduction to self-compassion • Self-compassion in chronic disease management • Goal setting
3	Importance of a whole-foods-based gluten-free diet in celiac disease	<ul style="list-style-type: none"> • Introduction to a whole-foods-based gluten-free diet • Mindful eating • Meal planning • Regular physical activity • Goal setting
4	Importance of sleep in effective management of celiac disease	<ul style="list-style-type: none"> • Introduction to action planning • Importance of quality sleep in chronic disease management • Sleep hygiene • Goal setting
5	When the gluten-free diet isn't enough . . . what else can I do?	<ul style="list-style-type: none"> • Naturopathic approach to celiac disease management • Communication strategies • Goal setting
6	What you may not know about celiac disease or the gluten-free diet	<ul style="list-style-type: none"> • Jeopardy style review of all information learned over the past 5 sessions

of musculoskeletal injury and improves oxygen transportation to the muscles.¹⁷ Each class will consist of warm-up, training period, cool-down, and flexibility exercises. Participants will have the option of using various pieces of equipment, including stationary bikes, treadmills, and ellipticals. All participants will wear Sportline™ HR monitors in order to monitor workout intensity. HIIT sessions will be comprised of 2 workouts per week, working up to 14 × 30-second intervals at 90% maximal heart rate (HRmax) followed by 2-minute recovery at 50% HRmax. Participant programs will be designed by a Certified Exercise Physiologist. Group exercise classes will be supervised by a Canadian Society for Exercise Physiology Certified Personal Trainer® or a Yoga Alliance Registered Yoga Teacher®. All instructors will also complete an online Cancer and Exercise training course with Thrive Health Services©.³⁵

Holistic GMCB education sessions. Participants in the HIIT+ group will participate in weekly group GMCB-based education sessions that will be approximately 20 minutes in duration. These sessions will cover general education on living with celiac disease as well as specific behavior change skills within a group environment. Specifically, participants will learn about the importance of following a GFD to effectively manage celiac disease and prevent the onset of other autoimmune conditions, communication strategies to ensure one's meal is safe to consume when dining outside the home, and strategies to

overcome barriers to following a strict GFD. The sessions, run by a trained interventionist, follow the evidence-based GMCB format which is designed to promote individual behavior change (ie, increases in exercise behavior) using the power of a cohesive group.³⁶ The purpose of the sessions is to help participants develop the self-regulatory skills necessary to engage in regular exercise (independently) after study completion. Specifically, participants learn how to self-monitor their behavior, set goals, plan regular exercise, and overcome barriers to exercise. See Table 1 for more information on the topics discussed in the GMCB holistic education sessions.

Measures

Primary Outcomes

Gut microbiota. Total bacterial DNA will be extracted using FastDNA Spin Kit for Feces (MP Biomedicals, Lachine, QC, Canada). Ethanol precipitation will be performed on extracted bacterial DNA to ensure a purified sample and then it will be quantified using Qubit dsDNA assay (Life Technologies, Grand Island, NY) and diluted to 5 ng/μL working concentration. Microbial profiling will be conducted using the Illumina MiSeq platform, according to the Illumina 16S Sequencing Library Preparation protocol and in accordance with our previous work (Centre for Health Genomics and Informatics, Calgary, AB, Canada).^{37,38}

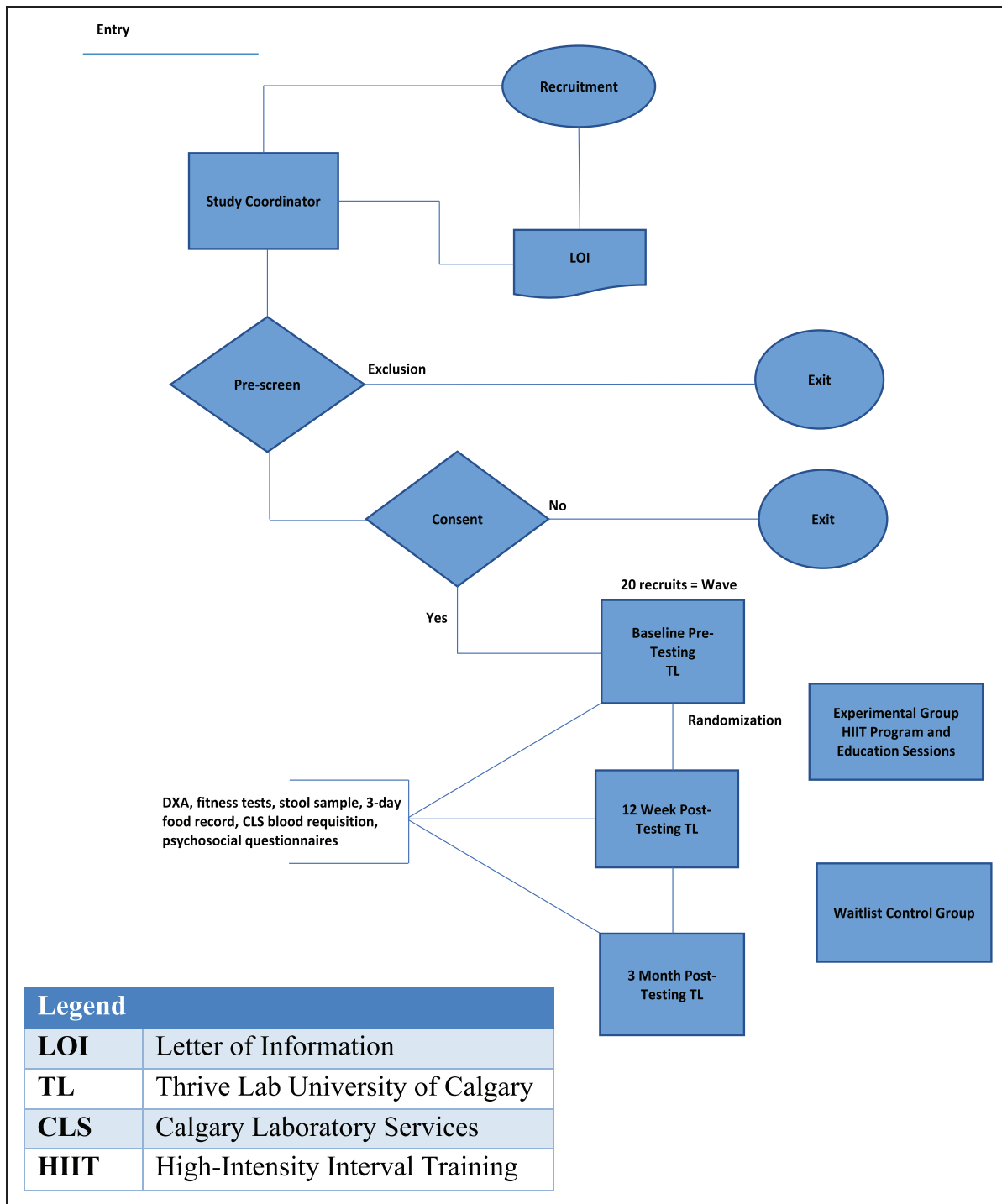


Figure 1. Flow diagram of the Understanding the Relationship Between the MicrobiOme, Vitality and Exercise in Celiac Disease Protocol. CLS, Calgary Laboratory Services; HIIT, high-intensity interval training; LOI, letter of information; TL, Thrive Lab University of Calgary.

Primary polymerase chain reactions (PCRs) will be used to amplify the V3-V4 region of the 16S rRNA gene and secondary PCRs will be used to attach dual indices to amplified regions with manufacturer recommended primers. Sequences will be trimmed to 250 nts and filtered

using the FASTX-toolkit. Chimeras will be removed and operational taxonomic units with 98% homology generated using USEARCH. Sequences will be classified from phylum to genus level using the Ribosomal Database Project MultiClassifier. Alpha and beta-diversity metrics

will be calculated in Quantitative Insights Into Microbial Ecology using rarefied data to control for the number of sequences in each sample.

Quality of life. A measure specific to living with celiac disease (Celiac Disease Quality of Life [CD-QoL])³⁹ will be used to assess participants' QoL. Participants will be asked to reflect over the last month of their lives and rate 20 statements relative to how they feel regarding coping with celiac disease. The statements consist of concerns such as increased risk of cancer, feeling depressed, thinking about food constantly, and the limitations from having celiac disease. The ratings for the extent of participant agreement range from 1 (*not at all*) to 5 (*a great deal*). Dorn et al.³⁹ reported acceptable convergent validity of the CD-QoL measure with abdominal pain and psychological distress ($r^2 = .35-.65$). In addition, they demonstrated acceptable divergent validity ($r = .62$) from the irritable bowel syndrome QoL assessment. Data derived from scores collected by Dowd and Jung⁴⁰ demonstrate acceptable internal consistency for this measure with an adult diagnosed celiac population (Cronbach $\alpha = .92$).

Secondary Outcomes

Metabolic assessments

Serum fasting glucose and lipids. Fasting (12 h) concentrations of glucose and serum lipids (triglyceride, high-density lipoprotein cholesterol, and low-density lipoprotein cholesterol) will be measured by Calgary Lab Services (Calgary, Canada).

Vascular assessments

Blood pressure. After the participant has been sitting quietly for at least 5 minutes, their blood pressure will be assessed. Following the Canadian Physical Activity, Fitness, and Lifestyle Approach (CPAFLA) Protocols, if the blood pressure is above 144/94, body composition assessments can be completed, but the exercise testing should not be. If the blood pressure is too high, the CEP can perform 2 trials to ensure accuracy.

Resting heart rate. Resting HR will be measured as a form of fitness screening during the assessments using a HR monitor. After at least 5 minutes of quiet sitting, HR will be taken. According to CPAFLA protocol, if the participant's HR is greater than 99 beats/minute, exercise testing will not be completed.

Body composition assessments. Using DXA (Hologic QDR 4500; Hologic, Inc, Bedford, MA), data regarding a participant's body composition and bone mineral density will be obtained.

Waist circumference. Two measurements will be taken on the right hip. According to CPAFLA Protocol, if there is more than a 0.5 cm difference between these measurements, another measurement should be taken. The final value (rounded to 1 decimal) will be the mean of the 2 values that are closest to each other.

Program measures

Attendance. Attendance will be calculated for the 12-week HIIT program by dividing the number of classes attended by the number of classes scheduled. The number of and reason for missed classes and testing assessments will be reported.

Physical fitness assessments

Submaximal exercise test. Direct measurement of VO_{2max} is an accurate method of determining cardiovascular fitness but requires time, equipment and highly trained personnel.⁴¹ The YMCA submaximal exercise test is effective at predicting VO_{2max} in subjects by extrapolating the relationship between HR and workload and eliminates many of the barriers of a direct aerobic test. At all 3 assessments, this test will be performed on a cycle ergometer to predict VO_{2max} and assess changes in submaximal HR.

Flexibility. A sit and reach test will be performed following 2 sets of a modified hurdler's stretch for 20 seconds on both sides. In addition, shoulder flexibility will be evaluated with the participant standing with the right arm overhead and bent at the elbow and the right palm resting on the back. Reaching behind with the left hand, palm outwards, both hands slide toward each other to try and make contact. The distance between fingertips or the overlap will be measured. The same test will be performed for the other side. For both the sit and reach test and the test for shoulder flexibility, 2 trials will be completed with the highest value being recorded.

Exercise intensity assessments

Heart rate. During each HIIT exercise class, the minimum, maximum, and average HRs of each participant will be assessed through HR monitors and recorded.

Rating of perceived exertion (RPE). The RPE scale will be used during the submaximal exercise test to obtain a subjective rating of how much effort the participant is putting into the task. A rating of 1 represents minimal effort and 10 is equivalent to exerting a lot of effort. The scale will also be utilized twice in the exercise classes: (1) after the fourth interval and (2) during the cool down period of the exercise classes.

Physical Activity Assessments

Self-reported exercise. Using the modified Godin-Shepard Leisure-Time Exercise Questionnaire (GLTEQ),⁴² adults can be classified as active and insufficiently active. Participants will self-report their average weekly exercise over the previous month for sessions that are at least 15 minutes in duration. The frequency and duration of strenuous, moderate, mild, resistance training, and flexibility training exercise that the participant completes will be reported. Amireault et al.⁴² determined that the GLTEQ is valid for classifying cancer survivors and that its use can go beyond their study to classify other insufficiently active respondents.

Psychosocial Assessments

Gastrointestinal symptoms. Using the Celiac Disease Specific Gastrointestinal Symptom Rating Scale (CeD-GSRS),⁴³ participants will be asked to choose the number that corresponds to the severity of the symptoms that they feel for 10 items. Responses range from 1 (*no discomfort at all*) to 7 (*very severe discomfort*). Symptoms include abdominal pain, hunger pains or a hollow feeling in the stomach in between meals, nausea, borborygmus (ie, rumbling or vibrations in the stomach), abdominal distension (ie, bloating), eructation (ie, burping), increased flatus (ie, passing gas), increased passage of stools, loose stools, and an urgent need for defecation. Svedlund et al.⁴⁴ found that the GSRS has a good interrater reliability of ≥ 0.86 .

Self-regulatory efficacy (SRE)—Exercise and GFD. Strachan and Brawley⁴⁵ developed a measure to assess participants' confidence in their abilities to self-manage their physical activity behavior. This measure was used to assess SRE to attend MOVE-C exercise sessions (10-items) and also adapted to assess participants' confidence in their own abilities to manage their dietary behavior to follow a strict GFD over the next month (8 items). The scale ranges from 0% (*not at all confident*) to 100% (*completely confident*) in 10% increments. Items on the exercise SRE questionnaire ask participants about their confidence to schedule MOVE-C classes, overcome barriers to attending MOVE-C classes and return to the MOVE-C classes if several in a row are missed. Items on the GFD questionnaire ask participants their confidence to be able to eat a strict GFD when outside the home, plan GF meals, read food labels, and adherence to a GFD after gluten is consumed. Data derived from the measure demonstrate acceptable levels of internal consistency (Cronbach $\alpha = .85$) for the exercise measure⁴⁵ and for the GFD measure (Cronbach $\alpha = .83$) among adults with celiac disease.⁴⁰

Sleep quality. Buysse et al.⁴⁶ created the Pittsburgh Sleep Quality Index (PSQI) to measure self-reported sleep quality and sleep disturbances. This 23-item questionnaire collects data on the following aspects of sleep: sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbance, use of medication, and daytime dysfunction. For example, participants are asked to report *time gone to bed, how long it takes to fall asleep (minutes), time of getting up in the morning, hours of actual sleep per night* and to assess the degree to which they have difficulties with each aspect. Buysse et al.⁴⁶ found that the PSQI was reported to be easy to use and understand and data derived from the instrument display acceptable levels of internal consistency (Cronbach $\alpha = .83$).

Self-compassion. Self-compassion was assessed using the short-form 12-item measure developed by Raes et al.⁴⁷ Participants were asked to respond to items regarding their self-compassion on a 1 (*almost never*) to 5 (*almost always*) scale. An exemplar item is "When I fail at something important to me I become consumed by feelings of inadequacy." Responses to negatively worded items are reverse scored and then the mean score across all 12 items is calculated with higher scores indicating higher self-compassion. Data derived from this measure have demonstrated acceptable reliability and validity in assessing self-compassion among adults (Cronbach $\alpha = .86$).⁴⁰

Energy and fatigue. Before and after each HIIT exercise class, participants will be asked to rate their energy and fatigue levels on a visual analog scale (VAS) from 0 (*none*) to 10 (*extreme*). Exercise has been found to improve energy levels and reduce fatigue (ACSM 2011).⁴⁸ These VAS have been successfully used in exercise settings to provide valid and reliable ratings of fatigue in relation to energy expenditure.⁴⁹

Feeling scale. The 1-item Feeling Scale (SC) by Hardy and Rejeski (1989) was used to assess how participants felt during the fourth interval and after the last interval. The scale ranges from +5 (*very good*) to -5 (*very bad*).

Feedback on program. During module 2 of the holistic education sessions and the questionnaire following the 12-week HIIT program, participants will be asked about their satisfaction with the MOVE-C program, their favorite part and any improvements they would like to see be made.

Nutritional Assessments

Three-day food record. Participants will be asked to complete 3-day food records prior to each assessment where

they will track their food intake for 2 days in the week and 1 day on the weekend. Food records will be analyzed using FoodWorks 14 Software (The Nutritional Company, Long Valley, NJ, USA).

GFD adherence. Adherence to a GFD will be measured using the 7-item measure developed by Leffler et al.⁵⁰ This measure assesses 4 different aspects of adherence to a GFD (ie, perceived adherence to a GFD, celiac symptoms, self-efficacy, reasons to follow a GFD) with 4 different scales. An exemplar item is “How important to your health are accidental gluten exposures?” assessed on a 1 (*very important*) to 5 (*not at all important*) scale. Responses to items are summed for a total score where lower scores indicate stricter adherence to a GFD. Data derived from this measure provide acceptable levels of test-retest reliability (Pearson $r = .82$).⁵¹

Discussion

The primary goal of the MOVE-C study will be to examine the effects of a 12-week aerobic HIIT exercise and holistic education program on QoL and changes in the composition of the microbiome among inactive adults with celiac disease. Secondary outcomes will include the intervention impact on behavioral (exercise behavior and adherence to a GFD), physiological (risk factors for metabolic syndrome), and social cognitions (SRE, self-compassion). In addition, we will also assess relationships between changes in the behavioral, physiological, and psychosocial outcomes among those in the intervention condition.

Collectively, the data from this study will enhance our understanding of the effects of a combined exercise and lifestyle intervention on important health related outcomes among a chronic disease population—inactive adults with celiac disease. Indeed, eligible participants are at risk of developing additional chronic diseases if they remain inactive. This study is the first to deliver an exercise + lifestyle intervention to inactive adults with celiac disease and to comprehensively examine behavioral, physiological, and psychosocial outcomes. Findings from this study may ultimately inform the development of similar exercise + lifestyle interventions for patients with other gastrointestinal conditions including inflammatory bowel disease and irritable bowel syndrome, who are likely to struggle with similar negative physical and psychosocial stresses as adults with celiac disease.

The following research themes will be assessed through the pilot data collected in the MOVE-C study:

1. QoL, composition of the microbiota and HIIT + holistic lifestyle education. The primary aim of this study is to examine the effects of a 12-week HIIT + holistic lifestyle education program on

changes in QoL and composition of the microbiota among inactive adults with celiac disease. While going on a strict GFD often leads to improvements in QoL among people diagnosed with celiac disease, in many cases people still report lower QoL, high treatment burden and symptoms despite following a strict GFD.^{5,7,52} An abundance of previous research indicates that engagement in regular exercise leads to improvements in QoL in chronic disease populations.⁹ In addition, engagement in exercise also leads to beneficial changes in the microbiota (increases in microbial diversity and reductions in pathogenic species) and intestinal health (preservation of healthy morphology in the small intestine).⁵³ To date, there have not been any studies examining the effects of exercise on either of these outcomes in people with celiac disease. Research is needed to determine if QoL and the composition of the microbiota can improve in adults with celiac disease in response to a 12-week HIIT + lifestyle program.

2. HIIT + lifestyle education and markers of metabolic syndrome. One of the secondary outcomes in this study is to assess the effects of the exercise + lifestyle intervention on metabolic health outcomes in inactive adults with celiac disease. HIIT training leads to improvements in body composition, insulin sensitivity and glucose control that are at least as beneficial as those found with MICT protocols. Specifically, Kilpatrick et al.²⁷ reported in a recent review that HIIT training led to significant reductions in abdominal visceral fat mass in patients with type 2 diabetes. Data from previous research also indicates that 2 weeks of aerobic HIIT leads to significant improvements in insulin sensitivity in overweight individuals and patients with type 2 diabetes mellitus.^{54–56} HIIT also leads to vascular improvements in terms of endothelial function and elasticity of arterial blood vessels.^{57,58} This study will examine if a HIIT + lifestyle education program can lead to improvements in key indicators of metabolic health in this population at risk for metabolic syndrome.
3. HIIT + lifestyle education, gastrointestinal symptoms, behavioral, and psychosocial outcomes. Drawing on the anticipated improvements in composition of the gut microbiome and research on the benefits of HIIT for gut health^{53,59} and patients with chronic¹⁶ and immune-based diseases,⁶⁰ we anticipate that the MOVE-C program will lead to improvements in reported gastrointestinal symptoms. Given the focus on exercise and healthy living in a group-based format, we anticipate improvements in behavioral (adherence to a GFD and exercise behavior) outcomes based on previous similar GMCB programs.^{29–31,36,61} Furthermore, we anticipate that participants will have more confidence to engage in

these behaviors on their own (SRE for exercise and GFD⁶²) as they have an opportunity to master them through the program. Neff and Germer⁶³ have demonstrated that self-compassion is a skill that can be taught, and accordingly, participants will learn to practice this skill in the biweekly education sessions. Finally, based on improvements in physical and psychological domains and learning sleep hygiene skills in the education sessions, we anticipate that participants will also report improvements in sleep quality after completing the program.

4. Relationship between changes in the physiological and psychosocial outcomes. Given the anticipated improvements in physiological and psychosocial outcomes after engaging in the MOVE-C intervention, this study will also allow us to elucidate relationship (s) between changes in both types of outcomes. To date, research has primarily focused on the etiology of celiac disease and treatment options—both important avenues to explore. However, improving our understanding of the relationship(s) between changes in these key outcomes will inform the development of future programs designed to empower patients to heal their guts after a celiac disease diagnosis and optimize QoL while living with a chronic disease.
5. Acceptability of HIIT for inactive adults with celiac disease. Over the past 5 years, there has been considerable debate regarding the acceptability of aerobic HIIT for relatively inactive populations. Indeed, some evidence suggests that higher intensities of exercise lead to negative affect and enjoyment, which may reduce the likelihood that inactive persons would continue this type of exercise.⁶⁴ Importantly, this research focused on assessment of affect *during* the high intensity interval. Other researchers have also examined this important question and have found that while affect is lower during high intensity exercise, when asked *after* the class if they would do it again, previously inactive participants are more likely to sign up for HIIT versus MICT.⁶² Following recommendations to optimize participant affective responses, MOVE-C HIIT sessions are relatively short (less than 60 s) and high intensity (ie, near maximal, approximately 90% of aerobic capacity). As such, it is anticipated that a progressive HIIT protocol will be well-tolerated (as indicated by attendance to the 12-week program and low levels of dropout) among this inactive population and that participants will continue to be active after the 12-week program has ended.

In summary, in this article, we provide a rationale for the MOVE-C program, including a detailed overview of the HIIT exercise + holistic lifestyle education sessions for inactive adults with celiac disease.

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Author Contributions

Principal responsibility for the study design and conduct was assumed by AJD and SNCR. All authors contributed to study design. AJD, LK, CP, and JTD drafted the manuscript. All authors read and commented on drafts and approved the final manuscript.

Declaration of Conflicting Interests


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