TITLE: A comparison between a standardized (GLA:D™ Canada) and an individualized (JointEffort) exercise program on functional mobility, quality of life, pain management, and inflammatory biomarkers in knee osteoarthritis patients.

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BACKGROUND: Osteoarthritis (OA) is the leading cause of disability worldwide and affects more than 4.4 million people in Canada (13% of Canadians) [1]. OA symptoms include joint pain, stiffness, range of motion loss, and inflammation, resulting in a significant decrease in quality of life [2, 3]. Current evidence-based guidelines for OA management recommend weight loss, patient education, exercise therapy, bracing, viscosupplementation, and anti-inflammatory/pain medications prior to joint replacement surgery [4]. Unfortunately, current practice trends are not consistent with these guidelines and focus largely on joint replacement. Recently, research from a group in Denmark has shown a reduction in the progression of knee OA symptoms, joint related painkiller use, individuals on sick leave, and higher physical activity levels 12 months after a combined patient education and standardized group exercise therapy program (GLA:D®) [5-7]. Based on the Danish success, the GLA:D® program has been made available in Canada. To date it is unclear if the GLA:D™ Canada program will result in outcomes similar to those seen in Denmark, or how the GLA:D™ program compares to existing individualized OA care programs (i.e. JointEffort).

RESEARCH QUESTIONS:
1. Is the GLA:D™ standardized education and exercise program associated with improvements in functional mobility, quality of life, pain management, and inflammatory biomarkers in knee OA patients in Calgary, Alberta?
2. Is the JointEffort individualized exercise and education program associated with improved functional mobility, quality of life, pain management, and inflammatory biomarkers in knee OA patients in Calgary, Alberta?
3. Do the improvements in functional mobility, quality of life, pain management, and inflammatory biomarkers in knee OA patients differ between those enrolled in the GLA:D™ and the JointEffort education and exercise programs?

OBJECTIVES: The objectives of the proposed study are to 1) assess the association between participation in the GLA:D™ standardized program and functional mobility, quality of life, pain management, and inflammatory biomarkers in knee OA patients, 2) assess the association between participation in the JointEffort individualized program and functional mobility, quality of life, pain management, and inflammatory biomarkers in knee OA patients, and 3) assess if there are any differences in outcomes between the standardized (GLA:D™) and individualized (JointEffort) exercise programs.

METHODOLOGY:
Study Participants: A convenience sample of 60 participants ≥50 years of age with a primary care physician or orthopedic surgeon knee OA diagnosis will be included in the study. Specifically, 30 individuals will participate in 1) the GLA:D™ program and 30 sex- and age-matched individuals will participate in 2) the JointEffort program. 50 participants is a conservative estimate based on the ability to detect a moderate effect between study groups ($1-\beta=0.8$, $\alpha=0.05$).

Study Recruitment: Study participants will be recruited from the current ongoing Active Living JointEffort Program and GLA:D Program (Calgary, AB). Participants in this study are patients (male and female) that include the following: have been diagnosed with OA by a primary care physician or orthopedic surgeon; ≥50 years of age; are able read, understand, and provide informed consent in English; and can attend exercise programming classes at the University of Calgary. Participants will be approached by the program staff to obtain consent to be contacted by the research coordinator to discuss the study and indicate if they are interested

in participating in either the JointEffort program or GLA:D program. Once consent is obtained, the research coordinator will contact these patients and screen them to confirm eligibility. Participants will be reimbursed for any additional parking costs associated with assessments. Participants will not incur any further costs as a result of participation in the study.

Inclusion and Exclusion Criteria

Inclusion criteria for participation in the study are the following:
(1) have been diagnosed with OA by a primary care physician or orthopedic surgeon;
(2) ≥50 years of age;
(3) are able read, understand, and provide informed consent in English; and
(4) can attend exercise programming classes at the University of Calgary.

Exclusion criteria for participation in the study are the following:
(1) have physical or neurological impairments or pre-existing medical conditions where physical activity is contraindicated;
(2) have inflammatory arthritis, a fracture, tumor, or acute trauma; and
(3) participated in the JointEffort or GLA:D program previously.

Exercise Programs: The GLA:D™ program consists of 1) pre and post program outcome measurement (self-reported and functional outcomes); 2) 2 1-1.5 hour education sessions including information on OA disease characteristics, treatments and self-help strategies; and 3) a neuromuscular exercise (warm-up, circuit training, and cool down) training program administered in 1 hour, small (up to 10 persons) group-based, supervised sessions twice weekly for 6 weeks. The goal of the exercises is to restore neutral, functional alignment of the legs by building compensatory functional stability and improving sensorimotor control. The JointEffort program consists of: 1) one appointment aimed at individualized program design; 2) a nutritional seminar taught by a registered dietician explaining dietary recommendations for OA patients and inflammatory conditions, including weight loss and/or management; and 3) an individualized exercise (strength and neuromuscular training, balance training, and range of motion exercises) training program administered in 1 hour, small (up to 10 persons) group-based, supervised sessions twice weekly for 6 weeks.

Study Outcomes:

1) Participant Characteristics, Adherence, and Medication Use: Demographic (age, sex, height, weight, and body mass index), comorbidity, attendance, exercise log, and medication use details will be recorded at each visit. Adherence will be measured by exercise program attendance (number of sessions).

2) Self-Reported of Symptoms, Function, and Quality of Life: The following self-report questionnaires will be completed at baseline, 2, and 12 months: the Knee Injury and Osteoarthritis Outcome Score (KOOS) [8], the Intermittent and Constant Osteoarthritis Pain (ICOAP) Score [9], and the EuroQOL-5 Dimensions (EQ-5D-5L) Score [10].

3) Disease Knowledge and Arthritis-Related Self-Efficacy*:* The patient knowledge questionnaire on OA (PKQ-OA) [11] and the arthritis self-efficacy questionnaire [12] will be completed at baseline, 2, and 12 months.

4) Physical Function: All participants will complete the 40m Face-Paced Walk Test and the 30s Chair Stand Test [13] at baseline, 2, and 12 months.

3) Biomarker Analysis: A blood serum sample, collected at baseline, 2, and 12 months will be analyzed to assess for inflammatory biomarkers using a Discovery Assay (42 Custom-Plex human assay) with Luminex®xMAP technology (Eve Technologies).

STATISTICAL ANALYSIS: Descriptive statistics (mean (95% CI), proportion (95% CI) or median (range) will be used report the baseline, 2, and 12 month change in self-report, functional and biomarker outcomes, as appropriate. To account for the matched design, mean within-pair difference (95% CI) will be used to compare treatment groups across outcomes. Finally, conditional logistic regression will be used to assess the relationship between attendance (number of sessions) and 12 month change in each outcome.

PROJECT FLOWCHART

TIME POINT	GLA:D™ Canada Group (Standardized Exercise Program)	JointEffort Group (Individualized Exercise Program)
Baseline Appointment	1) The GLA:D™ Canada program will be explained. 2) Participants will be asked to complete the questionnaires (KOOS, EQ-5D-5L, ICOAP, PKQ-OA, and the arthritis self-efficacy questionnaire). 3) Demographics, symptoms, comorbidities, and medication use will be recorded. 4) Blood draw for biomarker analysis. 5) Participants will be asked to complete physical function tests (40m Face-Paced Walk Test and the 30s Chair Stand Test).	1) The JointEffort program will be explained. 2) Participants will be asked to complete the questionnaires (KOOS, EQ-5D-5L, ICOAP, PKQ-OA, and the arthritis self-efficacy questionnaire). 3) Demographics, symptoms, comorbidities, and medication use will be recorded. 4) Blood draw for biomarker analysis. 5) Participants will be asked to complete physical function tests (40m Face-Paced Walk Test and the 30s Chair Stand Test). 6) Individualized program design.
Weeks 1-7	1) Two education sessions about OA (1-1.5 hours each), including the degeneration process in the joint, how the GLA:D™ Canada exercises improve joint stability, and how to retain joint stability through day to day self-management techniques. 2) Standardized neuromuscular training sessions twice a week for 6 weeks (60 minutes per session).	1) One nutritional seminar taught by a registered dietician explaining dietary recommendations for OA patients and patients with inflammatory conditions, and weight loss and/or weight management. 2) Individualized strength and neuromuscular training sessions twice a week for 6 weeks (60 minutes per session).
2 Months	1) Participants will be asked to complete the questionnaires (KOOS, EQ-5D-5L, ICOAP, PKQ-OA, and the arthritis self-efficacy questionnaire). 2) Symptoms and medication use will be recorded. 3) Blood draw for biomarker analysis. 4) Participants will be asked to complete physical function tests (40m Face-Paced Walk Test and the 30s Chair Stand Test).	1) Participants will be asked to complete the questionnaires (KOOS, EQ-5D-5L, ICOAP, PKQ-OA, and the arthritis self-efficacy questionnaire). 2) Symptoms and medication use will be recorded. 3) Blood draw for biomarker analysis. 4) Participants will be asked to complete physical function tests (40m Face-Paced Walk Test and the 30s Chair Stand Test).
12 Months	1) Participants will be asked to complete the questionnaires (KOOS, EQ-5D-5L, ICOAP, PKQ-OA, and the arthritis self-efficacy questionnaire). 2) Symptoms and medication use will be recorded. 3) Blood draw for biomarker analysis. 4) Participants will be asked to complete physical function tests (40m Face-Paced Walk Test and the 30s Chair Stand Test).	1) Participants will be asked to complete the questionnaires (KOOS, EQ-5D-5L, ICOAP, PKQ-OA, and the arthritis self-efficacy questionnaire). 2) Symptoms and medication use will be recorded. 3) Blood draw for biomarker analysis. 4) Participants will be asked to complete physical function tests (40m Face-Paced Walk Test and the 30s Chair Stand Test).

OTHER STUDY PROTOCOL DETAILS

Blood Collection

A certified phlebotomist will collect 4ml of blood (2 x 2ml collection tubes) from the participant by venipuncture. Samples will be stored on ice and then immediately centrifuged for 10 minutes at 1300rpm. The samples will be aliquoted into blood (3ml total) and serum (1ml total) and stored in a -80 degree freezer until biomarker analysis.

Data Collection and Storage

All questionnaires (KOOS, ICOAP, EQ-5D-5L, PKQ-OA, and arthritis self-efficacy questionnaire) will be collected in person (paper copies). Study data will be kept in a locked filing cabinet in the JointEffort Office (Active Living, University of Calgary) or on a secure password protected computer by the principal investigator or research coordinator. The study documents will be kept for 5 years after the completion of this project (anticipated by 2019) at which they will be destroyed by the professional company used by the University of Calgary (Enviroshred) in 2024.

Data Access

Research personnel including the following: the principal investigator, the research team (co-investigators), the research coordinator, and research trainees will have access to the participant data.

Research Locations:

Exercise Programming: Active Living, Fitness Centre, Faculty of Kinesiology (University of Calgary, Calgary, AB)

Biomarker analysis site: Centre for Mobility and Joint Health, McCaig Institute for Bone and Joint Health, Cumming School of Medicine (University of Calgary, Calgary, AB)

Data analysis site: Department of Physical Therapy, Faculty of Rehabilitation Medicine, University of Alberta, Edmonton, AB and McCaig Institute for Bone and Joint Health, Cumming School of Medicine (University of Calgary, Calgary, AB)

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