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Prescribing exercise for diabetes prevention

Submission date	Recruitment status	[ ] Prospectively registered
30/07/2009	No longer recruiting	[ ] Protocol
Registration date	**Overall study status**	[ ] Statistical analysis plan
11/02/2010	Completed	[ ] Results
Last Edited	**Condition category**	[ ] Individual participant data
11/02/2010	Nutritional, Metabolic, Endocrine	[ ] Record updated in last year

Plain English summary of protocol
Not provided at time of registration

Study website
http://dual.ca/artemis/index.html

Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
CCT-83029

Study information

Scientific Title
A multicentre, prospective, randomised study to determine the effects of an exercise managed intervention (ARTEMIStudy)

Acronym
ARTEMIS

Study objectives
Primary objective:
To compare the reduction in mean systolic blood pressure (SBP) within the first 4 hours of awakening using an automated home blood pressure device, in patients treated for 12 weeks with a combined aerobic and resistance exercise program versus usual care.

Secondary objectives:
1. To compare the reduction in mean SBP and diastolic blood pressure (DBP) as recorded by ambulatory home BP (A&D Medical Blood Pressure Monitor with Bluetooth®)
2. To compare the change in fasting glucose levels (LifeScan OneTouch Ultra II Blood Glucose Monitor + Polymap Bluetooth® Adaptor for the OneTouch Ultra II), and HbA1c levels
3. To compare the change in triglyceride, high density lipoprotein cholesterol (HDLc) and low density lipoprotein cholesterol (LDLc) levels
4. To compare the reduction in mean SBP and DBP, as recorded by clinic BP using BpTRU™
5. To compare the reduction in waist circumference and weight
6. To compare the improvement in mean steps per day using an Omron® pedometer
7. To compare the change in resting heart rate and heart rate variability over 24 hours
8. To compare the change in stage of change for physical activity (Prochaska and DiClemente's "Stage of Change" model)
9. To compare the change in predicted maximal oxygen consumption (VO2max) using the STEP™ test
10. To compare the change in quality of life (using 36-item short form health survey [SF-36], version 2)
11. To compare the change in vascular geometry and elastic properties of the carotid, aorta and femoral arteries
12. To compare the change in muscle sympathetic nerve activity discharge patterns and how this relates to peripheral (i.e., forearm) and systemic vascular resistance
13. To compare the change in C-reactive protein (CRP), insulin, catecholamines, vasopressin, plasma renin activity, angiotensin II, aldosterone, oestrogen, progesterone, cortisol, creatinine, microalbumin, homocysteine, heat shock proteins, adiponectin, and leptin
14. To compare the change in 3D ultrasound and cardiac function (echocardiography; including systolic function, diastolic function, ejection fraction, left ventricular wall dimensions and volume and stroke volume)
15. To compare the change in self efficacy (measured by diabetes and physical activity scales)

Phase 1 and 2 exercise intervention groups will then be compared at all timepoints (weeks 12, 24, 52). Because exercise interventions have appreciable attrition rates of up to 50% at six months; we will assess both intervention groups again at 6 months post study to determine decay effects.

Hypotheses:
Null hypotheses:

1. Improved exercise behaviours in either phase 1 or 2 will not enhance primary, secondary or tertiary outcomes
2. There will be more change of primary, secondary and tertiary outcomes in institutional versus community settings (phase 1 versus 2)

Alternative hypotheses:
1. Improved exercise behaviours in either phase 1 or 2 will enhance primary, secondary or tertiary outcomes
2. There will be equivalent change in primary, secondary and tertiary outcomes in phase 1 and 2 settings
3. The model of cardiovascular disease (CVD) risk factor diminution in metabolic syndrome described herein will be effectively deployed using a translational research approach using allied health care provider prescription

Ethics approval required
Old ethics approval format

Ethics approval(s)
The University of Western Ontario Research Ethics Board for Health Sciences Involving Human Subjects (HSREB) approved on the 10th March 2009 (ref: 15828)

Study design
Multicentre prospective randomised controlled trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet
Not available in web format, please use the contact details below to request a patient information sheet

Health condition(s) or problem(s) studied
Metabolic syndrome; cardiovascular complications of type 2 diabetes

Interventions
Patients with metabolic syndrome from an urban community (London, Ontario) will be randomly assigned to either the combined aerobic-resistance exercise intervention or exercise control groups in an institutional-academic research setting. At another study site (rural Ontario), participants representing each group will be randomly assigned to a combined aerobic-resistance exercise intervention or exercise control groups in a home-based setting where all

clinical data and intervention will be matched to the institutional site but delivered using wireless-enabled technology. The study will continue for one year for both interventional settings (rural and institutional). Follow up will be for one year.

Intervention Type
Other

Phase
Not Applicable

Primary outcome measure
1. Clinical blood pressure, recorded using a programmable automated device (BP-TRU™ 100 model, Vancouver, BC)
2. Blood glucose, lipid profiles, CRP and markers of RAS function: fasting blood glucose will be measured in the institutional setting using laboratory assays. In the rural setting, patients will use a remote monitoring glucometer (Bluetooth® enabled) as well as scheduled laboratory assays. Lipid profiles and CRP will be assessed using laboratory assays. Plasma catecholamines will be assessed by high pressure liquid chromatography whereas vasopressin, angiotensin and cortisol will be determined by radioimmunoassay approaches.
3. Predicted V02 max: subjects will perform a modified self-selected STEP™ test. Based on values of subject's height, weight, resting heart rate, training heart rate, and performance on the STEP™ test, V02 max values will be calculated.
4. Body composition, body mass index (BMI - kg/m^2), waist circumference

All measured at baseline, 3, 6, 9 and 12 months.

Secondary outcome measures
1. 3D ultrasound measurement of carotid artery: patients will undergo a 3D ultrasound exam to assess the extent of their carotid atheromatous disease
2. Behavioural measures: surveys to examine changes in behaviour change with exercise interventions and quality of life, i.e., stage of change, self efficacy, decisional balance, SF-36
3. Physiological measures:
3.1. Cardiac function: standard echocardiographic approaches using B-mode and M-mode echo Doppler imaging will be performed by a certified echocardiographic technologist. Image location and gain settings will be adjusted to yield optimal definition of endocardial and epicardial borders. Chamber and wall dimensions will be measured according to the standard methods of the American Society of Echocardiography and left ventricular (LV) fractional shortening will be calculated from the difference between systolic and diastolic cavity dimensions over 3 cardiac cycles at end diastole taken at the QRS peak. LVM will be calculated according to the method of Devereux et. al. and normalised to body surface area (BSA). Left ventricular diastolic filling will be assessed in the left lateral decubitus position (supine) or sitting (upright) and data manually traced and digitised from 5 cardiac cycles in each subject. Pulsed Doppler transmitral flow velocities will be taken from the apical 4-chamber view between the tips of the mitral valve leaflets. Doppler data will be manually traced and digitised in each subject. Measures of peak early flow velocity (E), atrial flow velocity (A), isovolumic relaxation time (IVRT) and early deceleration time (DT) will be recorded at a sweep speed of 50 or 100mm/s. Intimal-media thickness of the right common carotid artery will be assessed with longitudinal B-mode images of the carotid artery in the patient's supine position with the head turned 45 degrees away from the side examined at a straight portion of the artery 1 - 2 cm proximal to the bifurcation.
3.2. Vascular properties: major conduit vessels will be examined because these provide the major buffering capacity for systolic pressure and they provide enhanced spatial resolution for

analysis. Using B-mode echo Doppler imaging and the EchoPak software in the GE/Vingmed Ultrasound machines (System FiVe and Vivid I) we will measure the wall thickness (anterior and posterior wall) and cross-sectional diameter of each arterial segment at systole and again at end diastole. Electrocardiogram (ECG) markers will provide cues about the cardiac cycle phase. Measures of all variables will be made from three separate cardiac cycles in carotid, femoral and aortic vessels taken at end expiration. This procedure should take approximately 45 minutes, which includes setup time and verification of the data.
3.3. Muscle sympathetic nerve activity: microneurographic sympathetic activation will be obtained from the common peroneal nerve. A 200 µm-diameter, 35 mm long tungsten microelectrode that tapered to an uninsulated 1- to 5-µm tip is inserted transcutaneously into the perineal nerve just posterior to the fibular head. A reference electrode is positioned subcutaneously 1 - 3 cm from the recording site. Neuronal activity is amplified 1,000 times by a pre-amplifier and 50 - 100 times by a variable gain isolated amplifier. The signal is band-pass filtered with a bandwidth of 700 - 2,000 Hz and then rectified and integrated to obtain a mean voltage neurogram (0.1 sec time constant). A muscle sympathetic nerve activity (MSNA) site is confirmed by the characteristic pulse-synchronous burst pattern that does not produce skin paresthesias and that increases in frequency during a voluntary apnea but not during arousal to a loud noise.
3.4. Lower body negative pressure: the participant's lower body will be sealed inside an air-tight box at the hips. A small vacuum can be created in this box that mimics the effect of postural changes on the cardiovascular system. Levels of suction up to -40 mmHg will be used; this simulates levels of cardiovascular stress that are equivalent to the seated position.
3.5. Cardiovascular reactivity: the Stroop Test - subjects are asked to identify the colour of the text ignoring the semantic meaning of the word. Presentation of slide rate is increased over time to create an increasing stress level. Blood pressure, heart rate and MSNA will be measured as indices of the stress response.
3.6. Forearm endothelial function: using B-mode echo Doppler ultrasound we will make continuous measures of brachial artery diameters for 3 minutes following the release of a 5 - 10 minute period of forearm circulatory occlusion. This test is used as an index of endothelial function as the brachial artery dilation is related to shear stress. To test the effect of endothelial dysfunction the test will also be performed before and after the sublingual administration of 0.4 mg nitroglycerine. The nitroglycerine acts as a nitric oxide donor and will enhance both diameter and compliance responses under conditions where inadequate endothelial-derived nitric oxide is produced.
3.7. Continuous blood pressure: a finger cuff device (Finometer) will be used to measure blood pressure continuously. Similarly, a pulse oximeter will be placed around a toe in order to detect flow oscillations at that site. The finger cuff may feel a little tight and the finger may turn blue while in operation. However, these sensations go away immediately when the machine is turned off.

All measured at baseline, 3, 6, 9 and 12 months.

Overall study start date
01/08/2009

Completion date
31/12/2012

Eligibility

Key inclusion criteria

1. Male or female
2. Aged 18 to 70 years
3. Presents with metabolic syndrome as defined by having SBP greater than 130 mmHg and/or DBP greater than 85 mmHg and any two of the following criteria:
3.1. Abdominal obesity (waist circumference greater than 102 cm in males; greater than 88 cm in females)
3.2. Fasting triglycerides greater than 1.695 mmol/L
4. Low HDL cholesterol: males less than 1.04 mmol/L; females less than 1.29 mmol/L
5. Fasting glucose greater than 5.60 mmol/L

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
720

Key exclusion criteria
Any patient who:
1. Has an in-clinic mean SBP greater than or equal to 180 mmHg and/or DBP greater than or equal to 110 mmHg
2. Has a history of myocardial infarction, angioplasty, coronary artery bypass, or cerebrovascular ischaemia/stroke
3. Has symptomatic congestive heart failure
4. Has atrial flutter
5. Has uncontrolled hypertension
6. Has unstable angina
7. Has unstable pulmonary disease (e.g., asthma or obstructive lung disease)
8. Uses medications known to affect heart rate (e.g., beta-blockers)
9. Has second or third degree heart block
10. Has a history of alcoholism, drug abuse, or other emotional, cognitive or psychiatric problem that is likely to impair compliance to the study
11. Requires the continuation of other medication which might interfere with the objectives of the study
12. Has a pacemaker
13. Has unstable metabolic disease (e.g. uncontrolled thyroid disease)
14. Has orthopaedic or rheumatologic problems that could impair ability to exercise
15. Has a history of allergy to any of the study drugs
16. Started, or changed dose of, a lipid lowering agent(s) within the previous 3 months
17. Is currently enrolled in a clinical research trial

Date of first enrolment
01/08/2009

Date of final enrolment
31/12/2012

Locations

Countries of recruitment
Canada

Study participating centre
Aging, Rehabilitation & Geriatric Care Research Centre
London
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Sponsor information

Organisation
Aging, Rehabilitation & Geriatric Care Research Centre (Canada)

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Sponsor type
Research organisation

Funder(s)

Funder type
Research organisation

Funder Name
Canadian Institutes of Health Research (CIHR) (Canada) - http://www.cihr-irsc.gc.ca - CVC Diabetes Team (ref: CCT-83029)

Results and Publications

Publication and dissemination plan
Not provided at time of registration

Intention to publish date

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not provided at time of registration