ISRCTN29195046 https://doi.org/10.1186/ISRCTN29195046

Mobilising vitamin D sequestered in adipose tissue in humans with Exercise (VitaDEx)

Submission date
08/01/2019

Recruitment status
No longer recruiting

Registration date
21/01/2019

Overall study status
Completed

Last Edited
12/05/2025

Condition category
Nutritional, Metabolic, Endocrine

[X] Prospectively registered
[X] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol

Background and study aims
Vitamin D can become trapped in adipose (fat) tissue and lead to low levels of vitamin D in blood. Up to half of people in the UK have low levels of the important form of vitamin D in their blood. Physical activity may be an effective way to mobilise vitamin D from adipose tissue – even without weight loss. Exercise has a powerful effect on the concentration of the important form of vitamin D in blood and stimulates the release of this form of vitamin D from adipose tissue. Based on these observations, regular exercise may improve the mobilisation of vitamin D from adipose tissue and increase the amount and availability of the important form of vitamin D in blood. The aim of this study is to examine the impact of exercise on vitamin D status and metabolism in men and women who are overweight.

Who can participate?
Participants must be non-smoking, aged 25-65, not taking vitamin D supplements, and have a Fat Mass Index (FMI) determined using DEXA of 7.5-15 kg/m2 (men) and 11-21 kg/m2 (women). They must not currently be participating in any vigorous physical activity, and do less than 150 minutes of moderate intensity physical activity per week, with an objectively assessed Physical Activity Level (PAL) of less than 2.00 (total energy expenditure/resting energy expenditure).

What does the study involve?
Participants are randomly allocated to either maintain their current lifestyle or undertake an exercise intervention for 10 weeks. The study assesses the impact of exercise on the various forms of vitamin D that are found in blood, and whether these changes lead to an improvement in the function of cells known to be affected by vitamin D status (a type of white blood cell called monocytes). Stable isotopes (non-radioactive tracers) are used to examine how the turnover of vitamin D is affected by exercise, to understand the biological pathways and mechanisms that are involved in vitamin D mobilisation and how they are affected by exercise. These exercise-induced changes are compared with a group of lean active adults to understand the independent effects of overweight and exercise on vitamin D mobilisation, status and metabolism. A sub group of the participants undergo assessments of the differences in vitamin D and other metabolites between the blood that flows into muscle and adipose tissue, and the

blood that flows out of the muscle and adipose tissue. This will show whether exercise leads to changes in the amount of vitamin D the adipose tissue releases into the blood, and muscle tissue takes up from the blood. This part of the study takes place at the University of Birmingham.

What are the possible benefits and risks of participating?
The risks and burdens in the study are attributed to the measurement techniques, and the short-term lifestyle changes of 10 weeks of exercise training for participants in the exercise group. This study includes blood sampling, adipose and muscle tissue sampling, scanning techniques that use ionising radiation, and exercise capacity tests. The benefits for participants in taking part is that they will receive a personalised summary of their own results including cardiorespiratory fitness, body composition, physical activity levels, dietary analysis and blood test results. Participants also receive a personalised gym-based 10-week exercise programme (with those not in the exercise group receiving this after they finish the study). Everyone who completes the study will receive an inconvenience payment of £250 (Love2shop gift vouchers). If they also elect to undertake the optional element of the study in Birmingham, they will receive an additional inconvenience payment of £150 (Love2shop gift vouchers). Participants in the comparator group (lean) will be offered a voucher with value of £50 upon completion, and £75 for participation in the testing in Birmingham. Reasonable other travel costs incurred will be reimbursed, and they will be given a visitors parking permit to allow parking at the University.

Where is the study run from?
1. University of Bath (UK)
2. University Hospitals Clinical Research Facility (UK)

When is the study starting and how long is it expected to run for?
April 2018 to September 2022

Who is funding the study?
Biotechnology and Biological Sciences Research Council (BBSRC) (UK)

Who is the main contact?
Dr Oliver Perkin
o.j.perkin@bath.ac.uk

Contact information

Type(s)
Scientific

Contact name
Dr Oliver Perkin

ORCID ID
https://orcid.org/0000-0001-8921-8708

Contact details
Dept for Health
1W5.111
University of Bath
Claverton Down
Bath

United Kingdom
BA2 7AY
+44 (0)1225 384356
o.j.perkin@bath.ac.uk

Additional identifiers

Integrated Research Application System (IRAS)
254160

Protocol serial number
CPMS 40354, IRAS 254160

Study information

Scientific Title
Mobilising vitamin D sequestered in adipose tissue in humans with Exercise (VitaDEx)

Acronym
VitaDEx

Study objectives
The main study hypothesis is that the 10 weeks of regular exercise in overweight adults in the absence of weight loss will improve or maintain concentrations of vitamin D in the blood over the winter months, compared to a control group not participating in regular exercise.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Wales Research Ethics Committee 5, Bangor, Health and Care Research Wales, Castlebridge 4, 15-19 Cowbridge Road East, Cardiff, CF11 9AB, Tel: +44 (0)7825 244673, WalesREC5@wales.nhs.uk, 17/12/2018, ref: 18/WA/0392

Study design
Randomized; Both; Design type: Treatment, Prevention, Physical, Cross-sectional

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Vitamin D deficiency

Interventions
This study uses a classic randomised control trial study design, combined with cross-sectional group comparison.

For the randomised control trial (RCT) arm of the trial, 50 overweight adults who are currently not physically active will be randomly allocated to either maintain their current lifestyle for 10 weeks (lifestyle maintenance group; n=25), or to undertake an exercise intervention for 10 weeks (exercise group; n=25). The exercise group will be required to stay weight stable during the intervention period, thus allowing the effect of exercise alone to be investigated. Vitamin D status and metabolism will be compared pre- and post-intervention between groups.

To compare the effect of being overweight and inactive on vitamin status and metabolism, a group of 20 lean active adults will undertake the same measurements as the overweight adults in the RCT on one occasion only. This group will undertake no intervention.

All participants, whether they are in the RCT arm or the lean comparator group, will undergo the same screening meeting, and the first six visits will be the same between groups. After the sixth visit, the lean comparator groups participation in the study will be complete, and those in the RCT arm of the study will begin their 10-week intervention period, before post-intervention assessments will be made. Crucially, both groups will be tested in the winter months (October-March) to avoid vitamin D from sunlight exposure confounding the data, and participants will not be eligible if they are planning to travel to sunny climates during that winter. The study visits are described below:

Screening: participants will be invited to the University of Bath to sign an informed consent form and undertake eligibility screening. This will involve assessment of general health status, skin colour assessment (Fitzpatrick skin phototype), including blood pressure, a full DEXA body scan, height, weight, waist-to-hip circumference measurement, and a short easy walk on the treadmill. Habitual physical activity will be assessed with a questionnaire, and participants will be given a physical activity monitor mounted on a chest strap to wear for nine days after this visit. The data collected in this visit and subsequent physical activity monitoring will confirm eligibility to participate. This data will be used to allocate overweight participants to an RCT group by way of minimisation.

Across the whole study, measurements will be taken on 12-14 occasions for the RCT arm (two of the visits are optional and would involve a trip to Birmingham), and 6-7 visits for the lean comparator group (with one optional trip to Birmingham). Each measurement has a degree of flexibility on scheduling, and some measurements can be done taken outside the laboratory setting which will be discussed with participants to ensure participation is as convenient as possible. If scheduling constraints mean that some of the study measures fall in the weeks just outside October to March of time, participants will be asked to limit exposure to direct sunlight between the hours of 10:00 and 17:00 by wearing long sleeves and trousers, wearing a hat, and wearing sunscreen on the face, neck, and hands.

Visit 1 (day 0): After an overnight fast, participants will be given a standardised breakfast, which will contain a stable isotope vitamin D ‘tracer’. This is a nonradioactive form of vitamin D that occurs naturally, and it will allow us to measure how much vitamin D metabolism or ‘turnover’. For the three hours after this breakfast, participants will be asked not to lie down, do strenuous exercise, or eat or drink anything other than water. This visit could be done in participants homes if they prefer.

Visit 2 (day 5-7): After at least three hours without eating, a 5 mL blood sample will be taken from the vein on the inside of the elbow using a small needle and syringe. We will measure vitamin D concentrations in the blood and other health-related indicators from this. Participants will then be asked to perform an easy treadmill walk to calibrate the activity monitor they will be asked to wear after the next visit. This visit will take less than 45 minutes.

Visit 3 (day 6-10): After at least three hours without eating, a 5 mL blood sample will be taken as in the second visit. We will then provide a physical activity monitor and sleep monitor to wear for nine days, a sleep diary, and a diet diary to record everything eaten and drunk for three days. This visit will take less than 30 minutes and could be done at participants homes.

Visit 4 (day 24-28): After an overnight fast we will take a 5 mL fasted blood sample as previously described, and then undertake a full DEXA body scan for body composition and a CT scan of the lower leg. This visit will take approximately 45 minutes.

Visit 5 (day 27-31): This is one of the main study trial days. Participants will be asked to arrive at the laboratory in the fasted state with a faecal sample collected no earlier than the night before, using a kit we have provided. Participants will be asked to provide a urine sample and the trialists will measure their body mass. Resting metabolism (resting metabolic rate) will be measured by collecting the air the participant breathes out for 30 minutes whilst resting on a bed. A cannula will be inserted into a vein in the arm, and a 20 mL blood sample will be collected, and participants will be asked to provide a saliva sample. A small sample of body fat will then be taken from the waist 5 cm to the side of the belly button, and sample of muscle tissue taken from the thigh muscle. After this, the trialists will provide a standardised breakfast meal and ask participants to rest in bed for four hours whilst they intermittently take blood and expired gas samples. This visit will take less than six hours. The trialists will take participants for a lunch of their choice on campus once these measurements are completed.

Visit 6 (day 29-33): After an overnight fast, cardiorespiratory fitness will be determined with an exercise test on a treadmill, starting at walking speed. This test will also tell us how much fat is used during exercise. During this test heart rate and the air that participants breathe out through a mask will be measured, so participants will be allowed time to get used to wearing this whilst exercising before starting the test. For participants in the Exercise Group, this will count as the first exercise session. This will take approximately 1 hour, and participants will be taken for a breakfast of their choice after the measurement. The 10-week Exercise or Lifestyle Maintenance period will begin after this visit.

Visit 7 (day 65-70): After an overnight fast, the trialists will take a 5 mL blood sample, and will ask participants to consume the same breakfast and vitamin D ‘tracer’ as in visit one. This could be done at participants' homes.

Visit 8 (day 71-78): After an overnight fast participants will be asked to provide a urine sample and saliva sample. The trialists will then take a 5 mL fasted blood sample as previously described, and undertake a full body scan for body composition and a scan of then lower leg. Participants will then be asked to perform an easy treadmill walk for to calibrate the activity monitor they will be asked to wear after the next visit. This visit will take less than 1 hour.

Visit 9 (day 72-81): After at least three hours without eating, we will take a 5 mL blood sample as in previous visits. This visit will take less than 30 minutes and could be done at the home.

Visit 10 (day 90-99): After an overnight fast the trialists will take a 5 mL fasted blood sample as previously described, and then undertake a full DEXA body scan for body composition and a scan of the lower leg. The trialists will then provide participants with physical activity monitor and sleep monitor to wear for nine days, a sleep diary, and a diet diary to record everything participants eat and drink for three days. This visit will take approximately 45 minutes.

Visit 11 (day 91-102): This is the second main trial day – and will be an exact repeat of the measurements taken during visit 6. For participants in the exercise group, this must be at least 24 hours after the last exercise session.

Visit 12 (day 93-104): After an overnight fast, cardiorespiratory fitness will be determined with an exercise test on a treadmill, starting at walking speed, as in visit 7. This will take approximately 1 hour.

Visit aftercare: On all occasions that participants are asked to either provide a blood sample or exercise after an overnight fast, they will be offered a meal/snack and drink, and ensure that they feel fully recovered before departing.

Optional visits: In the 10 days before visits 5 and 11, should they choose to undertake this element of the study, they will be transported by car to and from the University of Birmingham to measure the difference in vitamin D concentration in arterial and venous blood leaving both muscle and fat tissue. This will tell us how much vitamin D leaves adipose tissue and how much is taken up by muscle. Participants opting to undertake this optional component will be required to undergo an ultrasound scan of their tummy area for identification of suitable veins for the procedure, and sign a separate informed consent form.

Continuous monitoring: Once a week during the 10-week intervention period, participants will be sent an electronic questionnaire by email, with up to 12 questions assessing whether they have experienced any cold or flu like symptoms in the past week. This can be completed at their convenience. All participants in the RCT arm of the study will be provided with a Garmin Vivifit 4 wrist band to continuously estimate daily energy expenditure throughout the intervention period.

Exercise training programme: Participants in the exercise group will undertake a closely-monitored 10-week gym-based exercise intervention commencing between October and January. Exercise will be conducted indoors. The intervention will be progressive and start at a moderate relative intensity with both intensity and duration increased over time similar to our previous intervention studies. By the end of the intervention, participants will be exercising 4 times a week at 70% maximum oxygen uptake. This type of exercise intervention successfully improves adipose tissue function.

Exercise group participants weight stability: A potential confounder during exercise interventions is variability in energy balance and weight loss due to varying degrees of dietary compensation. Thus, the trialists will compensate for the increase in energy expenditure with food prescribed to offset the energy expended during exercise to maintain energy balance. They will monitor energy expenditure through the collection and analysis of expired air samples (indirect calorimetry) during exercise once a week and replace the energy that is expended during exercise sessions with foods containing no vitamin D. Participant weight (body mass) will be recorded every two weeks. Participants will be asked to repeat a 3 day weighed food and fluid record at approximately 6-7 weeks.

Intervention Type
Behavioural

Primary outcome(s)
Vitamin D ‘status’ is measured using serum 25OHD, pre- and post- 10 weeks of exercise

Key secondary outcome(s))

1. Vitamin D metabolite and vitamin D binding protein concentrations are measured in serum by mass spectrometry, pre- and post- 10 weeks of exercise
2. Urinary excretion of vitamin D metabolites is measured pre- and post- 10 weeks of exercise
3. Whole-body vitamin D turnover and metabolism is measured using stable isotopes for 4 weeks before, and during the last 4 weeks, of 10 weeks of exercise
4. Vitamin D bioavailability is measured via the function of monocytes cultured in participant serum pre- and post- 10 weeks of exercise
5. Adipose and skeletal muscle vitamin D content is measured by mass spectrometry, pre- and post- 10 weeks of exercise
6. Adipose vitamin D mobilisation (ex vivo) is measured by adipose tissue explant culturing under conditions stimulating lipolysis, pre- and post- 10 weeks of exercise
7. Adipose tissue transcriptome is measured using RNAseq pre- and post- 10 weeks of exercise
8. Protein expression (based on targets from RNAseq) measured by Western blotting, pre- and post- 10 weeks of exercise
9. Adipose and muscle arteriovenous differences for vitamin D metabolites, acylcarnitine, and calcitroic acid, in response to stimulation is measured by mass spectrometry pre- and post- 10 weeks of exercise (in a subset of participants only)
10. Fasted and fed serum hormones (e.g., insulin, appetite regulatory hormones) in a mixed meal tolerance test are measured by ELISA, multiplex assay, and mass spectrometry, pre- and post- 10 weeks of exercise
11. Systemic cytokines in serum and plasma are measured by ELISA and multiplex assay, pre- and post- 10 weeks of exercise
12. Blood and adipose tissue (stromal vascular fraction) immune cell phenotypes are measured by flow cytometry pre- and post- 10 weeks of exercise
13. Incidence of upper-respiratory tract infections measured by weekly questionnaires for the 4 weeks before, and during 10 weeks of structured exercise (added 31/03/2022): along with salivary IgA and LL-37 levels pre-, mid-way-through-, and post-intervention
14. Gut microbiome taxonomic composition and metabolic potential are measured by ‘omic’ technologies (mass spectrometry and NMR), pre- and post- 10 weeks of exercise

To examine the effects of adiposity alone on the aforementioned outcomes, these measurements will also be taken from a lean, active comparator group at one timepoint only.

Completion date
30/09/2022

Eligibility

Key inclusion criteria
Group 1: 10-week RCT in overweight men and women
1. Aged 25-65 years
2. Fat Mass Index (FMI) determined using DEXA of 7.5-15 kg/m2 () and 11-21 kg/m2 ().
3. Self-reported participation in no vigorous intensity physical activity and less than 150 minutes of moderate intensity activity per week AND an objectively assessed Physical Activity Level (PAL) less than 2.00 (total energy expenditure/resting energy expenditure)
4. Available during the winter months (October-March)
5. Non-smoker

Group 2: Lean comparator group
1. Aged 25-65 years
2. Fat Mass Index (FMI) determined using DEXA of 2-6 kg/m2 () and 4-9 kg/m2 ().

3. Self-reported participation in either 150 minutes of moderate intensity or 75 minutes of vigorous intensity physical activity per week AND an objectively assessed Physical Activity Level (PAL) greater than 1.75
4. Available during the winter months (October-March)
5. Non-smoker

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
25 years

Upper age limit
65 years

Sex
All

Total final enrolment
71

Key exclusion criteria
Group 1: 10-week RCT in overweight men and women
1. Current or recent use of weight loss drugs
2. Any reported recent (i.e. last 6 months) shift (> 5%) in body mass or large change in habitual lifestyle
3. Individuals with coronary heart disease, chronic kidney disease, type 2 diabetes, stroke, heart failure and peripheral arterial disease
4. Individuals with 'severe hypertension' defined as a blood pressure greater than 180/110 mmHg (British Hypertension Society and NICE guidelines – CG127)
5. Individuals unable to change their physical activity (e.g. through disability)
6. Positive responses to the Physical Activity Readiness Questionnaire (PAR-Q)
7. Recent (i.e. last 2 months) participation in another research trial or lifestyle supportive intervention. (Participants will be asked not to donate blood whilst participating in the study)
8. Taking medication that might interfere with the study outcomes
9. Regular consumption of dietary supplements containing vitamin D
10. Regular use of sunbeds
11. Abnormal resting ECG (for arteriovenous difference participants, only)
12. Sensitivity or allergy to lidocaine or any local anaesthetic medicines.
13. Pregnancy

Group 2: Lean comparator group
1. Current or recent use of weight loss drugs
2. Any reported recent (i.e. last 6 months) shift (> 5%) in body mass or large change in habitual lifestyle

3. Individuals with coronary heart disease, chronic kidney disease, type 2 diabetes, stroke, heart failure and peripheral arterial disease
4. Individuals with ‘severe hypertension’ defined as a blood pressure greater than 180/110 mmHg (British Hypertension Society and NICE guidelines – CG127)
5. Positive responses to the Physical Activity Readiness Questionnaire (PAR-Q)
6. Recent (i.e. last 2 months) participation in another research trial or lifestyle supportive intervention. (Participants will be asked not to donate blood whilst participating in the study)
7. Taking medication that might interfere with the study outcomes
8. Regular consumption of dietary supplements containing vitamin D
9. Regular use of sunbeds
10. Abnormal resting ECG (for arteriovenous difference participants, only)
11. Sensitivity or allergy to lidocaine or any local anaesthetic medicines.
12. Pregnancy

Date of first enrolment
24/04/2019

Date of final enrolment
01/04/2022

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
University of Bath (lead centre)
Claverton Down
Bath
United Kingdom
BA2 7AY

Study participating centre
University Hospitals Clinical Research Facility
Queen Elizabeth Medical Centre
Edgbaston
Birmingham
United Kingdom
B15 2TH

Sponsor information

Organisation
University of Bath

ROR
https://ror.org/002h8g185

Funder(s)

Funder type
Research council

Funder Name
Biotechnology and Biological Sciences Research Council; Grant Codes: BB/R018928/1

Alternative Name(s)
UKRI - Biotechnology And Biological Sciences Research Council, Agricultural and Food Research Council, Biotechnology & Biological Sciences Research Council, BBSRC, BBSRC UK, AFRC

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan
The participant-level data will be made publicly available in a University of Bath repository

IPD sharing plan summary
Stored in publicly available repository

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article		11/05/2025	12/05/2025	Yes	No
HRA research summary			26/07/2023	No	No
Protocol file	version 1.2	13/05/2019	17/07/2024	No	No