ISRCTN23421591 https://doi.org/10.1186/ISRCTN23421591

Ergocalciferol vs. Cholecalciferol Food Fortification Study

Submission date	Recruitment status
29/07/2011	No longer recruiting
Registration date	**Overall study status**
29/07/2011	Completed
Last Edited	**Condition category**
04/12/2017	Nutritional, Metabolic, Endocrine

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

Plain English summary of protocol

Background and study aims
Vitamin D is the term used to describe two molecules: vitamin D2 and vitamin D3. Vitamin D2 is found in some fortified breakfast cereals and margarines. Vitamin D3 is made in your skin when exposed to the sunlight during the spring and summertime but is also found in foods such as oily fish and eggs. Vitamin D is an important part of the diet because it plays an essential role in keeping bones and muscles healthy and so helping to prevent diseases such as osteoporosis (weakening of the bones) and osteomalacia (muscle weakness, bone pain). Unfortunately vitamin D deficiency is a very common problem in the UK, which is worrying due to the potentially consequences to health that can occur. There is also no recommended intake of vitamin D to consume within the diet at present. Recent research into the dietary intake and vitamin D levels in women in the UK found that there are too few foods available in the typical UK diet that contain enough vitamin D to be beneficial to health, and that both South Asian and Caucasian women within the UK have very low levels of vitamin D in their blood, especially during the winter time. Therefore this study aims to investigate whether consuming food and drink items with a specific amount of added vitamin D will improve blood levels in both South Asian and Caucasian women during the wintertime. The study will also examine whether there is a difference between the two types of vitamin D by measuring how quickly the levels of vitamin D rise over time. This study will inform us the optimum level of vitamin D to consume every day to maintain healthy levels in blood and also determine which type of vitamin D is best for health.

Who can participate?
Women aged 20-64 of Caucasian ethnic origin or partly-veiled women of South Asian (i.e. India, Pakistan, Bangladesh) or Arabian ethic origin.

What does the study involve?
You will be required to visit the University of Surrey on three separate occasions: at the start of the study, after 6 weeks and after 12 weeks. The study investigators will also arrange telephone appointments with you at 2-3 weekly intervals between visits. All three visits will follow a very similar order of activities. Each visit will last about 45-60 minutes and all take place in the morning (appointments available 7am-11am). Before your first visit, you will have been sent in the post a diet diary and asked to complete it for four days in a row. At your first visit you will have a scan of your wrist bones, a blood sample (equivalent to 5 teaspoons) will be taken, and

your blood pressure, waist circumference and weight will be measured. You will be given a special badge (dosimeter) to wear on your clothes which measures how much sunlight you come into contact with for 7 days after your first visit. You will receive two products (one juice, one biscuit) to consume for each day of the study. One product will be a placebo (i.e., containing no vitamin D), and the other product may contain vitamin D2, vitamin D3 or no vitamin D at all - what the second product contains will be chosen completely at random. Follow-up telephone appointments and the next visit will be arranged. At your second visit you will provide a blood sample (equivalent to 4 teaspoons), and the body measurements and blood pressure recording will be repeated. You will then be supplied with more of the food and drink items that you have been randomly assigned to consume for the study. Follow-up telephone appointments and the final visit will be arranged. A dosimeter and diet diary will be sent to you about one week before the third visit, to be returned to the study investigator at the third visit, when a final blood sample (equivalent to 4 teaspoons), body measurements and blood pressure recording will be taken.

What are the possible benefits and risks of participating?
The main benefit to you (if assigned to the vitamin D2 or vitamin D3 products) will be the consistent supplementation of vitamin D through the winter months, when vitamin D availability is dramatically reduced due to the weak sunlight. In addition, the information that you provide in this study will be of value to science with respect to whether the UK should have a dietary recommendation for vitamin D. You will receive information on your diet, as well as the results of your bone health measurements and your vitamin D status. Due to the study being food based, the risk of side effects is likely to be minimal. However, you may experience a slight stomach ache as you adjust to eating or drinking your assigned product. You should also be aware that the combined amount of calories from the biscuit and juice will add 150 kcal per day to your normal diet. You will have a chance to speak to a study investigator at Visits 2 and 3 to discuss any issues you may be having; study investigators are also contactable via telephone or email throughout the study if the enquiry is more urgent. A blood sample must be taken at each trial visit, and this may cause some light bruising. Occasionally some people can feel faint when they have their blood taken and so to help reduce the risk of this, you will have your blood sample taken either whilst you are lying down on a bed or reclined in a chair. The bone scan involves extremely low levels of radiation, which you will be exposed to once during the course of the study. The amount of radiation absorbed from the scan is equivalent to two hours of natural background radiation found in the UK.

Where is the study run from?
University of Surrey (UK).

When is the study starting and how long is it expected to run for?
From September 2011 to March 2013.

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

Who is the main contact?
Dr Laura Tripkovic

Contact information

Type(s)
Scientific

Contact name
Dr Laura Tripkovic

Contact details
Department of Nutritional Sciences
School of Biosciences and Medicine
Faculty of Health and Medical Sciences
Guildford
United Kingdom
GU2 7XH

Additional identifiers

Protocol serial number
10695

Study information

Scientific Title
Ergocalciferol (Vitamin D2) vs. Cholecalciferol (Vitamin D3) Food Fortification: Comparative Efficiency in raising 25OHD Status in Caucasian & Asian Women and Mechanisms of Action (D2-D3 Study)

Acronym
D2D3

Study objectives
Vitamin D deficiency is a very common problem in the UK which is worrying due to the potentially serious consequences to health that can occur. There is also no recommended intake of vitamin D to consume within the diet at present. Therefore the D2D3 Study aims to investigate whether consuming a food or drink with a specific amount of added vitamin D everyday will improve blood levels in both South Asian and Caucasian women during the wintertime. The study will also examine whether there is a difference between the two types of vitamin D (vitamin D2 and vitamin D3) by measuring how quickly the levels of vitamin D rise in blood over time. This study will indicate the optimum level of vitamin D to consume everyday to maintain healthy levels in blood and also determine which type of vitamin D is best for health.

On 13/07/2015 the following changes were made to the trial record:
1. The overall trial end date was changed from 25/01/2013 to 29/03/2013.
2. The target number of participants was changed from 462 to 355.

Ethics approval required
Old ethics approval format

Ethics approval(s)
First MREC, 13/07/2011, ref: 11/LO/0708

Primary study design
Interventional

Study design
Randomised interventional treatment trial

Study type(s)
Treatment

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

Interventions
Current interventions as of 13/07/2015:
1. The study will aim to recruit 265 caucasian women and 90 south-asian women who will be randomly assigned to the intervention groups
2. Participants will receive both a food and drink item containing vitamin D2, vitamin D3 or a placebo everyday for 12 weeks as detailed below:
2.1. Orange juice - D2, an orange juice drink containing 600IU of vitamin D2 with a placebo biscuit
2.2. Orange juice - D3, an orange juice drink containing 600IU of vitamin D3 with a placebo biscuit
2.3. Orange juice - placebo, an orange juice drink containing no vitamin D with a placebo biscuit
2.4. Unsweetened biscuit - D2, an unsweetened biscuit containing 600IU of vitamin D2 with a placebo orange juice
2.5. Unsweetened biscuit - D3, an unsweetened biscuit containing 600IU of vitamin D3 with a placebo orange juice
3. The participants will visit the Study Team at the beginning of the study and then for two more visits at 6-week intervals
4. At each visit a blood sample will be taken to measure the levels of vitamin D in the blood
5. Bone health, weight, blood pressure and dietary intake will also be measured
6. A further blood sample may also be taken for genetic analysis; looking specifically at the genes that are activated by vitamin D
7. To be followed up at 6 weeks and 12 weeks

Previous interventions:
1. The study will aim to recruit 348 caucasian women and 114 south-asian women who will be randomly assigned to the intervention groups
2. Participants will receive a food or drink containing vitamin D2, vitamin D3 or a placebo everyday for 12 weeks as detailed below:
2.1. Orange juice - D2, an orange juice drink containing 600IU of vitamin D2
2.2. Orange juice - D3, an orange juice drink containing 600IU of vitamin D3
2.3. Orange juice - placebo, an orange juice drink containing no vitamin D
2.4. Unsweetened biscuit - D2, an unsweetened biscuit containing 600IU of vitamin D2
2.5. Unsweetened biscuit - D3, an unsweetened biscuit containing 600IU of vitamin D3
2.6. Unsweetened biscuit - placebo, an unsweetened biscuit containing no vitamin D
3. The participants will visit the Study Team at the beginning of the study and then for two more visits at 6-week intervals
4. At each visit a blood sample will be taken to measure the levels of vitamin D in the blood
5. Bone health, weight, blood pressure and dietary intake will also be measured
6. A further blood sample may also be taken for genetic analysis; looking specifically at the genes that are activated by vitamin D
7. To be followed up at 3 months

Intervention Type
Other

Primary outcome(s)
Serum 25-hydroxyvitamin D at baseline, week 6 and week 12

Key secondary outcome(s)
Current secondary outcome measures as of 13/07/2015:
1. 1,25 dihydroxyvitamin D at baseline, week 6, week 12 (for 48 participants, high and low responders)
2. Blood pressure at baseline, week 6, week 12
3. Bone mineral density at baseline
4. C-terminal telopeptide (CTX) at baseline, week 6, week 12
5. Dietary intake at baseline and week 12
6. Fasting glucose and insulin at baseline, week 6, week 12
7. Full blood count at baseline only
8. Height, weight, waist circumference at baseline, week 6, week 12
9. Kidney function (U&Es) at baseline only
10. Leukocyte RNA analysis at baseline, week 6, week 12 (for 48 participants, high and low responders)
11. Liver function (LFTs) at baseline only
12. Non-Esterified Fatty Acid and Triacyglcerol at baseline, week 6, week 12 14.
13. Parathyroid hormone at baseline, week 6, week 12
14. Serum calcium, corrected calcium and albumin at baseline, week 6, week 12
15. Single-nucleotide polymorphism analysis (SNP) at baseline only
16. Total and HDL Cholesterol at baseline, week 6, week 12
17. UV exposure at baseline and week 12
18. Vitamin D binding protein at baseline, week 6, week 12 (for 48 participants, high and low responders)
19. Vitamin D metabolites at baseline, week 6, week 12 (for 48 participants, high and low responders)
20. Vitamin D receptor at baseline, week 6, week 12 (for 48 participants, high and low responders)

Previous secondary outcome measures:
1. 1,25 dihydroxyvitamin D at baseline, week 6, week 12
2. Blood pressure at baseline, week 6, week 12
3. Bone mineral density at baseline, week 6, week 12
4. C-terminal telopeptide (CTX) at baseline, week 6, week 12
5. CYP27A1 at baseline, week 6, week 12
6. Dietary intake at baseline and week 12
7. Fasting glucose and insulin at baseline, week 6, week 12
8. Full blood count at baseline only
9. Height, weight, waist circumference at baseline, week 6, week 12
10. Kidney function (U&Es) at baseline only
11. Leukocyte RNA analysis at baseline, week 6, week 12
12. Liver function (LFTs) at baseline only
13. Non-Esterified Fatty Acid and Triacyglcerol at baseline, week 6, week 12 14. Parathyroid hormone at baseline, week 6, week 12
15. Serum calcium and albumin at baseline, week 6, week 12
16. Single-nucleotide polymorphism analysis (SNP) at baseline only
17. Total and HDL Cholesterol at baseline, week 6, week 12
18. UV exposure at baseline and week 12
19. Vitamin D binding protein at baseline, week 6, week 12

20. Vitamin D metabolites at baseline, week 6, week 12
21. Vitamin D receptor at baseline, week 6, week 12Current secondary outcome measures as of

Completion date
29/03/2013

Eligibility

Key inclusion criteria
1. Female, aged 20-64 years
2. Caucasian ethnic origin or partly-veiled women of South Asian (i.e. India, Pakistan, Bangladesh) or Arabian ethic origin
3. Body Mass Index 18-30 kg/m2
4. Pre-menopausal OR five years post-menopause
5. Written informed consent

Participant type(s)
Healthy volunteer

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
20 Years

Upper age limit
64 Years

Sex
Female

Key exclusion criteria
1. Currently receiving treatment for medical conditions likely to affect vitamin D metabolism
2. Regular use of sunbeds
3. Having a sun holiday one month prior to commencing the trial or plans for a sun holiday within the study period
4. Use of vitamin supplements containing vitamin D
5. Consumption of alcohol above recommended levels (>14units per week)
6. Those following a weightreducing diet or under dietary restriction (except vegetarianism)
7. Known intolerance/allergy to the constituent ingredients of the intervention products
8. Clinically significant haematological abnormalities other than mild anaemia (Hb>10.0g/dl)
9. Active malignancy
10. Postmenopause less than five years
11. Pregnant or planning a pregnancy during the study period
12. Breastfeeding mothers

Date of first enrolment

05/09/2011

Date of final enrolment
07/01/2013

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
University of Surrey
Guildford
United Kingdom
GU2 7XH

Sponsor information

Organisation
University of Surrey (UK)

ROR
https://ror.org/00ks66431

Funder(s)

Funder type
Research council

Funder Name
Biotechnology and Biological Sciences Research Council

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

IPD sharing plan summary
Data sharing statement to be made available at a later date

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	01/08/2017		Yes	No