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Biochemical Efficacy and Safety Trial of vitamin D (BEST-D)

Submission date	Recruitment status
12/03/2012	No longer recruiting
Registration date	**Overall study status**
12/04/2012	Completed
Last Edited	**Condition category**
24/08/2016	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 helps the body to absorb calcium and phosphorus from the diet and is important for keeping bones healthy. Low vitamin D levels are common in older people in the UK, especially during winter months. Moderate vitamin D deficiency may play a role in causing osteoporosis and fractures and has also been associated with an increased risk of cardiovascular disease, cancer and death. However, it is unclear whether supplementation with vitamin D has any beneficial effects on any of these diseases. Many people in Britain do not get enough sun exposure to maintain what are believed to be healthy vitamin D levels. Only small amounts of vitamin D are derived from food, chiefly from liver and oily fish.

There is substantial uncertainty about the optimal dose of vitamin D to use in large trials testing effects on bone health and other disease outcomes. It is possible that the doses of vitamin D used in previous trials to prevent fractures may have been too low to maintain healthy bones and to demonstrate other health benefits in older people.

The aim of the present study is to determine the optimal daily dose of vitamin D required to maintain blood levels of vitamin D in older people. It will assess the biochemical effects on blood levels of 25-hydroxy-vitamin D (25[OH]D) and parathyroid hormone of different amounts of vitamin D3 daily or a dummy tablet (placebo) when administered for one year.

Who can participate?
About 300 men and women aged 65 or older.

What does the study involve?
Participants will be randomly allocated to take either one of two different doses of vitamin D daily or a matching placebo for a year. The study will examine if these doses are effective at raising blood levels and are safe. The trial will assess the effects of vitamin D on blood levels of 25[OH]D, blood fats (lipids), biomarkers of inflammation, blood pressure, arterial stiffness and bone density. The results of this trial will help to select the optimal dose of vitamin D to be tested in a much larger trial assessing the effects of vitamin D on relevant disease outcomes.

What are the possible benefits and risks of participating?
It is unlikely that participants should gain materially or symptomatically from their participation in the study. However, the information resulting through their participation in the trial will be valuable for planning further larger trials of vitamin D assessing effects on major disease outcomes. The available evidence indicates that the doses of vitamin D used in the trial are likely to be safe and well-tolerated. In the unlikely event of any adverse effects, participants are advised to report any new unexplained symptoms to the study team, whose contact numbers are provided. These symptoms will also be evaluated at each study visit.

Where is the study run from?
The trial is being co-ordinated by the Clinical Trials Service Unit (CTSU), University of Oxford. The trial will be undertaken at a single GP practice, the Hightown Surgery, based in Banbury, Oxfordshire.

When is the study starting and how long is it expected to run for?
The study is expected to start in May 2012, and is anticipated to complete trial procedures by December 2013.

Who is funding the study?
University of Oxford (UK).

Who is the main contact?
Professor Jane Armitage
jane.armitage@ctsu.ox.ac.uk

Contact information

Type(s)
Scientific

Contact name
Prof Jane Armitage

Contact details
Clinical Trial Service Unit & Epidemiological Studies Unit
University of Oxford
Richard Doll Building
Old Road Campus
Roosevelt Drive
Oxford
United Kingdom
OX3 7LF
+44(0)1865 743743
jane.armitage@ctsu.ox.ac.uk

Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
CTSUBEST-D v 1.0

Study information

Scientific Title
Biochemical Efficacy and Safety Trial of vitamin D (BEST-D): a dose-finding trial assessing biochemical and vascular effects of high dose vitamin D

Acronym
BEST-D

Study objectives
Null hypothesis
Vitamin D3 in a dose of either 100mcg (4000 IU) or 50mcg (2000 IU) administered for 1 year, will not be sufficient to achieve blood 25(OH)D levels >90 nmol/L, in all older people living in the community.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Not provided at time of registration

Study design
Double-blind placebo controlled randomised trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Screening

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
Safety and efficacy of vitamin D

Interventions
50µg of vitamin D3 or 100 µg of vitamin D3 or matching placebo

Duration: 12 months of treatment

Intervention Type
Other

Phase
Not Applicable

Primary outcome measure
1. The primary efficacy assessment will involve an intention-to-treat analysis among all randomized subjects of daily dietary supplementation with vitamin D3 100 µg vs vitamin D3 50 µg on the proportion of individuals with levels of 25(OH)D above 90 nmol/L at the end of the study.
2. A co-primary endpoint will be the difference between those allocated 100 vs 50 µg daily in the mean 25(OH)D levels at the scheduled study end

Secondary outcome measures
All secondary assessments will involve intention-to-treat analyses among all randomized subjects of the effects of daily supplementation with vitamin D3 100µg vs placebo, vitamin D3 50µg vs placebo, and the difference between the two doses of vitamin D on:
1. Mean blood levels of 25(OH)D during follow-up
2. The proportions of participants with blood 25(OH)D levels >90 nmol/L at the 6 and 12 month visits
3. The proportion of participants with PTH levels suppressed into the normal range at the 6 and 12 month visits
4. The proportion of participants with calcium levels above the normal range at the 6 and 12 month visits
5. Other laboratory tests of safety: phosphate, albumin, creatinine, alkaline phosphatase
6. The changes from baseline in hsCRP, creatinine, nBNP, inflammatory cytokines (e.g. IL5, IL6, IL1β, IFNγ and TNFα) at 6 and 12 month visits, and mRNA expression markers of innate immunity at baseline and 12 month visits
7. The difference in the change from baseline in diastolic and systolic blood pressure, heart rate and arterial stiffness at 6 and 12 months
8. The difference in the changes from baseline in total cholesterol, LDL-C, HDL-C, triglycerides, apo-B and apo-A at 12 months

Overall study start date
30/04/2012

Completion date
30/10/2013

Eligibility

Key inclusion criteria
1. Age ≥ 65 years
2. Living in the community and ambulatory

Participant type(s)
Patient

Age group
Senior

Sex
Both

Target number of participants
300

Key exclusion criteria
1. Nursing home residents
2. Regular use of vitamin D supplements with >400 IU (10 µg) vitamin D daily
3. Use of alendronate, risedronate, zoledronic acid, parathyroid hormone, or calcitonin
4. Medically diagnosed dementia
5. History of hypercalcaemia, hyperparathyroidism, lymphoma, sarcoidosis, active tuberculosis
6. History of renal calculus
7. Known to be poorly compliant with clinic visits or with taking medication
8. Recent history of alcohol or substance misuse or abuse
9. Medical history that might limit the ability of the subject to take the study treatment for the duration of the study (e.g. terminal illness)
10. Regular prescribed calcium supplements

Date of first enrolment
30/04/2012

Date of final enrolment
30/10/2013

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
Clinical Trial Service Unit & Epidemiological Studies Unit
Oxford
United Kingdom
OX3 7LF

Sponsor information

Organisation
University of Oxford (UK)

Sponsor details
Clinical Trial Service Unit & Epidemiological Studies Unit
Richard Doll Building
Old Road Campus
Roosevelt Drive
Oxford
England
United Kingdom
OX3 7LF
+44(0)1865 743743
bestd@ctsu.ox.ac.uk

Sponsor type
University/education

Website
http://www.ctsu.ox.ac.uk/

ROR
https://ror.org/052gg0110

Funder(s)

Funder type
University/education

Funder Name
University of Oxford (UK) - Clinical Trials Service Unit (CTSU)

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

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
	results here:				

Results article	01/04/2015	Yes	No