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Natural vitamin D (cholecalciferol) versus standard care in patients receiving dialysis

Submission date
18/12/2015

Recruitment status
No longer recruiting

Registration date
30/12/2015

Overall study status
Ongoing

Last Edited
09/06/2025

Condition category
Urological and Genital Diseases

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

Plain English summary of protocol

Background and study aims
Vitamin D is essential for good health, because it helps our bodies to absorb calcium from the diet. There is a lot of evidence that having enough vitamin D can help prevent against many diseases, such as heart and blood vessel (cardiovascular) disease, bone diseases and cancer. Although vitamins generally come from the diet, in the case of vitamin D, the majority of people actually get most of it from sunlight. When the sun shines on our skin, a reaction in the body is triggered, causing the body to produce an active form of vitamin D called vitamin D3. Vitamin D deficiency is common patients with end stage renal disease (kidney failure), and is a strong predictor of death from cardiovascular disease, infection and cancer. Almost all kidney failure patients who are treated with dialysis are given pre-activated vitamin D to take, however this approach increases blood calcium concentrations which may be harmful, and even make vitamin D deficiency worse. International treatment guidelines therefore now recommend that kidney patients receive inactive vitamin D (cholecalciferol), since we now know that every organ activates its own vitamin D as required, even in patients with kidney failure. However, this is not currently used in the NHS as it has not yet been tested in a trial. The aim of this study is to test whether taking cholecalciferol supplements increases survival in UK dialysis patients.

Who can participate?
Adults living in the UK with dialysis-requiring end stage renal disease.

What does the study involve?
Participants are randomly allocated to one of two groups. Participants in the first group take Cholecalciferol (60,000IU) capsules by mouth once every fortnight for around five and a half years. Participants in the second group continue to receive normal care and are instructed not to take cholecalciferol containing supplements (no more than 1,000IU) for the 5.5 years study period. At the start of the study and then every six months until the end of the study, participants in both groups are contacted to complete questionnaires in order to find out about their quality of life. Seven years after the start of the study, the participants are looked up on the National Deaths Register so that the survival rate of participants in each group can be calculated.

What are the possible benefits and risks of participating?
There are no direct benefits or risks to participants taking part in this study.

Where is the study run from?
Addenbrooke's Hospital (Cambridge) and 35 other NHS hospitals in the UK.

When is the study starting and how long is it expected to run for?
March 2016 to April 2026

Who is funding the study?
National institute for health research (UK)

Who is the main contact?
Dr Rona Smith

Contact information

Type(s)
Scientific

Contact name
Dr Thomas Hiemstra

Contact details
Simplified Trial Office
Cambridge Clinical Trials Unit
Box 401 Cambridge Biomedical Campus
Cambridge
United Kingdom
CB2 0QQ

Additional identifiers

EudraCT/CTIS number
2015-005003-88

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
SIM15

Study information

Scientific Title
Natural vitamin D (cholecalciferol) versus standard care in patients receiving dialysis - The SIMPLIFIED randomised registry trial

Acronym

SIMPLIFIED

Study objectives
Cholecalciferol 60,000IU by mouth fortnightly will increase survival in patients receiving long term dialysis when compared with standard care.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Cambridgeshire East Regional Ethics Committee, 10/03/2016, ref: 16/EE/065

Study design
Multi-centre open-label blinded endpoint pragmatic interventional randomised registry 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
End stage renal disease

Interventions
Participants are randomly allocated to one of two groups.

Intervention group: Participants will receive oral cholecalciferol 60,000IU fortnightly for the duration of the trial mean follow-up 5.5 years.
Control group: Participants will receive standard care but will not be permitted to receive more than 1,000IU per day of cholecalciferol or ergocalciferol.

For all participants, questionnaire-based follow-up will be performed by phone, mail or electronically at 6 monthly intervals for the duration of the trial. Endpoints (death, hospital admissions, cardiovascular events, cancer, infections, fracture) will be obtained from routinely collected data sources including the national deaths register, hospital episode statistics, the UK renal registry, and the UK and Ireland Association of Cancer Registries. The trial will be event-driven, and will complete once 2,200 deaths have occurred.

Intervention Type
Drug

Phase
Phase IV

Drug/device/biological/vaccine name(s)
Cholecalciferol

Primary outcome measure
All cause mortality will be determined from the national deaths register at 7 years.

Secondary outcome measures
1. Health-related quality of life is measured using the EQ5D questionnaire , determined at 6-monthly intervals for the duration of the trial
2. Hospitalisation-requiring composite cardiovascular events (defined as CV death, acute coronary syndrome, heart failure or arrhythmia and stroke) is determined from Hospital Episode Statistics, and will be obtained at at least 6-monthly intervals for the duration of the trial
3. Hospitalisation for infection is determined from Hospital Episode Statistics, and will be obtained at at least 6-monthly intervals for the duration of the trial
4. Cancer incidence determined from the UK and Ireland Association of Cancer Registries (UKIACR) database after the end of the trial (after 2,200 deaths have occurred, estimated to be 7 years after enrolment of the first participant)
5. Hospitalisation for fracture is determined from Hospital Episode Statistics, and will be obtained at at least 6-monthly intervals for the duration of the trial
6. Cost-effectiveness of cholecalciferol is determined by calculating life years gained per patient (estimated from mortality data from the National Deaths Register (ONS) and Quality Adjusted Life Years (QALYs) gained (estimated from both ONS mortality data and EQ5D data converted to health state utilities relevant to the UK population) at 7 years

Overall study start date
01/03/2016

Completion date
30/04/2026

Eligibility

Key inclusion criteria
1. Aged 18 years or over
2. Have given written informed consent to participate
3. UK Resident
4. Have dialysis-requiring end stage renal disease (ESRD)

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
4,200

Key exclusion criteria
Current exclusion criteria as of 23/11/2017:
1. Current treatment with high dose (>1,000IU/day) cholecalciferol or ergocalciferol in the last 30 days
2. Persistent hypercalcaemia (>2.62 mmol/l on three separate and sequential occasions without precipitating cause)
3. Life expectancy of less than 6 months
4. Women who are pregnant / planning to become pregnant
5. Hypersensitivity to colecalciferol or any of the excipients
6. Not contributing, or willing to contribute, data to the UK Renal Registry (UKRR)

Previous exclusion criteria:
1. Current treatment with high dose (>1,000IU/day) cholecalciferol
2. Persistent hypercalcaemia (>2.62 mmol/l on three separate and sequential occasions without precipitating cause)
3. Life expectancy of less than 6 months
4. Women who are pregnant / planning to become pregnant
5. Inability to provide informed consent
6. Not contributing, or willing to contribute, data to the UK Renal Registry (UKRR)

Date of first enrolment
14/12/2016

Date of final enrolment
31/07/2025

Locations

Countries of recruitment
England

Scotland

United Kingdom

Wales

Study participating centre
Addenbrooke's Hospital
Hills Road
Cambridge
United Kingdom
CB2 0QQ

Study participating centre
The Royal London Hospital
Whitechapel Road
Whitechapel
London
United Kingdom
E1 1BB

Study participating centre
Bradford Hospital
Duckworth Lane
Bradford
United Kingdom
BD9 6RJ

Study participating centre
Doncaster Hospital
Thorne Road
Doncaster
United Kingdom
DN2 5LT

Study participating centre
Freeman Hospital
Freeman Road
Newcastle upon Tyne
United Kingdom
NE7 7DN

Study participating centre
Glasgow Royal Infirmary
84 Castle Street
Glasgow
United Kingdom
G4 0ET

Study participating centre

Gloucester Royal Hospital
Great Western Road
Gloucester
United Kingdom
GL1 3NN

Study participating centre
Guys and St Thomas' Hospital
Westminster Bridge Road
London
United Kingdom
SE1 9RT

Study participating centre
Ipswich Hospital
Heath Road
Ipswich
United Kingdom
IP4 5PD

Study participating centre
Leicester Royal infirmary
Infirmary Square
Leicester
United Kingdom
LE1 5WW

Study participating centre
Manchester Royal Infirmary
Oxford Road
Manchester
United Kingdom
M13 9WL

Study participating centre
Norfolk and Norwich University Hospital
Colney Lane
Norwich
United Kingdom
NR4 7UY

Study participating centre
Northern General Hospital
Herries Road
Sheffield
United Kingdom
S5 7AU

Study participating centre
Nottingham City Hospital
Hucknall Road
Nottingham
United Kingdom
NG5 1PB

Study participating centre
Royal Free Hospital
Pond Street
London
United Kingdom
NW3 2QG

Study participating centre
Royal Liverpool Hospital
Prescot Street
Liverpool
United Kingdom
L7 8XP

Study participating centre
Royal Shrewsbury Hospital
Mytton Oak Road
Shrewsbury
United Kingdom
SY3 8XQ

Study participating centre
Royal Sussex County Hospital
Eastern Road
Brighton

United Kingdom
BN2 5BE

Study participating centre
Salford Royal Hospital
Stott Lane
Salford
United Kingdom
M6 8HD

Study participating centre
Southend Hospital
Prittlewell Chase
Westcliff-on-Sea
United Kingdom
SS0 0RY

Study participating centre
Lister Hospital
Chelsea Bridge Road
London
United Kingdom
SG1 4AB

Study participating centre
Sunderland Royal Hospital
Kayll Road
Sunderland
United Kingdom
SR4 7TP

Study participating centre
University Hospital Aintree
Longmoor Lane
Liverpool
United Kingdom
L9 7AL

Study participating centre

University Hospital Wales
Heath Park
Cardiff
United Kingdom
CF14 4XW

Study participating centre
Broomfield Hospital
Court Road
Broomfield
Chelmsford
United Kingdom
CM1 7ET

Study participating centre
Kings College Hospital
Denmark Hill
London
United Kingdom
SE5 9RS

Study participating centre
Southmead Hospital
Dorian Way
Westbury-on-Trym
Bristol
United Kingdom
BS10 5NB

Study participating centre
St George's Hospital
Blackshaw Road
Tooting
London
United Kingdom
SW17 0QT

Study participating centre
St James' University Hospital
Beckett Street
Leeds

United Kingdom
LS9 7TF

Study participating centre
Northwick Park Hospital (Imperial- London)
Watford Road
Harrow
London
United Kingdom
HA1 3UJ

Study participating centre
Kent & Canterbury Hospital (East Kent)
Ethelbert Road
Canterbury
United Kingdom
CT1 3NG

Study participating centre
Basildon and Thurrock University
Nethermayne
Basildon
United Kingdom
SS16 5NL

Study participating centre
Churchill Hospital
Old Road
Headington
Oxford
United Kingdom
OX3 7LE

Study participating centre
Royal Preston Hospital (Lancashire)
Sharoe Green Lane North
Fulwood
Preston
United Kingdom
PR2 9HT

Study participating centre
Royal Devon & Exeter (Wonford)
Barrack Road
Exeter
United Kingdom
EX2 5DW

Study participating centre
Royal Stoke University Hospital
Newcastle Road
Stoke-on-Trent
United Kingdom
ST4 6QG

Study participating centre
Derriford Hospital
Derriford Road
Crownhill
Plymouth
United Kingdom
PL6 8DH

Sponsor information

Organisation
Cambridge University Hospitals NHS Foundation Trust

Sponsor details
Cambridge Biomedical Campus
Hills Road
Cambridge
England
United Kingdom
CB2 0QQ

Sponsor type
Hospital/treatment centre

ROR
https://ror.org/04v54gj93

Funder(s)

Funder type
Government

Funder Name
National Institute for Health Research

Alternative Name(s)
National Institute for Health Research, NIHR Research, NIHRresearch, NIHR - National Institute for Health Research, NIHR (The National Institute for Health and Care Research), NIHR

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Publication and dissemination plan
Planned dissemination of findings via presentations at national and international meetings, and through publication in peer-reviewed journals. In addition to meetings orientated to nephrology, publication of results at meetings aimed at allied health professionals and general practitioners involved in the care of patients receiving dialysis is also planned.

Intention to publish date
30/03/2026

Individual participant data (IPD) sharing plan
Regarding the participant level date set, the majority of data collections are made indirectly via UKRR and NHS DIGITAL and are saved on our secure data hosting server (SDHS- the University of Cambridge). The aggregated (not participant level) data might become available after publication.

IPD sharing plan summary
Stored in repository

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Abstract results		01/12/2015	10/05/2021	No	No