

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

<b>Submission date</b> 18/12/2015	<b>Recruitment status</b> No longer recruiting	<input checked="" type="checkbox"/> Prospectively registered <input type="checkbox"/> Protocol
<b>Registration date</b> 30/12/2015	<b>Overall study status</b> Ongoing	<input type="checkbox"/> Statistical analysis plan <input checked="" type="checkbox"/> Results
<b>Last Edited</b> 09/06/2025	<b>Condition category</b> Urological and Genital Diseases	<input type="checkbox"/> 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 in 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 data 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?
<a href="#">Abstract results</a>		01/12/2015	10/05/2021	No	No