ISRCTN12424842 https://doi.org/10.1186/ISRCTN12424842

Vitamin D supplementation compared to placebo in people presenting with their first episode of psychosis neuroprotection design

Submission date
25/02/2015

Recruitment status
No longer recruiting

Registration date
25/02/2015

Overall study status
Completed

Last Edited
30/12/2021

Condition category
Mental and Behavioural Disorders

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

Plain English summary of protocol

Background and study aims
Vitamin D is commonly known as the “sunshine hormone” – if your skin is regularly exposed to sunlight, it makes enough vitamin D to keep your body healthy. However, people living in the UK commonly have low vitamin D, because of our lack of strong sunshine. While vitamin D is known to be important for bone health, there is growing evidence that it may also help people recover from various brain diseases. In other words, having enough vitamin D may protect the brain (i.e. it could be ‘neuroprotective’). At this stage, there is a lack of evidence to clarify if adding vitamin D to the standard treatment of people recovering from their first episode of a psychotic disorder can help recovery. The best way to examine this question is with a Randomized Controlled Trial (RCT). To do this we need to compare vitamin D supplements to placebo. A computer program decides which group you are allocated to, so there is an equal chance (50:50) that you will be allocated to either of the two groups. The results are compared to see if one is better. In a ‘blind trial’ you will not know which treatment group you are in. This trial is ‘double blind trial‘, meaning that neither you nor the study team will know in which treatment group you are. If adding vitamin D supplements to standard treatment can help people make a better recovery, then in the future we will be able to provide this type of treatment routinely. The Vitamin D (or placebo) supplement will be given to you once a month by a clinician, alongside the regular treatment that you receive from your mental health team. The aim of this study is to explore if the addition of a vitamin D supplement to standard treatments (which may include medications, general support and talking therapies) can help people recover after having their first episode of a psychotic disorder. To do this, we will compare a group of people who are receiving a vitamin D supplement as well as their standard treatment versus those who receive a placebo supplement (dummy supplement that contains no vitamin D) and standard treatment alone.

What does the study involve
Current as of 11/10/2017:
Study participants are recruited from NHS Trust research sites (including Early Intervention Services (EIS), Home Treatment Teams, inpatient units, community teams and Patient Identification Centres (PICS)). Participation in the study is entirely voluntary. Half of the

participants who join the study are randomly allocated to receiving the vitamin D supplement while half receive a 'placebo' treatment (an identical looking treatment but without vitamin D). Each participant is asked to take six drops (just over one teaspoon) of the vitamin D supplement (or placebo) once a month for a total of 6 months. During their participation in the study (6 months), we ask each participant that they do not use other vitamin D supplements that exceed 400 IU/Daily, either alone or as part of a multivitamin preparation. During the study, the participants take part in a number of assessments. A trained research phlebotomist takes a small sample of blood (the equivalent of a few tablespoons). . The purpose of the blood test is to have a measure of what each participants vitamin D levels are when they enter the study and again at the 6 month assessment points. From the same blood sample we will also check on each participants general blood chemistry, including calcium levels and hormones that are linked to vitamin D. Participants are also asked if they would give another blood sample for genetic testing (in many cases, genes can alter vitamin D levels). Each participant is also asked various questions about symptoms, mood, plus any side effects caused by the treatments. To monitor their physical health we ask each participants permission to measure their weight, height, waist and blood pressure measurements. We will repeat questionnaires administered at the start of the study and at 6 months and will review each participants clinical notes to investigate changes over time. At 3 months we perform a blood test to check each participants calcium and hormone levels.

Previous:
Study participants are recruited from Early Intervention in Psychosis Services. Participation in the study is entirely voluntary. Half of the participants who join the study are randomly allocated to receiving the vitamin D supplement while half receive a 'placebo' treatment (an identical looking treatment but without vitamin D). Each participant is asked to take six drops (just over one teaspoon) of the vitamin D supplement (or placebo) once a month for a total of 12 months.. During their participation in the study (1 year), we ask each participant that they do not use other vitamin D supplements, either alone or as part of a multivitamin preparation. During the study, the participants take part in a number of assessments. A trained research phlebotomist takes a small sample of blood (the equivalent of a few tablespoons) from each . The purpose of the blood test is to have a measure of what each participants vitamin D levels were when they entered the study and again at the 6 and 12 month assessment points.. At the end of the study, with their permission, we will provide clinical team of each participant with their most recent Vitamin D level. From the same blood sample we will also check on each participants general blood chemistry, including calcium levels and hormones that are linked to vitamin D. Participants are also asked if they would give another blood sample for genetic testing (in many cases, genes can alter vitamin D levels). Each participant is also asked various questions about symptoms, mood, plus any side effects caused by the treatments. To monitor their physical health we ask each participants permission to measure their weight, height, waist and blood pressure measurements. We will repeat questionnaires administered at the start of the study at 6 and 12 months and will review each participants clinical notes to investigate changes over time. At 3 and 9 months we perform a blood test to check each participants calcium and hormone levels.

What are the possible benefits and risks of participating?
It is hoped that the participants will benefit from the treatment by having closer contact with the clinic. If they also receive the Vitamin D supplement then this may be good for bone and muscle health.

Where is the study run from?
South London and Maudsley NHS Foundation Trust (UK)

When is the study starting and how long is it expected to run for?
April 2015 to December 2019 (as of 26/10/2018)

Who is funding the study?
Stanley Medical Research Institute (USA)

Who is the main contact?
Dr. Gabriella Wojewodka, gabriella.wojewodka@kcl.ac.uk

Contact information

Type(s)
Scientific

Contact name
Dr Gabriella Wojewodka

Contact details
Department of Psychosis Studies
Institute of Psychiatry
Box PO63
De Crespigny Park
London
United Kingdom
SE5 8AF
-
gabriella.wojewodka@kcl.ac.uk

Type(s)
Public

Contact name
Dr Gabriella Wojewodka

Contact details
Department of Psychosis Studies
Institute of Psychiatry
Box PO63
De Crespigny Park
London
United Kingdom
SE5 8AF
-
gabriella.wojewodka@kcl.ac.uk

Additional identifiers

EudraCT/CTIS number
2014-002639-32

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
18385

Study information

Scientific Title
A randomised, double blind, placebo controlled parallel group trial of vitamin D supplementation compared to placebo in people presenting with their First Episode of psychosis Neuroprotection Design

Acronym
DFEND

Study objectives
The aim of this study is to investigate the effects of vitamin D supplementation in people presenting with their first episode of psychosis.

Ethics approval required
Old ethics approval format

Ethics approval(s)
14/LO/1588

Study design
Randomised; Interventional; Design type: Treatment

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 contact details to request a patient information sheet

Health condition(s) or problem(s) studied
Psychosis

Interventions

Vitamin D3: We will use a safe and convenient monthly treatment regimen in the DFEND trial. Under the direct supervision of trial staff, we will administer 120,000 IU of vitamin D3, using the widely used oral Vigantol oil preparation. This potent form of vitamin D has been used often in clinical trials, and comparable strategies are currently underway in large population based randomised controlled trials in the USA, New Zealand, Australia and the United Kingdom (total samples approx. 90,000 individuals).
Follow Up Length: 12 months (Updated 11/10/2017: 6 months)
Study Entry : Single Randomisation only

Intervention Type
Drug

Phase
Phase II

Primary outcome measure
Current primary outcome measure as of 24/05/2021:
Psychosis symptom severity assessed using the total Positive and Negative Syndrome Scale (PANSS) at 6-month follow-up

_____

Previous primary outcome measure as of 11/10/2017:
PANSS is used at baseline, 3 and 6 months.

_____

Previous primary outcome measure:
PANSS; Timepoint(s): 6 months, 12 months

Secondary outcome measures
Current secondary outcome measures as of 24/05/2021:
1. Psychosis symptom severity assessed using the total Positive and Negative Syndrome Scale (PANSS) at 6-month follow-up
2. Positive symptom severity assessed using the PANSS Positive Scale subscore at 3 and 6 months
3. Negative symptom severity assessed using the PANSS Negative Scale subscore at 3 and 6 months
4. Cognitive symptom severity assessed using the PANSS General Psychopathology Scale subscore at 3 and 6 months
5. Ability to function assessed using Global Assessment of Function (GAF) at 6 months
6. Depression assessed using the Calgary Depression Scale (CDS) at 6 months
7. Waist circumference (cm) at 6 months
8. Body mass index (BMI) (kg/m2) at 6 months
9. HbA1c (mmol/mol) at 6 months
10. Total cholesterol (mmol/l) at 6 months
11. C-reactive protein (CRP)(mg/l) at 6 months
12. Vitamin D (25(OH)D) concentrations at 6 months

_____

Previous secondary outcome measures as of 11/10/2017:
1. Calgary Depression Scale is used at baseline and 6 months
2. GAF scale is used at baseline and six months

Previous secondary outcome measures:
1. Calgary Depression Scale; Timepoint(s): 6, 12 months
2. GAF scale; Timepoint(s): 6, 12 months

Overall study start date
01/04/2015

Completion date
20/12/2019

Eligibility

Key inclusion criteria
Current inclusion criteria as of 11/10/2017:
1. Aged between 18-65 years including women of child-bearing age
2. Diagnosis of functional psychosis defined according to ICD-10 criteria
3. Willing to refrain from taking multivitamins or non-study vitamin D supplements (including cod liver oil), that exceed 400IU/day of vitamin D throughout the study
4. Patients who are willing to give a vitamin D blood sample
5. Patients who are able to and have given written informed consent

Previous inclusion criteria:
1. Patients experiencing their first episode of psychosis (or FEP, defined as first presentation in the last six months)
2. Attending clinical services run in the South London and Maudsley Hospital NHS Foundation Trust.
3. Aged 18-45 years
4. Must have capacity to provide written informed consent and have sufficient English language skills to complete the study
5. Subjects must agree to refrain from taking multivitamin or non-study vitamin D supplements throughout the study
6. Must be willing to provide a vitamin D blood sample at baseline

Psychosis will be defined according to ICD-10 criteria for psychosis (codes F20-29 and F3033) and confirmed with an OPCRIT (OPerational CRITeria) diagnosis.

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Upper age limit
65 Years

Sex
Both

Target number of participants
Planned Sample Size: 240; UK Sample Size: 240; Description: 120 (50%) will be randomized to the Active Treatment arm (120,000 IU monthly of vitamin D) and 50% (n=120) to the placebo arm.

Total final enrolment
149

Key exclusion criteria
Current exclusion criteria as of 11/10/2017:
1. Known intolerance of Vitamin D2 or D3 or known allergy to any of the trial medications
2. Those who are currently taking vitamin D supplements at a dose exceeding 400IU/day.
3. Those who have taken cardiac glycosides; calcium channel blockers; or oral, intramuscular, or intravenous corticosteroids;, bendroflumethiazide; isoniazid, or rifampicin in the past one month
4. Known active tuberculosis, sarcoidosis, hypo or hyperparathyroidism, past or present nephrolithiasis (renal stones), suspected or diagnosed hepatic or renal dysfunction, any malignancy other than non-melanoma skin cancer not in remission for ≥ 3 years, calcium disorders
5. Baseline corrected serum calcium > 2.6mmol/L
6. Patients with known history of hypercalcaemia
7. Pregnant or breast-feeding women and women planning a pregnancy
8. Patients lacking the capacity to provide written informed consent

Previous exclusion criteria:
1. Patients whose diagnosis was evaluated retrospectively and found not to fulfil the diagnostic criteria.
2. Individuals who are suicidal at baseline
3. Those with known endocrine disorders, CVS disease, or diabetes
4. Those with contraindications to Vigantol or prescribed cardiac glycosides
5. Pregnant women and women planning a pregnancy

Date of first enrolment
01/01/2016

Date of final enrolment
14/06/2019

Locations

Countries of recruitment
England

United Kingdom

Study participating centre

South London and Maudsley NHS Foundation Trust
King's College London
SLaM R&D and KCL joint office
Institute Of Psychiatry, Psychology and Neuroscience
16 De Crespigny Park
London
United Kingdom
SE5 8AF

Study participating centre
Southern Health NHS Foundation Trust
Tom Rudd Unit
Moorgreen Hospital
Botley Road
West End
Southampton
United Kingdom
SO30 3JB

Study participating centre
Kent and Medway NHS and Social Care Partnership Trust (KMPT)
Clinical Research Network: Kent Surrey Sussex (CRN:KSS)
KMPT Research & Development,
Beech House
Hermitage Lane
Maidstone
United Kingdom
ME16 9PH

Study participating centre
Cheshire and Wirral Partnership NHS Foundation Trust
Research Department
NIHR Clinical Research Network: North West Coast
Churton House
Countess of Chester Health Park
Chester
United Kingdom
CH2 1BQ

Study participating centre
South West London and St George's Mental Health NHS Foundation Trust
Clinical Research Unit
Barnes Hospital

South Worple Way
London
United Kingdom
SW14 8SU

Sponsor information

Organisation
King's College London

Sponsor details
Room 1.8
Hodgkin Building
Guy's Campus
London
England
United Kingdom
SE1 4UL

Sponsor type
Hospital/treatment centre

ROR
https://ror.org/0220mzb33

Funder(s)

Funder type
Research organisation

Funder Name
Stanley Medical Research Institute

Alternative Name(s)
The Stanley Medical Research Institute, SMRI

Funding Body Type
Private sector organisation

Funding Body Subtype
Research institutes and centers

Location
United States of America

Results and Publications

Publication and dissemination plan
Not provided at time of registration

Intention to publish date
31/12/2021

Individual participant data (IPD) sharing plan
Not provided at registration

IPD sharing plan summary
Not provided at time of registration

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol article	protocol	06/01/2020	08/01/2020	Yes	No
Results article		01/12/2021	30/12/2021	Yes	No
HRA research summary			28/06/2023	No	No