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Effects of vitamin D and probiotic supplements in older people

Submission date 04/04/2022	**Recruitment status** No longer recruiting	[X] Prospectively registered [X] Protocol [_] Statistical analysis plan [_] Results [_] Individual participant data [X] Record updated in last year
Registration date 06/04/2022	**Overall study status** Completed	
Last Edited 17/12/2024	**Condition category** Other	

Plain English summary of protocol

Background and study aims

As we age, our immune system becomes weaker and there is an increase in inflammation which contributes to common age-related diseases. These include heart disease, metabolic disease such as type 2 diabetes, the loss of muscle mass and strength known as sarcopenia, the weakening of bones known as osteoporosis, some cancers, and possibly dementia. A weaker immune system means older people can be more susceptible to infections and some vaccines may not work as well as in younger adults.

The “healthy” bacteria in our intestine (called gut microbiota) have an influence on our immune system and inflammation. Our intestinal bacteria also change with ageing and this can result in the loss of protective function and in the movement of harmful bacterial toxins and whole bacteria from the gut into the blood. Why these changes occur and how we can improve this in ageing are not understood. What we do know is that our intestinal bacteria can be altered by our diet. They can also be altered by probiotics, which are live healthy bacteria often found in yoghurts. In this study the researchers plan to investigate whether nutritional supplements of vitamin D and a probiotic improve measures of muscles, bone, the immune system, inflammation and intestinal bacteria. The probiotic organism used is called Lactobacillus plantarum. Vitamin D has an important role in maintaining healthy bones and a healthy immune system and preventing too much inflammation and has also been seen to positively affect the intestinal bacteria. Lactobacillus plantarum is commercially available and has been seen to positively affect the intestinal barrier but its effects on the immune system and inflammation have not been tested in older people.

The researchers plan to compare the effects of using either vitamin D and Lactobacillus plantarum individually or together in combination on intestinal bacteria, the immune system and inflammation, and other measures of ageing including bones and muscles.

Who can participate?

Healthy men and women over the age of 70 years

What does the study involve?

The study involves making two visits to the Clinical Research Facility at University Hospital Southampton. Each visit will last 1.5 to 2 hours. In between visits participants will be randomly allocated to consume supplements of either placebo, vitamin D, probiotic, or vitamin D plus

probiotic each day for 12 weeks.
At each clinic visit participants will be asked to answer a set of questions about their diet, quality of life, and physical activity. They will provide a blood sample for measurement of immune, inflammatory and metabolic markers as well as indicators of intestinal integrity.
In between the two visits participants will be asked to complete a daily paper diary to record ingestion of their supplement and complete a questionnaire every day about their respiratory health (if they are well they will not need to do this).
Participants will be asked to provide urine and faecal samples at the start and end of the study. On the days they provide urine samples they will complete a diary about their diet – this can be done as a paper diary or online.

What are the possible benefits and risks of participating?
Participants may benefit from positive effects on their immune system and/ or their intestinal bacteria. Knowledge gained from this study will help research and will ultimately be of use to other researchers and consumers.
With any procedure involving blood collection with a needle, there is a very small chance of infection and a chance of bleeding and bruising at the site of insertion of the needle. This will be minimised by using sterile techniques and trained members of staff.

Where is the study run from?
The University of Southampton (UK)

When is the study starting and how long is it expected to run for?
July 2018 to September 2024

Who is funding the study?
Medical Research Council (UK)

Who is the main contact?
Prof. Philip Calder
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Contact information

Type(s)
Principal Investigator

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Additional identifiers

EudraCT/CTIS number

IRAS number
304233

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
IRAS 304233, CPMS 51488

Study information

Scientific Title
Influence of vitamin D and a probiotic on inflammation and gut bacteria

Acronym
Nutriom

Study objectives
The objectives of this study are to identify the effect of vitamin D (calcifediol) and Lactobacillus plantarum TIFN101 alone and together on the intestinal microbiota, markers of immune function and inflammation and other health-related markers (blood lipids, body composition, muscle strength) in older adults.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 25/01/2022, South Central - Hampshire A Research Ethics Committee (Temple Quay House, 2 The Square, Temple Quay, Bristol, BS1 6PN, UK; +44 (0)2071048033/53; hampshirea.rec@hra.nhs.uk), ref: 21/SC/0403

Study design
Randomized controlled trial with a 2 x 2 factorial design

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Community

Study type(s)
Prevention

Participant information sheet
See study outputs table

Health condition(s) or problem(s) studied
Older people (aged 70+ years) living in the community

Interventions
Participants will be given IDs from 001 to 104. These IDs have been randomly allocated to treatment groups using a randomisation programme, with randomisation stratified for sex based upon a 50:50 distribution.

1. Control
2. Vitamin D (calcifediol) 10 micrograms/day
3. Lactobacillus plantarum TIFN101 5 billion colony forming units/day
4. Both vitamin D (calcifediol) and Lactobacillus plantarum TIFN101

Interventions will be delivered as capsules in blister packs with two capsules to be taken each day for 12 weeks.

Intervention Type
Supplement

Primary outcome measure
Measured at study entry and exit (week 12):
1. Serum 25-hydroxyvitamin D3 concentration (nmol/l) measured by immunoassay
2. Colonisation with the probiotic organism detected in faeces (number of organisms per g faeces) measured by 16S RNA
3. Serum CRP concentration measured by ELISA (mg/dl)

Secondary outcome measures
All measured at study entry and exit (12 weeks)
1. Blood immune cell phenotypes (number of each cell type per microlitre of blood) measured by flow cytometry
2. Plasma inflammatory markers (mg/l) measured by immunoassay
3. Faecal microbiome taxonomy (numbers of different organisms per g faeces) measured by 16S RNA
4. Weight (kg), body mass index (kg/m^2), body fat mass (kg and % body weight), body lean mass (kg and % body weight), mid arm upper circumference (cm), waist circumference (cm), hip circumference (cm), waist:hip ratio, measured by weighing scales, tape measure and bioelectric impedance
5. Hand grip strength (kg) measured using a dynamometer
6. Dietary intake (amounts of foods and nutrients) measured using the EPIC food frequency questionnaire and intake24 recall
7. Quality of life (questionnaire plus visual analog scale) measured using the EQ5D5L questionnaire
8. Physical activity measured using the Physical Activity Scale for the Elderly (PASE) questionnaire
9. Respiratory symptoms measured using the Wisconsin Upper Respiratory Symptom Survey

(WURSS)
10. Blood glucose (mml/l), insulin (U/l) and HOMA-IR measured by enzyme-linked colorimetric assays
11. Blood lipids (total, LDL and HDL cholesterol, triglycerides; all mmol/l) measured by enzyme-linked colorimetric assays
12. Blood adipokines (leptin, adiponectin, leptin/adiponectin ratio, visfatin and resistin; mg/l) measured by ELISA
13. Blood markers of intestinal barrier integrity (mg/l) measured by ELISA
14. Blood PTH (pg/ml) and calcium (mg/dl), as markers of vitamin D homeostasis
15. Faecal metabolome measured by nuclear magnetic resonance (NMR)
16. Urinary metabolome measured by NMR

Overall study start date
31/07/2018

Completion date
30/09/2024

Eligibility

Key inclusion criteria
1. Community dwelling males and females aged 70+ years
2. Body mass index 18.5-35 kg/m²
3. Willing to adhere to the study protocol
4. Able to provide written informed consent

Participant type(s)
Healthy volunteer

Age group
Senior

Lower age limit
70 Years

Sex
Both

Target number of participants
104

Total final enrolment
78

Key exclusion criteria
1. Living in a care or nursing home
2. Diagnosed with diabetes or other metabolic and endocrine disorders
3. Presence of active gastrointestinal disease (coeliac disease, Crohn’s disease, diagnosed IBD etc), autoimmune disease, or inflammatory disease (lupus, rheumatoid arthritis, multiple sclerosis)

4. Use of prescribed medicine to control inflammation (e.g. non-steroidal anti-inflammatory drugs; NSAIDs) or prescribed vitamin D or calcium+vitamin D or regular use of over-the-counter NSAIDs
5. Use of dietary supplements (will allow a 4-week washout period)
6. Use of probiotic drinks or yoghurts (will allow a 4-week washout period)
7. Blood donation in the previous 3 months
8. Participation in any other clinical trial in the previous 3 months

Date of first enrolment
21/04/2022

Date of final enrolment
31/05/2023

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
University of Southampton
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Organisation
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Sponsor type
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ROR
https://ror.org/01ryk1543

Funder(s)

Funder type
Research council

Funder Name
Medical Research Council

Alternative Name(s)
Medical Research Council (United Kingdom), UK Medical Research Council, MRC

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Publication and dissemination plan
Planned publication in high-impact peer-reviewed journals.

Intention to publish date
30/06/2025

Individual participant data (IPD) sharing plan
The anonymised datasets generated during and/or analysed during the current study will be available upon request from Philip Calder (pcc@soton.ac.uk)

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Participant information sheet	version 3	25/03/2022	05/04/2022	No	Yes

Protocol file	version 3	21/11/2022	16/02/2023	No	No
HRA research summary			28/06/2023	No	No