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PROTECTIVE-D: imPROving the effecTivenEss of vaccinaTion wIth positive mood and Vitamin D

Submission date	Recruitment status	[_] Prospectively registered
06/02/2024	No longer recruiting	[X] Protocol
Registration date	**Overall study status**	[_] Statistical analysis plan
08/02/2024	Completed	[_] Results
Last Edited	**Condition category**	[_] Individual participant data
04/03/2024	Infections and Infestations	[_] Record updated in last year

Plain English summary of protocol

Background and study aims
Vaccines help us prevent diseases and keep us well. Some vaccines work better than others and there are many reasons for this. It can be to do with the vaccine itself or to do with the person having the vaccine. It has already been found that people who report feeling happier on the day they are vaccinated produce more antibodies in response to the vaccination. Furthermore, giving people only 15 minutes of a positive mood intervention to watch before they are vaccinated improves their mood. Recent research also suggests that the amount of vitamin D in your body at the time of vaccination can affect how well vaccines work. This is a small study examining the effect of a positive mood intervention and vitamin D supplementation on the immunological responses to a boosting COVID-19 and/or influenza vaccination in healthy adults.

Who can participate?
People aged 65 to 85 years old who are eligible to receive a COVID-19 vaccination and/or influenza vaccination as part of their usual care

What does the study involve?
In this study, a small experiment will be conducted in which people who are about to receive a COVID-19 or influenza vaccination, or both, will be put in one of 4 groups at random.

Group 1 will not be offered anything other than their vaccine (this is called usual care).
Group 2 will receive a brief positive mood intervention, which has previously been shown to improve mood on the day they are vaccinated and for a further 6 days. They will also be advised to take a single dose of a vitamin D tablet just before they are vaccinated and once daily for the following 27 days.
Group 3 will also receive the positive mood intervention on the day they are vaccinated and for a further 6 days, but they will not take the vitamin D tablet.
Group 4 will be advised to take a vitamin D tablet at the time of vaccination and once daily for the following 27 days.

All participants will be asked to provide 15ml blood samples before vaccination and then at 28 days. This sample will help us measure antibody responses to the vaccination and determine how well people have responded. In addition, up to 20 people across all groups will be asked to provide up to a 60ml blood sample at baseline and day 28. These samples will help to understand how the interventions are changing the way the immune system works.

Finally, a small number of participants and people working in the vaccine clinics will be interviewed to gain their views on the approach to improving vaccine effectiveness. This work will help to identify if there is an easy and effective way to make vaccines work better that is acceptable to doctors and patients, doesn't have any side effects and which anyone, anywhere can try.

What are the possible benefits and risks of participating?
The benefits to participants in this trial are:
Participants may experience a more positive mood following the positive mood intervention. Routinely taking Vitamin D over the counter in the UK is advised due to lack of sunlight in the winter months. Vitamin D can keep bones, teeth and muscles healthy.

The risks to participants in this trial are:
Not taking vitamin D supplements as directed. Participant use of supplements including dose and strength will be checked regularly by the study team and participants will be advised if they are using them incorrectly. Complications arising from phlebotomy. These will be explained by the phlebotomist before the procedure. All participants will be encouraged to report any concerns and will have access to a 24-hour emergency mobile phone number held by a study clinician as well as usual NHS care.

Where is the study run from?
The University of Nottingham Health Service

When is the study starting and how long is it expected to run for?
October 2022 to April 2023

Who is funding the study?
NIHR Clinical Research Network East Midlands

Who is the main contact?
Dr Simon Royal, nnicb-nn.research@nhs.net

Contact information

Type(s)
Public, Scientific, Principal Investigator

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Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number
316876

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
IRAS 316876, CPMS 54065

Study information

Scientific Title
A feasibility randomised controlled trial examining the effect of a positive mood intervention and vitamin D supplementation on the immunological responses to a boosting COVID-19 and/or influenza vaccination in healthy adults

Acronym
PROTECTIVE-D

Study objectives
A feasibility study to identify compliance and adherence to vitamin D for 28 days from the day of vaccination, and a positive mood intervention for 7 days from the day of vaccination.

Ethics approval required
Ethics approval required

Ethics approval(s)
Approved 28/11/2022, London - Harrow Research Ethics Committee (Level 3, Block B Whitefriars Lewins Mead, Bristol, BS1 2NT, United Kingdom; +44 (0)207 104 8154; harrow.rec@hra.nhs.uk), ref: 22/LO/0714

Study design
Single-centre randomized interventional feasibility study

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
GP practice, Internet/virtual, Medical and other records, Telephone

Study type(s)
Treatment

Participant information sheet
See study outputs table

Health condition(s) or problem(s) studied
Vitamin D supplementation and/or positive mood intervention after vaccination

Interventions
This is a feasibility study to identify compliance and adherence to vitamin D for 28 days from the day of vaccination and a positive mood intervention for 7 days from the day of vaccination.

Patients aged 65 years or greater being targeted for COVID-19 and/or influenza vaccination will be recruited from primary care to participate in this feasibility trial. SMS text messages will be sent to potential participants with the PIS attached, a minimum of 24 hours before their appointment. They will be randomly allocated on a 1:1:1:1 basis using an electronic randomisation system to receive:
* No intervention (Usual Care)
* Positive mood intervention on the day of vaccination and for the following 6 days and vitamin D supplementation on the day of vaccination and once daily for the following 27 days
* Positive mood intervention on the day of vaccination and for the following 6 days
* Single dose oral vitamin D supplementation on the day of vaccination and once daily for the following 27 days

15 ml venous blood samples will be collected to detect antibodies to the vaccine antigens. These will be measured at baseline, 4 weeks and 6 months post-vaccine to assess intervention effects on peak vaccine responses and durability of protection. Participants will also receive a daily text message reminder with a link to the positive mood intervention and/or to take their vitamin D supplement, alongside an e-diary link to complete.

A sub-sample of around 20 patients will be invited to have blood samples collected to explore potential cellular and humoral mechanisms at day 0 and day 28. This will entail an additional maximum 60ml blood sample on each occasion.

Interviews will be conducted with patients and health care professionals involved in the pilot trial to identify barriers and facilitators to implementing the intervention in routine care.

Intervention Type
Supplement

Primary outcome measure
Compliance with study procedures measured using an e-diary from day 1 to day 28
Adherence to study procedures measured using an e-diary from day 1 to day 28

Secondary outcome measures
Vaccine-induced influenza antibody titres measured using an ELISA test at baseline and day 28

Overall study start date
01/10/2022

Completion date
01/04/2023

Eligibility

Key inclusion criteria
1. Able and willing to provide written informed consent to participate in the study
2. Able and willing (in the investigator's opinion) to comply with all the study requirements
3. Consent to allow investigators to discuss their medical information with their general practitioner and access medical records where relevant to the study
4. Eligible to receive a COVID-19 vaccination and/or influenza vaccination as part of usual care

Participant type(s)
Service user

Age group
Senior

Lower age limit
65 Years

Upper age limit
85 Years

Sex
Both

Target number of participants
28

Total final enrolment
28

Key exclusion criteria
1. Enrolled on a COVID-19 vaccine clinical trial of an investigational medicinal product (CTIMP) in the last 12 months
2. Clinically extremely vulnerable and received a third or fourth dose in Spring 2022
3. Aged less than 65 years old
4. Ineligible to receive a COVID-19 and/or influenza vaccination as part of usual care or those for whom a COVID-19 and/or influenza vaccination is contraindicated
5. Collection of blood samples is contraindicated
6. Deemed by health care provider to be:
6.1. Too physically frail to participate.
6.2. Diagnosed with dementia or other cognitive condition which would make participation

difficult
6.3. Insufficient command of the English language to complete surveys and provide informed consent
6.4. Participants who, in the past 3 months, have been prescribed oral vitamin D supplementation by a health care professional or who take over-the-counter supplements regularly on the advice of a health care professional

Date of first enrolment
01/02/2023

Date of final enrolment
28/02/2023

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
The Univ of Nottingham Health Serv
Cripps Health Centre
University Park
Nottingham
United Kingdom
NG7 2QW

Sponsor information

Organisation
University of Nottingham

Sponsor details
The University of Nottingham Health Service
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Sponsor type
Hospital/treatment centre

Website
https://unhs-research.co.uk

ROR
https://ror.org/01ee9ar58

Funder(s)

Funder type
Government

Funder Name
NIHR Clinical Research Network East Midlands

Results and Publications

Publication and dissemination plan
Planned publication in a high-impact peer-reviewed journal. The Chief Investigator will co-ordinate dissemination of data from this study. All publications (e.g., manuscripts, abstracts, oral /slide presentations, book chapters) based on this study will be reviewed by each sub-investigator and by the Sponsor before submission.

Intention to publish date
01/12/2024

Individual participant data (IPD) sharing plan
The datasets generated and analysed during the current study will be published as a supplement to the results publication.

IPD sharing plan summary
Published as a supplement to the results publication

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Participant information sheet	version 4.0	24/10/2022	07/02/2024	No	Yes
Protocol file	version 4.0	20/10/2022	07/02/2024	No	No