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

Participant Information Sheet & GDPR Privacy Notice
(Version 4.0 24/10/2022)

Date: 24th October 2022

Title of Study: 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

Name of Researcher(s): Dr Simon Royal, Dr Stephanie Pearson, Dr Kieran Ayling, Prof David Turner, Prof Lucy Fairclough, Prof Kavita Vedhara, Prof Holly Blake, Sir Prof Jonathan Van-Tam

We would like to invite you to take part in our research study. Before you decide we would like you to understand why the research is being done and what it would involve for you. One of our team will go through the information sheet with you and answer any questions you have. Talk to others about the study if you wish. Ask us if there is anything that is not clear.

What is the purpose of the study?

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. We have already found that people who report feeling happier on the day they are vaccinated produce more antibodies in response to the vaccination. We have also found that 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.

Before carrying out any research, please read over this information and ask any questions you have. You will then complete an informed consent form before any research activities take place.

We will conduct a small experiment in which people who are about to receive a COVID-19 vaccination 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 positive 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 will receive whatever material was agreed upon by the participants in stage 1 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.

We will also ask all participants to provide 15ml blood samples (two normal sized blood bottles) at day 0, day 28 and day 168 after their vaccination. This sample will help us measure antibody responses to the vaccination and determine how well people have responded. In addition, a small number of participants will be selected at random and asked if they would consent to provide a larger blood sample (up to 60ml) at day 0 and day 28 after they are vaccinated. These samples will allow us to understand how our interventions are changing the way the immune system works. If you are asked if you would like to be in this group but do not wish to provide this larger blood sample you can still participate it the study by providing the standard 15ml blood sample.

You may also be asked to be interviewed by the study team. This interview will last between 30-60 minutes and be audio recorded and transcribed.

Why have I been invited?

You are being invited to take part because you have been invited for a COVID-19 and/or flu booster vaccination at Cripps Health Centre. We are inviting 50 participants like you to take part.

Do I have to take part?

It is up to you to decide whether or not to take part. If you do decide to take part you will be given this information sheet to keep and be asked to sign a consent form (completion and return of a Questionnaire can be taken as implied consent). If you decide to take part you are still free to withdraw at any time and without giving a reason. This would not affect your legal rights.

What will happen to me if I take part?

If you decide to take part, you will be asked to read and complete an informed consent form. After this, one of the researchers on this project will ask you a few questions to see if you are eligible to take part. This may include your medical history, demographics and how many COVID-19 vaccines you've had. We will then take a 15ml blood sample from you and you will be asked to fill in some questionnaires. You will be randomly allocated into one of four groups. It is expected that this visit will last 60 minutes. At the end of this visit, you will also be given an ediary to complete for the next 28 days. Your GP will also be informed that you are taking part in this research.

If you are eligible to take part and have signed the informed consent form, you will then be randomised to one of 4 groups below:

- Group 1: Usual care (the COVID-19 and/or flu booster vaccine)
- Group 2: You will watch 15-20 minutes of positive mood intervention such as comedy on the day you are vaccinated and for 6 days following your vaccination. You will also receive a single dose of a Vitamin D tablet just before you receive your vaccine and for the next 27 days.

- Group 3: You will watch 15 minutes of positive mood intervention such as comedy on the day you are vaccinated and for a further 6 days at home.
- Group 4: You will be given the Vitamin D tablet at the time of vaccination and for the next 27 days.
- A small subgroup of participants will have a larger blood sample taken at Day 0 and at Day 28.

The second visit will happen at 4 weeks after the first visit, and you will have a follow-up blood sample taken. It is expected that this visit will last 15 minutes. At the end of this visit, you may also receive an invitation to take part in a one-off interview about the study. At 6 months after your first visit, we will collect data from your medical notes about your healthcare use (e.g. number of GP visits, antibiotic prescription, hospitalisation). If you wish to withdraw or lose capacity to consent during the study, any samples or tissues collected as part of the study will be kept by the study team.

During or after the study, you may be invited to be interviewed by the research team about your experience of the research study. The interview will last between 30-60 minutes. We want to listen to your views and help identify if there are any easy and effective ways to make vaccines work better that is acceptable to both doctors, nurses and patients. This interview may be audio recorded and transcribed. The audio recording will then be destroyed and the interview will be anonymised. Direct quotes from the interview may be used for publications, posters and research dissemination, though this will be anonymised, and any identifiable information will be removed.

Expenses and payments

Participants who are asked to take the vitamin D supplement will be offered a £10 boots vouchers to cover this expense

What are the possible disadvantages and risks of taking part?

Drawing blood may cause slight pain and occasionally bruising at the site where the needle enters. Some people feel light-headed or even faint when having blood taken. For the immunology cohort, over the course of the trial we will need to take up to 60ml of blood at a single visit. These amounts over the course of the year, should be below the limit of 470mL every 3 – 4 months for blood donations to the National Blood Transfusion Service. If abnormal results or undiagnosed conditions are found during the course of the study these will be discussed with you and, if you agree, your GP (or a hospital specialist, if more appropriate) will be informed. Any newly diagnosed conditions will be looked after within the NHS.

Vitamin D is safe when taken in recommended amounts. Most people don't experience side effects with vitamin D supplement tablets. Some side effects of taking too much vitamin D (above the amounts recommended on the packaging) include weakness, dry mouth, nausea, vomiting, and others. Taking vitamin D for long periods of time in doses higher than 4000 IU (100 mcg) daily is possibly unsafe and may cause very high levels of calcium in the blood.

There are no known side effects to the positive mood intervention.

What are the possible benefits of taking part?

We cannot promise the study will help you but the information we get from this study may help to improve how flu jabs work for people aged 65-85 years in the future.

- A positive mood intervention can uplift your mood and may make you feel happier. There is no known risk to this.

- Vitamin D helps regulate the amount of calcium and phosphate in the body. These nutrients are needed to keep bones, teeth, and muscles healthy. A lack of vitamin D can lead to bone deformities such as rickets in children, and bone pain caused by a condition called osteomalacia in adults. Government advice is that everyone should consider taking a daily vitamin D supplement during the autumn and winter. People at high risk of not getting enough vitamin D, all children aged 1 to 4, and all babies (unless they're having more than 500ml of infant formula a day) should take a daily supplement throughout the year.

- With all vaccines there is variability in the effectiveness and durability of protection, with the greatest variability evident in older people. Previous research has shown that a range of emotional and lifestyle factors alter vaccine effectiveness including positive and negative mood and vitamin D status. Interventions which target these factors can enhance vaccine success and help protect people.

What if there is a problem?

If you have a concern about any aspect of this study, you should ask to speak to the researchers who will do their best to answer your questions. If you remain unhappy and wish to complain formally, you can do this by contacting the Practice Manager at the University of Nottingham Health Service. All contact details are given at the end of this information sheet.

Will my taking part in the study be kept confidential?

We will follow ethical and legal practice and all information about you will be handled in confidence.

If you join the study, the data collected for the study will be looked at by authorised persons from the University of Nottingham who are organising the research. They may also be looked at by authorised people to check that the study is being carried out correctly. All will have a duty of confidentiality to you as a research participant and we will do our best to meet this duty.

All information which is collected about you during the course of the research will be kept **strictly confidential**, secured within the University of Nottingham. Any information about you which leaves the University will have your name and address removed (anonymised) and a unique code will be used so that you cannot be recognised from it. Anonymised data may also be stored in data archives for future researchers interested in this area.

Your personal data (address, telephone number) will be kept for 7 years for after the end of the study so that we are able to contact you about the findings of the study *and possible follow-up studies* (unless you advise us that you do not wish to be contacted). After this time your data will be

disposed of securely. During this time all precautions will be taken by all those involved to maintain your confidentiality, only members of the research team will have access to your personal data.

Your personal data (address, telephone number) will be kept for (12 months) after the end of the study so that we are able to contact you about the findings of the study *and possible follow-up studies* (unless you advise us that you do not wish to be contacted). All identifiable research data will be kept securely for 7 years. After this time your data will be disposed of securely. During this time all precautions will be taken by all those involved to maintain your confidentiality, only members of the research team will have access to your personal data.

Although what you say in the interview is confidential, should you disclose anything to us which we feel puts you or anyone else at any risk, we may feel it necessary to report this to the appropriate persons.

What will happen if I don't want to carry on with the study?

Your participation is voluntary and you are free to withdraw at any time, without giving any reason, and without your legal rights being affected. If you withdraw then the information collected so far may not be possible to extract and erase after (12 months) and this information may still be used in the project analysis.

The reason for withdrawal will be recorded in the study records, the withdrawn participants will not be replaced. Withdrawal from the study will not result in exclusion of the data generated by that participant from analysis unless requested by the participant.

What will happen to any samples I give?

The blood samples you provide will be analysed and securely stored, with a code unique to you, at the University of Nottingham and/or at Public Health England

We would also like to seek your consent so that any remaining samples may be stored and used in possible future research – this is optional (please indicate you agree to this on the consent form). The samples will be stored with a code unique to you and securely at the University of Nottingham under the University's Human Tissue Research Licence (no 12265). Some of these future studies may be carried out by researchers other than current team of Professor Kavita Vedhara, Dr Kieran Ayling, Dr Lucy Fairclough, Dr Heather Buchanan, Dr Simon Royal, Dr David Turner, Miss Michaela Brown, Miss Sophie Carlisle, who ran the first study, including researchers working for commercial companies. Any samples or data used will be anonymised, and you will not be identified in anyway. If you do not agree to this any remaining samples will be disposed of in accordance with the Human Tissue Authority's codes of practice.

Vitamin D insufficiency or deficiency may be identified during the analysis of samples collected for the study. This is a minor condition that does not require urgent treatment. Very rarely, major derangement of the immune system may be identified during analysis of the vaccine-induced antibody levels. If this occurs participants and their GPs will be notified by the Chief Investigator.
Participants with vitamin D levels below recommended norms will be notified after day 28 of the study and in line with local guidelines will be advised to obtain vitamin D supplements from a

pharmacy. They will further be advised to discuss the condition with their GP if they have any concerns.

What will happen to the results of the research study?

The results of this research trial may be presented at scientific meetings or conferences and published in a scientific medical journal. This may not happen until 1 or 2 years after the trial is completed. If you contact the researchers in the future, you can obtain a copy of the results. You will not be identified in any report or publication. Data from this trial may be used as part of a student post-graduate degree, for example a MD or PhD.

Who is organising and funding the research?

This research is being organised by the University of Nottingham Health Service in collaboration with the University of Nottingham. The project has been partially funded by NIHR CRN East Midlands and partially funded by the University of Nottingham Health Service, Cripps Health Centre.

Who has reviewed the study?

All research in the University of Nottingham is looked at by a group of people, called a Research Ethics Committee (REC), to protect your interests. This study has received a Favourable Ethical Opinion by XXXXXXXXXXXXXXX.

Further information and contact details

Please contact the Research Team at Cripps Health Centre on 0115 846 8888 or by emailing us at nnicb-nn.research@nhs.net