PARTICIPANT INFORMATION SHEET

Version 3.0 13th November 2019

VitaMIND: A randomised controlled trial of Vitamin D to improve cognition in people at risk of dementia

Invitation to take part in a research study

We would like to invite you to take part in our research study, VitaMIND, which is part of the Platform for Research Online to investigate Cognition and Genetics in Aging (PROTECT) study portfolio. If you take part in VitaMIND your involvement will be part of your PROTECT study journey. Before you decide, we would like you to understand why the research is being done and what it would involve for you.

Please take time to read the following information carefully and we recommend that you discuss it with family or friends if you wish. We recognise that there is a lot of information contained within this document. If you have any questions about this study, we would encourage you to contact a member of the study team (contact details are on the last page of this information sheet and on the study website).

You are under no obligation to take part in the study, and if you do take part you are free to withdraw at any time. If you decide to take part, we will ask you to read and sign a statement of consent on the PROTECT study website when you register.

Why are we doing the study?

As we get older our brains also begin to age, resulting in a 'slowing down' of abilities such as memory or reasoning. These mental processes are collectively known as 'cognition' and the 'slowing down' is called cognitive decline. In some people, cognition declines further, leading to cognitive impairment which is sometimes followed by the development of dementia, which affects over 800,000 people in the UK. There is a growing body of evidence that indicates that people may be able to reduce their risk of dementia through certain lifestyle habits or activities. This is particularly true for people who are at higher risk due to their current cognitive abilities or family history.

One promising avenue for reducing risk of dementia is through dietary supplementation of Vitamin D. Vitamin D is produced by the body when exposed to sunlight during summer months and is available in some foods such as fish and eggs. However, a large proportion of older adults do not receive enough Vitamin D and few people take regular dietary supplements despite recommendations from the National Institute of Clinical Excellence (NICE) for older adults. Vitamin D is known to play an important role in brain health and cognition, and research has shown that Vitamin D deficiency is linked to a risk of cognitive decline and dementia.

What is the purpose of the study?

VitaMIND is a three-year clinical trial. It aims to determine whether taking Vitamin D supplements improves brain function in older adults who may be at risk of cognitive decline in later life. Participants' level of risk will be determined through a series of potential 'risk factors'. These include:

- Family history of dementia
- Self-reported concerns about memory or brain health
- Performance on the PROTECT cognitive tests. As part of the study, we will compare the PROTECT cognitive test scores of VitaMIND participants to the average scores of all PROTECT participants of the same age to determine their level of risk for this category.

It is being led by the University of Exeter Medical School, in partnership with the Royal Devon & Exeter NHS Trust, Devon Partnership NHS Trust, and the South London and Maudsley NHS Trust.

The VitaMIND study will provide valuable new information about whether Vitamin D supplements should be used by older adults to reduce their risk of cognitive decline and dementia.

Why have I been invited?

All the adults invited to take part in this study are already participating in PROTECT. Over the next six months we will be looking for 584 people to join the VitaMIND study for a period of three years. **In order to participate you will need to have the ability to use a computer or a device like a smartphone or tablet with internet access.**

We are inviting PROTECT participants aged over 50 to volunteer to take part in this study who have a family history of cognitive impairment or dementia, and/or have concerns about their own memory or brain health.

For this study eligible participants will need to fulfil the following additional criteria:

1. Not already taking Vitamin D supplements
2. At risk of Vitamin D deficiency. This will be checked when you register using a questionnaire.

You should not take part if you:

1. Have been advised not to take vitamin D supplements due to an existing medical condition
2. Take the drug Digoxin.

If you wish to ask us any questions please use our contact details at the end of this information sheet.

Do I have to take part?

It is entirely up to you to decide whether or not to join the study. The purpose of this information sheet is to describe the study in detail and help you make your decision.

If you do wish to participate, you will need to read and sign a consent form on the PROTECT website. Please note that if you do participate, you will be free to withdraw at any time without giving a reason. Withdrawing will not affect the standard of care you receive through your own GP or local NHS services, or your legal rights. This study does not replace those services and if you feel less well during the time you are part of this study it is important that you seek help from your doctor or local health professionals in the usual way.

If you do not wish to participate this will not change your treatment or rights in any way, nor affect your participation in PROTECT or other studies currently affiliated with PROTECT. Please note the Vitamin D supplement used in this study is not suitable for vegans.

What will happen if I take part?

If you decide to take part the following steps will take place:

1. You will be directed to the trial section on the PROTECT website where all instructions, assessments and study information can be found.

2. You will be asked to complete a series of questions to confirm your eligibility. This will include completing a short questionnaire to establish your current risk of Vitamin D deficiency, letting us know about any concerns you have about your memory or brain health and checking whether you are taking certain medications or existing supplements.

3. Provided you are eligible, you will be asked to register with the study and confirm that you have read this Participant Information Sheet. A downloadable copy of this is available on the website.

4. You will be asked to read and sign the consent form to ensure you understand what the study involves and that you are happy to participate in the study.

5. You will then be asked to complete your first (baseline) study assessment. The assessments will be completed online through your PROTECT account and will be:

    a. A set of tests to measure brain function (called a cognitive test battery), which need to be completed in full once at each assessment date

    b. An Everyday Activities questionnaire, which measures your day-to-day activities

    c. A Quality of Life questionnaire, which measures your overall health on the day you take the tests

    d. An Everyday Emotions questionnaire, which measures your behaviour

6. Once you have completed your registration and baseline assessments you will be randomly allocated to receive Vitamin D supplements or a placebo (dummy). The placebo is an identical tablet that does not contain any Vitamin D or other active substance. There will be a 50:50 chance of receiving either Vitamin D or placebo and neither you nor the research team will know which study arm you are allocated to.

7. A study welcome pack will be sent to you in the post which will include:

    a. Information about the study including instructions for taking your tablets

    b. An activation code to enter in your online PROTECT account after you receive your welcome pack so we know to contact you a week later

    c. Fridge magnet as a reminder to take your tablets

    d. Your first batch of tablets. Tablets will be in blister packs of 28 tablets, with days of the week printed on each tablet space. You will receive three packs (12 weeks supply).

8. When you have received your welcome pack you can log into the PROTECT website and activate your study account by entering your activation code to let us know you have received your pack.

9. On the same day that you activate your study account you can take your first tablet at a time convenient to you. You will then be required to take one tablet daily for the study period of three years. Tablets will be sent to you every 12 weeks in blister packs. Please take one tablet each day. It is important that you do not take any multivitamin supplement containing Vitamin D during the course of this trial.

10. One week after you start taking your tablets you will receive a telephone call from our study team to check you are happy with the process and to answer any questions that you may have.

11. You will be asked to complete the same set of tests as mentioned above after six months, and again at one year, two years, and three years. These can all be found on your PROTECT account. We will send you an email reminder when your assessments are due.

12. You will also be asked to complete a report every three months to let us know how many tablets you have taken during that time. You will receive a reminder email to complete this activity. When you receive the reminder email we will ask you to log onto your study account and enter the tablet information into the relevant sections.

13. We would like to have a record of any ill health you experience during the course of the study. You will be asked to answer a set of simple questions related to your health each time you complete a tablet compliance check. This should take no longer than 3-5 minutes of your time depending on your answer. If you do report a serious health problem, we may contact you and / or your General Practitioner, with your permission, for further information. We also recommend that if you experience any ill health you contact your usual healthcare provider (usually your GP) for advice.

14. You may also receive a finger prick test kit to send a blood test for laboratory testing in order that we can check your Vitamin D levels. This will be sent to 10% of participants. If you are selected, we will provide you with a finger prick test in your welcome pack to be completed at home at the beginning of the study. You will also receive another finger prick test to be completed at the end of the study. The test is simple and relatively painless and is accompanied by full instructions. We will ask you to perform the test and send it in a postage paid envelope to our laboratory for analysis of Vitamin D levels in your blood. The laboratory will send the results back to us. They will not receive any of your personal information as your sample will be identified using an ID code. All data will be anonymous to the laboratory. The samples will be destroyed and not used in any other research.

15. At the end of the study we will ask you to complete a survey and provide us with suggestions and feedback on your experience from the study. We will also make the findings of the research available through the study website and newsletter.

16. We will be able to inform you of your treatment allocation at the end of the study.

All the information we collect will be secure and confidential. Analysis will be completed using anonymous data. We will keep all personal data for no more than 10 years after the study has finished and then it will be securely destroyed.

What will happen to the data I provide?

The University of Exeter is the sponsor for this study based in the United Kingdom. We will be using information from you in order to undertake this study and will act as data controller for this study. This means that we are responsible for looking after your information and using it properly. The University of Exeter will keep identifiable information about you for as long as it is required for the purposes of the study but no more than 10 years after the study has finished. Anonymised information, such as your trial results data, may be kept indefinitely and up until the study objectives have been achieved.

Your rights to access, change or move your information are limited, as we need to manage your information in specific ways in order for the research to be reliable and accurate. If you withdraw from the study, we will keep the information about you that we have already obtained. To safeguard your rights, we will use the minimum personally-identifiable information possible. You can find out more about how we use your information at www.exeter.ac.uk/dataprotection or by emailing dataprotection@exeter.ac.uk.

The University of Exeter will use your name and contact details to contact you about the research study, and make sure that relevant information about the study is recorded for your care, and to oversee the quality of the study. Individuals from the University of Exeter and regulatory organisations may look at your medical and research records to check the accuracy of the research study. NHS sites involved in the research (Royal Devon & Exeter, Devon Partnership Trust and South London and Maudsley) will pass these details to the University of Exeter along with the information collected from you and your medical records. The only people in the University of Exeter who will have access to information that identifies you will be people who need to contact you to discuss issues directly relating to the study or audit the data collection process. The people who analyse the information will not be able to identify you and will not be able to find out your name, NHS number or contact details. The research sites will keep identifiable information about you from this study for no more than 10 years after the study has finished.

When you agree to take part in a research study, the information about your health and care may be provided to researchers running other research studies in this organisation and in other organisations. These organisations may be universities, NHS organisations or companies involved in health and care research in this country or abroad. Your information will only be used by organisations and researchers to conduct research in accordance with the Policy Framework for Health and Social Care Research. This information will not identify you and will not be combined with other information in a way that could identify you. The information will only be used for the purpose of health and care research and cannot be used to contact you or to affect your care. It will not be used to make decisions about future services available to you, such as insurance.

What are the possible benefits and risks of taking part?

By taking part in this research you will also help move forward our understanding of how Vitamin D could play a role in maintaining cognition as we age. In addition to the potential benefit to brain health, findings from previous studies suggest that Vitamin D promotes good health including improved bone and tooth health, immune system and cardiovascular health. We are unable to guarantee that you will have the same benefit because taking part in the study means you will have a fifty percent chance of receiving Vitamin D (4000IU per day). The other 50% of participants will receive a placebo containing no Vitamin D. Neither you nor the study team will know whether you are receiving Vitamin D or placebo.

There are no known risks associated with taking Vitamin D. However, taking excessive amounts of Vitamin D can lead to symptoms such as fatigue, vomiting and poor appetite. Although this would only happen if you were to take very large amounts (60,000IU per day for several months), it is still important to follow the trial tablet course (regimen) and not take any additional Vitamin D supplements.

This study does not replace National Health Services and if you feel less well during the time you are part of this study it is important that you seek help from your doctor or local health professionals in the usual way.

What is in the tablets?

The following table lists the ingredients contained in both the placebo and treatment tablets used in the trial.

Tablet 1 - Placebo	Tablet 2 - Treatment
86 Mg Cellulose (E4460 i)	71.48 Mg Cellulose (E460 i)
38 Mg Hydroxypropyl Methycellulose	44.52 Mg Maltodextrin, Starch, Sucrose, Cholecalciferol
4 Mg Magnesium Stearate	38 Mg Hydroxypropylmethyl Cellulose
2 Mg Silicon Dioxide	4 Mg Magnesium Stearate

	2 Mg Silicon Dioxide

If you have any questions about whether any of the ingredients in either tablet will adversely affect your health, we recommend that you discuss this information with your GP.

The Vitamin D used in the treatment is Vitamin D3 and is not suitable for vegans because it is derived from sheep's wool.

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

You have the right to withdraw from the VitaMIND study at any time and without giving us a reason. You can do this through the 'Withdraw From Study' link on the website or by contacting us on the study helpline. You may withdraw at any point up until the end of this study. We will contact you to let you know when the study has ended. If you do decide to withdraw from the VitaMIND study we will not collect any further data from you for the purposes of this study. However, all anonymised data collected up until you withdraw will be kept and stored for analysis and regulatory purposes. Withdrawing from this study will not affect your participation in PROTECT or other studies currently affiliated with PROTECT.

There is a very small chance that people taking part in this study may develop cognitive impairment or dementia over the three-year period, though not as a result of participating in the study. Signs of cognitive decline will be monitored as usual for the PROTECT study, through your regular assessments. In the unlikely event we detect a clinically significant drop in your performance in the study tests we will contact you and your GP to recommend they arrange an appointment with you to carry out further tests. This follows the same process as the PROTECT study. If you are concerned about your cognition we recommend you contact your GP to discuss your concerns. You can also follow the links on the PROTECT website to talk to trained advisers at Alzheimer's Society UK.

If you receive a diagnosis of dementia or your cognitive performance is deemed to fulfil criteria for a loss of capacity, unfortunately you will need to withdraw from this study and PROTECT. If this happens we would retain all anonymous data collected up until withdrawal. We would like to keep any personal information (email address, home address, GP details, NHS number) that you have provided up until that date. However, if you would prefer for personal data collected up to that date to be removed from the study you can indicate this on the consent form. If you decide that you would like us to destroy your personal information please note that we will retain your name and participant ID to ensure we have a record of your consent when you registered for regulatory purposes.

You can change your mind about your preferences for data at any time by following the link on the website or by contacting the study helpline.

Who is organising and funding the research?

The study is supported by the JP Moulton Foundation and is sponsored by the University of Exeter. You will not receive payment for participating in this study.

Who has reviewed and approved this study?

The study has been reviewed by an independent NHS ethics committee Wales Research Ethics Committee 3, and the Health Research Authority who are the regulatory authority for clinical studies.

Will my taking part in this study be kept confidential?

Research data will be collected online through the PROTECT website over the three-year period, and is subject to the privacy terms of the PROTECT study. All data will be stored securely according to the General Data Protection Regulation 2018 and the security procedures in place at the University of Exeter. The research will also be covered by normal insurance policies at the University of Exeter.

Only members of the PROTECT research team will have access to your name for this study. The study database will not include your name, just a study number. Your data may be used by other researchers in the future, however your data will only be accessible in a completely anonymised format and it will not be possible to identify you. We will ask for your permission for this as part of the informed consent process.

All the data we collect will be stored confidentially, according to Data Protection Laws. Data will be analysed anonymously so no participant can be identified.

All study data will be stored securely according to Data Protection Laws* and the security procedures in place at the University of Exeter, Royal Devon & Exeter NHS Foundation Trust, Devon Partnership NHS Trust and South London and Maudsley NHS Trust.

For further information on how your personal information will be processed please visit our privacy policy on the study website.

***Data Protection Laws** *means (a) any law, statute, declaration, decree, directive, legislative enactment, order, ordinance, regulation, rule or other binding restriction (as amended, consolidated or re-enacted from time to time) which relates to the protection of individuals with regards to the Processing of Personal Data to which a Party is subject, including the Data Protection Act 1998 ("**DPA**") and EC Directive 95/46/EC (the "**DP Directive**") (up to and including 24 May 2018) and on and from 25 May 2018, the GDPR and all legislation enacted in the UK in respect of the protection of personal data; and (b) any code of practice or guidance published by the ICO (or equivalent regulatory body) from time to time.*

What will happen at the end of the study?

At the end of the study you will complete your final tests for the Vitamin D study on the PROTECT website. We will then contact you to let you know the study has ended and to thank you for your contribution. We will check if you wish to know your treatment allocation. The results of the study may be published in a scientific journal. We will provide you with a lay summary of our findings in the form of a newsletter which is sent to all PROTECT participants and is available on the website. The findings will also be available on the PROTECT website. The information collected will be totally confidential and no individuals will be identified in any reports/publications or presentations. A description of this clinical study will be available at www.clinicaltrialsregister.eu and at www.ClinicalTrials.gov.

What if there is a problem?

For independent advice and information you can contact the PALS Service at the Royal Devon & Exeter or Devon Partnership NHS Trusts.

Patient Advice and Liaison Service (PALS)

Royal Devon & Exeter NHS Trust PALS:

- Telephone: **01392 402093**
- Email: rde-tr.PALS@nhs.net

Devon Partnership NHS Trust PALS:

- Telephone: 0800 073 0741
- Email: dpn-tr.pals@nhs.net

South London & Maudsley PALS

- Telephone 0800 731 2864

- Email: pals@slam.nhs.uk

Additional contacts relating to this research

Research Team Contact (Study Helpline)

Tel: 01392 725010

Email: VitaMIND@exeter.ac.uk

VitaMIND Trial Co-ordinator

Mrs Ellie Pickering

Tel: 01392 726046

Email: e.pickering@exeter.ac.uk

Sponsor Contact

Ms Pam Baxter

Tel: 01392 723588

Email: P.R.Baxter2@exeter.ac.uk

Further Information

Thank you for taking the time to read the information about this study. If you would like to take part, please register for the study through the PROTECT website at www.protectstudy.org.uk. If you would like more information about the study before you decide whether or not to take part, you can contact a member of the study team by ringing the study help and information line 01392 725010.

Thank you for your interest in taking part.

Consent to Take Part

- I agree to take part in the above study.
- I am aged 50 or older, live in the UK and have access to a computer/smartphone/device and can access the internet.
- I confirm that I have read and understand the participant information sheet (version 3) dated 13/11/2019 for the above study. I have had the opportunity to consider the information, seek clarification and understand my involvement in the study.
- I confirm that I am knowingly entering the study
- I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reason and without my medical care or legal rights being affected.
- I understand that I may be selected to receive an at-home blood test kit, and that this is an optional part of the study
- I understand that relevant data collected during the study may be looked at by individuals representing the research team at the University of Exeter or from regulatory authorities, where it is relevant to my taking part in this research. I give permission for these individuals to have access to my data.
- I agree for anonymous data from this study to be used by other researchers in the future.
- In the event that a significant drop in my performance on the cognitive tests is detected during the study I give permission for the study team to contact my GP to recommend further testing.
- In the event that I lose capacity to consent during the period of this research I understand that I will immediately be withdrawn from the study.
- If I choose to withdraw or lose the capacity to consent as described in point 7, I understand that all anonymous data collected prior to my withdrawal will be retained and included in the study.
- I understand that if I withdraw from the study my personal details will be withdrawn from the VitaMIND study but will be retained in the main PROTECT study for as long as I remain a PROTECT participant
- I understand that all data will be stored in a way complying with the provisions of the General Data Protection Regulation 2018.