Older people and enhanced neurocognitive function

The OPEN Study

Participant Information Sheet

We would like to invite you to take part in a research project called the OPEN study. Before you decide whether or not to take part it is important for you to understand why the research is being done and what it will involve.

Please take your time to read this leaflet carefully and discuss it with family or friends if you wish. You may also wish to contact the Research Nurse at your general practice to ask for more information (see contact details at the end of this leaflet).

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What is the purpose of this study?

Older people in the UK are known to be at risk of vitamin B12 deficiency which may lead to increasing weakness in the limbs, and problems with communication and co-ordination.

This research is trying to find out if taking a daily vitamin B12 tablet for 12 months will improve the way the nerves work in your spine, arms and legs.

If your nerves work better it could possibly mean improved strength, greater independence and better quality of life. Alternatively, it is possible that taking the study tablets may have no beneficial effect.

Why have I been chosen?

We have invited you to take part because you are aged 75 years or over. We are sending this information to about 4,000 patients registered with 10 general practices in the South East of England.

Do I have to take part?

It is up to you to decide whether or not to take part. You do not have to agree to take part in this study. If you complete the "no" box on the reply slip, no further contact will be made with you about this study. This will not affect the care you receive from your general practice in any way.

What will happen if I agree to consider taking part?

If you return a completed reply slip and tick the "yes" box, you will be telephoned by the Research Nurse to make an appointment at the practice. If you have any questions about the study, you can ask the Research Nurse when s/he contacts you.

You will see from the reply slip that we ask whether you are already taking vitamin B12 tablets or whether you have had a vitamin B12 injection in the past 6 months. If you are currently taking vitamin B12 (either on its own or as part of a multi-vitamin tablet) or if you have had a vitamin B12 injection in the past 6 months you will not be able to join the study. Please record this information on the reply slip and we will not contact you further about the OPEN study.

First study visit

At the first appointment, the nurse will tell you more about the study. You can ask any questions you want. If you decide that you want to take part, the nurse will carry out an initial assessment of your memory. This is a short series of questions, which helps us to find out the current status of your memory. If the assessment suggests that you might have memory difficulties it will not be appropriate for you to take part in the study. If this is the case, you may wish to make an appointment with your GP to discuss this further.

If you are able to take part, the nurse will ask your permission to take a 5ml blood sample to check that you are not anaemic, and to check the

current level of vitamin B12 in your blood. If your blood test shows your level of vitamin B12 is low, or that you are anaemic, you will not be able to take part in the study, but the nurse will discuss the results with your GP and advise you if any treatment is required. Once all the relevant tests have been conducted on your blood, any remaining sample will be destroyed and not used for any other purposes.

If the results of your blood test fall within the levels required for the OPEN study then the Research Nurse will contact you to let you know, and will also pass your contact details on to the Study Manager of the OPEN study. The Study Manager will telephone you to arrange your second study visit and send you a brief questionnaire about your diet and frame of mind to complete at home.

Second study visit

The second study appointment will be at King's College Hospital, Denmark Hill, London, SE5 9RS. If you wish, we will arrange and pay for a registered taxi to take you from your home to the hospital and back again, or pay your travelling costs if you wish to travel by public transport or have a friend or relative to drive you to the appointment. When you arrive at the hospital you will be met by the Study Manager who will discuss the study with you and answer any questions you may have. The Study Manager will then give you two consent forms to read and sign if you want to take part in the study.

Once you have given your consent, the Study Manager will collect your completed questionnaire. He will then ask you to complete a second questionnaire which will assess your memory and concentration. The Study Manager will then measure your height, weight and mobility. We measure your mobility by recording the time it takes for you to stand up from a chair, walk 3 meters (10ft) in a line, turn around and walk back to the chair and sit down. These assessments are widely used in studies of older people.

A 15ml blood sample will be collected to check your levels of vitamin B12 and related vitamins. There is emerging evidence that our genes may define the way that our nerves and brain function changes over time. With your permission, part of your blood sample will therefore be stored for use in the future for analysis of the genetic differences that exist between people. Once all the relevant tests have been conducted on your blood and genetic material, any remaining sample will be destroyed and not used for any other purposes. This part of your visit will take approximately 30 minutes.

We will then collect information on how your nervous system is working by testing the reflexes in your knees and feet, and by using a series of standard nerve conduction tests.

What are nerve conduction tests?

Our muscles work because messages are sent to them from the brain via the nerves. Nerve conduction tests measure how fast and how well your nerves conduct these messages.

To test your nerves, small electrical pads are applied to your skin at various points on your arms and legs. The electrical pads will provide a small electrical impulse which will be detected at another point on your body. We will measure the size of the electrical impulse and the length of time it takes for the electrical impulse to reach the detection point.

We will also measure how well your brain manages to send messages to your muscles. To do this, we will place a stimulator that looks like a small hat on top of your head. When it sends an impulse, the stimulator makes a click sound and you will feel a slight tap on the top of your head. We will ask you to relax completely and then ask you to make a small movement of the muscle we are measuring. We will activate the stimulator at a very low level at first which will probably have no effect. We will then increase the size of the impulse until we detect a response in the muscle.

These techniques have been in general use for 25 years in people of all ages and there have been no serious side effects. A minor side effect that may rarely result from these techniques is a slight short-lasting headache.

Do I need to prepare for the procedure?

No special preparation is needed, but you may find it more convenient to wear loose clothing. Part of the test will involve your hands and legs, and you will be asked to remove jewellery, tights, stockings etc. so you may prefer to leave these at home. Please wear clothing which will allow the arm to be exposed to the elbow, and trousers or a skirt loose enough to be pulled up to knee level. If the weather is cold, or if your hands are naturally cold, please wear gloves so that your hands are warm when you attend the appointment. If you are on medication for any reason, this should be continued as normal but you should let the staff know what medicines you are taking when you come for your appointment. If possible, please avoid applying moisturising cream or lotion to your arms or legs as this can interfere with the recordings.

The dietary supplement

This study is designed as a randomised trial. This means that half of the participants in the study will be given tablets containing vitamin B12 and the other half will be given a placebo tablet. The placebo will look exactly the same as the vitamin B12 tablet but will have no active ingredient. You will have a 50% chance of getting the vitamin B12 tablets. Neither you, the Research Nurse, the Study Manager nor your GP will know which tablet you have been given. This is the best way to test whether vitamin B12 has any beneficial effect.

The Study Manager will telephone an automated computerised randomisation service which will decide which treatment you will receive. You will be asked to take one tablet every day for 12 months. You will be given a supply of tablets to take home with you. Additional tablets will be sent to you by post throughout the study.

Keeping in touch with you

The Study Manager will telephone you soon after you start taking the tablets and every two months during the study. You can tell him any information you wish to pass on to the study team.

12 month hospital appointment

After you have been taking the tablets for 12 months, we will make an appointment for you to return to the hospital to repeat the same tests as at the start of the study. This will allow us to check how you have changed over the year.

What is the treatment being tested – is it a drug?

The treatment being tested in this study is 1mg vitamin B12 consumed daily in one tablet. Vitamin B12 is not classified as a drug - it is available "off the shelf" as a dietary supplement. The tablets are suitable for vegetarians, vegans and coeliacs.

How do I know that this study is safe?

The study has been extensively reviewed by experts in nutrition research. Furthermore, the study has been approved by the appropriate research ethics committees and your local Primary Care Trust. Permission has been given for the study to take place.

What are the side effects of any treatment received when taking part?

There are no known side effects of vitamin B12. However, in extremely rare instances, some allergic skin reactions have been reported.

Do I have to change my every-day behaviour?

During the course of the study we ask that you do not take any supplementary vitamin B12 (either in a vitamin B12 tablet or as a part of a multi vitamin tablet) and do not have a vitamin B12 injection. There are no other restrictions on your way of life or on the use of any medications.

What are the possible disadvantages and risks of taking part in the study?

You will have to remember to take a tablet every day. You will be asked to make a return visit to King's College Hospital 12 months after joining the study.

What are the possible benefits of taking part?

Your health will be checked and if any memory or nerve function problems are diagnosed you will be referred to your GP. Also, you will be

participating in an important study that could improve the health of older people in the future.

What if new and relevant information becomes available during the study?

This is an important area of public health in which there is much academic research underway. New research information becomes available all the time. The study organisers will discuss any relevant research information that becomes available during the study period. We will inform you about the new information if it is important.

What happens when the research study stops?

After you have been taking your tablets for one year, we will not be able to provide you with more tablets. However, if you decide you want to take vitamin B12 tablets after the study has ended they are on sale in the UK.

The results of the study will not be available until all participants have completed their course of tablets. We may also have questions in the future relating to the study, and with this in mind we have asked on the consent form for your permission to contact you in the future if it is required.

What if something goes wrong?

If you are harmed by taking part in this research project, you may have grounds for legal action but you may have to pay for it. The London School of Hygiene & Tropical Medicine holds medical malpractice insurance, issued by Lloyd's of London, in the event that it is found legally liable for such harm. The London School of Hygiene & Tropical Medicine also holds an insurance policy, issued by Lloyd's of London, in respect of accidental harm to participants, as a result of taking part in the study.

Will my taking part be kept confidential?

Any information that you provide as part of the study will be completely confidential within the research team. Questionnaires will be made anonymous (i.e. we will replace your name and personal details with a special number which cannot be traced back to you by anyone except the Study Manager). Answers from all completed questionnaires will be combined and presented in such a way that individuals cannot be identified either directly or indirectly.

The principal researchers of this study are responsible for analysing, storing and ultimately destroying the data according to guidelines set by the National Health Service Research and Development Unit. However, we will ask your consent for your name and contact details to be sent to the NHS Central Register for future information, with regard to assessing your health.

What will happen to the results of the study?

The results will not be available until 2010. The research will be published in scientific journals and the results publicised widely. Participants in the study will be sent a summary of the results. Reference to the scientific publications and the research summary will be posted on the study website.

Who is organising and funding the research?

The study is co-ordinated by researchers at the London School of Hygiene & Tropical Medicine (LSHTM) and at the Medical Research Council General Practice Research Framework (GPRF).

The principal researcher is Dr Alan Dangour, Nutrition and Public Health Intervention Research Unit, LSHTM, Keppel Street, London, WC1E 7HT.

The study is funded by the Food Standards Agency, Aviation House, 125 Kingsway, London, WC2 6NH. Website: www.foodstandards.gov.uk

Who has reviewed this study?

All research in the NHS is looked at by an independent group of people, called a Research Ethics Committee to protect your safety, rights, wellbeing and dignity. This study has been reviewed and given a favourable opinion by the Cambridgeshire 4 Research Ethics Committee. The research has also been reviewed and given a favourable opinion by the LSHTM ethics committee.

Further Information and contact details

If you would like more information about the study please contact the Research Nurse at your Doctor's surgery:

General information about the study is available on the study website: www.OPEN-study.org.uk

If you have any specific questions, problems or concerns about this study then please contact the OPEN Study Manager, Ken Whyte at the London School of Hygiene & Tropical Medicine, Nutrition and Public Health Intervention Research Unit, Keppel Street, London WC1E 7HT.

Tel: 020 7958 8147 or by email: ken.whyte@LSHTM.ac.uk

Thank you very much for reading this information sheet.