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Anti-inflammatory supplement to reduce immune ageing

Submission date 18/02/2024	**Recruitment status** No longer recruiting	[_] Prospectively registered [X] Protocol [_] Statistical analysis plan [_] Results [_] Individual participant data [_] Record updated in last year
Registration date 19/02/2024	**Overall study status** Completed	
Last Edited 04/03/2024	**Condition category** Other	

Plain English summary of protocol

Background and study aims

People are living for longer, they are not necessarily enjoying good health in their old age. The number of people aged over 60 in the UK reached 15.5 million (23% of the population) in 2020 and this will continue rising. Changes within the immune system with advancing age, include increased inflammation, and we are investigating if this causes a number of diseases which mostly affect older people, such as heart disease, osteoporosis and dementia. The amount of inflammation in the blood has been shown to indicate how “aged” the immune system is and even how aged a person is overall (called their biological age).

Several food components (nutrients) can reduce inflammation and may reduce the degree of ageing of the immune system and have broad health benefits. However, these nutrients have not been tested in combination to see if their effects are even better.

We aim to test the effect of a nutritional supplement, developed by the company Bayer, which contains eight different nutrients that have been separately shown to reduce inflammation or improve immune function. We will measure inflammation and also whether the supplement improves physical function, quality of life and biological age.

Who can participate?

Adults aged 60 years or older.

What does the study involve?

The study overall lasts 3 months. If you agree to take part you will be invited to come to the Clinical Research Facility (CRF) in the Heritage Building on the Queen Elizabeth Birmingham hospital site. We will provide the full address with clear directions and transport links, including details of parking. You will be given a 3 months supply of the nutritional supplement, and will ask you to take one tablet every day for 12 weeks.

We will ask you to carry out some simple physical function tests, such as seeing how long it takes you to stand up from a sitting position 5 times.

Lastly, we will ask you to provide a saliva and a blood sample (20ml = 4 teaspoons) so that we can measure inflammation, immune age and biological age. As part of this, DNA will be extracted from the samples to look for specific DNA markers of ageing. The samples will be collected by one of the research team, who will take blood from a vein in your arm using a standard needle. For the saliva sample you will need to produce a small amount of spit into a specifically designed

collecting tube. The blood tests will be taken to the university laboratories where they will be processed and stored. The saliva will be sent to a company, Chronomics, to analyse as we do not do this sort of analysis at Birmingham. Chronomics is a company based in the UK that analyses biological samples.
We will ask you to fill in a questionnaire about your quality of life (QoL) and you will take away another questionnaire that asks you to record what you eat for the following week. We will also give you two copies of the QoL questionnaire to be filled in at home, 4 weeks and 8 weeks later, which can be brought to the 12 week visit, and repeat the food diary for the final week.
We will phone you at weeks 4 and 8 of the study to make sure that you are not experiencing any unexpected problems with the supplement and to remind you to fill in the questionnaires.
After 12 weeks we will ask you to return to the hospital and we will repeat all of the tests again.
We will not supply further nutritional supplements after the trial has ended.
We will use the blood sample to measure the amount of inflammation in your blood, this will tell us how "aged" your immune system is. We will also do another test which looks at chemical groups on the DNA in your blood cells; this tells us how biologically old you are. If we have any blood left over we would like to store this for up to 5 years for use in future ethically approved research, just in case new tests become available that will help us to understand the benefits of the nutritional supplement.
Although the study is funded by the company Bayer, they will not have access to your personal information and any left over blood will stay at the University of Birmingham. The sample will be destroyed at 5 years

What are the possible benefits and risks of participating?
The eight nutrients in the supplement (Vitamin D, Vitamin C, Vitamin B3, Omega 3 Poly Unsaturated Fatty Acids (EPA + DHA), Resveratrol, Olive fruit extract, Astaxanthin) have all been shown to be safe in the amounts we are using. Resveratrol is found naturally in grapes, blueberries, raspberries, mulberries, and peanuts. Astaxanthin is a keto-caratinoid that is found naturally in pink shelled sea creatures, such as shrimps. It is manufactured synthetically and is used primarily as a food dye. At much higher doses than we will be using, some of the nutrients affect medicines used for blood thinning, such as warfarin, and so we will not recruit people in to the study who are on this type of medication.

You may develop a bruise on the arm where the blood is taken, this will settle within a few days. There are no other side effects which you are likely to experience.

If the supplement does reduce inflammation and biological age you may see an improvement in your physical function and quality of life. You will be told if there is a reduction in inflammation and biological age at the end of the trial as well.

Where is the study run from?
The study is run from the Institute of Inflammation and Ageing at the University of Birmingham with the Clinical Research Facility at Queen Elizabeth Hospital, Birmingham (UK)

When is the study starting and how long is it expected to run for?
October 2022 to May 2024

Who is funding the study?
Bayer (Switzerland)

Who is the main contact?
Dr Thomas Jackson, t.jackson@bham.ac.uk

Contact information

Type(s)
Public, Scientific, Principal investigator

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Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

Integrated Research Application System (IRAS)
308774

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
IRAS 308774, CPMS 53163

Study information

Scientific Title
An uncontrolled open label trial of a nutritional supplement to reduce measures of biological and immune ageing and improve physical function and quality of life in healthy older people

Study objectives
To test the hypothesis that a 12-week treatment of Essentials, a nutritional supplement developed by Bayer, will improve biological ageing, immune ageing, quality of life (QoL), and physical function (SPPB) in healthy older adults, by conducting an uncontrolled open label trial in 76 participants.

Ethics approval required
Ethics approval required

Ethics approval(s)

approved 29/06/2022, London - Bromley Research Ethics Committee (Temple Quay House, 2 The Square, Temple Quay, Bristol, BS1 6PN, United Kingdom; +44 207 104 8134; bromley.rec@hra.nhs.uk), ref: 22/PR/0698

Study design
Uncontrolled open label trial

Primary study design
Interventional

Study type(s)
Efficacy

Health condition(s) or problem(s) studied
Age related inflammation and DNA methylation

Interventions
This trial will test the hypothesis that a combination of vitamins and nutraceuticals (“Essentials”), all known to have an effect on immune ageing or systemic inflammation will improve both biological markers of immune and biological age, and markers of physical function and general well-being.

The daily dose of the supplement, supplied by Bayer Consumer Care AG, contained Vitamin D3 (20 µg), Vitamin B3 (niacinamide, 50 mg), Vitamin C (85 mg), Omega-3 polyunsaturated fatty acids (eicosapentaenoic acid (EPA) and docosahexaenoic (DHA) acid, 250 mg), olive fruit extract (delivering 10 mg hydroxytyrosol), resveratrol (30 mg) and astaxanthin (3.2 mg). Participants were required to cease consumption of any multivitamins, dietary supplements containing (or any food/beverage products supplemented with) any of the study nutraceutical components, at least three weeks prior to commencement of the study.

Participants took the supplement daily for 12 weeks and all participants were included in this intervention – there was no control arm.

Intervention Type
Supplement

Primary outcome(s)
Immune ageing by measuring 51 different serum cytokines, chemokines and growth factors to give an iAGE score (Sayed et al 2021), hs-CRP will also be measured at baseline and 12 weeks

Key secondary outcome(s))
At baseline and 12 weeks we will measure
1. Biological ageing by DNA methylation in peripheral blood and saliva;
2. QoL (SF36) and diet (7 day food diary, to confirm there was no significant change in the diet of the participants) from questionnaires;
3. Physical function assessed by the SPPB (Guralink et al. 1994).

Completion date
01/05/2024

Eligibility

Key inclusion criteria
1. Age ≥60 years.
2. Ability to provide informed consent.
3. Willing to stop taking multivitamins, and dietary supplements containing vitamins C and D, B3, DHA/EPA, Olive polyphenols, resveratrol and astaxanthin or food/beverage products supplemented with the above ingredients 2 weeks prior to and throughout the study.
4. Able to travel to the clinic for initial and subsequent evaluations.

Participant type(s)
Healthy volunteer

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
60 years

Upper age limit
100 years

Sex
All

Total final enrolment
83

Key exclusion criteria
1. Current smokers, or ex smokers who have stopped within the last 12 months, or are using nicotine replacement products.
2. History of diabetes, myocardial infarction, congestive heart failure, kidney failure, liver disease or stroke.
3. Untreated thyroid disorder, cancer, active neoplasms.
4. Untreated gastrointestinal, or pulmonary diseases.
5. Surgery or trauma in last 60 days.
6. Inflammatory diseases, auto immune diseases or recent infection in last 60 days.
7. Allergies to any of the ingredients to be studied.
8. Currently taking or using multivitamins or dietary supplements containing vitamins C and D, B3, DHA/EPA, Olive polyphenols, resveratrol and astaxanthin or food/beverage products supplemented with the above ingredients.
9. Currently taking medication known to be metabolised by CYP3A.
10. Currently taking any of the following medications, which confound the effects of inflammation: Tamoxifen, Cyclosporine A, immunosuppressants or Anti TNF inhibitors, NSAIDs.
11. Currently taking any of the following anticoagulant drugs (blood thinners): Warfarin, Direct oral anticoagulant drugs (DOACs), and antiplatelet drugs including aspirin.
12. Individuals at risk of bleeding complications, including those with inherited bleeding

disorders (such as haemophilia), or increased risk hemorrhagic stroke or events.
13. Unable or unwilling to maintain current lifestyle throughout study such as eating habits, exercise habits, etc.
14. Assessed as being frail by Fried phenotype criteria.

Date of first enrolment
01/10/2022

Date of final enrolment
01/06/2023

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
University of Birmingham
University of Birmingham Research Laboratories
Queen Elizabeth Hospital
Birmingham
United Kingdom
B15 2TT

Sponsor information

Organisation
University of Birmingham

ROR
https://ror.org/03angcq70

Funder(s)

Funder type
Industry

Funder Name
Bayer

Alternative Name(s)
Bayer AG, Bayer Corporation, Friedr. Bayer et. comp.

Funding Body Type
Government organisation

Funding Body Subtype
For-profit companies (industry)

Location
Germany

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study will be available upon request from Dr Thomas Jackson (t.jackson@bham.ac.uk) for a 5 year period

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Participant information sheet	version 2.0	23/06/2022	19/02/2024	No	Yes
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes
Protocol file	version 2.0	06/09/2022	19/02/2024	No	No