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NNTV: NSA Nutritional supplementation Trial of fruit and vegetable extracts and Vascular function

Submission date	Recruitment status	[_] Prospectively registered
07/08/2013	No longer recruiting	[X] Protocol
Registration date	**Overall study status**	[_] Statistical analysis plan
27/02/2014	Completed	[X] Results
Last Edited	**Condition category**	[_] Individual participant data
10/05/2021	Circulatory System	

Plain English summary of protocol

Background and study aims
Cardiovascular disease (CVD) is the leading cause of death worldwide. Although CVD is associated with older adults, the signs of CVD, particularly atherosclerosis (when arteries become clogged up by fatty substances such as cholesterol), begin in early life and can progress through an individual's lifetime. Poor diet, lack of exercise and smoking are associated with atherosclerosis, and through lifestyle interventions the risk can be decreased. Regular consumption of five portions or more of fruit and vegetables (FV) as part of a healthy diet is thought to play an important role in the prevention of CVD. This is supported by evidence from observational studies. However, there is currently limited insight into the effects of FV supplements on the lining of blood vessels such as arteries, as well as insulin sensitivity, which are important steps on the pathway to CVD. In some longer term studies, JuicePlus+® supplements (containing antioxidants, polyphenols and other bioactive phytochemicals derived from 26 different FV) have been shown to decrease cardiovascular risk factors such as blood pressure. In this study, we propose to evaluate the effect of '5-A-Day' dietary advice and supplementation with JuicePlus+® capsules versus placebo (dummy) capsules on vascular function and CVD risk in a population of overweight/obese individuals. This study is expected to further our understanding of the short-term impact of FV constituents on CVD risk and has the potential to inform future dose selection and/or in-depth explanatory studies and dietary intervention studies using FV supplements.

Who can participate?
Overweight and obese males and females aged 25-65 years.

What does the study involve?
Pre-screening telephone call
Eligibility for the study will be assessed and if eligible you will be invited to the Medical Research Council (MRC) Human Nutrition Research Unit (HNR) for a screening visit.
Screening Visit
Study procedures will be fully explained to you and you will be shown all the equipment that will be used to take measurements during the study visits. If you are happy to take part written

consent will be taken.
A fasted blood sample will be taken to further assess your eligibility. Your height and weight will be measured. You will be asked to complete two short questionnaires about physical activity and consumption of fruit and vegetables. A nutritionist will provide you with '5-A-Day' dietary advice.
You will be randomly allocated to one of two groups:
Group 1: Three supplement capsules twice daily for 12 weeks. You will be given '5-A-Day' dietary advice plus written nutrition education material.
Group 2: Three placebo capsules twice daily for 12 weeks. You will be given '5-A-Day' dietary advice plus written nutrition education material.
You will not know which group you have been assigned to.
Study Visit 1
You will also be required to collect a 24-hour urine sample, starting the day before your visit and ending in the morning of the first test visit. This visit will last about 5 hours and you will have a number of measurements taken:
1. 45 ml blood sample (fasted)
2. Height and weight
3. Body fat percentage and waist circumference
4. Blood pressure
5. The thickness of the main artery on your neck will be measured using a specialised ultrasound machine
6. Electrocardiogram (ECG)
7. The thickness of an artery in your arm will be measured using a specialised ultrasound machine
8. The pulse in your wrist will be measured using a specialized machine
9. Blood flow will be assessed using electrical current
You will also complete a questionnaire to assess habitual fruit and vegetable intake and you will receive '5-A-Day' dietary advice and a 6-week supply of capsules.
In between study visit 1 and the follow up/intermediate visit, a member of the study team will phone weekly to monitor and provide ongoing support.
Follow-up/Intermediate Visit
Six weeks after Study Visit 1, you will attend the HNR and you will be given your next 6-week supply of capsules. A fasting blood sample will be taken. A nutritionist will provide you with '5-A-Day' dietary advice and you will be asked to complete a short questionnaire regarding your fruit and vegetable intake.
In between the follow-up/intermediate visit and study visit 2, a study team member will phone weekly to monitor and provide ongoing support.
Study Visit 2
This visit is the same as Study Visit 1 except you will not receive any more capsules following the visit.
Genetic and related metabolic tests on stored samples
In this study we plan to look at a range of genes and related metabolic tests which might affect your risk of CVD. The effects of these genes are not yet well understood, and this research is at a very early stage. For this reason, we will not be giving you any information on your genes. This is because the results will not be clinically relevant.
With your consent we will also store a small quantity of your blood for potential future research.

What are the possible benefits and risks of participating?
You will receive advice on how to reach the '5-A-Day' recommended intake of fruit and vegetables. Knowledge gained in this study will help our research into the prevention of heart disease.
If your blood measurements indicate anything clinical or that you may be at increased risk of developing conditions such as heart disease or diabetes, we will inform you and your GP (doctor). As a result your GP may want to order more tests. A new diagnosis could affect your

future insurance status (e.g. for life or private medical insurance). Your GP will arrange any specific treatment you may need in the usual way.

Where is the study run from?
Medical Research Council (MRC) Human Nutrition Research Unit (HNR), Cambridge, UK

When is the study starting and how long is it expected to run for?
April 2013 to December 2014

Who is funding the study?
The Medical Research Council (MRC), UK.

Who is the main contact?
Marietta Sayegh, Trial Co-ordinator
Dr Sumantra Ray, Chief Investigator

Study website
http://www.mrc-hnr.cam.ac.uk/volunteers/current-volunteer-projects

Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
6456

Study information

Scientific Title
Nutritional Supplementation study of fruit and vegetable extracts and vascular function: a randomised controlled trial of the effects of supplementation with fruit and vegetable extracts on vascular and endothelial function

Acronym
NNTV

Study objectives
Supplementation with capsules containing a combination of equal quantities of "Fruit Blend", "Vegetable Blend", and "Vineyard Blend" in addition to standard dietary advice to consume five portions of fruit and vegetables daily, will significantly improve bio-markers of vascular and metabolic function in overweight and obese adults, compared with a control group receiving identical dietary advice and placebo capsules.

Ethics approval required
Old ethics approval format

Ethics approval(s)
NRES Committee East of England - Essex, 03/06/2013, ref: 13/EE/0095

Study design
Single-centre double-blind randomised placebo-controlled trial with parallel group design

Primary study design
Interventional

Secondary study design
Randomised parallel trial

Study setting(s)
Other

Study type(s)
Treatment

Participant information sheet
Patient information can be found at http://www.mrc-hnr.cam.ac.uk/wp-content/uploads/Appendix-I-Study-protocol_PIS-1+2_v5-0.pdf

Health condition(s) or problem(s) studied

Vascular Function/Cardiovascular Prevention

Interventions
Eighty participants will be randomly assigned to one of two interventions with 40 participants in each intervention group:

1. Standard '5-A-Day' dietary advice and three fruit and vegetable extracts capsules twice daily (5+J) for 12 weeks.
2. Standard '5-A-Day' dietary advice and three placebo capsules twice daily (5+P) for 12 weeks

Total follow up for all study arms from test visit 1 (baseline) is 12 weeks duration.

Intervention Type
Supplement

Primary outcome measure
Change in Carotid Intimal Media Thickness (cIMT) between baseline and 12 weeks of intervention

Secondary outcome measures
1. Dynamic macrovascular changes: flow mediated dilatation, pulse wave analysis (Augmentation Index) and ambulatory blood pressure.
2. Dynamic microvascular changes: laser Doppler imaging following iontopheresis of acetylcholine and sodium nitroprusside.
3. Changes in laboratory blood markers including endothelial cell function and oxidative stress: isoprostanes, selectins and oxidised LDL (as markers of chronic low grade inflammation and vascular dysfunction); fasting insulin and C-peptide (markers of metabolic health); lipids, glucose and HbA1C (classical risk markers).
4. Changes in Knowledge, Attitudes and Practices (KAP): 5-A-Day KAP measured using scores from the FACET validated questionnaire to assess FV intake, and related lifestyle measures.
5. Changes to safety monitoring indicators: liver function, full blood count and ECG.

The secondary outcome measures are elicited in tandem with the primary outcomes at baseline (test visit 1) and 12 weeks (test visit 2).

Overall study start date
03/06/2013

Completion date
31/12/2015

Eligibility

Key inclusion criteria
Current inclusion criteria as of 27/10/2014:
Eighty, free-living, overweight and obese male and female adults deemed eligible for inclusion in this study. The inclusion criteria are:
1. BMI 25-35 kg/m²
2. Aged 25 - 65 years
3. Non-smoker
4. Willing and able to comply with the study procedures
5. No history of cardiovascular disease (CVD)

Previous inclusion criteria:
Eighty, free-living, overweight and obese male and female adults deemed eligible for inclusion in this study. The inclusion criteria are:
1. BMI 25-35 kg/m²
2. Aged 25 - 60 years
3. Non-smoker
4. Willing and able to comply with the study procedures
5. No history of cardiovascular disease (CVD)

Participant type(s)
Healthy volunteer

Age group
Adult

Sex
Both

Target number of participants
80 participants

Total final enrolment
82

Key exclusion criteria
1. Smokers
2. History of CVD

Date of first enrolment
03/06/2013

Date of final enrolment
31/12/2015

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
MRC Human Nutrition Research
Cambridge
United Kingdom
CB1 9NL

Sponsor information

Organisation
Medical Research Council (MRC) (UK)

Sponsor details
Human Nutrition Research
120 Fulbourn Road
Cambridge
United Kingdom
CB1 9NL

Sponsor type
Research council

ROR
https://ror.org/03x94j517

Funder(s)

Funder type
Research council

Funder Name
Medical Research Council (MRC) Human Nutrition Research (UK)

Funder Name
National Safety Associates LLC (USA)

Results and Publications

Publication and dissemination plan
Not provided at time of registration

Intention to publish date

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not provided at time of registration

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol article	protocol	04/02/2016		Yes	No
Abstract results	results presented at the Experimental Biology Meeting		10/05/2021	No	No
HRA research summary			28/06/2023	No	No