ISRCTN41926726 https://doi.org/10.1186/ISRCTN41926726

Supplementation with Folate (and vitamins B6 and B12) and/or Omega 3 Fatty Acids on the prevention of recurrent ischaemic events in patients who have already experienced a coronary or cerebrovascular event

Submission date 14/09/2005	**Recruitment status** No longer recruiting	[_] Prospectively registered [X] Protocol [_] Statistical analysis plan [X] Results [_] Individual participant data
Registration date 05/12/2005	**Overall study status** Completed	
Last Edited 16/06/2015	**Condition category** Circulatory System	

Plain English summary of protocol
Not provided at time of registration

Contact information

Type(s)
Scientific

Contact name
Prof Serge Hercberg

Contact details
U557 Inserm (UMR Inserm/Inra/Cnam)
5 rue Vertbois
Paris
France
75003

Additional identifiers

Study information

Scientific Title

Supplementation with Folate (and vitamins B6 and B12) and/or Omega 3 Fatty Acids on the prevention of recurrent ischaemic events in patients who have already experienced a coronary or cerebrovascular event

Acronym
SU.FOL.OM3 Study

Study objectives
Definitive proof that supplementation with B-vitamins or omega-3 fatty acids will lead to a reduced cardiovascular diseases morbidity and/or mortality is still scarce. The currently available intervention trials did either not have a study design that allows this conclusion or the results need to be reproduced before they can be regarded as definitive. (NB the trials with B vitamins evaluated mostly the effect on intermediate end-points).

Secondary intervention trials with hard endpoints and B-vitamin supplementation have recently started, but not all of these trials used a combination B vitamins and most trials used pharmacological doses. This has the disadvantage that the results will be difficult to translate into dietary advice. In addition, recent research has indicated that supplementation with 5-methyl tetrahydrofolate (5-methyl-THF), the most abundant natural folate vitamin, is safe and lowers homocysteine levels. This form of folate, in contrast to folic acid, does not lead to circulating unmetabolized folic acid. Unmetabolized folic acid is hypothesized to mask the hematological manifestations of a vitamin B12 deficiency, thereby predisposing subjects to irreversible neurological damage. Stable 5-methyl-THF was not available when other intervention studies started and therefore they all use folic acid.

Taking all this information together, there is a need for a large double-blind placebo-controlled randomized intervention trial evaluating the effect of supplementation with B-vitamins (exchanging folic acid for 5-methyl-THF) and n-3 fatty acids in nutritional doses on hard cardiovascular endpoints. Therefore, we propose the following intervention study in which participants are SUpplemented with natural FOLate, vitamin B6 and B12 and/or OMega-3 fatty acids: the SU.FOL.OM3 study.

Ethics approval required
Old ethics approval format

Ethics approval(s)
1. Ethics Committee of Paris-Cochin (Comité Consultatif pour la Protection des Personnes se prêtant à la Recherche Biomédicale) (ref: CCPPRB n°1933)
2. National Committee of information and liberty (La Commission Nationale de l'Informatique et des Libertés [CNIL]) (ref: CNIL n° 901230)

Primary study design
Interventional

Study design
Randomised controlled trial

Study type(s)
Prevention

Health condition(s) or problem(s) studied
Cardio and neurovascular diseases

Interventions
5-methyl-THF (560 µg), vitamin B6 (3 mg) and B12 (20 µg) and/or omega-3 supplements (600 mg with an eicosapentaenoic acid [EPA]:docosahexaenoic acid [DHA] ratio of 2:1) versus placebo

Intervention Type
Supplement

Phase
Not Specified

Drug/device/biological/vaccine name(s)
Folate, vitamins B6 and B12 and Omega 3 Fatty Acids

Primary outcome(s)
Combination of myocardial infarction, cerebral vascular ischemic accident or cardiovascular deaths

Key secondary outcome(s)
1. Hospitalisation for coronary diseases
2. Hospitalisation for cardiac diseases
3. Hospitalisation for vascular diseases
4. Total mortality
5. Cardiovascular mortality
6. Myocardial infarctions
7. Acute coronary syndrome without necrosis
8. Ischemic cerebral vascular accidents
9. Arteriopathies
10. Venous thrombosis
11. Cancers

Completion date
30/06/2009

Eligibility

Key inclusion criteria
1. Participants should have experienced a coronary or cerebral event during 1 to 12 months before baseline. A coronary or cerebral event is defined as:
a. Myocardial infarction (validated and documented by a combination of clinical, enzymatic, or electrocardiogram [ECG] parameters)
b. Acute coronary syndrome without necrosis (validated and documented by a combination of clinical, enzymatic or ECG parameters)
c. A cerebral vascular ischemic accident (defined by criteria validated in epidemiological studies)
2. The participants should be 45-80 years at baseline

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Sex
All

Key exclusion criteria
1. Age <45 years or >80 years
2. Cardiovascular pathology not well defined
3. Patients that are incapable of understanding the study protocol
4. Patients with a pathology that might interfere with homocysteine or omega-3 fatty acid metabolism, in particular those that use methotrexate for the treatment of a cancer or rheumatoid arthritis and chronic renal failure (plasma level of creatinine >200 µmol/l or creatinine clearance <40 ml/min)
5. Patients with a non-cardiovascular pathology with a suspected survival time less than the 5 years period of the study (solid cancer, evolved dementia, leukemia etc.)

Date of first enrolment
15/04/2003

Date of final enrolment
30/06/2009

Locations

Countries of recruitment
France

Study participating centre
U557 Inserm (UMR Inserm/Inra/Cnam)
Paris
France
75003

Sponsor information

Organisation
INSERM - Direction of Clinical Research (France)

ROR
https://ror.org/02vjkv261

Funder(s)

Funder type
Industry

Funder Name
National Institute for Health and Medical Research (INSERM) (France)

Funder Name
French National Institute for Agricultural Research (INRA)

Funder Name
Ministry of the Higher Education and Research (France)

Funder Name
Pierre Fabre

Funder Name
Eprova

Funder Name
Danone Vitapole/Lu

Funder Name
Unilever Bestfoods France

Funder Name
Candia/ Yoplait

Results and Publications

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?
Results article	results	29/11/2010		Yes	No
Results article	blood pressure results	01/03/2012		Yes	No
Results article	cancer prevention results	09/04/2012		Yes	No
Results article	depressive symptoms results	01/07/2012		Yes	No
Results article	biomarker results	01/06/2013		Yes	No
Results article	baseline plasma fatty acids profile results	07/04/2014		Yes	No
Protocol article	protocol	10/06/2008		Yes	No
Other publications	publication on background and rationale of the SU.FOL.OM3 study	01/02/2003		Yes	No