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

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

**Plain English summary of protocol**
Not provided at time of registration

## Contact information

**Type(s)**
Scientific

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## Additional identifiers

**EudraCT/CTIS number**

**IRAS number**

**ClinicalTrials.gov number**

### Secondary identifying numbers
N/A

# 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)

### Study design
Randomised controlled trial

### Primary study design

Interventional

## Secondary study design
Randomised controlled trial

## Study setting(s)
Not specified

## Study type(s)
Prevention

## Participant information sheet

## 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 measure
Combination of myocardial infarction, cerebral vascular ischemic accident or cardiovascular deaths

## Secondary outcome measures
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

## Overall study start date
15/04/2003

## 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

### Age group
Adult

### Sex
Both

### Target number of participants
2,400

### 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)

**Sponsor details**
101 rue de Tolbiac
Paris
France
75003

**Sponsor type**
Research organisation

**Website**
http://www.inserm.fr

**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

### 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? |
|---|---|---|---|---|---|
| Other publications | publication on background and rationale of the SU.FOL.OM3 study | 01/02/2003 | | Yes | No |
| Protocol article | protocol | 10/06/2008 | | Yes | No |
| Results article | results | 29/11/2010 | | Yes | No |
| Results article | blood pressure results | 01/03/2012 | | Yes | No |
| | cancer prevention results | 09/04 | | | |

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| Results article | | /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 |