

# Folic acid supplementation in the management of menopausal symptoms in cancer survivors and healthy postmenopausal women

<b>Submission date</b> 11/03/2015	<b>Recruitment status</b> No longer recruiting	<input checked="" type="checkbox"/> Prospectively registered <input type="checkbox"/> Protocol
<b>Registration date</b> 11/03/2015	<b>Overall study status</b> Completed	<input type="checkbox"/> Statistical analysis plan <input checked="" type="checkbox"/> Results
<b>Last Edited</b> 10/11/2022	<b>Condition category</b> Cancer	<input type="checkbox"/> Individual participant data

## Plain English summary of protocol

<http://www.cancerresearchuk.org/about-cancer/find-a-clinical-trial/a-study-looking-at-folic-acid-for-women-having-postmenopausal-symptoms-foam>

## Contact information

### Type(s)

Scientific

### Contact name

Ms Claire Gaunt

### Contact details

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## Additional identifiers

### Clinical Trials Information System (CTIS)

2013-004246-41

### Protocol serial number

18588

## Study information

**Scientific Title**

A phase III randomised study of folic acid supplementation in the management of menopausal symptoms in cancer survivors and healthy postmenopausal women

**Acronym**

FOAM

**Study objectives**

FOAM is a phase III, double-blind, placebo-controlled, randomised controlled trial designed to determine whether folic acid supplementation improves the frequency and severity of hot flushes in postmenopausal women, either healthy women or breast and endometrial cancer survivors compared to placebo. The frequency and severity of hot flushes will be recorded on self reporting patient diaries. Effectiveness of folic acid supplementation on other menopausal symptoms, and quality of life will also be investigated. If folic acid is demonstrated to be effective, it would represent a cheap, safe, well tolerated and easily deliverable alternative to the conventional hormone replacement therapy, particularly in cancer survivors who may be experiencing more intense symptoms and certainly cannot take hormone replacement.

**Ethics approval required**

Old ethics approval format

**Ethics approval(s)**

14/WM/0093; First MREC approval date 06/05/2014

**Study design**

Randomised; Interventional; Design type: Screening, Treatment

**Primary study design**

Interventional

**Study type(s)**

Treatment

**Health condition(s) or problem(s) studied**

Topic: Cancer; Subtopic: Breast Cancer; Disease: Breast

**Interventions**

Folic Acid: Folic acid is a member of the B group of vitamins. It participates in cellular division, DNA synthesis and maturation of red blood cells. Patients randomised to the Folic Acid arm will take 5 mg/day; Follow Up Length: 0 month(s); Study Entry : Single Randomisation only

**Intervention Type**

Supplement

**Primary outcome(s)**

Change in Hot Flush Score; Timepoint(s): Change in Hot Flush Score at 12 weeks from randomisation.

**Key secondary outcome(s)**

1. Change in 5-HIAA levels and MHPG metabolites; Timepoint(s): In urine from randomisation at week 12
2. Change in frequency of hot flushes; Timepoint(s): Change from randomisation in frequency of hot flushes (mild, moderate and severe) at weeks 4, 8 and 12
3. Change in longitudinal QoL data; Timepoint(s): As measured by the Utian Quality of Life Scale at weeks 4, 8 and 12
4. Change in other menopausal symptoms; Timepoint(s): Using the Greene Climacteric Scale at weeks 4, 8 and 12
5. Change in whole blood levels of serotonin, plasma nor-adrenaline and serum folic acid; Timepoint(s): From randomisation at week 12
6. Correlation of blood changes with clinical improvement; Timepoint(s): Changes in whole blood levels of serotonin, nor-adrenaline, and serum folic acid at week 12
7. Effects in specific prognostic subgroups; Timepoint(s): Healthy women vs cancer survivors and BMI <30 v >30
8. Interim Change in Hot Flush Score; Timepoint(s): Change from randomisation in Hot Flush Score at weeks 4, 8 and 12
9. Percentage of responders; Timepoint(s): The percentage of responders at weeks 4, 8 and 12; defined as a reduction in Hot Flush Score of =50%

**Completion date**

31/10/2017

## Eligibility

**Key inclusion criteria**

1. Experiencing =50 hot flushes per week, as quantified from daily patient Sloan Diary recordings for 7 days after consent and prior to randomisation
2. Being =40 and =70 years of age
3. Willing to participate in the trial and given informed consent; Target Gender: Female

**Participant type(s)**

Patient

**Healthy volunteers allowed**

No

**Age group**

Adult

**Sex**

Female

**Total final enrolment**

164

**Key exclusion criteria**

As of 25/08/2016:

1. Baseline red cell serum folic acid level above the normal laboratory range (3.1 to 20.0µg/L)
2. Smoking >5 cigarettes per day

3. Intestinal malabsorption e.g. coeliac, tropical sprue or Crohn's disease
4. Known chronic renal impairment or failure
5. Known established chronic conditions mimicking climacteric presentation e.g. poorly controlled hypertension, hyperglycaemia or thyroid instability
6. Pernicious anaemia due to vitamin B12 deficiency
7. Alcohol consumption more than 14 units per week
8. Women with pheochromocytoma or other medullary tumours or carcinoid syndrome
9. Known allergic reactions and/or hypersensitivity to folic acid
10. Women who are, in the opinion of the treating physician, unlikely to be able to give informed consent or successfully complete the trial intervention and procedure
11. Participation in another clinical trial within the last 4 weeks prior to enrolment
12. Administration of the following drugs during study and for the specified number of weeks prior to study entry:
  - 12.1. 24 weeks prior to randomisation:
    - 12.1.1 Bevacizumab (Avastin)
    - 12.1.2 Trastuzumab (Herceptin)
  - 12.2. 8 weeks prior to randomisation:
    - 12.2.1 HRT (women on oestrogen implants are excluded from trial entry)
    - 12.2.2 Herbal remedies
    - 12.2.3 Heparin
  - 12.3. 6 weeks prior to randomisation:
    - 12.3.1 Tamoxifen
    - 12.3.2 Fluoxetine
    - 12.3.3 Venlafaxine
  - 12.4. 4 weeks prior to randomisation:
    - 12.4.1 Phenytoin
    - 12.4.2 Phenobarbitol
    - 12.4.3 Primidone
  - 12.5. 2 weeks prior to randomisation:
    - 12.5.1 Warfarin
    - 12.5.2 Sertraline
    - 12.5.3 Mianserin
    - 12.5.4 Mirtazapine
  - 12.6. 1 week prior to randomisation:
    - 12.6.1 Raloxifen
    - 12.6.2 Chronic use of NSAIDs (including high dose Aspirin\* and Cox-2 inhibitors)
    - 12.6.3 Methotrexate
    - 12.6.4 Fluorouracil
    - 12.6.5 Trimethoprim
    - 12.6.6 Co-trimoxazole
    - 12.6.7 Chloramphenicol
    - 12.6.8 Sulfasalazine
    - 12.6.9 Paroxetine
    - 12.6.10 Duloxetine
    - 12.6.11 Clonidine
- \*low dose Aspirin (75mg daily) is not prohibited
- 12.7. Stop prior to study entry:
  - 12.8. Cholestyramine
  - 12.9. Antacids (containing aluminium or magnesium)
  - 12.10. Vitamin containing zinc or folic acid

## Initial

1. Hormonal or non hormonal treatment (including raloxifen) for menopausal symptoms within 8 weeks of enrolment
2. Baseline serum folic acid level which is above the normal laboratory range (3.1 to 20.0µg/L)
3. Smoking >5 cigarettes per day
4. Intestinal malabsorption e.g. celiac, tropical sprue or Crohn's disease
5. Known chronic renal impairment or failure
6. Pernicious anaemia due to vitamin B12 deficiency
7. Taking the following drugs:
  - 7.1. Nonsteroidal antiinflammatory drugs (NSAIDs) can interfere with folate metabolism
  - 7.2. Cholestrolowering agents such as cholestyramine may decrease folic acid absorption
  - 7.3. Chemotherapeutic agents such as fluorouracil and methotrexate can interfere with conversion of folate into tetrahydrofolate
  - 7.4. Antibiotics such as chloramphenicol, trimethoprim and cotrimoxazole may inhibit dihydrofolic reductase
  - 7.5. Sulfasalazine may decrease folic acid absorption
  - 7.6. Anticonvulsants such as phenytoin, phenobarbital and primidone can interfere with absorption of anticonvulsants
  - 7.7. Serotonin reuptake inhibitors such as fluoxetine, venlafaxine, sertraline and paroxetine may ameliorate hot flushes
  - 7.8. Serotonin disinhibitants such as mianserin and mirtazapine may ameliorate hot flushes
  - 7.9. a2adrenergic agonist such as yohimbine may aggravate hot flushes
  - 7.10. a2adrenergic antagonist such as clonidine may ameliorate hot flushes
  - 7.11. Antacids containing aluminium or magnesium can interfere with folate metabolism
  - 7.12. Preparations containing zinc such as vitamins or food supplements that may contain folic acid
  - 7.13. Anticoagulant or thrombolytic therapy can interfere with folate assays
8. Therapies containing human antimouse antibodies (e.g. Trastuzumab and Bevacizumab) can interfere with folate assays
9. Alcohol consumption more than 14 units per week
10. Women with phaeochromocytoma or other medullary tumours or carcinoid syndrome
11. Known allergic reactions and/or hypersensitivity to folic acid
12. Women who are, in the opinion of the treating physician, unlikely to be able to give informed consent or successfully complete the trial intervention and procedures
13. Participation in another clinical trial within the last 4 weeks prior to enrolment

## Date of first enrolment

15/04/2015

## Date of final enrolment

30/04/2019

## Locations

### Countries of recruitment

United Kingdom

England

**Study participating centre**  
**University of Birmingham**  
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## Sponsor information

### Organisation

University of Birmingham

### ROR

<https://ror.org/03angcq70>

## Funder(s)

### Funder type

Government

### Funder Name

National Institute for Health Research

### Alternative Name(s)

National Institute for Health Research, NIHR Research, NIHRresearch, NIHR - National Institute for Health Research, NIHR (The National Institute for Health and Care Research), NIHR

### Funding Body Type

Government organisation

### Funding Body Subtype

National government

### Location

United Kingdom

## Results and Publications

### Individual participant data (IPD) sharing plan

The current data sharing plans for this study are unknown and will be available at a later date

## IPD sharing plan summary

Not provided at time of registration

### Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
<a href="#">Results article</a>		01/11/2021	18/11/2021	Yes	No
<a href="#">HRA research summary</a>			28/06/2023	No	No
<a href="#">Plain English results</a>			10/11/2022	No	Yes