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The seAFOod (Systematic Evaluation of Aspirin and Fish Oil) polyp prevention trial and STOP-ADENOMA (STudy Of Prevention by Aspirin anD EPA; kNowledge Of Mechanism of Action) sub-study

Submission date 06/05/2011	**Recruitment status** No longer recruiting	[X] Prospectively registered [X] Protocol [_] Statistical analysis plan [X] Results [_] Individual participant data
Registration date 06/05/2011	**Overall study status** Completed	
Last Edited 17/12/2024	**Condition category** Cancer	

Plain English summary of protocol
Currently as of 29/05/2019:
https://www.cancerresearchuk.org/about-cancer/find-a-clinical-trial/a-trial-looking-aspirin-and-fish-oil-possible-way-preventing-small-growths-forming-bowel-seafood

Previously:
http://cancerhelp.cancerresearchuk.org/trials/a-trial-looking-aspirin-and-fish-oil-possible-way-preventing-small-growths-forming-bowel-seafood

Study website
https://www.nottingham.ac.uk/mczseafood/index.html

Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number
2010-020943-10

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
9734

Study information

Scientific Title
A randomised controlled trial of eicosapentaenoic acid (EPA) and/or aspirin for colorectal adenoma (or polyp) prevention during colonoscopic surveillance in the NHS Bowel Cancer Screening Programme: the seAFOod (Systematic Evaluation of Aspirin and Fish Oil) polyp prevention trial and the STudy Of Prevention by Aspirin anD EPA; kNowledge Of Mechanism of Action (STOP-ADENOMA): Understanding mechanisms of colorectal cancer chemoprevention using seAFOod Polyp Prevention Trial outcomes and its Biobank

Acronym
The seAFOod Polyp Prevention Trial and STOP-ADENOMA sub-study

Study objectives
Current study hypothesis as of 09/05/2022:
The seAFOod Polyp Prevention Trial has been designed to integrate fully into the screening and surveillance phases of the NHS Bowel Cancer Screening Programme (BCSP) so that participation will not alter routine clinical practice.
The STOP-ADENOMA sub-study will aim to understand mechanisms of colorectal cancer chemoprevention using seAFOod Polyp Prevention Trial outcomes and its biobank.

Previous study hypothesis:
The seAFOod Polyp Prevention Trial is a randomised, double-blind, placebo-controlled 2 x 2 factorial study. The trial has been designed to integrate fully into the screening and surveillance phases of the NHS Bowel Cancer Screening Programme (BCSP) so that participation will not alter routine clinical practice.

Ethics approval required
Old ethics approval format

Ethics approval(s)
The seAFOod Polyp Prevention Trial:
Approved 24/11/2010, East Midlands - Derby Research Ethics Committee (Equinox House, City Link, Nottingham, NG2 4LA, UK; +44 (0)207 1048211; derby.rec@hra.nhs.uk), ref: 10/H0405/90
STOP-ADENOMA sub-study:

Approved 16/10/2019, London-Surry Borders (Health Research Authority, Skipton House, 80 London Road, London, SE1 6LH, UK; +44 (0)207 104 8104; surreyborders.rec@hra.nhs.uk), ref. 19/LO/1655

Study design
A randomised, double-blind, placebo-controlled 2 x 2 factorial study with an observational retrospective analysis sub-study

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Prevention

Participant information sheet
Patient information can be found at https://www.nottingham.ac.uk/mczseafood/index.html

Health condition(s) or problem(s) studied
Topic: National Cancer Research Network, Oral and Gastrointestinal; Subtopic: Colorectal Cancer, Oral and Gastrointestinal (all Subtopics); Disease: Colon, Gastrointestinal

Interventions
Current interventions as of 29/08/2017:
The trial has a 2x2 factorial design with four treatment arms as follows:
1. EPA-FFA 2g daily or equivalent dose of EPA-TG plus aspirin 300mg once daily
2. EPA-FFA 2g daily or equivalent dose of EPA-TG plus aspirin placebo once daily
3. EPA placebo 2g daily plus aspirin 300mg once daily
4. EPA placebo 2g daily plus aspirin placebo 300mg once daily

Previous interventions:
The trial has a 2x2 factorial design with four treatment arms as follows:
1. EPA as the free fatty acid 1 g twice daily plus aspirin EC 300 mg once daily
2. EPA as the free fatty acid 1 g twice daily plus aspirin placebo once daily
3. EPA placebo twice daily plus aspirin EC 300 mg once daily
4. EPA placebo twice daily plus aspirin placebo once daily

Added 31/08/2017:
To keep power at 80% for the above figures, a simulation using Stata v10 and employing the proposed analysis method indicated that 192 individuals were required per arm (total 768 evaluable ‘high risk’ individuals). In the Trial protocol versions 1-3, a 15% drop-out rate was assumed . However, feedback from BCSP centres and experience from the first few months of the Trial suggested that the drop-out rate of ‘high risk’ BCSP patients would be lower than 15%. Allowance for a 10% drop-out rate increased the sample size to 768/0.9 = 853 individuals.

In October 2014, the trial secured an extension from the EME Programme, for a further 3 years until 31/10/2017. This allowed recruitment to continue to 12/06/2016 at the latest (limited by the shelf-life of EPA-TG approved by the MHRA). Projections based on past trial recruitment predicted that a maximum number of 755 participants might be randomised.

Intervention Type
Supplement

Primary outcome measure
Current primary outcome measure as of 10/05/2022:
seAFOod Trial:
1. The number of patients with one or more adenomas measured using BCSP surveillance colonoscopy at 12 months

STOP-ADENOMA sub-study:
1. Colorectal polyp number and the number of individuals with one or more polyps during a maximum of six years follow-up after involvement in the seAFOod trial
2. Red blood cell and rectal mucosal fatty acid levels at 6 and 12 months after the start of the intervention
3. Plasma and rectal mucosal oxylipin levels at 6 and 12 months after the start of the intervention
4. Urinary biomarkers of eicosanoid synthesis (PGE-M, 11-dehydro-TXB2) at 6 and 12 months after the start of the intervention.

Previous primary outcome measure:
The number of patients with one or more adenomas; Timepoint(s): BCSP surveillance colonoscopy at 12 months

Secondary outcome measures
Current secondary outcome measures as of 10/05/2022:
seAFOod Trial:
1. Number of adenomas per participant at the first BCSP surveillance colonoscopy (mean adenoma number per participant [MAP])
2. Detection of one or more ‘advanced’ (≥10 mm diameter, high-grade dysplasia or tubulo-villous /villous histology) adenomas at the first BCSP surveillance colonoscopy (advanced ADR [AADR])
3. Number of ‘advanced’ adenomas per participant at the first BCSP surveillance colonoscopy (advanced MAP).
4. Detection of one or more serrated adenomas at the first BCSP surveillance colonoscopy
5. Number of serrated adenomas per participant at the first BCSP surveillance colonoscopy (serrated MAP).
6. The region of the colorectum (right colon - any part of the colon proximal to the splenic flexure; left colon – the rectum and the colon distal to the splenic flexure) that adenomas(total, advanced, serrated) are detected at the first BCSP surveillance colonoscopy
7. Reclassification from ‘high risk’ to ‘intermediate risk’ after the first BCSP surveillance colonoscopy (BCSP risk stratification at the first surveillance colonoscopy states that any individual that does not continue to fulfil ‘high risk’ criteria is classified as ‘intermediate risk’ for further colonoscopic surveillance at three years)
8. Detection of colorectal cancer (CRC) prior to, or at, the first BCSP surveillance colonoscopy
9. Red blood cell (RBC) EPA and rectal EPA levels at baseline, 6 months (RBC only) and 12 months from randomisation
10. Absolute red blood cells (RBC) fatty acid (DHA, AA, EPA/AA ratio) levels and difference from

baseline at 6 months and 12 months
11. Dietary fish and other seafood intake at baseline and at the end of the study
12. Rectal mucosal fatty acid (DHA, AA, EPA/AA ratio) levels at surveillance colonoscopy
13. Adverse events, including clinically significant bleeding episodes (haemorrhagic stroke or GI bleeding requiring hospital admission or investigation)

STOP-ADENOMA sub-study:
1. Genetic polymorphisms in genes relevant to lipid mediator synthesis (eg. COX-2) and fatty acid synthesis (eg FADS) related to seAFOod trial colorectal polyp outcomes, fatty acid levels and urinary eicosanoid biomarkers
2. Rectal mucosal expression of COX-2 and 15-PGDH (by RT-PCR) related to seAFOod trial colorectal polyp outcomes and urinary eicosanoid biomarkers

Previous secondary outcome measures as of 29/08/2017:
1. Number of adenomas per participant at the first BCSP surveillance colonoscopy (mean adenoma number per participant [MAP])
2. Detection of one or more 'advanced' (≥10 mm diameter, high-grade dysplasia or tubulo-villous /villous histology) adenomas at the first BCSP surveillance colonoscopy (advanced ADR [AADR])
3. Number of 'advanced' adenomas per participant at the first BCSP surveillance colonoscopy (advanced MAP).
4. Detection of one or more serrated adenomas at the first BCSP surveillance colonoscopy
5. Number of serrated adenomas per participant at the first BCSP surveillance colonoscopy (serrated MAP).
6. The region of the colorectum (right colon - any part of the colon proximal to the splenic flexure; left colon – the rectum and the colon distal to the splenic flexure) that adenomas(total, advanced, serrated) are detected at the first BCSP surveillance colonoscopy
7. Reclassification from 'high risk' to 'intermediate risk' after the first BCSP surveillance colonoscopy (BCSP risk stratification at the first surveillance colonoscopy states that any individual that does not continue to fulfil 'high risk' criteria is classified as 'intermediate risk' for further colonoscopic surveillance at three years)
8. Detection of colorectal cancer (CRC) prior to, or at, the first BCSP surveillance colonoscopy
9. Red blood cell (RBC) EPA and rectal EPA levels at baseline, 6 months (RBC only) and 12 months from randomisation
10. Absolute red blood cells (RBC) fatty acid (DHA, AA, EPA/AA ratio) levels and difference from baseline at 6 months and 12 months
11. Dietary fish and other seafood intake at baseline and at the end of the study
12. Rectal mucosal fatty acid (DHA, AA, EPA/AA ratio) levels at surveillance colonoscopy
13. Adverse events, including clinically significant bleeding episodes (haemorrhagic stroke or GI bleeding requiring hospital admission or investigation)

Previous secondary outcome measures:
1. Adverse events, including clinically significant bleeding episodes; Timepoint(s): BCSP surveillance colonoscopy at 12 months
2. The number of 'advanced' adenomas per patient; Timepoint(s): BCSP surveillance colonoscopy at 12 months
3. The number of 'high risk' patients re-classified as 'intermediate risk'; Timepoint(s): BCSP surveillance colonoscopy at 12 months
4. The number of patients with one or more 'advanced' adenomas; Timepoint(s): BCSP surveillance colonoscopy at 12 months
5. The region of the colorectum that adenomas are detected; Timepoint(s): BCSP surveillance

colonoscopy at 12 months
6. The total number of adenomas per patient; Timepoint(s): BCSP surveillance colonoscopy at 12 months

Overall study start date
30/05/2011

Completion date
31/10/2017

Eligibility

Key inclusion criteria
Current inclusion criteria as of 04/07/2013:
Recruitment will be restricted to 55-73 year-old NHS Bowel Cancer Screening Programme (BCSP) patients who have been identified as 'high risk' (5 or more small adenomas or more than 3 adenomas with at least one being >10 mm in diameter) after their first screening colonoscopy by either Faecal Occult Blood test (FOBt) or Flexible Sigmoidoscopy (FS).
Target Gender: Male & Female; Upper Age Limit 73 years; Lower Age Limit 55 years.

Inclusion criteria from 29/05/2012 to 04/07/2013:
Recruitment will be restricted to 60-73 year-old NHS Bowel Cancer Screening Programme (BCSP) patients who have been identified as 'high risk' (5 or more small adenomas or more than 3 adenomas with at least one being >10 mm in diameter) after a single clearance screening colonoscopy.
Target Gender: Male & Female; Upper Age Limit 73 years; Lower Age Limit 60 years.

Original inclusion criteria:
Recruitment will be restricted to 60-75 year-old NHS Bowel Cancer Screening Programme (BCSP) patients who have been identified as 'high risk' (5 or more small adenomas or more than 3 adenomas with at least one being >10 mm in diameter) after a single clearance screening colonoscopy.
Target Gender: Male & Female; Upper Age Limit 75 years; Lower Age Limit 60 years.

Participant type(s)
Patient

Age group
Adult

Lower age limit
55 Years

Upper age limit
73 Years

Sex
Both

Target number of participants

Planned Sample Size: 755; UK Sample Size: 755

Total final enrolment
709

Key exclusion criteria
Current exclusion criteria as of 29/08/2017:
1. Current exclusion criteria as of 01/10/2012:
2. Requirement for more than one repeat colonoscopy or flexible sigmoidoscopy within the BCSP 3 month screening window
3. Malignant change in an adenoma requiring Colorectal Cancer Multi-disciplinary Team management
4. Regular (>3 doses per week) prescribed or over-the-counter (OTC) aspirin or regular (>3 doses per week) prescribed or OTC non-aspirin non-steroidal anti-inflammatory drug (NSAID) use
5. Aspirin intolerance or hypersensitivity, including aspirin-sensitive asthma
6. Active peptic ulcer disease within 3 months or previous peptic ulcer (not on proton pump inhibitor prophylaxis)
7. Fish or seafood allergy
8. Current or planned regular (>3 doses per week) use of fish oil supplements
9. Known clinical diagnosis or gene carrier of a hereditary colorectal cancer (CRC) predisposition (familial adenomatous polyposis (FAP), hereditary nonpolyposis colorectal cancer (HNPCC))
10. Previous or newly diagnosed inflammatory bowel disease
11. Previous or planned colorectal resection
12. Known bleeding diathesis or concomitant warfarin therapy or severe liver impairment
13. Severe liver impairment
14. Severe renal failure (creatinine clearance < 10 ml/min)
15. Current methotrexate use at a weekly dose of 15 mg or more
16. Inability to comply with study procedures and agents
17. Serious medical illness interfering with study participation
18. Failure to give written informed consent

Previous exclusion criteria from 01/10/2012 to 29/08/2017:
1. Requirement for more than one repeat colonoscopy or flexible sigmoidoscopy within the BCSP 3 month screening window
2. Malignant change in an adenoma requiring Colorectal Cancer Multi-disciplinary Team management
3. Regular (>3 doses per week) prescribed or over-the-counter (OTC) aspirin or regular (>3 doses per week) prescribed or OTC non-aspirin non-steroidal anti-inflammatory drug (NSAID) use
4. Aspirin intolerance or hypersensitivity, including aspirin-sensitive asthma
5. Active peptic ulcer disease within 3 months or previous peptic ulcer (not on proton pump inhibitor prophylaxis)
6. Fish or seafood allergy
7. Current or planned regular (>3 doses per week) use of fish oil supplements
8. Known clinical diagnosis or gene carrier of a hereditary colorectal cancer (CRC) predisposition (familial adenomatous polyposis (FAP), hereditary nonpolyposis colorectal cancer (HNPCC))
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10. Previous or planned colorectal resection
11. Known bleeding diathesis or concomitant warfarin therapy or severe liver impairment
12. Severe renal failure (creatinine clearance < 10 ml/min)
13. Current methotrexate use at a weekly dose of 15 mg or more
14. Inability to comply with study procedures and agents

15. Serious medical illness interfering with study participation
16. Failure to give written informed consent

Previous exclusion criteria from 29/05/2012 to 01/10/2012:
1. Need for repeat colonoscopy or flexible sigmoidoscopy to check for adenoma excision within a 3 month window

Previous exclusion criteria
1. Need for repeat colonoscopy or flexible sigmoidoscopy to check for adenoma excision within a 3 month window
2. Malignant change in an adenoma requiring Colorectal Cancer Multi-disciplinary Team management
3. Regular (>3 doses per week) prescribed aspirin or regular (>3 doses per week) prescribed nonaspirin nonsteroidal antiinflammatory drug (NSAID) use
4. Aspirin intolerance or hypersensitivity, including aspirin-sensitive asthma
5. Active peptic ulcer disease within 3 months or previous peptic ulcer (not on proton pump inhibitor prophylaxis)
6. Fish or seafood allergy
7. Current or planned regular (>3 doses per week) use of fish oil supplements
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11. Known bleeding diathesis or concomitant warfarin therapy or severe liver impairment
12. Severe renal failure (creatinine clearance < 10 ml/min)
13. Current methotrexate use at a weekly dose of 15 mg or more
14. Inability to comply with study procedures and agents
15. Serious medical illness interfering with study participation
16. Failure to give written informed consent

Date of first enrolment
11/11/2011

Date of final enrolment
12/06/2016

Locations

Countries of recruitment
United Kingdom

Study participating centre
Participating centres across England, go to http://www.nottingham.ac.uk/mczseafood/centres.html for a list of sites
United Kingdom
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Sponsor information

Organisation
University of Leeds (UK)

Sponsor details
Faculty of Medicine and Health
Joint Leeds Sponsor Office
Research & Innovation
34 Hyde Terrace
Leeds
England
United Kingdom
LS2 9LN

Sponsor type
University/education

ROR
https://ror.org/024mrxd33

Funder(s)

Funder type
Government

Funder Name
Efficacy and Mechanism Evaluation Programme

Alternative Name(s)
NIHR Efficacy and Mechanism Evaluation Programme, EME

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Publication and dissemination plan
The trialists are currently working on a dissemination plan and will share this when it is finalised.

Intention to publish date
31/10/2018

Individual participant data (IPD) sharing plan
The data sharing plans for the current study are unknown and will be made available at a later date.

IPD sharing plan summary
Data sharing statement to be made available at a later date

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol article	protocol	29/07/2013		Yes	No
Results article	results	15/12/2018		Yes	No
Funder report results		01/07/2019	10/05/2022	No	No
Protocol file	Sub-study protocol version 2.0	21/04/2021	10/05/2022	No	No
HRA research summary			28/06/2023	No	No
Results article	Results relating to colorectal polyp risk after short-term aspirin use	30/07/2023	31/07/2023	Yes	No
Results article	A secondary analysis of the seAFOod polyp prevention trial	13/06/2024	17/06/2024	Yes	No
Results article	The relationship between dietary and supplemental n-3 HUFA intake, blood and tissue n-3 HUFA levels, and colorectal polyp recurrence: A secondary analysis of the seAFOod polyp prevention trial	13/12/2024	17/12/2024	Yes	No