Eicosapentaenoic acid and/or aspirin for preventing colorectal adenomas during colonoscopic surveillance in the NHS Bowel Cancer Screening Programme: the seAFOod RCT

Mark A Hull,¹* Kirsty Sprange,² Trish Hepburn,² Wei Tan,² Aisha Shafayat,² Colin J Rees,³ Gayle Clifford,⁴ Richard F Logan,⁵ Paul M Loadman,⁶ Elizabeth A Williams,⁷ Diane Whitham² and Alan A Montgomery² on behalf of the seAFOod Collaborative Group

¹Leeds Institute of Medical Research, University of Leeds, St James’s University Hospital, Leeds, UK
²Nottingham Clinical Trials Unit, Queen’s Medical Centre, School of Medicine, University of Nottingham, Nottingham, UK
³Northern Institute for Cancer Research, Newcastle University, Newcastle upon Tyne, UK
⁴South Tyneside District Hospital, South Tyneside NHS Foundation Trust, South Shields, UK
⁵Nottingham Digestive Diseases Centre, Queen’s Medical Centre, University of Nottingham, Nottingham, UK
⁶School of Pharmacy and Medical Sciences, Institute of Cancer Therapeutics, University of Bradford, Bradford, UK
⁷Department of Oncology & Metabolism, Human Nutrition Unit, The Medical School, University of Sheffield, Sheffield, UK

*Corresponding author M.A.Hull@leeds.ac.uk

Declared competing interests of authors: Mark A Hull has received an unrestricted scientific grant for another project and also conference travel funding from SLA Pharma AG (Liestal, Switzerland). He has provided paid consultancy for Bayer AG (Leverkusen, Germany) and Thetis Pharmaceuticals LLC (Branford, CT, USA), and his institution received fees for his consultancy work for Thetis Pharma, which owns the rights to omega-3 fatty acid derivative molecules. Furthermore, he was a National Institute for Health Research (NIHR) Efficacy and Mechanism Evaluation Board member (2014–18). Colin J Rees has had research funded by Arc Medical Inc. (Tucker, GA, USA), Norgine (Amsterdam, the Netherlands) and Olympus Corporation (Tokyo, Japan), and has received paid honoraria and travel grants from Norgine, Boston Scientific (Marlborough, MA, USA) and Olympus. He has been a paid expert witness for Arc Medical. None of these bear any relation to the Systematic Evaluation of Aspirin and Fish Oil (seAFOod) trial. Alan A Montgomery is a member of the NIHR Health Technology Assessment Clinical Evaluation and Trials Board. Trish Hepburn has ownership of shares in AstraZeneca plc (Cambridge, UK).
Plain English summary

The seAFOod RCT
Efficacy and Mechanism Evaluation 2019; Vol. 6: No. 4
DOI: 10.3310/eme06040

NIHR Journals Library www.journalslibrary.nihr.ac.uk
Plain English summary

Bowel cancer kills > 15,000 people every year in England and Wales. Most bowel cancers develop from a polyp, also known as an adenoma, which is a fleshy growth on the bowel wall. Polyps are found and removed at colonoscopy, which is a large-bowel camera test, but colonoscopy does not prevent further polyps. Use of drugs or dietary supplements (called chemoprevention) may be able to reduce polyp growth and the possibility of developing bowel cancer.

The Systematic Evaluation of Aspirin and Fish Oil (seAFOod) trial tested the effects of naturally occurring omega-3 eicosapentaenoic acid (EPA) (a dose roughly equivalent to two oily fish portions every day) and aspirin on bowel polyp growth. Patients took EPA on its own, aspirin on its own, EPA and aspirin together or placebo (dummy) medication.

The trial recruited 709 participants who had three or more adenomas found and removed at a NHS Bowel Cancer Screening Programme colonoscopy and needed a check-up colonoscopy 1 year later. Allocation to one of the four treatment options before the check-up was by chance and ‘blinded’, so that all participants and trial staff did not know what treatment was taken.

The results showed that there was no reduction in the number of patients who had at least one adenoma at check-up (≈60%) in either EPA or aspirin users. However, EPA and aspirin were found to reduce the number of certain types of adenoma in different parts of the bowel by 10–20%. Both EPA treatment and aspirin treatment were safe for patients, with no increased bleeding risk, but EPA caused 10% more symptoms of mild stomach upset, including diarrhoea.

It is concluded that both EPA and aspirin have chemoprevention benefits, which are limited to certain bowel polyp types. The results also suggest that aspirin (possibly with EPA) could be used to help prevent bowel cancers that occur despite colonoscopy.
Criteria for inclusion in the Efficacy and Mechanism Evaluation journal
Reports are published in Efficacy and Mechanism Evaluation (EME) if (1) they have resulted from work for the EME programme, and (2) they are of a sufficiently high scientific quality as assessed by the reviewers and editors.

EME programme
The Efficacy and Mechanism Evaluation (EME) programme was set up in 2008 as part of the National Institute for Health Research (NIHR) and the Medical Research Council (MRC) coordinated strategy for clinical trials. The EME programme is broadly aimed at supporting ‘science driven’ studies with an expectation of substantial health gain and aims to support excellent clinical science with an ultimate view to improving health or patient care.

Its remit includes evaluations of new treatments, including therapeutics (small molecule and biologic), psychological interventions, public health, diagnostics and medical devices. Treatments or interventions intended to prevent disease are also included.

The EME programme supports laboratory based or similar studies that are embedded within the main study if relevant to the remit of the EME programme. Studies that use validated surrogate markers as indicators of health outcome are also considered.

For more information about the EME programme please visit the website: http://www.nets.nihr.ac.uk/programmes/eme

This report
The research reported in this issue of the journal was funded by the EME programme as project number 09/100/25. The contractual start date was in November 2010. The final report began editorial review in April 2018 and was accepted for publication in October 2018. The authors have been wholly responsible for all data collection, analysis and interpretation, and for writing up their work. The EME editors and production house have tried to ensure the accuracy of the authors’ report and would like to thank the reviewers for their constructive comments on the final report document. However, they do not accept liability for damages or losses arising from material published in this report.

This report presents independent research. The views and opinions expressed by authors in this publication are those of the authors and do not necessarily reflect those of the NHS, the NIHR, the MRC, NETSCC, the EME programme or the Department of Health and Social Care. If there are verbatim quotations included in this publication the views and opinions expressed by the interviewees are those of the interviewees and do not necessarily reflect those of the authors, those of the NHS, the NIHR, NETSCC, the EME programme or the Department of Health and Social Care.

© Queen’s Printer and Controller of HMSO 2019. This work was produced by Hull et al. under the terms of a commissioning contract issued by the Secretary of State for Health and Social Care. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

Published by the NIHR Journals Library (www.journalslibrary.nihr.ac.uk), produced by Prepress Projects Ltd, Perth, Scotland (www.prepress-projects.co.uk).
NIHR Journals Library Editor-in-Chief

Professor Ken Stein  Professor of Public Health, University of Exeter Medical School, UK

NIHR Journals Library Editors

Professor John Powell  Chair of HTA and EME Editorial Board and Editor-in-Chief of HTA and EME journals. Consultant Clinical Adviser, National Institute for Health and Care Excellence (NICE), UK, and Honorary Professor, University of Manchester, and Senior Clinical Researcher and Associate Professor, Nuffield Department of Primary Care Health Sciences, University of Oxford, UK

Professor Andrée Le May  Chair of NIHR Journals Library Editorial Group (HS&DR, PGfAR, PHR journals) and Editor-in-Chief of HS&DR, PGfAR, PHR journals

Professor Matthias Beck  Professor of Management, Cork University Business School, Department of Management and Marketing, University College Cork, Ireland

Dr Tessa Crilly  Director, Crystal Blue Consulting Ltd, UK

Dr Eugenia Cronin  Senior Scientific Advisor, Wessex Institute, UK

Dr Peter Davidson  Consultant Advisor, Wessex Institute, University of Southampton, UK

Ms Tara Lamont  Director, NIHR Dissemination Centre, UK

Dr Catriona McDaid  Senior Research Fellow, York Trials Unit, Department of Health Sciences, University of York, UK

Professor William McGuire  Professor of Child Health, Hull York Medical School, University of York, UK

Professor Geoffrey Meads  Professor of Wellbeing Research, University of Winchester, UK

Professor John Norrie  Chair in Medical Statistics, University of Edinburgh, UK

Professor James Raftery  Professor of Health Technology Assessment, Wessex Institute, Faculty of Medicine, University of Southampton, UK

Dr Rob Riemsma  Reviews Manager, Kleijnen Systematic Reviews Ltd, UK

Professor Helen Roberts  Professor of Child Health Research, UCL Great Ormond Street Institute of Child Health, UK

Professor Jonathan Ross  Professor of Sexual Health and HIV, University Hospital Birmingham, UK

Professor Helen Snooks  Professor of Health Services Research, Institute of Life Science, College of Medicine, Swansea University, UK

Professor Ken Stein  Professor of Public Health, University of Exeter Medical School, UK

Professor Jim Thornton  Professor of Obstetrics and Gynaecology, Faculty of Medicine and Health Sciences, University of Nottingham, UK

Professor Martin Underwood  Warwick Clinical Trials Unit, Warwick Medical School, University of Warwick, UK

Please visit the website for a list of editors: www.journalslibrary.nihr.ac.uk/about/editors

Editorial contact: journals.library@nihr.ac.uk