Improving outcomes for women aged 70 years or above with early breast cancer: research programme including a cluster RCT

Lynda Wyld,^{1,2*} Malcolm WR Reed,³ Karen Collins,⁴ Sue Ward,⁵ Geoff Holmes,⁵ Jenna Morgan, 1,2 Mike Bradburn, 6 Stephen Walters, 6 Maria Burton,⁴ Kate Lifford,⁷ Adrian Edwards,⁷ Kate Brain, Alistair Ring, Esther Herbert, 6 Thompson G Robinson,⁹ Charlene Martin,^{1,2} Tim Chater,⁶ Kirsty Pemberton,⁶ Anne Shrestha,^{1,2} Anthony Nettleship, 10 Paul Richards, 5 Alan Brennan, 5 Kwok Leung Cheung, 11 Annaliza Todd, 1,2 Helena Harder,³ Riccardo Audisio,¹² Nicolo Matteo Luca Battisti,⁸ Juliet Wright,³ Richard Simcock,³ Christopher Murray,¹⁰ Alastair M Thompson, 13 Margot Gosney, 14 Matthew Hatton, 15 Fiona Armitage, 15 Julietta Patnick,¹⁶ Tracy Green,¹⁷ Deirdre Revill,¹⁷ Jacqui Gath, 17 Kieran Horgan, 18 Chris Holcombe, 19 Matt Winter, 15 Jay Naik 20 and Rishi Parmeshwar 21

¹Department of Oncology and Metabolism, University of Sheffield Medical School, Sheffield, UK

²Jasmine Breast Centre, Doncaster and Bassetlaw Teaching Hospitals NHS Foundation Trust, Doncaster, UK

³Brighton and Sussex Medical School, Brighton, UK

⁴Faculty of Health and Wellbeing, Department of Allied Health Professions, Collegiate Cresent Campus, Sheffield Hallam University, Sheffield, UK

⁵Department of Health and Social Care Economics and Decision Science, School for Health and Related Research, University of Sheffield, Sheffield, UK

⁶Clinical Trials Research Unit, School for Health and Related Research, University of Sheffield, Sheffield, UK

⁷Division of Population Medicine, School of Medicine, Cardiff University, Cardiff, UK

⁸Breast Unit, Royal Marsden Hospital, London, UK

- ⁹Department of Cardiovascular Sciences, University of Leicester, Cardiovascular Research Centre, Glenfield General Hospital, Leicester, UK
- ¹⁰EpiGenesys, University of Sheffield, Sheffield, UK
- ¹¹Breast Unit, Royal Derby Hospital, Derby, UK
- ¹²Sahlgrenska Universitetssjukhuset, University of Gothenburg, Göteborg, Sweden
- ¹³Department of Surgery, Baylor College of Medicine, Houston, TX, USA
- ¹⁴School of Psychology and Clinical Language Sciences, University of Reading, Reading, UK
- ¹⁵Breast Unit, Weston Park Hospital, Sheffield, UK
- ¹⁶Cancer Epidemiology Unit, Nuffield Department of Population Health, University of Oxford, Oxford, UK
- ¹⁷Yorkshire and Humber Research Network Consumer Research Panel, Sheffield, UK
- ¹⁸Breast Unit, Leeds General Infirmary, Leeds, UK
- ¹⁹Royal Liverpool and Broadgreen University Hospitals NHS Trust, Liverpool, UK
- ²⁰Breast Unit, Pinderfields Hospital, Mid Yorkshire Hospitals NHS Trust, Wakefield, UK
- ²¹Breast Unit, Royal Lancaster Infirmary, University Hospitals of Morecambe Bay NHS Foundation Trust, Lancaster, UK

Disclosure of interests

Full disclosure of interests: Completed ICMJE forms for all authors, including all related interests, are available in the toolkit on the NIHR Journals Library report publication page at https://doi.org/10.3310/XZOE2552.

Primary conflicts of interest: Lynda Wyld reports membership of the National Institute for Health and Care Research (NIHR) Surgery Themed Call Board (3 October 2012-13 March 2013). Jenna Morgan reports being a NIHR Clinical Lecturer funded by NIHR. Stephen Walters reports membership of the Health Technology Assessment (HTA) Funding Committee Policy Group (28 May 2012-30 November 2017) and HTA Clinical Evaluation and Trials Committee (18 August 2010–30 November 2017). His main employer (School for Health and Related Research, University of Sheffield) has contracts and/or research grants with the Department of Health, NIHR, Medical Research Council (MRC) and the National Institute for Health and Care Excellence (NICE). He is a co-applicant or co-investigator on several NIHR portfolio grants [HTA, Public Health Research (PHR) and Efficacy and Mechanism Evaluation (EME) programmes, and Research for Patient Benefit (RfPB)] and grants from the MRC. He is a NIHR Senior Investigator and funded by the NIHR. He reports grants from other research grants, personal fees from book royalties and grants from the NIHR Senior Investigator Award outside the submitted work. Alistair Ring reports personal fees from F. Hoffman-La Roche Ltd (Basel, Switzerland), Novartis Pharmaceuticals UK Ltd (London, UK), Pfizer Inc. (New York, NY, USA), Eli Lilly and Company (Indianapolis, IN, USA) and Merck & Co. Inc. (Kenilworth, NJ, USA) outside the submitted work. Esther Herbert reports grants from NIHR during the conduct of the study (the Age Gap study). Thompson G Robinson is a NIHR Senior Investigator. Nicolo Matteo Luca Battisti reports grants from Genomic Health, Inc. (Redwood City, CA, USA), and grants and personal fees from Pfizer Inc. outside the submitted work. Margot Gosney reports membership of the HTA Prioritisation Committee A (1 November 2013–28 February 2019) and the HTA Elective and Emergency Specialist Care (EESC) Panel (1 November 2013-31 May 2018). Matt Winter reports personal fees and non-financial support from Easai Co., Ltd (Tokyo, Japan), personal fees from Pfizer Inc., personal fees and non-financial support from Eli Lilly and Company, personal fees from Genomic Health, Inc./ Exact Sciences Corporation (Madison, WI, USA), personal fees from Novartis Pharmaceuticals UK Ltd and personal fees and non-financial support from F. Hoffman-La Roche Ltd outside the submitted work.

^{*}Corresponding author L.wyld@sheffield.ac.uk

Published June 2022 DOI: 10.3310/XZOE2552

Plain English summary

Bridging the Age Gap in Breast Cancer research programme Programme Grants for Applied Research 2022; Vol. 10: No. 6

DOI: 10.3310/XZOE2552

NIHR Journals Library www.journalslibrary.nihr.ac.uk

Plain English summary

Older women make up 34% of all UK breast cancer cases. Many older women are not treated in the standard way, with lower rates of surgery and chemotherapy than younger women. Cancer outcomes are worse for older women than for younger women, partly because some treatments are not given to older women (e.g. chemotherapy, surgery or radiotherapy may not be given in some less fit older women). Full treatment is not essential for all older women, as some are unfit or have a reduced lifespan and will derive less benefit from treatment, which needs to be tailored to their needs. Treatment tailoring in older patients is not easy owing to the complex interplay of age, ill health, and frailty resulting from the cancer.

The Age Gap study recruited a large group of UK older women, aged \geq 70 years, with early-stage breast cancer, collecting data about health and fitness at the time of diagnosis, alongside detailed data about the cancer and the treatment received. Analysis by age and health subgroups was used to suggest thresholds at which patients may be offered full or fitness-adjusted treatment. The project also developed decision support tools to assist in decision-making, including a brief question and answer sheet, a series of booklets and an online tool. These tools were tested in a clinical trial in which half of participating breast units were asked to use the tool when counselling older women about their choices and the other half were asked to use normal counselling practices only. The trial evaluated whether or not this altered the treatment women chose, and whether or not it affected survival rates and quality-of-life outcomes.

The study recruited 3416 women aged \geq 70 years and found that older women generally cope well with treatment, but unfit older patients do not benefit much from surgery or chemotherapy, which may have an adverse impact on their quality of life in the short term. The decision tools received good feedback from patients and doctors and the online tools were accurate in predicting outcomes. The tools were compared with standard care in a clinical trial, and they improved the knowledge levels of women and altered treatment choice, with more women choosing less full treatment options in line with the fact that older women value quality of life and maintaining their independence very highly. Despite this decrease in rates of standard treatment, survival outcomes were similar after 3 years' follow-up, although longer follow-up will be needed.

Programme Grants for Applied Research

ISSN 2050-4322 (Print)

ISSN 2050-4330 (Online)

Programme Grants for Applied Research (PGfAR) was launched in 2013 and is indexed by Europe PMC, NCBI Bookshelf, DOAJ, Ulrichsweb and SCOPUS.

This journal is a member of and subscribes to the principles of the Committee on Publication Ethics (COPE) (www.publicationethics.org/).

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

The full PGfAR archive is freely available to view online at www.journalslibrary.nihr.ac.uk/pgfar. Print-on-demand copies can be purchased from the report pages of the NIHR Journals Library website: www.journalslibrary.nihr.ac.uk

Criteria for inclusion in the Programme Grants for Applied Research journal

Reports are published in *Programme Grants for Applied Research* (PGfAR) if (1) they have resulted from work for the PGfAR programme, and (2) they are of a sufficiently high scientific quality as assessed by the reviewers and editors.

Programme Grants for Applied Research programme

The Programme Grants for Applied Research (PGfAR) programme, part of the National Institute for Health and Care Research (NIHR), was established in 2006 to fund collaborative, multidisciplinary programmes of applied research to solve health and social care challenges. Findings are expected to provide evidence that lead to clear and identifiable patient benefits, in the relatively near future.

PGfAR is researcher led and does not specify topics for research; however, the research must be in an area of priority or need for the NHS and the social care sector of the Department of Health and Social Care, with particular emphasis on health and social care areas that cause significant burden, where other research funders may not be focused, or where insufficient funding is available

The programme is managed by the NIHR Central Commissioning Facility (CCF) with strategic input from the Programme Director. For more information about the PGfAR programme please visit the website: https://www.nihr.ac.uk/explore-nihr/funding-programmes/programme-grants-for-applied-research.htm

This report

The research reported in this issue of the journal was funded by PGfAR as project number RP-PG-1209-10071. The contractual start date was in July 2012. The final report began editorial review in February 2021 and was accepted for publication in February 2022. As the funder, the PGfAR programme agreed the research questions and study designs in advance with the investigators. The authors have been wholly responsible for all data collection, analysis and interpretation, and for writing up their work. The PGfAR 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 funded by the National Institute for Health and Care Research (NIHR). 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, CCF, PGfAR 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, the PGfAR programme or the Department of Health and Social Care.

Copyright © 2022 Wyld et al. This work was produced by Wyld et al. under the terms of a commissioning contract issued by the Secretary of State for Health and Social Care. This is an Open Access publication distributed under the terms of the Creative Commons Attribution CC BY 4.0 licence, which permits unrestricted use, distribution, reproduction and adaption in any medium and for any purpose provided that it is properly attributed. See: https://creativecommons.org/licenses/by/4.0/. For attribution the title, original author(s), the publication source – NIHR Journals Library, and the DOI of the publication must be cited.

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 Consultant Clinical Adviser, National Institute for Health and Care Excellence (NICE), UK, and Professor of Digital Health Care, Nuffield Department of Primary Care Health Sciences, University of Oxford, UK

Professor Andrée Le May Chair of NIHR Journals Library Editorial Group (HSDR, PGfAR, PHR journals) and Editor-in-Chief of HSDR, 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 Consultant in Public Health, Delta Public Health Consulting Ltd, UK

Dr Peter Davidson Interim Chair of HTA and EME Editorial Board. Consultant Advisor, School of Healthcare Enterprise and Innovation, University of Southampton, UK

Ms Tara Lamont Senior Adviser, School of Healthcare Enterprise and Innovation, University of Southampton, UK

Dr Catriona McDaid Reader in Trials, 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 Emeritus Professor of Wellbeing Research, University of Winchester, UK

Professor James Raftery Professor of Health Technology Assessment, School of Healthcare Enterprise and Innovation, University of Southampton, UK

Dr Rob Riemsma Consultant Advisor, School of Healthcare Enterprise and Innovation, University of Southampton, UK

Professor Helen Roberts Professor of Child Health Research, Child and Adolescent Mental Health, Palliative Care and Paediatrics Unit, Population Policy and Practice Programme, UCL Great Ormond Street Institute of Child Health, London, 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

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

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