Insights from UKCTOCS for design, conduct and analyses of large randomised controlled trials

Usha Menon,[1*] Aleksandra Gentry-Maharaj,[1,2] Matthew Burnell,[1] Sophia Apostolidou,[1] Andy Ryan,[1] Jatinderpal K Kalsi,[3] Naveena Singh,[4] Lesley Fallowfield,[5] Alistair J McGuire,[6] Stuart Campbell,[7] Steven J Skates,[8] Anne Dawnay,[9] Mahesh Parmar[1] and Ian J Jacobs[2] on behalf of the UKCTOCS team

[1]MRC Clinical Trials Unit, Institute of Clinical Trials and Methodology, University College London, London, UK
[2]Department of Women's Cancer, Elizabeth Garrett Anderson Institute for Women's Health, University College London, London, UK
[3]Institute of Epidemiology and Health Care, University College London, London, UK
[4]Department of Cellular Pathology, Barts Health NHS Trust, London, UK
[5]Sussex Health Outcomes Research and Education in Cancer (SHORE-C), Brighton and Sussex Medical School, University of Sussex, Brighton, UK
[6]London School of Economics and Political Science, London, UK
[7]Create Health, London, UK
[8]Massachusetts General Hospital and Harvard Medical School, Boston, USA
[9]Department of Clinical Biochemistry, Barts Health NHS Trust, London, UK

[*]Corresponding author u.menon@ucl.ac.uk

Disclosure of interests of authors

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/CLDC7214.

Primary conflicts of interest: Usha Menon had stock ownership awarded by University College London (UCL) until October 2021 in Abcodia, which holds the licence for ROCA. She has received grants from the Medical Research Council (MRC), Cancer Research UK, the National Institute for Health and Care Research (NIHR), and The Eve Appeal. She holds patent number EP10178345.4 for Breast Cancer Diagnostics. She received an honorarium for a lecture from NY Obstetrical Society (USA), and was reimbursed for travel by NY Obstetrical Society, National Cancer Policy Forum, USA and Robinson College, Cambridge. She has been a member of International Alliance for Cancer Early Detection (ACED); Tina's Wish Scientific Advisory Board (USA); Data Monitoring Committee: Mixed COVID Vaccines study, India; Research Advisory Panel, Yorkshire Cancer Research; GCP Professional Certification Scheme Steering committee, CDSA, India; Clinical and Public Health Fellowship Selection Committee, Wellcome Trust DBT India Alliance; Prevention Expert Review Panel, Population Research Committee, CRUK; Early Career Fellowship Selection Committee, Wellcome Trust DBT India Alliance; and Chair of Data Monitoring Committee for GEM3. Usha Menon reports funding from UCL Hospital Biomedical Research

Centre, paid to UCL. Usha Menon, Aleksandra Gentry-Maharaj, Andy Ryan, Matthew Burnell and Sophia Apostolidou report funding from CRUK, The Eve Appeal, NIHR HTA, MRC and NIHR, all paid to UCL. Usha Menon, Aleksandra Gentry-Maharaj and Sophia Apostolidou report research collaboration contracts with Cambridge University, QIMR Berghofer Medical Research Institute, iLOF (intelligent Lab on Fiber), RNA Guardian, Micronoma, Mercy Bioanalytics, Synteny Biotechnology, Imperial College, London and Dana Farber Cancer Institute Inc., University of Innsbruck and National Health and Medical Research Council (NHMRC), Australia. Alexandra Gentry-Maharaj is a member of ACED Gynaecological Cancer Working Group and is ACED Co-Director Research Domain Trials. Sophia Apostolidou reports funding to UCL from Abodia. Mahesh Parmar was an Associate Member of the EME funding committee while the project was active. Mahesh Parmar has received grants and Aleksandra Gentry-Maharaj, Matthew Burnell and Andy Ryan have been funded by grants from MRC, Cancer Research UK, NIHR, and The Eve Appeal. Steven J Skates co-developed ROCA in 1995. It was patented by Massachusetts General Hospital and Queen Mary University of London and is owned by these universities. The patent has expired. Massachusetts General Hospital and Queen Mary University of London granted a licence for the ROCA to Abcodia in 2014. He reports stock options from SISCAPA Assay Technologies. Steven J Skates reports grant support from National Cancer Institute (USA), NIHR (UK) and Mercy Bioanalytics. He participated in the Independent Data Monitoring Committee for GRAIL, served on the clinical advisory board for Guardant Health and Scientific Advisory Board for LUNGevity, and holds stock options for service on Scientific Advisory Board of SISCAPA Assay Technologies. He also has a collaboration agreement with Freenome. Ian J Jacobs reports grants from Eve Appeal Charity, MRC, Cancer Research UK, and NIHR during the conduct of the study. He co-invented the ROCA in 1995; it was patented by Massachusetts General Hospital and Queen Mary University of London and is owned by these universities. Massachusetts General Hospital and Queen Mary University of London granted a licence for the ROCA to Abcodia in 2014. Ian J Jacobs is non-executive director, shareholder, and consultant to Abcodia and has rights to royalties from sales of the ROCA. He founded (1985), was a trustee of (2012–4), and is now an Emeritus trustee (2015–present) of The Eve Appeal, one of the funding agencies for UKCTOCS. Lesley Fallowfield reports MRC funding for the psychosocial arm of the UKCTOCS study 2001–13, paid to University of Sussex. Naveena Singh received honoraria from Astra-Zeneca-MSD and GlaxoSmithKline for participation in advisory boards. Alistair McGuire was a member of NIHR HTA and EME Editorial Board (2012 to 2022). Ranjit Manchanda reports funding from The Eve Appeal, Rosetrees Charity, Barts Charity, Yorkshire Cancer Research, Ovacure, British Gynaecological Cancer society (BGCS), Astrazeneca and GlaxoSmithKline (GSK). All other authors declare no competing interests.

Published August 2023
DOI: 10.3310/CLDC7214

Plain language summary

Insights from UKCTOCS for design, conduct and analyses of large randomised controlled trials

Health Technology Assessment 2025; Vol. 29: No. 10
DOI: 10.3310/CLDC7214

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

Plain language summary

Randomised controlled trials help us decide whether new health-care approaches are better than those in current use. To successfully complete these on time and within budget, there is a constant need to review and revise the procedures used for delivering various aspects such as invitation, enrolment, follow-up of participants, delivery of the new test, data collection, and analysis. We report on the processes used in the United Kingdom Collaborative Trial of Ovarian Cancer Screening, one of the largest such trials. The United Kingdom Collaborative Trial of Ovarian Cancer Screening enrolled over 202,000 women (2001–5), delivered over 670,000 yearly screens (2001–11) and followed all participants until 2020. Key to our successful completion were the involvement of senior investigators in day-to-day running of the trial, a pre-emptive approach to issues, a willingness to innovate, and the use of technology. Our underlying ethos was that trial participants should always be at the centre of all our processes. We ensured that they were able to always contact either their local or the central team for clarifications and rescheduling of appointments. To facilitate this, we shared participant contact details (with consent) with both teams. We built a comprehensive electronic system to manage all aspects of the trial. This included online forms that the teams completed in real time (resulting in an almost paperless trial) and systems to check and manage trial processes and track blood samples. We automated key steps such as checking whether participants were eligible, assigning correct action based on results of screening tests, scheduling appointments and printing letters. As a result, all participants were treated as set out in the trial plan. Our engagement with participants ensured that they continued participating and we had a low rate of complaints. We faced issues with regard to our initial trial design and the way we planned to analyse the data. We feel that our solutions are highly relevant, especially as there is a renewed focus on trials for early detection of cancer.