

The AgeX Trial

Draft minutes of Trial Management Group (TMG)
26 July 2022 11.00 – 13.00
Via videoconference

Present

Professor Julietta Patnick (Chair) (JP)
Associate Professor Isobel Barnes (IB)
Mrs Claire Borrelli (CB)
Mrs Jacquie Jenkins (JJ)
Associate Professor Hongchao Pan (HP)
Professor Sir Richard Peto (RP)
Professor Sian Taylor-Phillips (invited guest) (STP)
Professor Malcolm Reed (MR)
Professor Gillian Reeves (GR)
Mr Keith Shaw (KS)
Dr Louise Wilkinson (LW)
Ms Krys Baker (minutes) (KB)

Apologies received

Professor Dame Valerie Beral (VB)
Professor David Hunter (DH)
Dr Suzanne Wright (SW)

1. Welcome and introductions

JP welcomed TMG members and investigators. It was noted that Dr Lucy Carpenter and Professor Mike Richards had resigned as members of the TMG.

2. Minutes of the last meeting (05/05/2021) and matters arising

The minutes of the last meeting were accepted as an accurate record.

3. Presentation of progress report

3.1 The AgeX should be thought of as two separate trials. One trial is of the effects of one extra breast screening invitation at ages 47-49 years. The other is of the effects of one extra breast screening invitation at ages 71-73 years. The primary analyses will be of breast cancer mortality and the subsidiary main analyses will be of breast cancer incidence and treatment.

3.2 AgeX began in 2009 and over about an 11-year period 65 NHS Breast Screening Centres in England randomized 20,000 clusters containing 4.5 million women. While randomisation ended in March 2020 (when the NHS Breast Screening Programme was paused due to COVID) electronic follow-up continues.

3.2 Follow-up involves linkage to several different national databases to determine cause-specific mortality; hospital admissions; breast cancer incidence; and information about the characteristics and treatment of any breast cancers. The relevant datasets all get provided to AgeX but arrive intermittently (typically about once a year).

3.4 The main analyses will be restricted to 3 million women (2 million younger, and 1 million older) who were of the right age and linkable to national electronic datasets; had not already had any breast disease or cancer or breast surgery; and were likely to attend for breast screening if invited, as they had attended their previous cervical or breast cancer screening invitation. All these criteria are based unbiasedly on information recorded before randomisation.

3.5 AgeX is large because only small effects on breast cancer mortality can plausibly be expected from just one extra invitation with $\sim 3/4$ compliance. The estimates of the Independent Panel suggest reductions in breast cancer mortality of about 0.2/1000 younger women and 0.6/1000 older women. As even these small effects may take many years to materialise, AgeX will need prolonged follow-up.

4. DMEC report to TMG June 2022

The DMEC report was presented to the TMG congratulating the trial team on the continued successful progress of the trial. In particular, the continued high quality and timely data linkages were noted. There were no concerns raised by the DMEC.

5. Discussion on protocol revision and publication strategy

The investigators hope to publish the protocol and the results of the main subsidiary analyses once electronic linkage to all the relevant datasets is available for all participants. This first mortality report will include all deaths up to 2026, yielding an average of 10 woman-years of follow-up. A further report on mortality is scheduled to include all deaths up to 2031.

6. Date of next meeting

It was agreed that, unless there are unexpected events, the next meeting of the AgeX TMG should take place in mid-2023.

7. Any other business

There was discussion about additional linkage to the National Radiotherapy Dataset for follow-up information on radiotherapy, which is typically given as an outpatient appointment and therefore not covered by data on hospital admissions.