NHSBSP AGE EXTENSION TRIAL

Minutes of the Trial Management Group
3rd February 2011
11:00 – 13:00
Cancer Epidemiology Unit, Richard Doll Building, University of Oxford

Present
Professor Julietta Patnick (Chair)
Professor Dame Valerie Beral
Dr Lucy Carpenter
Kath Moser
Professor Sir Richard Peto
Professor Amanda Ramirez
Professor Malcolm Reed
Professor Sir Mike Richards
Sarah Sellars
Margot Wheaton
Dr Robin Wilson
Richard Winder

In attendance
Professor Tom Meade
Dr Gillian Reeves

Documents circulated in advance:
- agenda
- draft protocol (Jan 2011)

Plus for background information:
- original application for ethical approval
- patient information leaflet
- final report of the pilot study

1. Welcome and introductions

2. Background (JP)

The background to the trial was outlined.

Originally randomisation was planned to continue over three years i.e. through one screening round. Now, as announced in January 2011 in *Improving Outcomes: A Strategy for Cancer*, randomisation will continue for at least six years i.e. over two screening rounds.

Several breast screening units (approx 10% of all units) are not able to participate in the trial:

1. Gateshead (unsuitable method of batch creation)
2. Several East Anglian units (unsuitable method of batch creation)
3. North Devon (private sector unit)

3. Results from the pilot study (KM)

KM tabled a 2-page summary of the pilot study.

The pilot study included 60,000 women across 5 pilot breast screening units. Overall, the pilot was deemed successful and it has provided a firm basis from which to proceed with the main trial. Although women randomised out could request to be screened very few did so. Screening uptake was lower than hoped for. [Pilot study results have subsequently been published: Moser et al. Extending the age range for breast screening in England: pilot study to assess the feasibility and acceptability of randomisation. J Medical Screening 2011;18:96-102]

The following issues were discussed:

a. Women randomised out.

Individual women who were randomised out were not informed of this, nor that they were part of a trial. This approach has ethical approval. Women randomized out can, nevertheless, request screening and their GPs and breast screening units were informed that any woman randomised out could ask to be screened.

b. Digital mammography

Installing digital equipment across the country is proceeding slowly. Although most screening units now have one digital machine this is mostly used for assessment rather than screening. Most women in the trial to date will have been screened using analogue equipment; this is not ideal for the trial. It is expected that the use of digital machines for screening will increase over time and so, with randomisation now continuing over 6 years, a higher proportion of women will be screened with digital equipment in the second screening round than the first. A record needs to be kept of whether screening was performed using digital or analogue equipment.

There was discussion on the advantages and disadvantages of digital as compared with analogue mammography.
Action: SS to circulate papers on the benefits and disadvantages of digital vs analogue equipment

c. Uptake rates

Screening uptake was 62% in the pilot study. This is lower than the uptake of 74% for women aged 50-70 invited for routine screening.

There was discussion on how uptake could be improved as the difference between an uptake of 60% or 70% would make a large difference to the power of the main trial:

1) Monitoring which screening invitation letters did not reach the addresee. What percentage of women do not live at the address the invite goes to? Could look at population movements in/out of area. It is not in the interest of GP consortia to delete ghost patients. This is an issue to revisit at a future meeting.
2) Offering an ‘out of hours’ service. Research in Manchester and Bristol some years ago indicated that offering an ‘out of hours’ service to previous non-

attenders did not improve uptake. This was now being revisited to see if attitudes had changed.

3) Convenient access and car parking.
4) Using text messaging/emailing to remind women of appointments had been tested although they did not specifically consider uptake of non-attendees. It was suggested that non-attendees could be randomised to see if these techniques made a difference.
5) As many people do not work in the same area as they live, offering women screening in areas other than their home address may improve uptake especially for younger women. This approach will be coming into effect soon in some areas.
6) Past research has established that determinants of uptake of breast cancer screening include post code, car ownership, and previous screening history.

d. 'false positives' and terminology

The term 'negative assessment'. is preferred over 'false positive'.
Action: Avoid use of 'false positive' on trial documents and publications.

The preliminary results of the pilot indicate that women aged 47-49 had a higher 'negative assessment' rate than women aged 71-73. It would be interesting to examine whether having a negative assessment discourages women from subsequent attendance at breast screening.

4. The main trial

a) Additional ethics approval (JP)

Since obtaining ethical approval for the trial in February 2010, additional approval has been obtained to:

1) extend the trial to cover two screening rounds i.e. 6 years
2) include data from the pilot study in the main trial

b) protocol (JP)

Since making the original application for ethical approval, it has become apparent that a more refined analysis is required. A revised protocol had therefore been drafted for discussion at the meeting. This included several differences form the original ethics application - specifically linkage with:

- historic screening records
- HES data
- other, as yet unspecified, NHS data

Although it is known that attending previous screening invitation is strongly related to attending current invitation, it may be hard to justify looking at attending cervical screening as a predictor of attending breast screening as cervical screening is so much more invasive than breast screening. It was suggested we look at data on historic screening and other determinants of screening uptake, to see what is shown, and then decide how to proceed with main trial analysis.
Action: KM to do exploratory analysis looking at predictors of screening uptake including historical screening acceptance, postcode, car ownership etc. It may be possible to use data from the pilot study for this analysis.

Action: KM to amend protocol

i) **to say the analysis will be done firstly including all women, and subsequently restricted to women most likely to attend screening. The way in which the latter group of women is defined will depend on what the exploratory analyses come up with in terms of predictors of taking up screening invitation.**
ii) **to make clear that it is batches that are randomised and not individual women.**
iii) **to make clearer that all women randomised in will be invited.**

c) progress to date (KM)

KM tabled a 1-page summary of progress of the trial to end January 2011.

19 breast screening units have started randomising. The total number of study participants by the end of January 2011 was 128, 871. By the end of March 2011, it is estimated that there will be over 155, 000 study participants.

Before starting randomisation, sites need to:
- have at least one digital machine
- be keeping to NHSBSP targets
- have local R&D approval

Obtaining digital equipment is proving the biggest hurdle to starting randomisation due to equipment cost, and also maintenance costs which are very high for digital machines.

Action: SS to compile a document listing all 73 units and identifying which of the above criteria screening units have fulfilled/not yet fulfilled. MR suggested this could be reviewed at the Cancer Programme Board.

Action: KM to calculate numbers that will be randomised in six years and add to protocol

Clarification was requested as to what the endpoint of the trial was. It was clarified that the primary endpoint is breast cancer mortality. For the 47-49 age group this is defined as the cumulative risk of breast cancer mortality by 60 and for the 71-73 year age group it is defined as the cumulative risk of breast cancer mortality by age 80.

5. Discussion and adoption of terms of reference

The terms of reference were reviewed. It was noted that the terms of reference should include a reference to patient safety which is built into NHSBSP procedures.

6. Any other business

- **Patient information leaflet**

Leaflet needs updating to cover extension of randomisation to 2 screening rounds. In addition several suggested amendments to the current information leaflet were proposed.

Action: Suggested changes to information leaflet to be discussed with JP. KM to coordinate update and changes to leaflet, including clearance with ethics committee

- **Extension of trial over 2 screening rounds**

Sites that have already obtained local R&D approval will need to inform their R&D department that the trial is now running over two screening rounds (rather than one as previously planned); sites in the process of obtaining approval will need to ensure their application is for 72 months and the appropriate number of women.

Action: SS to inform all sites (including previous pilot sites) to proceed as above, and to send sites the letter from ethics committee giving approval for the trial to extend over 2 screening rounds

Pilot sites will have completed two screening rounds by summer 2015. As things stand currently they will at that point start inviting all women in the extended age groups.

- **A potential third round and setting completion dates**

The idea of extending the trial for a third screening round was raised; this would increase the power of the trial and enable longer term outcomes to be examined. In case this becomes a possibility at a future date, it was stressed that it was important to say in the protocol that the trial will continue until '*at least'* 2016.

The possibility of setting completion dates was raised so as to synchronise completion of rounds. This issue should be discussed at a further meeting.

7. Date of next meeting

The Data Monitoring Committee meeting due to be held in the afternoon was postponed. It will now meet as a teleconference.

It was agreed that the Age Extension Trial Management Group should meet annually face-to-face, with the next meeting in January/ February 2012. It was felt that the next meeting should be for at least 3hrs with a break in the middle.

NHSBSP AGE EXTENSION TRIAL

Minutes of the Trial Management Group
11 January 2012
11:00 – 12:00
**** Phone conference ****

Present
Professor Julietta Patnick (Chair)
Professor Dame Valerie Beral
Kath Moser
Professor Sir Richard Peto
Professor Amanda Ramirez
Professor Malcolm Reed
Professor Sir Mike Richards
Sarah Sellars
Margot Wheaton
Dr Robin Wilson
Richard Winder

Apologies
Dr Lucy Carpenter

Documents circulated in advance:
- Agenda
- Draft revised trial protocol (Jan 2012)
- Minutes of TMG meeting 3 February 2011
- Correspondence regarding complaint received regarding the NHSBSP Age Extension trial
- Correspondence with the HTA regarding the proposal to extend the NHSBSP Age Extension trial to older age groups

Plus for background information (4 papers on digital equipment + publication on the number needed to screen to prevent one breast cancer death):

1. Welcome and introductions

2. Minutes of the last meeting (3 February 2011) and matters arising

The minutes of the last meeting (3 February 2011) were accepted as an accurate record of the meeting.

Matters arising:

Sarah Sellars circulated a background document about digital screening. 74 (92.5% of units) breast screening units have at least one digital mammography machine while just over half (42) are fully digital; 6 units have no digital machines.
Action: Sarah Sellars to circulate recently compiled table with details of the sites with digital mammography.

3. Trial update

a) progress to date (KM)

As of October 2011, 40 of the 73 breast screening units due to randomise had started randomising. It is estimated that 330,000 women had been randomised by the end of October 2011. SS said that by the end of January 2012, 47 units will have started randomising. No trial data are available yet.

A complaint has been received from a patient randomised in at the age of 72 regarding the information provided in the patient information leaflet.

It was agreed that in the future, complaints should be referred to Professor Janet Darbyshire, Chair of the Data Monitoring and Ethics Committee (DMEC), to advise on such matters. Any complaints received by individual breast screening units, and regarding this trial, should also be referred to the Chair of the DMEC.
Action: KM to refer this complaint to Janet Darbyshire.

b) protocol

The protocol has been substantially revised. The plan is for it to be agreed, re-submitted to the ethics committee and published soon. It was agreed that members of the TMG would be listed as co-authors on the published protocol.

The protocol should refer via a link to the version of the standard NHSBSP leaflet (that accompanies all invitations to screening) that is currently in use. This would therefore allow for any future changes that may occur in this standard NHSBSP leaflet.

Patient information leaflet

The trial patient information leaflet has not yet been updated. Any revisions will need ethical approval and will be published as part of the protocol. It was clarified that in areas participating in the Age Extension Trial, every woman invited for screening receives the trial patient information leaflet.
Action: The revised trial patient information leaflet will need to be submitted for ethical approval and will form part of the published protocol.

Richard Peto highlighted two proposed major scientific changes to the protocol:- increasing the power of the trial, and extending the trial at older ages.

Increasing the power of the trial

Even with two rounds of randomisation (i.e. recruiting over 6 years), it may still be difficult to guarantee a reliable result for the women in the younger age group (47-49). In order to increase the power of the study, he advocated excluding from the main comparisons any woman who – at the point of randomisation - on the basis of objective information is unlikely to accept an invitation for breast screening:
- women who did not accept their invitation to attend cervical screening
- women who have moved out the area
- women who have died
- women who developed breast cancer prior to batch creation

Excluding women clear of breast cancer when first invited for routine screening at the average age of 51 would also improve the power of the trial, but it is not yet clear whether it is feasible to do this.

The possibility was raised of undertaking a detailed sub-group analysis into the effect of the type of mammography screening used (digital or analogue). Another sub-group analysis could look into the characteristics of tumours detected (e.g ER positive or ER negative).

An end point committee will need to be convened to determine objectively which deaths can be attributed to breast cancer, as they are sometimes miscertified as lung and bone cancer or pneumonia, particularly in old age.

Action: Any comments regarding the trial protocol should be sent to Kath Moser before the end of January 2012.

4. Proposal to extend the trial at older ages

A proposal has been submitted to the Health Technology Assessment (HTA) programme to extend the trial by inviting the women randomised in aged 71-73 for a further two extra screens (at ages 74-76 and 77-79 years). This is important because it would provide a bigger signal as to the effect of continuation of screening and provide a clear result by 2020, with no chance of a false negative result. It would also mean that the effect of screening for each separate age group could be seen.

In response to the queries raised by the HTA regarding how extending the trial to older ages would increase the power of the study, Richard Peto read the reply he provided to the HTA (see below).

"*Thanks for your thoughtful letter. I'd like to talk over my concerns, but meanwhile please read the attached revision of the age extension study protocol, and in particular the "Statistical power" section on page 6. We could well get a false negative for the effects of adding an early screen at ages 47-49, in which case the effects at ages 70+ need to be overwhelmingly reliable. At these older ages, however, if women were randomly allocated 0, 1 or 2 extra screens after 70 (in the ratio 2:1:1) then a trend test would have about the same power as randomisation of 0 vs 1 extra screens (in the ratio 2:2), but a trial of 0 vs 2 extra screens (in the ratio 2:2) would have a lot more power, especially for breast cancer deaths at ages 75-84. The appropriate criterion isn't just "power to detect at p=0.01", however; what we need is a narrow CI on the effects, and a p=0.01 result has a lower confidence limit of a negligibly small effect. A study of at least 2 extra screens vs none would offer this, and one of screening to age 79 would do so even better. If we get massively statistically reliable evidence about size of the effects of 2 extra screens, then we could infer reasonably reliably what just one would have offered, achieving what your HTA call was for in a more unambiguous way than a 3-way randomisation would*."

Extending the trial for these two extra screening rounds would not affect the trial costs (for follow-up, record linkage etc). However there would be extra costs to breast screening units in providing more mammograms to the older women (1/6 of the women in the trial). This cost would increase gradually over time, and would not reach the full amount for a few years. The cost of these extra screens is estimated at £12m for 2 extra screening rounds.

It was agreed that it would be of great benefit to extend the trial for two extra screens in the upper age group. Subject to ethical approval, this could be tested in the 5 pilot sites by inviting the women randomised in aged 71-73 for a further

screen 3 years later; this would indicate what issues might arise, as well as the uptake rates and costs. There may be some reduction in treatment costs due to cancers being detected earlier.

5. Any other business

The group were told about a separate trial that is being undertaken to look at treatment versus no treatment in low risk DCIS. This trial should shed light on the debate over under diagnosis and over–treatment.

6. Date of next meeting

It was agreed that the next meeting of the Trial Management Group should be January 2013 and should be coordinated with the meeting of the Data Monitoring and Ethics Committee.

Action: Kath Moser to circulate an email to fix a date for the next meeting of the Trial Management Group.

NHSBSP AGE EXTENSION TRIAL

Minutes of the Trial Management Group
9 January 2013
11:00 – 13:00
Cancer Epidemiology Unit, University of Oxford

Present
Professor Julietta Patnick (Chair)
Professor Dame Valerie Beral
Dr Lucy Carpenter
Kath Moser
Professor Sir Richard Peto
Professor Amanda Ramirez
Professor Malcolm Reed
Professor Sir Mike Richards
Sarah Sellars
Margot Wheaton
Richard Winder

In attendance
Professor Janet Darbyshire
Jenny Rusby
Hayley Abbiss (notes)

Apologies
Dr Robin Wilson

Documents circulated in advance:
- Agenda
- Draft revised trial protocol (Dec 2012)
- Draft patient information leaflet (Dec 2012)
- Minutes of TMG meeting 11 January 2012

Documents circulated at meeting:
- Trial progress at end of 2012; graphs of trial cumulative numbers by date
- Article: Extending the age range for breast screening in England: pilot study to assess the feasibility and acceptability of randomization (JMedScr)
- Article: The benefits and harms of breast cancer screening: an independent review (The Lancet)

1. Welcome and introductions (Julietta Patnick (JP))

Janet Darbyshire (JD) and Jenny Rusby from the trial Data Monitoring and Ethics Committee (DMEC) were welcomed to observe the meeting.

It has been one year since the last TMG meeting (by telephone conference). Progress on revising the protocol and information leaflet was delayed while we awaited the outcome of the Marmot Review. The Review (reporting at the end of Oct 2012) supported the continuation of the screening programme and, importantly

for this trial, said "The impact of breast screening outside the ages 50-69 years is very uncertain. The Panel supports the principle of the ongoing trial in the UK for randomising women under age 50 and above age 70 to be invited for breast screening."

2. Minutes of the last meeting (11 January 2012) and matters arising

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

Matters arising:
Sarah Sellars (SS) gave an update on digital mammography: out of the 80 breast screening units, 66 were now fully digital and 4 had no digital machines (due to drop to 3 by the end of Jan 2013).

Kath Moser (KM) confirmed that the complaint received from a patient randomised in aged 72 had been referred to Janet Darbyshire (JD), Chair of the DMEC.

JP reported that the National Research Ethics Service recently received a Freedom of Information Request about the trial; they are going to supply the information requested with names redacted.

3. Trial update

a) revised protocol and patient information leaflet

Following the outcome of the Marmot Review the protocol and the trial patient information leaflet have been revised.

The group discussed the protocol and some further minor revisions were suggested. It is not intended to revise the protocol again and therefore it needs to be phrased in such a way to avoid necessitating further revision. KM confirmed that all members of the TMG will be co-authors of the protocol, and linked publication, as agreed at the TMG Jan 2012. JD requested that her DMEC membership details be amended to remove 'statistician' and replace with 'epidemiologist'.
Action: KM to amend JD's details.

Any further comments to be sent to KM by 18 January. KM to action the changes already agreed and any further suggested changes.
Action: All to send any further comments regarding the protocol to KM by 18 January 2013.

Finalising the protocol will be delegated to the co-investigators. Once finalised, the revised protocol will be submitted to the ethics committee as part of a notice of substantial amendment.
Action: KM to make further revisions to protocol and patient information leaflet and send to Ethics for approval, by end February 2013.

It was agreed that the final protocol should be submitted to a journal for peer-reviewed publication. Lancet Oncology was suggested.
Action: KM to submit protocol to journal for publication.

JD suggested that the co-investigators develop a statistical analysis plan although the full plan could be finalised at a later date before conducting the final analysis.
Action: Co-investigators to consider developing a statistical analysis plan.

The TMG agreed the appointment of Dr Gillian Reeves (GR) as the independent statistician on the DMEC. It was noted that GR, being located within the Cancer Epidemiology Unit, will have access to data that will not be available to the TMG, and as such the proprieties of the role must be observed in order not to compromise the integrity of the trial.

The revised patient information leaflet, which will form part of the published protocol, was discussed. Many comments were made and amendments suggested. It was agreed that some further extensive revisions were required following which it would be circulated again.
Action: KM to further revise the patient information leaflet and circulate by 18 January 2013 for approval.

The possibility that a woman may wish to attend for screening but opt out of the trial was discussed. However the TMG agreed it was not necessary to mention this within the leaflet as, should a woman object to being in the trial, then she could be removed from the trial analysis at that time.

b) progress to date

KM described trial progress as outlined in the 2 circulated handouts. An estimated 800,000 women have now been randomised. As there was not time to describe other aspects of progress it was agreed that KM would circulate the committee with this information.
Action: KM to email the TMG with an update on progress.

4. Any other business

Proposal to extend the trial at older ages

Richard Peto (RP) highlighted the benefits of extending the trial by inviting the older women who had been randomised in aged 71-73 to a further two extra screens (at ages 74-76 and 77-79 years). Life expectancy in women is increasing and women in their mid 70's are generally still in good health. Stopping sending invitations could send the message that there is a lowering of risk, which is erroneous. Offering this additional screening will add to the power of the trial.

The 5 pilot sites started randomising women in June 2009. As this is over 3 years ago, there would be older women who had been randomised in aged 71-73 and who would now be eligible, once the approvals are in place, to be invited in the next screening round. By June 2013, five other centres will be in this position. VB said it was important to start offering additional screening to the older women as soon as possible so as not to miss too many women. JP commented that the units need time to prepare for the changes, but if ethical approval was obtained in March they should be able to start in autumn 2013.

The trial, as currently formulated, is mandatory. Discussions should be had regarding the compulsory/voluntary nature of offering additional screening beyond

the age of 73. If this is not mandatory, some screening units will opt out due to workload issues and this could result in the participating units being unrepresentative of the whole.

Margot Wheaton (MW) commented that offering additional screening will require changes to the NBSS software.
Action: MW to start discussing computing implications and software developments required.

The costs of offering additional screening were discussed. Overall around 0.5M women could be offered additional screening after age 73. Costs incurred will include this additional screening, although uptake is not expected to be high, and also the computing development. It was agreed that Public Health England (PHE) should be approached now and with a view to seeking approval for 18 months funding (until March 2015), estimated at £1.5-2M, on the recommendation of the TMG. Mike Richards (MR) suggested that the group could use 2014/15 to make a case for requesting further funding in the following years, looking at the long run and potential for reduced costs. He suggested that once recruitment stops then the money saved could be used to continue screening the existing older women within the study as they age; the advantage being that a cohort getting older will give a more reliable answer.
Action: Submit funding request for additional 18 months to PHE.

VB suggested the possibility of going to a research funding body if PHE won't provide funding.

MR suggested that the different options are costed at this stage so that it is clear what the funding profile will be. This was agreed.
Action: KM to prepare costings.

5. Date of next meeting

January 2014, date to be confirmed.
Action: KM/HA to email TMG with proposed date.

NHSBSP AGE EXTENSION TRIAL

Minutes of the Trial Management Group
23 January 2014
11:00 – 13:00
Cancer Epidemiology Unit, University of Oxford

Present
Professor Julietta Patnick (Chair)
Professor Dame Valerie Beral
Kath Moser
Professor Sir Richard Peto
Professor Malcolm Reed
Sarah Sellars
Margot Wheaton
Dr Robin Wilson
Richard Winder

In attendance
Keith Shaw
Hayley Abbiss (notes)

Apologies
Dr Lucy Carpenter
Dr Kevin Fenton
Professor Amanda Ramirez
Professor Sir Mike Richards

Documents circulated in advance:
- Agenda
- Minutes of TMG meeting 9 January 2013
- Trial progress as at January 2014
- Data progress as at January 2014
- Report on study population data for the first 4 years of the trial
- Report on screening data for the first 3 years of the trial
- Report of the parliamentary inquiry into older age and breast cancer

1. Welcome and introductions

Keith Shaw (KS) was welcomed to the meeting. KS is Data Manager for the trial (Cancer Epidemiology Unit).

Kevin Fenton (KF), Director of Health and Wellbeing for Public Health England (PHE), has agreed to join the Trial Management Group. He sent apologies due to a prior commitment.

Apologies were received from Lucy Carpenter (LC) and Mike Richards.

Amanda Ramirez (AR) has resigned following a change in her job which means she is now focussing on clinical work.

2. Minutes of the last meeting (9 January 2013) and matters arising

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

Matters arising:

Julietta Patnick (JP) reported a positive meeting recently with Cancer Research-UK who were very supportive of the NHS Breast Screening Programme.

JP reported that she had received a complaint from Susan Bewley in November 2013 expressing concerns about the ethical and scientific underpinning of the trial.

3. Trial update (KM)

a) Randomisation, numbers, data

There has been much progress in obtaining trial data over the last year and KS has been central in managing this process. Reports were circulated in advance of the meeting. KS confirmed there have been no issues with accessing the data from the Quality Assurance Reference Centres (QARCs) since their transfer from the NHS to PHE.

There are 9 breast screening units that have not yet started randomising. 6 of these plan to start by the end of March 2014. There is no start date for the remaining three. Sarah Sellars (SS) reported that from April 2015 all women are likely to be screened using digital machines.

Valerie Beral (VB) requested that all future reports be marked as confidential and that all such material should be treated confidentially and not discussed outside the TMG.

b) Ethical approval, protocol

A substantial amendment (to cover linkage to HES and other NHS datasets; offer screening throughout their 70s to women randomised in aged 71-73; revise patient leaflet) was submitted to the Research Ethics Committee (REC) February 2013 but was not approved.

Julietta Patnick (JP), the principal investigator, has since had discussions with the Chair of the REC to clarify their concerns. The main issues are around the leaflet and informing the control group.

It had been decided that rather than put in an appeal, it was better to submit a new substantial amendment that only covered linkage to NHS datasets, and a revised patient leaflet.

JP and KM have been redrafting the leaflet, and Public Health England is now assisting in reformatting the leaflet. As soon as the leaflet is finalised we will go back to the REC with a new substantial amendment. References in the protocol to continuing to send invitations to women over 73 will be removed.

SS stressed the importance of the new leaflet not looking similar to the NHSBSP information leaflet that is sent to all women as this could cause confusion. MW was concerned that if the new leaflet was bigger than.at present it would impact on postage costs.

It was agreed that it was urgent to finalise the new leaflet and go back to the REC as soon as possible.

Malcolm Reed (MR) requested that the new leaflet is sent to the TMG before it is submitted to Ethics with the new substantial amendment.

Action: KM to send patient information leaflet to TMG before submitting it to the REC with the substantial amendment.

4. Discussion of future plans

Funding is needed to continue to offer screening to women (who were randomised in aged 71-73) throughout their 70s. JP estimated that offering screening to 74-76 year olds would cost an extra £4 million per annum. Due to cuts within the NHS and PHE they will not be able to provide additional funding. JP confirmed PHE are supportive of the TMG reorganising current funds in order to generate funding for offering screening to 74-76 year olds.

The Health Technology Assessment Programme will not fund the continuation of an existing trial. Richard Winder asked whether approaching public/private partnerships for funding was an option. The NIHR was suggested as a potential funder. RP warned it would be unwise to seek any commercial sponsorship and VB agreed funding would need to be at 'arms-length'. It was agreed that the TMG should get approval from the Ethics Committee, calculate what funding is required, and then talk to Professor Dame Sally Davies.

JP highlighted the main problems would be obtaining funding and recruiting services. It was discussed whether offering one more screening round was deliverable. Margot Wheaton (MW) stressed that staffing levels across the service are currently at a critical level.

MR suggested a 3 prong strategy – (i) getting the protocol right (ii) obtaining ethics approval (iii) obtaining funding. The costs would need to be worked out in parallel with this.

JP is expecting to be called to give evidence to the Commons Select Committee on Science and Technology inquiry into National Health Screening. VB advised that she will be providing written evidence to the Committee. The deadline is 26 February 2014.

PHE supports the continuation of randomisation beyond the two screening rounds currently agreed. They will require good evidence before deciding to extend, or not, routine screening to women under age 50 and over age 70, and support randomising until such a point is reached. Evidence for the younger women should be available in the early 2020s, for the older women in the late 2020s. The primary endpoints are breast cancer mortality up to age 60 for the younger, and up to age 80 for the older, women. The Data Monitoring and Ethics Committee will advise the TMG when, in their opinion, there is proof beyond any reasonable doubt that an additional screening invitation at ages 47-49 years or at ages 71-73 years will reduce breast cancer mortality by age 60 or by age 80 respectively. It will then be up to the TMG to decide what to do.

5. Any other business

TMG membership.
SS, MW and Richard Winder are due to retire by Jan 2015. They were asked if they would be interested in staying on the TMG to contribute their expertise – all said they would be. Mike Richards has stepped back from the TMG but agreed to remain a semi-sleeping partner. Amanda Ramirez has resigned her membership of the TMG. Robin Wilson plans to retire in 2016 and so we will need to find a radiologist to replace him.

It was agreed to invite someone currently working in the screening programme. Suggestions included Kim Stoddard, Programme Manager for North London Breast Screening Service; Monica Dale, Breast Screening Superintendent Radiographer. RP proposed inviting Dr Hongchao Pan, from CTSU, who is involved in the Early Breast Cancer Trialists' Collaborative Group.

Publications.
It was agreed that we cannot write substantive papers at this stage. We plan to publish the protocol once it has been finalised, possibly in Lancet Oncology or Health Informatics; some process data could be included.

Next years meeting.
MR requested a longer meeting next year in order to allow for academic discussions and to look at detailed numbers, costs and times. It was proposed to include some presentations including one from RP on screening women through their 70's. JP requested that a time line be drawn up. The DMEC will be invited to observe the TMG meeting and attend the presentations. It was agreed that the DMEC meeting should follow on after the TMG meeting.

Action: KM to submit the new substantial amendment including the revised patient information leaflet to the Ethics Committee, as soon as possible.

Action: VB to submit written evidence to Commons Select Committee

Action: JP/KM to invite new members to the TMG

6. Date of next meeting
TBA

NHSBSP AGE EXTENSION TRIAL

Minutes of the Trial Management Group
28 January 2015
11:00 – 13:30
Cancer Epidemiology Unit, University of Oxford

Present
TMG Members
Professor Julietta Patnick (Chair)
Professor Dame Valerie Beral
Kath Moser
Professor Sir Richard Peto
Professor Malcolm Reed
Dr Lucy Carpenter
Dr Hongchao Pan
Margot Wheaton

DMEC Members
Professor Janet Darbyshire
Professor Gillian Reeves
Dr Jenny Rusby
Dr Rosalind Given-Wilson (from 13.00hours)

In attendance
Keith Shaw
Krys Baker (notes)

Apologies
Dr Kevin Fenton
Professor Sir Mike Richards
Dr Robin Wilson
Professor Tom Meade (DMEC)

Documents circulated in advance:
- Agenda
- Minutes of TMG meeting 23 January 2014
- Trial progress as at January 2015
- Data progress as at January 2015
- Report on study population data for the first 5 years of the trial
- Report on screening data for the first 4 years of the trial

1. Welcome and Introductions

New Member of TMG Honchao Pan (HP) was welcomed to the meeting. Keith Shaw (KS) Data Manager and Krys Baker (KB) Trial Administrator were also welcomed.

Apologies were received from Kevin Fenton (KF), Mike Richards (MR), Robin Wilson (RW) and Tom Meade (TM).

2. Minutes of the last meeting (23rd Jan 2014) and matters arising

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

Matters arising:

TMG membership – Sarah Sellars and Richard Winder have now retired from their posts. They will continue to be named as authors of the protocol but a footnote will state that they have retired. HP is a new member. New membership of the TMG will be discussed later in the meeting.

The recent criticisms of the trial were discussed, and it was decided that this would not be the focus of the meeting.

Malcolm Reed (MR) asked for there to be more communication with the TMG between meetings; it was agreed that KB would circulate periodic updates.

3. Trial Update – Kath Moser (KM)

a) Randomisation, numbers, data

As at the end of December 2014, 64 out of the 69 breast screening units due to take part in the trial had started randomising. Of the 5 remaining units, 1 is due to start soon. There was some discussion as to whether it would be better to exclude these 5 units from the trial. The TMG felt that a final date should be set for them to commence the trial. However the DMEC meeting later that day decided that these 5 units should not be excluded from the trial. There are a further 9 units which will not be participating in the trial – one is private, and 8 use a non-standard method of creating screening batches. An estimated 1,846,000 women have been randomised to date, with the number randomised increasing by 44,700 per month.

Keith Shaw (KS) is receiving data downloads; there is currently a delay due to changes in PHE data release procedures; the application to PHE for data release is in hand. 1.5 million women have so far been flagged at the NHS Central Register for deaths and cancers.

Members of the TMG were not concerned with the variation in batch sizes across units, and agreed that it would not compromise the statistical power of the trial.

b) Ethical approval, protocol

The updated protocol (version 3.0) had been circulated together with the new Patient Information Sheet; also a poster, which will be circulated to GP surgeries for them to display. Ethical Approval for Substantial Amendment 3, which included these documents, was granted on 4 November 2014.

The TMG agreed that the leaflet is more detailed, and that the Protocol is more comprehensive.

4. Discussion of future plans and 5. Discussion of scientific matters

LC suggested collecting data on characteristics of women who had not attended breast screening; Richard Peto (RP) agreed that this would be a good idea, but it would need to be a separate project.

KS and KB will be setting up a trial website. TMG suggestions for content included Protocol, minutes of meetings, links to trial registers, and to breast cancer charities for patients. Also include up to date numbers of women in the trial.

The intention is to publish the protocol very soon.

JP informed the meeting that PHE were keen for a response to published criticisms. MR felt that publishing a response would distract from the main scientific points. This was discussed and it was agreed not to respond in print to the criticisms. Trial documents would be made available on the trial website.

The changed context of the trial was outlined: whereas initially the trial was opportunistic, now PHE have stated that future decisions about extending routine NHS breast cancer screening outside the age range 50-70 years should await the emergence of reliable evidence as to its effects. The trial can provide this information.

The TMG discussed recommendation 3 from the parliamentary inquiry into older age and breast cancer *"to gather evidence for the benefits and risks of breast screening for women above the current screening age"*. It was decided that a sub-group of the TMG would be set up to explore this recommendation. This would include Kevin Fenton (KF) amongst others.

Valerie Beral (VB) described the 5 datasets that will be linked to the trial records thereby providing a wealth of data – screening history and screening going forward, death registration, cancer registration, cancer outcomes, and Hospital Episode Statistics.

6. Any other business

Janet Darbyshire (JD) raised discussion of the name of the DMEC and their role. She said the DMEC can provide advice on data monitoring and safety. In terms of ethics their role is advisory, they do not make decisions in relation to ethics – that is for the REC to do.

There was some discussion on the various models of trial management and oversight. It was agreed that although members had not experienced this model before, they were happy with the model adopted for the Age Extension Trial.

TMG members would be informed once the website was up and running.

7. Date of next meeting

TBA

NHSBSP AGE EXTENSION TRIAL

Minutes of the Trial Management Group
11 January 2016
11:00 – 13:00
PHE Wellington House, London

Present

TMG Members

Professor Julietta Patnick (Chair)
Professor Dame Valerie Beral
Mrs Claire Borrelli
Mrs Jacquie Jenkins
Professor Iain Lyburn
Ms Kath Moser
Dr Hongchao Pan
Professor Sir Richard Peto
Professor Malcolm Reed (by phone conference)

DMEC Members

Professor Janet Darbyshire
Professor Gillian Reeves
Ms Jenny Rusby

Visitors

Professor David Heymann (PHE)
Ms Anne Stevenson (PHE)

In attendance

Mr Keith Shaw
Ms Krys Baker

Apologies

Professor Kevin Fenton
Professor Sir Mike Richards
Dr Lucy Carpenter
Mrs Margot Wheaton
Dr Rosalind Given-Wilson (DMEC)
Professor Tom Meade (DMEC)

1. Welcome and Introductions

New members, Professor Iain Lyburn (Consultant Radiologist), Claire Borrelli (Radiographer and Education & Training Manager) and Jacquie Jenkins (National Breast Screening Programme Manager), were welcomed to the meeting. Visitors Professor David Heymann (Chair of Public Health England) and Anne Stevenson (National Programmes Lead for the Young Person and Adult Screening Programmes - representing Prof Kevin Fenton) were also welcomed. Introductions were made from all committee members.

Apologies were received from Prof Kevin Fenton (KF), Prof Sir Mike Richards (MR), Dr Lucy Carpenter (LC), Margot Wheaton (MW), Dr Rosalind Given-Wilson (RGW) and Prof Tom Meade (TM).

DH needed to leave the meeting early and so it was agreed to bring agenda item 4 forward.

2. Minutes of the last meeting (28th Jan 2015) and matters arising

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

Matters arising:

TMG members found the mid-year newsletter useful. A similar communication will be sent to TMG and DMEC members in 2016. There was a discussion about how many participants were required to produce a reliable result from the trial. It was agreed that randomisation needed to continue until the mid 2020s to inform policy.

The trial website is up and running with web address http://www.agex.uk/

Action: Send mid-year newsletter to TMG and DMEC members later in 2016

4. Screening women throughout their 70s

- The TMG agreed that scientifically it makes sense for the older women to be invited for additional screenings beyond 71-73.
- It would take time for screening units to implement adding the older age group into their batches and there will also be implications on staffing and resources within BSU's.
- PHE said that the trial budget was fixed
- The priority for PHE is to make sure that the BSUs prioritise the clinical work and do not miss their targets.
- The PHE budget is currently being prepared for the 2016/17 financial year.
- It was agreed that the TMG need to see a breakdown of the funds being allocated to all units. PHE agreed to provide these figures.
- Software would need to be written to implement any change.
- Ethics approval would need to be sought for any changes.

Actions: A timeline was agreed as follows:

1. **In the next month the budget will be reviewed by PHE. They will provide the budget to the TMG well before April 2016.**

2. **In the next month Cancer Epidemiology Unit (CEU) will provide estimates of numbers of women in their 70s by BSU.**

3. **IL, CB and JJ will assess the workload and clinical implications at the local BSU level.**

4. **The application for ethics approval for additional invitations to women in their 70s will be prepared over the next month.**
5. **3-5 units to be selected to pilot extending screening to women in this age group. The pilot will begin when ethics approval has been granted and funding for the pilot is available.**

6. **A further pilot will be conducted in one of the units currently inviting all women aged 47-49 (paid for out of trial funds but not contributing to the trial) to assess the feasibility and acceptability of being requested to no longer invite this age group and withdrawal of the associated funds.**

7. **By March 2017 it was hoped that all participating units should be inviting for screening the trial women aged 74+**

8. **PHE to assess the possibility of providing screening on request for women aged 47-49 in BSUs not participating in the trial who are being requested to stop inviting all women in this age group for screening.**

3. Trial Update

- As at the end of December 2015, 65 out of the 69 breast screening units due to take part in the trial had started randomising. Of the 4 remaining units which had not yet started, 3 plan to commence randomisation in 2016.
- 2.4 million women had been randomised as at Dec 2015
- The study population data for the first 6 years of the trial was described. 10,229 screening batches had been randomised during this period, which included 1,974,712 trial participants. Currently around 500,000 women are being randomised per year.
- The screening data for the first 5 years of the trial was described; date of first offered appointment, screening date, recall, biopsy, etc - for the women randomised in.
- The surgical procedures data were discussed and further detail requested.

Action: Further information on surgical procedures (from HES if possible) will be prepared for the next meeting

It was confirmed that all screening is now digital.

Action: Self-referrals derived from screening history data to be prepared for next meeting.

Action: Uptake by breast screening units using routine screening data, to compare with trial data, to be prepared for next meeting.

Action: Use screening history data to investigate whether women invited aged 47-49 in the trial come back when routinely invited for screening aged 50-52.

6. Any other business

Future Publications

- Interim analyses and publication of protocol requested by JP and KM. RP suggested that the protocol should be published in a major journal such as Lancet Oncology once the revision of adding the 74-79 age group has been approved. It was also agreed to add the protocol to the website once published, and in the meanwhile a summary may be added to the website once ethical approval has been obtained.

Meeting for participating BSUs

- It was agreed that a meeting would be arranged during 2016 for all participating BSUs, to feedback information about the trial including some interim numbers.

Action: Arrange meeting during 2016 in Oxford for participating BSUs

HSCIC

- The study is currently awaiting approval from HSCIC for release of HES data, the application is being reviewed in the next couple of weeks.

Leaflet (PIS)

- When putting together the next ethics application, to include changed wording of the PIS to ask those invited for screening to cancel appointment if they do not wish to attend screening.

7. Date of next meeting

Feb 2017 KB will send doodle poll

AgeX Trial

Minutes of the Trial Management Group
20th February 2017
11:00 – 13:30
Cancer Epidemiology Unit, NDPH, Oxford

Present

TMG Members
Professor Julietta Patnick (Chair)
Ms Krys Baker
Professor Dame Valerie Beral
Dr Lucy Carpenter
Mrs Jacquie Jenkins (via conference phone)
Ms Kath Moser
Dr Hongchao Pan
Professor Sir Richard Peto
Professor Malcolm Reed
Mr Keith Shaw

DMEC Members
Professor Janet Darbyshire (chair of DMEC)
Dr Ros Given-Wilson
Professor Gillian Reeves
Ms Jenny Rusby

Apologies
Professor Kevin Fenton
Professor Sir Mike Richards
Mrs Claire Borrelli
Professor Iain Lyburn
Professor Tom Meade

1. Welcome and Introductions

Apologies were received from Prof Kevin Fenton (KF), Prof Sir Mike Richards (MR), Mrs Claire Borrelli (CB), Professor Iain Lyburn (IL) and Tom Meade. It was noted that Margot Wheaton had retired.

2. Minutes of the last meeting (11th Jan 2016) and matters arising

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

Matters arising:

Action points:

JJ explained that the new budget showed an overall reduction as 9 BSUs who were not part of the trial but were inviting all women 47-49 had been asked to stop inviting these women from Dec 2016. This released money which in due course could be put towards inviting some trial women 74+. For screening JJ said it was unlikely to be possible to start inviting women 74+ until 2018, possibly slightly earlier if IT issues could be sorted. VB explained that the trial has ethical and CAG approval to add two follow up screening invites at 74-76yrs and 77-79yrs in the women randomised in aged 71-73. We are waiting for an IT program to be written and for a review of capacity in Breast Screening Units (BSUs). This would be piloted first in one or two centres in the next 12 months or so.

VB reported on self-referrals. The self-referral rate among women aged 47-49 randomised not to be screened is 0.9%, whereas among women aged 71-73 it is about 10%. As there were so many women not invited at 71-73 who self-referred, the degree of contamination could be greater than anticipated following the pilot and greater numbers of women to be randomised could consequently be required. RGW reported that previous trials had encouraged women over 70 to self-refer for breast screening. JJ also reported that PHE does encourage women to return for breast screening in their 70s despite there being little evidence in support of this.

There was some discussion on how this number could be minimised. RP said that it gave a greater case for recruiting as many over 70 women as possible to increase numbers.

Action: Discuss with PHE the inconsistency in their approach to women over 70.

Action: Start inviting those aged 74-76 ASAP. Look at BSUs that have a high self-referral rate.

It was noted that the meeting held in the Richard Doll Building in Oxford in September 2016 for representatives from Breast Screening Units (BSUs) had been well received and had a good attendance from BSUs.

3. Mid-year update

TMG members found the mid-year newsletter useful. A similar communication will be sent to TMG and DMEC members in 2017.

Action: JP/KB Send mid-year newsletter to TMG and DMEC members later in 2017

4. Updated Protocol with recent Amendment

Amendment 4.0 approved Sept 2016 included an:

- Updated protocol to include option for two extra breast screening invitations in 74-79 age group, reference to the trial as "AgeX" in the protocol's title, text, and descriptive material, revision of the Introduction and Background to bring them up to date.
- Updated patient Information sheet which include changes to reflect possibly inviting women for screening throughout their 70s, ask women to let their screening office know if they are unable to attend their appointment, mention that record linkage to routinely collected NHS data will use data from NHS Digital (previously HSCIC),following a request from NHS Digital that this be mentioned. There was some discussion to clarify the intended exclusion from analyses of women who had had previous breast disease or breast surgery. It was agreed that the types of previous breast disease and of previous breast surgery would be looked at when relevant hospital data were available.

It was also agreed that the implementation of the extra screens should be carried out paying attention to a shortage of workforce within the BSUs.

Action: Discuss types of previous breast disease at next TMG meeting when relevant data are available.

5. External review

A document was circulated containing all data sources. The study has recently had approval from NHS Digital for the provision of hospital admissions data (HES) data earlier this year. HES records for 2.5 million women will be provided this spring/summer. Other data sources include PHE for screening data, cancer outcomes data and cancer screening history. ONS provide mortality and incident cancer data via NHS Digital.

Public Health England (PHE) have recently asked for an independent external review of the AgeX trial to be carried out, and a letter describing the results of the review was circulated to members. The anonymous reviewers wrote a strongly favourable report in support of the trial with an average score of 9.3 out of 10. The reviewers asked for a clarification of a couple of points. The TMG discussed response to the reviewers proposed by RP. It was agreed to clarify some of the responses and give more succinct replies to the questions and send our response to PHE.

Action: RP to edit our response to PHE and send it to them.

6. Plans for inviting women 74-79

2016 Summary of European Commission Recommendations on Breast Cancer Screening was circulated. They conditionally recommend screening for women 70-
74. The fact that there is no evidence for recommending this gives good grounds for supporting the trial.

RP stated that the EBCTCG was currently undertaking a review of individual data from all previous trials of breast screening; results should be available by 2018.

7. Trial update

As at the end of December 2016:

- 65 breast screening units are randomising
- 2,933,000 women are estimated to have been randomised to date
    - 1,873,000 aged 47-49
    - 1,060,000 aged 71-73
- the number of women randomised is increasing by an estimated 45,300 per month
    - 29,000 aged 47-49
    - 16,400 aged 71-73
- Almost all mammography now digital
- Inner city BSUs tend to have lower uptake

8. Any other business

RGW reported a concern regarding a shortage of Radiographers and Radiologists which may have an impact on the trial that was expressed at the British Society of Breast Radiology meeting in Nov 2016. VB was attending a meeting of Breast Screening Radiologists on the 23rd February 2017. It was suggested that the investigators describe the trial at scientific meetings.

Action: Trial needs to be actively communicating with BSUs in order to explain its rationale and importance, as was done in the early years of the trial. In particular present information about AgeX at scientific meetings.

Action: Need to start pilots for adding screening invitations 74+

AgeX Trial

Minutes of the Trial Management Group
12th March 2018
10:30 – 12:30
Cancer Epidemiology Unit, NDPH, Oxford
Minutes

Present
Professor Julietta Patnick (Chair) (JP)
Ms Krys Baker (KB)
Dr Isobel Barnes (IB)
Professor Dame Valerie Beral (VB)
Dr Lucy Carpenter (LC)
Professor David Hunter (DH)
Dr Hongchao Pan (HCP)
Professor Malcolm Reed (MR)
Professor Sir Mike Richards (MAR)
Mr Keith Shaw (KS)

Apologies
Mrs Claire Borrelli (CB)
Professor Kevin Fenton (KF)
Mrs Jacquie Jenkins (JJ)
Professor Iain Lyburn (IL)
Professor Sir Richard Peto (RP)

1. Welcome and Introductions
Apologies were received from Prof Kevin Fenton (KF), Mrs Claire Borrelli (CB), Professor Iain Lyburn (IL) and Mrs Jacquie Jenkins (JJ). JP welcomed Professor David Hunter and Dr Isobel Barnes to the TMG. Isobel has succeeded Kath Moser who retired in April 2017. The committee also thanked Kath for her work in setting up the trial.

2. Minutes of the last meeting (20th Feb 2017) and matters arising
The minutes of the last meeting were accepted as an accurate record.

Matters arising:

It was noted that some DMEC Members were present at the 2017 TMG meeting. However this year the DMEC met earlier, on the 22nd February 2018, and a note from the DMEC to the TMG was circulated in the papers for this meeting.

Action points:

The “Be Clear about Cancer” campaign run by PHE inviting over 70s to attend for breast screening is not evidence based and has had some unwanted effects on the trial, by increasing screening among the controls. PHE has agreed to consider the AgeX TMG views on suspending these campaigns.

It has not yet been possible to commence sending the invitations to the 74-76 years olds. Some funds for this will come from the money released from the Breast Screening Units that were screening 47-49 year olds, without randomisation.

3. Mid-year update

TMG members found the mid-year newsletter useful.

4. Trial Update

VB presented a report prepared by the AgeX investigators for the meeting of the PHE Breast Screening Programme Research Advisory Committee (RAC) in January 2018 (which she had attended). VB explained that, at the meeting, PHE representatives unexpectedly suggested that some women who were randomised into AgeX when they were aged 70 should have been offered routine screening instead. The trial investigators found, however, that there were discrepancies between the definition of age used by PHE and that used for routine breast screening invitation procedures (which also applied to AgeX). PHE asked that this apparent discrepancy be reported to the DMEC and regulatory authorities. The AgeX DMEC met on 22 February 2018 and agreed that no change to the AgeX trial materials or procedures was necessary at present, and this information was conveyed to members of the TMG.

The TMG discussed if there were any steps that the trial might have taken to avoid this issue, pointing out that the method that the screening programme procedures currently use to define age was based on year of birth and that women aged 70 who were due to turn 71 by the end of the year were not eligible for routine screening. VB reported that the trial investigators continued to be in discussion with PHE about this.

VB presented the report based on other work to date:

4.1 Recruitment: 3.1 million women have been randomised up to 31/03/17; 67% of those aged <50 and 69% of those aged 71+ allocated to be invited for screening have accepted.

4.2 Numbers randomised: The study is now randomizing just over 500k women per year. The annual number of women randomised is likely to be stable from now on, as no more screening services are joining the trial. Recently the proportion of older women has increased slightly, largely because women born in the post-war baby boom are now reaching their 70s.

4.3 Randomised batches: There has been some increase in the average batch size over the last few years. The number of batches randomising women to be invited or not are similar.

4.4 Excluded records: The number of women who could not be flagged has increased in the last two years. This is due to the care.data episode which led to about 3% of people requesting that their health data not be passed on to others.

4.5 Data sources: Data on those randomised and follow-up data come from 7 different sources. The numbers randomised, screening outcomes and death data were available up to 31/3/2017, but information on tumour characteristics

(COSD data) was last available in 2013 and on past cancer screening history in 2015. It is hoped that planned improvements in PHE data systems will reduce these delays and simplify data transfer. There are still relatively small numbers of women with 5 years follow-up. SMR reported asked to be kept updated about the timeliness of provision of cancer data (including COSD).

5. Report by DMEC

The report issued by the DMEC who met in 22nd Feb 2018 had been circulated.

6. Presentations about AgeX at Scientific Meetings

JP will be presenting information about the Trial at the Symposium Mammographicum conference in July 2018. The audience is people working in breast screening, mostly radiographers. The TMG agreed that since the trial started new radiologists and radiographers have been appointed and stressed the importance of keeping them informed about the trial.

HCP and RP have been working on a meta-analysis of breast screening around the world to present at the Early Breast Cancer Trialists' Collaborative Group meeting in April 2018.

The TMG agreed that more conference presentations and liaison with PHE were important.

7. Membership of TMG

It was agreed that all TMG members who had not attended 2 consecutive meetings would receive a letter to ask if they wished to continue as members of the TMG. If a meeting was missed for the third time, the member would generally be replaced on the committee. The TMG members agreed that it is essential to have Radiologist and Radiographer representation on the TMG. MR suggested that a second lay representative such as a patient representative was appointed and offered suggestions on where to find lay representation

It was suggested that Suzanne Wright (Head of Implementation & Training for PHE Screening) replace Margot Wheaton as a member of the TMG.

Action: KB contact MR to find and appoint a 2nd lay representative

Action: JP to invite Suzanne Wright to become a member of TMG

Action: JP/KB write to TMG members who have not attended for 2 consecutive meetings to ask if they wish to continue as members of the committee.