

NHSBSP AGE EXTENSION TRIAL

**Minutes of the Data Monitoring and Ethics Committee
9th January 2013
14:00 – 15:30
Cancer Epidemiology Unit, University of Oxford**

Present

Professor Janet Darbyshire (chair)
Dr Rosalind Given-Wilson
Professor Tom Meade
Dr Gillian Reeves
Ms Jenny Rusby

In attendance

Kath Moser
Professor Sir Richard Peto
Hayley Abbiss (notes)

Documents circulated in advance:

- Agenda
- Minutes of DMC meeting 8 November 2011
- Draft revised trial protocol (Dec 2012)
- Draft patient information leaflet (Dec 2012)
- Letter dated 10 Dec 2010, from Julietta Patnick, REC reference 10/H0710/9
- Letter of reply dated 16 Dec 2010, from NRES, REC reference 10/H0710/9

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 randomisation
- Article: The benefits and harms of breast cancer screening: an independent review

1. Welcome and introductions

Janet Darbyshire (JD) (chair) welcomed the members of the committee to the meeting. It was agreed that the first part of the meeting would be an open session.

2. Minutes of the last meeting and matters arising

The minutes of the last meeting (8th Nov 2011) were accepted as an accurate record of the meeting.

Matters arising:

Tom Meade (TM) queried the meaning of 'implied consent' on p4 of the minutes. It was clarified that if a woman attends for screening then this is taken as implied consent. The trial information leaflet will be sent out with the woman's invitation to attend.

Jenny Rusby (JR) commented that women who were randomised out would not be aware of this fact or that their data were being used. It was confirmed that the trial design, including this aspect, had received ethical approval. It was noted that of over 800,000 women randomised to date, only one objection had been raised. JD as chair of the DMEC had been informed of this objection.

The Trial Management Group (TMG) has discussed and agreed the appointment of Gillian Reeves (GR) to act as the independent statistician on the DMEC. It was clarified that Richard Peto (RP) was the Trial Statistician. He and Kath Moser (KM) will present trial data to the DMEC.

3. 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 patient information leaflet will form part of the protocol.

JD requested that her DMEC membership details be amended to remove 'statistician' and replace with 'epidemiologist'.

JD said she was comfortable with the proposal to invite the women randomised at ages 71-73 for further screening during their 70s but that this plan needed to be made clearer in the protocol. The protocol will not specify the upper age limit for screening invitations and therefore needs to be written flexibly.

TM drew attention to the confused wording in the primary analyses section and it was agreed that this should be made clearer.

The revised protocol will be sent to Ethics as part of a notice of substantial amendment. The protocol will also be submitted for publication in a journal.

Action: Any further comments regarding the protocol to be sent to KM by 18 January 2013. KM to amend protocol.

Action: KM to further revise the patient information leaflet and circulate for approval.

4. Trial update

RP highlighted the importance of the outcome of the Marmot Review 2012 which supported this trial and the continuation of the screening programme.

Subject to funding and ethical approval, the aim now is to continue screening the women who were randomised at ages 71-73 during their 70s. The TMG will look into the costs of this.

JD is keen that the investigators write a **statistical analysis plan** that documents the analyses they expect to be showing to the DMEC. In early meetings the DMEC will want to see process measures (as was done for the pilot study using NBSS clinical data).

Some discussion of this followed:

JD asked how inter-cluster correlation will be handled. RP said it can safely be ignored as the clusters are small. This can be mentioned in the statistical analysis plan.

Should the DMEC be comparing the data from the trial with the expected cancer detection rate? And what happens if the trial data show much lower rates? Futility of the trial?

RGW asked if the cause-distribution of deaths would be examined in women in both arms of the trial. Small numbers would be an issue here.

Are there reasons for stopping the trial for futility? For example, if uptake was extremely low?

What should the DMEC be looking for? What is their remit?

Action: Investigators to produce a statistical analysis plan.

Action: KM to send DMEC draft analyses two months before next DMEC meeting i.e. in Nov 2013 (for the Jan 2014 meeting). JD can then say if there is anything else they will require.

KM provided an update on the progress of the trial as at the end of December 2012. There have been delays in obtaining trial study population data due to software and other technical problems; however it is estimated that over 800,000 women have been randomised to date. Data on 0.5 million women will be extracted shortly and it will then be possible to say how many screening batches (clusters) have been randomised so far. It is hoped that some NBSS data on screening outcomes will be available in time for the next DMEC meeting; by definition, this will only be for women randomised for screening invitation. It is expected that all 72 breast screening units (BSUs) will be using digital equipment by the beginning of 2014.

5. Any other business

It was 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.

6. Date of next meeting

January 2014, date to be confirmed.

Several members of the DMEC proposed that the next meeting is held in London.

Action: KM/HA to email DMEC with proposed date.

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RP, KM and HA left the meeting at this point and a closed session was held.

Draft statement from the DMEC Closed Session to the Trial Management Group

“The DMEC is encouraged by the progress to date in implementing the trial, and will be interested to see data from the trial at our next meeting, particularly on uptake of screening.

It will be helpful to see an outline of the intended monitoring analyses before the next meeting, as discussed in the Open Session, and the draft Statistical Analysis Plan although we appreciate that this will evolve over time until the database is locked for the final analysis.”