NRES Committee London - Harrow
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15 March 2013

Ms Kath Moser
Cancer Epidemiology Unit
Richard Doll Building
Roosevelt Drive
Oxford
OX3 7LF

Dear Ms Moser

Study title:	**EVALUATING THE NET EFFECTS OF EXTENDING THE AGE RANGE FOR BREAST SCREENING IN THE NHS BREAST SCREENING PROGRAMME IN ENGLAND FROM 50-70 YEARS TO 47-73 YEARS**
REC reference:	**10/H0710/9**
Amendment number:	**1**
Amendment date:	**14 February 2013**
IRAS project ID:	**29856**

The above amendment was reviewed by the Sub-Committee in correspondence.

Ethical opinion

The members of the Committee taking part in the review decided that they could not give a favourable ethical opinion of the amendment, for the following reasons:

This amendment seeks to shift the emphasis from a pragmatic opportunity (while resources were being expanded) to compare women who were or were not invited for breast screening in the extended age range, almost a service evaluation, to a randomised trial. The name of the study has changed from evaluation to randomised to reflect this intention.

Ethical concerns

1) Participants in a Control Group who do not know that they are in such a group, as randomisation is done before women are invited for screening:

Women should be randomised after agreeing to be included in a trial of screening in the extended ages. A strong case would have to be made to not arrange the trial in this way.

The original justification for having a group that did not receive screening was that this would have to happen to some women anyway, as on a practical level, there was not the capacity to offer such screening to all in the age extension group. However, as now the researchers are offering more than one additional three yearly scan to those in the screening group, this lack of resources argument loses its validity, as the screening and

control groups were going to be selected in batches of 100 within the same geographical area.
The researchers had previously said that any woman could request a mammogram, thus no one who wanted screening would in fact be excluded, but the Substantial Amendment submission states that only those patients in the areas that are taking part in the age extension study can ask for a mammogram every 3 years after the age of 70.

However, the standard screening leaflet says that any woman over 70 can request screening every 3 years, and there is no geographical qualification required - this point also needs clarification.

It may be a reasonable approach for those over 70 years as they will have been aware of the screening program and might have received a screening leaflet, but the younger women at 47 will not be aware that they might be able to ask for an early screening visit, and this is not even mentioned as an option in the standard leaflet either.

The Committee's concern is that the control group do not know that they are in such a group, that is being used to compare their outcomes with others who are having additional screening. It is not sufficient to say that they can request screening – how would they know as they would not have received any breast screening leaflet in recent years let alone the recent more informative leaflet?

2) There is a lack of equipoise in the approach as to the value of screening in the age extension group:

The standard leaflet is for women aged 50yrs to 70yrs and does reflect current evidence and the view of the Marmott report which concluded that screening does offer benefit.
The researchers have stated that the study is to answer the question regarding the value of screening at the edges of the current screening age range, but still gives these women the standard leaflet, albeit with an extra sheet for those in the age extension study. This extra sheet does not demonstrate equipoise or explain the reason for investigating the pros and cons of screening at the extended age range; it just says that 'we need more evidence for benefit at the extremes of age' and there is no mention of the disadvantages.
This additional leaflet needs revising.

3) No consent form has been provided:

Verbal consent or attendance is used for the routine breast screening and might be suitable for this study, if the additional information sheet is expanded. However, the Committee do think that first, the use of randomisation before obtaining consent needs to be resolved and written consent to allow randomisation is strongly preferable.

I regret to inform you that the amendment is therefore not approved. The study should continue in accordance with the documentation previously approved by the Committee.

If you would find it helpful to discuss any of the matters raised above or seek further clarification from a member of the Committee, you are welcome to contact Libby Watson, Committee Co-ordinator.

Options for further ethical review

1. **Modifying the amendment**

You may modify or adapt the amendment, taking into account the Committee's concerns. Modified amendments should be submitted on the standard Notice of Amendment form.

The form should indicate that it is a modification of the above amendment. Please ensure that you resubmit those documents that have been added or revised and need to be reviewed. There is no requirement to *resubmit* any documents that were submitted with the original amendment and are still relevant to it but have not changed. However, the standard Notice of Amendment form must *list* all documents that are still relevant to the amendment, clearly indicating those which are new or have been modified and those which remain unchanged.

The REC must receive a revised Notice of Amendment form at least 14 days before you plan to implement the amendment. The Committee will then have 14 days from the date of receiving the notice in which to notify you that the amendment is rejected, otherwise the amendment may be implemented.

2. Appeal against the opinion

Alternatively, you may appeal against the decision of the Committee by notifying the relevant Research Ethics Service appeals manager (see below) in writing within 90 days of the date of this letter, setting out your representations with respect to the opinion. The appeal would be based on the notice of substantial amendment and supporting documentation reviewed previously, without revision. If the appeal is allowed, the amendment will be reviewed again at the next scheduled full meeting of this Committee, taking into account your representations together with the comments of a second REC on the amendment. The second REC will be appointed by the appeals manager.

You will be notified of the arrangements for the meeting of the REC and will be able to attend and/or make further written representations if you wish to do so.

The appeals manager is:

Joan Kirkbride
Director of Operations
National Research Ethics Service

Email: joan.kirkbride@nhs.net

Documents reviewed

The documents reviewed at the meeting were:

Document	Version	Date
Participant Information Sheet	2	08 February 2013
Protocol	2	08 February 2013
Notice of Substantial Amendment (non-CTIMPs)	1	14 February 2013

Membership of the Committee

The members of the Committee who took part in the review are listed on the attached sheet.

Statement of compliance

The Committee is constituted in accordance with the Governance Arrangements for Research Ethics Committees and complies fully with the Standard Operating Procedures for Research Ethics Committees in the UK.

We are pleased to welcome researchers and R & D staff at our NRES committee members' training days – see details at http://www.hra.nhs.uk/hra-training/

10/H0710/9:	**Please quote this number on all correspondence**

Yours sincerely

pp.

Dr Jan Downer
Chair

E-mail: nrescommittee.london-harrow@nhs.net

Enclosures: *List of names and professions of members who took part in the review*

Copy to: *Ms Heather House, Clinical Trials & Reserach Governance*
Professor Julietta Patnick, NHS Cancer Screening Programmes

NRES Committee London - Harrow

Attendance at Sub-Committee of the REC meeting by correspondence

Committee Members:

Name	*Profession*	*Present*
Dr Jan Downer - Chair	Consultant Anaesthetist	Yes
Dr Sanober Haq	Doctor of Medicine	Yes