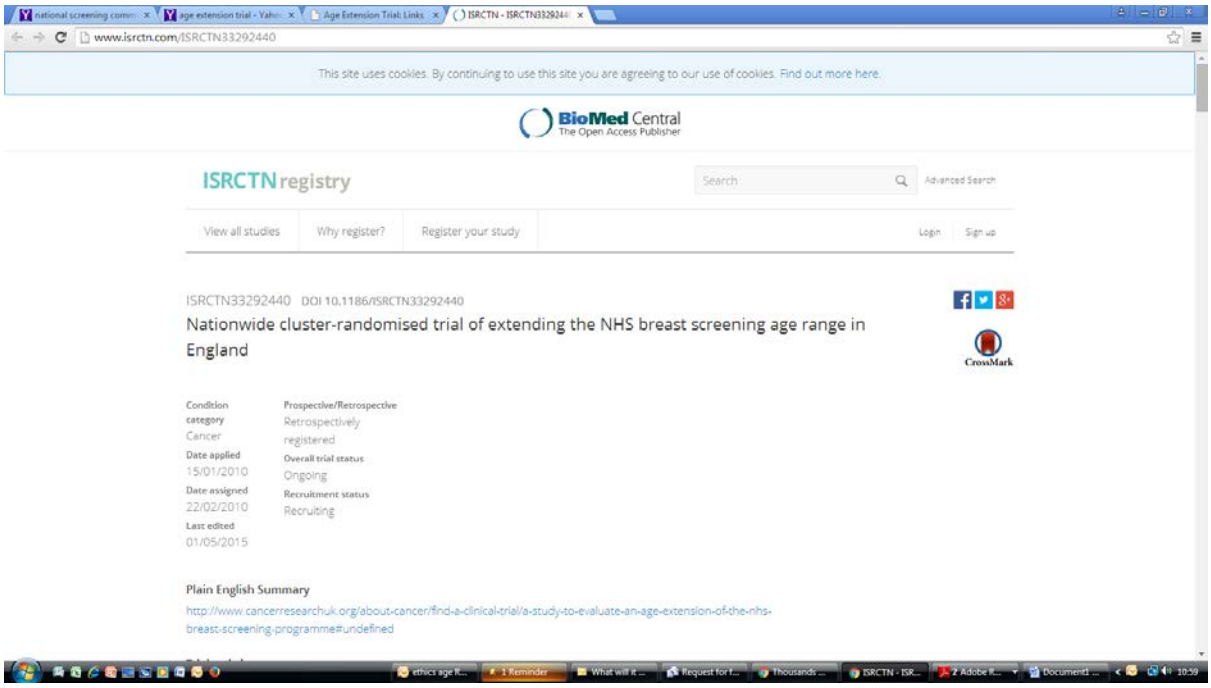
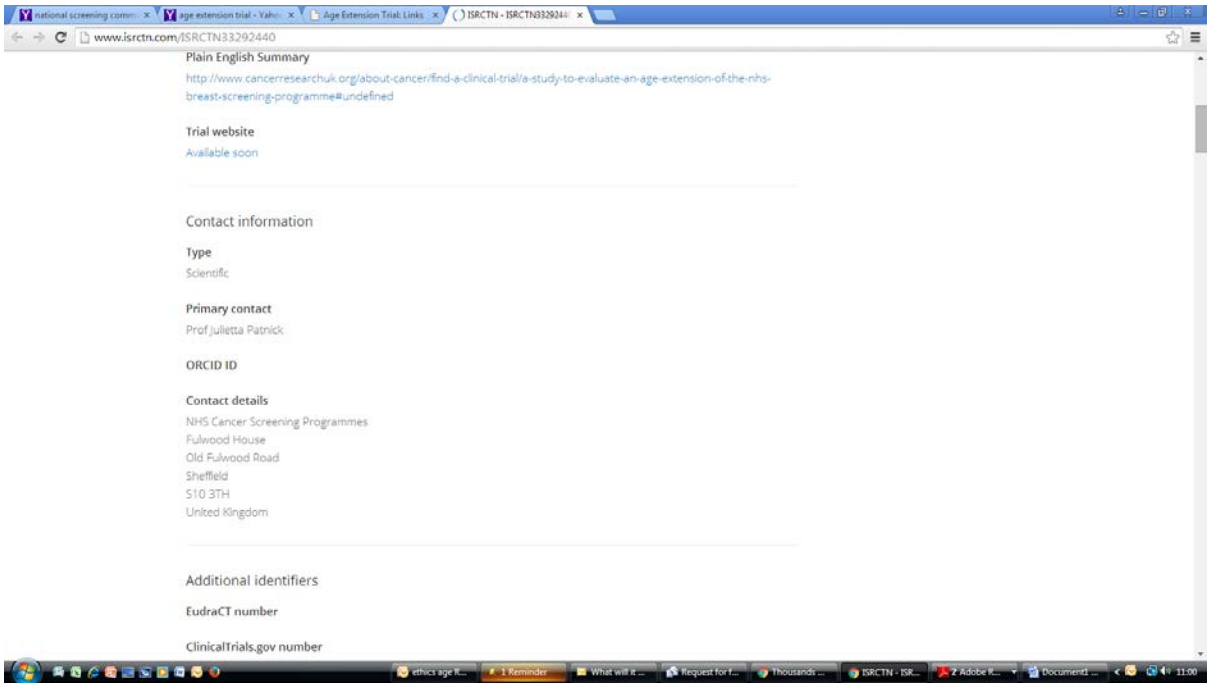
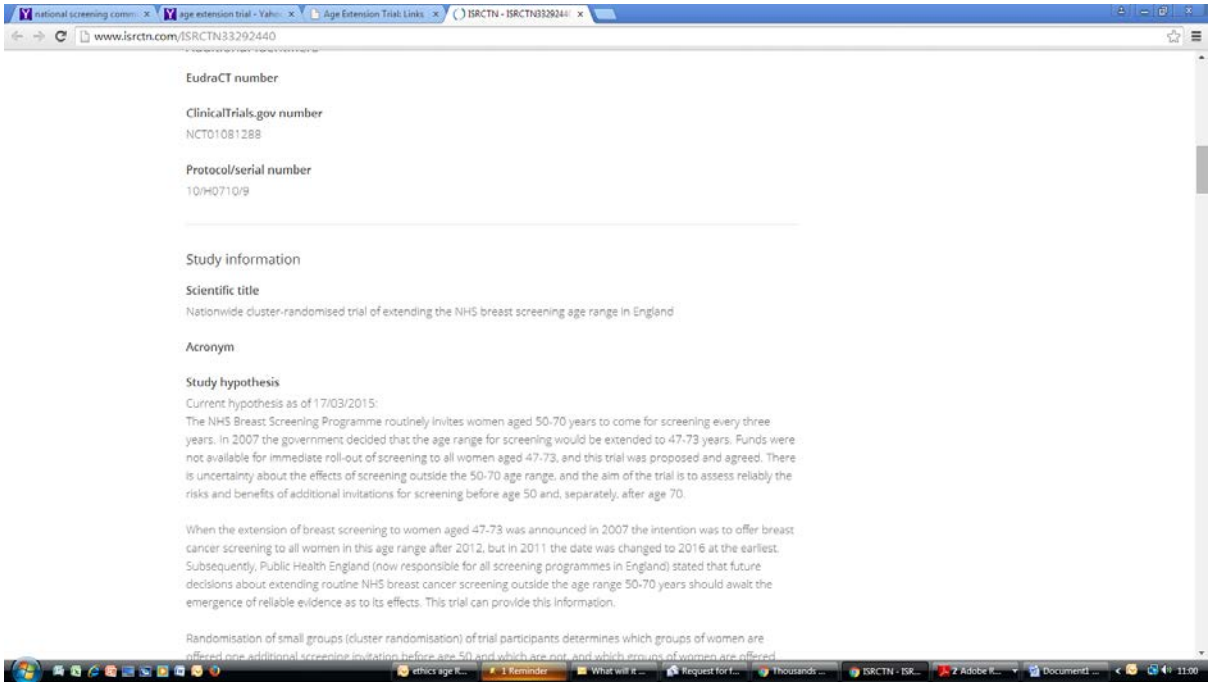
Screen shots 2 nov 2015-11-02







www.isrctn.com/ISRCTN33292440

EudraCT number

ClinicalTrials.gov number
NCT01081288

Protocol/serial number
10/H0710/9

Study information

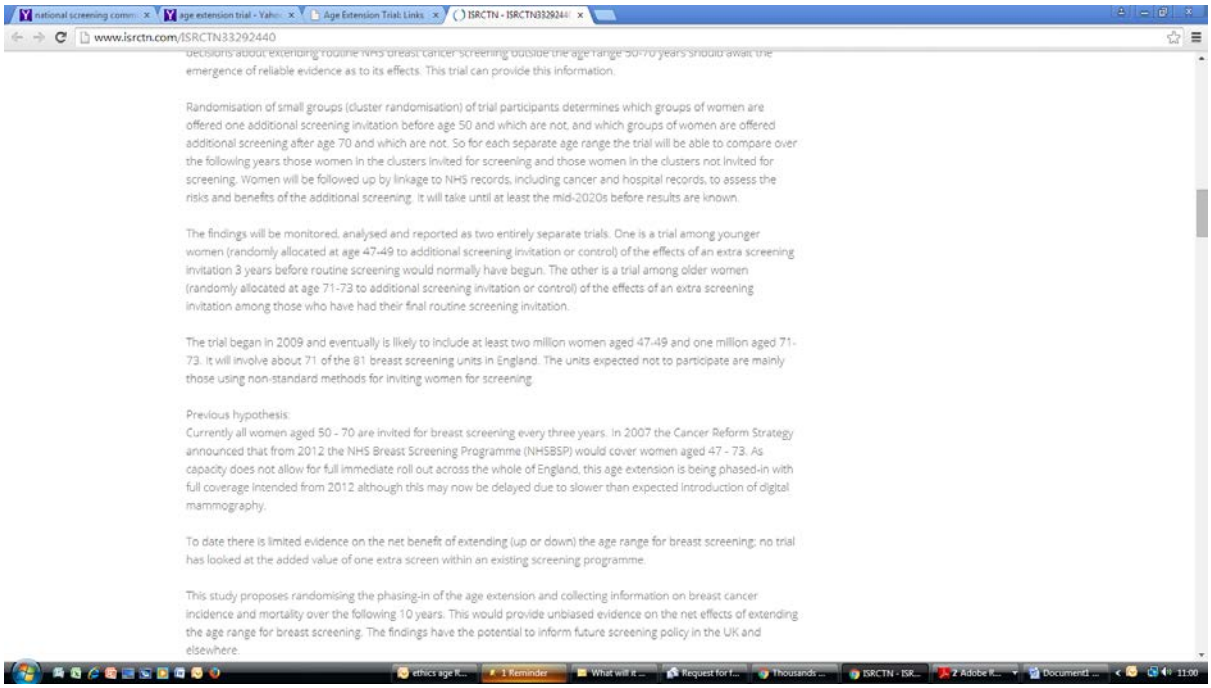
Scientific title
Nationwide cluster-randomised trial of extending the NHS breast screening age range in England

Acronym

Study hypothesis
Current hypothesis as of 17/03/2015:
The NHS Breast Screening Programme routinely invites women aged 50-70 years to come for screening every three years. In 2007 the government decided that the age range for screening would be extended to 47-73 years. Funds were not available for immediate roll-out of screening to all women aged 47-73, and this trial was proposed and agreed. There is uncertainty about the effects of screening outside the 50-70 age range, and the aim of the trial is to assess reliably the risks and benefits of additional invitations for screening before age 50 and, separately, after age 70.

When the extension of breast screening to women aged 47-73 was announced in 2007 the intention was to offer breast cancer screening to all women in this age range after 2012, but in 2011 the date was changed to 2016 at the earliest. Subsequently, Public Health England (now responsible for all screening programmes in England) 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. This trial can provide this information.

Randomisation of small groups (cluster randomisation) of trial participants determines which groups of women are offered one additional screening invitation before age 50 and which are not, and which groups of women are offered



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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. This trial can provide this information.

Randomisation of small groups (cluster randomisation) of trial participants determines which groups of women are offered one additional screening invitation before age 50 and which are not, and which groups of women are offered additional screening after age 70 and which are not. So for each separate age range the trial will be able to compare over the following years those women in the clusters invited for screening and those women in the clusters not invited for screening. Women will be followed up by linkage to NHS records, including cancer and hospital records, to assess the risks and benefits of the additional screening. It will take until at least the mid-2020s before results are known.

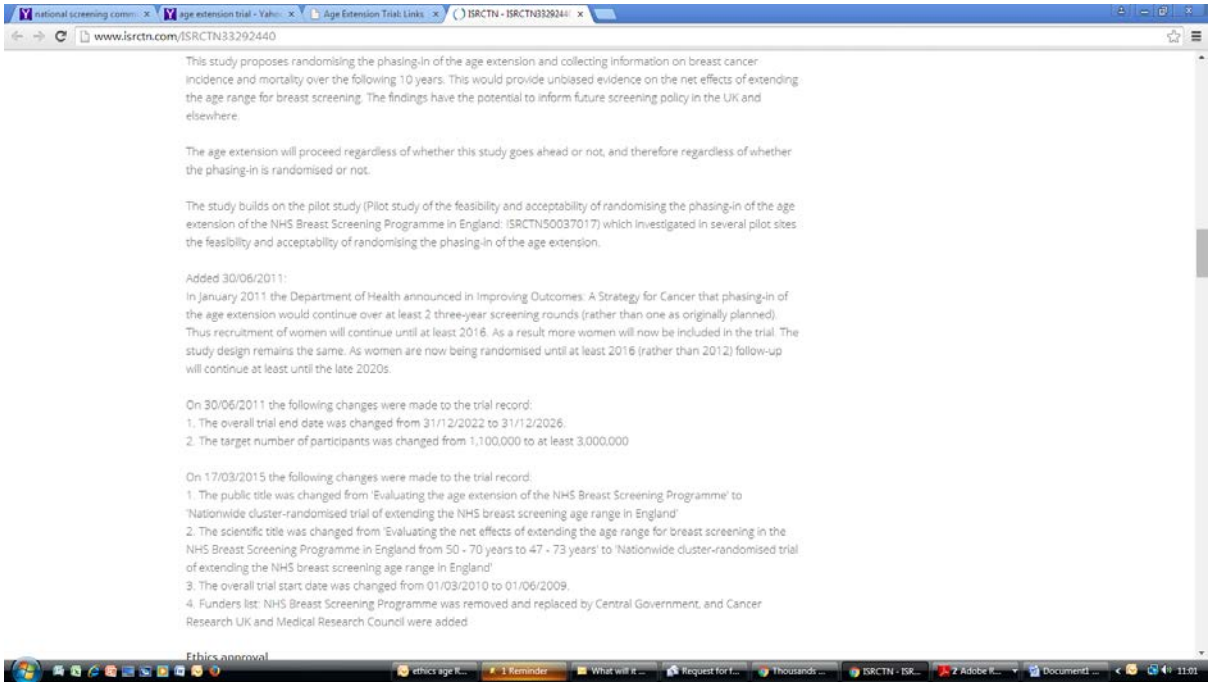
The findings will be monitored, analysed and reported as two entirely separate trials. One is a trial among younger women (randomly allocated at age 47-49 to additional screening invitation or control) of the effects of an extra screening invitation 3 years before routine screening would normally have begun. The other is a trial among older women (randomly allocated at age 71-73 to additional screening invitation or control) of the effects of an extra screening invitation among those who have had their final routine screening invitation.

The trial began in 2009 and eventually is likely to include at least two million women aged 47-49 and one million aged 71-73. It will involve about 71 of the 81 breast screening units in England. The units expected not to participate are mainly those using non-standard methods for inviting women for screening.

Previous hypothesis:
Currently all women aged 50 - 70 are invited for breast screening every three years. In 2007 the Cancer Reform Strategy announced that from 2012 the NHS Breast Screening Programme (NHSBSP) would cover women aged 47 - 73. As capacity does not allow for full immediate roll out across the whole of England, this age extension is being phased-in with full coverage intended from 2012 although this may now be delayed due to slower than expected introduction of digital mammography.

To date there is limited evidence on the net benefit of extending (up or down) the age range for breast screening; no trial has looked at the added value of one extra screen within an existing screening programme.

This study proposes randomising the phasing-in of the age extension and collecting information on breast cancer incidence and mortality over the following 10 years. This would provide unbiased evidence on the net effects of extending the age range for breast screening. The findings have the potential to inform future screening policy in the UK and elsewhere.



This study proposes randomising the phasing-in of the age extension and collecting information on breast cancer incidence and mortality over the following 10 years. This would provide unbiased evidence on the net effects of extending the age range for breast screening. The findings have the potential to inform future screening policy in the UK and elsewhere.

The age extension will proceed regardless of whether this study goes ahead or not, and therefore regardless of whether the phasing-in is randomised or not.

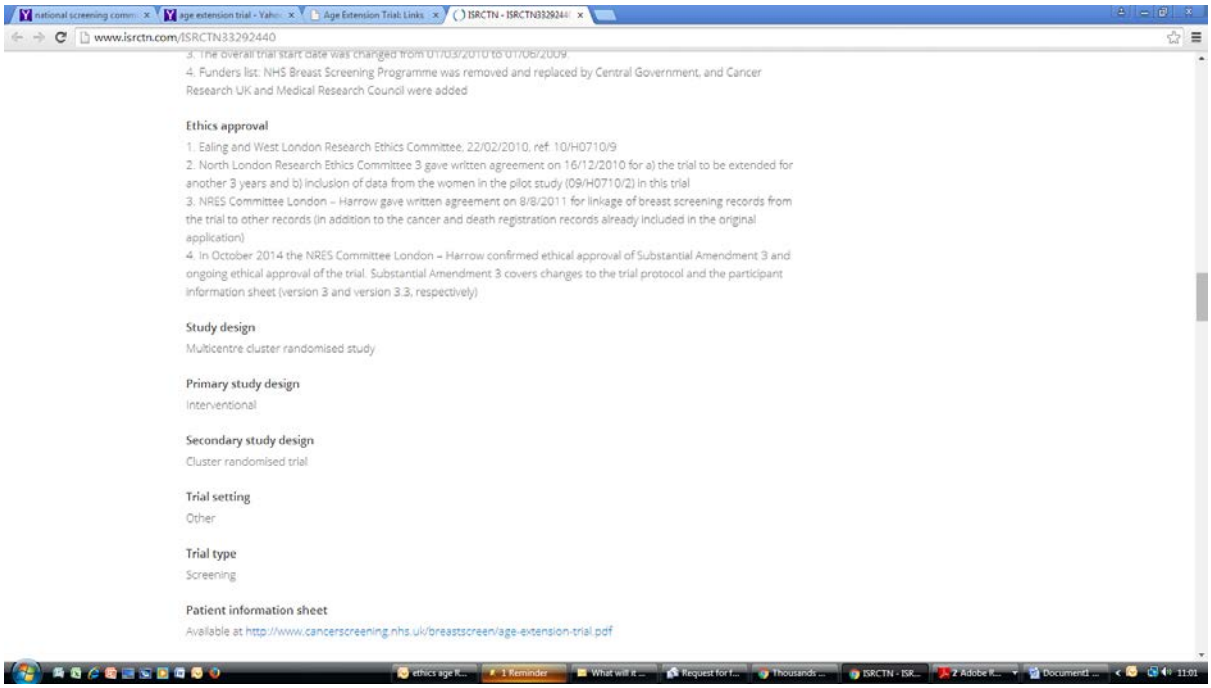
The study builds on the pilot study (Pilot study of the feasibility and acceptability of randomising the phasing-in of the age extension of the NHS Breast Screening Programme in England: ISRCTN50037017) which investigated in several pilot sites the feasibility and acceptability of randomising the phasing-in of the age extension.

Added 30/06/2011:
In January 2011 the Department of Health announced in Improving Outcomes: A Strategy for Cancer that phasing-in of the age extension would continue over at least 2 three-year screening rounds (rather than one as originally planned). Thus recruitment of women will continue until at least 2016. As a result more women will now be included in the trial. The study design remains the same. As women are now being randomised until at least 2016 (rather than 2012) follow-up will continue at least until the late 2020s.

On 30/06/2011 the following changes were made to the trial record:
1. The overall trial end date was changed from 31/12/2022 to 31/12/2026.
2. The target number of participants was changed from 1,100,000 to at least 3,000,000

On 17/03/2015 the following changes were made to the trial record:
1. The public title was changed from 'Evaluating the age extension of the NHS Breast Screening Programme' to 'Nationwide cluster-randomised trial of extending the NHS breast screening age range in England'
2. The scientific title was changed from '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' to 'Nationwide cluster-randomised trial of extending the NHS breast screening age range in England'
3. The overall trial start date was changed from 01/03/2010 to 01/06/2009.
4. Funders list: NHS Breast Screening Programme was removed and replaced by Central Government, and Cancer Research UK and Medical Research Council were added

Ethics approval



3. The overall trial start date was changed from 01/03/2010 to 01/06/2009.
4. Funders list: NHS Breast Screening Programme was removed and replaced by Central Government, and Cancer Research UK and Medical Research Council were added

Ethics approval

1. Ealing and West London Research Ethics Committee, 22/02/2010, ref: 10/H0710/9
2. North London Research Ethics Committee 3 gave written agreement on 16/12/2010 for a) the trial to be extended for another 3 years and b) inclusion of data from the women in the pilot study (09/H0710/2) in this trial
3. NRES Committee London – Harrow gave written agreement on 8/8/2011 for linkage of breast screening records from the trial to other records (in addition to the cancer and death registration records already included in the original application)
4. In October 2014 the NRES Committee London – Harrow confirmed ethical approval of Substantial Amendment 3 and ongoing ethical approval of the trial. Substantial Amendment 3 covers changes to the trial protocol and the participant information sheet (version 3 and version 3.3, respectively)

Study design

Multicentre cluster randomised study

Primary study design

Interventional

Secondary study design

Cluster randomised trial

Trial setting

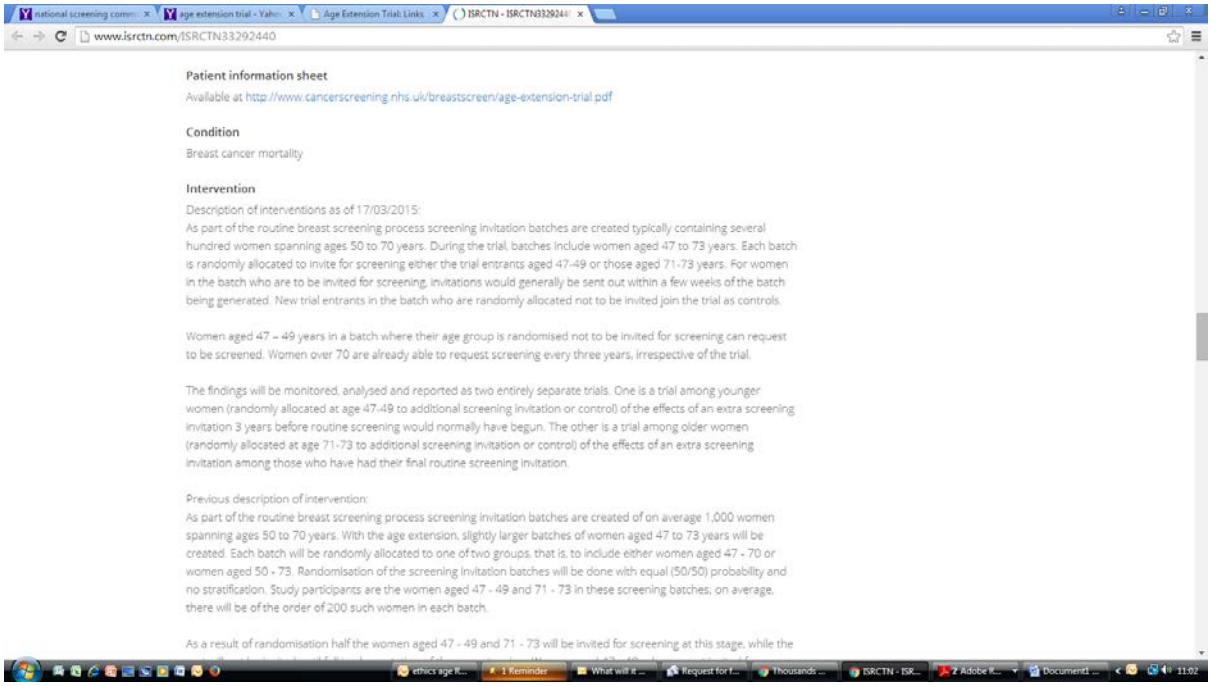
Other

Trial type

Screening

Patient information sheet

Available at http://www.cancerscreening.nhs.uk/breastscreen/age-extension-trial.pdf



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Patient information sheet

Available at http://www.cancerscreening.nhs.uk/breastscreen/age-extension-trial.pdf

Condition

Breast cancer mortality

Intervention

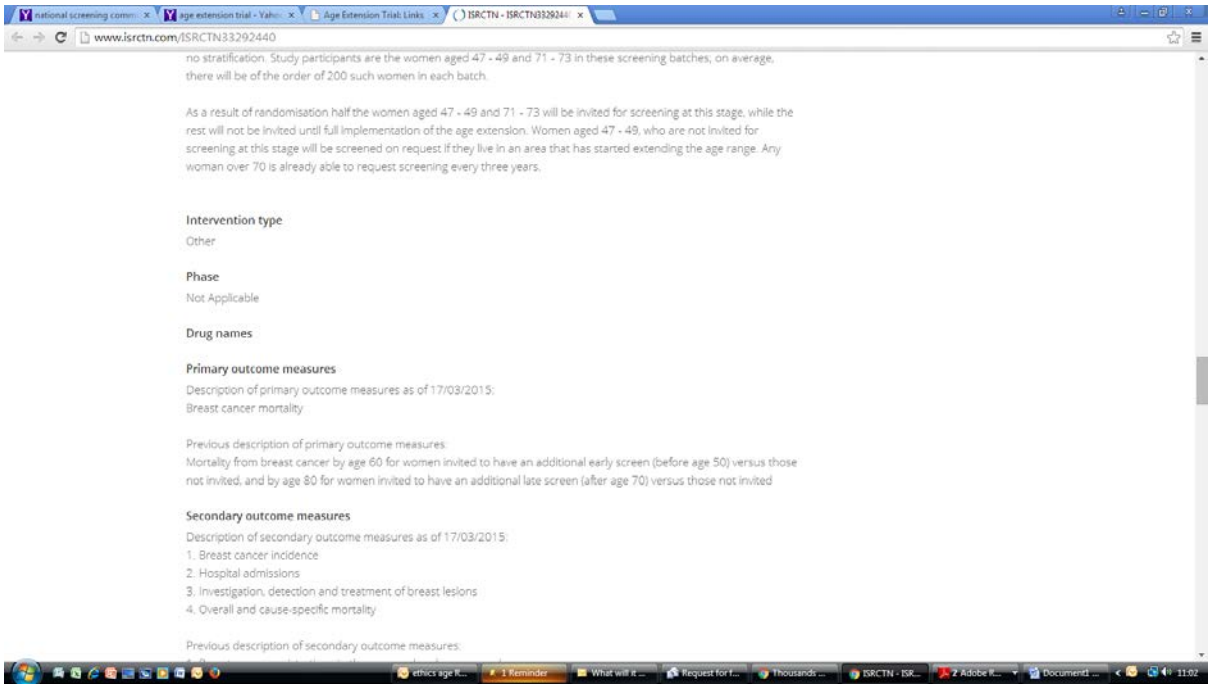
Description of interventions as of 17/03/2015:
As part of the routine breast screening process screening invitation batches are created typically containing several hundred women spanning ages 50 to 70 years. During the trial, batches include women aged 47 to 73 years. Each batch is randomly allocated to invite for screening either the trial entrants aged 47-49 or those aged 71-73 years. For women in the batch who are to be invited for screening, invitations would generally be sent out within a few weeks of the batch being generated. New trial entrants in the batch who are randomly allocated not to be invited join the trial as controls.

Women aged 47 – 49 years in a batch where their age group is randomised not to be invited for screening can request to be screened. Women over 70 are already able to request screening every three years, irrespective of the trial.

The findings will be monitored, analysed and reported as two entirely separate trials. One is a trial among younger women (randomly allocated at age 47-49 to additional screening invitation or control) of the effects of an extra screening invitation 3 years before routine screening would normally have begun. The other is a trial among older women (randomly allocated at age 71-73 to additional screening invitation or control) of the effects of an extra screening invitation among those who have had their final routine screening invitation.

Previous description of intervention:
As part of the routine breast screening process screening invitation batches are created of on average 1,000 women spanning ages 50 to 70 years. With the age extension, slightly larger batches of women aged 47 to 73 years will be created. Each batch will be randomly allocated to one of two groups, that is, to include either women aged 47 - 70 or women aged 50 - 73. Randomisation of the screening invitation batches will be done with equal (50/50) probability and no stratification. Study participants are the women aged 47 - 49 and 71 - 73 in these screening batches, on average, there will be of the order of 200 such women in each batch.

As a result of randomisation half the women aged 47 - 49 and 71 - 73 will be invited for screening at this stage, while the



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no stratification. Study participants are the women aged 47 - 49 and 71 - 73 in these screening batches, on average, there will be of the order of 200 such women in each batch.

As a result of randomisation half the women aged 47 - 49 and 71 - 73 will be invited for screening at this stage, while the rest will not be invited until full implementation of the age extension. Women aged 47 - 49, who are not invited for screening at this stage will be screened on request if they live in an area that has started extending the age range. Any woman over 70 is already able to request screening every three years.

Intervention type

Other

Phase

Not Applicable

Drug names

Primary outcome measures

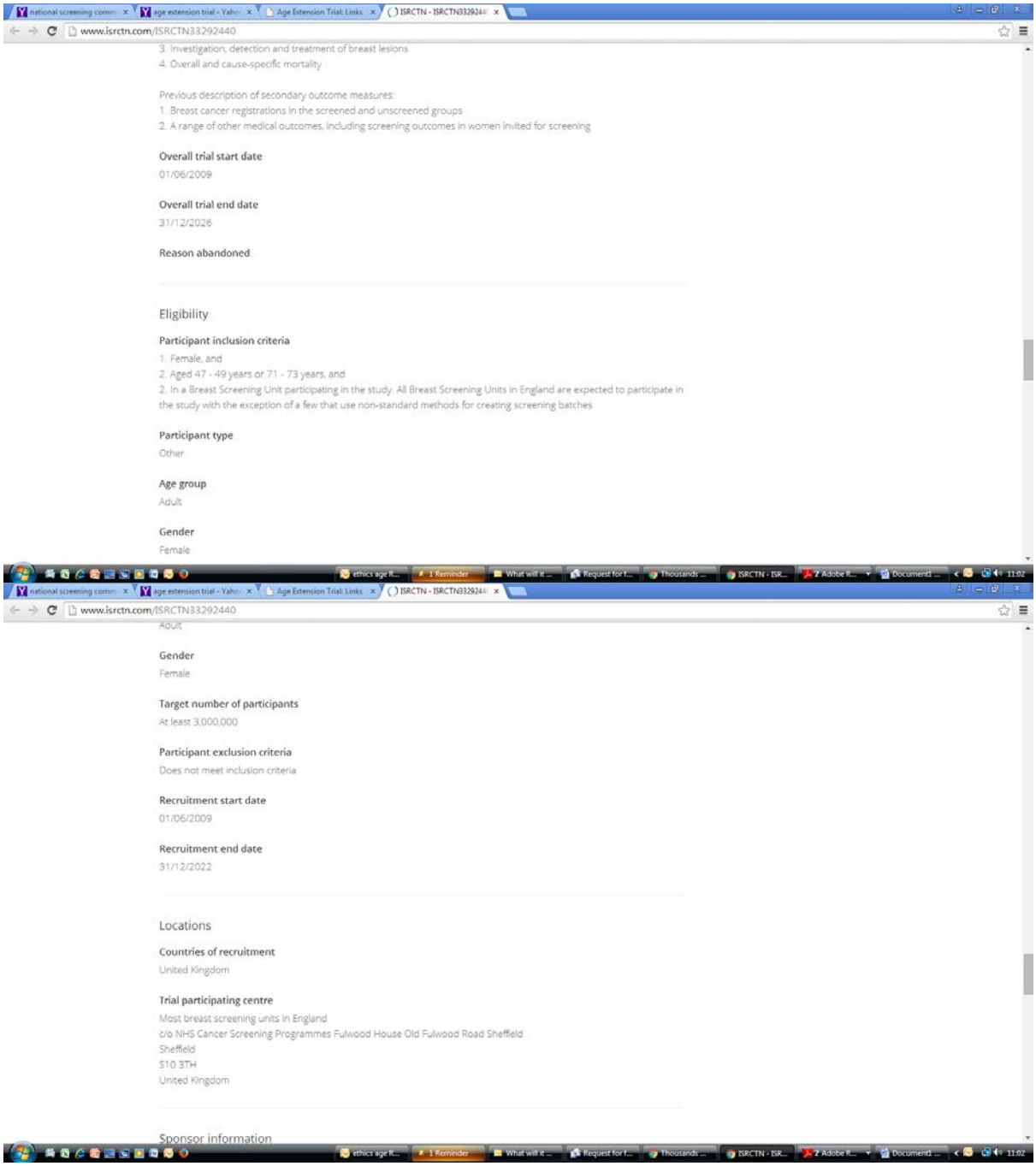
Description of primary outcome measures as of 17/03/2015:
Breast cancer mortality

Previous description of primary outcome measures:
Mortality from breast cancer by age 60 for women invited to have an additional early screen (before age 50) versus those not invited, and by age 80 for women invited to have an additional late screen (after age 70) versus those not invited

Secondary outcome measures

Description of secondary outcome measures as of 17/03/2015:
1. Breast cancer incidence
2. Hospital admissions
3. Investigation, detection and treatment of breast lesions
4. Overall and cause-specific mortality

Previous description of secondary outcome measures: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3. Investigation, detection and treatment of breast lesions
4. Overall and cause-specific mortality
Previous description of secondary outcome measures:
1. Breast cancer registrations in the screened and unscreened groups
2. A range of other medical outcomes, including screening outcomes in women invited for screening
Overall trial start date
01/06/2009
Overall trial end date
31/12/2026
Reason abandoned
Eligibility
Participant inclusion criteria
1. Female, and
2. Aged 47 - 49 years or 71 - 73 years, and
2. In a Breast Screening Unit participating in the study. All Breast Screening Units in England are expected to participate in the study with the exception of a few that use non-standard methods for creating screening batches
Participant type
Other
Age group
Adult
Gender
Female
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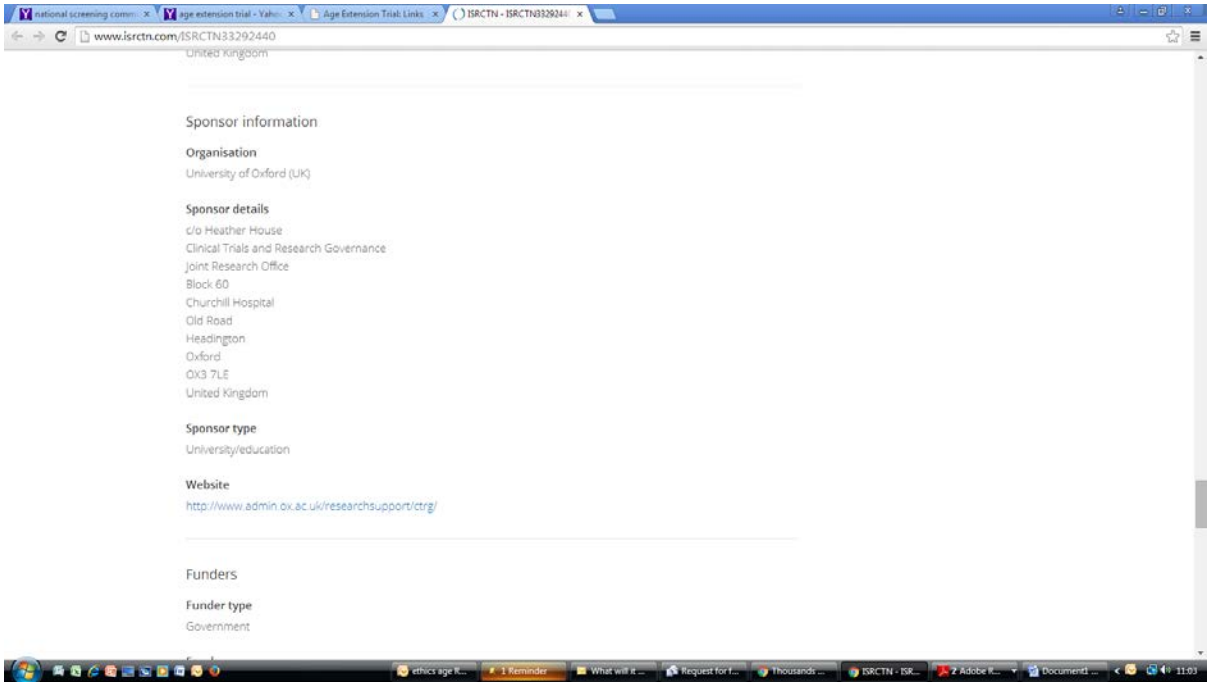
Adult
Gender
Female
Target number of participants
At least 3,000,000
Participant exclusion criteria
Does not meet inclusion criteria
Recruitment start date
01/06/2009
Recruitment end date
31/12/2022
Locations
Countries of recruitment
United Kingdom
Trial participating centre
Most breast screening units in England
c/o NHS Cancer Screening Programmes Fulwood House Old Fulwood Road Sheffield
Sheffield
S10 3TH
United Kingdom
Sponsor information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United Kingdom
Sponsor information
Organisation
University of Oxford (UK)
Sponsor details
c/o Heather House
Clinical Trials and Research Governance
Joint Research Office
Block 60
Churchill Hospital
Old Road
Headington
Oxford
OX3 7LE
United Kingdom
Sponsor type
University/education
Website
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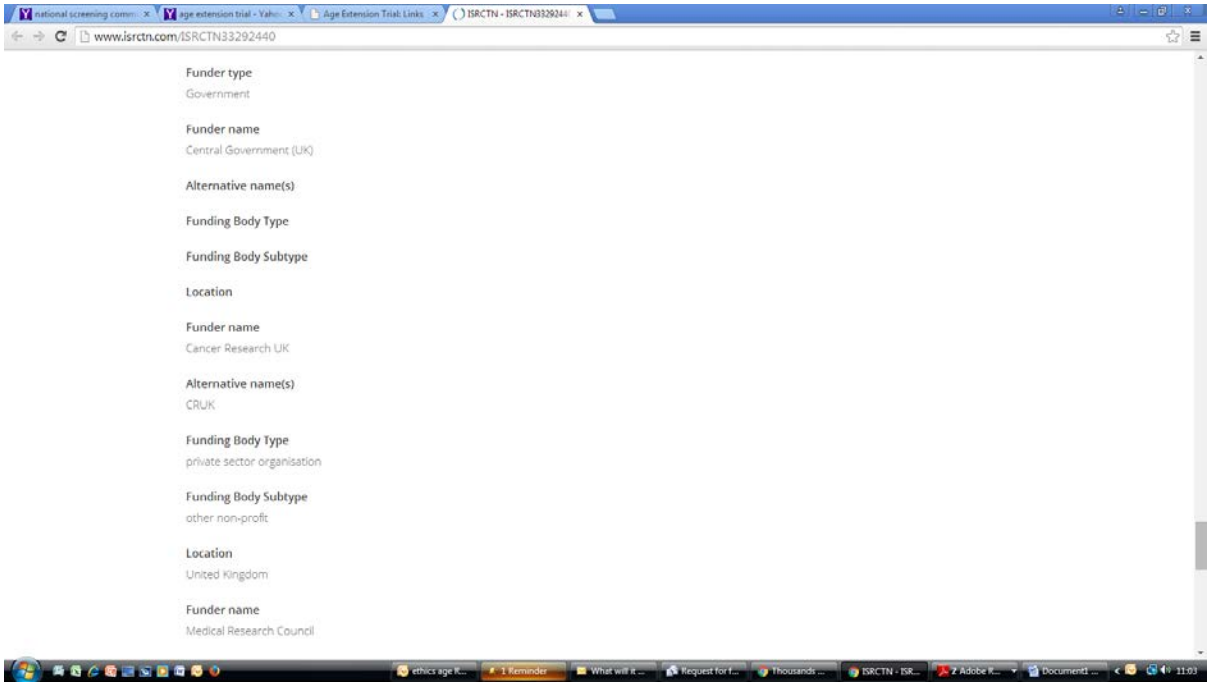
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Funder type
Government
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Alternative name(s)
Funding Body Type
Funding Body Subtype
Location
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Cancer Research UK
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CRUK
Funding Body Type
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Funding Body Subtype
other non-profit
Location
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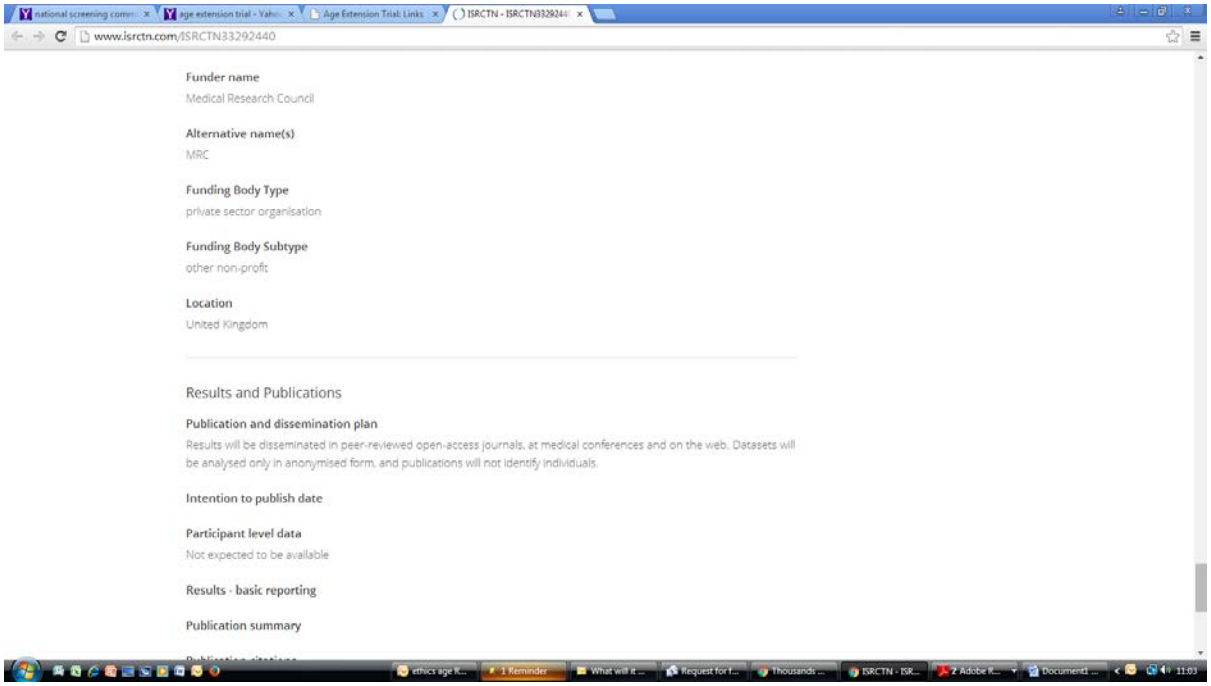
Funder name
Medical Research Council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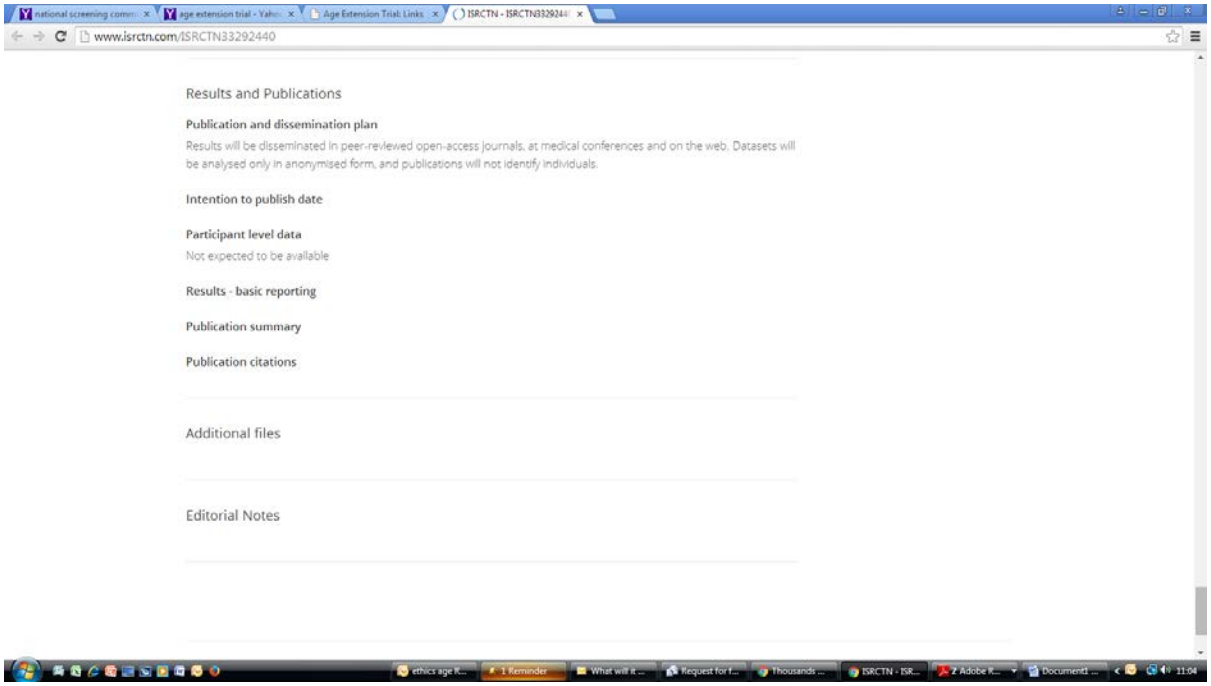
Funder name
Medical Research Council
Alternative name(s)
MRC
Funding Body Type
private sector organisation
Funding Body Subtype
other non-profit
Location
United Kingdom
Results and Publications
Publication and dissemination plan
Results will be disseminated in peer-reviewed open-access journals, at medical conferences and on the web. Datasets will be analysed only in anonymised form, and publications will not identify individuals.
Intention to publish date
Participant level data
Not expected to be available
Results - basic reporting
Publication summary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Results and Publications
Publication and dissemination plan
Results will be disseminated in peer-reviewed open-access journals, at medical conferences and on the web. Datasets will be analysed only in anonymised form, and publications will not identify individuals.
Intention to publish date
Participant level data
Not expected to be available
Results - basic reporting
Publication summary
Publication citations
Additional files
Editorial Notes