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

PROTOCOL FOR THE STUDY

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SUMMARY

Currently all women are invited for breast screening between the ages of 50 and 70. The 2007 Cancer Reform Strategy announced that from 2012 the NHS Breast Screening Programme (NHSBSP) would be extended to cover women between the ages of 47 and 73. As capacity does not allow for full immediate roll out across the whole of England, the age extension is being phased-in with full coverage from 2012.

The purpose of this study is to evaluate the net effects of extending the age range for breast screening in the NHSBSP in England from 50-70 years to 47-73 years. To date there is limited evidence on the net benefit of extending the age range for breast screening, nor on whether an extra screen at younger or older ages is more worthwhile. Randomising the phasing-in would provide unbiased evidence on this.

This study will randomise the phasing-in of the age extension and collect information on breast cancer incidence and mortality over the following ten years. The findings have the potential to inform future screening policy in the UK and elsewhere. If the study is not carried out, this unique opportunity of establishing the risks and benefits of adding an extra early and an extra late screen to an existing screening programme will be missed.

Aim

To evaluate 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

Background

The NHS Breast Screening Programme (NHSBSP) was established by the Department of Health in 1988 in response to the recommendations of the Forrest working group which had been set up to consider whether or not to implement a population screening programme in the UK. It was the first programme of its kind in the world. It began inviting women for screening in 1988 and national coverage was achieved by mid 1990s. Currently free breast screening is offered every three years to women aged between 50 and 70. Around 1.5 million women are screened in the UK each year.

The NHSBSP is nationally coordinated. It sets national standards which are monitored through a national quality assurance network. For England, there is a national coordination office, based in Sheffield, and an advisory committee which oversees the programme and reports to government ministers. There are around 80 breast screening units across the UK, each inviting eligible women through their GP practices.

Rationale

In 2007 the Cancer Reform Strategy (1) announced that from 2012 the NHSBSP would be extended to cover women between the ages of 47 and 73. This means that women will get 2 extra screening invitations in their lifetime with the first one before they are age 50. 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 and few trials have looked at women in their 70s at all, let alone at the effect of one extra screen when they have already had up to seven previous screens.

Randomising the phasing-in provides a unique opportunity to obtain unbiased evidence on the net effects of extending the age range for breast screening and the findings have the potential to inform 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 subsequent years thereby filling this gap in the evidence base. Additionally, by collecting data on breast cancer incidence in the groups invited and not invited for screening, it will generate information that can be used to evaluate the harms and benefits of breast screening, and thereby look into recent criticisms of breast screening, so-called overdiagnosis and associated harms (2).

The study builds on the pilot study which is investigating the feasibility and acceptability of randomising the phasing-in of the age extension in several pilot sites and demonstrated no significant problems of feasibility or acceptability. The pilot has paved the way for randomised phasing-in of the age extension

across the rest of England and the information gathered during the pilot will inform the planning and implementation of this process.

Study outline

The study aims to evaluate the risks and benefits of extending the age range for breast screening in the NHS Breast Screening Programme in England from 50-70 years to 47-73 years. This will be done by randomising the phasing-in of the age extension and collecting information on subsequent breast cancer incidence and mortality over the following years. As it takes many years for any reduction in mortality associated with screening to become evident, follow-up for at least 10 years is needed to ensure that any benefit from screening will not be missed. If randomised phasing-in is carried out 2010-12 then follow-up will be needed until 2022.

As it is government policy, the age extension will be phased in over the next 3 to 4 years regardless of the study outlined here. This study, however, proposes the phasing-in is carried out in a randomised way, and that women are subsequently followed up for breast cancer incidence and mortality. Other than the randomisation, all other aspects of screening will be done in exactly the same way as always in the NHSBSP, following all NHSBSP routine permissions and procedures.

Study sites

The study will take place in all screening centres in England with the exception of a handful of centres that use a non-standard method of inviting women into screening batches. Sites included in the pilot study will also be part of this study.

Study participants

As part of the routine breast screening process, the NHAIS system creates screening invitation batches of on average 1,000 women spanning ages 50 to 70 years. Invitations to attend for breast screening are sent out at the same time to all the women in such a batch.

In this study slightly larger batches will be created of women aged 47 to 73 years. Each batch will be randomly allocated to one of two groups, that is, to include ages 47 to 70 years or ages 50 to 73 years, instead of, as now, 50 to 70 years. Randomisation will be by cluster not by individual, where the cluster is the screening invitation batch. The randomisation of the screening invitation batches will be done with equal (50/50) probability and no stratification.

The study participants are the women aged 47-49 and 71-73 in these screening batches. In other words, both the women randomised for screening invitation and those randomised not to get a screening invitation form the study population. On average, there will be of the order of 200 such women in each batch.

Women aged 50 to 70 are not study participants as they will be unaffected by the randomisation process; they are in the age group already eligible for routine

screening, and their invitations for screening will continue as normal regardless of the age extension.

Women aged 47-49 who are in a screening batch selected for randomisation but who are not invited for screening (because in that batch the 71-73 year age group is randomised for screening invitation) can request to be screened 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.

Study materials
All women who are invited for screening, regardless of their age, will receive an information leaflet about the study enclosed with their invitation for screening and the standard NHS breast screening information booklet ("The Facts").

Data collection and storage
Relevant data items held on the National Breast Screening System (NBSS) will be downloaded annually from each screening centre for all study participants. This will take place during 2010-12 as the age extension is phased-in. Data items will include the patient identifiers needed for tracing women on the NHS Central Register (NHSCR) and for women invited for screening, information on screening, assessments and outcomes. These data will be held at the Cancer Epidemiology Unit (CEU) where they will be stored securely in accordance with CEU procedures and policies.

All study participants will be traced and flagged at the NHSCR in order to find subsequent breast cancer incidence and mortality. In addition, breast cancer registrations prior to batch randomisation date will need to be obtained in order that women with a breast cancer diagnosis prior to screening invitation can be omitted from the analysis.

Analysis
The main outcome will be mortality from breast cancer by age 60 for women having an additional early screen and by age 80 for those having an additional later screen. All comparisons will be on an intention to treat basis with the screening batch as the unit of comparison. For each age group, women in batches where that age group was randomised in (i.e. invited for screening) will be compared with women of that age group in batches where randomisation for screening invitation was offered to the alternative age group. In order to minimise the dilution of any effect by pre-existent breast cancer, women with prior breast cancer will be omitted from analyses of breast cancer mortality.

Breast cancer incidence will be compared in the screened and unscreened groups in order to generate information on the recent concern about so-called overdiagnosis.

Consent and confidentiality
It is essential to include all study participants in this study; 100% coverage is essential for the scientific validity of the study, and excluding participants for whom we cannot get consent could seriously bias the results particularly as they are unlikely to be randomly spread throughout the population. Women

randomised to be invited for screening are informed in the information leaflet of the fact that the phasing-in of the age extension is randomised in order that the net benefit of extending the age range for breast screening can be scientifically evaluated, and that researchers will be analysing the results on behalf of the NHSBSP. Consent is implied for those who attend for screening because of the standard procedures of the NHSBSP which uses implied consent, and the information leaflet. It is not possible to ask consent of women randomised not to be invited for screening, without whom the study would be meaningless; however, information about the study will be sent to all women invited for screening in a community and therefore widely known. Application is being made to the National Information Governance Board for Health and Social Care for Section 251 approval for the use of patient identifiable data without consent and access to medical records by those outside the direct healthcare team.

We will not be informing General Practitioners (GPs) that specific patients of theirs are taking part in the study but screening units will inform local GPs that the study is taking place in their area. However the NHSBSP always informs GPs when their patients have been invited for screening and then what the outcome was even if they did not attend. The participants invited for screening in this study will be treated in exactly the same way. In general GPs will be unaware which patients of theirs have been randomized not to receive an invitation for screening.

Although this study will link individual patient records there is no interest in individual identities. The study will be conducted in accordance with relevant aspects of the Data Protection Act. The data will be treated with utmost confidentiality and used only for medical research. Data will be held securely at the CEU where they will be stored securely in accordance with CEU procedures and policies. The data will be anonymised once data linkage has been completed. All data will be analysed only in anonymised form and future publications will not identify any individual women.

Approvals and permissions
Before proceeding with the study ethical approval will need to be obtained from the Research Ethics Committee, and Section 251 support obtained from the National Information Governance Board for Health and Social Care.

Timetable
Prepare application to the Research Ethics Committee and to the National Information Governance Board for Health and Social Care for submission autumn 2009
Prepare patient information leaflet, Aug/Sept 2009
Convene Data Monitoring Committee and Steering Group, early 2010
Register study on trial public registers, Dec 2009
Start study in each area, from Jan 2010 onwards
Establish mechanism for data download from NBSS system, Spring 2010

Funding of the study
The age extension of the breast screening programme is funded by central government; this will therefore cover the phasing-in of the extension whether it

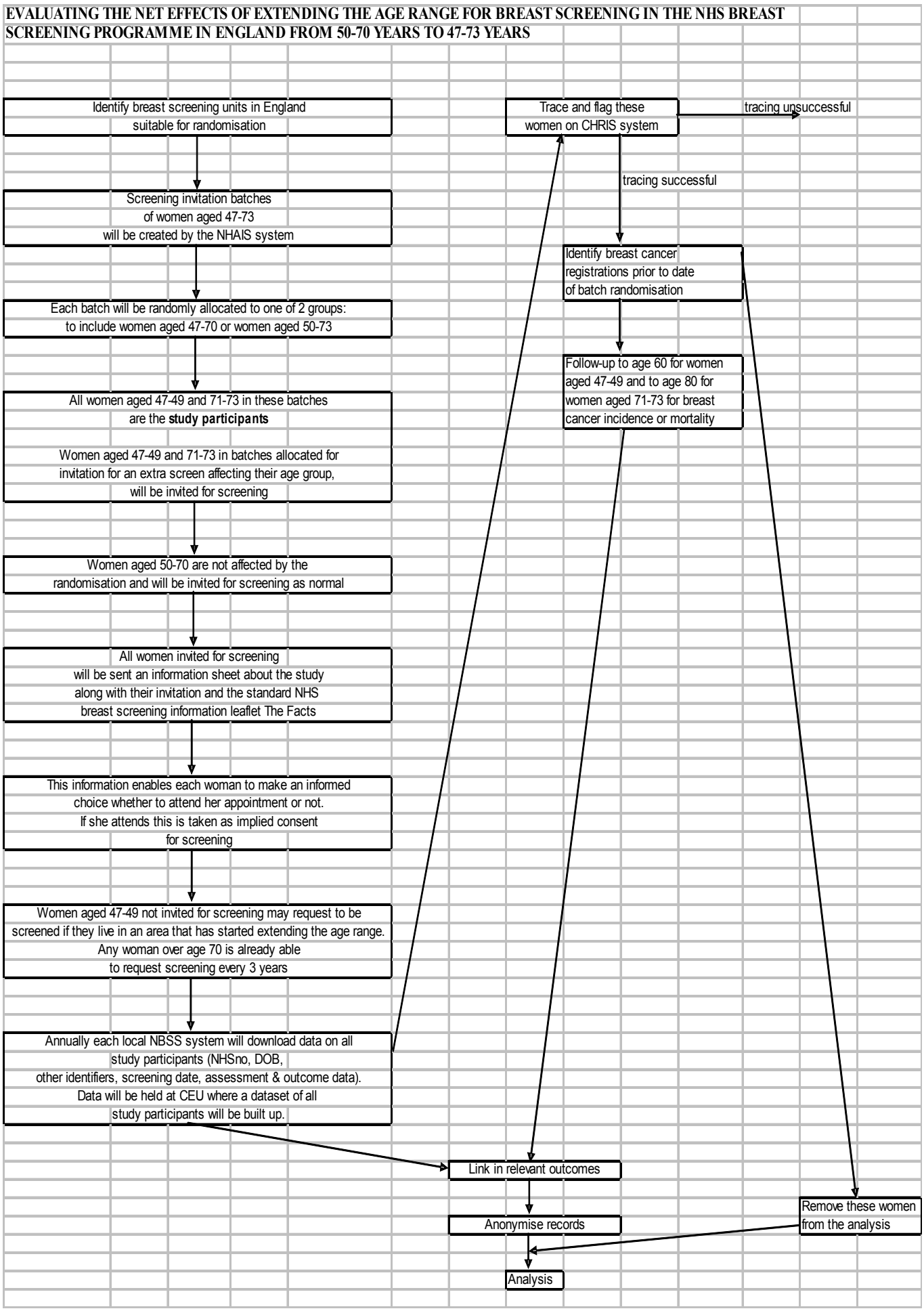
is randomised or not. The flagging of study members at NHSCR, and follow-up for breast cancer incidence and mortality will be funded by the NHSBSP.

Publication of results
Results of the study will be disseminated in peer-reviewed journals, at conferences and on the NHSBSP website.

References

1.Department of Health. *Cancer Reform Strategy*. NHS: London, 2007.

2.KJ Jørgensen & PC Gøtzsche. Overdiagnosis in publicly organised mammography screening programmes: systematic review of incidence trends BMJ 2009;339:b2587


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
Identify breast screening units in England suitable for randomisation
Screening invitation batches of women aged 47-73 will be created by the NHAIS system
Each batch will be randomly allocated to one of 2 groups: to include women aged 47-70 or women aged 50-73
All women aged 47-49 and 71-73 in these batches are the study participants
Women aged 47-49 and 71-73 in batches allocated for invitation for an extra screen affecting their age group, will be invited for screening
Women aged 50-70 are not affected by the randomisation and will be invited for screening as normal
All women invited for screening will be sent an information sheet about the study along with their invitation and the standard NHS breast screening information leaflet The Facts
This information enables each woman to make an informed choice whether to attend her appointment or not. If she attends this is taken as implied consent for screening
Women aged 47-49 not invited for screening may request to be screened if they live in an area that has started extending the age range. Any woman over age 70 is already able to request screening every 3 years
Annually each local NBSS system will download data on all study participants (NHSno, DOB, other identifiers, screening date, assessment & outcome data). Data will be held at CEU where a dataset of all study participants will be built up.
Trace and flag these women on CHRIS system
tracing unsuccessful
tracing successful
Identify breast cancer registrations prior to date of batch randomisation
Follow-up to age 60 for women aged 47-49 and to age 80 for women aged 71-73 for breast cancer incidence or mortality
Link in relevant outcomes
Anonymise records
Remove these women from the analysis
Analysis