**Systematic review and meta-analysis: Interventions designed to improve participation, amongst under-served population groups, in national screening programmes**

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# Abbreviations

AAA abdominal aortic aneurysm programme

AABR automated auditory brainstem response

AOAE automated otoacoustic emission

BCSP bowel cancer screening programme

BSP breast screening programme

CASP Critical Appraisal Skills Programme

cRCT cluster randomised controlled trial

CSP cervical screening programme

CF cystic fibrosis

CHT congenital hypothyroidism

DES diabetic eye screening programme

FASP fetal anomaly screening programme

FIT faecal immunochemical test

FOBT faecal occult blood test

GA1 glutaric aciduria type 1

HCU homocystinuria

HR-HPV high risk human papillovirus

IDSP infectious diseases in pregnancy screening programme

ICC intracluster correlation coefficient

IRR incidence rate ratio

IVA isovaleric acidaemia

LTGAH Long-term gender-affirming hormones

LGBT+ Lesbian, gay, bisexual, trans\* (+ queer, intersex, asexual)

MSUD maple syrup urine disease

MCADD medium-chain acyl-CoA dehydrogenase deficiency

NBS newborn blood spot screening programme

NIHR National Institute for Health Research

NHSP newborn hearing screening programme

NIPE newborn and infant physical examination screening programme

NN4B numbers for babies (NHS scheme)

PHE Public Health England

PKU phenylketonuria

qRCT quasi-randomised controlled trial

RCT randomised controlled trial

RR relative risk

SCT sickle cell and thalassaemia screening programme

SCD sickle cell disease

SPH Solutions for Public Health

UKCTG UK Clinical Trials Gateway

# Introduction

Public Health England (PHE) is seeking to further develop its commitment to reducing health inequalities as outlined in its recently published inequalities strategy (PHE, 2018).

Solutions for Public Health (SPH) has been commissioned to produce a systematic review and, where possible, meta-analysis of interventions to improve participation amongst under-served population groups in national screening programmes.

## NHS screening programmes

There are 11 different NHS national screening programmes. Some screen for more than one condition and some include more than one screening method. Each of the programmes is summarised briefly below. The numbered subheadings contain links to more detailed information from the NHS about the programmes.

A brief description of each screening programme is given below with some relevant extracts taken from “Supporting the health system to reduce inequalities in screening, PHE Screening inequalities strategy” (PHE, 2018). Superscript references in the quoted text are contained in the original PHE 2018 report (linked in the reference section of this report).

### [NHS abdominal aortic aneurysm (AAA) programme](https://www.gov.uk/topic/population-screening-programmes/abdominal-aortic-aneurysm)

Men are invited for a single ultrasound scan in the year they turn 65 with results being available at the time of the scan. Materials include an information leaflet and informed consent obtained at the clinic. (NHS AAA, 2015)

Transgender people whose gender is recorded as male by their GP will be invited for screening. Transgender women are believed to have the same higher risk as cisgender men but an invitation may not be issued if their gender is recorded correctly on their medical records. Transgender men are not considered to be at higher risk but may attend if they receive an invitation. (NHS-SP Trans Health, 2017)

#### Examples of inequalities identified by PHE

“Within the NHS AAA screening programme those people experiencing social deprivation, are less likely to attend and participate in screening and the proportion of aneurysms detected is inversely correlated with increasing deprivation.”

### [NHS bowel cancer screening programme (BCSP)](https://www.gov.uk/topic/population-screening-programmes/bowel)

Bowel cancer screening is offered every 2 years to people aged 60-74. An information leaflet is sent a week in advance of a home test kit. A faecal immunochemical test (FIT) kit is being introduced in England from 2018 and will eventually replace the faecal occult blood test (FOBT) kit. Bowel scope screening by flexible sigmoidoscopy is also being introduced as an additional test for people at age 55 but is not yet available everywhere. (NHS BCSP, 2015)

#### Examples of inequalities identified by PHE

“People in more deprived groups are less likely to complete bowel screening (35% for the most deprived group compared to 61% for the least deprived)ix and are more likely to die from bowel cancerx.”

“Uptake of bowel screening in England is lower in the ethnically diverse areas (38% compared to 52 to 58% in other areas)xv.”

“Women reporting any disability are less likely to participate in bowel screening (RR 0.75 compared to those without disabilities). This is particularly the case for those with disabilities relating to self-care or vision, or for those with 3 or more disabilitiesxxiii. People with learning disabilities are also less likely to participate in bowel screening (IRR 0.86 compared to those without learning disabilities)xxiv.”

“Men have a lower uptake of bowel screening (51% compared to 56% for women)xxvi but are more likely to be diagnosed and die from bowel cancer (male:female ratio 12:10)xxvii.”

### [NHS breast screening programme (BSP)](https://www.gov.uk/topic/population-screening-programmes/breast)

Mammography is offered every 3 years to women aged 50-70 and women over 70 may request continued screening. (NHS BSP, 2015)

Transgender men and women may need to attend for breast screening but only those whose gender is recorded as female by their GP will be invited. Transgender women who are using long-term gender-affirming hormones should attend for screening and transgender men should attend screening if they have any breast tissue regardless of whether or not they have had chest reconstruction. (NHS-SP Trans Health, 2017)

#### Examples of inequalities identified by PHE

“Women in the most deprived groups are generally less likely to participate in breast screening (relative risk (RR) 0.89 for the most deprived groups compared to the least deprived)xiii but are more likely to die from breast cancerxiv.”

“There is some evidence that women from ethnic minority groups are less likely to attend breast screening compared to White British women, but estimates vary by study and by minority ethnic groupxviii.”

“Women with disabilities are less likely to participate in breast screening (RR 0.64 compared to those without disabilities). This is particularly the case for those with disabilities relating to self-care or vision, or for those with 3 or more disabilitiesxxi. Women with learning disabilities are also less likely to participate in breast screening (incident rate ratio (IRR) 0.76 compared to those without learning disabilities)xxii.”

### [NHS cervical screening programme (CSP)](https://www.gov.uk/topic/population-screening-programmes/cervical)

Women are invited for a cervical screening (pap smear) test every 3 years from ages 25-49 and every 5 years from ages 50-64. Women over the age of 65 will only be screened further if recent tests have shown abnormal cells. Abnormal findings are triaged through a high risk human papillomavirus (HR-HPV) test with positive findings being referred for colposcopy. Women who have received the HPV vaccination (introduced in 2008) are still invited to screening. (NHS CSP, 2015)

Transgender men whose gender is recorded as female by their GPs will be invited and should attend if they still have a cervix. Transgender women may receive an invite if their gender is recorded as female but they do not need to attend. (NHS-SP Trans Health, 2017)

#### Examples of inequalities identified by PHE

“Women in the most deprived groups (most deprived quintile) are less likely to attend cervical screening (odds ratio (OR) 0.91 to 0.94 when compared to the least deprived quintilexi) yet are more likely to have high risk HPV, and a higher risk of being diagnosed with/dying from cervical cancerxii.”

“Women from ethnic minority groups are less likely to attend cervical screening compared to White British women (OR 2.20 for White British women compared to ethnic minority women)xvi. The disparity is particularly great for certain ethnic minority groups – for example the likelihood of non-attendance reaches OR 10.69 and OR 12.86 for Indian and Bangladeshi women respectively compared to White British womenxvii.”

“In cervical screening uptake is markedly higher among 50 to 64 year olds than among 25 to 49 year oldsxx.”

“Women with learning disabilities are less likely to participate in cervical screening (IRR 0.54 compared to those without learning disabilities)xxv.”

### [NHS diabetic eye screening (DES) programme](https://www.gov.uk/topic/population-screening-programmes/diabetic-eye)

All people with type 1 and type 2 diabetes aged 12 or over are invited to screening for diabetic retinopathy every year at their local screening service, which may be at their GP, local hospital, an optician or another local clinic. Additional screening is offered in pregnancy after the first antenatal visit and after 28 weeks of pregnancy. Screening is not necessary for gestational diabetes. (NHS DES, 2014)

#### Examples of inequalities identified by PHE

“People from South Asian communities are known to be up to 6 times more likely to have type 2 diabetes than the general population. In addition, this population group tend to have poorer diabetes management, putting them at higher risk of serious health complications including diabetic retinopathy. Data analysed from the Clinical Practice Research Datalink (CPRD) showed the prevalence of diabetic retinopathy to be highest in the South Asian population and also in the most deprived geographical groupxix.”

### [NHS fetal anomaly screening programme (FASP)](https://www.gov.uk/topic/population-screening-programmes/fetal-anomaly)

Antenatal screening is offered by healthcare professionals to everyone in pregnancy for early detection of anencephaly, open spina bifida, cleft lip, diaphragmatic hernia, gastroschisis, exomphalos, serious cardiac abnormalities, bilateral renal agenesis, lethal skeletal dysplasia, Edwards’ syndrome (T18), and Patau’s syndrome (T13). Initial screening includes a sonograph to measure nuchal translucency and a blood test. The quadruple blood test for Down’s may be used for late screening. Those identified as higher risk based on these tests are offered either chorionic villus sampling or amniocentesis. (NHS FASP, 2013)

#### Examples of inequalities identified by PHE

“Overall, there is limited published evidence on inequalities in antenatal and newborn screening programmes. However, 2013 UK research using large survey data consolidated evidence that single women, those from ethnic minorities and younger women are more likely to make late bookings for antenatal care, have fewer antenatal checks and engage less with screeningxxviii.”

“In NHS London an equity audit undertaken in 2015/16 found:

* evidence of inequalities in access to timely antenatal care across London
* many of the characteristics of women at greater risk of booking at more than 10 weeks gestation were also associated with social disadvantage, poorer pregnancy outcomes and poorer infant health
* there was considerably longer wait from referral to booking for women living in higher deprivation areas
* for several maternal characteristics (including first language other than English, Jewish religion, unemployment and most black and minority ethnicities), a later referral is compounded by a longer wait from referral to booking”

### [NHS infectious diseases in pregnancy screening (IDPS) programme](https://www.gov.uk/topic/population-screening-programmes/infectious-diseases-in-pregnancy)

Midwives and other healthcare professionals offer a blood test as part of antenatal care to screen for HIV, hepatitis B and syphilis. (NHS IDPS, 2015)

#### Examples of inequalities identified by PHE

“Overall, there is limited published evidence on inequalities in antenatal and newborn screening programmes. However, 2013 UK research using large survey data consolidated evidence that single women, those from ethnic minorities and younger women are more likely to make late bookings for antenatal care, have fewer antenatal checks and engage less with screeningxxviii.”

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* for several maternal characteristics (including first language other than English, Jewish religion, unemployment and most black and minority ethnicities), a later referral is compounded by a longer wait from referral to booking”

### [NHS newborn and infant physical examination (NIPE) screening programme](https://www.gov.uk/topic/population-screening-programmes/newborn-infant-physical-examination)

Healthcare professionals offer physical examinations for newborn babies born in England for congenital heart disease, developmental dysplasia of the hip, congenital cataracts and cryptorchidism (undescended testes). (NHS NIPE, 2013)

#### Examples of inequalities identified by PHE

“Overall, there is limited published evidence on inequalities in antenatal and newborn screening programmes.”

### [NHS newborn blood spot (NBS) screening programme](https://www.gov.uk/topic/population-screening-programmes/newborn-blood-spot)

Healthcare professionals will take a blood spot sample from the heel usually when a child is 5 days old but may offer screening up to one year old. Nine conditions are screened from the blood spot: sickle cell disease (SCD), cystic fibrosis (CF), congenital hypothyroidism (CHT), phenylketonuria (PKU), medium-chain acyl-CoA dehydrogenase deficiency (MCADD), maple syrup urine disease (MSUD), isovaleric acidaemia (IVA), glutaric aciduria type 1 (GA1), homocystinuria (HCU). (NHS NBS, 2013)

#### Examples of inequalities identified by PHE

“Overall, there is limited published evidence on inequalities in antenatal and newborn screening programmes.”

### [NHS newborn hearing screening programme (NHSP)](https://www.gov.uk/topic/population-screening-programmes/newborn-hearing)

Healthcare professionals offer hearing screening within 4-5 weeks of birth and up to 3 months old. Either automated otoacoustic emission (AOAE) or automated auditory brainstem response (AABR) may be used. Babies at high risk of hearing impairment from another condition are referred straight to full audiological assessment. (NHS NHSP, 2013)

#### Examples of inequalities identified by PHE

“Overall, there is limited published evidence on inequalities in antenatal and newborn screening programmes.”

### [NHS sickle cell and thalassaemia (SCT) screening programme](https://www.gov.uk/topic/population-screening-programmes/sickle-cell-thalassaemia)

Healthcare professionals offer screening in pregnancy and to fathers where the screening identifies the mother as a carrier. If both parents are carriers then counselling and prenatal diagnosis will be offered, with the option of termination if a diagnosis is obtained early enough. The programme aims to offer initial screening by 10 weeks of pregnancy. Newborns are tested for sickle cell disease as part of NBS screening. (NHS SCT, 2013)

#### Examples of inequalities identified by PHE

“Overall, there is limited published evidence on inequalities in antenatal and newborn screening programmes. However, 2013 UK research using large survey data consolidated evidence that single women, those from ethnic minorities and younger women are more likely to make late bookings for antenatal care, have fewer antenatal checks and engage less with screeningxxviii.”

“In NHS London an equity audit undertaken in 2015/16 found:

* evidence of inequalities in access to timely antenatal care across London
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* there was considerably longer wait from referral to booking for women living in higher deprivation areas
* for several maternal characteristics (including first language other than English, Jewish religion, unemployment and most black and minority ethnicities), a later referral is compounded by a longer wait from referral to booking”

### Summary of the screening programmes

|  |  |  |
| --- | --- | --- |
| **Screening programme** | **Population** | **Repeated** |
| AAA | Men aged 65 | No |
| BCSPa. FOBT or FITb. sigmoidoscopy | Adultsa. 60-74b. 55 | a. Yes (every 2 years)b. No |
| BSP | Women aged 50-70 | Yes (every 3 years) |
| CSP | Womeni. 25-49ii. 50-64 | i. Yes (every 3 years)ii. Yes (every 5 years) |
| DES | People with diabetes aged 12+ | Yes (annual) |
| FASP | Pregnancy | No |
| IDPS | Pregnancy | No |
| NIPE | Newborn (in England) | No |
| NBS | Newborn & infancy | No |
| NHSP | Newborn up to 3 months | No |
| SCT1. Mother
2. Father
3. Foetus
 | Pregnancy(aim to begin step-wise screening by 10 weeks of pregnancy) | No |

## Under-served groups

The under-served groups defined by the commissioning brief are as follows:

* groups experiencing socio-economically deprived backgrounds
* those with protected characteristics as described in the 2010 Equality Act
	+ age
	+ disability
	+ gender reassignment
	+ marriage and civil partnership
	+ pregnancy and maternity
	+ race
	+ religion or belief
	+ sex
	+ sexual orientation
* those who are not registered with a GP
* homeless people and rough sleepers
* asylum seekers
* gypsy and traveller groups
* sex workers
* those in prison
* those experiencing severe and enduring mental health problems
* those with drug or alcohol harm issues
* those with communication difficulties

This review will, of necessity, include only what evidence is available for any of these groups for each screening programme. We anticipate finding little or no evidence for some sub-questions whereas others, especially socio-economic status, ethnicity and language- or literacy-related communication difficulties are likely to have a reasonably large body of evidence. A rapid review of this question, commissioned by PHE for the cancer screening programmes only (Duffy *et al*, 2017), found 68 trials making 71 comparisons. 26 were conducted in the UK, 21 of these were randomised (including 5 cluster randomised), with 11 of these randomised trials including some information about under-served groups or subgroups, primarily defined by socio-economic status, ethnicity and language barriers.

### Barriers to accessing health care

The PHE report referenced earlier (PHE, 2018) discusses broad barriers to healthcare affecting under-served groups, citing a “determinants of health” framework (Dahlgren & Whitehead, 1992) and the Marmot Review (Fair Society, Healthy Lives, 2010).



**The Determinants of Health. (Dahlgren & Whitehead, 1992)**

While recognising the important differences between groups who are disadvantaged with respect to accessing some or all healthcare services, and the diversity within groups defined by broad labels, we anticipate that there will be a number of over-arching factors including, but not necessarily limited to:

* communication barriers related to language, literacy and education
* transience, lack of address or insecure accommodation
* difficulty with time and transport, including getting time off work, transport time and costs and loss of hourly pay
* lack of time and energy due to factors like disability, poor mental health, long working hours or difficult shift patterns
* fear of the authorities, due to factors like the “hostile environment”, poor treatment by officialdom or criminalisation

This is not an exhaustive list and there will be some very specific barriers for certain groups as already noted, for example, for transgender people and sex-specific screening programmes. These group-specific barriers may nevertheless be exacerbated by the elements of socio-economic deprivation listed above.

## Interventions to improve participation in screening

PHE previously commissioned a rapid review of interventions to improve participation in screening services, restricted to cancer screening but not to the UK (Duffy *et al*, 2017). This provides a very useful starting point for identifying the sorts of interventions we might anticipate for the adult screening programmes. A schematic diagram from the paper is reproduced below, summarising interventions along the screening timeline.

The interventions for antenatal, newborn and infant screening are likely to be quite different as screening is usually initiated directly by midwives or other healthcare professionals who are already in clinical contact with the mother and child. The NHS baby number, or “numbers for babies (NN4B)”, introduced in 2002/3, is an example of a tool designed to improve screening rates for newborns and infants (RCM, 2008).

Timely initiation of antenatal screening is particularly important as these are intended to allow early treatment to prevent or minimise harm to the unborn child and to allow parents to make an informed decision about continuing with the pregnancy. The entire screening pathway, from initial invitation to any actions based on screening results, needs to take place in a very defined (and very short) period of time and so efficient systems for identification and referral are likely to be an especially important part of interventions in these programmes.

### Mixed interventions

A number of the trials identified by the rapid review (Duffy *et al*, 2017) included mixed interventions which are not easily categorised. The final classification scheme will depend on what evidence we find but we anticipate the following sorts of mixed categories will arise:

* mixed (invite-based)
* mixed (community-based)
* mixed (invite & community)
* mixed (systems-based)

These trials will be considered alongside, but separately from, trials of single interventions which are included in the mixed intervention.

### Opting out

Improved participation in screening is a public health objective which may not be shared by individuals in the population. A benefit of improved identification and communication with candidates for screening includes improving information about the risks and benefits of screening and providing the opportunity to opt out (NHS-SP, 2016).

# Aims and objectives

To identify interventions which are effective in improving participation in national screening programmes amongst under-served groups.

## Relevant evidence

This review is restricted to UK-based trials of NHS national screening programmes conducted since 1990 and so the control arms will typically be standard NHS screening practice at the time the trial was conducted. However, this practice has changed over time and may vary between regions. There will inevitably be some heterogeneity between studies in the control arms used to evaluate interventions for each screening programme. There may also be trials which compare 2 non-standard interventions and these will also be included.

Some more complex interventions are difficult to evaluate using an RCT, being heavily reliant on local insights and services, difficult to scale, with often intensive and costly interventions. Single cohort studies without a comparator group will often be designed around local needs and circumstances or as pilots for controlled trials. These will not be included in this evidence review as they cannot give reliable estimates of benefit.

Outcomes of screening, including referral for treatment and especially the ultimate impact on the burden of disease, are the end goals of improving uptake. However these endpoints are extremely difficult to study in the context of a controlled trial of an intervention that aims to increase uptake. Only a very small proportion of people screened will have any kind of disease detected. Trials of screening vs no screening typically require sample sizes of tens or hundreds of thousands of people to measure realistic differences in outcomes due to screening. To detect differences due to a percentage increase in uptake of screening would, in most cases, be unrealistic and we anticipate finding little evidence for these outcomes from prospective, controlled trials.

## Resource considerations

This review has been commissioned in 2 stages to establish the size of the project and funding required to complete it. The end of Phase 1 includes a report to PHE summarising the type and volume of evidence identified in each of the numerous sub-categories for this review, summarised in the table below.

This protocol covers the full review, Phase 1 and Phase 2, to ensure that our intended approach is pre-registered in full before the literature searches are conducted.

The evidence for each screening programme may include several different under-served groups. Some of those groups will have been identified at a demographic level (eg areas of high deprivation) and others at the individual level (eg community nurses visiting traveller sites). Some trials will have been targeted specifically at the deprived group they report on and others will have conducted subgroup analysis, possibly for a number of different disadvantaged groups included in their sample. These characteristics will be noted as part of the Phase 1 paper selection.

**Summary of evidence table**

|  |  |
| --- | --- |
| **Design** | **NHS screening programme** |
| Under-served group 1 | Under-served group 2 |  … |
| *Area-based* | *Individual* | *Area-based* | *Individual* |  |
| **Intervention type 1** |  RCT | *wholegroup* | n(N) | n(N) | n(N) | n(N) |  |
| *subgroup* | n(N) | n(N) | n(N) | n(N) |  |
|  Cluster RCT | *wholegroup* | n(C)(N) | n(C)(N) | n(C)(N) | n(C)(N) |  |
| *subgroup* | n(C)(N) | n(C)(N) | n(C)(N) | n(C)(N) |  |
|  Quasi-randomised | *wholegroup* | n(N) | n(N) | n(N) | n(N) |  |
| *subgroup* | n(N) | n(N) | n(N) | n(N) |  |
|  Controlled | *wholegroup* | n(N) | n(N) | n(N) | n(N) |  |
| *subgroup* | n(N) | n(N) | n(N) | n(N) |  |
|  Cluster controlled | *wholegroup* | n(C)(N) | n(C)(N) | n(C)(N) | n(C)(N) |  |
| *subgroup* | n(C)(N) | n(C)(N) | n(C)(N) | n(C)(N) |  |
| … |  |  |  |  |  |  |  |

# Methods

## Pre-registration

This protocol will be registered on [PROSPERO](https://www.crd.york.ac.uk/prospero/#aboutregpage) (an NIHR-funded international prospective register of systematic reviews) when the search strategy has been finalised and this protocol document is agreed with our funders, PHE.

It is anticipated that further protocol amendments will be necessary after the paper selection is completed as we will not have a definitive list of interventions, or under-served populations with evidence available, until that stage is completed. We have also agreed with PHE that we will produce a report at the end of Phase 1 (protocol development through to paper selection) summarising the type and quality of evidence available with, where possible, some options to either expand the evidence base or contain costs if required.

Protocol amendments will be made on PROSPERO and in an updated version of this document, with an audit trail for both sources.

## **Data managemen**t

Documentation relating to the design and production of the search and review will be saved centrally on SPH’s shared access drive, which is automatically backed up. Backups of draft documents produced by SPH associates will be saved directly to the cloud, Interim versions of documents will be frozen to check for discrepancies with the final versions.

Search results will be entered into an excel database which will be used to document all decisions regarding title, abstract and full paper review. Versions of the database completed by individual reviewers will be saved separately from an agreed final version. SPH will produce and maintain a quality assurance framework to provide a documented audit trail of all stages of the review process.

Trial summaries will be entered directly into evidence tables in Word. Quality assessment and numerical results for the primary endpoint will be entered into Excel.

## Search strategy

A systematic search strategy of Medline, EMBASE and Cochrane databases has been devised in conjunction with the specialist healthcare information scientists at the Bodleian Healthcare Library, University of Oxford. The PICOS agreed with PHE was used to inform the literature search design and key terms to be included.

Two test searches were carried out, followed by review of the search terms, number of studies returned by each and detailed assessment of the first 100 results. Search terms were then amended following discussion between the information scientist, the 2 reviewers and the SPH quality assurance (QA) lead for this project, to ensure that relevant terms are included. The search design will be shared and agreed with PHE.

The final search strategy can be found in the appendix to this protocol, including the date range of the search, databases searched, search strategy, key search terms and the number of studies found at each stage of the search. In addition, we will check studies included in previous systematic reviews and will search the UK Clinical Trials Gateway (UKCTG) database of registered trials for trials in progress.

## Paper selection

Titles will be reviewed by an experienced reviewer at SPH and those that are clearly out of scope of the inclusion criteria will be excluded.

The remaining abstracts will be independently reviewed by two reviewers to identify studies which are eligible or possibly eligible. Full papers will be obtained for all potentially eligible studies after resolution of any disagreements. If there is any doubt about eligibility the full paper will be reviewed.

The full papers will be screened for eligibility by JS with decisions reviewed by VdS as the QA lead and any disagreements resolved by discussion, with a third party where necessary.

For included studies, the screening programme(s) and study design will be noted. For the trials, details of whether under-served groups were targeted by area demographics or individual characteristics and whether they were specifically targeted by the trial or reported as subgroups, will also be recorded along with total sample size, the interventions compared and the under-served groups included.

The number of studies excluded at each stage will be recorded via a PRISMA flow diagram, including reasons for exclusion during the review of full papers. An interim report will be produced for PHE with summary tables showing the volume of evidence found.

### Inclusion criteria

* parallel group trials comparing methods to improve participation in one of the 11 NHS national screening programmes (listed in section 1.1 above) with the following designs:
	+ randomised controlled trials
	+ quasi-randomised controlled trials where predictable allocation did not affect inclusion
	+ cluster randomised trials
	+ non-randomised cohort and quasi-experimental studies1
* at least one under-served group targeted by the trial or reported as a subgroup
* conducted in the UK
* systematic reviews which include at least one trial which would meet these inclusion criteria2
* cost-effectiveness studies, or reviews including cost-effectiveness studies, of interventions to improve participation in screening using UK costs

*1 Non-randomised controlled trials will be considered for inclusion for questions where there is little or no randomised evidence.*

*2 We anticipate finding a very large number of systematic reviews, many of which will include substantial amounts of evidence from outside the UK. These will be tabulated by the question addressed and volume of UK evidence, for PHE to consider which they would like included in Phase 2 of this review.*

### Exclusion criteria

* case-reports, case-series, uncontrolled cohort studies, case-control studies
* grey literature
* not published as full text articles in peer-reviewed journals
* non-English language
* published before 1990

### Final paper selection

An interim report will be produced summarising the evidence found by screening programme, under-served group and type of intervention. No information on outcomes will be included in the interim report. The final inclusion criteria, with respect to non-randomised studies, and also systematic reviews to be included in a “review of reviews”, will be agreed with the funder, depending on the availability of randomised evidence for specific questions and resource considerations.

All systematic reviews found will be cross-checked with our own search results to ensure we have found all the relevant trials.

## Outcomes

Methods to improve participation in screening are of interest at all stages of the screening process:

* cohort identification (invitation)
* information about screening
* access to screening services
* access to treatment
* onward referral
* disease outcomes

There is likely to be very little evidence from comparative trials about most of these stages. We have therefore specified the primary outcome as uptake of screening, which will include interventions relating to information and access, the second and third bullet points above.

### Primary outcome

Screening uptake

### Secondary outcomes

* identification of people to be invited to participate in screening
* progress through referral pathways following screening
* disease outcomes
* recorded preference to opt out of screening programme

Any other reported outcomes will be recorded in evidence summary tables.

## Quality assessment (risk of bias) tools

Quality assessment of studies will be done by JS, who will discuss with VdS where there is uncertainty, and with a third reviewer if uncertainty persists.

### Parallel group trials

We do not anticipate that many of the relevant studies will include individual informed consent because of the nature of the question. Quasi-randomised trials where predictable allocation has no influence on inclusion in the trial may therefore be considered strong evidence and will be treated similarly to RCTs. Where predictable allocation may have influenced inclusion in the trial these will be grouped with non-randomised controlled trials for the purposes of selection and analysis.

The updated RoB 2.0 risk of bias tool (RoB 2, 2018) covers individually and cluster randomised trials and will be used to assess the quality of randomised trials. The related ROBINS-I tool (Sterne *et al*, 2016) will be used to assess any non-randomised studies included in the review.

### Systematic reviews

Systematic reviews included in the “review of reviews” will be assessed using the ROBIS tool (Whiting *et al*, 2016).

### Cost-effectiveness studies

Cost-effectiveness studies will be summarised through a narrative review guided by the York CRD guidance for economic evaluations in systematic reviews (York CRD) with quality assessment informed by the more detailed tools for assessing economic studies provided by the Cochrane Handbook (Cochrane 15) and the Consensus on Health Economic Criteria (CHEC) checklist (Evers *et al*, 2005).

## Data extraction

Details of the trial design, interventions, population and outcomes will be extracted into evidence summary tables in Word. Quality assessment of included trials and numerical data for analysis of the primary endpoint will be recorded in Excel.

Data extraction will be done by JS. VdS will review the evidence summary tables and discuss any issues with JS, reviewing papers where there are ambiguities or inconsistencies or where JS requests a second opinion, and we envisage that through this process data extraction will be checked by VdS for at least 10% of papers. If the number of papers reviewed in this way by VdS covers less than 10% of the total included papers, further papers will be chosen at random for review of data extraction by VdS.

## Analysis

Numerical data for analysis will be extracted into Excel with interim versions frozen for checking against the final dataset. Analysis will be conducted in R using the metafor package (Viechtbauer, 2017).

All extractable results on the primary endpoint (screening uptake) will be displayed visually using forest plots of relative risk (RR) with absolute differences compared to control also summarised for ease of interpretation with respect to practical impact.

Forest plots will be presented in multiple formats driven by screening programme, under-served group and intervention type to allow this complex dataset to be viewed in different ways depending on the item of interest to decision-makers.

Trials with missing data will be included on the plots to indicate where data exists but has not been adequately reported. Other outcomes will be summarised in the evidence tables and considered in the narrative summary. It is not anticipated that there will be many clinically homogeneous groups of trials for these outcomes but forest plots will be produced where there is enough information to make a visual overview useful, with meta-analysis where appropriate.

Systematic reviews and economic evaluations will be quality assessed and summarised through a narrative review.

### Cluster trials

We will follow the detailed guidance on reporting cluster trials within systematic reviews from a review of the quality of Cochrane reviews (Richardson *et al*, 2016). Results of cluster trials will be adjusted for clustering, using imputed values for the intracluster correlation coefficient (ICC) where the original trials are poorly analysed or reported, using methods recommended in the Cochrane handbook (Cochrane Handbook 16.3). Where ICC values are not reported and difficult to estimate, conservative estimates will be applied where possible. Where results could not be reliably adjusted this will be clearly indicated.

### Meta-analysis across screening programmes and under-served groups

Of necessity meta-analysis can only be done within groups of similar interventions as there is no reason to believe that very different methods to improve participation will have similar impact. We can pool subgroups of studies across screening programmes and under-served groups where there are sufficient features in common to believe that the result will be interpretable. Structural similarities between screening programmes and barriers in common across under-served groups are considered in section 1 of this protocol.

Primary analysis will be driven by type of intervention and meta-analysed within groups and across groups with structural similarities. Results will also be presented grouped by screening programme, under-served group and barriers to accessing health care.

The additive random effects model (Dersimonian & Laird, 1986) will be used to pool studies regardless of the extent of heterogeneity. If there is substantial heterogeneity a multiplicative random effects model will also be applied to examine the influence of smaller trials, which may have a large influence on the central estimate of the additive model (Thompson & Sharp, 1999). Study size is associated with study quality and so the additive model can have the effect of exaggerating bias in some circumstances.

### Assessing publication bias

Formal assessment of publication bias is unlikely to be possible in this review as we do not anticipate having a sufficiently large number of clinically homogeneous trials within any one group. Funnel plots will be difficult to interpret as smaller trials are likely to have used more intensive community-based interventions or to have targeted a very low participation group, and so the reasons for any asymmetry we can observe will not be obvious.

This question will be considered in the narrative but we do not anticipate strong empirical evidence either way. Exclusion of the grey literature and the use of a UK-specific search filter means that some publication bias is likely and we will try to assess the impact of missing trials on interpretation.

## Open data

Data and code for analysis will be made available to peer reviewers and others on request.

# References

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Duffy SW, Myles JP, Maroni R, Mohammad A (2017) Rapid review of evaluation of interventions to improve participation in cancer screening services. *J Med Screen* **24**: 127–145, doi:10.1177/0969141316664757.

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Whiting P, Savović J, Higgins JPT, Caldwell DM, Reeves BC, Shea B, Davies P, Kleijnen J, Churchill R, group R (2016) ROBIS: A new tool to assess risk of bias in systematic reviews was developed. *J Clin Epidemiol* **69**: 225, doi:10.1016/J.JCLINEPI.2015.06.005.

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# Appendices

## Searches

### Medline

Search date: 28th November 2018

|  |  |  |
| --- | --- | --- |
| # ▲ | Searches | Results |
| 1 | "Early Detection of Cancer"/ | 19603 |
| 2 | Mass Screening/ | 95514 |
| 3 | Mammography/ | 28139 |
| 4 | papanicolaou test/ or vaginal smears/ | 22239 |
| 5 | ((nhs or national) adj5 screening programme\*).ti,ab. | 1387 |
| 6 | ((population or mass) adj3 screening).ti,ab. | 14458 |
| 7 | ((bowel or colon\* or colorectal or colo-rectal or breast or cervical or cervix) adj5 screening).ti,ab. | 34621 |
| 8 | (cancer adj5 screening).ti,ab. | 42815 |
| 9 | (f?ecal occult blood test\* or f?ecal immunochemical test\* or f?ecal immuno-chemical test\*).ti,ab. | 3765 |
| 10 | ((sigmoidoscop\* or colonoscop\* or flexisig\* or bowel scop\*) and screening).ti,ab. | 7214 |
| 11 | mammogra\*.ti,ab. | 30087 |
| 12 | ((chest adj2 (x-ray\* or xray\* or imag\* or radiogra\*)) and screening).ti,ab. | 2421 |
| 13 | ((vagina\* or cervi\* or pap\*) adj2 smear\*).ti,ab. | 13215 |
| 14 | ((pap or papanicolaou or smear) adj2 (test\* or screen\*)).ti,ab. | 6152 |
| 15 | (("carcinoma in situ" or cervical intraepithelial neoplas\* or cervical intra-epithelial neoplas\* or cin2 or cin3 or cervical dyskaryosis or cervical dyplasia\*) adj5 screening\*).ti,ab. | 296 |
| 16 | exp Congenital Abnormalities/ and screening.mp. | 16117 |
| 17 | exp Prenatal Diagnosis/ | 69954 |
| 18 | Neonatal Screening/ | 9245 |
| 19 | ((neonat\* or newborn or pregnan\* or prenatal or antenatal or pre-natal or ante-natal or fetal or foetal or fetus or foetus) adj5 screening).ti,ab. | 21819 |
| 20 | ("newborn and infant physical exam\*" or NIPE).ti,ab. | 38 |
| 21 | ("newborn blood spot" or "neonatal blood spot").ti,ab. | 71 |
| 22 | (((neonat\* or newborn) adj3 hearing) and (screening or test\*)).ti,ab. | 1600 |
| 23 | (automated otoacoustic emission\* or aoae or automated auditory brainstem response or aabr).ti,ab. | 242 |
| 24 | ((hip dysplasia or ((congenital or newborn\* or neonat\*) adj2 (cataract\* or hypothyroid\*)) or cryptorchidism or cystic fibrosis or phenylketonuria or dehydrogenase deficiency or maple syrup urine disease or acid?emia or aciduria or homocystinuria or pku or scd or cf or cht or mcadd or hcu or iva or gai or ((gene\* or carrier\*) adj3 h?emoglobin)) and screening).ti,ab. | 8213 |
| 25 | ((fetal or foetal or fetus or foetus) adj (anatomy or defect? or malformation? or abnormalit\* or anomal\* or syndrome?)).ti,ab. | 6276 |
| 26 | ((congenital\* or cardiac or heart) adj2 (defect? or malformation? or abnormalit\* or anomal\*)).ti,ab. | 74714 |
| 27 | (structural adj2 (defect? or malformation? or abnormalit\* or anomal\*)).ti,ab. | 15676 |
| 28 | ((non-chromosomal or nonchromosomal) adj2 (defect? or malformation? or abnormalit\* or anomal\*)).ti,ab. | 93 |
| 29 | 25 or 26 or 27 or 28 | 93820 |
| 30 | (ultrasound\* or ultra-sound or ultrasonogra\* or ultra-sonogra\* or sonogra\* or echocardiogra\* or screen\* or scan\* or structural assessment\* or structural survey\*).ti,ab. | 1553818 |
| 31 | 29 and 30 | 18720 |
| 32 | ((down\* syndrome or edward\* syndrome or patau\* syndrome or trisomy or t13 or t18) adj5 (screening\* or test\*)).ti,ab. | 3124 |
| 33 | ((chorionic vill\* adj2 (sampl\* or test\* or screen\*)) or amniocentesis or nuchal translucenc\*).ti,ab. | 10816 |
| 34 | ((anencephal\* or spina bifida or (cleft adj (lip? or palate?)) or (diaphragm\* adj hernia?) or gastroschisis or exomphalos or ((renal or kidney) adj agenesis) or skeletal dysplasia) and screening).ti,ab. | 992 |
| 35 | (((diabetes or diabetic) adj3 (eye? or retin\* or macul\*)) and (screening or test\*)).ti,ab. | 4578 |
| 36 | ((pregnan\* or antenatal or ante-natal) and (hiv or human immunodeficiency virus or hepatitis or hepb or hep-b or syphilis or sexually transmitted infection\* or sexually transmitted disease\*) and screening).ti,ab. | 2821 |
| 37 | Vision Screening/ and diabet\*.mp. | 282 |
| 38 | ((sickle cell or thalass?emia? or h?emoglobinopath\*) and screening).ti,ab. | 3497 |
| 39 | ((aaa or ((aorta or aortic) adj2 aneurysm?)) and screening).ti,ab. | 1532 |
| 40 | 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 31 or 32 or 33 or 34 or 35 or 36 or 37 or 38 or 39 | 307814 |
| 41 | Patient Participation/ | 23151 |
| 42 | Patient Compliance/ | 54800 |
| 43 | ((improv\* or increase\* or enhanc\* or promot\*) adj5 (participat\* or "use" or uptake or utili?ation or utili?ed or attendance? or attending)).ti,ab. | 212144 |
| 44 | (screening adj5 (participat\* or "use" or uptake or utili?ation or utili?ed or access\* or attendance? or attending)).ti,ab. | 23124 |
| 45 | ((improv\* or increase\* or enhanc\* or promot\*) adj5 screening).ti,ab. | 20911 |
| 46 | ((improv\* or increase\* or enhanc\* or promot\*) and (participat\* or "use" or uptake or utili?ation or utili?ed or attendance? or attending)).ti. | 25227 |
| 47 | (screening and (participat\* or "use" or uptake or utili?ation or utili?ed or access\* or attendance? or attending)).ti. | 6148 |
| 48 | ((improv\* or increase\* or enhanc\* or promot\*) and screening).ti. | 4486 |
| 49 | 41 or 42 or 43 or 44 or 45 or 46 or 47 or 48 | 334464 |
| 50 | Reminder Systems/ | 3141 |
| 51 | Patient Navigation/ | 512 |
| 52 | (reminder\* or alert? or automated messag\*).ti,ab. | 37469 |
| 53 | (letter? adj2 (invitation? or invite?)).ti,ab. | 590 |
| 54 | ((personal\* or tailor\* or target\*) adj2 (letter? or invit\*)).ti,ab. | 1408 |
| 55 | ((provider? or professional? or physican? or doctor? or general practi\* or midwi\* or community) adj5 (letter? or endorse\* or recommend\*)).ti,ab. | 11400 |
| 56 | (text messag\* or sms or telephone call\* or phone call\* or call centre? or call center? or helpline? or hotline?).ti,ab. | 15515 |
| 57 | incentiv\*.ti. or (((financial or economic or cash) adj3 (incentive? or transfer?)) or reimburs\* or re-imburs\* or voucher? or token? or reward\*).ti,ab. | 84415 |
| 58 | health communication/ or persuasive communication/ | 5048 |
| 59 | health education/ or consumer health information/ or exp health promotion/ or exp patient education as topic/ | 200938 |
| 60 | (health adj2 (promotion or education or communication)).ti,ab. | 65939 |
| 61 | ((patient or public or parent? or parental) adj2 education).ti,ab. | 29586 |
| 62 | ((community or population or public) adj2 engagement).ti,ab. | 2903 |
| 63 | ((personali\* or tailor\* or target\*) adj5 (mail\* or communicat\* campaign? or initiative? or strateg\* or program\*)).ti,ab. | 55798 |
| 64 | ((promotion\* or publicity or education\* or media) adj5 (campaign? or initiative? or strateg\* or program\*)).ti,ab. | 79111 |
| 65 | ((promotion\* or publicity or education\*) adj5 (material? or tool? or information)).ti,ab. | 22121 |
| 66 | (information\* adj3 (material? or tool? or sheet?)).ti,ab. | 6997 |
| 67 | (leaflet? or pamphlet? or booklet? or book let?).ti,ab. | 25063 |
| 68 | ((translat\* or pict\* or photo\*) adj5 (material? or tool? or information)).ti,ab. | 17762 |
| 69 | (translator? or interpreter? or chaperone? or multilingual\* or multi-lingual or bilingual or bi-lingual or ((multiple or many or several) adj2 language?)).ti,ab. | 42383 |
| 70 | (((community adj3 (nurse? or aide? or advocate? or volunteer?)) or lay health) and (enhanc\* or promot\* or educat\*)).ti,ab. | 2643 |
| 71 | (cultural\* adj2 (sensitiv\* or adapt\* or chang\* or appropriat\*)).ti,ab. | 14265 |
| 72 | (dvd? or audiovisual\* or audio-visual\* or video\* or screencast\* or podcast\* or stream\*).ti,ab. | 174436 |
| 73 | (social media or twitter or facebook\* or youtube or instagram).ti,ab. | 10056 |
| 74 | Reagent Kits, Diagnostic/ or Self Care/ | 46937 |
| 75 | (self-sampl\* or self-test\* or self-collect\* or home-sampl\* or home-test\* or home-collect\*).ti,ab. | 3109 |
| 76 | (direct mail\* or pre-addressed envelope\* or pre-addressed packag\* or free post\* or prepaid post\* or pre-paid post\*).ti,ab. | 962 |
| 77 | ((timed or fixed or booked or extended or screening) adj3 appointment?).ti,ab. | 326 |
| 78 | ((improv\* or increase\* or enhanc\* or promot\*) adj5 access\*).ti,ab. | 35716 |
| 79 | ("out of hour?" or extended hour? or evening? or weekend? or week-end? or saturday? or sunday?).ti,ab. | 29104 |
| 80 | (travel\* or transport).ti,ab. | 394004 |
| 81 | ("baby number?" or "number for babies" or nn4b or n4b).ti,ab. | 271 |
| 82 | intervention?.ti,ab. | 812708 |
| 83 | 50 or 51 or 52 or 53 or 54 or 55 or 56 or 57 or 58 or 59 or 60 or 61 or 62 or 63 or 64 or 65 or 66 or 67 or 68 or 69 or 70 or 71 or 72 or 73 or 74 or 75 or 76 or 77 or 78 or 79 or 80 or 81 or 82 | 1948432 |
| 84 | 40 and 49 and 83 | 9708 |
| 85 | limit 84 to (english language and yr="1990 -Current") | 9191 |
| 86 | limit 85 to "reviews (maximizes specificity)" | 416 |
| 87 | exp United Kingdom/ | 348420 |
| 88 | (national health service\* or nhs\*).ti,ab,in. | 162683 |
| 89 | (english not ((published or publication\* or translat\* or written or language\* or speak\* or literature or citation\*) adj5 english)).ti,ab. | 90196 |
| 90 | (gb or "g.b." or britain\* or (british\* not "british columbia") or uk or "u.k." or united kingdom\* or (england\* not "new england") or northern ireland\* or northern irish\* or scotland\* or scottish\* or ((wales or "south wales") not "new south wales") or welsh\*).ti,ab,jw,in. | 1873869 |
| 91 | (bangor or "bangor's" or cardiff or "cardiff's" or newport or "newport's " or st asaph or "st asaph's" or st davids or swansea or "swansea's").ti,ab,in. | 48025 |
| 92 | (aberdeen or "aberdeen's" or dundee or "dundee's" or edinburgh or "edinburgh's" or glasgow or "glasgow's" or inverness or (perth not australia\*) or ("perth's" not australia\*) or stirling or "stirling's").ti,ab,in. | 185555 |
| 93 | (armagh or "armagh's" or belfast or "belfast's" or lisburn or "lisburn's" or londonderry or "londonderry's" or derry or "derry's" or newry or "newry's").ti,ab,in. | 22557 |
| 94 | (bath or "bath's" or ((Birmingham not alabama\*) or ("birmingham's" not alabama\*) or bradford or "bradford's" or brighton or "brighton's" or bristol or "bristol's" or carlisle\* or "carlisle's" or (cambridge not (massachusetts\* or boston\* or harvard\*)) or ("cambridge's" not (massachusetts\* or boston\* or harvard\*)) or (canterbury not zealand\*) or ("canterbury's" not zealand\*) or chelmsford or "chelmsford's" or chester or "chester's" or chichester or "chichester's" or coventry or "coventry's" or derby or "derby's" or (durham not (carolina\* or nc)) or ("durham's" not (carolina\* or nc)) or ely or "ely's" or exeter or "exeter's" or gloucester or "gloucester's" or hereford or "hereford's" or hull or "hull's" or lancaster or "lancaster's" or leeds\* or leicester or "leicester's" or (lincoln not nebraska\*) or ("lincoln's" not nebraska\*) or (liverpool not (new south wales\* or nsw)) or ("liverpool's" not (new south wales\* or nsw)) or ((london not (ontario\* or ont or toronto\*)) or ("london's" not (ontario\* or ont or toronto\*)) or manchester or "manchester's" or (newcastle not (new south wales\* or nsw)) or ("newcastle's" not (new south wales\* or nsw)) or norwich or "norwich's" or nottingham or "nottingham's" or oxford or "oxford's" or peterborough or "peterborough's" or plymouth or "plymouth's" or portsmouth or "portsmouth's" or preston or "preston's" or ripon or "ripon's" or salford or "salford's" or salisbury or "salisbury's" or sheffield or "sheffield's" or southampton or "southampton's" or st albans or stoke or "stoke's" or sunderland or "sunderland's" or truro or "truro's" or wakefield or "wakefield's" or wells or westminster or "westminster's" or winchester or "winchester's" or wolverhampton or "wolverhampton's" or (worcester not (massachusetts\* or boston\* or harvard\*)) or ("worcester's" not (massachuse tts\* or boston\* or harvard\*)) or (york not ("new york\*" or ny or ontario\* or ont or toronto\*)) or ("york's" not ("new york\*" or ny or ontario\* or ont or toronto\*))))).ti,ab,in. | 1240081 |
| 95 | 87 or 88 or 89 or 90 or 91 or 92 or 93 or 94 | 2419644 |
| 96 | (exp africa/ or exp americas/ or exp antarctic regions/ or exp arctic regions/ or exp asia/ or exp oceania/) not (exp great britain/ or europe/) | 2640052 |
| 97 | 95 not 96 | 2290325 |
| 98 | 85 and 97 | 1041 |
| 99 | 86 or 98 | 1364 |

Similar searches will be conducted in Embase and Cochrane.