Public Health England

SPH
Solutions for Public Health

Systematic review of interventions designed to improve participation in UK national screening programmes amongst underserved population groups – young person and adult screening programmes

Report produced by Solutions for Public Health in conjunction with Public Health England Screening

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Appendices (available separately)

Executive summary

Objective

Participation in screening programmes varies and tends to be lower amongst those more likely to develop the condition targeted by screening. This systematic review explores interventions that improve participation by underserved groups in screening programmes in the UK. This paper reports the findings for young person and adult (YPA) screening programmes.

Data sources

Medline, EMBASE, Cochrane, CINAHL, HMIC, and PsycINFO to 10th October 2019.

Review methods

Randomised trials in national screening programmes in the UK were included if they reported results related to participation in screening for underserved groups at any stage of the screening pathway. Risk of bias was assessed using RoB 2. The primary outcome was uptake of screening. Secondary outcomes were any outcomes related to cohort identification, patient information about screening, access to screening and to treatment, onward referral, disease outcomes and preference to opt out of screening.

Results

Thirty six trials relating to YPA screening programmes were identified, reporting 193 comparisons of screening uptake within underserved groups. Most of the evidence related to uptake of screening tests in cancer screening programmes and by underserved groups defined by socioeconomic status, ethnicity, age, sex, and screening history.

There was strong and consistent evidence in favour of: reminders that include a timed appointment, General Practitioner (GP) letters for non-responders, and human papillomavirus (HPV) self-test kits for non-responders.

There was some evidence favouring annual reminders for non-responders and pre-appointment reminders by post or text message, and weaker or unconfirmed evidence favouring: timed office hours appointments with an offer to switch to out-of-hours, GP letters near the time of invitation, GP endorsed invitations, enhanced reminder letters and telephone reminders for non-responders and a psychoeducational booklet. There was little or no evidence favouring: reminders by text message for non-responders, nurse or link worker telephone calls or home visits, pre-notification letters in cervical screening, tailored invitations referencing screening history, simplified leaflets, narrative leaflets, anticipated regret questions, or planning tools addressing barriers to screening.

There was reasonably strong evidence from a single trial of diabetic eye screening that financial incentives do not improve uptake.

Conclusion

This review identified several mostly reminder-based interventions for which there was good evidence of improvement in screening uptake amongst underserved groups in the UK. Areas where further research would be useful include participation at other stages of the screening pathway, non-cancer screening programmes, less-researched underserved groups, and whether interventions have different effects in different groups.

1 Introduction

Variation in participation in screening programmes exists both within and between national screening programmes. Moreover, groups at higher risk of the condition targeted by screening tend to be less likely to participate.[1,2] This inequality in screening participation can be due to barriers making it harder for some groups of people to engage with screening services. Screening inequalities can occur at any point along the screening pathway and barriers that persist once a person has started screening may result in some people being unable to maximise the benefits of screening.

Public Health England (PHE) is committed to reducing inequalities in screening as outlined in its screening inequalities strategy.[3] PHE therefore commissioned this systematic review in order to support and encourage actions to address these inequalities. The review looked at interventions which may improve participation at any stage in the screening pathway by underserved population groups in national screening programmes in the UK. This follows an earlier rapid review of a similar question for cancer screening.[4]

Screening can do harm as well as good and invitations are based on the principle that all individuals should be able to choose if a screening test is right for them. PHE defines personal informed choice as a decision made to accept or decline a screening test based on access to accessible, accurate, evidence-based information covering: the condition being screened for; the testing process; the risks, limitations, benefits and uncertainties; potential outcomes, and treatment pathways.

“Improving” participation aims to maximise informed decision-making and remove barriers to engagement in NHS screening programmes. The primary focus of this report is inequalities in screening participation. It covers the evidence found for interventions that increase participation in young person and adult (YPA) screening programmes.

2 Methods

The methods are described in detail in the published protocol and more briefly below.

2.1 Protocol

The protocol was developed using the PRISMA[5,6] guidelines and registered on PROSPERO (CRD42019118866) in December 2018. Protocol amendments are listed on PROSPERO.

2.2 Eligibility criteria

The eligibility criteria were: randomised, quasi-randomised, or cluster-randomised trials; comparing methods to improve participation in one of the NHS screening programmes at any stage of the screening pathway; reporting subgroup analysis or results for at least one underserved group; excluding outdated controls or

interventions which have already been adopted as standard in the UK (trials reporting at least one relevant comparison remained eligible but ineligible arms were excluded from the analysis); published from 1990 onwards with a full-text peer-reviewed report available.

Systematic reviews and economic analyses were also sought based on similar criteria; systematic reviews had to include at least one trial which would be eligible for this review and economic analyses had to be directly relevant to the UK context to be considered for inclusion. Results of these studies provided context to some of our findings.

The current YPA NHS screening programmes include: Abdominal Aortic Aneurysm (AAA)[7], Breast Screening Programme (BSP),[8] Cervical Screening Programme (CSP),[9] Diabetic Eye Screening (DES),[10] and the NHS Bowel Cancer Screening Programme. Until recently, the NHS offered two types of tests for bowel cancer: a home completed self-test kit every two years from age 60 to 74 (BCSP)[11] and a single flexi sigmoidoscopy to people at the age of 55 (BSS). The two components of this screening programme have been considered separately due to these very different screening strategies. Screening using single flexi sigmoidoscopy has now been decommissioned and is no longer offered. The screening programmes are listed alongside their abbreviations in Table 1 for convenience.

Underserved groups were defined as: those experiencing socioeconomic deprivation, those with any of the protected characteristics described in the UK 2010 Equality Act, those not registered with a General Practitioner (GP), homeless people, rough sleepers, asylum seekers, gypsy and traveller groups, sex workers, those in prison, and those experiencing severe and enduring mental health problems, drug or alcohol harm issues or communication difficulties. In addition, first-time invitees were included as an underserved group because younger age groups were considered underserved in every screening programme and because this group is of interest in its own right. Non-responders were also included as a useful proxy for underserved groups, and were categorised in three groups: recent non-responders who had missed a recent screening invitation and were at the reminder stage; previous non-responders who had not participated in previous screening rounds, and long-term non-responders who had not participated in multiple previous screening rounds.

Only UK trials were included because of the potential for differences in screening programmes, health services and underserved groups to substantially complicate interpretation of non-UK trials.

2.3 Outcomes

All outcomes relating to participation in screening at any point in the screening pathway, from cohort identification to management after screening, were considered relevant. The primary outcome was pre-specified in the protocol as uptake of screening because it was anticipated that it would be the only outcome with reasonably consistent measurement across trials and would be reported by most trials. Participation, measured as uptake in response to the offer of a test, is an important metric of a screening programme as it identifies the number and characteristics of the groups from the target population who are accessing the service. Secondary outcomes included any outcomes related to cohort identification,

patient information about screening, access to screening, onward referral, access to treatment, disease outcomes and preference to opt out of screening.

The time period over which uptake is measured following an invitation or reminder for screening varies by screening programme and reporting is not consistent across all trials within screening programmes. For the forest plots the longest time period reported by each trial was used, to maximise the information available; data for all reported time periods were extracted along with other outcomes reported. It was anticipated that there would be very little clinically homogeneous evidence suitable for meta-analysis and so the primary objective was to provide a clear visual summary of the evidence with respect to uptake across this heterogeneous group of trials, with the narratives informed by information from other endpoints where available.

2.4 Literature searches

Searches of Medline(OvidSP), EMBASE(OvidSP), Cochrane Database of Systematic Reviews(Cochrane Library, Wiley), CINAHL(EBSCOHost), Health Management Information Consortium (HMIC)(OvidSP) and PsycINFO(OvidSP) databases were conducted on 17th December 2018 and updated on 10th October 2019. The search strategies included a UK filter, based on a validated published filter with some additional geographical terms included.[12] The searches were further limited to 1990 onwards and English language. The search strategy is included in the protocol (Appendix 1). All titles were screened by two reviewers and all abstracts retained by at least one title screener were independently screened by two reviewers. Disagreements were resolved by discussion and full papers obtained for review where there was any doubt. One reviewer screened the full papers, consulting with a second and if necessary a third reviewer. All trials excluded solely because they did not report on any underserved groups were checked by a second reviewer. Systematic reviews and economic analyses were short-listed and classified by relevance to the UK context and whether or not there was substantial evidence relating to underserved groups in the reported results. Reference lists of relevant trials and systematic reviews were checked for additional trials.

2.5 Risk of bias assessment

The RoB 2 instrument[13] was used to assess risk of bias, which was assessed at the study level. Quasi-randomised trials were treated as equivalent to fully randomised trials where the quasi-randomisation was likely to produce a truly random sample. This does not introduce bias when there is no informed consent or opportunity for researchers to selectively include or exclude people based on predictable allocation.

2.6 Data extraction

Data extraction tables were developed and piloted on four of the more complex trials included in the review. Two reviewers independently completed data extraction for each included trial, including risk of bias and reported results within underserved groups. Disagreements were resolved by discussion, consulting a third reviewer where necessary. Authors were contacted to request missing information. The completed summary tables are provided in Appendix 2.

2.7 Analysis

The specific focus of this review concerns interventions which may improve participation in screening for underserved population groups. Some trials randomise a general population of those eligible for screening and report relevant subgroup analyses. Other trials target a specific underserved group and so cannot report differences in effects between underserved groups and groups with higher screening uptake (interactions).[14] This anticipated heterogeneity in the type of data available, with some trials only including a subset of the eligible population, led to the approach taken, which is to extract uptake data for each relevant underserved group and comment on any evidence of an interaction, if reported, in the narrative.

In this review most trials contribute several different results for uptake, defined by the underserved groups they report and, for trials with more than two arms, the comparison made. It is therefore difficult to present the results as each one is defined by multiple criteria: the trial (and screening programme), the comparison being made, and the underserved group. A system for labelling the results was developed, described in full in Appendix 3. The criteria and abbreviations used for graphical presentation of the results are listed in Table 1. Interventions are defined using three criteria: the stage of the screening process, the nature of the intervention, and the mode of delivery.

The preferred outcome measure is absolute risk difference (RD) as this is the most useful number to consider from a public health perspective. We have also produced forest plots of the best available odds ratio (OR) for each trial, defined as: the raw (unadjusted) OR for trials which used simple randomisation of individuals; adjusted for stratification factors if the randomisation was stratified, and adjusted for clustering if it was cluster-randomised. In some cases, the preferred OR was not reported, and authors were unable to provide additional information. In these cases, the most appropriate OR was selected from the information available. All the reported results for uptake are included in the trial summary tables in Appendix 2.

Where the reported results of cluster trials were not adjusted for clustering they have been adjusted[15] using either the reported intra-cluster correlation coefficient (ICC) or an estimate of 0.03 for the ICC, with this value based on rounding up ICCs reported by other included cluster trials.

Forest plots for the primary endpoint of uptake were produced in R (version 4.0.4) using the dmetar,[16] meta,[17] and metafor[18] packages with missing data indicated by blank lines on the plots.

Table 1 Abbreviations used in presentation of results

Screening programme		**Underserved group**		
AAA	Abdominal Aortic Aneurysm	**Category**	**Code**	
BCSP	Bowel Cancer Screening Programme	Socioeconomic	**IMD20** **SIMD20**	Most deprived quintile (English IMD or Scottish IMD)
BSS	Bowel Scope Screening		**IMD40** **SIMD40**	Two most deprived quintiles (English IMD or Scottish IMD)
BSP	Breast Screening Programme		**IMD33**	Most deprived tertile (English)
CSP	Cervical Screening Programmes		**SES33**	Most deprived tertile (Townsend score or measure not reported)
DES	Diabetic Eye Screening		**NoQual**	No formal qualifications
			Unemp	Unemployed
			Tenant	Housing status (renting)
Basis of underserved group result		Ethnicity	**ETH**	Minority ethnicity
.w	whole trial population		**ASIAN**	Asian family origin
.s	subgroup of whole trial population		**PAK**	Pakistani family origin
.i	individual demographic		**BGD**	Bangladeshi family origin
.a	area-based demographic	Age	**<65**	Under 65
			70+	Over 70
			50-54, 55-60	Age range as specified
		Sex	**MEN**	Men
		Screening history	**FTI**	First-time invitee
			pNON	Previous non-attender
			ltNON	Long-term non-attender
		Current screening status	**rNON**	Recent non-attender (population recruited to trials of reminders)

Intervention description					
Event / stage of screening pathway		**Type of intervention**		**Mode of intervention**	
I	invitation	**NFA**	no further action	**PO**	post
A	appointment	**INV**	standard invite	**TEL**	telephone
K	home test kit	**PIL**	patient information leaflet	**TXT**	text message
R	reminder	**SWI**	simplified patient information	**F2F**	face-to-face
2R	second reminder	**EWI**	enhanced patient information	**GP**	general practice
LT	long-term non-responder	**PNL**	pre-notification letter		
		HCP	healthcare professional		
pre.	prefixes to modify the event	**PSY**	psychological/barriers		
post.	codes where needed	**AR**	anticipated regret		
		REM	(standard) reminder	**Other**	
		ERM	enhanced reminder	**ICC**	intra-cluster correlation
		Combi	combined invites or leaflets		
		GPE	GP endorsed		coefficient
		GPL	GP letter		
		HTK	home test kit		
		IMP	implementation intentions		
		INDIV	tailored to the individual		
		FIXED	Fixed/timed appointment		
		HLOC	health locus of control		
		svy	survey (not an intervention)		
		ann	annual (prefix)		

3 Results

3.1 Literature search

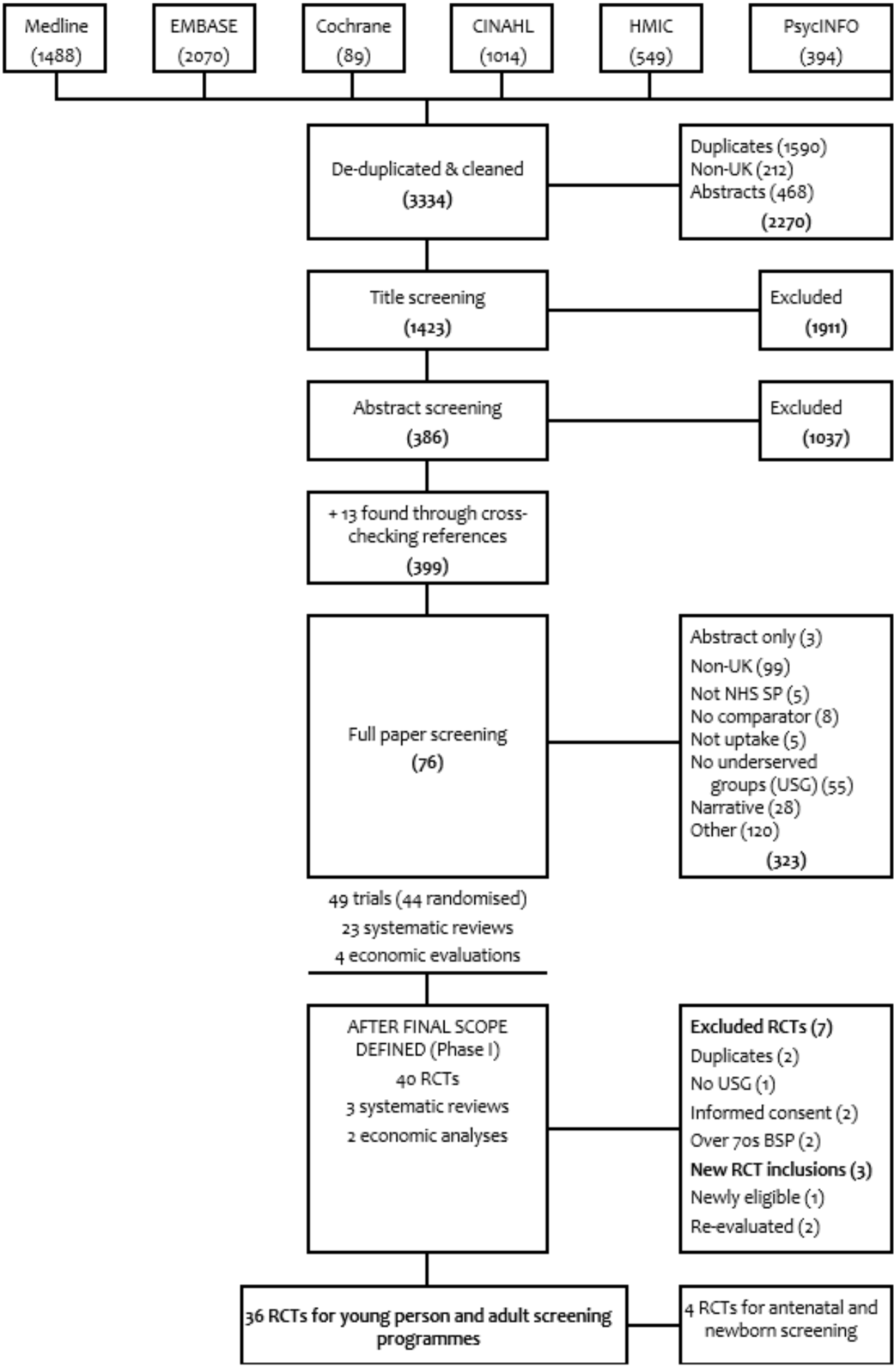
Searches of the six databases identified 5,604 records, with 3,334 potentially eligible reports after deduplication in Endnote (including an update search in October 2019). Following title and then abstract screening, 2,948 were excluded, leaving 386 full papers for review. A further 13 papers were identified through cross checking of references. After final inclusion/exclusion decisions, 40 trials reporting relevant randomised comparisons were found. Of these, 36 trials were in YPA screening programmes, which is the focus of this paper, and four were for antenatal and newborn screening programmes. Of the trials in YPA screening programmes, 35 trials reported 193 results relating to uptake of screening in underserved groups, including nine results (from two trials) comparing two different control arms. One trial was a pilot study that did not report uptake.[19] Of these trials, one reported results for both BSP and CSP,[20] and two trials in CSP were reported in a single paper.[21]

No eligible trials were found for other points in the screening pathway, such as identification of people to be invited for screening, and diagnostic testing and management following a positive screening test result.

Most of the eligible trials were in the cancer screening programmes: BCSP[19,22–30]; BSS[31,32]; BSP[33-47], and CSP[20,48-51]. Very little eligible evidence was identified for DES,[52,53] and none for AAA. All the underserved groups reported by these trials were defined by some measure related to socioeconomic status, ethnicity, age, sex, or screening history. Three systematic reviews[54-56] and two economic analyses[57,58] were also appraised (Appendix 4).

A PRISMA diagram summarising the results of the literature searches is given in Figure 1.

Figure 1 PRISMA diagram (including updated searches on 10/10/19



3.2 Quality of trials

The overall quality of the trials, as assessed using RoB 2, is shown in Table 2. Summary tables including the detail of the risk of bias assessments for each trial are provided in Appendix 2. The majority of the trials (26) were assessed as having a low risk of bias. Three trials were assessed as having a high risk of bias. Potential sources of bias were most often related to imbalances in baseline characteristics between the groups or a lack of sufficient data reported to assess this. Other issues included “pseudo” randomisation, and a relatively small number of clusters or failure to adjust for clustering. For practical reasons some trials excluded participants after randomisation, technically a violation of intention-to-treat (ITT), but in most cases this is unlikely to introduce bias because the exclusions were usually done blind of allocation and were consistent with the usual screening process. In some cases, there was a risk that post-randomisation exclusion may have been influenced by allocation and these concerns were noted. Results were not corrected for ITT because this was only possible for a subset of trials and it made no substantive difference in those which reported sufficient information.

Table 2 Summary of trials identified and their overall risk of bias (RoB)

a) Bowel cancer screening programme and bowel scope screening

	Trial (size*)	Interventions tested	Underserved groups	RoB
BCSP	Libby 2011[22] (n=59,953)	Information booklet sent with the pre-notification letter or later, with the home test kit	- SIMD20/40 - age <65, 70+ - men - first-time invitees	Low
	Lo 2014[23] (n=23,182)	Implementation intentions (planning tool to overcome barriers to participation)	- IMD33 - age <65 - men	Low
	Shankleman[24] 2014 (n=3,886)	Health promotion delivered by phone or group sessions	- men - first-time invitees - previous non-attenders	High
	O'Carroll 2015[25] (n=60,000)	Anticipated regret questions with HLOC questionnaire included for explanatory purposes	- IMD20/40 - age <65, 70+ - men - first-time invitees - previous non-attenders	Low
	Smith 2017[26] (n=163,525)	Simplified 'gist' leaflet	- IMD20/40 - age <65, 70+ - men - first-time invitees - previous non-attenders	Low
	McGregor 2016[27] (n=150,417)	Narrative leaflet using short testimonies from people who had been screened	- IMD20/40 - age <65, 70+ - men - first-time invitees - previous non-attenders	Low
	Raine 2016a[28] (n=265,434)	Sentence on GP-endorsement included in invitation sent from screening hubs	- IMD20/40 - age <65, 70+ - men - first-time invitees - previous non-attenders	Low
	Raine 2016b[29] (n=168,480)	Enhanced reminders, included additional lines in standard reminder letters	- recent non-attenders[#] - IMD20/40 - age <65, 70+ - men - first-time invitees - previous non-attenders	Some
	Hirst 2017[30] (n=8,269)	Text message reminders	- recent non-attenders[#] - IMD20/40 - age <65, 70+ - men - first-time invitees	Some
BSS	Wardle 2003[31] (n=2,966)	Psychoeducational leaflet	- most deprived tertile	Low
	Kerrison 2018[32] (n=1,383)	Annual reminders	- recent non-attenders[#]	Low

b) Breast screening programme

	Trial (size*)	Interventions tested	Underserved groups	RoB
BSP	Lancaster 1992[20] (n=2,131)	Dual invitations for breast and cervical screening compared to an offer of cervical screening on attendance for mammography	- Asian	High
	Turner 1994[33] (n=465)	GP letter sent in addition to routine reminder	- recent non-attenders[#] - first-time invitees - previous non-attenders	Low
	Meldrum 19943[4] (n=3,083)	Tailored invitations making reference to screening history	- first-time invitees - previous non-attenders	Low
	Hoare 1994[35] (n=527)	Home visits to encourage attendance at screening	- Asian[#] - Pakistani - Bangladeshi	Low
	Sharp 1996[36] (n=799)	GP letter compared to home visits	- recent non-attenders[#] - age <60	Some
	Atri 1997[37] (n=2,064)	Telephone call or letter from GPs for those not responding to reminders	- recent non-attenders[#] - minority ethnicity - Indian	Some
	Stead 1998[38] (n=2,229)	Open reminder vs reminder including a fixed/timed appointment	- recent non-attenders[#] - socioeconomic status - first-time invitees - previous non-attenders - long-term non-attenders	Low
	O'Connor 1998[39] (n=473)	GP letters	- first-time invitees - previous non-attenders	Low
	Bankhead 2001[40] (n=1,158)	GP letters and flags in notes (factorial design)	- recent non-attenders[#] - first-time invitees	Low
	Richards 2001[41] (n=6,133)	GP letters and flags in notes (factorial design)	- first-time invitees - previous non-attenders	Low
	Rutter 2006[42] (n=2,082)	Implementation intentions (planning tools to overcome barriers to attendance)	- first-time invitees - previous non-attenders	Some
	Offman 2013[43] (n=19,409)	Office hours vs out-of-hours appointments	- age <60 - previous non-attenders	Some
	Kerrison 2015[44] (n=2,240)	Pre-appointment text message reminders	- IMD20/40 - first-time invitees	Low
	Chambers 2016[45] (n=856)	Telephone reminders with or without additional telephone support and anticipated regret questions	- recent non-attenders[#]	Low
	Allgood 2016[46] (n=22,828)	Pre-appointment postal reminders	- IMD20/40 - age <60 - first-time invitees - previous non-attenders	Low
	Allgood 2017[47] (n=26,054)	Open reminder vs reminder including a fixed/timed appointment	- recent non-attenders[#] - IMD20/40 - first-time invitees - long-term non-attenders	Low

c) Cervical screening programme

	Trial (size*)	Interventions tested	Underserved groups	RoB
CSP	McAvoy 1991[48] (n=737)	Posted written information compared to home visits with written information or video	- Asian[#]	Low
	Lancaster 1992[20] (n=2,131)	Dual invitations for breast and cervical screening compared to an offer of cervical screening on attendance for mammography	- previous non-attenders	Some
	Stein 2005[49] (n=1,140)	Nurse phone call compared to a letter from a local screening commissioner or celebrity (Claire Rayner)	- long-term non-attenders[#]	Low
	Szarewski 2011[50] (n=3,000)	HPV self-test kits for non-attenders	- recent non-attenders[#] - IMD20/40	Low
	Cadman 2015[51] (n=6,000)	HPV self-test kits for non-attenders	- recent non-attenders[#] - IMD20/40 - age <35 - long-term non-attenders	Low
	Kitchener 2018a[21] (n=20,879)	Pre-notification letters with or without an online booking option	- first-time invitees[#]	Low
	Kitchener 2018b[21] (n=10,126)	Five interventions compared to standard (open) reminder: fixed/timed appointment; HPV self-test kits sent, HPV self-test kits offered, nurse navigator phone call offered, choice of nurse navigator or HPV self-test kit	- recent non-attenders[#]	Low

d) Diabetic eye screening

	Trial (size*)	Interventions tested	Underserved groups	RoB
DES	Bush 2014[52] (n=851)	Telephone reminder for non-attenders	- recent non-attenders[#]	High
	Judah 2018[53] (n=1,274)	Financial incentives (£10 or 1% chance of winning £1000 in a lottery)	- long-term non-attenders[#] (from the most deprived 60% of post codes)	Low

* includes all those randomised, some may be not eligible for this review, number of clusters may be much smaller; # – whole trial population; High – high risk of bias; Low – low risk of bias; RoB – risk of bias assessed using RoB 2 tool; Some – some concerns. See Table 1 for screening programme abbreviations

3.3 Trial results

Table 2 summarises the trials identified for each screening programme including the interventions tested and the underserved groups for which results were reported. Appendix 5 provides forest plots for RD and OR which summarise the results for uptake within underserved groups by type of intervention. Where stronger evidence was identified, plots are also provided alongside the narrative below. In addition, Appendix 6 provides forest plots for RD and OR by NHS screening programme and Appendix 7 provides the same by underserved group.

There are very few groups of trials which are sufficiently clinically homogeneous to justify meta-analysis and none where meta-analysis would change our conclusions. The forest plots therefore do not include any pooled results. A narrative synthesis aided by the plots is provided.

The plots provide an overview of reported results within underserved groups; they should not be used to attempt to identify underserved groups for which the interventions do or do not work, particularly where subgroup sizes are small or multiple subgroups have been reported. There was little clear evidence from reported subgroup analysis that the effect of interventions was different for different subgroups and most of the trials identified were too small to reliably detect such interactions, especially in the context of multiple hypothesis tests. The four ASCEND trials[26-29] were the only trials explicitly designed to develop and test interventions that might reduce the socioeconomic gradient in uptake of screening.

All results pertain to trials in the context of NHS screening programmes and hence, unless otherwise stated, are applicable to UK populations.

3.3.1 HPV self-test kits for recent non-responders (CSP)

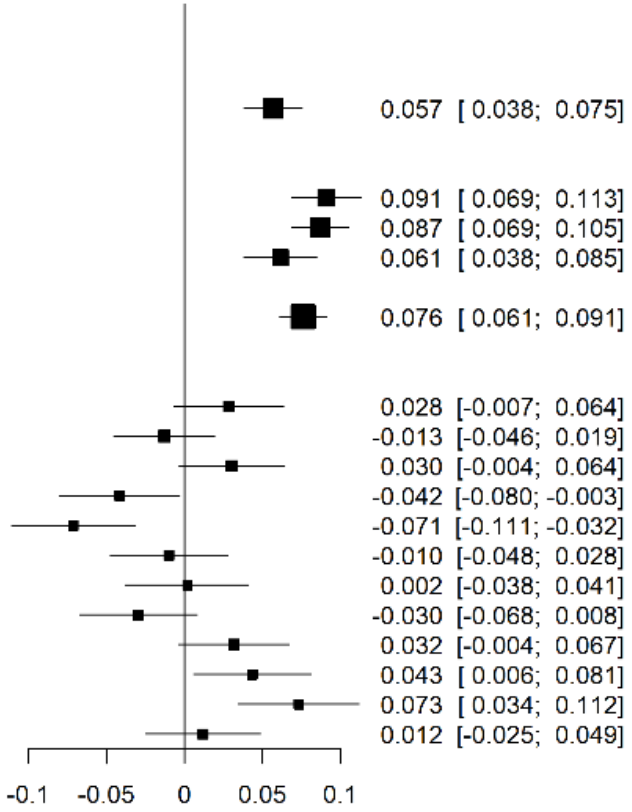
Three trials (Szarewski 2011,[60] Cadman 2015,[61] Kitchener 2018b[62]), all assessed as having a low risk of bias, collectively report strong evidence of an increase in overall uptake (of the order of 3 to 9%) with the addition of posted HPV self-test kits compared to standard reminders alone for recent non-responders. This was based on a combined endpoint of return of kit or attendance for screening (Figure 2).

Szarewski 2011[50] and Cadman 2015[51] do not report the details of the control arm other than a “standard reminder” was used; Kitchener 2018b specifies that the “standard” control was an open reminder invitation, and also included an intervention arm that included a fixed/timed appointment with the reminder invitation. Kitchener 2018b[62] also tested the offer of an HPV self-test kit (rather than posting one to all participants), and it included only first-time invitees.

The results of these three trials were consistent and relatively precise. They therefore provide substantial good quality evidence that including HPV self-test kits with reminder letters increases uptake in underserved groups when measured by either return of a kit or attendance for screening.

Figure 2 HPV self-test kits for recent non-responders (CSP)

Trial, screening programme, comparison & underserved group	control	N	test	N	Risk of Bias	RD	95%-CI
Szarewski 2011 (CSP).i 2R-REM-PO v 2R-HTK-PO IMD20.sa	.	.	.	.	Low		
Szarewski 2011 (CSP).i 2R-REM-PO v 2R-HTK-PO IMD40.sa	.	.	.	.	Low		
Szarewski 2011 (CSP).i 2R-REM-PO v 2R-HTK-PO rNON.wi	68	1500	153	1500	Low	0.057	[0.038; 0.075]
Cadman 2015 (CSP).i 2R-REM-PO v 2R-HTK-PO IMD20.sa	73	1372	198	1375	Low	0.091	[0.069; 0.113]
Cadman 2015 (CSP).i 2R-REM-PO v 2R-HTK-PO IMD40.sa	100	1946	268	1937	Low	0.087	[0.069; 0.105]
Cadman 2015 (CSP).i 2R-REM-PO v 2R-HTK-PO <35.si	63	1098	136	1145	Low	0.061	[0.038; 0.085]
Cadman 2015 (CSP).i 2R-REM-PO v 2R-HTK-PO ltNON.si	.	.	.	.	Low		
Cadman 2015 (CSP).i 2R-REM-PO v 2R-HTK-PO rNON.wi	183	3000	411	3000	Low	0.076	[0.061; 0.091]
Kitchener 2018b (CSP).c R-REM-PO v R-HTK-PO rNON.wi	1026	3782	342	1141	Low	0.028	[-0.007; 0.064]
Kitchener 2018b (CSP).c R-REM-PO v R-HTK-OFFER rNON.wi	1026	3782	333	1290	Low	-0.013	[-0.046; 0.019]
Kitchener 2018b (CSP).c R-REM-PO v R-NN/HTK-TEL/PO rNON.wi	1026	3782	385	1277	Low	0.030	[-0.004; 0.064]
Kitchener 2018b (CSP).c R-HTK-PO v R-HTK-OFFER rNON.wi	342	1141	333	1290	Low	-0.042	[-0.080; -0.003]
Kitchener 2018b (CSP).c R-HTK-PO v R-NN-TEL rNON.wi	342	1141	230	1007	Low	-0.071	[-0.111; -0.032]
Kitchener 2018b (CSP).c R-HTK-PO v R-FIXED-PO rNON.wi	342	1141	472	1629	Low	-0.010	[-0.048; 0.028]
Kitchener 2018b (CSP).c R-HTK-PO v R-NN/HTK-TEL/PO rNON.wi	342	1141	385	1277	Low	0.002	[-0.038; 0.041]
Kitchener 2018b (CSP).c R-HTK-OFFER v R-NN-TEL rNON.wi	333	1290	230	1007	Low	-0.030	[-0.068; 0.008]
Kitchener 2018b (CSP).c R-HTK-OFFER v R-FIXED-PO rNON.wi	333	1290	472	1629	Low	0.032	[-0.004; 0.067]
Kitchener 2018b (CSP).c R-HTK-OFFER v R-NN/HTK-TEL/PO rNON.wi	333	1290	385	1277	Low	0.043	[0.006; 0.081]
Kitchener 2018b (CSP).c R-NN-TEL v R-NN/HTK-TEL/PO rNON.wi	230	1007	385	1277	Low	0.073	[0.034; 0.112]
Kitchener 2018b (CSP).c R-FIXED-PO v R-NN/HTK-TEL/PO rNON.wi	472	1629	385	1277	Low	0.012	[-0.025; 0.049]



See Table 1 for abbreviations

Note that Kitchener 2018b includes five different intervention arms, three of which include an HPV self-test kit (posted kit, offer of kit, choice of kit or nurse navigator). These interventions are sometimes designated as the control arm in the plot above. The first three lines compare the three HPV self-test kit arms to the standard (open) reminder.

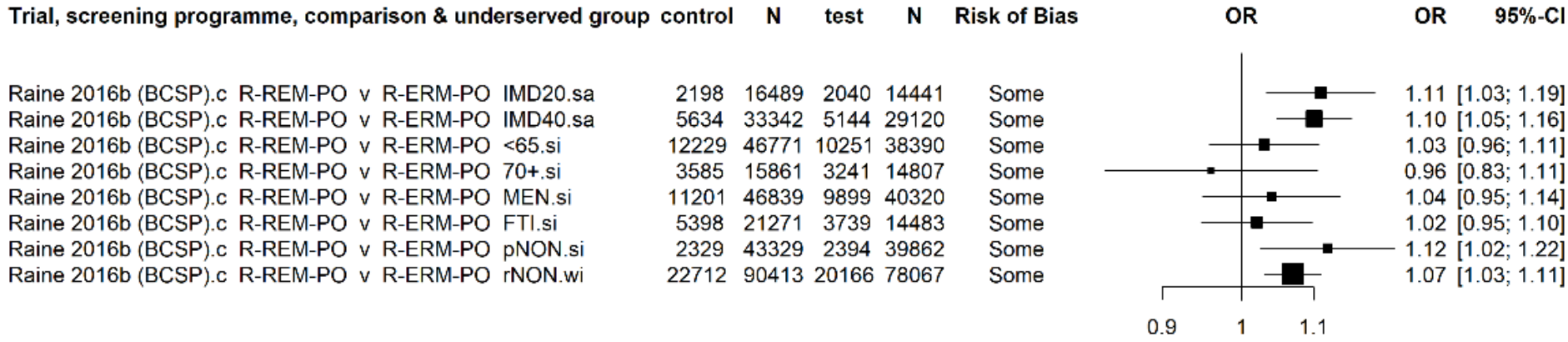
3.3.2 Enhanced reminders for recent non-responders (BCSP)

One trial in BCSP (Raine 2016b[29]), for which there were some concerns of bias, assessed enhanced reminders that included "two additions to the usual letter: a banner reading 'A reminder to you' at the start of the letter and a brief restatement of the screening offer at the end of the letter" for those who did not return test kits. The study reported an increase in overall uptake with an adjusted OR of 1.07 (95% confidence interval (CI) 1.03 to 1.11). It was the only trial to report strong evidence of an interaction (p=0.005) by socioeconomic status (IMD quintiles), with a stronger effect in the most deprived quintile, OR 1.11 (95% CI 1.04 to 1.20), compared to OR 1.00 (95% CI 0.94 to 1.06) in the least deprived quintile. There was a reasonably consistent gradient of effects from least deprived to most deprived population quintiles.

Raine 2016b[29] randomised 20 days within each of the five English screening hubs, treating each 'hub-day' as a cluster. One hub-day was excluded due to the wrong intervention being delivered. There were moderate imbalances between groups in age and previous screening history and, on review, it was considered that the imbalances in screening history may be greater than what would be expected by chance. However, adjusted ORs were reported, adjusted for IMD quintile, screening history, age, sex and screening hub to attempt to account for these imbalances. Given this, forest plots for adjusted OR rather than RD have been provided (Figure 3; see Appendix 5 for forest plots of RD).

Although there were some concerns regarding the risk of bias, the results of this trial suggest that enhanced reminder letters increase uptake of screening in BCSP and that this effect is greater in the more deprived population groups. Although this single trial's result is not confirmed, it suggests that this intervention has the potential to reduce screening inequalities in BCSP.

Figure 3 Enhanced reminders for recent non-responders (BCSP), adjusted OR



See Table 1 for abbreviations

3.3.3 Fixed/timed appointment vs open reminders for non-responders (BSP, CSP)

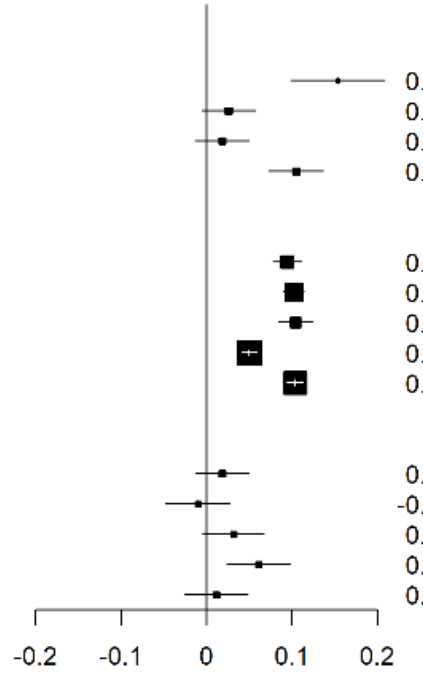
Two trials in BSP (Stead 1998,[38] Allgood 2017[47]), both assessed as having a low risk of bias, reported an overall increase in uptake of the order of 10% with reminders that included a fixed appointment time compared to open invitations to book an appointment for non-responders. One trial in CSP that also had a low risk of bias (Kitchener 2018b[21]) reported a smaller overall increase in uptake of the order of 2% (not statistically significant) for the fixed/timed appointment reminder.

Results for underserved groups are plotted in Figure 4. For BSP, both Stead 1998[38] and Allgood 2017[47] report smaller absolute effects for long-term non-attenders and Stead 1998 also for previous non-attenders. This is not unexpected given the lower baseline attendance for these groups, and the ORs are more similar across the different groups. Kitchener 2018b[62] only reported results of recent non-attenders.

The two trials in BSP together report consistent good quality evidence that reminders that included a fixed/timed appointment for non-responders substantially improve uptake in underserved groups. The single trial in CSP reported weaker evidence of a relatively small effect.

Figure 4 Fixed/timed appointment vs open reminders for non-responders (BSP, CSP)

Trial, screening programme, comparison & underserved group	control	N	test	N	Risk of Bias	RD	95%-CI
Stead 1998 (BSP).i R-OPEN-PO v R-FIXED-PO SES.sa	.	.	.	.	Low		
Stead 1998 (BSP).i R-OPEN-PO v R-FIXED-PO FTI.si	35	389	76	312	Low	0.154	[0.098; 0.209]
Stead 1998 (BSP).i R-OPEN-PO v R-FIXED-PO pNON.si	27	512	35	446	Low	0.026	[-0.006; 0.057]
Stead 1998 (BSP).i R-OPEN-PO v R-FIXED-PO ltNON.si	21	429	26	386	Low	0.018	[-0.014; 0.051]
Stead 1998 (BSP).i R-OPEN-PO v R-FIXED-PO rNON.wi	151	1228	228	1001	Low	0.105	[0.073; 0.137]
Allgood 2017 (BSP).i R-OPEN-PO v R-FIXED-PO IMD20.sa	386	3623	682	3395	Low	0.094	[0.078; 0.111]
Allgood 2017 (BSP).i R-OPEN-PO v R-FIXED-PO IMD40.sa	820	7326	1507	7040	Low	0.102	[0.090; 0.114]
Allgood 2017 (BSP).i R-OPEN-PO v R-FIXED-PO FTI.si	163	2072	369	2017	Low	0.104	[0.084; 0.125]
Allgood 2017 (BSP).i R-OPEN-PO v R-FIXED-PO ltNON.si	97	4445	307	4283	Low	0.050	[0.041; 0.059]
Allgood 2017 (BSP).i R-OPEN-PO v R-FIXED-PO rNON.wi	1784	13247	3054	12807	Low	0.104	[0.094; 0.113]
Kitchener 2018b (CSP).c R-REM-PO v R-FIXED-PO rNON.wi	1026	3782	472	1629	Low	0.018	[-0.013; 0.050]
Kitchener 2018b (CSP).c R-HTK-PO v R-FIXED-PO rNON.wi	342	1141	472	1629	Low	-0.010	[-0.048; 0.028]
Kitchener 2018b (CSP).c R-HTK-OFFER v R-FIXED-PO rNON.wi	333	1290	472	1629	Low	0.032	[-0.004; 0.067]
Kitchener 2018b (CSP).c R-NN-TEL v R-FIXED-PO rNON.wi	230	1007	472	1629	Low	0.061	[0.024; 0.098]
Kitchener 2018b (CSP).c R-FIXED-PO v R-NN/HTK-TEL/PO rNON.wi	472	1629	385	1277	Low	0.012	[-0.025; 0.049]



See Table 1 for abbreviations

Note that Kitchener 2018b includes six different arms; the plot above shows fixed/timed appointments compared to all the other arms (and is the control arm for the final comparison).

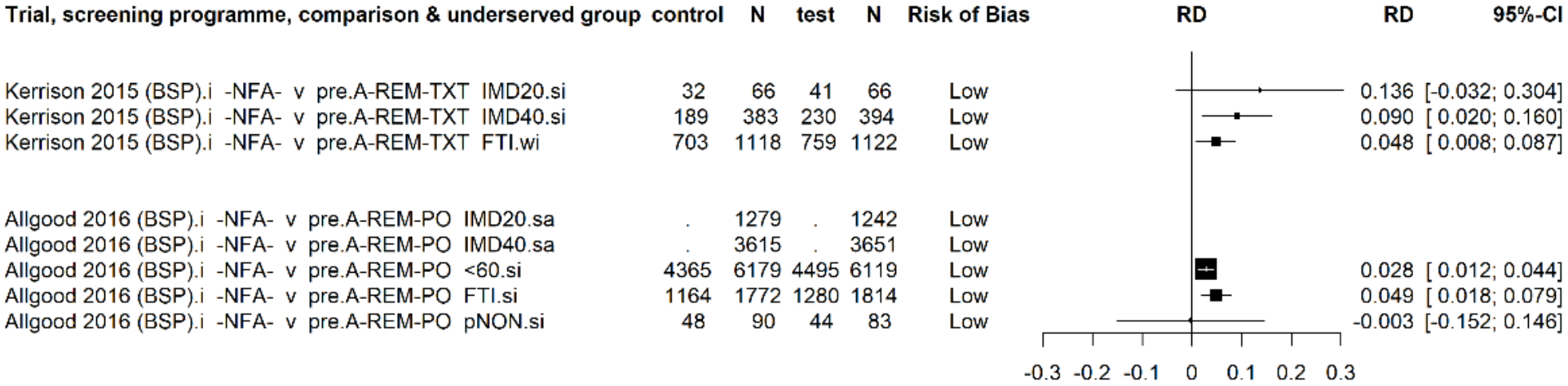
3.3.4 Pre-appointment reminders (BSP)

Two trials in BSP (Allgood 2016[46], Kerrison 2015[44]), both assessed as having a low risk of bias, reported evidence of a substantial increase in uptake with pre-appointment reminders, the increase being of the order of 3 to 9% for the groups with reasonably large sample sizes (Figure 5). One trial sent reminders by post (Allgood 2016[46]) and one by text message (Kerrison

2015[44]). These results were obtained despite valid mobile phone numbers only being available for 40% of randomised individuals in the trial of text messages.

Overall, there is encouraging evidence that pre-appointment reminders, by text or post, increase uptake in underserved groups. However, although the two trials have a low risk of bias, they are single trials for two different reminder methods and so they do not directly confirm each other.

Figure 5 Pre-appointment reminders (BSP)



See Table 1 for abbreviations

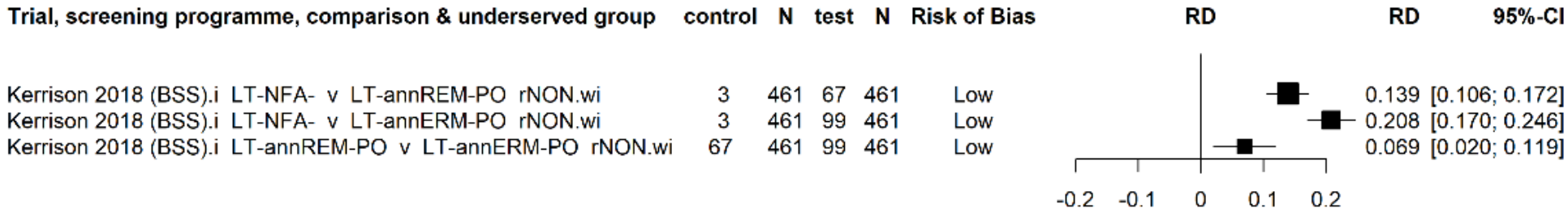
3.3.5 Annual reminders for non-responders (BSS)

One trial in BSS (Kerrison 2018[32]), with a low risk of bias, provided strong evidence that annual reminders for non-responders improve uptake by 15 to 20% (after two annual reminders) and some evidence that an enhanced leaflet based on the Behaviour Change Wheel was more effective than the standard leaflet (Figure 6).

This result based on a single good quality trial, provided plausible, relatively precise evidence of a large effect. The effectiveness of reminders is consistent with results in other screening programmes which have already implemented reminders. The reported

difference in effectiveness between the two types of leaflet is also relatively large but this result is less secure and may require further corroboration.

Figure 6 Annual reminders for non-responders (BSS)



See Table 1 for abbreviations

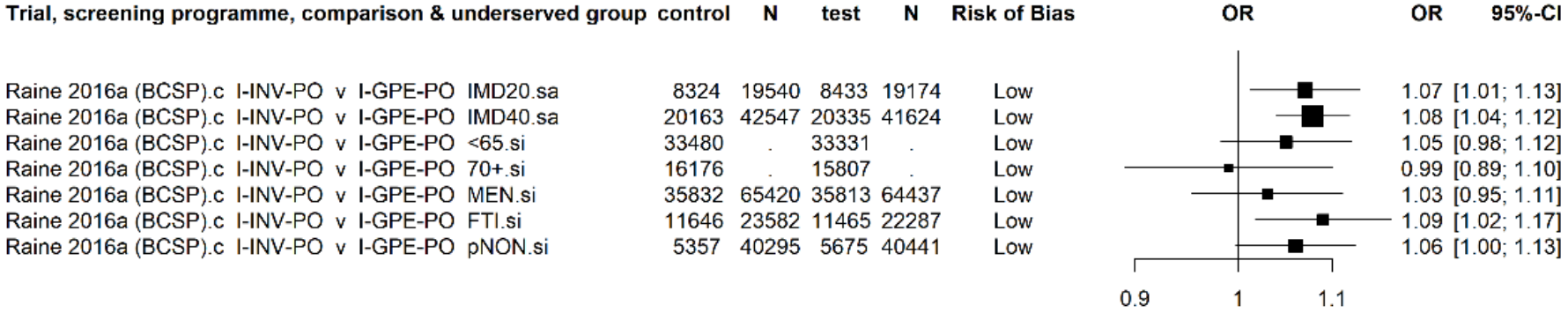
3.3.6 GP endorsed invitations (BCSP)

One trial in BCSP (Raine 2016a[28]), assessed as having a low risk of bias, tested the addition of a statement that the individual's GP supported bowel cancer screening in the pre-notification letter. The trial reported an increase in overall uptake of the order of 1% (Figure 7), with an adjusted OR of 1.07 (1.04 to 1.10). There was no evidence of a difference in effect by deprivation quintile.

Raine 2016a[28] randomised 20 days within each of the five English screening hubs, treating each 'hub-day' as a cluster. Two hub-days were excluded due to the wrong intervention being delivered. Although some imbalances between the groups in screening history were noted, on review, these were considered likely to fall within what might be expected by chance. Given these imbalances, forest plots for the adjusted OR rather than RD have been provided (Figure 7; see Appendix 5 for RD).

Although this is an unconfirmed result from a single trial, the risk of bias was considered low, and the trial suggests that the inclusion of a GP endorsement on screening invitation letters may increase uptake in underserved groups in BCSP. A similar intervention was addressed in ASCEND 2 (ISRCTN11660314), which has recently been published[59].

Figure 7 GP endorsed invitations (BCSP), adjusted OR



See Table 1 for abbreviations

3.3.7 Text or telephone reminders for non-responders (BCSP, BSP)

One trial of text message reminders for non-responders in BCSP (Hirst 2017[30]), for which there were some concerns of bias, reported no overall effect on uptake. One trial of telephone reminders for non-responders in BSP (Chambers 2016[45]), with a low risk of bias, provided some evidence that a simple telephone reminder increases uptake by an order of 10%. Results of these trials within underserved groups are shown in Figure 8.

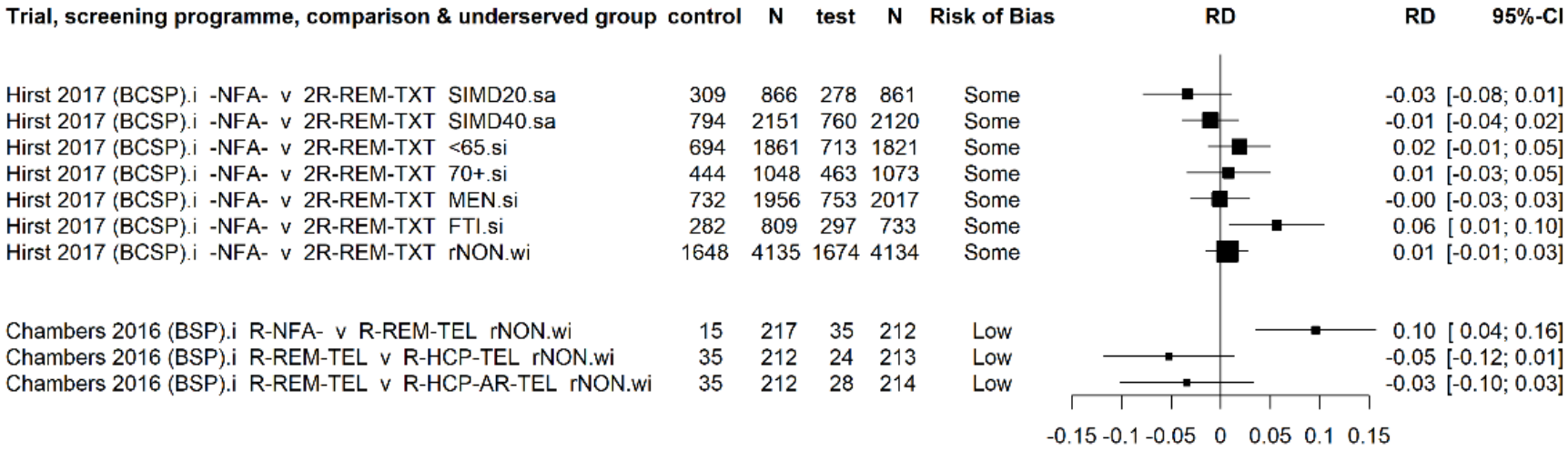
Hirst 2017[30] (BCSP) reported no evidence of a benefit for text message reminders compared to no further action after an unsuccessful written reminder. There was some evidence of a benefit for first-time invitees, but this is a small subgroup in the context of a number of subgroup analyses and this result cannot be considered reliable. It was difficult to assess the success of randomisation in this trial and the results should be treated with caution.

Chambers 2016[45] (BSP) reported relatively strong evidence of an increase in uptake of the order of 10% with a simple telephone reminder compared to no further action after postal reminders had failed, with no evidence that more intensive phone interventions improved uptake further.

There is thus limited evidence from one good quality trial in BSP that a telephone reminder for non-responders results in a relatively large increase in screening uptake. However, the trial was small and the result has not been reliably confirmed. For

text reminders, there was no evidence of an increase in screening uptake from a single trial in BCSP in which there were some concerns of bias.

Figure 8 Text or telephone reminders for non-responders (BCSP, BSP)



See Table 1 for abbreviations

3.3.8 GP letters and other GP-based interventions (BSP, CSP)

Six trials of GP letters[33,36,37,39-41] and one of a letter from a screening commissioner[49] in BSP and CSP, five with a low risk of bias[42, 48, 49, 50, 59] and two with some concerns[45, 46], provided some evidence that these interventions increase screening uptake, mostly by around 3 to 7%, although the details of the interventions varied. Two trials[49,50] also suggested that a flag in (pre-computerised) notes was similarly effective.

Two trials of GP letters in BSP reported consistent evidence of improved uptake, one in the whole population due to be screened (Richards 2001[41]) and one in those who had recently missed a screening appointment (Bankhead 2001[40]). Both these trials also reported that a flag in paper notes was similarly effective; the additional benefit of combining both interventions was unclear. These trials included a cost-effectiveness analysis reported in more detail in Brown 2006[57], but the costs are of limited relevance with the current computerisation of notes.

Turner 1994[33] (BSP) reported an increase in uptake with a GP letter sent with the standard second reminder. Sharp 1996[36] (BSP) reported an increase for non-attenders after reminders had failed for a GP letter compared with a nurse visit. Atri 1997[37] (BSP) compared GP letters (if phone calls failed) for non-responders against no further action and reported some evidence of benefit but this trial encountered some problems with the cluster randomisation.

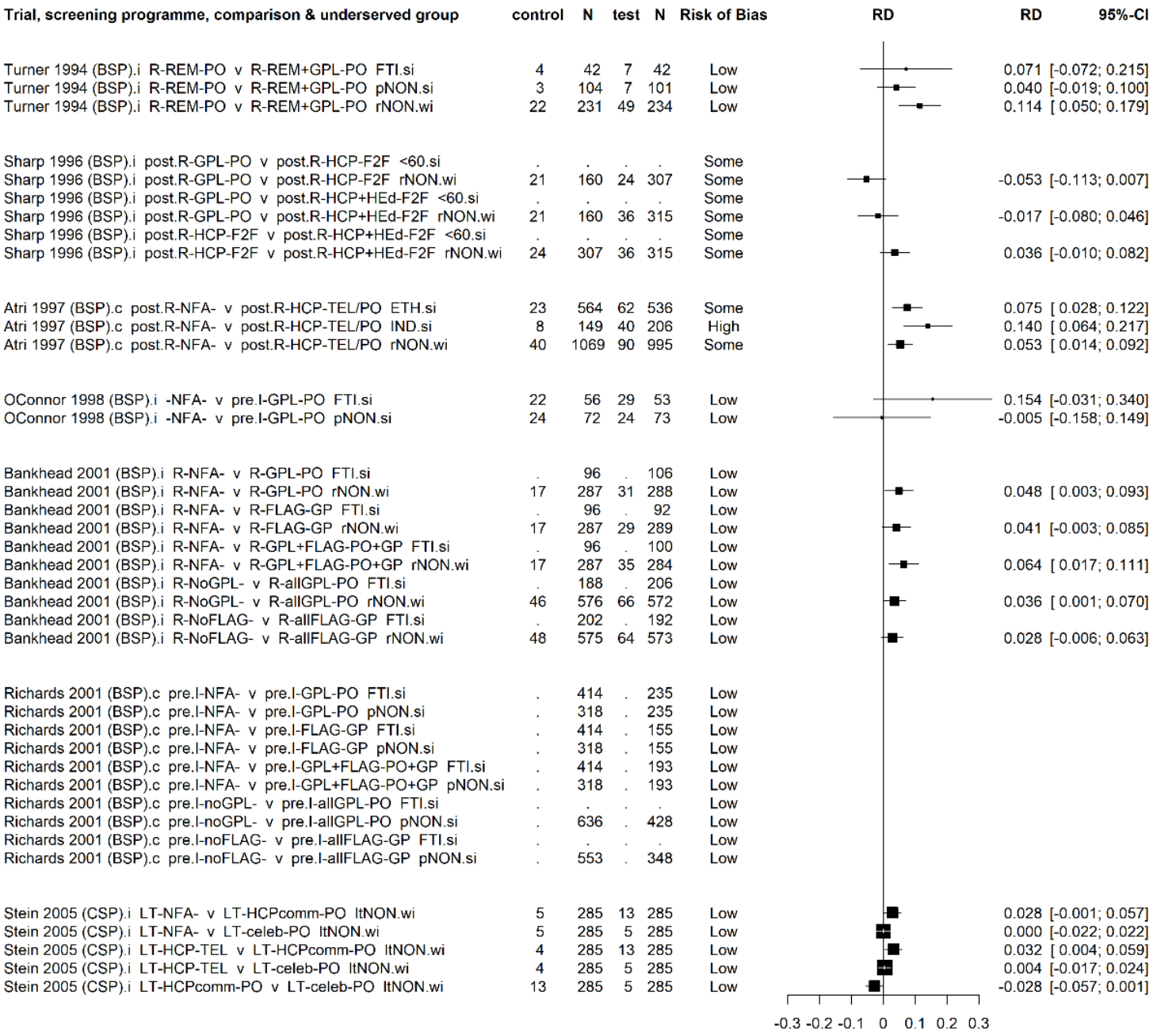
O'Connor 1998[39] (BSP) compared pre-invitation GP letters against no further action; it was too small to draw any firm conclusions about the benefit overall or in subgroups but the reported results are not inconsistent with Richards 2001[41] (BSP) which posed a similar question.

Although not strictly involving GP letters, there was also one trial in CSP (Stein 2005[49]) which compared a nurse phone call with letters from a local screening commissioner or a celebrity (Claire Rayner) for long-term non-attenders. The trial reported some evidence that the letter from a local screening commissioner was substantially more effective than nurse phone calls or letters from a celebrity. Following the interventions, uptake was still very low at less than 5% in this group in all three arms of the trial.

These results for each underserved group reported are shown in Figure 9.

These trials provide consistent evidence from four relatively small trials of variable quality that GP letters have a small to moderate effect on uptake in the reminder setting amongst underserved groups. One relatively small good quality trial suggests that they are also useful at the time of invitation. One good quality trial in each of these settings also suggests that flags in paper notes are similarly effective. Although the trials are relatively old, the same or similar interventions, such as flags in electronic patient records, would still be applicable today.

Figure 9 GP letters and other GP-based interventions (BSP, CSP)



See Table 1 for abbreviations
Assumes ICC of 0.03 for Atri 1997 as ICC not reported

3.3.9 Link worker or nurse telephone calls (BCSP, BSP, CSP, DES)

Six trials, three of which had a low risk of bias[21,45,49] and three with a high risk or some concerns[24,37,52] investigated the effect of a link worker or nurse telephone call on screening uptake in four different screening programmes. Overall, they provided little reliable evidence in favour of this intervention, especially when compared to other simpler interventions.

Shankleman 2014[24] (BCSP) reported results for a cluster trial comparing telephone health promotion with group sessions (and a non-randomised control arm, not eligible for this

review). The measure of uptake was based on aggregate practice data over the period of the trial and includes some screens which pre-date the trial and excludes some screens completed after the trial finished. The results do not provide evidence of a difference in effectiveness between these interventions.

Atri 1997[37] (BSP) compared phone calls from GP practices (and GP letters if phone calls failed) for non-responders with no further action and reported some evidence of benefit but this trial encountered some problems with the cluster randomisation.

One small trial with a low risk of bias in BSP (Chambers 2016[45]) reported no evidence that more intensive phone interventions improved uptake compared to a simple telephone reminder.

A larger multi-arm trial with a low risk of bias for recent non-responders in CSP (Kitchener 2018b[21]) included a nurse navigator arm (and also an arm offering a choice between a nurse navigator or an HPV self-sampling kit). The control arm was a standard reminder with open appointments. The other test arms were fixed/timed appointments, posted HPV self-sampling kit, or an offer of an HPV self-sampling kit. Uptake was lower on the nurse navigator arm compared to every other arm, although results were a little more encouraging for a choice of HPV self-test kit or nurse navigator.

Stein 2005[49] (CSP) compared a nurse phone call with letters from a local screening commissioner or a celebrity (Claire Rayner) for long-term non-attenders and reported some evidence that the letter from a local screening commissioner was substantially more effective than the other two arms, although uptake was less than 5% in all three arms in this very low uptake group (and less than 2% in the nurse phone call arm).

One small cluster trial in DES (Bush 2014[52]) compared the use of link worker telephone calls the day before a second (reminder) appointment against no further action. It reported a large increase in uptake of the order of 30% but this trial did not achieve balanced groups through the cluster randomisation. The results should be treated with caution, although the direction of effect is not implausible given that there was no intervention on the control arm.

These results for each underserved group reported are provided in Appendix 5.

Overall, these trials do not provide reliable evidence that link worker or nurse telephone calls increase screening uptake among underserved groups. While two trials provided positive results, they had a medium and high risk of bias and the results of the four other trials, three of which had a low risk of bias, were not consistent with this. In particular, three of the trials with a low risk of bias[21,45,49] found a greater increase in uptake with other reminder interventions, such as a simple telephone reminder, letter from a commissioner, or a fixed/timed appointment or HPV self-test kit sent in the post.

3.3.10 Link worker or nurse home visits or group sessions (BCSP, BSP, CSP)

Three trials (two with a low risk of bias[35,48] and one with some concerns regarding bias[36]) of link worker or nurse home visits and one trial (with a high risk of bias[24]) of group sessions did not provide consistent or reliable evidence that these types of intervention increase screening uptake in cancer screening programmes.

A small trial targeting Asian women in BSP (Hoare 1994[35]) reported no conclusive evidence of an increase in uptake with link worker home visits but it was not powered to detect a small difference.

Another trial in BSP (Sharp 1996[36]), after standard reminders had failed, reported no benefit of nurse home visits with or without health education compared to a simple GP letter.

A small trial for Asian women conducted by McAvoy 1991,[48] carried out in the 1980s before the CSP was fully established, reported a benefit for home visits compared to posted information materials but no benefit of video over written information provided at the home visit. The applicability of this trial to the current context is uncertain.

Shankleman 2014[24] (BCSP) compared group sessions with a telephone call and reported no reliable evidence of a difference, in a relatively small trial which encountered substantial methodological difficulties.

These results for each underserved group reported are provided in Appendix 5.

Overall, there is no reliable evidence in favour of these types of intervention in underserved groups. Although one trial, with a low risk of bias, carried out before the CSP was fully established, suggested that home visits may increase cervical screening uptake, it was a small trial and may not be applicable to the CSP today, and results from the other three trials were not consistent with this.

3.3.11 Office hours vs out-of-hours appointments (BSP)

One trial in BSP (Offman 2013[43]), assessed as having some risk of bias, reported evidence that provision of an office hours appointment with an option to switch to out-of-hours may be effective at increasing uptake in underserved groups.

Offman 2013[43] compared office hours appointments (with or without the option to book an out-of-hours appointment) with evening or weekend appointments. Limited data were reported for subgroups (see Appendix 5), but overall, the trial reported a benefit for office hours compared to out-of-hours, reporting the highest uptake for office hours with the option to switch to out-of-hours.

This single trial's finding that office hours appointments with an option to switch to out-of-hours was the most effective is not implausible. However, as it was a single trial, with some inconsistency between subgroups and some risk of bias, confirmation would be desirable.

3.3.12 Simplified 'gist' patient information leaflet (BCSP)

One trial in BCSP (Smith 2017[26] piloted in Smith 2015[19]), assessed as having a low risk of bias, did not report reliable evidence that screening uptake was affected by the addition of a 'gist' leaflet (a supplementary leaflet with simplified information) sent along with the kit and standard information booklet.

Smith 2017[26] randomised ten days within each of the five English screening hubs, treating each 'hub-day' as a cluster. The overall results and those within underserved groups slightly favour the intervention, by an order of 1%, but the effect is not large enough to rule out the play of chance (see Appendix 5 for forest plot). The authors noted that the

simplified leaflets did not replace the standard information leaflet and combining the two leaflets may have limited the effectiveness of providing simplified information.

Although this single trial with a low risk of bias did not provide reliable evidence in favour of the addition of a simplified leaflet to the screening invitation materials, it may be useful to consider testing the use of this type of leaflet in place of the standard leaflet if the simplified information was considered sufficient to allow participants to make an informed choice.

3.3.13 Narrative patient information leaflet (BCSP)

One trial in BCSP (McGregor 2016[27]), assessed as having a low risk of bias, tested the addition of a supplementary leaflet with short testimonies from people who had been screened, sent along with the kit and standard information booklet. The trial found no evidence of an increase in screening uptake overall (adjusted OR of 1.00 (95% CI 0.96 to 1.03)) or for any underserved subgroup (see Appendix 5).

McGregor 2016[27] randomised ten days within each of the five English screening hubs, treating each 'hub-day' as a cluster. There were relatively large imbalances in screening status between the groups. On review, these imbalances were considered likely to fall within what might be expected by chance, and adjusted ORs were reported, adjusted for age, gender, hub and screening history, to take account of imbalances. The authors noted that the narrative leaflet did not replace the standard information leaflet and combining the two leaflets may have affected the impact of the narrative information.

This single trial with a low risk of bias provided no evidence of an effect in favour of the addition of a narrative leaflet that included testimonies from people who had been screened to the screening invitation materials.

3.3.14 Information sent with pre-notification letter or home test kit (BCSP)

One trial in BCSP (Libby 2011[22]), with a low risk of bias, did not report reliable evidence that screening uptake was affected by whether the information booklet for BCSP was sent later with the kit or at the time of the pre-notification letter.

Libby 2011[22] tested the timing of the information booklet for BCSP (with a third arm of no pre-notification letter, not eligible for this review). Reported uptake was slightly higher when sending the booklet later with the kit, but this difference is consistent with chance (see Appendix 5). The authors also point out that earlier receipt of the booklet may inform individuals of the screening pathway earlier so they may make an informed choice to opt out of screening sooner.

This single trial with a low risk of bias reported results for underserved groups with wide confidence intervals and did not provide reliable evidence regarding the timing of the information booklet in BCSP. A confirmatory trial designed to detect a smaller difference and address informed opt outs might be useful.

3.3.15 Pre-notification letters (CSP)

A single trial in CSP (Kitchener 2018a[21]), with a low risk of bias, found no strong evidence of benefit from sending pre-invitation letters to first-time cervical screening invitees compared to no pre-invitation contact. This trial also found no strong evidence of benefit from providing information on how to book an appointment online at the same time as the pre-invitation letter. The online booking arm reported somewhat higher uptake than the pre-invitation letter alone, but this was not statistically significant (see Appendix 5).

This intervention is already standard for BCSP. However, for CSP, this single good quality trial offers no support for pre-notification letters for first-time invitees, although the online booking option may be worth testing further.

3.3.16 Tailored invitations (BSP)

One trial in BSP (Meldrum 1994[34]), with a low risk of bias, reported no overall benefit for tailored invitations which included details of screening history (see Appendix 5). There was some indication that the effect may vary by screening history, reducing uptake for previous non-attenders and weaker evidence of a possible increase for first-time invitees.

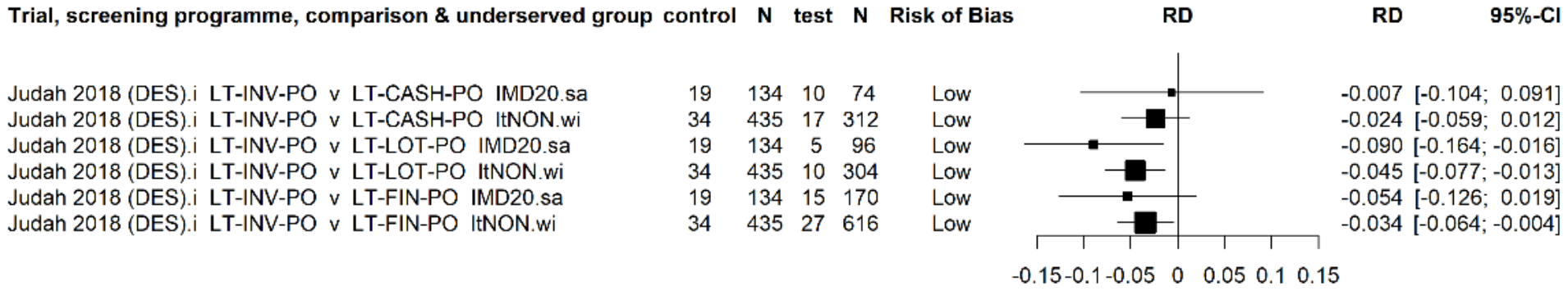
This single relatively small good quality trial offers no overall support for tailored invitations that include details of a person's previous screening history but suggests that it may be beneficial for first-time invitees. This result is not implausible, and a confirmatory trial may be useful. Increasing participation by first-time invitees has the potential to improve uptake for further rounds of screening if the first invite is accepted but reminding previous non-responders that they have previously not responded may be unhelpful.

3.3.17 Financial incentives (DES)

A single trial in DES (Judah 2018[53]), with a low risk of bias, reported evidence of a negative impact on uptake for financial incentives in a group who had not attended screening for at least two years (selected from the most deprived three quintiles by IMD). Two intervention arms offered either a £10 cash incentive or a 1% chance of winning a £1000 lottery (Figure 10).

This single good quality trial, although relatively small, provided strong evidence that financial incentives do not improve uptake, and this intervention is unlikely to be useful. Note however that financial incentives are not the same as removing financial barriers such as transport or postage costs.

Figure 10 Financial incentives (DES)



See Table 1 for abbreviations

3.3.18 Anticipated regret (BCSP, BSP)

One trial in BCSP (O'Carroll 2015[25]) and one in BSP (Chambers 2016[45]), both with a low risk of bias, found no evidence of an increase in screening uptake with the addition of questions about anticipated regret (for example asking the participant whether, if they did not complete the test, they believed they would regret this later) to communications about screening (see Appendix 5).

O'Carroll 2015[25] (BCSP) included a questionnaire with the pre-notification letter, combining questions about anticipated regret with a health locus of control questionnaire (HLOC) and used two control arms, one with HLOC alone and one with no intervention. Chambers 2016[45] (BSP) used anticipated regret questions in one arm of a trial testing three telephone interventions in addition to a standard postal reminder for recent non-responders: a simple telephone reminder, telephone support, and telephone support with anticipated regret questions.

These two good quality trials, one of which was relatively large, found no benefit in terms of uptake from including questions about anticipated regret to pre-invitation letters for BCSP and to telephone reminders for BSP respectively.

3.3.19 Implementation intentions, planning (BCSP, BSP)

One trial in BCSP (Lo 2014[23]), assessed as having a low risk of bias, and one in BSP (Rutter 2006[42]), for which there was some concern regarding bias, found no evidence of an increase in screening uptake with the addition of tools to aid planning to overcome common barriers to screening.

Lo 2014[23] (BCSP) tested the addition of three preformulated intention plans addressing three common barriers to screening: practicalities, forgetting, and negative feelings about the test. It reported no increase in uptake overall. There was some suggestion of a small benefit (of the order of 2%) for the most deprived tertile and weak evidence of an interaction by socioeconomic status, but this result is not secure in the context of multiple analyses. Baseline characteristics were not reported.

Rutter 2006[42] (BSP) tested the inclusion of a planning tool to overcome barriers to screening sent shortly before the screening invitation was due. The barriers addressed were: changing an inconvenient appointment, arranging travel, and getting time off work. The planning intervention included a survey, based on the Theory of Planned Behaviour as an explanatory tool for the researchers, and was compared to two control arms, one including the survey only and one with no additional intervention. Uptake was no higher with the intervention and a substantial reduction was observed for previous non-attenders (with no evidence of a difference for first-time invitees).

These results are included in forest plots in Appendix 5.

These two trials, for which there was some concern regarding bias for one, failed to provide consistent or reliable evidence in favour of addressing intentions and barriers to uptake of screening within communications around the time of the screening invitation.

3.3.20 Psychoeducational booklet (BSS)

One trial in BSS (Wardle 2003[31]), with a low risk of bias, found a small increase in uptake of around 3 to 4% with a psychoeducational booklet sent prior to the screening invitation. There was very weak evidence of an interaction by socioeconomic status, with higher uptake in more deprived tertiles.

This trial was nested within a larger trial of the effectiveness of flexible sigmoidoscopy, in a subgroup of people included in that trial who had indicated they would “probably” but not “definitely” attend for BSS screening. This group therefore had a relatively high propensity to attend. The paper does not report sufficient numerical evidence to plot the results.

Although this is a single trial, with the results not confirmed, it was moderately sized with a low risk of bias and one of the few trials that attempted to assess whether the benefit was affected by level of socioeconomic deprivation. The trend observed was not statistically significant and it may be worth assessing this approach in an adequately powered trial.

3.3.21 Combining invitations for BSP and CSP

One trial (Lancaster 1992[20]), with a moderate to high risk of bias, found a higher uptake of cervical screening together with a very weak suggestion that breast screening uptake may be reduced when a cervical screening invitation was added to the breast screening invitation (see Appendix 5).

This trial offered walk-in cervical screening on attendance at mammography. The results are complicated to interpret because one group was invited to cervical screening (with the breast screening invitation) and the other only if they attended for breast screening. There was no true control group. Uptake of cervical screening was higher with the combined invitation. There was very weak evidence that uptake for BSP might have been reduced in a subgroup of Asian women who received a combined invitation but this was a data-driven analysis, motivated by the observation that some practices with very low BSP uptake also had a very high proportion of Asian patients and this result cannot be considered reliable.

This was a small low quality trial that is difficult to interpret, providing mixed results. It suggests that combining breast and cervical invitations might be worth investigating further, although this may not be straightforward because of differences between the programmes.

4 Discussion

4.1 Summary of findings

All the eligible evidence identified by this systematic review relates to screening invitation and reminder strategies, with none identified for other points in the screening pathway. The strongest evidence for increasing uptake in underserved groups in YPA screening programmes was for people who had not responded to an invitation for screening who were sent reminders in different ways, including being sent fixed/timed appointments; GP letters; and HPV self-test kits (for CSP), as well as unconfirmed results favouring annual reminders (for BSS) and enhanced reminder letters (for BCSP). The evidence for reminders involving text or telephone contact following non-attendance was less robust. Reminder interventions are relatively cost-effective to implement as they apply only to a subgroup of those eligible for screening. The strong evidence in favour of HPV self-test kits is promising but this would entail a major change to the CSP and would need to take into account a range of other factors such as screening test performance, the manufacture of test kits and pathology laboratory resourcing.

There was strong evidence that financial incentives do not improve uptake, from a single good quality trial of persistent non-attenders for DES in the most deprived three quintiles by IMD. This result is consistent with observations made by a previous systematic review which did not include this trial (Jepson 2000[54]).

Interventions for which there was some, but weaker or unconfirmed, evidence included a range of different types of interventions: pre-appointment reminders by post or text message, where only one trial was found for each mode of delivery; an office hours appointment with the offer of a switch to an out-of-hours appointment; GP letters near the time of invitation; GP endorsed invitations; and an unpublished psychoeducational booklet (for BSS).

There was little or no evidence favouring: nurse or link worker telephone calls or home visits, pre-notification letters in cervical screening, tailored invitations referencing screening history, simplified leaflets, narrative leaflets, anticipated regret questions, or planning tools addressing barriers to screening.

Very few trials concerned with screening uptake in the general population reported an analysis of differences in the effectiveness of the intervention between underserved groups and the remainder of the population (interaction), to assess whether the intervention is likely to reduce inequalities in screening uptake. The four ASCEND trials[26-29] tested whether interventions might reduce the socioeconomic gradient in uptake of screening and Raine 2016b[29], which tested an enhanced reminder letter for non-responders in BCSP, was the only trial that reported strong evidence of an interaction (p=0.005) by socioeconomic status (IMD quintiles), with a stronger effect in the more deprived quintiles.

4.2 Strengths and weaknesses of this review

This review was primarily an exercise in organizing a very heterogeneous set of trials, covering different screening programmes, at different stages in the screening process, involving several different controls, interventions and underserved groups. There are some reasonably strong and consistent sets of results both for and against specific types of interventions. Some, such as fixed/timed reminder appointments in BSP and GP letters in BSP and CSP, are now used in the NHS while others such as HPV self-test kits are being considered.

This review only included RCTs, and some potentially useful interventions do not lend themselves to RCT designs. For example, intensive community-based interventions for extremely marginalised groups, addressing factors such as language, financial barriers and transport difficulties, are often heavily reliant on local context and would be complex to test in a randomised setting. Even in non-randomised settings, enhanced health promotion activities related to screening are difficult to evaluate as they may well be prompted by particular local circumstances.

The review only included trials specifically targeting underserved groups and trials aimed at the general population eligible for screening reporting results for at least one underserved subgroup. As a result, around two thirds of the UK trials identified in the searches were not included as they only reported results for a general screening population. Interventions shown to improve uptake in the general population may well improve uptake in underserved groups and this evidence also needs to be taken into account. Note, however, that trials of interventions for previous non-responders should all have been included because previous non-responders were considered an underserved group, and hence the search strategy should have identified all the UK trials of reminder-based interventions relating to the general population of previous non-responders.

Some trials included the general population eligible for screening and reported relevant subgroup results, while other trials only included patients in one or more underserved groups (results being for the whole trial population). This heterogeneity, as well as differences in trial design, population included, and intervention, in addition to the well documented problems associated with relying on subgroup results, led to the approach of extracting reported data for underserved groups from all trials and presenting them visually on forest plots without pooling the results. These plots provide an overview of results in underserved groups and

should not be used to identify specific groups for which the interventions do or do not work, particularly where results were reported for multiple small subgroups.

The review only included evidence from the UK, in order to appraise the interventions likely to be the most applicable to the undeserved groups in this country. In addition, differences in screening programmes elsewhere, the nature of socioeconomic disadvantage and its association with ethnicity would substantially complicate interpretation of non-UK trials. This does not imply that there is no useful information from elsewhere. In particular, the lack of eligible studies about decision aids does leave an important gap, with only non-UK studies available [76–81].

There is limited information on uptake by ethnicity. As noted in the review by Sokal 2010,[55] ethnicity is strongly associated with socioeconomic status and so questions about ethnicity and uptake are confounded by deprivation, a problem encountered frequently in health care research.[60,61]

5 Conclusions

5.1 Results in context with previous reviews

Many of our findings were in concordance with an earlier review, Jepson 2000,[54] which addressed a similar question but with a much broader scope, including both randomised and non-randomised evidence worldwide from any type of screening. Jepson 2000[54] also included an analysis of factors related to screening uptake.

Jepson 2000[54] recommended that studies of uptake include measures of informed choice. We agree with this but would also note that this would introduce both a (self-) selection bias and the possibility of a reduction in uptake because of the need for participants to read additional materials and complete the questionnaires. This observation is supported by another systematic review by Myers 2020.[56] The authors had planned a complex analysis of combined interventions with a view to identifying promising strategies but the dataset was too heterogeneous for this purpose. They reported a simplified analysis of interventions exploring the volume of printed materials received by people invited for screening, finding that additional printed materials appeared to reduce uptake. We had also reached this conclusion based on observations by Smith 2017[26], McGregor 2016[27], and McGregor 2016b[62] and some weak trends in O'Carroll 2015[25] and Rutter 2006[42]. O'Carroll 2015 and Rutter 2006 both included an additional questionnaire regarding beliefs alongside the intervention and neither included an arm with the intervention alone (without the additional questionnaire) for a straightforward comparison with the untreated control group.

This review reports results for specific underserved groups rather than more traditional (and strictly correct[14]) subgroup analysis, although reported interactions are included in the narratives and the more detailed trial summary tables. The reason for this is illustrated by the difficulties Myers 2020[56] ran into when trying to pool subgroups across trials in BCSP. This is a very heterogeneous set of trials, with substantial variation in both intervention and control arms, and not all trials recruited a general population of people eligible for screening. Attempting a meta-analytic subgroup analysis in this way has very little methodological

validity, and a meta-analysis of interactions (i.e. attempting to maintain the trial level results within a meta-analysis of interactions) would run into similar difficulties.

5.2 Gaps in the evidence

5.2.1 Non-cancer screening programmes

All but one of the trials included in this review related to cancer screening programmes, with one for DES and none for AAA screening. As AAA screening has some structural similarities with BSS, being a one-time screen of older adults, the evidence in favour of annual reminders for BSS provides a useful hypothesis for AAA screening and would be worth investigating in this context. There may also be sufficient similarity between the screening processes for BSP and CSP to prompt trials of interventions in one screening programme which have been shown to work well in another. Other interventions for which there was the strongest evidence in cancer screening programmes could also be considered as a priority for testing in the DES and AAA programmes.

5.2.2 Underserved groups that are more difficult to engage in research

Most of the evidence identified for underserved groups related to socioeconomic disadvantage, age, gender and previous non-response to invitations. It is important to also investigate interventions that would improve screening uptake in other groups that are more difficult to engage but also often at high risk of the condition being targeted by screening, such as those not registered with a GP, homeless people, rough sleepers, asylum seekers, gypsy and traveller groups, sex workers, those in prison, those experiencing severe and enduring mental health problems, people with drug or alcohol harm issues or communication difficulties and those with other protected characteristics described in the 2010 Equality Act. Difficulties in engaging these groups would need to be considered in designing the trials. It is also important that larger trials have the power to investigate whether interventions are more or less effective in underserved groups compared to the screening population as a whole.

5.2.3 Other aspects of screening participation

Screening inequalities can occur at multiple points in the screening pathway whereas all the evidence identified by this systematic review for YPA screening programmes related to screening test uptake. It is important to understand the inequalities in general knowledge and attitudes about screening and informed choice before receiving an invitation for screening as this is likely to be crucial in the decision to participate (Young 2018[63]). Further along the pathway, a high proportion of people with a positive screening result typically go on to receive diagnostic tests and treatment. It is not completely clear which population groups are less likely to complete the screening pathway or why (Dalton 2018,[64] Plumb 2017[65]). It is plausible that people who face barriers at one stage in the screening pathway will also face barriers at other stages. Designing trials to examine this can be complex, because of the confounding effects of the questionnaires used to assess screening knowledge, attitudes and informed choice and because of the large numbers required and the need for informed consent for trials relating to diagnosis and treatment. However, improvements at all stages of the screening pathway are important if screening inequalities and the burden of diseases that are being targeted by screening are to be reduced.

5.3 Implications for future research design

5.3.1 Introduction of new interventions

The introduction of new interventions, especially where the evidence is less secure, should be done via a research design that allows further evaluation in real-world practice. The ability of NHS screening programmes to facilitate this, for example by individually randomising people eligible for screening, is important.

5.3.2 Cluster trials

Cluster trials should include enough clusters to achieve reasonable balance across sociodemographic factors which often vary considerably between smaller geographical clusters, such as GP practices, especially with respect to granular details of minority ethnicity and the factors contributing to socioeconomic deprivation.

5.3.3 Competing questions

Trials addressing theories from behavioural psychology should ensure that real-world uptake questions can successfully be answered at the same time. There is some evidence that large volumes of printed materials may reduce uptake and this should be avoided where possible.

5.3.4 Testing interventions that do not lend themselves to RCT designs

For interventions that, because of their nature, cannot be tested through an RCT design, research should aim to include comparator groups that are as closely matched as possible and include collection of data on potential confounding variables.

6 Summary box

What is already known

- Participation in screening varies both within and between screening programmes, and groups at higher risk of the condition being screened for are often also less likely to participate in screening.
- Little is known about which interventions specifically improve screening uptake amongst these underserved groups.

What this study adds

- There is relatively strong evidence of improvement in screening uptake amongst underserved groups in the UK for a number of reminder-based interventions and these warrant further consideration.
- Further research is needed in relation to aspects of screening participation other than uptake, non-cancer screening programmes, less-researched underserved groups, and whether interventions have different effects in different groups.

7 References

1. Whitehead M. The concepts and principles of equity and health. Int J Health Serv Plan Adm Eval 1992; 22: 429–445.

2. Health Equity in England: The Marmot Review 10 Years On. The Health Foundation, https://www.health.org.uk/publications/reports/the-marmot-review-10-years-on (accessed 18 July 2020).

3. PHE. Supporting the health system to reduce inequalities in screening, PHE Screening inequalities strategy, https://phescreening.blog.gov.uk/wp-content/uploads/sites/152/2018/03/Supporting-the-health-system-to-reduce-inequalities-in-screening.pdf (2018).

4. Duffy SW, Myles JP, Maroni R, et al. Rapid review of evaluation of interventions to improve participation in cancer screening services. J Med Screen 2017; 24: 127–145.

5. Moher D, Liberati A, Tetzlaff J, et al. Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLOS Med 2009; 6: e1000097.

6. Moher D, Shamseer L, Clarke M, et al. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015 statement. Syst Rev 2015; 4: 1.

7. Population screening programmes: NHS abdominal aortic aneurysm (AAA) programme - GOV.UK, https://www.gov.uk/topic/population-screening-programmes/abdominal-aortic-aneurysm (accessed 23 June 2020).

8. Population screening programmes: NHS breast screening (BSP) programme - GOV.UK, https://www.gov.uk/topic/population-screening-programmes/breast (accessed 23 June 2020).

9. Population screening programmes: NHS cervical screening (CSP) programme - GOV.UK, https://www.gov.uk/topic/population-screening-programmes/cervical (accessed 23 June 2020).

10. Population screening programmes: NHS diabetic eye screening (DES) programme - GOV.UK, https://www.gov.uk/topic/population-screening-programmes/diabetic-eye (accessed 23 June 2020).

11. Population screening programmes: NHS bowel cancer screening (BCSP) programme - GOV.UK, https://www.gov.uk/topic/population-screening-programmes/bowel (accessed 23 June 2020).

12. Adams PR, Barrett E, Finnegan A. The development of validated UK geographic search filters for MEDLINE and Embase.

13. Sterne JAC, Savović J, Page MJ, et al. RoB 2: a revised tool for assessing risk of bias in randomised trials. BMJ 2019; 366: l4898.

14. Altman DG, Bland JM. Interaction revisited: the difference between two estimates. BMJ 2003; 326: 219.

15. Higgins J, Eldridge S, Li T. Cochrane Handbook Chapter 23: Including variants on randomized trials, https://training.cochrane.org/handbook/current/chapter-23 (accessed 23 June 2020).

16. Harrer M, Cuijpers P, Furukawa TA, et al. 2.2 The dmetar package | Doing Meta-Analysis in R, https://bookdown.org/MathiasHarrer/Doing_Meta_Analysis_in_R/dmetar.html (accessed 23 June 2020).

17. Schwarzer G, Carpenter JR, Rücker G. Meta-Analysis with R. Springer International Publishing, 2015.

18. Viechtbauer W. Conducting meta-analyses in R with the metafor package. J Stat Softw 2010; 36: 1–48.

19. Smith SG, Raine R, Obichere A, et al. The effect of a supplementary ('gist-based') information leaflet on colorectal cancer knowledge and screening intention: a randomized controlled trial. J Behav Med 2015; 38: 261–272.

20. Lancaster G, Elton P. Does the offer of cervical screening with breast screening encourage older women to have a cervical smear test? J Epidemiol Community Health 1992; 46: 523–527.

21. Kitchener H, Gittins M, Cruickshank M, et al. A cluster randomized trial of strategies to increase uptake amongst young women invited for their first cervical screen: The strategic trial. J Med Screen 2018; 25: 88–98.

22. Libby G, Bray J, Champion J, et al. Pre-notification increases uptake of colorectal cancer screening in all demographic groups: A randomized controlled trial. J Med Screen 2011; 18: 24–29.

23. Lo SH, Good A, Sheeran P, et al. Preformulated implementation intentions to promote colorectal cancer screening: A cluster-randomized trial. Health Psychol 2014; 33: 998–1002.

24. Shankleman J, Massat NJ, Khagram L, et al. Evaluation of a service intervention to improve awareness and uptake of bowel cancer screening in ethnically-diverse areas. Br J Cancer 2014; 111: 1440–1447.

25. O'Carroll RE, Chambers JA, Brownlee L, et al. Anticipated regret to increase uptake of colorectal cancer screening (ARTICS): A randomised controlled trial. Soc Sci Med 2015; 142: 118–127.

26. Smith SG, Wardle J, Atkin W, et al. Reducing the socioeconomic gradient in uptake of the NHS bowel cancer screening Programme using a simplified supplementary information leaflet: A cluster-randomised trial. BMC Cancer 2017; 17: 1–9.

27. McGregor LM, von Wagner C, Atkin W, et al. Reducing the Social Gradient in Uptake of the NHS Colorectal Cancer Screening Programme Using a Narrative-Based Information Leaflet: A Cluster-Randomised Trial. Gastroenterol Res Pract 2016; 2016: 3670150.

28. Raine R, Duffy SW, Wardle J, et al. Impact of general practice endorsement on the social gradient in uptake in bowel cancer screening. Br J Cancer 2016; 114: 321–326.

29. Raine R, Moss SM, Von Wagner C, et al. A national cluster-randomised controlled trial to examine the effect of enhanced reminders on the socioeconomic gradient in uptake in bowel cancer screening. Br J Cancer 2016; 115: 1479–1486.

30. Hirst Y, Skrobanski H, Kerrison RS, et al. Text-message Reminders in Colorectal Cancer Screening (TRICCS): a randomised controlled trial. Br J Cancer 2017; 116: 1408–1414.

31. Wardle J, Williamson S, McCaffery K, et al. Increasing attendance at colorectal cancer screening: testing the efficacy of a mailed, psychoeducational intervention in a community sample of older adults. Health Psychol Off J Div Health Psychol Am Psychol Assoc 2003; 22: 99–105.

32. Kerrison RS, McGregor LM, Counsell N, et al. Use of Two Self-referral Reminders and a Theory-Based Leaflet to Increase the Uptake of Flexible Sigmoidoscopy in the English Bowel Scope Screening Program: Results From a Randomized Controlled Trial in London. Ann Behav Med Publ Soc Behav Med 2018; 52: 941–951.

33. Turner KM, Wilson BJ, Gilbert FJ. Improving breast screening uptake: Persuading initial non-attenders to attend. J Med Screen 1994; 1: 199–202.

34. Meldrum P, Turnbull D, Dobson HM, et al. Tailored Written Invitations for Second round Breast Cancer Screening: A Randomised Controlled Trial. J Med Screen 1994; 1: 245–248.

35. Hoare T, Thomas C, Biggs A, et al. Can the uptake of breast screening by Asian women be increased? A randomized controlled trial of a linkworker intervention. J Public Health Med 1994; 16: 179–85.

36. Sharp DJ, Peters TJ, Bartholomew J, et al. Breast screening: A randomised controlled trial in UK general practice of three interventions designed to increase uptake. J Epidemiol Community Health 1996; 50: 72–76.

37. Atri J, Falshaw M, Gregg R, et al. Improving uptake of breast screening in multiethnic populations: a randomised controlled trial using practice reception staff to contact non-attenders. BMJ 1997; 315: 1356–1359.

38. Stead MJ, Wallis MG, Wheaton ME. Improving uptake in non-attenders of breast screening: Selective use of second appointment. J Med Screen 1998; 5: 69–72.

39. O'Connor AM, Griffiths CJ, Underwood MR, et al. Can postal prompts from general practitioners improve the uptake of breast screening? A randomised controlled trial in one east London general practice: J Med Screen 1998; 5: 49–52.

40. Bankhead C, Richards SH, Peters TJ, et al. Improving attendance for breast screening among recent non-attenders: a randomised controlled trial of two interventions in primary care: J Med Screen 2001; 8: 99–105.

41. Richards SH, Bankhead C, Peters TJ, et al. Cluster randomised controlled trial comparing the effectiveness and cost-effectiveness of two primary care interventions aimed at improving attendance for breast screening. J Med Screen 2001; 8: 91–98.

42. Rutter DR, Steadman L, Quine L. An implementation intentions intervention to increase uptake of mammography. Ann Behav Med 2006; 32: 127–134.

43. Offman J, Wilson M, Lamont M, et al. A randomised trial of weekend and evening breast screening appointments. Br J Cancer 2013; 109: 597–602.

44. Kerrison RS, Shukla H, Cunningham D, et al. Text-message reminders increase uptake of routine breast screening appointments: a randomised controlled trial in a hard-to-reach population. Br J Cancer 2015; 112: 1005–1010.

45. Chambers JA, Gracie K, Millar R, et al. A pilot randomized controlled trial of telephone intervention to increase Breast Cancer Screening uptake in socially deprived areas in Scotland (TELBRECS): J Med Screen 2016; 23: 141–9.

46. Allgood PC, Maxwell AJ, Hudson S, et al. A randomised trial of the effect of postal reminders on attendance for breast screening. Br J Cancer 2016; 114: 171–176.

47. Allgood PC, Maroni R, Hudson S, et al. Effect of second timed appointments for non-attenders of breast cancer screening in England: a randomised controlled trial. Lancet Oncol 2017; 18: 972–980.

48. McAvoy BR, Raza R. Can health education increase uptake of cervical smear testing among Asian women? BMJ 1991; 302: 833–836.

49. Stein K, Lewendon G, Jenkins R, et al. Improving uptake of cervical cancer screening in women with prolonged history of non-attendance for screening: a randomized trial of enhanced invitation methods. J Med Screen 2005; 12: 185–189.

50. Szarewski A, Cadman L, Mesher D, et al. HPV self-sampling as an alternative strategy in non-attenders for cervical screening – a randomised controlled trial. Br J Cancer 2011; 104: 915–920.

51. Cadman L, Wilkes S, Mansour D, et al. A randomized controlled trial in non-responders from Newcastle upon Tyne invited to return a self-sample for Human Papillomavirus testing versus repeat invitation for cervical screening. J Med Screen 2015; 22: 28–37.

52. Bush K, Thomas R, Raymond NT, et al. Cluster randomised controlled trial evaluation of a Link Worker-delivered intervention to improve uptake of diabetic retinopathy screening in a South Asian population. Diab Vasc Dis Res 2014; 11: 294–297.

53. Judah G, Darzi A, Vlaev I, et al. Financial disincentives? A three-armed randomised controlled trial of the effect of financial Incentives in Diabetic Eye Assessment by Screening (IDEAS) trial. Br J Ophthalmol 2018; 102: 1014–1020.

54. Jepson R, Clegg A, Forbes C, et al. The determinants of screening uptake and interventions for increasing uptake: a systematic review. Health Technol Assess; 4.

55. Sokal R. A critical review of the literature on the uptake of cervical and breast screening in British South Asian women. Qual Prim Care 2010; 18: 251–261.

56. Myers L, Goodwin B, March S, et al. Ways to use interventions to increase participation in mail-out bowel cancer screening: a systematic review and meta-analysis. Transl Behav Med 2020; 10: 384–393.

57. Brown J, Welton NJ, Bankhead C, et al. A Bayesian approach to analysing the cost-effectiveness of two primary care interventions aimed at improving attendance for breast screening. Health Econ 2006; 15: 435–445.

58. Asaria M, Griffin S, Cookson R, et al. Distributional cost-effectiveness analysis of health care programmes--a methodological case study of the UK Bowel Cancer Screening Programme. Health Econ 2015; 24: 742–754.

59. Including a general practice endorsement letter with the testing kit in the Bowel Cancer Screening Programme: Results of a cluster randomised trial, ASCEND 2. J Med Screen 2021 Feb; 27 (online ahead of print)

60. Nazroo JY. The structuring of ethnic inequalities in health: economic position, racial discrimination, and racism. Am J Public Health 2003; 93: 277–284.

61. Saini A. Stereotype threat. The Lancet 2020; 395: 1604–1605.

62. McGregor L, Isitt J, von Wagner C, et al. Improving uptake of flexible sigmoidoscopy screening: a randomized trial of nonparticipant reminders in the English Screening Programme. Endoscopy 2016; 49: 35–43.

63. Young B, Bedford L, Kendrick D, Vedhara K, Robertson JFR, das Nair R. Factors influencing the decision to attend screening for cancer in the UK: a meta-ethnography of qualitative research. Journal of Public Health 2018, Vol. 40, No. 2, pp. 315–339

64. Dalton A. Incomplete diagnostic follow-up after a positive colorectal cancer screening test: a systematic review. Journal of Public Health 2018, Vol. 40, No. 1, pp. e46–e5887.

65. Plumb A, Ghanouni A , Rainbow S ,Djedovic N , Marshall S , Stein J, Taylor S, Halligan S, Lyratzopoulos G ,von Wagner C. Patient factors associated with non-attendance at colonoscopy after a positive screening faecal occult blood test J Med Screen 2017 Mar;24(1):12-19

8 Glossary

Cluster trials	Trials where groups of people (such as households, GP practices, or hospitals) are randomised, usually because the intervention can only be applied at that level (eg training GPs and measuring the outcome for their patients). Analysis of cluster randomised trials needs to account for the fact that individuals within clusters are more similar to each other than they are to the trial population as a whole. Clustering reduces the effective sample size by an amount which depends on the strength of the intra-cluster correlation coefficient, the number of clusters and the size of the clusters.[1]
Confounding	When a factor associated with an outcome is associated with another factor which is also associated with the outcome, making it difficult to establish the true relationship (eg whether ethnicity has an impact on uptake independently of socioeconomic status)
Factorial design	A trial design which tests two interventions simultaneously and allows for testing any interaction between them. The whole population is randomised to A or not A and also to B or not B, creating four groups who receive: neither treatment, A only, B only, or A and B combined. Each group may be compared to each of the others but the most powerful approach is to analyse A vs not A and B vs not B. An interaction (non-additive effects for A combined with B) can complicate interpretation, and require much larger sample sizes to measure than the main effects, but may also be of interest in its own right.
Intention-to-treat	The principle that all randomised individuals (or clusters) should be analysed in the group they were originally allocated to regardless of the treatment delivered. This is to preserve the integrity of randomisation. Post-randomisation exclusion risks introducing bias because the decision to exclude (or look for reasons to exclude) may be influenced by knowledge of the group allocation.
Interaction	The difference between the effect sizes measured within each level of a subgroup.[2]

[1] Higgins JPT, Eldridge S, Li T. Cochrane Handbook, Chapter 23.
[2] Matthews JNS, Altman DG. Statistics Notes: Interaction 2: Compare Effect Sizes Not P Values. *BMJ*, 1996; 313: 808

Quasi-randomisation	Using a factor which is essentially random, such as day of attendance or odd/even clinic numbers, to allocate individuals to groups. This is generally not an acceptable form of randomisation because the group allocation is predictable in advance and that knowledge may influence the decision to include an individual in the trial. This is of less concern in the group of trials included in this review because pre-randomisation consent cannot be used in trials which are designed to measure effects on uptake and the researchers usually do not have any clinical relationship with the individuals included in the trials.