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Promoting colorectal cancer screening: A systematic review and meta-analysis of randomised controlled trials of interventions to increase uptake

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Running heading: COLORECTAL CANCER SCREENING INTERVENTIONS

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Abstract

Colorectal cancer (CRC) represents a global public health concern. CRC screening is associated with significant reductions in CRC incidence and mortality, however, uptake is suboptimal. This systematic review and meta-analysis of randomised controlled trials explored the effectiveness of interventions designed to increase screening uptake, plus the impact of various moderators. Data from 102 studies including 1.94 million participants were analysed. Results showed significant benefit of all interventions combined (OR, 1.49, 95% CI: 1.43, 1.56, $p < 0.001$). The effects were similar in studies using objective versus self-reported uptake measures and lower in studies judged to be at high risk of bias. Moderator analyses indicated significant effects for aspects of behaviour (effects lower for studies on non-endoscopic procedures), and intervention (effects higher for studies conducted in community settings, in healthcare systems that are not free, and that use reminders, health-professional providers, paper materials supplemented with in-person or phone contact, but avoid remote contact). Interventions that included behaviour change techniques targeting social support (unspecified or practical), instructions or demonstration of the behaviour, and that added objects to the environment produced stronger effects. The way in which findings can inform interventions to improve CRC screening uptake is discussed.

Keywords: meta-analysis, colorectal cancer, screening uptake, health interventions, behaviour change techniques.

This systematic review and meta-analysis explores the effectiveness of interventions to increase colorectal cancer (CRC) screening behaviours in the general population. It provides evidence on the overall effectiveness of interventions on uptake and potential moderators of these effects including an exploration of how the use of various behaviour change techniques might be differentially effective.

Colorectal cancer is among the leading causes of mortality and morbidity, representing the third most commonly diagnosed malignancy, following lung and breast cancer, and is the fourth leading cause of cancer death worldwide (Torre et al., 2015). CRC accounts for over 9% of all cancer incidence with approximately 1.8 million new cases and 862,000 deaths occurring annually (based on 2018 data; World Health Organisation, 2018).

Encouragingly, evidence demonstrates that CRC incidence and mortality rates have been stabilising or reducing for several decades. Recent declining trends have largely been attributed to population-based screening programmes, which facilitate early-stage CRC detection and the prevention of CRC through the removal of precancerous polyps (Arnold et al., 2017; Center, Jemal, & Ward, 2009; Holme, Bretthauer, Fretheim, Odgaard-Jensen, & Hoff, 2013; Levin et al., 2008). The majority of developed countries have implemented organised CRC screening programmes.

A number of CRC screening methods are currently in use, with a range of invasiveness levels and recommended screening intervals (see Sarma, Silver, Kobrin, Marcus, & Ferrer, 2019 for a useful overview and comparison to other forms of cancer screening). The least invasive screening methods are various stool-based tests. These include the faecal occult blood test, the faecal immunochemical test, and the DNA stool test in conjunction with the faecal immunochemical test. The faecal occult blood test usually involves an individual using a provided kit to self-collect one or more stool samples at home and then sending it by postal service to a centralised facility for analysis (i.e., checking for the presence of blood that might indicate the presence of a polyp, cancer, or other abnormality). If abnormalities are detected, a follow-up diagnostic colonoscopy is usually

recommended. The faecal immunochemical test uses a similar procedure but requires a single stool sample to be collected and is a more sensitive test. Similarly a DNA stool test checks for genetic mutations that could be indicative of cancer. Direct visualisation tests principally include sigmoidoscopy and colonoscopy. Both involve using a scope to internally examine the rectum and/or colon for polyps, other abnormalities, or cancer (sigmoidoscopy examines only the lower colon and rectum; colonoscopy examines the entire colon and rectum) and usually take place in a centralised location (e.g., hospital, specialised CRC centre). International screening programmes vary in focus, although the use of the faecal occult blood test/faecal immunochemical test is the most common. Programmes also vary in terms of who qualifies for screening (e.g., most programmes specifically focus upon individuals over 50 years of age) and screening frequencies (e.g., every 1-3 years for faecal occult blood test/faecal immunochemical test; every 5-10 years for sigmoidoscopy/ colonoscopy) (see Sarma et al., 2019 for a useful recent discussion of these issues). The main benefit of CRC screening is earlier detection of cancer that can subsequently be more easily and effectively treated – leading to reductions in cancer-specific mortality. Results from several randomised controlled trials indicate that regular participation in CRC screening at a population level has led to significantly more favourable disease prognosis, improved overall patient outcomes, and a measurable impact on the overall global burden of CRC (Atkin et al., 2010; Lindholm, Brevinge, & Haglind, 2008; Schoen et al., 2012). A meta-analysis of four randomised controlled trials, including data from a sample of 320,000 participants, reported that annual or biennial faecal occult blood test screening had no effect on CRC incidence but was associated with a 16% reduction in the relative risk of CRC mortality (Hewitson et al., 2008). Moreover, CRC screening programmes are considered highly cost-effective and therefore investing public resources in early detection initiatives is likely to not only have strong health benefits but also to substantially reduce the estimated financial burden (Lansdorp-Vogelaar, Knudsen, & Brenner, 2011; Vanness et al., 2011).

However, for individuals, there are costs associated with participating in screening. These

costs include physical discomfort and potential complications associated with the screening tests, negative affective reactions linked to the tests (e.g., embarrassment, disgust), and the worry linked to awaiting test results or receiving false positive results.

Previous systematic reviews that have examined intervention effectiveness for increasing CRC screening uptake are scarce in the existing literature. One systematic review (Sabatino et al., 2008) examined the effectiveness, applicability and economic efficiency, and barriers-to-implementation for provider-directed interventions in relation to breast, cervical and colorectal cancers. Their findings suggested that interventions demonstrating some effectiveness for all three cancers were those that incorporated healthcare provider assessment and feedback. Another review (Baron et al., 2008) examined the effectiveness of different types of patient-directed interventions – including patient reminders/recall systems, incentives, small media, mass media and group education – to increase breast, cervical and colorectal cancer screening. Interventions using small media (e.g., leaflets providing information about screening) were associated with improved screening uptake across cancer types. Other existing reviews have focused on non-endoscopic screening modalities and/or USA-based studies only (Rat et al., 2017).

Previous reviews are predominantly limited by their narrative approach and by their focus on either provider- or patient-directed interventions as well as the restricted range of moderators examined. Interventions aimed at increasing CRC screening uptake are usually complex and heterogeneous across several dimensions. This includes the target population, the format, the mode of delivery, the setting in which interventions were delivered, the intervention provider, the screening modality, and other parameters relating to methodological quality (e.g., risk of bias, outcome assessment). All of these aspects are likely to influence the magnitude of intervention effectiveness, and yet they have rarely been reported in existing reviews.

In the present review we examined a range of key moderators of intervention effectiveness across the general population. The moderators examined fall into four groups: participant

characteristics, nature of the behaviour, methodological factors, and intervention characteristics.

In terms of participant characteristics we examined four moderators: age, gender, family history of cancer, and previous CRC screening. There is mixed evidence in relation to the effectiveness of interventions to increase CRC screening rates in younger versus older participants (Denberg et al., 2005; Klabunde, Meissner, Wooten, Breen, & Singleton, 2007) and this has not been explored in previous meta-analytic reviews. We therefore explored mean age of the sample in each study as a potential moderator. There is more evidence in relation to participant gender, although the results are inconclusive with women generally more likely to take part in less invasive procedures (faecal occult blood test/faecal immunochemical test; Weller et al., 2007) and men more likely to take part in more invasive procedures (sigmoidoscopy/colonoscopy; Ananthakrishnan, Schellhase, Sparapani, Laud, & Neuner, 2007; McGregor, Hilsden, Li, Bryant, & Murray, 2007; Meissner, Breen, Klabunde, & Vernon, 2006; Wardle, Miles, & Atkin, 2005). We therefore explored the percentage of males in a study as a potential moderator. A family history of cancer makes the risk of the disease more salient and may make CRC screening uptake more likely (Han, Moser, & Klein, 2007), and therefore the present meta-analysis examined whether intervention effectiveness varied as a function of the proportion of people in the sample with a family history of CRC. Finally, participants' previous CRC screening behaviour may also influence the effects of an intervention, although the direction of effect is unclear. For example, previous screening could lead to future consistent behaviour as has been found in other health behaviours (McEachan, Conner, Taylor, & Lawton, 2011). Alternatively, individuals could decide that having been previously screened reduces their desire or perceived need to be screened again. Therefore, we explored the percentage of the sample who had previously been screened in a study as a potential moderator.

In terms of the nature of the behaviour, we examined one moderator: screening modality. The screening modality used may influence intervention effectiveness because participants may be more or less receptive to preventive health messages depending on whether the screening procedure

provided is endoscopic or non-endoscopic in nature. What might attract patients to endoscopic procedures (e.g., lower chances of false negative results, possibility of removing polyps during the screening) might be different from what attracts patients to non-endoscopic procedures (e.g., less invasive, can be conducted from home). Therefore, we examined differences between studies that focused on: more invasive endoscopic procedures, less invasive non-endoscopic procedures (mainly faecal occult blood test/faecal immunochemical test), or those that included both procedures.

In terms of methodological moderators, we examined the effects of two moderators: outcome assessment and risk of bias. An important methodological difference between studies is the use of self-reported or objectively assessed screening behaviour. Although the former may be easier to collect, the latter is usually considered more important in this area given that such data is often routinely collected. Therefore the current meta-analysis explored differences between studies reporting objective versus self-report measures of screening. In addition, given the focus of the review was on randomised controlled trials, we examined the impact of different sources of bias using a standardised tool. In particular, we examined effects in studies classified as having low, unclear, or high bias. Confirming that interventions are effective in studies with a low risk of bias is an important component of this test.

In terms of intervention characteristics we examined effects of eight moderators: type of contact, mode of delivery, provider, intervention materials, intervention setting, use of reminders, type of healthcare system, and use of behaviour change techniques. First, interventions to increase CRC screening vary in terms of contact type and how the intervention was delivered. Most interventions use a remote means to contact individuals, although face-to-face contact is used in some studies to individuals or groups, and even combinations of face-to-face and remote contact is used. Therefore, in relation to type of contact, this review explored differences by studies using face-to-face, remote, or mixed contact methods. Second, group or community-based interventions offer participants the opportunity to connect with aspects of their social environment, which can

enhance collaborative/community decision-making and encourage collective action for behaviour change (Anderson, Scrimshaw, Fullilove, & Fielding, 2003; Swan, 2009; Wallerstein & Duran, 2010). We therefore explored individual versus group or mixed modes of delivery as a moderator. Third, despite past research identifying intervention provider as an important factor to consider with regards to intervention effectiveness, previous reviews and meta-analyses in the CRC screening literature have not examined this as a potential moderator. There is evidence to suggest that the involvement of health professionals (clinically trained or not) might be particularly beneficial in implementing interventions within the community (Gorin et al., 2006; Holmes et al., 2008; Palmer & Schneider, 2005; Shavers, Fagan, & McDonald, 2007). The fact that lay health educators are often 'rooted' within the community and hold indigenous knowledge enables them to handle intervention delivery with greater cultural sensitivity and to adapt their communication style to the cultural context of their local communities (e.g., participant ethnicity or social class). Therefore, the current review examined moderating effects of intervention provider being clinically-trained health professionals, non-clinically-trained health professionals, research staff, or not being person dependent.

Fourth, intervention materials can be provided in a variety of formats (mode of delivery) including electronic, paper-based, phone-based, personally delivered, or different combinations of these formats. This has not been explicitly explored in reviews of CRC screening, although this has been examined in other areas such as physical activity (Beall, Baskerville, Golfam, Saeed, & Little, 2014; Foster, Richards, Thorogood, & Hillsdon, 2013), cardiovascular medication adherence (Cutrona et al., 2010), and obesity prevention (Greaves et al., 2011; Kozica et al., 2015). Therefore the current review examined the moderating effect of the mode of delivery between electronic plus paper-based, paper-based only, paper plus phone-based, phone-based, in-person delivery, and paper-based plus in-person delivery. Fifth, CRC screening mainly takes place either in primary care or in the community. Therefore in relation to intervention setting we examined differences in

effectiveness between studies conducted in community or primary care settings. Sixth, CRC screening programmes vary in their use of reminders and we therefore examined differences in effectiveness between studies in terms of whether reminders were employed or not. Seventh, the healthcare systems that interventions take place within differ considerably. A potentially important dimension is the extent to which the healthcare system provides free access to all (as is the case in the UK) or some form of payment is required (as is mainly the case in the USA).

Eighth, in addition to the above intervention characteristics, we also coded studies in terms of the behaviour change techniques employed. Behaviour change techniques have been defined as the 'active ingredients' of behaviour change interventions and constitute the smallest intervention components whose detailed specification is crucial for observing, implementing and replicating effective interventions (Michie et al., 2013). The Behaviour Change Technique Taxonomy Version 1 (BCTTv1) consists of 93 distinctive, non-overlapping behaviour change techniques, each with a clear definition and hierarchically clustered into 16 groups (Michie et al., 2013). This taxonomy enables researchers on the one hand to specify and describe the key 'active ingredients' of interventions, which is critical for promoting replication of specific intervention strategies, and reviewers on the other hand to take a detailed approach in extracting and synthesising information about intervention content in an attempt to understand which specific strategies are responsible for changes in behaviour. We coded all studies in relation to the presence or absence of each of the 93 behaviour change techniques, although it was only possible to explore the effect of seven behaviour change techniques based on their use across studies (see Method). As for other moderators, we explored the impact of the presence of each behaviour change technique (in the intervention versus control conditions) on study effectiveness. To our knowledge, the present meta-analytic review is the first in the field of CRC screening to investigate the effectiveness of individual behaviour change techniques to increase screening uptake using the BCTTv1 among average-risk populations.

In summary, the present systematic review and meta-analysis investigated the effectiveness

of interventions to increase CRC screening in the general population. It also assessed the impact of various important moderators of intervention effectiveness, including the use of various behaviour change techniques.

Method

Search strategy and selection criteria

Methods were applied according to the Preferred Reporting Items for Systematic reviews and Meta-analyses (PRISMA) guidelines. The review was preregistered on PROSPERO (https://www.crd.york.ac.uk/prospero/display_record.php?RecordID=33782). We searched electronic databases (Embase, PsycINFO and MEDLINE) from inception until May, 15, 2016, to identify randomised controlled trials of interventions aiming to increase CRC screening uptake (See Supplementary Table 1 for database search strategy). The search strategy was developed based on the Participants, Interventions, Comparisons, Outcomes, Study design (PICOS) framework. Trials were eligible for inclusion provided they: (1) randomly allocated participants to condition; (2) included participants over 50 years at point of randomisation; (3) included participants with no personal history of CRC; (4) reported outcome data quantitatively; (5) reported unique data; and (6) were published in a peer-reviewed journal. There was no restriction on nature of control group and only studies using randomised controlled trials or cluster randomised controlled trials were included. Only studies reporting screening behaviour were included (studies only reporting intention were excluded). Non-English language trials were ineligible for inclusion (See Supplementary Table 2 for characteristics of included studies including details on each study arm). After removing duplicate publications, one author (AT) pre-screened all search results (titles, abstracts) against inclusion criteria. A second author (LH) independently reviewed 20% of abstracts. AT assessed the selected full-text articles for inclusion and 20% of relevant citations were checked independently by LH. There was 100% agreement between reviewers at each of these two steps. All analyses were conducted independently by three authors (AT, NT, SW) and any disagreements were resolved

through discussion.

Data extraction

Quantitative information was extracted using a standardised, pre-piloted data extraction form (Supplementary Appendix A). In order to help with coding, study authors were contacted to provide additional information as required. Risk of bias was assessed by AT according to the Cochrane Collaboration's tool (Higgins et al., 2011) (i.e., random sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data, selective reporting and intention-to-treat analysis) and studies were coded into low, unclear or high risk of bias (See Supplementary Table 3 for risk of bias in individual studies). We report overall levels of risk of bias and also consider risk of bias as a methodological moderator.

The moderators coded fell into four groups: participant characteristics, nature of the behaviour, methodological factors, and intervention characteristics. In terms of participant characteristics these were all continuous measures. *Age* was coded as mean age of the sample in a study (data available for 140 tests). *Gender* was coded as the percentage of males in the sample in a study (data available for 139 tests). *Family history* of cancer was coded as percentage of sample with a family history of CRC in a study (data available for 40 tests). *Screening status at time of study* was coded as percentage of participants in a study with up-to-date baseline CRC screening (data available for 60 tests).

In terms of the nature of the behaviour, we coded *screening modality*. Studies were coded as involving only endoscopic (data available for 10 tests), only non-endoscopic (data available for 56 tests), or either (data available for 86 tests) procedure. In terms of methodological moderators we coded *outcome assessment* and *risk of bias*. Studies were coded as using an objective measure of screening outcome if data was based on objective records of CRC (data available for 119 tests) or as self-report if based on patient responses (data available for 21 tests). Risk of bias in each study was coded using the tool noted earlier (Higgins et al., 2011) into high (data available for 69 tests), unclear

(data available for 52 tests) or low (data available for 31 tests) bias.

In terms of intervention characteristics, we coded eight moderators: *contact type, mode of delivery, provider, intervention materials, intervention setting, use of reminders, type of healthcare system,* and *use of behaviour change techniques*. Contact type was coded as face-to-face (data available for 18 tests), remote (i.e., not delivered face-to-face and used a variety of modes such as standard mail, internet and telephone; data available for 121 tests) or mixed (i.e., when both face-to-face and remote contact were used; data available for 14 tests). Mode of delivery was coded as individual (i.e., when delivered one-to-one; data available for 137 tests) or group/mixed (i.e., when not delivered one-to-one; data available for 15 tests). Provider was coded as clinically-trained health professionals (data available for 7 tests), non-clinically-trained health professionals (data available for 35 tests), research staff (data available for 15 tests), or non-person dependant (i.e., when there was no direct contact with health professionals or research staff; data available for 88 tests). Intervention materials were coded as electronic plus paper-based media (data available for 29 tests), paper-based media only (data available for 61 tests), paper-based media plus phone (data available for 25 tests), phone only (data available for 12 tests), in-person delivery (data available for 13 tests), or paper-based media plus in person delivery (data available for 9 tests). Intervention setting was coded as either community (data available for 42 tests) or primary care (data available for 107 tests). Use of reminders was coded as reminders used (data available for 47 tests) or not used (data available for 58 tests). Type of healthcare system was coded as free (data available for 46 tests) or not free (data available for 106 tests) healthcare.

Data on each of the above moderators was coded by AT using a standardised form (See Supplementary Appendix A for data extraction form). A second author (LH) independently coded data from 20% of eligible articles. The degree of inter-rater agreement was 95% and ranged from 79 (risk of bias) to 100% (modality, outcome, contact type, mode of delivery, provider). Any disagreements were resolved by discussion. See Supplementary Appendix B for an overview of

coding strategies for each of these different moderators.

Based on Michie et al. (2013), information was extracted on the presence of behaviour change techniques in both the intervention and control arms. Table 1 provides definitions and examples of the 7 behaviour change techniques identified across the 102 studies reviewed that occurred in at least 10 studies and we were therefore able to analyse (See Supplementary Figure 1 for frequency of occurrence of each of the 35 behaviour change techniques that appeared in at least one study; See Supplementary Table 4 for definitions and examples of all 35 behaviour change techniques identified across studies). Only behaviour change techniques that were present in the intervention and absent in the control condition were included in the moderator analyses. This approach has been reported elsewhere (MacDonald, Lorimer, Knussen, & Flowers, 2016; Peters, de Bruin, & Crutzen, 2015; Samdal, Eide, Barth, Williams, & Meland, 2017) and was used to ensure that any observed difference in effect could be attributed to the inclusion of specific behaviour change techniques in any given intervention. Data on the presence of each behaviour change technique in each study arm were extracted by two researchers independently (AT plus DBB or LH) and only coded as present if identified as present by both researchers (100% agreement).

Data analysis

The primary outcome was the proportion of participants completing CRC screening at follow-up. All summary effects and associated statistics were computed using Comprehensive Meta-Analysis (Version 3). Effect size estimates were calculated based on number of events screened per number of participants in a given study arm and pooled under the random effects model, with data expressed as odds ratios (ORs) with 95% confidence intervals (CIs). A Cohen's *d* effect size with Hedge's *g* correction for small sample bias was calculated for all study comparisons (g = 0.20, 0.50, 0.80 represented small, moderate, and large effect sizes respectively). Where studies had more than one experimental condition compared with a single control condition, the number of participants in the control condition was divided across experimental conditions to avoid double counting. We

comment further on this strategy in the discussion. Small-study bias is suggested when observed effect sizes increase with smaller sample sizes (and thus larger standard errors). A potential cause underlying this bias is publication bias (where the likelihood of publication is affected by the results of studies). Small-study bias was examined using Egger's test.

Between-study heterogeneity was assessed by Cochran's *Q*-statistic (measure of weighted squared deviations) and the I^2 statistic (proportion of total observed variance attributable to between-study variation in effect size as opposed to random error). Investigation of the potential causes of heterogeneity (i.e., moderator effects) was undertaken when $p < .05$ for the *Q*-test (Cochran, 1954; Higgins, Thompson, Deeks, & Altman, 2002). The Q-statistic ($Q_{between}$) was used to compare categorical subgroups and meta-regression was used for continuous moderators.

Pearson's correlations were computed to examine interdependence between moderators. Variables were considered confounded if shared variance exceeded 25% (i.e. $r > 0.50$).

Results

Overall Sample

Our search strategy identified 8783 articles, of which 260 articles met criteria for full-text review (Figure 1). A total of 102 randomised controlled trials, incorporating 152 study comparisons[1] ($k = 152$) met study criteria and included 1,941,165 participants (study median $N = 769$) (See Supplementary Appendix C for references to included publications; See Supplementary Table 2 for included study details; see https://osf.io/kx48g/?view_only=2e78a039727f4cec92302121a3927b92 for raw data). A total of 919,037 and 1,022,128 participants were assigned to intervention and control arms respectively. Median study publication year was 2012 (range 2000-2016). Mean participant age was 61.3 years (range 50-80 years). The majority of participants were female (59.1%), and the majority of studies were conducted in the USA ($N = 75$) or Europe ($N = 17$). The median follow-up period was 10 months (range 4 weeks-3 years). The modal control condition was

[1] Thirty articles included several treatment arms and a single control arm. Each comparison of a treatment arm to a control arm was referred to here as a 'study comparison'.

usual care (70 trials, 68.6%; 32 trials, 31.4% used enhanced usual care). Thirty trials (29.4%) involved multiple study comparisons (several intervention conditions compared against a single control condition). Approximately one fifth of trials were graded as being at low (k = 23, 21.9%), about one-third (k = 40, 38.1%) as unclear and two-fifths (k = 42, 40.0%) as high risk of bias (Figure 2). Public health interventions were associated with significantly greater CRC screening uptake rates compared with controls (g = .221, OR = 1.49, 95% CI: 1.43, 1.56, $p < 0.001$; $Q(151) = 4067.06$, $p < .001$, $I^2 = 96.3$), i.e., a small effect size. Egger's regression revealed significant asymmetry ($\beta = 6.19$, 95% CI 4.47 to 7.92, $p < .001$), suggesting the findings were susceptible to small-study bias which may be indicative of publication bias.

In relation to the overall effect, significant heterogeneity was observed ($Q = 4067.306$, $p < .001$, $I^2 = 96.287$), supporting the need to investigate the influence of various moderators of effect size.

Continuous Moderators

Table 2 reports the results of the assessment of sample moderators using weighted meta-regressions. This revealed that age of the sample, proportion of sample who were male, family history of CRC, and being up-to-date with screening at baseline were each unrelated to intervention effects (Table 2), i.e., the interventions showed similar levels of effectiveness across these groups.

Categorical Moderators

Table 3 reports effects of the moderators of nature of the behaviour, methodological factors, and intervention characteristics (consideration of the use of behaviour change techniques as moderators is reported in Table 4). In relation to nature of the behaviour, Table 3 shows that interventions were differentially effective across endoscopic only, non-endoscopic only and either (endoscopic or non-endoscopic) *screening modalities* ($Q(2) = 26.36$, $p < .001$). Pairwise comparisons showed that interventions were more effective for endoscopic only screening compared to the non-endoscopic only category ($Q(1) = 5.13$, $p = .02$); while interventions in the either modality

category were more effective than interventions in non-endoscopic only category ($Q(1) = 25.75$, $p < .001$), the endoscopic and either categories did not significantly differ from one-another ($Q(1) = 0.01$, $p = .92$).

Moving on to methodological moderators, in relation to *outcome assessment*, interventions were no more effective in studies reporting objective (e.g., Dietrich et al., 2006; Fiscella et al., 2011) compared to self-report (e.g., Horne et al., 2015; Walsh et al., 2010) measures of screening uptake ($Q(1) = 0.64$, $p = .42$). In relation to *risk of bias*, there was evidence of differential effectiveness of interventions across bias categories for the categories of bias ($Q(2) = 18.20$, $p < .001$). Pairwise comparisons demonstrated that the high bias versus unclear bias ($Q(1) = 6.32$, $p = .012$), and high bias versus low bias ($Q(1) = 13.06$, $p < .001$) categories were significantly different from one-another, with the high bias studies reporting the smallest effect sizes. The difference between the unclear bias and low bias categories was not significant ($Q(1) = 0.05$, $p = .82$). It is notable that interventions in the low bias category (e.g., Green et al., 2013; Hendren et al., 2014) that used objective measures were demonstrated to have significant effect sizes.

In relation to intervention characteristics, Table 3 also shows the results of the moderator analyses for *contact type, mode of delivery, provider, intervention materials, intervention setting, use of reminders* and *type of healthcare.* In relation to *contact type*, interventions using face-to-face, remote or mixed types of contact showed differential effectiveness ($Q(2) = 10.74$, $p = .005$). Pairwise comparisons demonstrated that mixed contact was more effective than remote contact ($Q(1) = 10.72$, $p < .001$), but that mixed versus face-to-face contact ($Q(1) = 0.58$, $p = .44$) and face-to-face versus remote contact ($Q(1) = 0.56$, $p = .45$) were not significantly different from one-another. In relation to *mode of delivery*, interventions were similarly effective in increasing screening uptake when delivered individually or by group/mixed modes ($Q(1) = 1.54$, $p = .215$). In relation to *provider*, all four types of provider (i.e., clinically trained health professionals, non-clinically trained health professionals, research staff, not person dependent) showed significant effects, but also

showed differential effectiveness ($Q(3) = 107.24$, $p < .001$). Pairwise tests indicated that interventions provided by clinically-trained and non-clinically-trained providers did not differ from one-another ($Q(1) = 1.11$, $p = .29$), although they were each significantly more effective than interventions that were non-person dependent (versus clinically trained: $Q(1) = 64.33$, $p < .001$; versus non-clinically trained: $Q(1) = 61.03$, $p < .001$). However, they were not significantly different to those provided by research staff (versus clinically-trained: $Q(1) = 0.13$, $p = .72$; versus non-clinically trained: $Q(1) = 0.27$, $p = .607$). Research staff interventions were more effective than non person-dependent interventions ($Q(1) = 18.82$, $p < .001$).

In relation to *intervention materials*, all types of intervention materials were associated with significant effect sizes although there were significant differences between types of materials ($Q(5) = 81.03$, $p < .001$) (Table 3). The use of paper-based media plus phone was the most effective (Table 3), this significantly differed to electronic plus paper ($Q(1)= 42.63$, $p < .001$), paper only ($Q(1) = 69.84$, $p < .001$), and in person only ($Q(1)= 5.28$, $p = .02$). Paper-based media plus phone did not significantly differ to paper plus person ($Q(1) = 2.62$, $p = .106$) or phone only ($Q(1) = 2.37$, $p = .12$). Electronic plus paper was significantly less effective than in person only ($Q(1) = 4.34$, $p = .04$), paper plus in person ($Q(1) = 8.88$, $p = .003$), and phone only ($Q(1) = 6.54$, $p = .01$). Electronic plus paper did not significantly differ to paper based only ($Q(1) = 3.24$, $p = .07$). In person delivery alone was not significantly different to paper plus in person ($Q(1) = .21$, $p = .64$), paper only ($Q(1) = 1.88$, $p = .17$), and phone only ($Q(1) = .19$, $p = .66$). Paper plus in person delivery was significantly more effective than paper only ($Q(1) = 9.58$, $p = .002$) but not significantly different to phone only ($Q(1) = .001$, $p = .97$). Finally, phone only was significantly more effective than paper only ($Q(1) = 5.22$, $p = .02$).

In relation to *intervention setting*, both community and primary care settings were associated with significant effect sizes (Table 3). Studies using community settings were demonstrated to report significantly greater effect sizes than those using primary care settings ($Q(1) = 12.15$, $p = .002$). In

relation to *use of reminders*, studies that did and did not use reminders were each associated with significant effect sizes, however the size of effect was greater in studies using reminders ($Q(1) = 15.32$, $p < .001$). Finally, studies using samples with free and paid-for type of *healthcare* were both associated with significant effect sizes. The effect sizes reported in studies conducted in free healthcare systems were significantly lower than those conducted in non-free healthcare systems ($Q(1) = 48.66$, $p < .001$).

Behaviour Change Technique Moderators

A total of 35 different behaviour change techniques were used across studies. The median number of behaviour change techniques used was *three* and the range was between one and 10. The five most commonly identified behaviour change techniques were *information about health consequences, prompts/cues, social support (practical), adding objects to the environment* and *problem solving.* The five least commonly reported behaviour change techniques were *imaginary punishment, non-specific incentive, specific incentive, social incentive* and *information about social and environmental consequences* (See Supplementary Figure 1 for full frequency data on behaviour change techniques used).

Individual behaviour change techniques were included in moderator analyses if they were coded as present for at least $k = 10$ studies. Seven behaviour change techniques met this criterion and are reported in Table 4. Significant effects were observed for five behaviour change techniques. The presence of each of the following four behaviour change techniques was associated with significant increases in the effect size: *social support (unspecified)* ($Q(1) = 16.58$, $p < .001$); *social support (practical)* ($Q(1) = 6.13$, $p < .001$); *instructions on how to perform the behaviour* ($Q(1) = 33.86$, $p < .001$); *demonstration of the behaviour* ($Q(1) = 10.11$, $p = .001$). Finally, use of the behaviour change technique *adding objects to the environment*[2] also significantly increased study effect sizes ($Q(1) = 49.01$, $p < .001$). This behaviour change technique was coded as present only for USA-based studies that included a free, stool-based screening kit irrespective of participants'

insurance status or only for studies with universal healthcare when it involved adding an object other than a free screening kit, given that the inclusion of the kit constitutes usual care in countries with healthcare free at the point of access.

Despite the significant effects of the moderators explored and reported in Tables 3 and 4, it is also notable that significant heterogeneity in the effect sizes remained even after controlling for each moderator considered individually.

Relationships between Moderators

In a final analysis we examined the relationship between the categorical moderators reported in Table 3. In only two cases did the correlation exceed our set criterion ($r > .50$), whereby there was an association between either modality category (endoscopic or non-endoscopic screening behaviour) and type of healthcare (free or not free), where either modality was less likely in a country with free healthcare ($r = -.63$, $p < .001$). Remote contact was also associated with the provider being non-person dependent ($r = .53$, $p < .001$).

Discussion

This meta-analysis examined the effectiveness of public health interventions to improve CRC screening rates in the general population. We identified 102 trials incorporating 152 independent study comparisons in a sample population of 1.94 million. Studies used a range of methods to increase CRC screening uptake. Most interventions were conducted in the USA, delivered remotely, on a one-to-one basis, used paper-based educational materials and were conducted through primary care settings. The majority of studies used non-endoscopic CRC screening. Studies predominantly assessed screening uptake objectively and were classified as having high or unclear risk of bias. The principal finding of this review is that, across studies, interventions had a small-sized ($g = .221$) but significant impact on increasing CRC screening rates that did not seem to be unduly affected by publication bias. It was notable that failure to using intention-to-treat analysis, failure to blind outcome assessment and incomplete outcome data were particular sources of bias in included studies

(Figure 2). Surprisingly, although Egger's test was significant, effects were actually significantly weaker in studies judged to be of high risk of bias. It was also reassuring that effect sizes were not significantly different in studies using objective versus self-report measures of uptake (Table 3).

A range of significant moderators of this overall effect size were identified. In relation to sample characteristics (Table 2), it was notable that interventions were similarly effective across age groups, genders, those with and without a family history of CRC, and those who had or had not been screened previously. The current findings contrast with the existing literature on age (Denberg et al., 2005; Klabunde et al., 2007), gender (Ananthakrishnan et al., 2007; McGregor et al., 2007; Meissner et al., 2006; Wardle et al., 2005; Weller et al., 2007) and family history of cancer (Han et al., 2007), although our findings are based on a very large sample of studies. Alternatively, it may be that the relatively crude measures we used (i.e., sample percentages) disguised these effects. Nevertheless, based on the current large review, we would note the effectiveness of CRC screening interventions across various samples.

In relation to the nature of the behaviour, interventions targeting non-endoscopic only procedures were significantly less effective than those targeting either endoscopic only or either procedure (Table 3). Non-endoscopic procedures differ in a number of ways including characteristics that may be considered both positive (e.g., lower cost, lower invasiveness) and negative (e.g., being more routine and more frequent, being less diagnostic). However, it is notable that relatively modest numbers of studies within the review targeted endoscopic only procedures (k = 10). Nevertheless, the disadvantage of targeting non-endoscopic procedures only may be useful information for those designing CRC screening interventions.

Perhaps the most useful aspect of the review was in identifying the intervention characteristics and behaviour change techniques employed that were associated with increased CRC screening uptake. In relation to intervention characteristics, a number of significant moderators emerged (Table 3). First, there was evidence that interventions using a mixed contact type reported

the greatest effect sizes overall and significantly stronger effects than remote access. It was notable that remote contact had been used more frequently (k = 121/152) than either of the other contact types. Studies have previously suggested that interventions delivered face-to-face can better engage participants in open dialogue about their own healthcare, and that this is associated with greater informed decision-making and willingness to take independent actions to manage one's own health (Alston et al., 2012; Carman et al., 2013; Couët et al., 2015; Hibbard & Greene, 2013).

Second, interventions provided by health professionals (clinically-trained or not) or research staff were significantly more effective at increasing screening uptake rates than those provided by those that were not person-dependent (Table 3). This finding is perhaps not surprising given the higher level of trust given to health professionals (Gorin et al., 2006; Holmes et al., 2008; Palmer & Schneider, 2005; Shavers et al., 2007). It would suggest that there is value to ensuring health professionals (clinically trained or not) deliver such interventions despite potential additional costs.

Third, providing intervention materials on paper-based media that is supplemented by in-person or phone contact was the most effective. This is consistent with results from previous systematic reviews in which systematic telephone contact has been associated with increased screening uptake for colorectal, breast and cervical cancer screening (Baron et al., 2008; Everett et al., 2011; Jepson et al., 2000). Over-the-phone health communication may act as a reminder and adjunct to paper-based materials as it offers the opportunity for personal contact with someone knowledgeable about CRC screening. This might be an effective intervention for service-users anxious about the screening process but apprehensive about discussing it directly with their doctor.

Fourth, there was evidence that interventions delivered in the community were more effective in increasing CRC screening rates compared to those delivered in a primary care setting (Table 3). This finding supports previous evidence highlighting that community-based approaches motivate greater behaviour change, partly due to connecting participants to aspects of their social environment (Bonevski et al., 2014; Kreuter, McQueen, Boyum, & Fu, 2016).

Fifth, interventions employing reminders were found to be more effective than those not employing reminders and this is consistent with an earlier review and recommendations to increase cancer-related screening uptake (Baron et al., 2010). Therefore, given the relatively minor costs of using reminders this would seem like a useful and easy to administer intervention for studies to employ going forward.

Sixth, the type of healthcare system was found to moderate intervention effectiveness. Studies conducted in countries that do not provide free healthcare (e.g., USA) reported higher effects of CRC interventions on uptake compared to those countries providing free healthcare for all (e.g., UK). This basis for this difference remains unclear, although it is possible that the interventions conducted in non-free healthcare systems actually address the financial costs of CRC screening uptake. It would be useful for future research to explore the basis of differences in effectiveness within different healthcare systems.

We also look at intervention characteristics as moderators of the effectiveness of CRC screening interventions by exploring their use of behaviour change techniques (Table 4). Two behaviour change techniques from the social support domain, *unspecified social support* and *practical social support*, were associated with significant increases in screening uptake. This would support the use of social support to promote CRC screening uptake (e.g., friends or family supporting individuals to screen by attending with the individual). Certain factors are known to negatively impact the social support-health relationship; for instance, satisfaction with social support may moderate the social support-health behaviour relationship and satisfaction may be driven by expectations (Morrison, 2015).

In addition, practical information on the behaviour such as *instructions on how to perform the behaviour* and *demonstration of the behaviour* were each associated with more effective interventions. This would suggest the value of these behaviour change techniques in relation to increasing CRC screening rates and the importance of such practical information. Finally, *adding*

objects to the environment, was also found to be associated with more effective interventions. This is perhaps not surprising for USA-based studies where such objects included a free, stool-based screening kit irrespective of participants' insurance status, but more surprising for studies outside the US where the screening kit would be normally provided for free. Further analyses indicated the use of this behaviour change technique to be significant in both non-free (OR = 3.75, 95%CI 3.19, 4.30, $p < .001$) and free healthcare systems (OR = 1.89, 95%CI 1.12, 2.66, $p < .001$). It is notable that the effect was attenuated in the free healthcare sub-sample and was only based on four studies.

Despite the present review identifying some effective and some ineffective behaviour change techniques, the lack of detail with regards to intervention descriptions of included studies may have limited our ability to code the full range of techniques used and to explore combinations of behaviour change techniques. Greater transparency and more detailed descriptions of intervention elements (as required by various recommendations: http://www.equator-network.org/wp-content/uploads/2014/03/TIDieR-Checklist-PDF.pdf; https://www.equator-network.org/reporting-guidelines/tidier-php-a-reporting-guideline-for-population-health-and-policy-interventions/) could remove this problem in future published studies. It was surprising that some of the more efficacious behaviour change techniques such as *self-monitoring*, *review of behavioural goals*, *setting graded tasks*, and *prompting intention formation* (Prestwich, Kenworthy, & Conner, 2017) were seldom used in included studies. Future research might usefully explore the impact of such behaviour change techniques in relation to CRC screening. For example, because CRC screening is a behaviour that is often composed of multiple steps and requires careful planning, it might be that the behaviour change technique *action planning* might be effective. *Action planning* is thought to facilitate behaviour change by providing a clear pathway for identifying the context, duration and frequency of the required behaviour and provides individuals the opportunity to develop effective strategies to overcome situational barriers associated with enacting the behaviour. Relatedly, implementation intentions (simple if-then plans) have been shown to be effective across a range of behaviours

(Avery, Flynn, van Wersch, Sniehotta, & Trenell, 2012; Cradock et al., 2017; Hankonen et al., 2015; Lara et al., 2014) but rarely applied to cancer screening (Browne & Chan, 2011; Sheeran & Orbell, 2000) with only two studies using this behaviour change technique in the present review (Lo et al., 2014; Neter, Stein, Barnett-Griness, Rennert, & Hagoel, 2014). The demonstration of effectiveness for interventions employing behaviour change techniques from the goals and planning domain might help support the view that changing motivation or intentions to be screened is an important mechanism of action through which CRC screening uptake can be changed. This would be consistent with two previous meta-analyses of correlational studies that indicated strong, positive correlations between motivation/intention and screening uptake (Cooke & French, 2008; Godin & Kok, 1996).

Previous studies also highlight that increased self-efficacy may also be an important mechanism of action that explains the effectiveness of cancer screening interventions. For example, one study found that self-efficacy was a significant independent predictor of colonoscopy attendance (McQueen et al., 2007). While Orbell et al. (2017) showed that self-efficacy and also response costs but not vulnerability, response efficacy or severity from Protection Motivation Theory (Norman, Boer, Seydel, & Mullen, 2015) mediated the effects of both socio-economic status and Asian ethnicity on CRC screening rates. These findings might suggest that incorporating behaviour change techniques that target self-efficacy such as *setting graded tasks, verbal persuasion about capability,* and *mental rehearsal of successful performance* from the self-belief domain may be useful within this context. More generally, research that attempts to explore what mechanisms of action (e.g., protection motivation, self-efficacy, response costs, vulnerability, response efficacy, severity) CRC screening interventions target and successfully change in order to produce behaviour change would be a useful direction for research and would add considerably to our understanding in this behavioural domain.

The current review has a number of limitations. First, additional variables had been scheduled

a priori to be included in moderator analyses, including variables related to socio-economic status, past screening history (e.g., number of past invites, screening episode, percentage of people ever screened), intensity of intervention (e.g., number of contacts in intervention and control arms, number of contacts with physician), and intervention latency (i.e., average duration from screening invite to screening behaviour). However, insufficient data was reported in the included studies on these variables to allow robust moderator analyses.

Second, we did not consider combinations of moderators. For example, some recent studies have examined how combinations of behaviour change techniques might be particularly effective in changing behaviour (Sheeran et al., 2019). Similarly, examining the effectiveness of different moderator effects in free versus non-free healthcare systems may be important. Future studies might usefully explore these and related issues (e.g., being provided a screening kit or appointment slot versus having to request one). Relatedly, it was notable that heterogeneity of effect sizes remained, even after controlling each moderator considered (Tables 2-4). Consideration of combinations of moderators might have helped explain this heterogeneity although limited numbers of studies within particular combinations may restrict the power of such analyses.

Third, there are a number of potential shortcomings with the analyses employed. In particular, we employed the Egger's test to examine publication bias, although it might be better considered as a test of small-study bias which may be reflective of possible publication bias. There are alternatives available including trim and fill analysis and PET-PEESE analyses (Carter, Schonbrodt, Gervais, & Hilgard, 2019) although these are not without problems. While Egger's test may be more sensitive than other related tests, it may also have a higher risk of false positives. Moreover, as Egger's test is based on funnel plot asymmetry, the observed small-study bias may be reflective of various factors such as poorer methodological quality in studies with smaller sample sizes leading to inflated effects or outlying studies rather than, or in addition to, publication bias.

In addition, in the 30 studies that had more than one experimental condition compared with a

single control condition, we divided the number of participants in the control condition by the number of comparisons to avoid double counting. There are other ways of managing such dependency. For example, Borenstein et al., (2009) suggests a correction whereby the multiple comparison groups are aggregated and compared against control. However, use of this method produced only minor changes compared to our original calculation suggesting that this non-optimal approach did not unduly influence our results.

In summary, the present meta-analysis identifies intervention approaches drawn from all the available randomised evidence, and provides an evidentiary basis on which future public health interventions aiming to increase CRC screening can be developed. It is important that future trials provide more detailed accounts of intervention descriptions in order to establish the relative effectiveness of the various intervention components and build on existing evidence (Rychetnik, Frommer, Hawe, & Shiell, 2002). Cost-effectiveness analysis of interventions to increase CRC screening should also be prioritised to direct efficient allocation of public resources and facilitate informed decision-making on the financial scope of public health interventions.

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Table 1. Coded behaviour change techniques identified in the reviewed studies that were included in the moderator analyses.

Behaviour change technique[a]	Definition	Example – study and details
1.2 Problem solving	Analyse, or prompt the person to analyse, factors influencing the behaviour and generate or select strategies that include overcoming barriers and/or increasing facilitators (includes 'Relapse Prevention' and 'Coping Planning').	Christi et al (2008)[b]: "The patient navigator mailed the colonoscopy preparation instructions as well as any necessary prep prescriptions to the patient. A tracking form was completed by the navigator during this initial telephone call, including general demographic and clinical patient information as well as some information about the barriers that the patient may have that could prevent him or her from completing the recommended screening colonoscopy."
3.1 Social support (unspecified)	Advise on, arrange or provide social support (e.g. from friends, relatives, colleagues,' buddies' or staff) or non-contingent praise or reward for performance of the behaviour. It includes encouragement and counselling, but only when it is directed at the behaviour.	Costanza et al (2007): "In brief, using a computer-assisted interviewing technique described by others [48–52], we developed a counseling protocol that tailors counseling to a subject's responses to questions that the computer prompts the counselor to ask. When the answer is entered into the computer, the computer automatically displays the counseling script appropriate to the subject's responses and stage of adoption."
3.2 Social support (practical)	Advise on, arrange, or provide practical help (e.g. from friends, relatives, colleagues, 'buddies' or staff) for performance of the behaviour.	Blumenthal et al (2010): "A health educator was available to assist with negotiating direct payment and arranging transportation to the physician's office or medical clinic for the screening test."
4.1 Instructions on how	Advise or agree on how to	Coronado et al (2010):

to perform the behaviour	perform the behaviour (includes 'Skills training').	"Patients in the second arm (n = 168) were mailed a packet containing a letter, an FOBT card, a pamphlet with instructions on how to complete the FOBT, and a pre-stamped, addressed envelope for mailing the card to the clinic."
5.1. Information about health consequences	Provide information (e.g. written, verbal, visual) about health consequences of performing the behaviour.	Boguradzka et al (2014): "The scheme of the discussion was standardized and included the following issues: (1) basic information on a burden and biology of CRC, (2) a rationale for CRC screening in asymptomatic individuals and benefits of early treatment of the disease and prevention by removal of polyps, (3) recommendation to participate in an ongoing primary colonoscopy screening program, (4) information on colonoscopy procedure, including need for sedation, bowel preparation, and adverse events."
6.1 Demonstration of the behaviour	Provide an observable sample of the performance of the behaviour, directly in person or indirectly e.g. via film, pictures, for the person to aspire to or imitate (includes 'Modelling').	Braun et al (2005): "Following this, free FOBT kits were distributed, and the Native Hawaiian physician provided instructions on testing and demonstrated how to use the FOBT kit to collect stool samples using a child's potty and Play-Doh stools, a strategy that has proved effective in New York State."
12.5 Adding objects to the environment	Add objects to the environment in order to facilitate performance of the behaviour.	Hendren et al (2013): "A second letter was sent at week 12 of the intervention to patients who remained unscreened. Patients in need of CRC screening were mailed kits for stool testing [Fecal Immunochemical Test (FIT) kit] with the second letter."

[a]Categorization from Michie et al. (2013). [b]See supplementary appendix C for reference to these papers and all included papers.

Table 2. Continuous sample characteristic moderator analyses on screening uptake.

			95% CI		
Predictor	***k***	**Beta**	**Lower limit**	**Upper limit**	***p***
Age (mean)	140	-0.03	-0.015	0.09	0.65
Gender (%males)	139	-0.004	-0.025	0.017	0.70
Family history (%yes)	40	0.04	-0.05	0.13	0.40
Screening status at time of study (%yes)	64	-0.027	-0.06	0.011	0.16

Notes. ***k*** = number of comparisons, CI = confidence interval.

Table 3. Nature of behaviour, methodological factors and intervention characteristics moderator analyses on screening uptake

Analysis[a]	Random-effects model		Sig.	Heterogeneity	Within subgroup differences
	k	**g, OR (95% CI)**	***p***	**Q, p*h*, I^2**	**Q_b, df, *p***
NATURE OF BEHAVIOUR					
Moderator: Screening modality					
Endoscopic only	10	0.269, 1.629 (1.337-1.986)	<0.001	64.23, <0.001, 86.0%	26.36, 2, <0.001
Non-endoscopic only	56	0.151, 1.314 (1.238-1.396)	<0.001	1927.00, <0.001, 97.1%	
Either endoscopic or non-endoscopic	86	0.269, 1.629 (1.537-1.727)	<0.001	1123.73, <0.001, 92.4%	
METHODOLOGICAL FACTORS					
Moderator: Outcome assessment[e]					
Objective	119	0.231, 1.521 (1.448-1.598)	<0.001	3882.74, <0.001, 97.0%	0.64, 1, 0.42
Self-report	21	0.265, 1.616 (1.405-1.860)	<0.001	112.17, <0.001, 82.2%	
Moderator: Risk of bias					

High bias	69	0.155, 1.324 (1.245-1.408)	<0.001	527.08, <0.001, 87.1%	18.203, 2, <0.001
Unclear bias	52	0.253, 1.583 (1.480-1.693)	<0.001	1136.57, <0.001, 95.5%	
Low bias	31	0.247, 1.565 (1.444-1.697)	<0.001	1072.01, <0.001, 97.2%	
INTERVENTION CHARACTERISTICS					
Moderator: Contact type					
Face-to-face	17	0.238, 1.540 (1.335-1.776)	<0.001	160.29, <0.001, 90.0%	10.739, 2, 0.005
Remote	121	0.206, 1.452 (1.383-1.525)	<0.001	3560.54, <0.001, 96.6%	
Mixed	14	0.353, 1.900 (1.628-2.218)	<0.001	264.78, <0.001, 95.1%	
Moderator: Mode of Delivery					
Individual (i.e. one-to-one)	137	0.227, 1.509 (1.440-1.582)	<0.001	3899.34, <0.001, 96.5%	1.539, 1, 0.215

Group/Mixed	15	0.177, 1.378 (1.203-1.578)	<0.001	155.44, <0.001, 91.0%	
Moderator: Provider[b]					
Clinically-trained health professionals	7	0.555, 2.739 (2.270-3.304)	<0.001	160.76, <0.001, 96.3%	107.24, 3, <0.001
Non-clinically trained health professionals	35	0.367, 1.948 (1.771-2.142)	<0.001	298.47, <0.001, 88.6%	
Research staff	15	0.326, 1.806 (1.554-2.098)	<0.001	215.91, <0.001, 93.5%	
Not person dependant	88	0.140, 1.289 (1.224-1.357)	<0.001	2587.44, <0.001, 96.6%	
Moderator: Intervention Materials[c]					
Electronic plus paper-based media	29	0.112, 1.225 (1.111-1.351)	<0.001	232.81, <0.001, 88.0%	81.03, 5, <0.001
Paper-based media only	61	0.168, 1.356 (1.277-1.441)	<0.001	1987.15, <0.001, 97.0%	

Paper-based media plus phone	23	0.465, 2.328 (2.062-2.629)	<0.001	229.23, <0.001, 90.4%	
Phone only	12	0.279, 1.659(1.393-1.976)	<0.001	183.05, <0.001, 94.5%	
In-person delivery	13	0.223, 1.499(1.303-1.724)	<0.001	149.91, <0.001, 92.5%	
Paper-based media plus in person delivery	14	0.289, 1.691(1.475-1.938)	<0.001	249.33, <0.001, 94.8%	
Moderator: Intervention Setting[d]					
Community	42	0.283, 1.671 (1.526-1.829)	<0.001	534.985, <0.001, 92.3%	12.15, 1, 0.002
Primary care	107	0.201, 1.440 (1.374-1.509)	<0.001	2629.42, <0.001, 95.9%	
Moderator: Use of reminders					
Reminders used	74	0.276, 1.650 (1.545-1.762)	<0.001	2082.00, <0.001, 96.5%	15.31, 1, <0.001
No reminders used	78	0.175, 1.373 (1.288-1.464)	<0.001	1973.57, <0.001, 96.1%	

Moderator: Healthcare					
Free healthcare	46	0.123, 1.675 (1.587-1.769)	<.*001*	1849.33, <.001, 97.6	48.657, 1, <0.001
Not free	106	0.284, 1.25 (1.175-1.330)	<.*001*	1269.74, <.001, 91.7	

Notes. k = number of comparisons, *g*= Hedge's g measure of effect size, OR = odds ratio, CI = confidence interval, p*h*=p value of Q test for heterogeneity test, Q_b = Q value indicating the between-group effect.Q_b value reported from subgroup analysis conducted across k=152 but the effect sizes reported in the table are taken from individual sensitivity analyses for non-low and low SES studies. [a]Three papers were not included in the analysis (Groups 1 and 2 from Church et al 2004; Groups 1, 2 and 3 from Marcus et al, 2005; Walsh et al, 2005) as it was unclear, or not reported, who delivered the intervention. [b]One paper was not included in the analysis (Price-Haywood et al., 2014) as it was unclear who delivered the intervention. [c]Three papers were not included in the analysis (Cameron et al, 2011; Clouston et al 2014; Group 3 from Green et al, 2013) as they did not meet inclusion criteria for any of the moderator categories. [d]Two papers not included in the analysis (Krok-Schoen et al, 2015; Groups 3 and 4 from White et al, 2015) as they did not meet inclusion criteria for any of the moderator categories. [e]Five papers not included in the analysis (Barthe et al., 2015; Clouston et al., 2014; Groups 1, 2 and 3 from Cole et al., 2002; Groups 1, 2 and 3 from Cole et al., 2007; Guiriguet et al., 2016) as it was either unclear or not reported how screening uptake was assessed.

Table 4. Behaviour change technique moderator analyses on screening uptake.

Analysis	*k*	Random effects model		Heterogeneity	Test for subgroup differences
	105	**g, OR (95% CI)**	***p***	**Q, p*h*, I^2**	**Q_{BET}, df, *p***
BCT: Problem solving					
Yes	36	0.247, 1.564, (1.424-1.719)	<0.001	355.89, <.001, 90.2%	1.221, 1, 0.269
No	116	0.213, 1.473 (1.401-1.549)	<0.001	3621.00, <.001, 96.8%	-
BCT: Social support (unspecified)					
Yes	17	0.362, 1.931 (1.689-2.207)	<0.001	261.603, <.001, 93.9%	16.577, 1, <0.001
No	135	0.201, 1.440 (1.377-1.506)	<0.001	3134.977, <.001, 95.7%	-
BCT: Social support (practical)					
Yes	47	0.266, 1.620 (1.497-1.753)	<0.001	653.644, <.001, 93.0%	6.126, 1, 0.013

No	105	0.200, 1.437 (1.363-1.515)	<0.001	3239.738, <.001, 96.8%	-
BCT: Instructions on how to perform the behaviour					
Yes	35	0.356, 1.908 (1.737-2.095)	<0.001	990.264, <.001, 96.6%	33.860, 1, <0.001
No	117	0.182, 1.392 (1.324-1.463)	<0.001	2930.501, <.001, 96.0%	-
BCT: Information about health consequences					
Yes	80	0.237, 1.538 (1.446-1.636)	<0.001	1720.602, <.001, 95.4%	1.417, 1, 0.233
No	72	0.207, 1.455 (1.360-1.557)	<0.001	2278.987, <.001, 96.9%	-
BCT: Demonstration of the behaviour					
Yes	22	0.319, 1.784 (1.585-2.009)	<0.001	431.508, <.001, 95.1%	10.114, 1, 0.001
No	130	0.205, 1.450 (1.383-1.521)	<0.001	3529.698, <.001, 96.3%	-
BCT: Adding objects to the environment					

Yes	45	0.338, 1.846 (1.712-1.990)	<0.001	1184.064, <.001, 96.3%	49.010, 1, <0.001
No	107	0.162, 1.343 (1.280-1.409)	<0.001	1939.635, <.001, 94.5%	-

Notes. k = number of comparisons, g = Hedge's g, OR = Odds Ratio, CI = Confidence Interval, ph = p value of Q-test for heterogeneity, Q_b = Q value indicating the between-group effect.

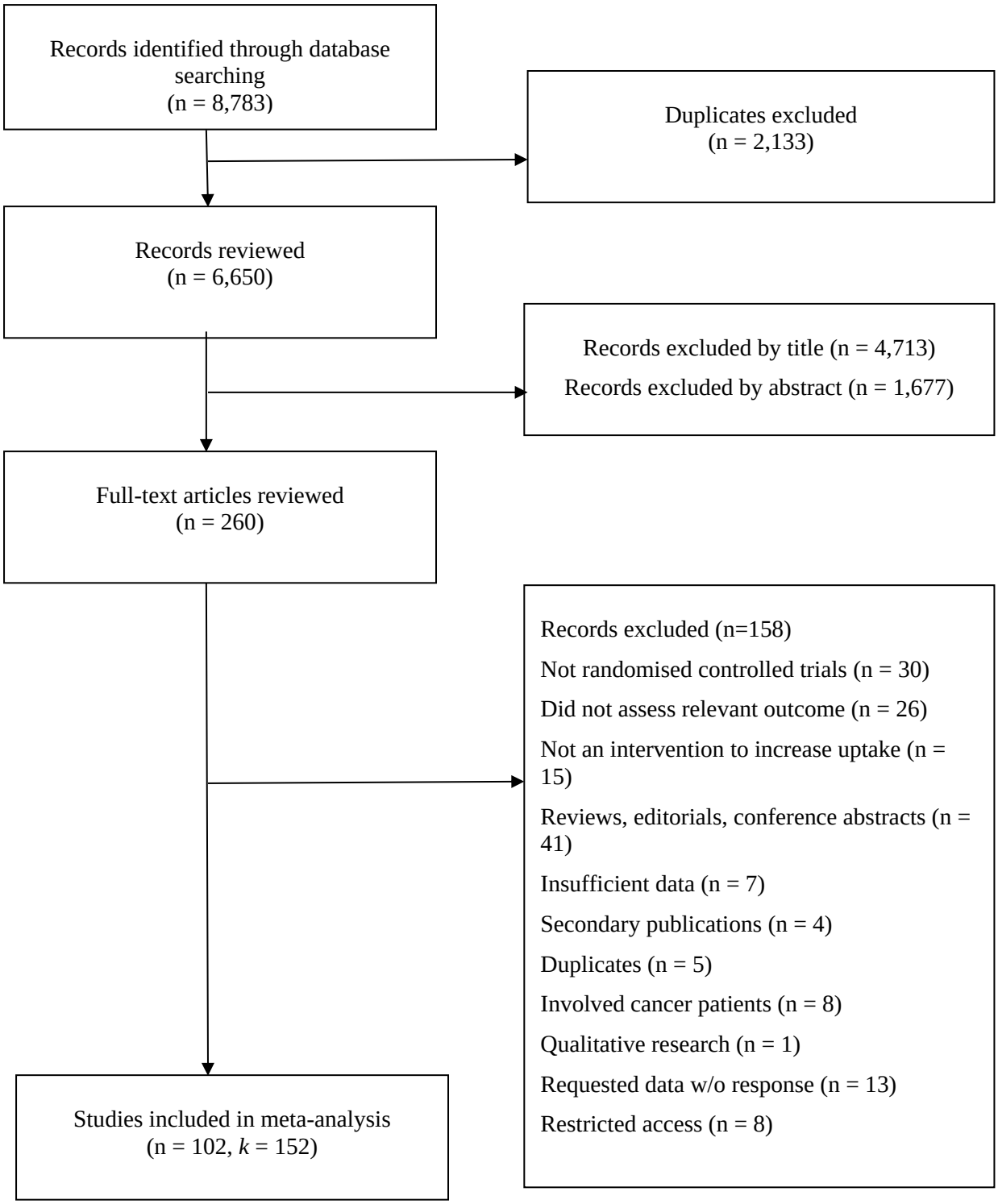


Figure 1. PRISMA flow diagram presenting a schematic overview of the selection process for interventions eligible for full review.

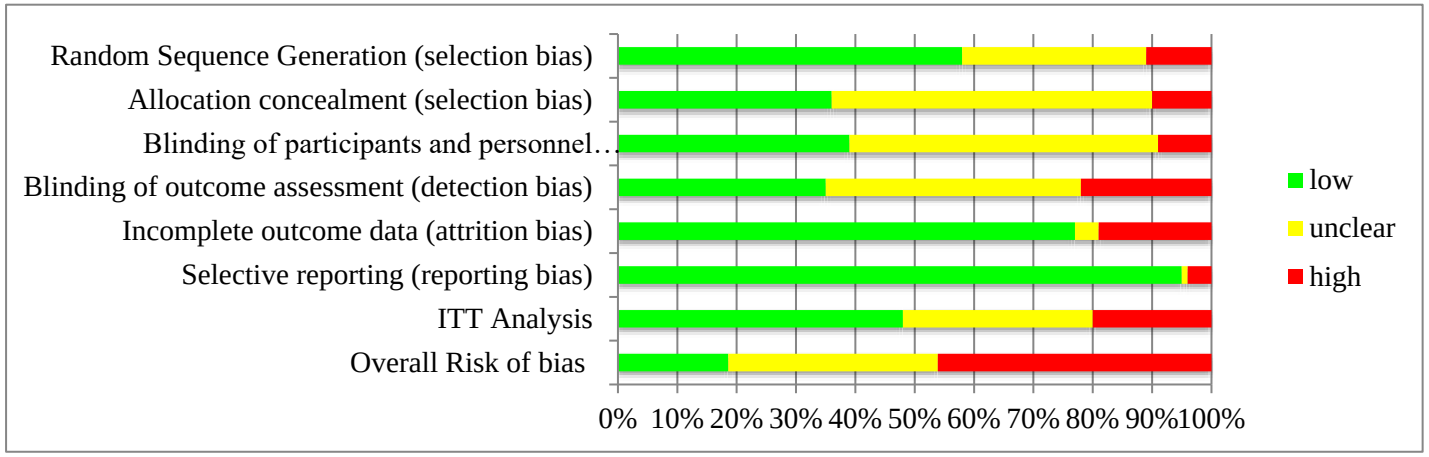
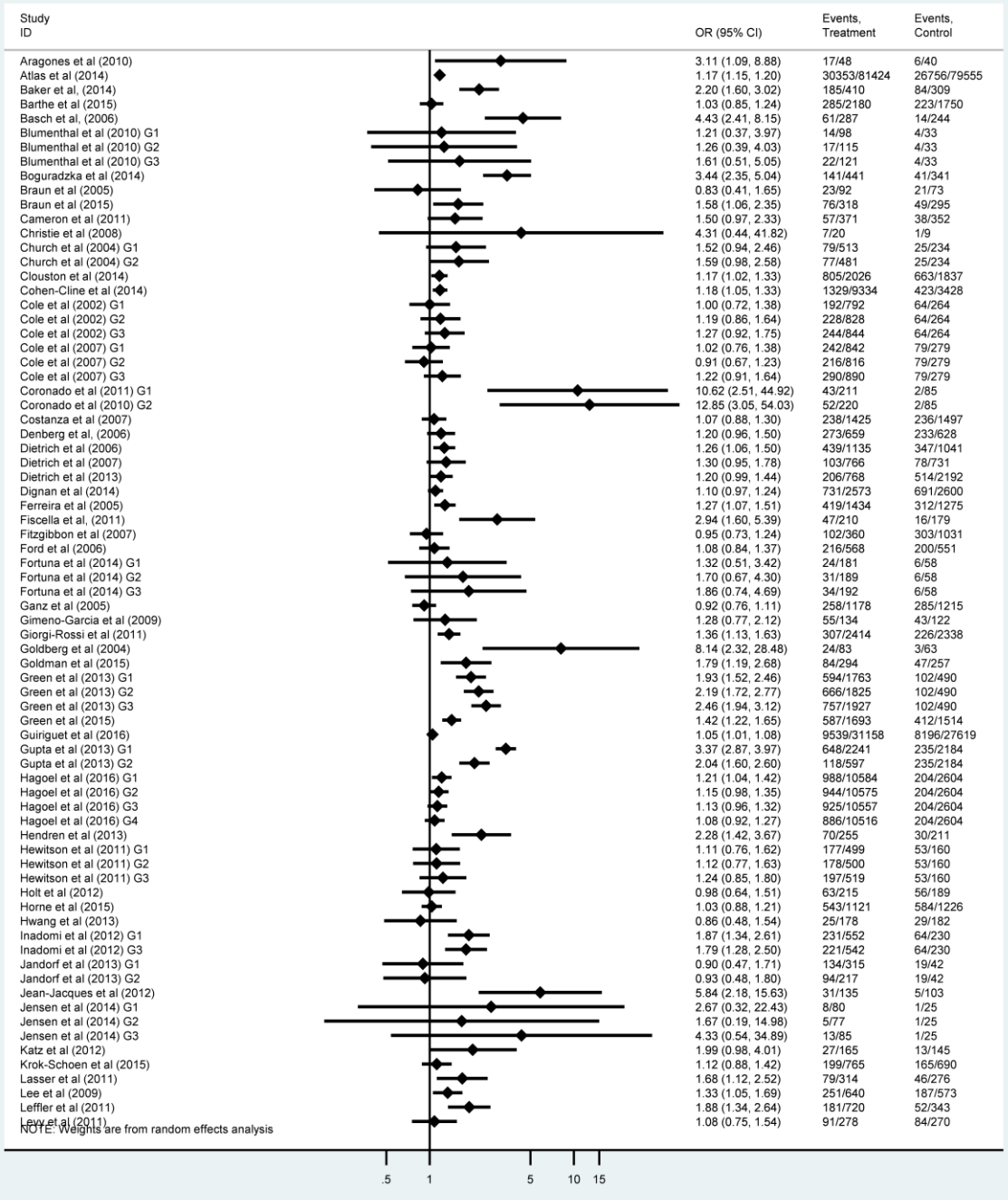


Figure 2. Risk of bias assessment for all included studies.


Study ID
OR (95% CI)
Events, Treatment
Events, Control
Aragones et al (2010) 3.11 (1.09, 8.88) 17/48 6/40
Atlas et al (2014) 1.17 (1.15, 1.20) 30353/81424 26756/79555
Baker et al, (2014) 2.20 (1.60, 3.02) 185/410 84/309
Barthe et al (2015) 1.03 (0.85, 1.24) 285/2180 223/1750
Basch et al, (2006) 4.43 (2.41, 8.15) 61/287 14/244
Blumenthal et al (2010) G1 1.21 (0.37, 3.97) 14/98 4/33
Blumenthal et al (2010) G2 1.26 (0.39, 4.03) 17/115 4/33
Blumenthal et al (2010) G3 1.61 (0.51, 5.05) 22/121 4/33
Boguradzka et al (2014) 3.44 (2.35, 5.04) 141/441 41/341
Braun et al (2005) 0.83 (0.41, 1.65) 23/92 21/73
Braun et al (2015) 1.58 (1.06, 2.35) 76/318 49/295
Cameron et al (2011) 1.50 (0.97, 2.33) 57/371 38/352
Christie et al (2008) 4.31 (0.44, 41.82) 7/20 1/9
Church et al (2004) G1 1.52 (0.94, 2.46) 79/513 25/234
Church et al (2004) G2 1.59 (0.98, 2.58) 77/481 25/234
Clouston et al (2014) 1.17 (1.02, 1.33) 805/2026 663/1837
Cohen-Cline et al (2014) 1.18 (1.05, 1.33) 1329/9334 423/3428
Cole et al (2002) G1 1.00 (0.72, 1.38) 192/792 64/264
Cole et al (2002) G2 1.19 (0.86, 1.64) 228/828 64/264
Cole et al (2002) G3 1.27 (0.92, 1.75) 244/844 64/264
Cole et al (2007) G1 1.02 (0.76, 1.38) 242/842 79/279
Cole et al (2007) G2 0.91 (0.67, 1.23) 216/816 79/279
Cole et al (2007) G3 1.22 (0.91, 1.64) 290/890 79/279
Coronado et al (2011) G1 10.62 (2.51, 44.92) 43/211 2/85
Coronado et al (2010) G2 12.85 (3.05, 54.03) 52/220 2/85
Costanza et al (2007) 1.07 (0.88, 1.30) 238/1425 236/1497
Denberg et al, (2006) 1.20 (0.96, 1.50) 273/659 233/628
Dietrich et al (2006) 1.26 (1.06, 1.50) 439/1135 347/1041
Dietrich et al (2007) 1.30 (0.95, 1.78) 103/766 78/731
Dietrich et al (2013) 1.20 (0.99, 1.44) 206/768 514/2192
Dignan et al (2014) 1.10 (0.97, 1.24) 731/2573 691/2600
Ferreira et al (2005) 1.27 (1.07, 1.51) 419/1434 312/1275
Fiscella et al, (2011) 2.94 (1.60, 5.39) 47/210 16/179
Fitzgibbon et al (2007) 0.95 (0.73, 1.24) 102/360 303/1031
Ford et al (2006) 1.08 (0.84, 1.37) 216/568 200/551
Fortuna et al (2014) G1 1.32 (0.51, 3.42) 24/181 6/58
Fortuna et al (2014) G2 1.70 (0.67, 4.30) 31/189 6/58
Fortuna et al (2014) G3 1.86 (0.74, 4.69) 34/192 6/58
Ganz et al (2005) 0.92 (0.76, 1.11) 258/1178 285/1215
Gimeno-Garcia et al (2009) 1.28 (0.77, 2.12) 55/134 43/122
Giorgi-Rossi et al (2011) 1.36 (1.13, 1.63) 307/2414 226/2338
Goldberg et al (2004) 8.14 (2.32, 28.48) 24/83 3/63
Goldman et al (2015) 1.79 (1.19, 2.68) 84/294 47/257
Green et al (2013) G1 1.93 (1.52, 2.46) 594/1763 102/490
Green et al (2013) G2 2.19 (1.72, 2.77) 666/1825 102/490
Green et al (2013) G3 2.46 (1.94, 3.12) 757/1927 102/490
Green et al (2015) 1.42 (1.22, 1.65) 587/1693 412/1514
Guiriguet et al (2016) 1.05 (1.01, 1.08) 9539/31158 8196/27619
Gupta et al (2013) G1 3.37 (2.87, 3.97) 648/2241 235/2184
Gupta et al (2013) G2 2.04 (1.60, 2.60) 118/597 235/2184
Hagoel et al (2016) G1 1.21 (1.04, 1.42) 988/10584 204/2604
Hagoel et al (2016) G2 1.15 (0.98, 1.35) 944/10575 204/2604
Hagoel et al (2016) G3 1.13 (0.96, 1.32) 925/10557 204/2604
Hagoel et al (2016) G4 1.08 (0.92, 1.27) 886/10516 204/2604
Hendren et al (2013) 2.28 (1.42, 3.67) 70/255 30/211
Hewitson et al (2011) G1 1.11 (0.76, 1.62) 177/499 53/160
Hewitson et al (2011) G2 1.12 (0.77, 1.63) 178/500 53/160
Hewitson et al (2011) G3 1.24 (0.85, 1.80) 197/519 53/160
Holt et al (2012) 0.98 (0.64, 1.51) 63/215 56/189
Horne et al (2015) 1.03 (0.88, 1.21) 543/1121 584/1226
Hwang et al (2013) 0.86 (0.48, 1.54) 25/178 29/182
Inadomi et al (2012) G1 1.87 (1.34, 2.61) 231/552 64/230
Inadomi et al (2012) G3 1.79 (1.28, 2.50) 221/542 64/230
Jandorf et al (2013) G1 0.90 (0.47, 1.71) 134/315 19/42
Jandorf et al (2013) G2 0.93 (0.48, 1.80) 94/217 19/42
Jean-Jacques et al (2012) 5.84 (2.18, 15.63) 31/135 5/103
Jensen et al (2014) G1 2.67 (0.32, 22.43) 8/80 1/25
Jensen et al (2014) G2 1.67 (0.19, 14.98) 5/77 1/25
Jensen et al (2014) G3 4.33 (0.54, 34.89) 13/85 1/25
Katz et al (2012) 1.99 (0.98, 4.01) 27/165 13/145
Krok-Schoen et al (2015) 1.12 (0.88, 1.42) 199/765 165/690
Lasser et al (2011) 1.68 (1.12, 2.52) 79/314 46/276
Lee et al (2009) 1.33 (1.05, 1.69) 251/640 187/573
Leffler et al (2011) 1.88 (1.34, 2.64) 181/720 52/343
Lew et al (2011) 1.08 (0.75, 1.54) 91/278 84/270
NOTE: Weights are from random effects analysis
.5
1
5
10
15

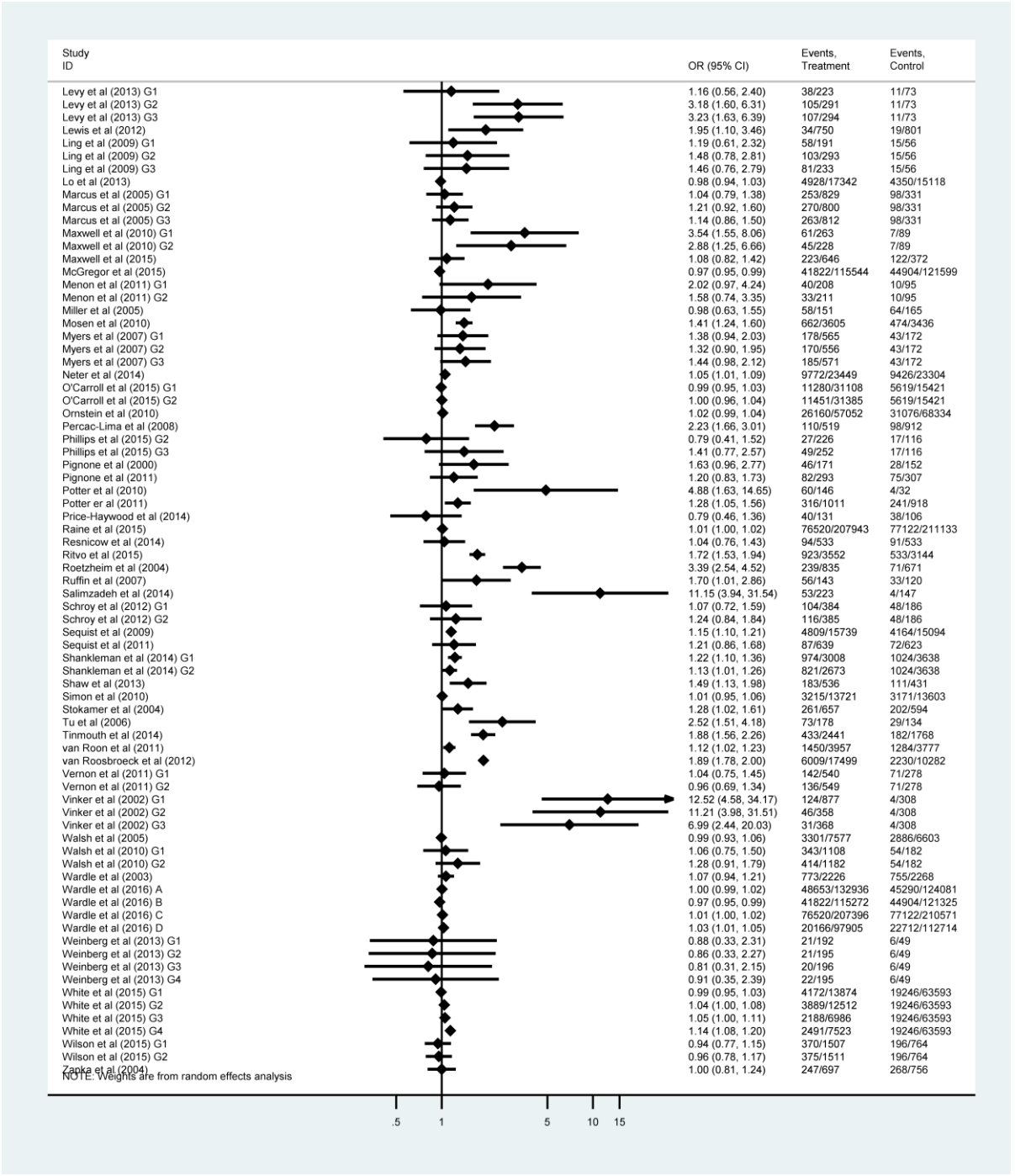


Figure 3. Effect of health interventions on CRC uptake.