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Cluster randomized controlled trial of volitional and motivational interventions to improve bowel cancer screening uptake: A population-level study

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ABSTRACT

Objectives. Colorectal cancer (CRC) is a leading cause of cancer death worldwide, although effective uptake of bowel cancer screening is below 60% in England. This trial investigated the influence of volitional and motivational interventions and their combination on increasing guaiac fecal occult blood testing (gFOBT) screening uptake. *Method.* In total, 34,633 participants were recruited (via North-East of England bowel cancer screening hub) into a 2×2 factorial cluster randomized controlled trial. Social norm-based motivational intervention (SNA); Implementation intention-based Volitional Help Sheet (VHS); Combined intervention (SNA+VHS); Treatment as usual control. Screening rate (gFOBT kit return rate within 8 weeks of invitation) was the primary outcome. *Results.* Screening kits were returned by 60% of participants (*N*=20,847/34,633). A substantial imbalance was observed in participant characteristics, participants in the combined intervention group were younger and more likely to be first time invitees. Adjusted analyses found insufficient evidence that any of the interventions were different to control (Combined: *OR* = 1.18, 95% *CI* 0.97-1.44; SNA alone: *OR*=0.93; 95% *CI*: 0.76-1.15; VHS alone *OR*= 0.88; *95% CI*: 0.75-1.03). Subgroup analyses demonstrated a significant beneficial effect of the combined intervention in the youngest age group compared to control (*OR* = 1.27; 95% *CI:* 1.05-1.54). *Conclusions.* The study did not support any benefit of either VHS or SNA interventions alone on bowel cancer screening uptake. The combined SNA+VHS intervention was significantly different from control only in the youngest age group in adjusted analyses. However, the magnitude of effect in the youngest age group suggests that further testing of VHS plus SNA interventions in carefully targeted populations may be warranted.

1. Introduction

Colorectal cancer (CRC) is the fourth most commonly diagnosed cancer in the UK and the third most common worldwide; it is also the fourth leading cause of cancer death globally (World Cancer Research Fund Network, 2017). CRC mortality could be reduced by periodic

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screening (Hewitson et al., 2008) and the majority of European countries have a screening program implemented, although uptake rates vary considerably by country and remain below the recommended level of 65% (Navarro et al., 2017).

In England, the NHS Bowel Cancer Screening Program (NHSBCSP) was implemented in 2006 and routinely offers biennial gFOBT screening to all adults aged 60–74 years. General uptake in England is around 59% (Public Health England, 2018) although by area-based levels of deprivation, this ranges from 61% in the least deprived areas to 35% in the most deprived areas of the country (Solmi et al., 2015; Von Wagner, Semmler, Good and Wardle, 2009). Studies also report that low socioeconomic status (SES) and black, Asian and minority ethnic (BAME) populations are more likely to experience both emotional and practical barriers concerning screening, including more negative beliefs regarding screening procedures, greater cancer fatalism and lower perceived self-efficacy (Miller et al., 2019; Power et al., 2009; Von Wagner et al., 2009).

Interventions to increase CRC screening have demonstrated that receiving an invitation letter via the post along with reminders are effective methods of increasing screening uptake (Rat et al., 2018; Tsipa et al., 2020). However, these are already components of the NHS BCSP and yet uptake is still sub-optimal. Therefore, it is important to identify effective behavior change interventions that can be applied at a population level. Brief interventions have been demonstrated to be an effective way to modify behavior (Gollwitzer, 1993, 1999; Lindberg et al., 2009). Several previous studies have supported the effectiveness of implementation intentions to improve uptake of medical screening, particularly in individuals with high intentions (Greiner et al., 2014; Lo et al., 2014; Neter et al., 2014; Rutter et al., 2006; Sheeran and Orbell, 2000). Briefly, implementation intentions involve the formation of an if-then plan e.g. 'IF I feel embarrassed when I am about to take my sample, THEN I will remind myself that I am doing this because I care about my health') (Gollwitzer, 1993, 1999). Recent randomized controlled trials (RTCs) have demonstrated that delivery of an implementation intention intervention significantly increased uptake of colorectal cancer screening (Neter et al., 2014), including in a low-income and ethnically diverse population (Greiner et al., 2014).

One method used to aid the formation of implementation intentions is a Volitional Help Sheet (VHS), a tool that has been developed by Armitage (2008). In Armitage's original study, smokers randomized to the VHS condition were asked to draw lines linking temptations to smoke (from a list of options, e.g. "If I am tempted to smoke when things are not going the way I want and I am frustrated") with appropriate behavioral responses (e.g. "then I will tell myself I can quit if I want to"). By drawing lines between temptations to smoke and behavioral responses, participants were actively forming implementation intentions. The results of this study found significantly higher levels of quitting in the VHS condition compared to the control condition. Subsequently, Armitage and colleagues have demonstrated the effectiveness of the VHS for other health behaviors (Armitage, 2008; Armitage and Arden, 2010; 2012; O'Connor et al., 2015). To date, no studies have utilized the VHS technique to help facilitate the formation of implementation intentions within the context of bowel cancer screening. However, the utilization of the VHS technique could represent a substantial improvement on previous research by encouraging respondents to actively form plans that help overcome salient barriers (e.g., feeling negative about the test, lack of confidence to manage the practicalities of the stool sampling) and/or engage in behaviors associated with successful screening uptake (e.g., Tell yourself that the test has proven benefits, planning precisely when you will collect the sample).

Individual CRC interventions are demonstrated to show modest effects (Usher-Smith et al., 2018; Tsipa et al., 2020), it is suggested that interventions may need to be combined together using factorial designs to assess synergistic effects (Myers et al., 2019). One suggested moderator of the effectiveness of implementation intentions is the level of motivation that individuals have toward performing the target behavior (Prestwich and Kellar, 2014), whereby the influence of implementation intentions is suggested to be greater in individuals with stronger intentions to act. The combination of motivational-volitional approaches has been shown to be effective for improving physical activity and reducing alcohol consumption (Hagger and Luszczynska, 2014). The present study therefore aimed to test the effectiveness of a motivational intervention, an implementation intentions-based volitional intervention, and their combination on subsequent screening behavior using a factorial design with usual care as the control condition. There are also a number of factors which may influence the potential effectiveness of these interventions, including whether individuals have completed CRC before, were receiving an invitation for the first time, or their age. The study, therefore, also aimed to assess whether key differences between participants (including previous screening behavior and age) influenced the intervention impact.

One potential motivational intervention suggested to influence subsequent health behavior is based on a social norms approach (SNA). Social norms theory suggests that people falsely perceive the attitudes and/or behaviors of important others to be different from their own (Berkowitz, 2005; Schultz et al., 2007). As a result, there is a tendency for individuals to underestimate the extent to which their peers engage in health behaviors (Perkins, 2014) which may discourage performance of different behaviors. SNA interventions aim to provide participants with more accurate information about actual behavior of other people like them to increase behavioral motivation. However, little work has been carried out testing a SNA approach, or combined motivational-volitional interventions in relation to health screening behavior (Dempsey et al., 2018).

The steps towards increasing bowel cancer screening (STIBCS) trial aimed to test an implementation intentions-based Volitional Help Sheet (VHS) and a SNA-based motivational intervention, to increase CRC screening uptake in a sample in the North East of England. This was a cluster randomized controlled (RCT) trial using a factorial design to examine the effectiveness of SNA and VHS interventions alone and in combination, compared to usual care. Secondary aims were to: i) assess whether effects varied by gender, age, screening history and area-level socioeconomic deprivation, and ii) estimate the potential costs and gains of the interventions using cost-effectiveness analysis. Economic analysis was therefore also conducted to assess the potential costs and gains of the interventions.

2. Method

2.1. Participants and design

Participants were men and women aged 60–74 years receiving a first or repeat bowel cancer screening, sent a biennial fecal occult screening test between 5 March, 2018 and 10 April, 2018 in the region of the UK served by the North-East England screening hub.

The research design employed a 2 × 2 factorial cluster randomized controlled trial to assess the influence of a volitional intervention (VHS) and a motivational intervention (SNA), individually and in combination, as compared with usual care. The trial protocol was pre-registered at ISRCTN, (registration number 39941749; http://www.isrctn.com/ISRCTN39941749). A cluster-randomized approach was used due to practicalities of the postal system used by the screening service making individual randomization not feasible. Intervention groups were randomly allocated by day. Block randomization was used within strata defined by week of mailing the invitation, with blocks randomly assigned using a random number generator. The randomization sequence was generated by the statistician and the rest of the research team remained blinded to the allocation procedures. All participants received a letter of invitation and information sheet and were unaware of alternative interventions (see Fig. 1).

2.2. Ethical approvals

The study received the following approvals: The NHSBCSP Research Advisory Committee (ID_184), Confidentiality Advisory Group (CAG; 17/CAG/0119) for Section 251 exemption of the NHS Act 2006. The study received ethical approval from the National Research Ethics Services Committee East of Scotland (REC ref: 17/ES/0085) and the University of Leeds Ethics Committee.

2.3. Interventions and procedure

Participants were randomized to one of four experimental conditions in order to evaluate the individual and combined effects of: (1) a motivational intervention using a SNA leaflet, and (2) a volitional intervention using a Volitional Help Sheet (VHS).

All participants received an initial letter of invitation for CRC screening and a standard NHS information booklet (usual care). Each participant was allocated to one of four conditions, depending on the day their invitation was sent: a Volitional Help Sheet (VHS) intervention based on implementation intentions, a motivational intervention based on the Social Norms Approach (SNA), both of these interventions combined (SNA + VHS), or usual care (no intervention). This was followed by a guaiac fecal occult blood test (gFOBT) kit sent eight days after the initial letter, four days after any interventional material.

The implementation intentions intervention pack contained an information sheet and a short task (the VHS; supplementary file 2) designed to help participants to construct effective 'if-then' plans. This involved drawing lines to connect barriers likely to be encountered (IFs) with effective responses (THENs) to aid participants' decision-making process with regards to completion of the gFOBT screening kit. The list of barriers and responses identified was based on qualitative pilot work, interviewing 27 individuals across a range of ethnic and socio-economic groups (supplementary file 1).

The motivational intervention pack contained an information sheet and a motivational-intervention leaflet with information regarding the social norms surrounding bowel cancer screening (i.e. how many people currently engage in screening) and was designed to motivate participants to take part in gFOBT screening (supplementary file 2).

2.4. Outcomes

The primary outcome measure was defined as the recorded return of a gFOBT screening kit to the North East screening hub within 8 weeks of the initial screening invitation. Recorded data on gender, age, area-level socioeconomic deprivation derived from the 2015 Index of Multiple Deprivation (IMD) based on individual postcodes, and previous bowel cancer screening uptake were also used. The time taken to return the screening kit was also assessed as a secondary outcome. All measures were obtained from records.

2.5. Sample size

Previous studies had used week as the unit of allocation but found negligible clustering (ICC = 0.0004) (Lo et al., 2014). We were able to use day (not week) as the unit of allocation, so anticipated an even weaker clustering effect, but used ICC = 0.0005 for our sample size calculations to be conservative. Based on figures provided by the screening center, we anticipated at least 2000 invitations posted per day, giving a cluster size of 2000. Based on recent national average uptake we assumed an uptake of approximately 52% in the control arm (Moss et al., 2012). To have 95% power to detect a 4% improvement in absolute terms between the two intervention arms containing VHS and the two

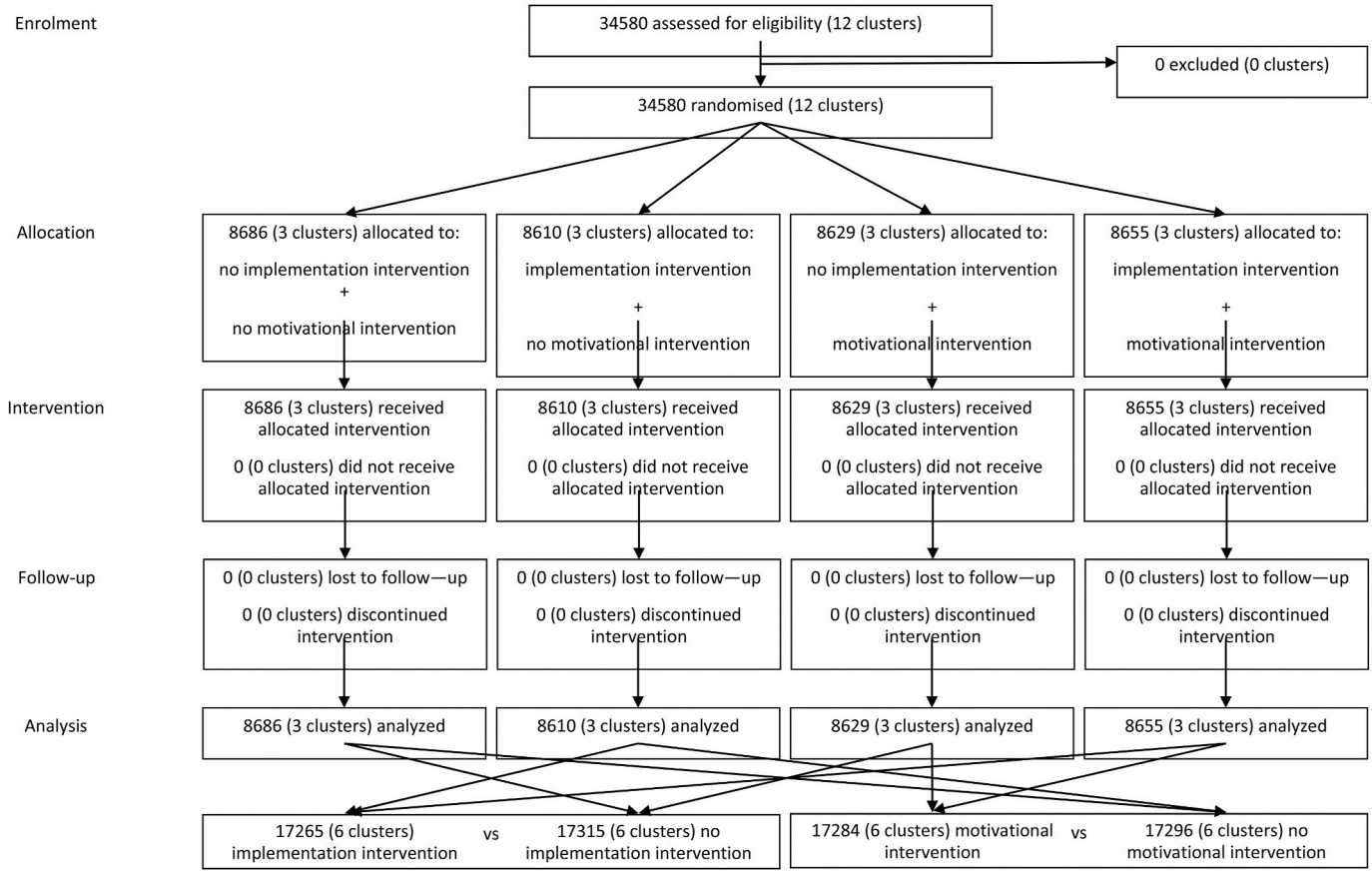

Fig. 1. Flow diagram of the progress of clusters and participants through the trial.

arms containing SNA (e.g. a 56% uptake) at two-tailed $p < 0.05$, would require approximately 5000 individuals in each of the four arms. This would also give 80% power to detect a 3% improvement between these combined groups, 80% power to detect a 4% improvement between any of the four arms on their own, and 80% power to detect a 5% improvement between VHS and SNA in the most deprived third of participants. This sample size also provides approximately 80% power to detect a 6% synergistic improvement for participants receiving both interventions, or a 6% antagonistic interaction, where having both interventions is worse than one intervention on its own.

2.6. Statistical analyses

The baseline balance of characteristics of the participants was explored to assess the success of the randomization and to assess the extent to which the results can be generalized.

A linear mixed effects regression model was used for the primary outcome of samples being returned within eight weeks, with intervention group as a fixed effect adjusting for participants' age, gender, IMD score, previous screening history and week of invitation (the blocking variable used in the randomization process) to improve precision and control for potential imbalance. The date the invitation was sent was included as a random effect to take account of clustering. Adjusted estimates are presented as the primary results to improve precision, because of the potential for bias through lack of blinding and the potential for imbalance with the small number of clusters.

Given the factorial design, the approach taken to the statistical analysis depends on whether groups receiving the same intervention, with or without the second intervention, can be combined. Therefore, a statistical interaction between VHS and SNA interventions was included to estimate the extent to which the motivation intervention (SNA) improves any effect of the volitional intervention (VHS). Where interactions between interventions were not significant, all participants receiving that intervention were compared against all participants receiving a control for that intervention (VHS vs no VHS, SNA vs no SNA) therefore benefitting from the potential efficiency gains of the factorial design. The intraclass correlation was also estimated from this model to evaluate the strength of clustering and to compare with assumptions used in estimating the required sample size. Where interactions between interventions existed, the main results were based on comparing the four separate groups (usual care, VHS, SNA, VHS plus SNA combined).

Cox's proportional hazards regression was used for the secondary outcome of time (days) to return a sample, restricted to those who returned them, with shared frailty within each cluster to take account of clustering. Results were adjusted for participants' age, gender, IMD score, previous screening history and week of invitation (the blocking variable used in the randomization process) as fixed effects to improve precision and control for potential imbalance.

Variation in the success of the interventions (measured using the primary outcome of return of a gFOBT sample within eight weeks of being sent an invitation) was assessed by the following pre-defined participant characteristics: age (in years), gender, IMD score, past screening history (i.e. whether a participant had completed and returned a sample before), and by IMD quintile. Subgroups were formally compared using interaction terms included in the models, presented as the estimated effects of the intervention for each subgroup category. For continuous variables (age, IMD score) the tests of interaction are based on the continuous variable. An intention-to-treat approach was taken throughout analysis, with outcome measures available on all included participants. All analyses were conducted using Stata version 15.1.

Table 2
Primary and secondary outcomes of participants by separate intervention groups.

Characteristic	Usual care only n = 8686	Volitional Help Sheet (VHS) n = 8610	Social Norms Approach (SNA) n = 8629	Volitional Help Sheet (VHS) + Social Norms Approach (SNA) n = 8655
Returned screening sample within 8 weeks				
Number returned (%)	5331 (61%)	5284 (61%)	5373 (62%)	4825 (56%)
Unadjusted odds ratios (95% *CI*)	1.00	1.00 (0.79, 1.26)	1.04 (0.83, 1.32)	0.79 (0.63, 1.00)
Adjusted[a] odds ratios (95% *CI*)	1.00	0.88 (0.75, 1.03)	0.93 (0.76, 1.15)	1.18 (0.97, 1.44)
Time taken to return kit amongst those who returned samples				
Median time (IQR)	14 (9–21)	13 (10–22)	13 (9–21)	14 (9–23)
Unadjusted hazard ratio (95% *CI*)	1.00	0.99 (0.86, 1.15)	1.06 (0.91, 1.23)	0.93 (0.80, 1.08)
Adjusted[a] hazard ratio (95% *CI*)	1.00	0.94 (0.90, 0.99)	0.96 (0.90, 1.03)	0.98 (0.92, 1.05)

An interaction ratio was calculated to assess how much more the combined VHS + SNA group is over and above what would be expected from the combined group if the two interventions were independent (Combined *OR*/(VHS *OR* x SNA *OR*), i.e. 1.18/(0.88 × 0.93). Interaction ratio = 1.44; *95% CI*: 1.13 to 1.84; $p = 0.01$).

[a] Adjusted for participants' age, gender, index of multiple deprivation score, previous screening history and week of invitation.

Table 1
Demographic and clinical characteristics of participants by separate randomization groups.

Characteristic	Usual care	Implementation intervention	Motivational intervention	Implementation and motivational interventions	Total
	Usual care only n = 8686	Volitional Help Sheet (VHS) n = 8610	Social Norms Approach (SNA) n = 8629	Volitional Help Sheet (VHS) + Social Norms Approach (SNA) n = 8655	Total n = 34580
Age in Years					
Mean (*SD*)	66 (5)	66 (5)	66 (5)	64 (5)	66 (5)
Gender					
Male (%)	4282 (49%)	4224 (49%)	4173 (48%)	4349 (50%)	17028 (49%)
Female (%)	4404 (51%)	4386 (51%)	4456 (52%)	4306 (50%)	17552 (51%)
Index of Multiple Deprivation					
Mean (*SD*)	23 (17)	23 (17)	23 (17)	24 (17)	23 (17)
Previously invited before					
No (%)	1581 (18%)	1452 (17%)	1614 (19%)	4062 (50%)	8709 (25%)
Yes (%)	7105 (82%)	7158 (83%)	7015 (81%)	4593 (53%)	25871 (75%)
Previously returned screening sample					
No (%)	3596 (41%)	3446 (40%)	3597 (42%)	5458 (63%)	16097 (47%)
Yes (%)	5090 (59%)	5164 (60%)	5032 (58%)	3197 (37%)	18483 (53%)

2.7. Health economics analysis

Cost-effectiveness analysis was performed using the return on investment (ROI) tool developed by Public Health England (Public Health England, 2016). This tool is constructed to estimate the potential costs and gains of an intervention designed to increase uptake rate of the gFOBT test.

The ROI tool uses aggregate data on cost, scanning and diagnosis pathways, treatment scenarios, follow-up/surveillance results, and end of life care. The costs included in the ROI are: costs of scanning, diagnosis, treatment of patients per bowel cancer stage (I, II, III and IV), and costs of recurrence. The SNA and VHS instruments were added to the screening costs and were estimated based on the actual costs of printing, preparing and posting the instruments to the randomized population. The tool uses quality-adjusted life years (QALYs) as an outcome measure (Whitehead and Ali, 2010). The model estimates the number of life years saved per cancer stage which are then used to estimate the lifetime QALYs gains per instrument. The generic utility values used for these estimations were updated to match the UK population (Szende et al., 2014).

The tool's base costs are from 2013, however, these have been updated using annual inflation rates to represent 2018 figures. The tool also discounts costs at 3.5% and outcomes at 1.5%. The tool was originally designed to enable comparison in cost and outcomes between different Clinical Commissioning Groups (CCGs) in England. Our analysis was restricted to CCGs operating in North East England. The effectiveness of the instruments was estimated following the same procedure described in the statistical analyses section. A sensitivity analysis on alternative utility values based on Ness and colleagues (Ness et al., 1999) and uptake rate of relevant strategies were also carried out.

3. Results

3.1. Study participants

In total, 34,633 people were mailed an invitation in the 12 days included in the study. All individuals who received an invitation were included in the study, 20,847 (60%) of these individuals returned a screening kit within eight weeks of being invited. A slightly higher proportion of women (N = 10,960, 62%) than men (9,887, 58%) returned the kit. Those that returned the kit did so within a median time of 13 days (IQR 9 to 22). Among those previously invited, participants who had returned a kit before were more likely to return one (N = 15,798, 85%) than those who had not done so previously (N = 5,257, 33%).

Baseline characteristics of participants and clusters by each of the four separate randomly allocated groups are outlined in Table 1. There was substantial imbalance observed in important participant characteristics, with the clusters receiving both VHS and SNA differing markedly from the other groups. The participants in this group had a younger mean age, with a substantially lower proportion of participants having previously been offered screening, reflected in a lower proportion who had returned screening samples before. Reported analyses therefore control for these imbalances.

3.2. Primary outcomes

The effect of the intervention on the primary endpoint of samples being returned within eight weeks is reported by separate intervention groups in Table 2. Given the cluster-level imbalance in participant characteristics, we focus on the adjusted results.

Given the 2 × 2 factorial design, we first tested the interaction between the two interventions. There was a significant interaction between the two (interaction ratio 1.44; 95% *CI*: 1.13 to 1.84; p = 0.01) based on the fully adjusted models. This effect was strongly dependent on the covariate adjustments because of the imbalance. Thus, the interventions were not independent and thus should not be presented as main effects (VHS vs no-VHS, SNA vs no-SNA), but should instead be based on the four separate intervention groups (usual care, VHS, SNA, VHS and SNA combined) as presented below and in Table 2.

Compared to control, there was no evidence of any benefit from the VHS implementation intervention alone (Adj. *OR* = 0.93, 95% CI 0.76 to 1.15), the SNA motivational intervention alone (Adj. *OR* = 0.88; 95% CI: 0.75 to 1.03), nor the combined intervention (Adj. *OR* = 1.18, 95% CI 0.97 to 1.44) in the adjusted models. The sample return rate in the VHS only group also did not significantly differ from the SNA only group (Adj. *OR* = 1.06; 0.87 to 1.30).

The intraclass correlation for this model was 0.0016 (95% *CI*: 0.0005, 0.0051), considerably higher than that assumed in the sample size calculations.

3.3. Secondary outcome

The secondary outcome (time to return) is reported by separate intervention groups in Table 2. Based on the same adjusted models for separate intervention groups (Table 2) there was no significant

Table 3
Subgroup analyses for primary outcomes of participants for separate intervention groups compared to usual care.

Returned screening sample within 8 weeks	Volitional Help Sheet (VHS) vs usual control		Social Norms Approach (SNA) vs usual control		Volitional Help and Social Norms Approach (VHS + SNA) vs usual control	
	Adjusted *OR*[a] (95% *CI*) *vs.* usual care	Interaction *p*-value	Adjusted *OR*[a] (95% *CI*) *vs.* usual care	Interaction *p*-value	Adjusted *OR*[a] (95% *CI*) *vs.* usual care	Interaction *p*-value
Age						
<62.5 years	0.80 (0.68, 0.95)	0.08	0.90 (0.73, 1.10)	0.3	1.27 (1.05, 1.54)	<0.001
62.5–67.5 years	0.98 (0.80, 1.19)		1.02 (0.80, 1.28)		1.05 (0.82, 1.33)	
68–72.5 years	0.93 (0.78, 1.11)		1.03 (0.83, 1.28)		0.89 (0.72, 1.11)	
>72.5 years	0.99 (0.75, 1.31)		1.13 (0.82, 1.55)		1.05 (0.76, 1.46)	
Gender						
Male	0.88 (0.73, 1.05)	0.9	0.96 (0.76, 1.21)	0.7	1.15 (0.93, 1.43)	0.4
Female	0.89 (0.74, 1.06)		0.93 (0.74, 1.17)		1.23 (0.99, 1.53)	
Index of multiple deprivation fifths (quintiles)						
Q1	0.83 (0.68, 1.02)	0.2	0.97 (0.75, 1.24)	0.9	1.06 (0.84, 1.34)	0.4
Q2	0.92 (0.74, 1.15)		1.02 (0.79, 1.32)		1.25 (0.98, 1.60)	
Q3	0.86 (0.70, 1.07)		0.85 (0.66, 1.10)		1.28 (1.00, 1.64)	
Q4	0.86 (0.70, 1.07)		0.96 (0.74, 1.24)		1.15 (0.91, 1.47)	
Q5	0.93 (0.74, 1.17)		0.90 (0.69, 1.17)		1.24 (0.96, 1.60)	
Previously returned screening sample						
Yes	0.97 (0.86, 1.09)	0.9	0.92 (0.79, 1.08)	0.9	0.84 (0.72, 0.98)	0.3
No	0.99 (0.81, 1.21)		0.94 (0.75, 1.17)		0.96 (0.77, 1.21)	

[a] Adjusted for participants' age, gender, index of multiple deprivation score, previous screening history and week of invitation.

Table 4
Base case cost-effectiveness analysis.

Intervention	Costs	QALYs[a]	Incremental costs	Incremental QALYs	ICER[b]	Result
Usual care	£26,144,386	2367				Not cost-effective
VHS[c]	£26,147,039	2362	–	–	–	Dominated
SNA[d]	£26,169,259	2365	–	–	–	Dominated
SNA + VHS	£26,259,052	2373	£114,665	6.08	£18,861	Cost-effective

[a] QALYs: Quality-adjusted life year.
[b] ICER: Incremental cost-effectiveness ratio.
[c] VHS: Volitional Help Sheet intervention.
[d] SNA: Social Norm approach intervention.

interaction ($p = 0.07$) nor any evidence that samples were returned any quicker after the SNA or combined interventions compared to control (SNA intervention: *HR* = 0.96; 95% *CI*: 0.89 to 1.03; combined: *HR* = 0.98; 95% *CI*: 0.92–1.05). Time to return in the VHS only condition was significantly shorter in the VHS condition compared to control (*HR* = 0.94; 95% *CI*: 0.90 to 0.99), however this was significant in the adjusted analyses only. The VHS only and SNA only conditions did not differ from one another on time to return (*HR* = 0.98; 0.92 to 1.05).

3.4. Subgroup analyses

The effects of the combined intervention were demonstrated to vary by age ($p < 0.001$), with a significant effect of the combined intervention compared to control in the youngest age group only (Age <62.5; Adj. *OR* = 1.27; 95% *CI* 1.05 to 1.54). There was no evidence that the effects of VHS or SNA alone varied by age, gender, IMD score, previous invitation for screening, or previous participation in screening. The results from the predefined subgroup analyses are reported in Table 3.

3.5. Economic analysis

Combining SNA and VHS together was the costliest intervention, followed by SNA and VHS alone, while usual care was the cheapest alternative. In terms of effectiveness, SNA + VHS offers the highest QALYs gains while VHS alone offers the lowest. These results indicate that VHS and SNA alone were costlier and less effective than usual care. While the SNA + VHS estimated incremental cost-effectiveness ratio (ICER) indicates that using this combined strategy over usual care would require over £18,861 to gain a QALY. This value is below the UK National Institute for Health and Care Excellence's £20,000 per QALY threshold, indicating that this is the most cost-effective strategy. The sensitivity analysis performed did not change the estimated results (see Table 4).

Given that the cost-effectiveness results are driven by the modest differences in the uptake rate, we carried out a Monte-Carlo simulation of uptake rates assuming a beta distribution. We ran 10,000 iterations of the uptake of both interventions. The results indicated that in 97% of them, the uptake rate of SNA + VHS was equal to or higher than the mean difference in the uptake rate between the relevant interventions (0.027; difference between 0.628 and 0.601). The latter finding suggests that in 97% of potential combinations between different uptake rates, the combined SNA + VHS intervention would be a cost-effective strategy. These results were observed as the SE of the uptake estimates (0.01 for both interventions) is relatively small given the large sample size.

4. Discussion

This large-scale cluster randomized controlled trial aimed to investigate the influence of two theory based brief behavior change interventions and their combination on increases in bowel cancer screening uptake in a sample from the North of England, conducted in collaboration with the NHS bowel cancer screening program. Over 34,000 people were included in the study, uptake rates were around 60% in all conditions. There was no evidence supporting the benefit of either individual intervention on screening uptake rate, although there was some evidence supporting the combined intervention in the youngest age group. Considerable cluster imbalance within the combined intervention was found. Health economic analysis based on the adjusted results supported the combined condition as the most cost-effective strategy, despite the null results of the combined intervention.

The imbalance in baseline characteristics evident between clusters appeared to be due to an unexpected postal delay resulting from the intervention delivery period taking place during the end of a public holiday. People who are receiving their first invitation are effectively those turning 60. On a Monday, invitees are those who have turned 60 on Saturday, Sunday or Monday. On a Tuesday, invitees are only people who've turned 60 on that day. Due to the invitations covering the Easter weekend, invitees on 3rd April (who were randomized to the combined condition) had turned 60 on Good Friday, Saturday, Easter Sunday, Easter Monday and Tuesday. Conversely, when someone has been invited before, the way their next "screening due date" (i.e. when they will be invited) is calculated means this is almost certainly on a Monday-Friday. Therefore, there are fewer invitees with screening due dates falling on a weekend. As a result of this, participants in the combined condition had some sociodemographic differences compared to the other three conditions, including a greater likelihood of being first-time screeners as a result of having just turned 60 years old.

When adjusting for covariates, there was a significant interaction found between the two interventions, providing tentative support for the combination of both interventions improving the effect of either the implementation intentions based volitional (VHS) intervention or social norms (SNA) based intervention alone. Future research ought to investigate the interaction effect further. Adjusted subgroup analyses also demonstrated a significant effect of the combined condition on uptake in the youngest age group compared to control, although none of the other age groups significantly differed. However, the failure of randomization demonstrated in the combined condition supports a need to further test these tentative effects in a properly randomized study.

The literature suggests that implementation intention formation is more effective in individuals who have a strong motivation toward performing the target behavior (Prestwich and Kellar, 2014). The results of the present study show that neither intervention alone was enough to change behavior. There are a number of barriers to bowel cancer screening that have been identified in previous literature, including motivation along with poor social support and fatalistic beliefs (Jones et al., 2010). Little is known about the effectiveness of applying a social norms approach to increase motivation in health promotion behaviors, where the majority of previous studies have focused on alcohol use and other risk behaviors (Dempsey et al., 2018). While the present study developed and piloted the intervention materials within the target population, it has been demonstrated that SNA interventions tend to be more influential when norm messaging is targeted at specific characteristics of the individual, as well as when individuals identify with the messaging (Dempsey et al., 2018). The norm messaging used as part of the SNA intervention was fairly broad (relating to 'some form of screening') and did not target the specific age group of the participant.

This was in part to reduce any potential negative impact of providing information on the current sub-optimal rates of CRC screening. Limitations of the study design also meant that all participants were sent the same materials, regardless of their age or gender. It would be beneficial for further research to be conducted, focusing on social norms in cancer screening behaviors and comparing the impact of targeted versus untargeted social norm information on subsequent screening.

Participants were not asked to return the intervention materials and therefore it is not possible to ascertain how many participants receiving the VHS materials engaged with this, or whether the situations and solutions provided were relevant to them. It has been demonstrated previously that CRC screening is associated with strong affective reactions, including disgust concerning thinking about screening (Chambers, O'Carroll, Brownlee, Libby and Steele, 2016), which may reduce the likelihood of participant engagement in activities which encourage thinking about the screening process. In 2019, the gFOBT screening was replaced with the single-sample Fecal Immunochemical Test (FIT) in England. Disgust reactions toward the FIT are suggested to be lower than to the gFOBT (Chambers et al., 2016); it would therefore be worthwhile testing the impact of administering a VHS intervention to individuals invited to complete the FIT.

The cost-effectiveness analysis suggests that SNA and VHS on their own are not a good use of public resources as current practice is less costly and more effective. However, when combining them together, although more expensive, the QALYs gained overall would add 6 years of full health to the targeted population. The results are robust as demonstrated by the sensitivity analysis. . In cost-effectiveness analyses, both costs and outcomes are analyzed (QALYs) consequently, results are based on the combined measures of both costs and outcomes. Therefore, and despite finding a non-significant result of the intervention, the economic evaluation can still produce a cost-effectiveness recommendation (Claxton, 1999; Johnston et al., 2003). The slight average increase in the uptake rate in the SNA + VHS condition versus control (0.628 vs 0.601) indicates that some individuals (although a small number) will be affected by the intervention. This is then translated into better overall long-term outcomes on average (i.e. fewer patients detected at later stages) which translates into a slightly higher population QALY gained which overcomes the increase in costs due to using SNA and VHS combined. Given the established threshold in the UK (£20, 000 per QALY gained) the SNA + VHS intervention is considered cost-effective.

4.1. Strengths and limitations

Strengths of the study include its large sample size and collaboration with the NHS bowel cancer screening hub, which demonstrates the ability of similar interventions to be administered alongside routine screening invitations. The study additionally provides up-to-date uptake rates for the FOBT, where the 60% uptake rate in the present study is consistent with the latest data provided by Public Health England for England as a whole (Public Health England, 2018).

Further strengths are the use of an objective measure of screening uptake assessed by the bowel cancer screening hub, rather than relying on self-reported data, the cost-effectiveness of the intervention and the ease with which it could be introduced to the national screening program. The interventions materials were additionally developed and piloted in individuals from a range of sociodemographic backgrounds.

One of the key limitations of the study was the considerable imbalance in participant characteristics in the combined condition which limits any conclusions that can be drawn, in particular with regards to the significant interaction effect. Additional limitations of the study include the lower than intended power for the stated effects, although estimated power was based on previous studies. Additionally, due to the design of the intervention, it is not possible to know whether participants engaged with the intervention materials. The cost effectiveness analysis also has some limitations, as the ROI tool allows only for deterministic sensitivity analysis. This type of analysis assesses the sensitivity of results to variations of individual parameters but does not provide information on the probability of each intervention being cost effective. Although it is likely that the overall conclusion would remain the same, the lack of a probabilistic sensitivity analysis prevents us to fully account for the uncertainty of the model and estimating the probability of SNA + VHS of being cost-effective. This limitation, however, could be addressed in future RCTs focused on the combined instruments.

5. Conclusions

The present study demonstrates that, despite the absence of a positive effect, a brief behavior change interventions can be practically incorporated into routine NHS screening. However, at this time, the limitations of the study due to the imbalance found between conditions limits the conclusions that can be drawn regarding the effectiveness of the combined motivational (SNA) and volitional (VHS) intervention. Nevertheless, the current results are promising and ought to be tested again in a new randomized controlled trial.

Credit author statement

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.socscimed.2020.113496.

References

Armitage, C.J., 2008. A volitional help sheet to encourage smoking cessation: a randomized exploratory trial. Health Psychol. 27 (5), 557–566. https://doi.org/10.1037/0278-6133.27.5.557.

Armitage, C.J., Arden, M.A., 2010. A volitional help sheet to increase physical activity in people with low socioeconomic status: a randomised exploratory trial. Psychol. Health 25 (10), 1129–1145. https://doi.org/10.1080/08870440903121638.

Armitage, C.J., Arden, M.A., 2012. A volitional help sheet to reduce alcohol consumption in the general population: a field experiment. Prev. Sci. 13 (6), 635–643. https://doi.org/10.1007/s11121-012-0291-4.
Berkowitz, A.D., 2005. An Overview of the Social Norms Approach. Changing the Culture of College Drinking: A Socially Situated Health Communication Campaign, pp. 193–214.
Chambers, J., O'Carroll, R., Brownlee, L., Libby, G., Steele, R., 2016. Colorectal cancer screening and perceived disgust: the importance of the "Ick" factor in faecal occult blood test uptake. Colorectal Canc. Open Access 2 (1).
Claxton, K., 1999. The irrelevance of inference: a decision-making approach to the stochastic evaluation of health care technologies. J. Health Econ. 18 (3), 341–364.
Dempsey, R.C., McAlaney, J., Bewick, B., 2018. A critical appraisal of the Social Norms Approach as an interventional strategy for health-related behaviour and attitude change. Front. Psychol. 9, 2180.
Gollwitzer, P.M., 1993. Goal achievement: the role of intentions. Eur. Rev. Soc. Psychol. 4 (1), 141–185.
Gollwitzer, P.M., 1999. Implementation intentions: strong effects of simple plans. Am. Psychol. 54 (7), 493.
Greiner, K.A., Daley, C.M., Epp, A., James, A., Yeh, H.-W., Geana, M., Hester, C.M., 2014. Implementation intentions and colorectal screening: a randomized trial in safety-net clinics. Am. J. Prev. Med. 47 (6), 703–714.
Hagger, M.S., Luszczynska, A., 2014. Implementation intention and action planning interventions in health contexts: state of the research and proposals for the way forward. Appl. Psychol.: Health Well-Being 6 (1), 1–47.
Hewitson, P., Glasziou, P., Watson, E., Towler, B., Irwig, L., 2008. Cochrane systematic review of colorectal cancer screening using the fecal occult blood test (hemoccult): an update. Am. J. Gastroenterol. 103 (6), 1541–1549. https://doi.org/10.1111/j.1572-0241.2008.01875.x.
Johnston, K., Gray, A., Moher, M., Yudkin, P., Wright, L., Mant, D., 2003. Reporting the cost-effectiveness of interventions with nonsignificant effect differences: example from a trial of secondary prevention of coronary heart disease. Int. J. Technol. Assess. Health Care 19 (3), 476.
Jones, R.M., Devers, K.J., Kuzel, A.J., Woolf, S.H., 2010. Patient-reported barriers to colorectal cancer screening: a mixed-methods analysis. Am. J. Prev. Med. 38 (5), 508–516.
Lindberg, N.M., Stevens, V.J., Smith, K.S., Glasgow, R.E., Toobert, D.J., 2009. A brief intervention designed to increase breast cancer self-screening. Am. J. Health Promot. 23 (5), 320–323.
Lo, S.H., Good, A., Sheeran, P., Baio, G., Rainbow, S., Vart, G., Wardle, J., 2014. Preformulated implementation intentions to promote colorectal cancer screening: a cluster-randomized trial. Health Psychol. 33 (9), 998–1002. https://doi.org/10.1037/a0033507.
Miller, B.C., Bowers, J.M., Payne, J.B., Moyer, A., 2019. Barriers to mammography screening among racial and ethnic minority women. Soc. Sci. Med. 239, 112494. https://doi.org/10.1016/j.socscimed.2019.112494.
Moss, S.M., Campbell, C., Melia, J., Coleman, D., Smith, S., Parker, R., Weller, D.P., 2012. Performance measures in three rounds of the English bowel cancer screening pilot. Gut 61 (1), 101–107. https://doi.org/10.1136/gut.2010.236430.
Myers, L., Goodwin, B., March, S., Dunn, J., 2019. Ways to use interventions to increase participation in mail-out bowel cancer screening: a systematic review and meta-analysis. Trans. Behav. Med. 10 (2), 384–393.
Navarro, M., Nicolas, A., Ferrandez, A., Lanas, A., 2017. Colorectal cancer population screening programs worldwide in 2016: an update. World J. Gastroenterol. 23 (20), 3632.
Ness, R.M., Holmes, A.M., Klein, R., Dittus, R., 1999. Utility valuations for outcome states of colorectal cancer. Am. J. Gastroenterol. 94 (6), 1650–1657.
Neter, E., Stein, N., Barnett-Griness, O., Rennert, G., Hagoel, L., 2014. From the bench to public health: population-level implementation intentions in colorectal cancer screening. Am. J. Prev. Med. 46 (3), 273–280.
O'Connor, D.B., Armitage, C.J., Ferguson, E., 2015. Randomized test of an implementation intention-based tool to reduce stress-induced eating. Ann. Behav. Med. 49 (3), 331–343. https://doi.org/10.1007/s12160-014-9668-x.
Perkins, H.W., 2014. Misperception is reality: the "reign of error" about peer risk behaviour norms among youth and young adults. In: The Complexity of Social Norms. Springer, pp. 11–36.
Power, E., Miles, A., Von Wagner, C., Robb, K., Wardle, J., 2009. Uptake of colorectal cancer screening: system, provider and individual factors and strategies to improve participation. Future Oncol. 5 (9), 1371–1388.
Prestwich, A.J., Kellar, I., 2014. How can the impact of implementation intentions as a behaviour change intervention be improved? Revue Européenne de Psychologie Appliquée/Eur. Rev. Appl. Psychol. 64 (1), 35–41.
Public Health England, 2016. Return on Investment Tool: Colorectal Cancer. Retrieved from. https://www.gov.uk/government/publications/return-on-investment-tool-colorectal-cancer.
Public Health England, 2018. Public Health Profiles: Cancer Services. Retrieved from. https://fingertips.phe.org.uk/profile/cancerservices/data#page/11/gid/1938132830/pat/152/par/E38000001/ati/7/are/B83620.
Rat, C., Latour, C., Rousseau, R., Gaultier, A., Pogu, C., Edwards, A., Nguyen, J.-M., 2018. Interventions to increase uptake of faecal tests for colorectal cancer screening: a systematic review. Eur. J. Canc. Prev. 27 (3), 227–236, 27(3), 227-236.
Rutter, D.R., Steadman, L., Quine, L., 2006. An implementation intentions intervention to increase uptake of mammography. Ann. Behav. Med. 32 (2), 127–134.
Schultz, P.W., Nolan, J.M., Cialdini, R.B., Goldstein, N.J., Griskevicius, V., 2007. The constructive, destructive, and reconstructive power of social norms. Psychol. Sci. 18 (5), 429–434.
Sheeran, P., Orbell, S., 2000. Using implementation intentions to increase attendance for cervical cancer screening. Health Psychol. 19 (3), 283.
Solmi, F., Von Wagner, C., Kobayashi, L.C., Raine, R., Wardle, J., Morris, S., 2015. Decomposing socio-economic inequality in colorectal cancer screening uptake in England. Soc. Sci. Med. 134, 76–86. https://doi.org/10.1016/j.socscimed.2015.04.010.
Szende, A., Janssen, B., Cabases, J., 2014. Self-reported Population Health: an International Perspective Based on EQ-5D. Springer Netherlands, Dordrecht, The Netherlands.
Tsipa, A., O'Connor, D.B., Branley-Bell, D., Day, F., Hall, L.H., Sykes-Muskett, B., Conner, M., 2020. Promoting colorectal cancer screening: a systematic review and meta-analysis of randomised controlled trials of interventions to increase uptake. Health Psychol. Rev. https://doi.org/10.1080/17437199.2020.1760726.
Usher-Smith, J.A., Silarova, B., Sharp, S.J., Mills, K., Griffin, S.J., 2018. Effect of interventions incorporating personalised cancer risk information on intentions and behaviour: a systematic review and meta-analysis of randomised controlled trials. BMJ Open 8 (1), e017717.
Von Wagner, C., Semmler, C., Good, A., Wardle, J., 2009. Health literacy and self-efficacy for participating in colorectal cancer screening: the role of information processing. Patient Educ. Counsel. 75 (3), 352–357.
Whitehead, S.J., Ali, S., 2010. Health outcomes in economic evaluation: the QALY and utilities. Br. Med. Bull. 96 (1), 5–21.
World Cancer Research Fund Network, 2017. Colorectal Cancer. Retrieved from. https://www.wcrf.org/dietandcancer/colorectal-cancer.