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A randomized trial to evaluate the effectiveness and impact of offering post-office visit decision support and assistance in obtaining physician-recommended colorectal cancer screening: The e-assist Colon Health Study

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ABSTRACT

Introduction. How to provide practice-integrated decision support to patients remains a challenge. We are testing the effectiveness and impact of a practice-integrated program targeting patients with a physician recommendation for colorectal cancer (CRC) screening.

Methods and analysis. In partnership with health care teams, we developed "e-assist: Colon Health:" a patient-targeted, post-visit CRC screening decision support program. The program is housed within an electronic health record (EHR)-embedded patient portal. It leverages a physician screening recommendation as the cue to action and uses the portal to enroll and intervene with patients. Program content complements patient-physician discussions by encouraging screening for those eligible, addressing common questions, and assisting with barrier removal. Patients are randomized to receive e-assist: Colon Health or one of two controls (usual care plus or usual care). Trial participants are average-risk, aged 50-75 years, due for CRC screening, and received a physician order for stool testing or colonoscopy. Effectiveness will be evaluated by comparing CRC screening use, as documented in the EHR, between trial enrollees in the e-assist: Colon Health and usual care plus (CRC screening information receipt) groups. Secondary outcomes include patient-perceived benefits of, barriers to and support for CRC screening, and patient-reported CRC screening intent. The usual care group will be used to estimate screening use without intervention and program impact at the population level. Differences in outcomes by study arm will be estimated with hierarchical logit models where patients are nested within physicians.

Ethics and dissemination. All aspects of the trial are being monitored by the Institutional Review Board of the health system in which the trial is being conducted. We will disseminate findings in diverse scientific venues and will target clinical and quality improvement audiences

via other venues. The intervention could serve as a model for filling the gap between physician recommendations and patient action.

Trial registration number: NCT02798224

ARTICLE SUMMARY

Strengths and limitations of this study

- Trial addresses how EHR-embedded, online decision support and assistance can be used following patients' receipt of physician order for CRC screening
- Use of EHR-embedded patient portal to enroll patients and deliver intervention facilitates practice integration and provides efficient and sustainable platform for intervention
- Program facilitates informed decision making and addresses common barriers to and questions regarding CRC screening, thereby filling known gaps in office visit discussions
- Enrolling and intervening with patients via the patient portal limits the program's reach to those already engaged with portal technology
- Study findings may be limited in that they may not generalize to other settings

INTRODUCTION

Despite the availability of multiple effective colorectal cancer (CRC) screening tests, CRC screening remains underutilized relative to other cancer screening tests.[1] We have found that a driving factor behind this under-utilization for insured individuals is the gap that exists between physician recommendation and patient receipt of care. We previously found that while the overwhelming majority (93%) of insured people due for CRC screening when visiting a physician office received a recommendation for screening, only 54% were screened in the following year.[2] Despite the known importance of physician recommendations to CRC screening use,[3 4] the gap between recommendation and screening use, in part, may be explained by the poor quality of typical patient-physician CRC screening discussions which have been shown to fall short of recommended decision making processes, and omit addressing common patient questions and CRC screening barriers.[3 5-23] To address these shortfalls, and close the gap between physician recommendation and care receipt, interventions are needed that encourage patient follow through, address lingering patient questions, and assist with barrier removal following a physician recommendation for screening.

How to offer such decision support and assistance to patients in a way that is practice-integrated remains a challenge. Individual health navigators hold promise, especially for low literacy patients, but costs associated with such programs limit scalability.[24 25] Patient reminders and the removal of structural barriers can increase screening use, but these techniques leave many unscreened and are disconnected from physician recommendations and other existing clinic processes.[24 26-37] Similarly, traditional decision aids provided before an office visit often result in improved patient knowledge, but limited (if any) changes in screening behaviors and have proven difficult to integrate within practice.[38-43] The effectiveness of such previously tested CRC screening programs may be limited by a combination of factors. These include their failure to be practice-integrated and thus capitalize on the powerful patient-physician relationship and

cue to action that exists once a physician recommends CRC screening, and the missed opportunity to intervene *after* an office visit in which CRC has been recommended with program content that is complementary to typical office-based CRC screening discussions.

By leveraging the platform of an online patient portal that is embedded within the electronic health record (EHR), we have developed a practice-integrated, patient-targeted CRC screening program, e-assist: Colon Health. The program is delivered to patients via an EHR-embedded patient portal after an office visit in which CRC screening has been recommended, thereby leveraging physician recommendations as a cue to action. Program content reinforces screening benefits, and addresses typical patient questions and the personal and structural barriers faced once a physician recommendation has been received. We are evaluating e-assist: Colon Health using a practice-embedded trial in which patients are randomized to receive e-assist: Colon Health or one of two control arms (usual care plus or usual care).

Aims and Hypotheses

The primary outcome of interest for the randomized trial is receipt of EHR-documented CRC screening within 12 months of physician recommendation. The overall aims of the evaluation include:

Aim 1. To compare screening use, intent to screen, and patient perceptions among trial enrollees receiving e-assist: Colon Health and usual care plus.

H1: A larger proportion of trial enrollees receiving e-assist: Colon Health, compared to trial enrollees receiving usual care plus, will be screened for CRC within 12 months of receiving the physician recommendation.

H2: A larger proportion of trial enrollees receiving e-assist: Colon Health, compared to enrollees receiving usual care plus, will report intending to be screened at the time of the follow-up survey.

H3: Trial enrollees receiving e-assist: Colon Health will perceive more benefits from CRC screening, more screening support, and fewer CRC screening barriers at the time of the follow-up survey as compared to trial enrollees receiving usual care plus.

Aim 2. To evaluate whether the effectiveness of e-assist: Colon Health is moderated by factors including patient health literacy, decision-making preference, and CRC screening decision stage as reported by trial enrollees at baseline.

H4: The effectiveness of e-assist: Colon Health will be greater among patients with low health literacy (compared to those with high health literacy), a preference for less directed decision making (compared to those with a preference for directed decision making), and a low decision stage (compared to those with a higher decision stage).

Aim 3. To characterize the impact of e-assist: Colon Health at a primary care population level by describing the ability of the program to reach the target population and by comparing CRC screening use across the three study arms.

METHODS

Conceptual Framework

Intervention and trial design are guided by the Health Belief Model (HBM),[44] the Precaution Adoption Process Model and Self Determination Theory.[45-48] The HBM suggests that people's use of preventive services is explained by their perceived threat of disease, benefits of the service, barriers to and self-efficacy for obtaining screening. The model also acknowledges the need for a stimulus, or cue to action, to trigger the behavior. The HBM provides overarching

guidance for intervention design (e.g., provision of information regarding the risks and consequences of CRC, and the benefits of screening; offering assistance overcoming barriers to screening; addressing structural barriers to completing screening by providing direct access to stool testing and assistance with completing screening; etc.) as well as the impetus for targeting patients immediately following a primary care visit with an order for CRC screening (i.e., an external cue to action that has occurred within established clinic processes). The HBM, however, does not provide guidance on how to personalize health communications and other intervention components to maximize message salience and accompanying action. The Precaution Adoption Process Model provides this guidance by building upon the core elements of the HBM, and considering how a person comes to decisions to take action.[46] Specifically, the individual's readiness to engage in the healthful behavior is based on their "decision stage." The premise behind the model is that different factors influence different stage transitions and that messages can be strategically designed to move individuals through the stages.[49-51] For example, the e-assist: Colon Health program offers patients who indicate they are not ready to be screened suggestions for how to overcome common personal barriers to screening. Likewise, patients who indicate they are undecided about how to be screened are provided with information about the pros and cons of different test options, while those indicating they are ready to be screened are provided with tips for completing their preferred screening test and assistance removing structural barriers that may arise. Finally, we use principles from Self Determination Theory to guide the tone of the written messages and ensure they are autonomy supporting,[48] and are not overly directive or controlling. For example, the program provides information on other types of CRC screening tests only to those who express an interest in this information and then emphasizes that modality choice is up to the patient.

Study Setting

The trial is being conducted within the primary care practice of an integrated health system. The practice's 33 primary care clinics are located throughout the city of Detroit and the surrounding suburban tri-county area. Clinics are staffed by approximately 150 salaried, adult primary care (i.e., general internal medicine and family medicine) physicians. The health system uses a commercial EHR that includes an embedded patient portal.[52]

Patient and Public Involvement

The design of the program and its integration with clinic workflow and practice were achieved via continual partnerships with care delivery and support teams. The user-centered design was used to ensure program acceptability, scalability and sustainability. Patient input via focus groups, in-depth interviews and beta testing was used to develop the content of the e-assist: Colon Health program.[53]

Study Design

We are evaluating the e-assist: Colon Health program using a three-arm, randomized practice-embedded trial. To be consistent with the health system's preventive health practices, the inclusion and exclusion criteria for the trial was guided by the U.S. Preventive Services Task Force guidelines for CRC screening.[54] As such, average-risk patients, aged 50-75 years, due for CRC screening were randomized to receive (1) an online patient portal message with links to the interactive e-assist: Colon Health program (experimental treatment); (2) an online patient portal message with links to Healthwise CRC and CRC screening educational material (usual care plus);[55] or (3) usual care. For the effectiveness evaluation, we will use an intent-to-treat analysis among those consenting to study participation in the experimental treatment and usual care plus arms. Because an outreach communication specific to CRC screening following a physician recommendation may itself serve as a reminder and cue to action, we will use the

third arm, for which there is no outreach communication or consent, to describe screening use in a population without any post-visit communication about CRC screening (usual care). The latter will be used to estimate program impact at the population level. The evaluation framework is depicted in Figure 1.

Eligible Patient Identification and Randomization

Because of the desire to automate the workflow to recruit and intervene with patients and the inability to conduct randomization within the EHR environment, we randomized all ***potentially*** trial-eligible patients before opening the trial to enrollment. This was done by using the EHR data repository to identify patients who would become study eligible if they were to receive a physician recommendation for CRC screening during the trial enrollment period. This list of ***potentially*** trial-eligible participants was generated by identifying average-risk men and women aged 50-75 years who were due for CRC screening as recommended by the US Preventive Services Task Force Guidelines,[54] had an activated online patient portal account, and per administrative records were assigned to a primary care physician practicing in one of the health system's 33 primary care clinics. Patients with EHR-documented colonoscopy in the past 10 years, sigmoidoscopy in the past 5 years, or fecal occult blood test (FOBT) or fecal immunochemical test (FIT) in the past 12 months were excluded as were patients known to be above average risk for CRC (i.e., those with a personal or family history of CRC, those with prior polyps, or a history of inflammatory bowel disease, familial adenomatous polyposis, or hereditary nonpolyposis). Patients without an activated portal account and who were not aligned to a primary care physician were also excluded.

SAS® software Version 9.4 was used to randomly allocate potentially trial-eligible patients to the experimental treatment, usual care plus, or usual care study arms. To ensure adequate sample size for the primary effectiveness analyses that will compare CRC screening use between the

experimental treatment and the usual care plus groups (both of which require patient consent), we used a 2:2:1 ratio for randomization.

Study Enrollment and Baseline Assessment

Figure 2 outlines the study processes from the identification of potentially trial-eligible patients through outcome measurement. As indicated in Figure 2, while the trial is open for enrollment, the list of potentially trial-eligible participants (as identified above) is monitored electronically and continuously to identify those with an ambulatory care visit to a primary care physician that includes a referral for a colonoscopy, an order for stool testing (i.e., FOBT or FIT), or both. Once a potentially eligible patient receives such an order they become trial eligible. When the physician closes the encounter (i.e., visit note within the EHR), if the patient has a pre-assigned randomization code reflective of either the experimental treatment or usual care plus group, a secure message is sent automatically to the patient's online portal account inviting them to access an attached link that contains the decision support intervention appropriate to their study arm. Once an eligible patient opens the attached link, they are invited to participate in the study. Those continuing past an online consent page are considered enrolled in the trial. Trial enrollment is continuing until 900 patients are enrolled in each of the two study arms requiring consent (i.e., the experimental treatment and usual care plus). At that time, any individual who was randomized to usual care and received a primary care physician order for CRC screening will be included in the usual care arm.

Figure 3 provides an overview of the study contact procedures by study arm as well as a brief synopsis of the intervention content (the latter of which is described in more detail below). For those in the experimental treatment and usual care plus groups, the online programs contain a brief baseline questionnaire consisting of six measures that are being collected to assess balance between the experimental treatment and active comparison study arms, and to enable

the testing of patient-level factors that may moderate the effectiveness of e-assist: Colon Health. As indicated in Table 1, these include previously validated measures of health literacy,[56 57] and measures adapted for CRC screening such as perceived worry,[58] decision-making preference,[59-62] perceived susceptibility,[63 64] screening history,[65] and CRC screening decision-making stage.[66] No similar assessment is given to the usual care group.

Table 1. Measures and Schedule of Measurement for Trial Participants Receiving e-assist: Colon Health or the Usual care plus

	Measure	Baseline Questionnaire	Follow- up Survey[2]	Medical Record Documented[1]
Primary Outcome	CRC Screening			X
Secondary Outcomes	CRC Screening Intent[66]		X	
	Barriers to CRC Screening[67 68]		X	
	CRC Screening Benefits[69 70]		X	
	Patient-Provider Supportive Communication[71]		X	
Moderating Factors	Health Literacy[56 57]	X	X	
	CRC Decision Stage[66]		X	
	Decision-Making Preference[59-62]	X	X	
	Perceived Worry[58]	X	X	
	CRC Screening History[65]	X		
	Perceived CRC Susceptibility[63,64]	X	X	

1. CRC screening as indicated by receipt of colonoscopy, flexible sigmoidoscopy, fecal occult blood testing, fecal immunochemical testing or stool DNA testing within 12 months of physician recommendation for screening as documented in the electronic health record (EHR).
2. Follow-up survey administered 4-8 weeks following for trial enrollment

Outcome Measures and Follow-up Assessment

As indicated in Table 1, the primary effectiveness outcome for the trial is a binary variable reflecting CRC screening use in the 12-month period following the date of physician recommendation. Screening use is being determined by an EHR-documented occurrence of any of the following: colonoscopy, flexible sigmoidoscopy, fecal occult blood testing, fecal immunochemical testing or stool DNA testing. Patients for whom no indication of testing is identified in the EHR will be assumed not to have received screening.

Secondary outcomes include patient-perceived benefits of,[69 70] barriers to and support for CRC screening, and patient-reported CRC screening intent (Table 1).[67 68 71] The latter of which is obtained using a measure of behavioral intent adapted for CRC screening.[66] These secondary outcomes are being assessed via a telephone survey administered to participants enrolled in the experimental treatment and usual care plus arms only. The telephone survey is being administered 4 to 8 weeks following trial enrollment.

Experimental Treatment: e-assist: Colon Health

The e-assist: Colon Health program is designed to serve as an online visit extender, filling known voids in typical office-based CRC screening decision-making processes and addressing key personal and structural barriers to CRC screening once a physician order has been placed. Program content includes images, newly developed text and seven videos that were developed in the context of another NCI-funded trial (NCT01885351). After consenting to study participation and answering the baseline questionnaire, patients randomized to receive e-assist: Colon Health are able to view the content of the initial module. There are five central components to the initial module: (1) messaging and a video to reiterate that CRC screening is recommended; (2) messaging to provide information on different screening modalities and associated benefits/risks; (3) a screening test option comparison to assist patients in

determining their screening test preference; (4) messaging and videos addressing ways to overcome common personal barriers to screening; and (5) messaging to assist with completing screening once a decision to screen has been made. The majority (89%) of e:assist: Colon Health text content assesses at or below a sixth grade reading level with the remainder (11%) at a seventh grade level, as evaluated by the Flesch–Kincaid Grade Level test.[72]

Although messaging regarding the benefits of CRC screening and testing guidelines are seen by everyone, much of the program's content is self-directed, enabling users to choose the material they want to view and the order in which they view it. Patients' readiness to screen along with their informational and CRC screening preferences are assessed through questions embedded throughout the program. Participant responses are used to tailor the program content seen to the participants' decision stage and preferences. The specific assistance a patient receives (e.g., instructions for how to schedule a colonoscopy; instructions for how to prepare for a colonoscopy screening; requesting mailed delivery of stool test; or instructions for how to complete stool test) is similarly tailored based on the participant's responses to embedded questions. What participants view and the order in which they view it are being tracked as part of the implementation effectiveness component of the evaluation. Although participants can return to the initial module as often as they want until they submit it as completed, we anticipate most participants completing the initial module in one session that lasts between 8 and 12 minutes, depending up information viewed.

Near the end of the initial module, a course of action is negotiated that is aligned with the patient's preferences and willingness to be screened. If a participant's responses indicate he/she is ready to be screened, the e-assist: Colon Health program facilitates receipt of screening by assisting with the removal of structural barriers that may arise (e.g., how to call the endoscopy nurse schedulers with questions). For participants expressing a desire to be

screened using a test different from what their physician ordered, the program assists in obtaining their desired CRC screening test by providing contact information for the central scheduling line or messaging the patient's physician directly.

Any participant that does not indicate they have completed CRC screening when they submit their initial module receives a follow-up module. Much of the content in this follow up is similar to that available in the initial module albeit targeted based upon the information and preferences shared via question responses within the initial module. For example, if during the first module a participant elected to send a secure message to their primary care physician requesting a stool test, the content in the follow-up module would confirm that the participant received the stool test and offer tips for completion. For patients that do not express a desire to be screened, the follow-up module presents information using a motivational counseling approach.[73 74] This approach is aimed at moving patients who are undecided or not considering screening towards a concrete decision. It does so by highlighting the personal relevance of screening, the risks of CRC, and the benefits of screening, while identifying personally relevant barriers. There are a total of 11 different follow-up modules. As with the initial module, program navigation within each of these modules is self-directed with participants' responses to embedded questions used to tailor the program content seen. All follow-up modules are delivered two weeks after the initial module was submitted as completed, with the exception of those targeting participants who indicated they were not ready to be screened or those who abandoned the program without submitting it. For the former, the follow-up module is sent 28 days later; for the latter, 7 days later.

Usual Care Plus

Patients randomized to usual care plus receive the identical recruitment message as those in the experimental arm (Figure 3). The consent form page and introductory screens reiterating

that CRC screening has been recommended for them and outlining the benefits of screening are also identical. In lieu of the interactive e-assist: Colon Health program, individuals in usual care plus receive links to four webpages, one of which contains a video, that are stored within the patient portal's health information library. The educational material is currently distributed by Healthwise and includes information on the etiology, symptoms, and treatment of CRC as well as screening modalities and the interpretation of screening results.[55] With the exception of the one video, all material is static, and none is individually tailored.

Similar to participants in the experimental treatment group, participants enrolled in usual care plus are sent a follow-up module. The reminder module, which is also not tailored, is sent two weeks after the initial module. It includes a welcome screen and a link to the National Cancer Institute's CRC screening website.[75] This webpage provides patients with information on CRC screening and serves as a comparable alternative to the Healthwise information initially provided to the usual care plus. This allows the usual care plus group to run parallel to the experimental treatment in both timing as well as breadth of content provided (Figure 3).

Usual Care

Patients randomized to usual care receive CRC screening information and instructions as routinely provided by the health system. While the same Healthwise material that is being pushed to patients enrolled in usual care plus is available to these participants via the health library accessible within the EHR, unlike in usual care plus, participants are not being systematically directed to this material. Thus, while patients in this arm, by virtue of their portal account, have access to the same Healthwise material on CRC and CRC screening, access to the library containing these documents is not readily identifiable within the portal. Similarly, those materials could be printed for patients at the time of an office visit, but to our knowledge this rarely, if ever, happens.

Analysis Plan

Each outcome Y will be conditional on treatment assignment T and consent C, (the interaction terms of) which will identify four groups: consenters (C=1) and nonconsenters (C=0) assigned to treatment (T=1) and usual care plus or control (T=0). The primary outcome for the evaluation is a binary variable (EHR-documented CRC screening use within 12 months as defined above) which will be available regardless of treatment assignment or consent status. Secondary outcomes, all measured at the time of the follow-up survey, are ordinal categorical (e.g., screening intent and benefits) or continuous (e.g., barriers and screening support), and available among consenters only, regardless of treatment assignment.

For the effectiveness evaluation (H1), differences in CRC screening between experimental treatment and usual care plus will be estimated by a hierarchical logit model where patients who consented are nested within physicians. We anticipate no missing data in the primary outcome, as CRC screening use will be obtained from the EHR, and the absence of screening test data will be coded as no screening. For secondary outcomes (H2 and H3), we will use hierarchical generalized linear models and hierarchical linear models to analyze categorical and continuous outcomes, respectively, where patients who consented are nested within physicians.[76] We will compare the treatment effects for consenters, moderated by patient characteristics, to test H4 for aim 2. For H2-H4, we will handle missing data from survey item- and unit-nonresponses efficiently by analyzing all observed data.[77-79]

For the impact evaluation, we will compare screening rates across the three trial arms for consenters and nonconsenters by a hierarchical logit model, analyzing the entire sample. The effects of consenters will be compared to each other and those of nonconsenters to describe the population represented by the experiment. We will also analyze a hierarchical model for the

consent outcome C, which will describe who the beneficiaries of the treatment and usual care plus are in terms of their characteristics. One difficulty is that each patient in the usual care arm is missing the consent status. That is, if the patient was assigned to the other arms, he/she would have or would not have consented to study participation. We will view missing consent as missing data, and estimate the hierarchical models by efficient handling of missing data, i.e., by all observed data.[77-81]

Power and Sample Size Calculations

To account for the clustering of patients nested within physicians, statistical power for the primary effectiveness evaluation (i.e., the comparison of outcomes between the experimental treatment and usual care plus) was estimated using an R program written by Dr. Jessaca Spybrook implementing the method in Spybrook and Hedberg, and Moerbeek et al.[82 83]. With randomization at the patient level, we consider a 95% plausible interval for CRC screening use in the experimental treatment (66%±5%) at alpha=0.05 in the usual care plus arm. With 1800 patients seen by 150 primary care physicians, or 12 patients per physician (6 in the experimental treatment and 6 in the usual care plus), we have 0.86 power to detect a 7% change in CRC screening rates between the experimental treatment and the usual care plus (i.e., 66% vs. 59%, respectively).

Trial Status

As indicated in Figure 2, prior to opening trial enrollment, 19,085 patients were identified as potentially eligible and randomized (7,752 to the experimental treatment, 7,626 to usual care plus, and 3,707 to usual care). The trial opened for enrollment at 1:00 pm eastern standard time on June 14, 2017 with recruitment planned to end in early 2019. Seven months into trial recruitment (1/14/18), 2,175 of the potentially eligible patients have received a primary care physician order for CRC screening (1,110 in the experimental group and 1,065 in the usual care

plus group) This has resulted in n=328 patients being enrolled in the experimental group and n=376 in the usual care plus group. We have identified two barriers to trial enrollment among those receiving a physician order for CRC screening, and thus an invitation for trial participation. First, approximately 30% of patients who are sent an email notification that they have a new portal message never log into their portal account to read the message. In addition, among patients who log into their portal account and read the message, about 50% elect not to open the attachment which includes information on the trial (e.g. consent information) and the decision support programs. We are currently using in-depth interviews with patients who elected not to log into their portal account or not to open the attachment to gain insights into other means by which to engage such patients with decision support following physician recommendations for care.

ETHICS AND DISSEMINATION PLAN

All aspects of the trial protocol have been approved by the Institutional Review Board of the health system in which the trial is being conducted. The IRB approved the trial under an expedited review and, given the benefit/risk ratio, waived the need for written patient consent. A HIPAA waiver of authorization was received to enable the inclusion of the usual care group. The trial is funded by the National Cancer Institute (7R01CA197205) and registered with Clinical Trials.gov (NCT02798224).

Findings, whether positive or negative, will enable clinicians and other health care stakeholders to make informed decisions about how to integrate new portal technology to support primary care patients in their decision making and service receipt. We will disseminate emerging stories, lessons learned, and findings on an ongoing basis. To do so requires attention to packaging and context as well as diversity in dissemination strategies. Manuscripts and presentations will be prepared for publication in diverse scientific venues, and we will target brief reports and

presentations for the clinical, quality improvement, and EHR communities as well as make use of emerging repositories like Cancer Control Planet.

Data requests can be submitted to the corresponding author at the UNC Eshelman School of Pharmacy, University of North Carolina at Chapel Hill, Chapel Hill, North Carolina, after conclusion of the trial and publication of the primary manuscript.

DISCUSSION

To our knowledge, this is the first trial to test an online practice-integrated, post-visit CRC screening decision support program that does not rely on direct human resources to help patients address lingering questions about CRC screening, and overcome personal and structural barriers to screening use once a physician recommendation is in hand. As such, we are testing an intervention that fills an important gap in clinical care that has yet to be addressed. Our trial and program are unique in their use of clinical workflow-integrated automation. By automating patient identification and program delivery we are facilitating program sustainability should e-assist: Colon Health succeed. By intervening with patients following a regularly scheduled office visit in which they received a physician recommendation for CRC screening, we are able to use a naturally occurring clinical event as the cue for patient action, thereby capitalizing on the known powerful relationships between patients and their physicians. By using the patient portal to do so, we are ensuring that e-assist: Colon Health is fully integrated within existing clinic processes. The e-assist: Colon Health program will extend, in a personalized and autonomy-supporting manner, the patient-physician CRC screening decision-making process beyond the confines of office visits. Thus, unlike traditional decision aids administered prior to a visit, we do not anticipate that e-assist: Colon Health will alter the patient-physician office visit interaction per se; instead we expect e-assist: Colon Health to extend the patient's ability to consider CRC screening in a supportive setting post-receipt of

physician recommendation and to improve the patient's perception of the autonomy support they receive from their doctor's office. The fact that the program is accessed via an existing patient portal furthers its integration with increasingly common clinic processes, streamlines patient accessibility, and begins to address prior challenges of implementation faced by previous decision aid studies.[84-87]

Recent reviews indicate that, compared to usual care, people who use decision aids benefit from improved knowledge, a better understanding of their values, and enhanced participation in the decision-making process.[43 88 89] Despite the known benefits of decision aid use, physicians voice concerns regarding their practicality and,[42 90] to date, their integration within practice is limited.[41 42] Our trial, via our ongoing engagement with clinician and other health care stakeholders, is illustrating how these barriers can be overcome. The challenge is that while communication outreach strategies embedded within a patient portal may be sustainable and acceptable to health care stakeholders, they engage only a small subset of the patient population.[91] Further, there is increasing evidence that use of a portal among those with an account varies, with patients from traditionally disadvantaged publications being relatively less engaged even once they have a portal account, and our trial and its decision support intervention appears to be no exception.[92 93] Thus, an overarching limitation of the trial is that its reach is limited to those already engaged with the portal. Prior studies have repeatedly shown this to be a relatively small segment of the population, and one in which minorities and other traditionally disadvantaged populations are under-represented.[94-111] In addition, our trial is limited by its implementation and recruitment within one health system which may further limit the ability to generalize results.

Facilitating the timely use of CRC screening among primary care patients requires that scalable programs be designed to address not only barriers to obtaining a physician recommendation for

care, but also the quality of that recommendation and the personal and system barriers faced once patients have a physician recommendation for care. Identifying sustainable strategies to support patient adherence to evidence-based care is critical for patient-centered medical homes and other delivery settings if we are to effectively and efficiently deliver preventive health services. Supporting patient adherence to known effective preventive health services is also critical to the ability to reduce the morbidity and mortality associated with preventable diseases such as CRC.

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References

1. Siegel R, Desantis C, Jemal A. Colorectal cancer statistics, 2014. *CA Cancer J Clin* 2014;64(2):104-17. doi: 10.3322/caac.21220 [published Online First: 2014/03/19]

2. Lafata JE, Cooper G, Divine G, et al. Patient-physician colorectal cancer screening discussion content and patients' use of colorectal cancer screening. *Patient Educ Couns* 2014;94(1):76-82. doi: S0738-3991(13)00361-3 [pii]10.1016/j.pec.2013.09.008 [published Online First: 2013/10/08]

3. Peterson EB, Ostroff JS, DuHamel KN, et al. Impact of provider-patient communication on cancer screening adherence: A systematic review. *Preventive Medicine* 2016;93:96-105. doi: https://doi.org/10.1016/j.ypmed.2016.09.034

4. Vernon SW. Participation in Colorectal Cancer Screening: A Review. *JNCI: Journal of the National Cancer Institute* 1997;89(19):1406-22. doi: 10.1093/jnci/89.19.1406

5. Lafata JE, Divine G, Moon C, et al. Patient-physician colorectal cancer screening discussions and screening use. *Am J Prev Med* 2006;31(3):202-9. doi: S0749-3797(06)00202-9 [pii]10.1016/j.amepre.2006.04.010 [published Online First: 2006/08/15]

6. Hoffman RM, Lewis CL, Pignone MP, et al. Decision-making processes for breast, colorectal, and prostate cancer screening: The DECISIONS survey. *Med Decis Making* 2010;30(5 Suppl):53S-64S. doi: 0272989X10378701 [pii]10.1177/0272989X10378701 [published Online First: 2010/10/15]

7. Cairns CP, Viswanath K. Communication and colorectal cancer screening among the uninsured: Data from the Health Information National Trends Survey (United States). *Cancer Causes & Control* 2006;17(9):1115-25. [published Online First: 2006/09/29]

8. Carcaise-Edinboro P, Bradley CJ. Influence of patient-provider communication on colorectal cancer screening. *Med Care* 2008;46(7):738-45. doi: 10.1097/MLR.0b013e318178935a00005650-200807000-00014 [pii] [published Online First: 2008/06/27]

9. Feeley TH, Cooper J, Foels T, et al. Efficacy expectations for colorectal cancer screening in primary care: Identifying barriers and facilitators for patients and clinicians. *Health Communication* 2009;24(4):304-15. doi: 10.1080/10410230902889241 [published Online First: 2009/06/06]

10. Fenton JJ, Jerant AF, von Friederichs-Fitzwater MM, et al. Physician counseling for colorectal cancer screening: Impact on patient attitudes, beliefs, and behavior. *Journal of the American Board of Family Medicine : JABFM* 2011;24(6):673-81. doi: 10.3122/jabfm.2011.06.110001 [published Online First: 2011/11/17]

11. Flocke SA, Stange KC, Cooper GS, et al. Patient-rated importance and receipt of information for colorectal cancer screening. *Cancer Epidemiol Biomarkers Prev* 2011;20(10):2168-73. doi: 1055-9965.EPI-11-0281 [pii]10.1158/1055-9965.EPI-11-0281 [published Online First: 2011/08/05]

12. Fox SA, Heritage J, Stockdale SE, et al. Cancer screening adherence: Does physician-patient communication matter? *Patient Educ Couns* 2009;75(2):178-84. doi: S0738-3991(08)00535-1 [pii]10.1016/j.pec.2008.09.010 [published Online First: 2009/03/03]

13. Guerra CE, Schwartz JS, Armstrong K, et al. Barriers of and facilitators to physician recommendation of colorectal cancer screening. *Journal of general internal medicine* 2007;22(12):1681-8. doi: 10.1007/s11606-007-0396-9 [published Online First: 2007/10/17]

14. Katz ML, James AS, Pignone MP, et al. Colorectal cancer screening among African American church members: A qualitative and quantitative study of patient-provider communication. *BMC Public Health* 2004;4:62. doi: 1471-2458-4-62 [pii]10.1186/1471-2458-4-62 [published Online First: 2004/12/17]

15. Lafata JE, Cooper GS, Divine G, et al. Patient-physician colorectal cancer screening discussions: delivery of the 5A's in practice. *Am J Prev Med* 2011;41(5):480-6. doi: 10.1016/j.amepre.2011.07.018

16. Ling BS, Klein WM, Dang Q. Relationship of communication and information measures to colorectal cancer screening utilization: Results from HINTS. *Journal of health communication* 2006;11 Suppl 1:181-90. doi: 10.1080/10810730600639190 [published Online First: 2006/04/28]

17. Ling BS, Trauth JM, Fine MJ, et al. Informed decision-making and colorectal cancer screening: Is it occurring in primary care? *Med Care* 2008;46(9 Suppl 1):S23-9. doi: 10.1097/MLR.0b013e31817dc49600005650-200809001-00005 [pii] [published Online First: 2008/09/09]

18. McQueen A, Bartholomew LK, Greisinger AJ, et al. Behind closed doors: Physician-patient discussions about colorectal cancer screening. *Journal of general internal medicine* 2009;24(11):1228-35. doi: 10.1007/s11606-009-1108-4 [published Online First: 2009/09/19]

19. Wackerbarth SB, Tarasenko YN, Joyce JM, et al. Physician colorectal cancer screening recommendations: An examination based on informed decision making. *Patient Educ Couns* 2007;66(1):43-50. doi: 10.1016/j.pec.2006.10.003 [published Online First: 2006/11/14]

20. Walsh JM, Karliner L, Burke N, et al. Physicians' approaches to recommending colorectal cancer screening: A qualitative study. *Journal of cancer education : the official journal of the American Association for Cancer Education* 2010;25(3):385-90. doi: 10.1007/s13187-010-0058-1 [published Online First: 2010/03/06]

21. Wunderlich T, Cooper G, Divine G, et al. Inconsistencies in patient perceptions and observer ratings of shared decision making: The case of colorectal cancer screening. *Patient Educ Couns* 2010;80(3):358-63. doi: S0738-3991(10)00396-4 [pii]10.1016/j.pec.2010.06.034 [published Online First: 2010/07/30]

22. Jones RM, Vernon SW, Woolf SH. Is discussion of colorectal cancer screening options associated with heightened patient confusion? *Cancer Epidemiol Biomarkers Prev* 2010;19(11):2821-25. doi: 10.1158/1055-9965.EPI-10-0695

23. O'Farrell CM, Green BB, Reid RJ, et al. Physician-patient colorectal cancer screening discussions by physicians' screening rates. *Journal of the American Board of Family Medicine* 2012;25(6):771-81.

24. Holden DJ, Jonas DE, Porterfield DS, et al. Systematic review: enhancing the use and quality of colorectal cancer screening. *Ann Intern Med* 2010;152(10):668-76. doi: 0003-4819-152-10-201005180-00239 [pii]10.7326/0003-4819-152-10-201005180-00239 [published Online First: 2010/04/15]

25. Lairson DR, Dicarlo M, Deshmuk AA, et al. Cost-effectiveness of a standard intervention versus a navigated intervention on colorectal cancer screening use in primary care. *Cancer* 2014;120(7):1042-9. doi: 10.1002/cncr.28535 [published Online First: 2014/01/18]

26. Sabatino SA, Lawrence B, Elder R, et al. Effectiveness of Interventions to Increase Screening for Breast, Cervical, and Colorectal Cancers Nine Updated Systematic Reviews for the Guide to Community Preventive Services. *American Journal of Preventive Medicine* 2012;43(1):97-118. doi: DOI 10.1016/j.amepre.2012.04.009

27. Myers RE, Ross E, Jepson C, et al. Modeling adherence to colorectal cancer screening. *Prev Med* 1994;23(2):142-51. doi: S0091-7435(84)71020-6 [pii]10.1006/pmed.1994.1020 [published Online First: 1994/03/01]

28. Dietrich AJ, Tobin JN, Cassells A, et al. Telephone care management to improve cancer screening among low-income women: a randomized, controlled trial. *Ann Intern Med* 2006;144(8):563-71. doi: 144/8/563 [pii] [published Online First: 2006/04/19]

29. Basch CE, Wolf RL, Brouse CH, et al. Telephone outreach to increase colorectal cancer screening in an urban minority population. *Am J Public Health* 2006;96(12):2246-53. doi: AJPH.2005.067223 [pii]10.2105/AJPH.2005.067223 [published Online First: 2006/11/02]

30. Myers RE, Ross EA, Wolf TA, et al. Behavioral interventions to increase adherence in colorectal cancer screening. *Med Care* 1991;29(10):1039-50. [published Online First: 1991/10/01]

31. Goldberg D, Schiff GD, McNutt R, et al. Mailings timed to patients' appointments: a controlled trial of fecal occult blood test cards. *Am J Prev Med* 2004;26(5):431-5. doi: 10.1016/j.amepre.2004.02.009S0749379704000364 [pii] [published Online First: 2004/05/29]

32. Mosen DM, Feldstein AC, Perrin N, et al. Automated telephone calls improved completion of fecal occult blood testing. *Med Care* 2010;48(7):604-10. doi: 10.1097/MLR.0b013e3181dbdce7

33. Hardcastle JD, Chamberlain JO, Robinson MH, et al. Randomised controlled trial of faecal-occult-blood screening for colorectal cancer. *Lancet* 1996;348(9040):1472-7. doi: S0140-6736(96)03386-7 [pii]10.1016/S0140-6736(96)03386-7 [published Online First: 1996/11/30]

34. Hardcastle JD, Armitage NC, Chamberlain J, et al. Fecal occult blood screening for colorectal cancer in the general population. Results of a controlled trial. *Cancer* 1986;58(2):397-403. [published Online First: 1986/07/15]

35. Church TR, Yeazel MW, Jones RM, et al. A randomized trial of direct mailing of fecal occult blood tests to increase colorectal cancer screening. *J Natl Cancer Inst* 2004;96(10):770-80. [published Online First: 2004/05/20]

36. Baron RC, Rimer BK, Breslow RA, et al. Client-directed interventions to increase community demand for breast, cervical, and colorectal cancer screening. *American Journal of Preventive Medicine* 2008;35(1):S34-S55. doi: DOI 10.1016/j.amepre.2008.04.002

37. Baron RC, Mercer SL, Se TFCP. Recommendations for client- and provider-directed interventions to increase breast, cervical, and colorectal cancer screening. *American Journal of Preventive Medicine* 2008;35(1):S21-S25. doi: DOI 10.1016/j.amepre.2008.04.004

38. Stacey D, Légaré F, Col NF, et al. Decision Aids for People Facing Health Treatment or Screening Decisions. *Cochrane Database Syst Rev* 2014;1

39. Stacey D, Bennett CL, Barry MJ, et al. Decision Aids for People Facing Health Treatment or Screening Decisions. *Cochrane Database Syst Rev* 2011;10(10)

40. O'Connor AM, Bennett CL, Stacey D, et al. Decision Aids for People Facing Health Treatment or Screening Decisions. *Cochrane Database Syst Rev* 2009;3(3)

41. Jimbo M, Rana GK, Hawley S, et al. What is Lacking in Current Decision Aids on Cancer Screening? *CA: A Cancer Journal for Clinicians* 2013;63(3):193-214.

42. Brace C, Schmocker S, Huang H, et al. Physicians' awareness and attitudes toward decision aids for patients with cancer. *J Clin Oncol* 2010;28(13):2286-92. doi: 10.1200/JCO.2009.25.2874

43. Volk RJ, Linder SK, Lopez-Olivo MA, et al. Patient Decision Aids for Colorectal Cancer Screening: A Systematic Review and Meta-analysis. *Am J Prev Med* 2016;51(5):779-91. doi: 10.1016/j.amepre.2016.06.022

44. Janz NK, Becker MH. The Health Belief Model: a decade later. *Health Educ Q* 1984;11(1):1-47. [published Online First: 1984/01/01]

45. Weinstein ND, Lyon J, Sandman P, et al. Experimental evidence for stages of health behavior change: the precaution adoption process model applied to home radon testing. *Health Psychol* 1998;17(5):445-53. [published Online First: 1998/10/17]

46. Weinstein N, Sandman P. The Precaution Adoption Process Model and its application. San Francisco, CA: Jossey-Bass 2002:16-39.

47. Ryan RM, Deci EL. Intrinsic and Extrinsic Motivations: Classic Definitions and New Directions. *Contemp Educ Psychol* 2000;25(1):54-67. doi: 10.1006/ceps.1999.1020S0361476X99910202 [pii] [published Online First: 2000/01/06]

48. Deci EL, Koestner R, Ryan RM. A meta-analytic review of experiments examining the effects of extrinsic rewards on intrinsic motivation. *Psychol Bull* 1999;125(6):627-68. doi: Doi 10.1037/0033-2909.125.6.627

49. Weinstein ND, Rothman AJ, Sutton SR. Stage theories of health behavior: conceptual and methodological issues. *Health Psychol* 1998;17(3):290-9. [published Online First: 1998/06/10]

50. Sutton S. Stage models of health behaviour change stage theories of health.behaviour: Introduction, overview and current status. *Psychol Health* 2005;20:261-61.

51. EW Maibach DC. Moving people to behavior change: A staged social cognitive approach to message design. Newbury Park, CA: Sage 1995:41-64.

52. *Epic - with the patient at the heart*. Available from: https://www.epic.com/ Accessed February 2018

53. Dyer KE, Shires DA, Flocke SA, et al. Patient-reported needs after receiving a physician recommendation for colorectal cancer screening. Manuscript submitted for publication

54. United States Preventive Services Task Force. *Screening for Colorectal Cancer: U.S. Preventive Services Task Force Recommendation Statement*. 2008; Available from: http://www.uspreventiveservicestaskforce.org/uspstf08/colocancer/colors.htm Accessed February 2018

55. *Healthwise – for every health decision.* (n.d.). Colorectal Cancer. Retrieved from https://www.healthwise.net Accessed February 2018

56. Chew LD, Griffin JM, Partin MR, et al. Validation of screening questions for limited health literacy in a large VA outpatient population. *Journal of general internal medicine* 2008;23(5):561-6. doi: 10.1007/s11606-008-0520-5 [published Online First: 2008/03/13]

57. Chew LD, Bradley KA, Boyko EJ. Brief questions to identify patients with inadequate health literacy. *Fam Med* 2004;36(8):588-94. [published Online First: 2004/09/03]

58. National Cancer Institute. *Health Information National Trends Survey 4 Cycle 4*. 2014; https://hints.cancer.gov/docs/Instruments/HINTS_4_Cycle_4_English_Annotated_Form.pdf Accessed February 2018

59. Degner LF, Sloan JA, Venkatesh P. The Control Preferences Scale. *Can J Nurs Res* 1997;29(3):21-43.

60. Degner LF. Preferences to participate in treatment decision making: the adult model. *J Pediatr Oncol Nurs* 1998;15(3 Suppl 1):3-9.

61. Williams GC, Rodin GC, Ryan RM, et al. Autonomous regulation and long-term medication adherence in adult outpatients. *Health Psychol* 1998;17(3):269-76. [published Online First: 1998/06/10]

62. Williams GC, Grow VM, Freedman ZR, et al. Motivational predictors of weight loss and weight-loss maintenance. *J Pers Soc Psychol* 1996;70(1):115-26. [published Online First: 1996/01/01]

63. National Cancer Institute. *Health Information National Trends Survey 2*. 2005; https://hints.cancer.gov/docs/Instruments/HINTS_2005_Final_Report.pdf Accessed February 2018

64. McQueen A, Tiro JA, Vernon SW. Construct validity and invariance of four factors associated with colorectal cancer screening across gender, race, and prior screening. *Cancer Epidemiol Biomarkers Prev* 2008;17(9):2231-7. doi: 17/9/2231 [pii]10.1158/1055-9965.EPI-08-0176 [published Online First: 2008/09/05]

65. National Cancer Institute. *Health Information National Trends Survey 3.* 2008; https://hints.cancer.gov/docs/Instruments/HINTS2007FinalReport.pdf Accessed February 2018

66. Sifri R, Rosenthal M, Hyslop T, et al. Factors associated with colorectal cancer screening decision stage. *Preventive Medicine* 2010;51(3):329-31. doi: https://doi.org/10.1016/j.ypmed.2010.06.015

67. Jones RM, Magnusson BM, Dumenci L, et al. Psychometric Properties of a Fecal Occult Blood Test Barrier Scale. *Am J Epidemiol* 2011;173:S170-S70.

68. Jones RM, Magnusson BM, Dumenci L, et al. Measuring Barriers to Flexible Sigmoidoscopy and Colonoscopy: A Validation Study. *Am J Epidemiol* 2011;173:S169-S69.

69. Vernon SW, Myers RE, Tilley BC. Development and validation of an instrument to measure factors related to colorectal cancer screening adherence. *Cancer Epidemiology Biomarkers & Prevention* 1997;6(10):825-32.

70. Hibbard JH, Mahoney ER, Stockard J, et al. Development and testing of a short form of the patient activation measure. *Health Serv Res* 2004;40(6 Pt 1):1918-30. doi: HESR438 [pii]10.1111/j.1475-6773.2005.00438.x [published Online First: 2005/12/13]

71. AHRQ. *Patient Experience Measures from the CAHPS® Clinician & Group Surveys* 2011 [Available from: https://cahps.ahrq.gov/surveys-guidance/cg/cgkit/1309_CG_Measures.pdf Accessed September 26 2014.

72. Flesch R. A new readability yardstick. *J Appl Psychol* 1948;32(3):221-33.

73. Fiore M. Treating Tobacco Use and Dependence: 2008 Update: Clinical Practice Guideline: DIANE Publishing 2008.

74. Fiore D, Bailey M, Cohen W, et al. Smoking Cessation Clinical Guideline Number 18: AHCPR, 1996.

75. PDQ® Screening and Prevention Editorial Board. PDQ Colorectal Cancer Screening. Bethesda, MD: National Cancer Institute. Updated 02/23/2018 Available at: https://www.cancer.gov/types/colorectal/patient/colorectal-screening-pdq. Accessed 04/06/2018. [PMID: 26389230]

76. Raudenbush SW, & Bryk, A. S. Hierarchical linear models: Applications and data analysis methods. 2 ed. Thousand Oaks: Sage Publications 2002.

77. Rubin D. Inference and missing data. *Biometrika* 1976;63:581-92.

78. Shin YR, SW Joint Distribution of Site-Specific causal effects, Complier Means and Noncomplier Means Given Data MAR from a Multisite Trial. Manuscript in preparation

79. Shin Y, Raudenbush SW. Just-Identified Versus Overidentified Two-Level Hierarchical Linear Models with Missing Data. *Biometrics* 2007;63(4):1262-68. doi: 10.1111/j.1541-0420.2007.00818.x

80. Rubin DB. Bayesian Inference for Causal Effects: The Role of Randomization. *Ann Statist* 1978;6(1):34-58. doi: 10.1214/aos/1176344064

81. Angrist JD, Imbens GW, Rubin DB. Identification of Causal Effects Using Instrumental Variables. *Journal of the American Statistical Association* 1996;91(434):444-55. doi: 10.2307/2291629

82. Spybrook J, Hedberg E. A Framework for Designing Cluster Randomized Trials with Binary Outcomes. *Evaluation Review*, 23(4):445-469, 20x1

83. Moerbeek M, Van Breukelen G, MPF B. Optimal experimental designs for multilevel logistic models. *Journal of the Royal Statistical Society: Series D (The Statistician),* 2001;50(1):17-30.

84. Miller WL, McDaniel RR, Jr., Crabtree BF, et al. Practice jazz: understanding variation in family practices using complexity science. *J Fam Pract* 2001;50(10):872-8. doi: jfp_1001_08720 [pii] [published Online First: 2001/10/25]

85. Miller WL, Crabtree BF, McDaniel R, et al. Understanding change in primary care practice using complexity theory. *J Fam Pract* 1998;46(5):369-76. [published Online First: 1998/05/23]

86. Carpiano RM, Flocke SA, Frank SH, et al. Tools, teamwork, and tenacity: an examination of family practice office system influences on preventive service delivery. *Prev Med* 2003;36(2):131-40. doi: S0091743502000245 [pii] [published Online First: 2003/02/20]

87. Carney PA, Dietrich AJ, Keller A, et al. Tools, teamwork, and tenacity: an office system for cancer prevention. *J Fam Pract* 1992;35(4):388-94. [published Online First: 1992/10/01]

88. Trikalinos TA, Wieland LS, Adam GP, et al. Decision Aids for Cancer Screening and Treatment. Rockville (MD)2014.

89. Stacey D, Legare F, Lewis K, et al. Decision aids for people facing health treatment or screening decisions. *Cochrane Database Syst Rev* 2017;4:CD001431. doi: 10.1002/14651858.CD001431.pub5

90. Graham ID, Logan J, O'Connor A, et al. A qualitative study of physicians' perceptions of three decision aids. *Patient Educ Couns* 2003;50(3):279-83.

91. Krist AH, Woolf SH, Hochheimer C, et al. Harnessing Information Technology to Inform Patients Facing Routine Decisions: Cancer Screening as a Test Case. *Ann Fam Med* 2017;15(3):217-24. doi: 10.1370/afm.2063

92. Tieu L, Schillinger D, Sarkar U, et al. Online patient websites for electronic health record access among vulnerable populations: portals to nowhere? *J Am Med Inform Assoc* 2017;24(e1):e47-e54. doi: 10.1093/jamia/ocw098

93. Lafata JE MC, Shires DA, Dyer K, Raliff S, Schreiber M. Patients' Use of Electronic Patient Portals and Their Features. *Am J Managed Care* In press

94. Price-Haywood EG, Luo Q, Monlezun D. Dose effect of patient-care team communication via secure portal messaging on glucose and blood pressure control. *J Am Med Inform Assoc* 2018 doi: 10.1093/jamia/ocx161

95. Krist AH, Aycock RA, Etz RS, et al. MyPreventiveCare: implementation and dissemination of an interactive preventive health record in three practice-based research networks serving disadvantaged patients--a randomized cluster trial. *Implement Sci* 2014;9:181. doi: 10.1186/s13012-014-0181-1

96. Griffin A, Skinner A, Thornhill J, et al. Patient Portals: Who uses them? What features do they use? And do they reduce hospital readmissions? *Appl Clin Inform* 2016;7(2):489-501. doi: 10.4338/ACI-2016-01-RA-0003

97. Gerber DE, Laccetti AL, Chen B, et al. Predictors and intensity of online access to electronic medical records among patients with cancer. *J Oncol Pract* 2014;10(5):e307-12. doi: 10.1200/JOP.2013.001347

98. Yamin CK, Emani S, Williams DH, et al. The digital divide in adoption and use of a personal health record. *Arch Intern Med* 2011;171(6):568-74. doi: 10.1001/archinternmed.2011.34

99. Tenforde M, Nowacki A, Jain A, et al. The association between personal health record use and diabetes quality measures. *Journal of general internal medicine* 2012;27(4):420-4. doi: 10.1007/s11606-011-1889-0

100. Smith SG, O'Conor R, Aitken W, et al. Disparities in registration and use of an online patient portal among older adults: findings from the LitCog cohort. *J Am Med Inform Assoc* 2015;22(4):888-95. doi: 10.1093/jamia/ocv025

101. Sarkar U, Karter AJ, Liu JY, et al. Social disparities in internet patient portal use in diabetes: evidence that the digital divide extends beyond access. *J Am Med Inform Assoc* 2011;18(3):318-21. doi: 10.1136/jamia.2010.006015

102. Roblin DW, Houston TK, 2nd, Allison JJ, et al. Disparities in use of a personal health record in a managed care organization. *J Am Med Inform Assoc* 2009;16(5):683-9. doi: 10.1197/jamia.M3169

103. Peacock S, Reddy A, Leveille SG, et al. Patient portals and personal health information online: perception, access, and use by US adults. *J Am Med Inform Assoc* 2017;24(e1):e173-e77. doi: 10.1093/jamia/ocw095

104. McClellan SR, Panattoni L, Chan AS, et al. Patient-initiated Electronic Messages and Quality of Care for Patients With Diabetes and Hypertension in a Large Fee-for-Service Medical Group: Results From a Natural Experiment. *Med Care* 2016;54(3):287-95. doi: 10.1097/MLR.0000000000000483

105. Lyles CR, Harris LT, Jordan L, et al. Patient race/ethnicity and shared medical record use among diabetes patients. *Med Care* 2012;50(5):434-40. doi: 10.1097/MLR.0b013e318249d81b

106. Kruse CS, Bolton K, Freriks G. The effect of patient portals on quality outcomes and its implications to meaningful use: a systematic review. *J Med Internet Res* 2015;17(2):e44. doi: 10.2196/jmir.3171

107. Irizarry T, DeVito Dabbs A, Curran CR. Patient Portals and Patient Engagement: A State of the Science Review. *J Med Internet Res* 2015;17(6):e148. doi: 10.2196/jmir.4255

108. Goel MS, Brown TL, Williams A, et al. Disparities in enrollment and use of an electronic patient portal. *Journal of general internal medicine* 2011;26(10):1112-6. doi: 10.1007/s11606-011-1728-3

109. Crotty BH, Tamrat Y, Mostaghimi A, et al. Patient-to-physician messaging: volume nearly tripled as more patients joined system, but per capita rate plateaued. *Health Aff (Millwood)* 2014;33(10):1817-22. doi: 10.1377/hlthaff.2013.1145

110. Chen C, Garrido T, Chock D, et al. The Kaiser Permanente Electronic Health Record: transforming and streamlining modalities of care. *Health Aff (Millwood)* 2009;28(2):323-33. doi: 10.1377/hlthaff.28.2.323

111. Ancker JS, Barron Y, Rockoff ML, et al. Use of an electronic patient portal among disadvantaged populations. *Journal of General Internal Medicine* 2011;26(10):1117-23. doi: 10.1007/s11606-011-1749-y

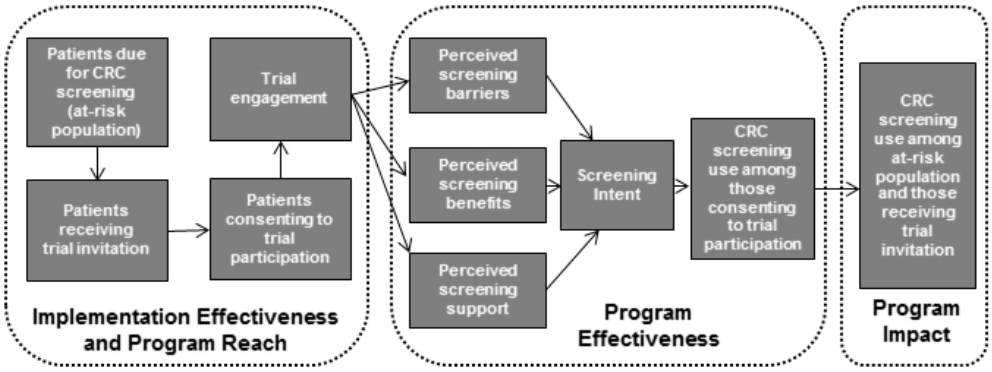

Figure 1. Evaluation Framework

180x68mm (96 x 96 DPI)

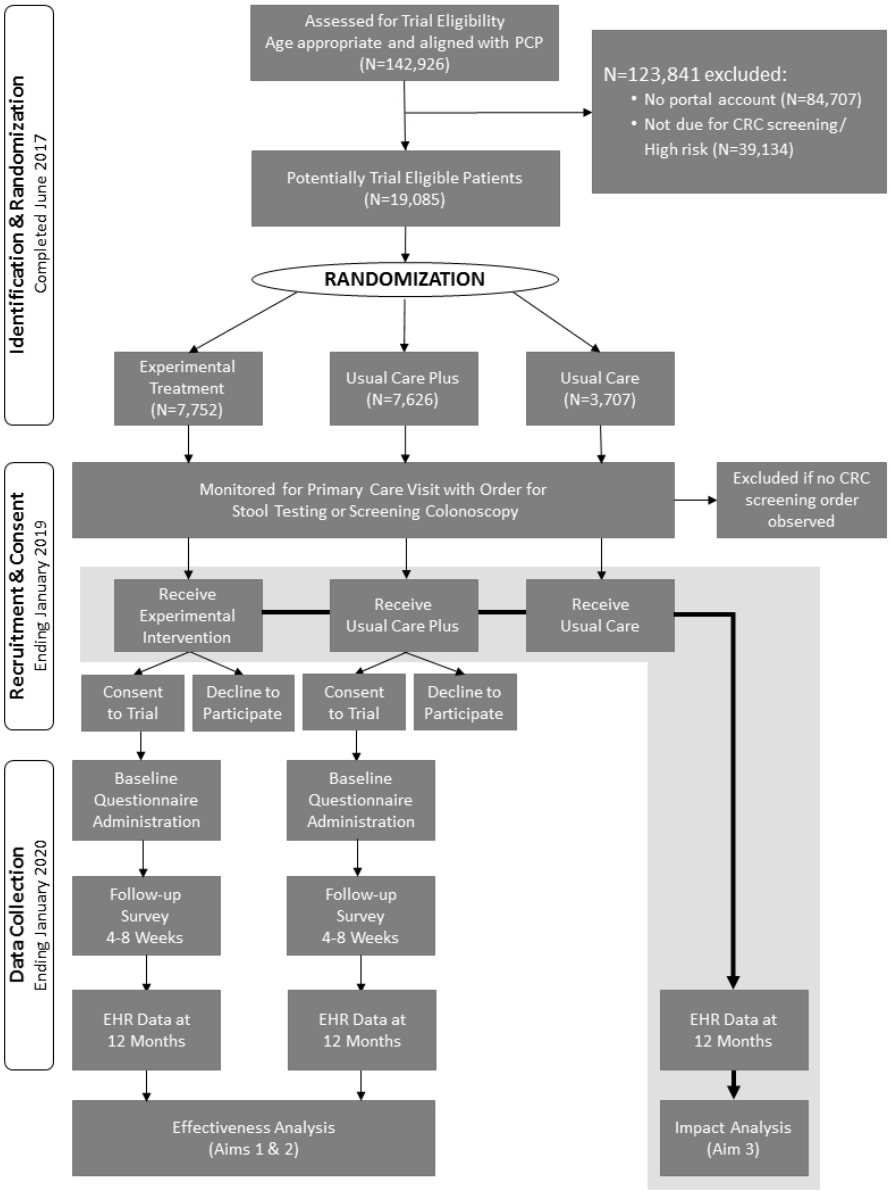

Figure 2. Study Process

215x279mm (96 x 96 DPI)

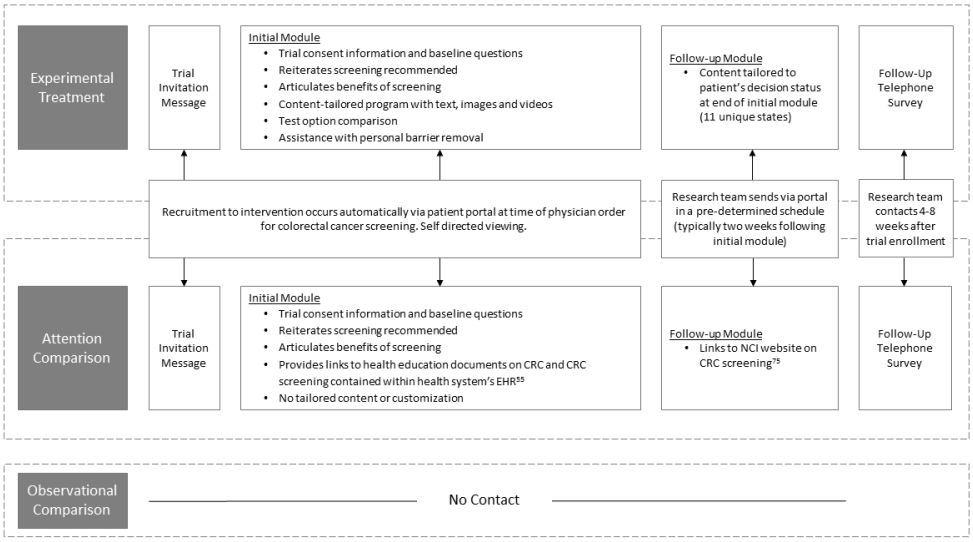

Figure 3. Intervention Content and Contact Procedures by Study Arm

317x177mm (96 x 96 DPI)

Reporting checklist for protocol of a clinical trial.

Based on the SPIRIT guidelines.

		Reporting Item	Page Number
Title	#1	Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym	1
Trial registration	#2a	Trial identifier and registry name. If not yet registered, name of intended registry	3
Trial registration: data set	#2b	All items from the World Health Organization Trial Registration Data Set	N/A
Protocol version	#3	Date and version identifier	N/A
Funding	#4	Sources and types of financial, material, and other support	21
Roles and responsibilities: contributorship	#5a	Names, affiliations, and roles of protocol contributors	1, 21
Roles and responsibilities: sponsor contact information	#5b	Name and contact information for the trial sponsor	N/A
Roles and responsibilities: sponsor and funder	#5c	Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have	N/A

		ultimate authority over any of these activities	
Roles and responsibilities: committees	#5d	Composition, roles, and responsibilities of the coordinating centers, steering committee, endpoint adjudication committee, data management team, and other individuals or groups overseeing the trial, if applicable (see Item 21a for data monitoring committee)	N/A
Background and rationale	#6a	Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention	4
Background and rationale: choice of comparators	#6b	Explanation for choice of comparators	4-5
Objectives	#7	Specific objectives or hypotheses	5-6
Trial design	#8	Description of trial design including type of trial (eg, parallel group, crossover, factorial, single group), allocation ratio, and framework (eg, superiority, equivalence, non-inferiority, exploratory)	5
Study setting	#9	Description of study settings (eg, community clinic, academic hospital) and list of countries where data will be collected. Reference to where list of study sites can be obtained	8
Eligibility criteria	#10	Inclusion and exclusion criteria for participants. If applicable, eligibility criteria for study centers and individuals who will perform the interventions (eg, surgeons, psychotherapists)	9
Interventions: description	#11a	Interventions for each group with sufficient detail to allow replication, including how and	12-15

		when they will be administered	
Interventions: modifications	#11b	Criteria for discontinuing or modifying allocated interventions for a given trial participant (eg, drug dose change in response to harms, participant request, or improving / worsening disease)	N/A
Interventions: adherence	#11c	Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return; laboratory tests)	10
Interventions: concomitant care	#11d	Relevant concomitant care and interventions that are permitted or prohibited during the trial	N/A
Outcomes	#12	Primary, secondary, and other outcomes, including the specific measurement variable (eg, systolic blood pressure), analysis metric (eg, change from baseline, final value, time to event), method of aggregation (eg, median, proportion), and time point for each outcome. Explanation of the clinical relevance of chosen efficacy and harm outcomes is strongly recommended	10-12 & Table 1
Participant timeline	#13	Time schedule of enrolment, interventions (including any run-ins and washouts), assessments, and visits for participants. A schematic diagram is highly recommended (see Figure)	Figures 2 & 3
Sample size	#14	Estimated number of participants needed to achieve study objectives and how it was determined, including clinical and statistical assumptions supporting any sample size calculations	17

Recruitment	#15	Strategies for achieving adequate participant enrolment to reach target sample size	17-18
Allocation: sequence generation	#16a	Method of generating the allocation sequence (eg, computer-generated random numbers), and list of any factors for stratification. To reduce predictability of a random sequence, details of any planned restriction (eg, blocking) should be provided in a separate document that is unavailable to those who enroll participants or assign interventions	9
Allocation concealment mechanism	#16b	Mechanism of implementing the allocation sequence (eg, central telephone; sequentially numbered, opaque, sealed envelopes), describing any steps to conceal the sequence until interventions are assigned	9
Allocation: implementation	#16c	Who will generate the allocation sequence, who will enroll participants, and who will assign participants to interventions	9
Blinding (masking)	#17a	Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how	N/A
Blinding (masking): emergency unblinding	#17b	If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during the trial	N/A
Data collection plan	#18a	Plans for assessment and collection of outcome, baseline, and other trial data, including any related processes to promote data quality (eg, duplicate measurements, training of assessors) and a description of study	10-12

		instruments (eg, questionnaires, laboratory tests) along with their reliability and validity, if known. Reference to where data collection forms can be found, if not in the protocol	
Data collection plan: retention	#18b	Plans to promote participant retention and complete follow-up, including list of any outcome data to be collected for participants who discontinue or deviate from intervention protocols	16
Data management	#19	Plans for data entry, coding, security, and storage, including any related processes to promote data quality (eg, double data entry; range checks for data values). Reference to where details of data management procedures can be found, if not in the protocol	N/A
Statistics: outcomes	#20a	Statistical methods for analyzing primary and secondary outcomes. Reference to where other details of the statistical analysis plan can be found, if not in the protocol	16-17
Statistics: additional analyses	#20b	Methods for any additional analyses (eg, subgroup and adjusted analyses)	16-17
Statistics: analysis population and missing data	#20c	Definition of analysis population relating to protocol non-adherence (eg, as randomized analysis), and any statistical methods to handle missing data (eg, multiple imputation)	16-17
Data monitoring: formal committee	#21a	Composition of data monitoring committee (DMC); summary of its role and reporting structure; statement of whether it is independent from the sponsor and competing interests; and reference to where further details about its charter can be found, if not in the protocol. Alternatively, an explanation of why a DMC is	N/A

		not needed	
Data monitoring: interim analysis	#21b	Description of any interim analyses and stopping guidelines, including who will have access to these interim results and make the final decision to terminate the trial	N/A
Harms	#22	Plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial conduct	N/A
Auditing	#23	Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor	N/A
Research ethics approval	#24	Plans for seeking research ethics committee / institutional review board (REC / IRB) approval	18-19
Protocol amendments	#25	Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators, REC / IRBs, trial participants, trial registries, journals, regulators)	N/A
Consent or assent	#26a	Who will obtain informed consent or assent from potential trial participants or authorized surrogates, and how (see Item 32)	18
Consent or assent: ancillary studies	#26b	Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable	N/A
Confidentiality	#27	How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial	N/A
Declaration of	#28	Financial and other competing interests for	21

interests		principal investigators for the overall trial and each study site	
Data access	#29	Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators	N/A
Ancillary and post trial care	#30	Provisions, if any, for ancillary and post-trial care, and for compensation to those who suffer harm from trial participation	N/A
Dissemination policy: trial results	#31a	Plans for investigators and sponsor to communicate trial results to participants, healthcare professionals, the public, and other relevant groups (eg, via publication, reporting in results databases, or other data sharing arrangements), including any publication restrictions	18-19
Dissemination policy: authorship	#31b	Authorship eligibility guidelines and any intended use of professional writers	N/A
Dissemination policy: reproducible research	#31c	Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code	19
Informed consent materials	#32	Model consent form and other related documentation given to participants and authorized surrogates	N/A
Biological specimens	#33	Plans for collection, laboratory evaluation, and storage of biological specimens for genetic or molecular analysis in the current trial and for future use in ancillary studies, if applicable	N/A

BMJ Open

A study protocol for a randomized trial to evaluate the effectiveness and impact of offering post-office visit decision support and assistance in obtaining physician-recommended colorectal cancer screening: The e-assist Colon Health Study

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A study protocol for a randomized trial to evaluate the effectiveness and impact of offering post-office visit decision support and assistance in obtaining physician-recommended colorectal cancer screening: The e-assist Colon Health Study

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ABSTRACT

Introduction. How to provide practice-integrated decision support to patients remains a challenge. We are testing the effectiveness of a practice-integrated program targeting patients with a physician recommendation for colorectal cancer (CRC) screening.

Methods and analysis. In partnership with healthcare teams, we developed "e-assist: Colon Health:" a patient-targeted, post-visit CRC screening decision support program. The program is housed within an electronic health record (EHR)-embedded patient portal. It leverages a physician screening recommendation as the cue to action and uses the portal to enroll and intervene with patients. Program content complements patient-physician discussions by encouraging screening, addressing common questions, and assisting with barrier removal. For evaluation, we are using a randomized trial in which patients are randomized to receive e-assist: Colon Health or one of two controls (usual care plus or usual care). Trial participants are average-risk, aged 50-75 years, due for CRC screening, and received a physician order for stool testing or colonoscopy. Effectiveness will be evaluated by comparing screening use, as documented in the EHR, between trial enrollees in the e-assist: Colon Health and usual care plus (CRC screening information receipt) groups. Secondary outcomes include patient-perceived benefits of, barriers to and support for CRC screening, and patient-reported CRC screening intent. The usual care group will be used to estimate screening use without intervention and program impact at the population level. Differences in outcomes by study arm will be estimated with hierarchical logit models where patients are nested within physicians.

Ethics and dissemination. All trial aspects have been approved by the Institutional Review Board of the health system in which the trial is being conducted. We will disseminate findings in

diverse scientific venues and will target clinical and quality improvement audiences via other venues. The intervention could serve as a model for filling the gap between physician recommendations and patient action.

Trial registration number: NCT02798224

ARTICLE SUMMARY

Strengths and limitations of this study

- Trial addresses how EHR-embedded, online decision support and assistance can be used following patients' receipt of physician order for CRC screening
- Use of EHR-embedded patient portal to enroll patients and deliver intervention facilitates practice integration and provides efficient and sustainable platform for intervention
- Program facilitates informed decision making and addresses common barriers to and questions regarding CRC screening, thereby filling known gaps in office visit discussions
- Enrolling and intervening with patients via the patient portal limits the program's reach to those already engaged with portal technology
- Study findings may be limited in that they may not generalize to other settings

INTRODUCTION

Despite the availability of multiple effective colorectal cancer (CRC) screening tests, CRC screening remains underutilized relative to other cancer screening tests.[1] We have found that a driving factor behind this under-utilization for insured individuals is the gap that exists between physician recommendation and patient receipt of care. We previously found that while the overwhelming majority (93%) of insured people due for CRC screening when visiting a physician office received a recommendation for screening, only 54% were screened in the following year.[2] Despite the known importance of physician recommendations to CRC screening use,[3,4] the gap between recommendation and screening use, in part, may be explained by the poor quality of typical patient-physician CRC screening discussions which have been shown to fall short of recommended decision making processes, and omit addressing common patient questions and CRC screening barriers.[3,5,6] To address these shortfalls, and close the gap between physician recommendation and care receipt, interventions are needed that encourage patient follow through, address lingering patient questions, and assist with barrier removal following a physician recommendation for screening.

How to offer such decision support and assistance to patients in a way that is practice-integrated remains a challenge. Individual health navigators hold promise, especially for low literacy patients, but costs associated with such programs limit scalability.[7,8] Patient reminders and the removal of structural barriers can increase screening use, but these techniques leave many unscreened and are disconnected from physician recommendations and other existing clinic processes.[7,9-19] Similarly, traditional decision aids provided before an office visit often result in improved patient knowledge, but limited (if any) changes in screening behaviors and have proven difficult to integrate within practice.[20-23] The effectiveness of such previously tested CRC screening programs may be limited by a combination of factors. These include their failure to be practice-integrated and thus capitalize on the powerful patient-physician relationship and

cue to action that exists once a physician recommends CRC screening, and the missed opportunity to intervene *after* an office visit in which CRC has been recommended with program content that is complementary to typical office-based CRC screening discussions.

By leveraging the platform of an online patient portal that is embedded within the electronic health record (EHR), we have developed a practice-integrated, patient-targeted CRC screening program, e-assist: Colon Health. The program is delivered to patients via an EHR-embedded patient portal after an office visit in which CRC screening has been recommended, thereby leveraging physician recommendations as a cue to action. Program content reinforces screening benefits, and addresses typical patient questions and the personal and structural barriers faced once a physician recommendation has been received. We are evaluating e-assist: Colon Health using a practice-embedded trial in which patients are randomized to receive e-assist: Colon Health or one of two control arms (usual care plus or usual care).

Aims and Hypotheses

The primary outcome of interest for the randomized trial is receipt of EHR-documented CRC screening within 12 months of physician recommendation. The overall aims of the evaluation include:

Aim 1. To compare screening use, intent to screen, and patient perceptions among trial enrollees receiving e-assist: Colon Health and usual care plus.

H1: A larger proportion of trial enrollees receiving e-assist: Colon Health, compared to trial enrollees receiving usual care plus, will be screened for CRC within 12 months of receiving the physician recommendation.

H2: A larger proportion of trial enrollees receiving e-assist: Colon Health, compared to enrollees receiving usual care plus, will report intending to be screened at the time of the follow-up survey.

H3: Trial enrollees receiving e-assist: Colon Health will perceive more benefits from CRC screening, more screening support, and fewer CRC screening barriers at the time of the follow-up survey as compared to trial enrollees receiving usual care plus.

Aim 2. To evaluate whether the effectiveness of e-assist: Colon Health is moderated by factors including patient health literacy, decision-making preference, and CRC screening decision stage as reported by trial enrollees at baseline.

H4: The effectiveness of e-assist: Colon Health will be greater among patients with low health literacy (compared to those with high health literacy), a preference for less directed decision making (compared to those with a preference for directed decision making), and a low decision stage (compared to those with a higher decision stage).

Aim 3. To characterize the impact of e-assist: Colon Health at a primary care population level by describing the ability of the program to reach the target population and by comparing CRC screening use across the three study arms.

METHODS

Conceptual Framework

Intervention and trial design are guided by the Health Belief Model (HBM),[24] the Precaution Adoption Process Model and Self Determination Theory.[25-28] The HBM suggests that people's use of preventive services is explained by their perceived threat of disease, benefits of the service, barriers to and self-efficacy for obtaining screening. The model also acknowledges the

need for a stimulus, or cue to action, to trigger the behavior. The HBM provides overarching guidance for intervention design (e.g., provision of information regarding the risks and consequences of CRC, and the benefits of screening; offering assistance overcoming barriers to screening; addressing structural barriers to completing screening by providing direct access to stool testing and assistance with completing screening; etc.) as well as the impetus for targeting patients immediately following a primary care visit with an order for CRC screening (i.e., an external cue to action that has occurred within established clinic processes). The HBM, however, does not provide guidance on how to personalize health communications and other intervention components to maximize message salience and accompanying action. The Precaution Adoption Process Model provides this guidance by building upon the core elements of the HBM, and considering how a person comes to decisions to take action.[26] Specifically, the individual's readiness to engage in the healthful behavior is based on their "decision stage." The premise behind the model is that different factors influence different stage transitions and that messages can be strategically designed to move individuals through the stages.[29,30] For example, the e-assist: Colon Health program offers patients who indicate they are not ready to be screened suggestions for how to overcome common personal barriers to screening. Likewise, patients who indicate they are undecided about how to be screened are provided with information about the pros and cons of different test options, while those indicating they are ready to be screened are provided with tips for completing their preferred screening test and assistance removing structural barriers that may arise. Finally, we use principles from Self Determination Theory to guide the tone of the written messages and ensure they are autonomy supporting,[28] and are not overly directive or controlling. For example, the program provides information on other types of CRC screening tests only to those who express an interest in this information and then emphasizes that modality choice is up to the patient.

Study Setting

The trial is being conducted within the primary care practice of an integrated health system. The practice's 33 primary care clinics are located throughout the city of Detroit and the surrounding suburban tri-county area. Clinics are staffed by approximately 150 salaried, adult primary care (i.e., general internal medicine and family medicine) physicians. The health system uses a commercial EHR that includes an embedded patient portal.[31]

Patient and Public Involvement

The design of the program and its integration with clinic workflow and practice were achieved via continual partnerships with care delivery and support teams. The user-centered design was used to ensure program acceptability, scalability and sustainability. Patient input via focus groups, in-depth interviews and beta testing was used to develop the content of the e-assist: Colon Health program.[32]

Study Design

We are evaluating the e-assist: Colon Health program using a three-arm, randomized trial. The trial is pragmatic and practice-embedded, in that it uses available EHR data to identify, recruit and follow up eligible patients.[33,34] By embedding these processes within the health system's infrastructure, we are able to invite a broad, generalizable group of patients and to do so in an efficient and sustainable way should the intervention be found effective under such 'real world' conditions.

To be consistent with the health system's preventive health practices, the inclusion and exclusion criteria for the trial was guided by the U.S. Preventive Services Task Force guidelines for CRC screening.[35] As such, average-risk patients, aged 50-75 years, due for CRC screening were randomized to receive (1) an online patient portal message with links to the interactive e-assist: Colon Health program (experimental treatment); (2) an online patient portal message

with links to Healthwise CRC and CRC screening educational material (usual care plus);[36] or (3) usual care. For the effectiveness evaluation, we will use an intent-to-treat analysis among those consenting to study participation in the experimental treatment and usual care plus arms. Because an outreach communication specific to CRC screening following a physician recommendation may itself serve as a reminder and cue to action, we will use the third arm, for which there is no outreach communication or consent, to describe screening use in a population without any post-visit communication about CRC screening (usual care). The latter will be used to estimate program impact at the population level. The evaluation framework is depicted in Figure 1.

Eligible Patient Identification and Randomization

Because of the desire to automate the workflow to recruit and intervene with patients and the inability to conduct randomization within the EHR environment, we randomized all ***potentially*** trial-eligible patients before opening the trial to enrollment. This was done by using the EHR data repository to identify patients who would become study eligible if they were to receive a physician recommendation for CRC screening during the trial enrollment period. This list of ***potentially*** trial-eligible participants was generated by identifying average-risk men and women aged 50-75 years who were due for CRC screening as recommended by the US Preventive Services Task Force Guidelines,[35] had an activated online patient portal account, and per administrative records were assigned to a primary care physician practicing in one of the health system's 33 primary care clinics. Patients with EHR-documented colonoscopy in the past 10 years, sigmoidoscopy in the past 5 years, or fecal occult blood test (FOBT) or fecal immunochemical test (FIT) in the past 12 months were excluded as were patients known to be above average risk for CRC (i.e., those with a personal or family history of CRC, those with prior polyps, or a history of inflammatory bowel disease, familial adenomatous polyposis, or

hereditary nonpolyposis). Patients without an activated portal account and who were not aligned to a primary care physician were also excluded.

SAS® software Version 9.4 was used to randomly allocate potentially trial-eligible patients to the experimental treatment, usual care plus, or usual care study arms. To ensure adequate sample size for the primary effectiveness analyses that will compare CRC screening use between the experimental treatment and the usual care plus groups (both of which require patient consent), we used a 2:2:1 ratio for randomization.

Study Enrollment and Baseline Assessment

Figure 2 outlines the study processes from the identification of potentially trial-eligible patients through outcome measurement. As indicated in Figure 2, while the trial is open for enrollment, the list of potentially trial-eligible participants (as identified above) is monitored electronically and continuously to identify those with an ambulatory care visit to a primary care physician that includes a referral for a colonoscopy, an order for stool testing (i.e., FOBT or FIT), or both. Once a potentially eligible patient receives such an order they become trial eligible. When the physician closes the encounter (i.e., visit note within the EHR), if the patient has a pre-assigned randomization code reflective of either the experimental treatment or usual care plus group, a secure message is sent automatically to the patient's online portal account inviting them to access an attached link that contains the decision support intervention appropriate to their study arm. Once an eligible patient opens the attached link, they are invited to participate in the study. Those continuing past an online consent page are considered enrolled in the trial. Trial enrollment is continuing until 900 patients are enrolled in each of the two study arms requiring consent (i.e., the experimental treatment and usual care plus). At that time, any individual who was randomized to usual care and received a primary care physician order for CRC screening will be included in the usual care arm.

Figure 3 provides an overview of the study contact procedures by study arm as well as a brief synopsis of the intervention content (the latter of which is described in more detail below). For those in the experimental treatment and usual care plus groups, the online programs contain a brief baseline questionnaire consisting of six measures that are being collected to assess balance between the experimental treatment and active comparison study arms, and to enable the testing of patient-level factors that may moderate the effectiveness of e-assist: Colon Health. As indicated in Table 1, these include previously validated measures of health literacy,[37] and measures adapted for CRC screening such as perceived worry,[38] decision-making preference,[39-41] perceived susceptibility,[42,43] screening history,[44] and CRC screening decision-making stage.[45] No similar assessment is given to the usual care group.

Outcome Measures and Follow-up Assessment

As indicated in Table 1, the primary effectiveness outcome for the trial is a binary variable reflecting CRC screening use in the 12-month period following the date of physician recommendation. Screening use is being determined by an EHR-documented occurrence of any of the following: colonoscopy, flexible sigmoidoscopy, fecal occult blood testing, fecal immunochemical testing or stool DNA testing. Patients for whom no indication of testing is identified in the EHR will be assumed not to have received screening.

Secondary outcomes include patient-perceived benefits of,[46] barriers to and support for CRC screening, and patient-reported CRC screening intent (Table 1).[47-49] The latter of which is obtained using a measure of behavioral intent adapted for CRC screening.[45] These secondary outcomes are being assessed via a telephone survey administered to participants enrolled in the experimental treatment and usual care plus arms only. The telephone survey is being administered 4 to 8 weeks following trial enrollment.

Table 1. Measures and Schedule of Measurement for Trial Participants Receiving e-assist: Colon Health or the Usual care plus

	Measure	Baseline Questionnaire	Follow-up Survey[2]	Medical Record Documented[1]
Primary Outcome	CRC Screening			X
Secondary Outcomes	CRC Screening Intent[45]		X	
	Barriers to CRC Screening[47,48]		X	
	CRC Screening Benefits[46]		X	
	Patient-Provider Supportive Communication[49]		X	
Moderating Factors	Health Literacy[37]	X	X	
	CRC Decision Stage[45]		X	
	Decision-Making Preference[39-41]	X	X	
	Perceived Worry[38]	X	X	
	CRC Screening History[44]	X		
	Perceived CRC Susceptibility[42,43]	X	X	

1. CRC screening as indicated by receipt of colonoscopy, flexible sigmoidoscopy, fecal occult blood testing, fecal immunochemical testing or stool DNA testing within 12 months of physician recommendation for screening as documented in the electronic health record (EHR).
2. Follow-up survey administered 4-8 weeks following for trial enrollment

Experimental Treatment: e-assist: Colon Health

The e-assist: Colon Health program is designed to serve as an online visit extender, filling known voids in typical office-based CRC screening decision-making processes and addressing key personal and structural barriers to CRC screening once a physician order has been placed. Program content includes images, newly developed text and seven videos that were developed

in the context of another NCI-funded trial (NCT01885351). After consenting to study participation and answering the baseline questionnaire, patients randomized to receive e-assist: Colon Health are able to view the content of the initial module. There are five central components to the initial module: (1) messaging and a video to reiterate that CRC screening is recommended; (2) messaging to provide information on different screening modalities and associated benefits/risks; (3) a screening test option comparison to assist patients in determining their screening test preference; (4) messaging and videos addressing ways to overcome common personal barriers to screening; and (5) messaging to assist with completing screening once a decision to screen has been made. The majority (89%) of e:assist: Colon Health text content assesses at or below a sixth grade reading level with the remainder (11%) at a seventh grade level, as evaluated by the Flesch–Kincaid Grade Level test.[50]

Although messaging regarding the benefits of CRC screening and testing guidelines are seen by everyone, much of the program's content is self-directed, enabling users to choose the material they want to view and the order in which they view it. Patients' readiness to screen along with their informational and CRC screening preferences are assessed through questions embedded throughout the program. Participant responses are used to tailor the program content seen to the participants' decision stage and preferences. The specific assistance a patient receives (e.g., instructions for how to schedule a colonoscopy; instructions for how to prepare for a colonoscopy screening; requesting mailed delivery of stool test; or instructions for how to complete stool test) is similarly tailored based on the participant's responses to embedded questions. What participants view and the order in which they view it are being tracked as part of the implementation effectiveness component of the evaluation. Although participants can return to the initial module as often as they want until they submit it as completed, we anticipate most participants completing the initial module in one session that lasts between 8 and 12 minutes, depending up information viewed.

Near the end of the initial module, a course of action is negotiated that is aligned with the patient's preferences and willingness to be screened. If a participant's responses indicate he/she is ready to be screened, the e-assist: Colon Health program facilitates receipt of screening by assisting with the removal of structural barriers that may arise (e.g., how to call the endoscopy nurse schedulers with questions). For participants expressing a desire to be screened using a test different from what their physician ordered, the program assists in obtaining their desired CRC screening test by providing contact information for the central scheduling line or messaging the patient's physician directly.

Any participant that does not indicate they have completed CRC screening when they submit their initial module receives a follow-up module. Much of the content in this follow up is similar to that available in the initial module albeit targeted based upon the information and preferences shared via question responses within the initial module. For example, if during the first module a participant elected to send a secure message to their primary care physician requesting a stool test, the content in the follow-up module would confirm that the participant received the stool test and offer tips for completion. For patients that do not express a desire to be screened, the follow-up module presents information using a motivational counseling approach.[51] This approach is aimed at moving patients who are undecided or not considering screening towards a concrete decision. It does so by highlighting the personal relevance of screening, the risks of CRC, and the benefits of screening, while identifying personally relevant barriers. There are a total of 11 different follow-up modules. As with the initial module, program navigation within each of these modules is self-directed with participants' responses to embedded questions used to tailor the program content seen. All follow-up modules are delivered two weeks after the initial module was submitted as completed, with the exception of those targeting participants who indicated they were not ready to be screened or those who abandoned the program without

submitting it. For the former, the follow-up module is sent 28 days later; for the latter, 7 days later.

Usual Care Plus

Patients randomized to usual care plus receive the identical recruitment message as those in the experimental arm (Figure 3). The consent form page and introductory screens reiterating that CRC screening has been recommended for them and outlining the benefits of screening are also identical. In lieu of the interactive e-assist: Colon Health program, individuals in usual care plus receive links to four webpages, one of which contains a video, that are stored within the patient portal's health information library. The educational material is currently distributed by Healthwise and includes information on the etiology, symptoms, and treatment of CRC as well as screening modalities and the interpretation of screening results.[36] With the exception of the one video, all material is static, and none is individually tailored.

Similar to participants in the experimental treatment group, participants enrolled in usual care plus are sent a follow-up module. The reminder module, which is also not tailored, is sent two weeks after the initial module. It includes a welcome screen and a link to the National Cancer Institute's CRC screening website.[52] This webpage provides patients with information on CRC screening and serves as a comparable alternative to the Healthwise information initially provided to the usual care plus. This allows the usual care plus group to run parallel to the experimental treatment in both timing as well as breadth of content provided (Figure 3).

Usual Care

Patients randomized to usual care receive CRC screening information and instructions as routinely provided by the health system. While the same Healthwise material that is being pushed to patients enrolled in usual care plus is available to these participants via the health

library accessible within the EHR, unlike in usual care plus, participants are not being systematically directed to this material. Thus, while patients in this arm, by virtue of their portal account, have access to the same Healthwise material on CRC and CRC screening, access to the library containing these documents is not readily identifiable within the portal. Similarly, those materials could be printed for patients at the time of an office visit, but to our knowledge this rarely, if ever, happens.

Analysis Plan

Each outcome Y will be conditional on treatment assignment T and consent C, (the interaction terms of) which will identify four groups: consenters (C=1) and nonconsenters (C=0) assigned to treatment (T=1) and usual care plus or control (T=0). The primary outcome for the evaluation is a binary variable (EHR-documented CRC screening use within 12 months as defined above) which will be available regardless of treatment assignment or consent status. Secondary outcomes, all measured at the time of the follow-up survey, are ordinal categorical (e.g., screening intent and benefits) or continuous (e.g., barriers and screening support), and available among consenters only, regardless of treatment assignment.

For the effectiveness evaluation (H1), differences in CRC screening between experimental treatment and usual care plus will be estimated by a hierarchical logit model where patients who consented are nested within physicians. Because we will obtain CRC screening use data from the EHR with the absence of screening data coded as 'no screening,' there will not be known missing values for the primary outcome. For a limited number of trial participants (who, for whatever reason, elect to receive screening elsewhere), this may result in unknown missing values. While this will represent a trial limitation, we do not have reason to expect this missingness to differ by study arm.

For secondary outcomes (H2 and H3), we will use hierarchical generalized linear models and hierarchical linear models to analyze categorical and continuous outcomes, respectively, where patients who consented are nested within physicians.[53] We will compare the treatment effects for consenters, moderated by patient characteristics, to test H4 for aim 2. For H2-H4, we will handle missing data from survey item- and unit-nonresponses efficiently by analyzing all observed data.[54-56]

For the impact evaluation, we will compare screening rates across the three trial arms for consenters and nonconsenters by a hierarchical logit model, analyzing the entire sample. The effects of consenters will be compared to each other and those of nonconsenters to describe the population represented by the experiment. We will also analyze a hierarchical model for the consent outcome C, which will describe who the beneficiaries of the treatment and usual care plus are in terms of their characteristics. One difficulty is that each patient in the usual care arm is missing the consent status. That is, if the patient was assigned to the other arms, he/she would have or would not have consented to study participation. We will view missing consent as missing data, and estimate the hierarchical models by efficient handling of missing data, i.e., by all observed data.[54-58]

Power and Sample Size Calculations

To account for the clustering of patients nested within physicians, statistical power for the primary effectiveness evaluation (i.e., the comparison of outcomes between the experimental treatment and usual care plus) was estimated using an R program written by Dr. Jessaca Spybrook implementing the method in Spybrook and Hedberg, and Moerbeek et al.[59,60]. With randomization at the patient level, we consider a 95% plausible interval for CRC screening use in the experimental treatment (66%±5%) at alpha=0.05 in the usual care plus arm. With 1800 patients seen by 150 primary care physicians, or 12 patients per physician (6 in the

experimental treatment and 6 in the usual care plus), we have 0.86 power to detect a 7% change in CRC screening rates between the experimental treatment and the usual care plus (i.e., 66% vs. 59%, respectively).

Trial Status

As indicated in Figure 2, prior to opening trial enrollment, 19,085 patients were identified as potentially eligible and randomized (7,752 to the experimental treatment, 7,626 to usual care plus, and 3,707 to usual care). The trial opened for enrollment at 1:00 pm eastern standard time on June 14, 2017 with recruitment planned to end in early 2019. Seven months into trial recruitment (1/14/18), 2,175 of the potentially eligible patients have received a primary care physician order for CRC screening (1,110 in the experimental group and 1,065 in the usual care plus group) This has resulted in n=328 patients being enrolled in the experimental group and n=376 in the usual care plus group. We have identified two barriers to trial enrollment among those receiving a physician order for CRC screening, and thus an invitation for trial participation. First, approximately 30% of patients who are sent an email notification that they have a new portal message never log into their portal account to read the message. In addition, among patients who log into their portal account and read the message, about 50% elect not to open the attachment which includes information on the trial (e.g. consent information) and the decision support programs. We are currently using in-depth interviews with patients who elected not to log into their portal account or not to open the attachment to gain insights into other means by which to engage such patients with decision support following physician recommendations for care.

ETHICS AND DISSEMINATION PLAN

All aspects of the trial protocol have been approved by the Henry Ford Health System Institutional Review Board (protocol number 10060). The IRB approved the trial under an

expedited review and, given the benefit/risk ratio, waived the need for written patient consent. A HIPAA waiver of authorization was received to enable the inclusion of the usual care group. The trial is funded by the National Cancer Institute (7R01CA197205) and registered with Clinical Trials.gov (NCT02798224).

Findings, whether positive or negative, will enable clinicians and other health care stakeholders to make informed decisions about how to integrate new portal technology to support primary care patients in their decision making and service receipt. We will disseminate emerging stories, lessons learned, and findings on an ongoing basis. To do so requires attention to packaging and context as well as diversity in dissemination strategies. Manuscripts and presentations will be prepared for publication in diverse scientific venues, and we will target brief reports and presentations for the clinical, quality improvement, and EHR communities as well as make use of emerging repositories like Cancer Control Planet.

Data requests can be submitted to the corresponding author at the UNC Eshelman School of Pharmacy, University of North Carolina at Chapel Hill, Chapel Hill, North Carolina, after conclusion of the trial and publication of the primary manuscript.

DISCUSSION

To our knowledge, this is the first trial to test an online practice-integrated, post-visit CRC screening decision support program that does not rely on direct human resources to help patients address lingering questions about CRC screening, and overcome personal and structural barriers to screening use once a physician recommendation is in hand. As such, we are testing an intervention that fills an important gap in clinical care that has yet to be addressed. Our trial and program are unique in their use of clinical workflow-integrated automation. By automating patient identification and program delivery we are facilitating

program sustainability should e-assist: Colon Health succeed. By intervening with patients following a regularly scheduled office visit in which they received a physician recommendation for CRC screening, we are able to use a naturally occurring clinical event as the cue for patient action, thereby capitalizing on the known powerful relationships between patients and their physicians. By using the patient portal to do so, we are ensuring that e-assist: Colon Health is fully integrated within existing clinic processes. The e-assist: Colon Health program will extend, in a personalized and autonomy-supporting manner, the patient-physician CRC screening decision-making process beyond the confines of office visits. Thus, unlike traditional decision aids administered prior to a visit, we do not anticipate that e-assist: Colon Health will alter the patient-physician office visit interaction per se; instead we expect e-assist: Colon Health to extend the patient's ability to consider CRC screening in a supportive setting post-receipt of physician recommendation and to improve the patient's perception of the autonomy support they receive from their doctor's office. The fact that the program is accessed via an existing patient portal furthers its integration with increasingly common clinic processes, streamlines patient accessibility, and begins to address prior challenges of implementation faced by previous decision aid studies.

Recent reviews indicate that, compared to usual care, people who use decision aids benefit from improved knowledge, a better understanding of their values, and enhanced participation in the decision-making process.[23,61,62] Despite the known benefits of decision aid use, physicians voice concerns regarding their practicality and,[22,63] to date, their integration within practice is limited.[21,22] Our trial, via our ongoing engagement with clinician and other health care stakeholders, is illustrating how these barriers can be overcome. The challenge is that while communication outreach strategies embedded within a patient portal may be sustainable and acceptable to health care stakeholders, they engage only a small subset of the patient population.[64] Further, there is increasing evidence that use of a portal among those with an

account varies, with patients from traditionally disadvantaged publications being relatively less engaged even once they have a portal account.[65,66] Our trial and its decision support intervention appears to be no exception. Thus, an overarching limitation of the trial is that its reach is limited to those already engaged with the portal. Prior studies have repeatedly shown this to be a relatively small segment of the population, and one in which minorities and other traditionally disadvantaged populations are under-represented.[67-76] In addition, our trial is limited by its implementation and recruitment within one health system which may further limit the ability to generalize results.

Facilitating the timely use of CRC screening among primary care patients requires that scalable programs be designed to address not only barriers to obtaining a physician recommendation for care, but also the quality of that recommendation and the personal and system barriers faced once patients have a physician recommendation for care. Identifying sustainable strategies to support patient adherence to evidence-based care is critical for patient-centered medical homes and other delivery settings if we are to effectively and efficiently deliver preventive health services. Supporting patient adherence to known effective preventive health services is also critical to the ability to reduce the morbidity and mortality associated with preventable diseases such as CRC.

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Competing Interests: None declared

Figure Titles and Legends

Figure 1. Evaluation Framework

The figure provides an overview of the implementation and patient outcomes that are being assessed as part of the e-assist: Colon Health study.

Figure 2. Study Processes

The figure identifies how patients were identified, randomized, recruited and followed during the e-assist: Colon Health study.

Figure 3. Intervention Content and Contact Procedures by Study Arm

The figure summarizes the points and content of participant contact during the e-assist: Colon Health study.

References

1. Siegel R, Desantis C, Jemal A. Colorectal cancer statistics, 2014. *CA Cancer J Clin* 2014;64(2):104-17. doi: 10.3322/caac.21220 [published Online First: 2014/03/19]

2. Lafata JE, Cooper G, Divine G, et al. Patient-physician colorectal cancer screening discussion content and patients' use of colorectal cancer screening. *Patient Educ Couns* 2014;94(1):76-82. doi: S0738-3991(13)00361-3 [pii]10.1016/j.pec.2013.09.008 [published Online First: 2013/10/08]

3. Peterson EB, Ostroff JS, DuHamel KN, et al. Impact of provider-patient communication on cancer screening adherence: A systematic review. *Preventive Medicine* 2016;93:96-105. doi: https://doi.org/10.1016/j.ypmed.2016.09.034

4. Vernon SW. Participation in Colorectal Cancer Screening: A Review. *JNCI: Journal of the National Cancer Institute* 1997;89(19):1406-22. doi: 10.1093/jnci/89.19.1406

5. Lafata JE, Divine G, Moon C, et al. Patient-physician colorectal cancer screening discussions and screening use. *Am J Prev Med* 2006;31(3):202-9. doi: S0749-3797(06)00202-9 [pii]10.1016/j.amepre.2006.04.010 [published Online First: 2006/08/15]

6. Flocke SA, Stange KC, Cooper GS, et al. Patient-rated importance and receipt of information for colorectal cancer screening. *Cancer Epidemiol Biomarkers Prev* 2011;20(10):2168-73. doi: 1055-9965.EPI-11-0281 [pii]10.1158/1055-9965.EPI-11-0281 [published Online First: 2011/08/05]

7. Holden DJ, Jonas DE, Porterfield DS, et al. Systematic review: enhancing the use and quality of colorectal cancer screening. *Ann Intern Med* 2010;152(10):668-76. doi: 0003-4819-152-10-201005180-00239 [pii]10.7326/0003-4819-152-10-201005180-00239 [published Online First: 2010/04/15]

8. Lairson DR, Dicarlo M, Deshmuk AA, et al. Cost-effectiveness of a standard intervention versus a navigated intervention on colorectal cancer screening use in primary care. *Cancer* 2014;120(7):1042-9. doi: 10.1002/cncr.28535 [published Online First: 2014/01/18]

9. Sabatino SA, Lawrence B, Elder R, et al. Effectiveness of Interventions to Increase Screening for Breast, Cervical, and Colorectal Cancers Nine Updated Systematic Reviews for the Guide to Community Preventive Services. *American Journal of Preventive Medicine* 2012;43(1):97-118. doi: DOI 10.1016/j.amepre.2012.04.009

10. Myers RE, Ross E, Jepson C, et al. Modeling adherence to colorectal cancer screening. *Prev Med* 1994;23(2):142-51. doi: S0091-7435(84)71020-6 [pii]10.1006/pmed.1994.1020 [published Online First: 1994/03/01]

11. Dietrich AJ, Tobin JN, Cassells A, et al. Telephone care management to improve cancer screening among low-income women: a randomized, controlled trial. *Ann Intern Med* 2006;144(8):563-71. doi: 144/8/563 [pii] [published Online First: 2006/04/19]

12. Basch CE, Wolf RL, Brouse CH, et al. Telephone outreach to increase colorectal cancer screening in an urban minority population. *Am J Public Health* 2006;96(12):2246-53. doi: AJPH.2005.067223 [pii]10.2105/AJPH.2005.067223 [published Online First: 2006/11/02]

13. Myers RE, Ross EA, Wolf TA, et al. Behavioral interventions to increase adherence in colorectal cancer screening. *Med Care* 1991;29(10):1039-50. [published Online First: 1991/10/01]

14. Goldberg D, Schiff GD, McNutt R, et al. Mailings timed to patients' appointments: a controlled trial of fecal occult blood test cards. *Am J Prev Med* 2004;26(5):431-5. doi: 10.1016/j.amepre.2004.02.009S0749379704000364 [pii] [published Online First: 2004/05/29]

15. Mosen DM, Feldstein AC, Perrin N, et al. Automated telephone calls improved completion of fecal occult blood testing. *Med Care* 2010;48(7):604-10. doi: 10.1097/MLR.0b013e3181dbdce7

16. Hardcastle JD, Chamberlain JO, Robinson MH, et al. Randomised controlled trial of faecal-occult-blood screening for colorectal cancer. *Lancet* 1996;348(9040):1472-7. doi: S0140-6736(96)03386-7 [pii]10.1016/S0140-6736(96)03386-7 [published Online First: 1996/11/30]

17. Church TR, Yeazel MW, Jones RM, et al. A randomized trial of direct mailing of fecal occult blood tests to increase colorectal cancer screening. *J Natl Cancer Inst* 2004;96(10):770-80. [published Online First: 2004/05/20]

18. Baron RC, Rimer BK, Breslow RA, et al. Client-directed interventions to increase community demand for breast, cervical, and colorectal cancer screening. *American Journal of Preventive Medicine* 2008;35(1):S34-S55. doi: DOI 10.1016/j.amepre.2008.04.002

19. Baron RC, Mercer SL, Se TFCP. Recommendations for client- and provider-directed interventions to increase breast, cervical, and colorectal cancer screening. *American Journal of Preventive Medicine* 2008;35(1):S21-S25. doi: DOI 10.1016/j.amepre.2008.04.004

20. Stacey D, Légaré F, Col NF, et al. Decision Aids for People Facing Health Treatment or Screening Decisions. *Cochrane Database Syst Rev* 2014;1

21. Jimbo M, Rana GK, Hawley S, et al. What is Lacking in Current Decision Aids on Cancer Screening? *CA: A Cancer Journal for Clinicians* 2013;63(3):193-214.

22. Brace C, Schmocker S, Huang H, et al. Physicians' awareness and attitudes toward decision aids for patients with cancer. *J Clin Oncol* 2010;28(13):2286-92. doi: 10.1200/JCO.2009.25.2874

23. Volk RJ, Linder SK, Lopez-Olivo MA, et al. Patient Decision Aids for Colorectal Cancer Screening: A Systematic Review and Meta-analysis. *Am J Prev Med* 2016;51(5):779-91. doi: 10.1016/j.amepre.2016.06.022

24. Janz NK, Becker MH. The Health Belief Model: a decade later. *Health Educ Q* 1984;11(1):1-47. [published Online First: 1984/01/01]

25. Weinstein ND, Lyon J, Sandman P, et al. Experimental evidence for stages of health behavior change: the precaution adoption process model applied to home radon testing. *Health Psychol* 1998;17(5):445-53. [published Online First: 1998/10/17]

26. Weinstein N, Sandman P. The Precaution Adoption Process Model and its application. San Francisco, CA: Jossey-Bass 2002:16-39.

27. Ryan RM, Deci EL. Intrinsic and Extrinsic Motivations: Classic Definitions and New Directions. *Contemp Educ Psychol* 2000;25(1):54-67. doi: 10.1006/ceps.1999.1020S0361476X99910202 [pii] [published Online First: 2000/01/06]

28. Deci EL, Koestner R, Ryan RM. A meta-analytic review of experiments examining the effects of extrinsic rewards on intrinsic motivation. *Psychol Bull* 1999;125(6):627-68. doi: 10.1037/0033-2909.125.6.627

29. Weinstein ND, Rothman AJ, Sutton SR. Stage theories of health behavior: conceptual and methodological issues. *Health Psychol* 1998;17(3):290-9. [published Online First: 1998/06/10]

30. EW Maibach DC. Moving people to behavior change: A staged social cognitive approach to message design. Newbury Park, CA: Sage 1995:41-64.

31. *Epic - with the patient at the heart*. Available from: https://www.epic.com/ Accessed February 2018

32. Dyer KE, Shires DA, Flocke SA, et al. Patient-reported needs after receiving a physician recommendation for colorectal cancer screening. Manuscript submitted for publication

33. Ford I, Norrie J. Pragmatic Trials. *New England Journal of Medicine* 2016;375(5):454-63. doi: 10.1056/NEJMra1510059

34. Loudon K, Treweek S, Sullivan F, et al. The PRECIS-2 tool: designing trials that are fit for purpose. *BMJ : British Medical Journal* 2015;350 doi: 10.1136/bmj.h2147

35. United States Preventive Services Task Force. *Screening for Colorectal Cancer: U.S. Preventive Services Task Force Recommendation Statement*. 2008; Available from: http://www.uspreventiveservicestaskforce.org/uspstf08/colocancer/colors.htm Accessed February 2018

36. *Healthwise – for every health decision.* (n.d.). Colorectal Cancer. Retrieved from https://www.healthwise.net Accessed February 2018

37. Chew LD, Griffin JM, Partin MR, et al. Validation of screening questions for limited health literacy in a large VA outpatient population. *Journal of general internal medicine* 2008;23(5):561-6. doi: 10.1007/s11606-008-0520-5[published Online First: 2008/03/13]

38. National Cancer Institute. *Health Information National Trends Survey 4 Cycle 4*. 2014; https://hints.cancer.gov/docs/Instruments/HINTS_4_Cycle_4_English_Annotated_Form.pdf Accessed February 2018

39. Degner LF, Sloan JA, Venkatesh P. The Control Preferences Scale. *Can J Nurs Res* 1997;29(3):21-43.

40. Williams GC, Rodin GC, Ryan RM, et al. Autonomous regulation and long-term medication adherence in adult outpatients. *Health Psychol* 1998;17(3):269-76. [published Online First: 1998/06/10]

41. Williams GC, Grow VM, Freedman ZR, et al. Motivational predictors of weight loss and weight-loss maintenance. *J Pers Soc Psychol* 1996;70(1):115-26. [published Online First: 1996/01/01]

42. National Cancer Institute. *Health Information National Trends Survey 2*. 2005; https://hints.cancer.gov/docs/Instruments/HINTS_2005_Final_Report.pdf Accessed February 2018

43. McQueen A, Tiro JA, Vernon SW. Construct validity and invariance of four factors associated with colorectal cancer screening across gender, race, and prior screening. *Cancer Epidemiol Biomarkers Prev* 2008;17(9):2231-7. doi: 17/9/2231 [pii]10.1158/1055-9965.EPI-08-0176 [published Online First: 2008/09/05]

44. National Cancer Institute. *Health Information National Trends Survey 3.* 2008; https://hints.cancer.gov/docs/Instruments/HINTS2007FinalReport.pdf Accessed February 2018

45. Sifri R, Rosenthal M, Hyslop T, et al. Factors associated with colorectal cancer screening decision stage. *Preventive Medicine* 2010;51(3):329-31. doi: https://doi.org/10.1016/j.ypmed.2010.06.015

46. Vernon SW, Myers RE, Tilley BC. Development and validation of an instrument to measure factors related to colorectal cancer screening adherence. *Cancer Epidemiology Biomarkers & Prevention* 1997;6(10):825-32.

47. Jones RM, Magnusson BM, Dumenci L, et al. Psychometric Properties of a Fecal Occult Blood Test Barrier Scale. *Am J Epidemiol* 2011;173:S170-S70.

48. Jones RM, Magnusson BM, Dumenci L, et al. Measuring Barriers to Flexible Sigmoidoscopy and Colonoscopy: A Validation Study. *Am J Epidemiol* 2011;173:S169-S69.

49. AHRQ. *Patient Experience Measures from the CAHPS® Clinician & Group Surveys* 2011 [Available from: https://cahps.ahrq.gov/surveys-guidance/cg/cgkit/1309_CG_Measures.pdf Accessed September 26 2014.

50. Flesch R. A new readability yardstick. *J Appl Psychol* 1948;32(3):221-33.

51. Fiore M. Treating Tobacco Use and Dependence: 2008 Update: Clinical Practice Guideline: DIANE Publishing 2008.

52. PDQ® Screening and Prevention Editorial Board. PDQ Colorectal Cancer Screening. Bethesda, MD: National Cancer Institute. Updated 02/23/2018 Available at: https://www.cancer.gov/types/colorectal/patient/colorectal-screening-pdq. Accessed 04/06/2018. [PMID: 26389230]

53. Raudenbush SW, & Bryk, A. S. Hierarchical linear models: Applications and data analysis methods. 2 ed. Thousand Oaks: Sage Publications 2002.

54. Rubin D. Inference and missing data. *Biometrika* 1976;63:581-92.

55. Shin YR, SW Joint Distribution of Site-Specific causal effects, Complier Means and Noncomplier Means Given Data MAR from a Multisite Trial. Manuscript in preparation

56. Shin Y, Raudenbush SW. Just-Identified Versus Overidentified Two-Level Hierarchical Linear Models with Missing Data. *Biometrics* 2007;63(4):1262-68. doi: 10.1111/j.1541-0420.2007.00818.x

57. Rubin DB. Bayesian Inference for Causal Effects: The Role of Randomization. *Ann Statist* 1978;6(1):34-58. doi: 10.1214/aos/1176344064

58. Angrist JD, Imbens GW, Rubin DB. Identification of Causal Effects Using Instrumental Variables. *Journal of the American Statistical Association* 1996;91(434):444-55. doi: 10.2307/2291629

59. Spybrook J, Hedberg E. A Framework for Designing Cluster Randomized Trials with Binary Outcomes. *Evaluation Review*, 23(4):445-469, 20x1

60. Moerbeek M, Van Breukelen G, MPF B. Optimal experimental designs for multilevel logistic models. *Journal of the Royal Statistical Society: Series D (The Statistician),* 2001;50(1):17-30.

61. Trikalinos TA, Wieland LS, Adam GP, et al. Decision Aids for Cancer Screening and Treatment. Rockville (MD)2014.

62. Stacey D, Legare F, Lewis K, et al. Decision aids for people facing health treatment or screening decisions. *Cochrane Database Syst Rev* 2017;4:CD001431. doi: 10.1002/14651858.CD001431.pub5

63. Graham ID, Logan J, O'Connor A, et al. A qualitative study of physicians' perceptions of three decision aids. *Patient Educ Couns* 2003;50(3):279-83.

64. Krist AH, Woolf SH, Hochheimer C, et al. Harnessing Information Technology to Inform Patients Facing Routine Decisions: Cancer Screening as a Test Case. *Ann Fam Med* 2017;15(3):217-24. doi: 10.1370/afm.2063

65. Tieu L, Schillinger D, Sarkar U, et al. Online patient websites for electronic health record access among vulnerable populations: portals to nowhere? *J Am Med Inform Assoc* 2017;24(e1):e47-e54. doi: 10.1093/jamia/ocw098

66. Lafata JE MC, Shires DA, Dyer K, Raliff S, Schreiber M. Patients' Use of Electronic Patient Portals and Their Features. *Am J Managed Care* In press

67. Krist AH, Aycock RA, Etz RS, et al. MyPreventiveCare: implementation and dissemination of an interactive preventive health record in three practice-based research networks serving disadvantaged patients--a randomized cluster trial. *Implement Sci* 2014;9:181. doi: 10.1186/s13012-014-0181-1

68. Griffin A, Skinner A, Thornhill J, et al. Patient Portals: Who uses them? What features do they use? And do they reduce hospital readmissions? *Appl Clin Inform* 2016;7(2):489-501. doi: 10.4338/ACI-2016-01-RA-0003

69. Yamin CK, Emani S, Williams DH, et al. The digital divide in adoption and use of a personal health record. *Arch Intern Med* 2011;171(6):568-74. doi: 10.1001/archinternmed.2011.34

70. Smith SG, O'Conor R, Aitken W, et al. Disparities in registration and use of an online patient portal among older adults: findings from the LitCog cohort. *J Am Med Inform Assoc* 2015;22(4):888-95. doi: 10.1093/jamia/ocv025

71. Sarkar U, Karter AJ, Liu JY, et al. Social disparities in internet patient portal use in diabetes: evidence that the digital divide extends beyond access. *J Am Med Inform Assoc* 2011;18(3):318-21. doi: 10.1136/jamia.2010.006015

72. Roblin DW, Houston TK, 2nd, Allison JJ, et al. Disparities in use of a personal health record in a managed care organization. *J Am Med Inform Assoc* 2009;16(5):683-9. doi: 10.1197/jamia.M3169

73. Peacock S, Reddy A, Leveille SG, et al. Patient portals and personal health information online: perception, access, and use by US adults. *J Am Med Inform Assoc* 2017;24(e1):e173-e77. doi: 10.1093/jamia/ocw095

74. Kruse CS, Bolton K, Freriks G. The effect of patient portals on quality outcomes and its implications to meaningful use: a systematic review. *J Med Internet Res* 2015;17(2):e44. doi: 10.2196/jmir.3171

75. Irizarry T, DeVito Dabbs A, Curran CR. Patient Portals and Patient Engagement: A State of the Science Review. *J Med Internet Res* 2015;17(6):e148. doi: 10.2196/jmir.4255

76. Ancker JS, Barron Y, Rockoff ML, et al. Use of an electronic patient portal among disadvantaged populations. *Journal of General Internal Medicine* 2011;26(10):1117-23. doi: 10.1007/s11606-011-1749-y

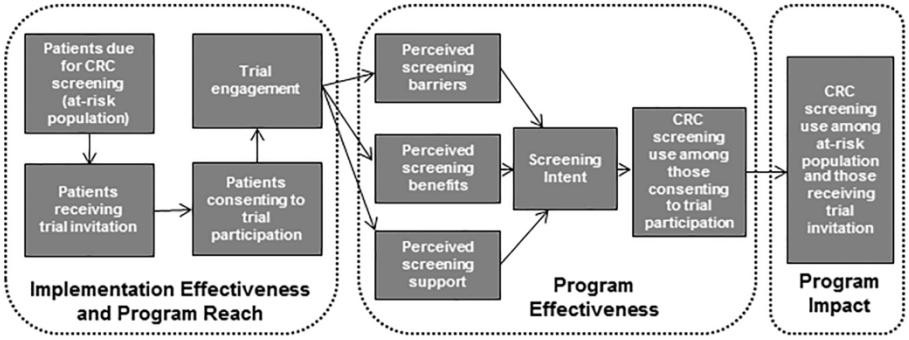

Figure 1. Evaluation Framework

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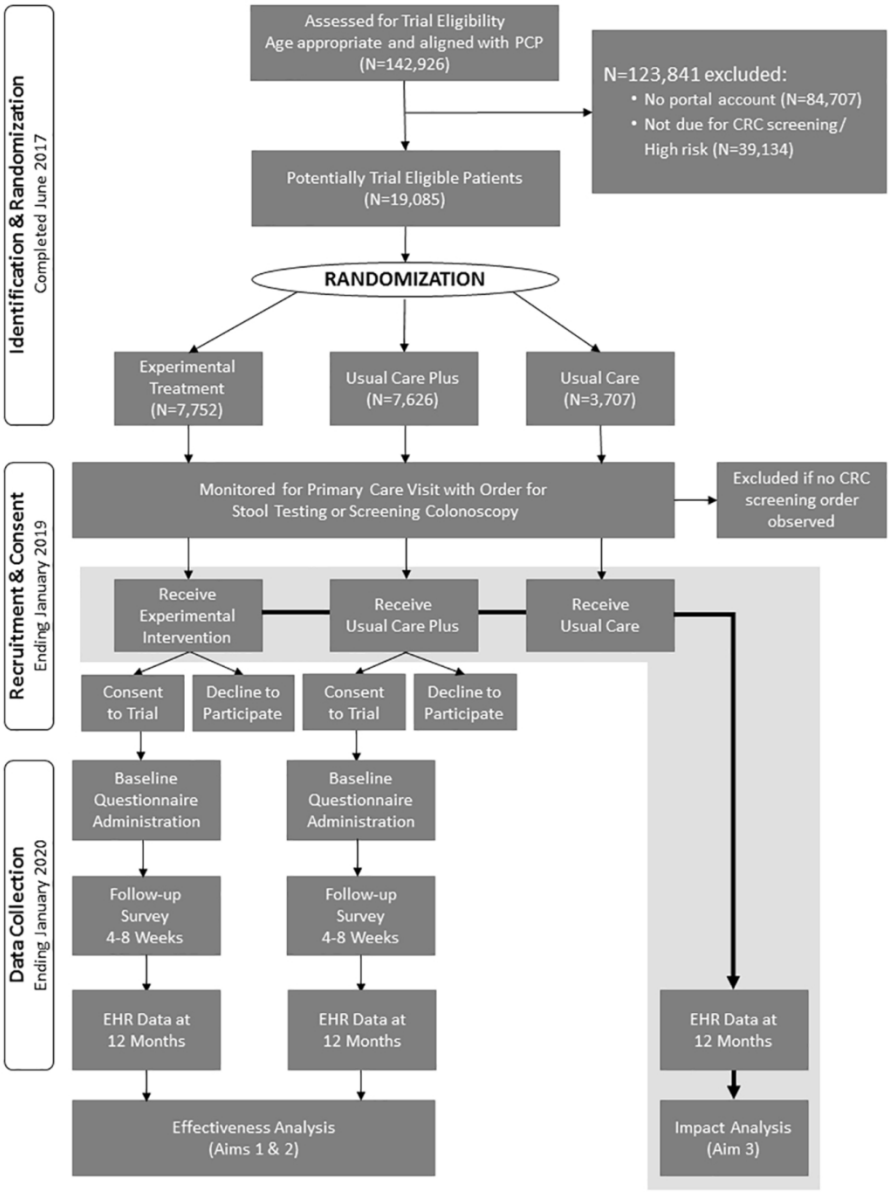

Figure 2. Study Process

119x154mm (300 x 300 DPI)

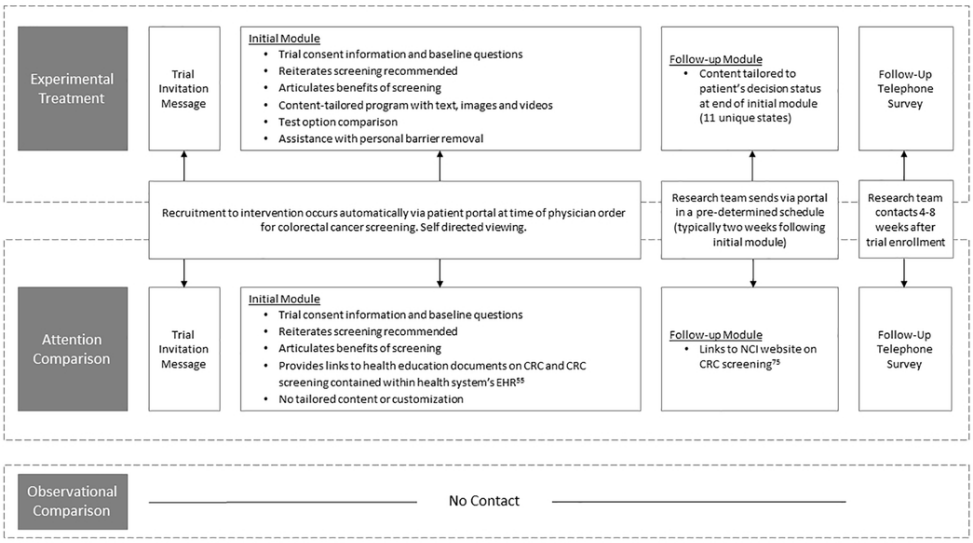

Figure 3. Intervention Content and Contact by Study Arm

90x50mm (300 x 300 DPI)

Reporting checklist for protocol of a clinical trial.

Based on the SPIRIT guidelines.

		Reporting Item	Page Number
Title	#1	Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym	1
Trial registration	#2a	Trial identifier and registry name. If not yet registered, name of intended registry	3
Trial registration: data set	#2b	All items from the World Health Organization Trial Registration Data Set	N/A
Protocol version	#3	Date and version identifier	N/A
Funding	#4	Sources and types of financial, material, and other support	21
Roles and responsibilities: contributorship	#5a	Names, affiliations, and roles of protocol contributors	1, 21
Roles and responsibilities: sponsor contact information	#5b	Name and contact information for the trial sponsor	N/A
Roles and responsibilities: sponsor and funder	#5c	Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have	N/A

		ultimate authority over any of these activities	
Roles and responsibilities: committees	#5d	Composition, roles, and responsibilities of the coordinating centers, steering committee, endpoint adjudication committee, data management team, and other individuals or groups overseeing the trial, if applicable (see Item 21a for data monitoring committee)	N/A
Background and rationale	#6a	Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention	4
Background and rationale: choice of comparators	#6b	Explanation for choice of comparators	4-5
Objectives	#7	Specific objectives or hypotheses	5-6
Trial design	#8	Description of trial design including type of trial (eg, parallel group, crossover, factorial, single group), allocation ratio, and framework (eg, superiority, equivalence, non-inferiority, exploratory)	5
Study setting	#9	Description of study settings (eg, community clinic, academic hospital) and list of countries where data will be collected. Reference to where list of study sites can be obtained	8
Eligibility criteria	#10	Inclusion and exclusion criteria for participants. If applicable, eligibility criteria for study centers and individuals who will perform the interventions (eg, surgeons, psychotherapists)	9
Interventions: description	#11a	Interventions for each group with sufficient detail to allow replication, including how and	12-15

		when they will be administered	
Interventions: modifications	#11b	Criteria for discontinuing or modifying allocated interventions for a given trial participant (eg, drug dose change in response to harms, participant request, or improving / worsening disease)	N/A
Interventions: adherence	#11c	Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return; laboratory tests)	10
Interventions: concomitant care	#11d	Relevant concomitant care and interventions that are permitted or prohibited during the trial	N/A
Outcomes	#12	Primary, secondary, and other outcomes, including the specific measurement variable (eg, systolic blood pressure), analysis metric (eg, change from baseline, final value, time to event), method of aggregation (eg, median, proportion), and time point for each outcome. Explanation of the clinical relevance of chosen efficacy and harm outcomes is strongly recommended	10-12 & Table 1
Participant timeline	#13	Time schedule of enrolment, interventions (including any run-ins and washouts), assessments, and visits for participants. A schematic diagram is highly recommended (see Figure)	Figures 2 & 3
Sample size	#14	Estimated number of participants needed to achieve study objectives and how it was determined, including clinical and statistical assumptions supporting any sample size calculations	17

Recruitment	#15	Strategies for achieving adequate participant enrolment to reach target sample size	17-18
Allocation: sequence generation	#16a	Method of generating the allocation sequence (eg, computer-generated random numbers), and list of any factors for stratification. To reduce predictability of a random sequence, details of any planned restriction (eg, blocking) should be provided in a separate document that is unavailable to those who enroll participants or assign interventions	9
Allocation concealment mechanism	#16b	Mechanism of implementing the allocation sequence (eg, central telephone; sequentially numbered, opaque, sealed envelopes), describing any steps to conceal the sequence until interventions are assigned	9
Allocation: implementation	#16c	Who will generate the allocation sequence, who will enroll participants, and who will assign participants to interventions	9
Blinding (masking)	#17a	Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how	N/A
Blinding (masking): emergency unblinding	#17b	If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during the trial	N/A
Data collection plan	#18a	Plans for assessment and collection of outcome, baseline, and other trial data, including any related processes to promote data quality (eg, duplicate measurements, training of assessors) and a description of study	10-12

		instruments (eg, questionnaires, laboratory tests) along with their reliability and validity, if known. Reference to where data collection forms can be found, if not in the protocol	
Data collection plan: retention	#18b	Plans to promote participant retention and complete follow-up, including list of any outcome data to be collected for participants who discontinue or deviate from intervention protocols	16
Data management	#19	Plans for data entry, coding, security, and storage, including any related processes to promote data quality (eg, double data entry; range checks for data values). Reference to where details of data management procedures can be found, if not in the protocol	N/A
Statistics: outcomes	#20a	Statistical methods for analyzing primary and secondary outcomes. Reference to where other details of the statistical analysis plan can be found, if not in the protocol	16-17
Statistics: additional analyses	#20b	Methods for any additional analyses (eg, subgroup and adjusted analyses)	16-17
Statistics: analysis population and missing data	#20c	Definition of analysis population relating to protocol non-adherence (eg, as randomized analysis), and any statistical methods to handle missing data (eg, multiple imputation)	16-17
Data monitoring: formal committee	#21a	Composition of data monitoring committee (DMC); summary of its role and reporting structure; statement of whether it is independent from the sponsor and competing interests; and reference to where further details about its charter can be found, if not in the protocol. Alternatively, an explanation of why a DMC is	N/A

		not needed	
Data monitoring: interim analysis	#21b	Description of any interim analyses and stopping guidelines, including who will have access to these interim results and make the final decision to terminate the trial	N/A
Harms	#22	Plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial conduct	N/A
Auditing	#23	Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor	N/A
Research ethics approval	#24	Plans for seeking research ethics committee / institutional review board (REC / IRB) approval	18-19
Protocol amendments	#25	Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators, REC / IRBs, trial participants, trial registries, journals, regulators)	N/A
Consent or assent	#26a	Who will obtain informed consent or assent from potential trial participants or authorized surrogates, and how (see Item 32)	18
Consent or assent: ancillary studies	#26b	Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable	N/A
Confidentiality	#27	How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial	N/A
Declaration of	#28	Financial and other competing interests for	21

interests		principal investigators for the overall trial and each study site	
Data access	#29	Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators	N/A
Ancillary and post trial care	#30	Provisions, if any, for ancillary and post-trial care, and for compensation to those who suffer harm from trial participation	N/A
Dissemination policy: trial results	#31a	Plans for investigators and sponsor to communicate trial results to participants, healthcare professionals, the public, and other relevant groups (eg, via publication, reporting in results databases, or other data sharing arrangements), including any publication restrictions	18-19
Dissemination policy: authorship	#31b	Authorship eligibility guidelines and any intended use of professional writers	N/A
Dissemination policy: reproducible research	#31c	Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code	19
Informed consent materials	#32	Model consent form and other related documentation given to participants and authorized surrogates	N/A
Biological specimens	#33	Plans for collection, laboratory evaluation, and storage of biological specimens for genetic or molecular analysis in the current trial and for future use in ancillary studies, if applicable	N/A