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Title: Feasibility of a Colorectal Cancer Screening Web App in Primary Care Patients

ClinicalTrials.gov: NCT06241768

Participating Institution(s): Wake Forest Baptist Comprehensive Cancer Center

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IRB Protocol Approval Date: January 25, 2024

Confidential

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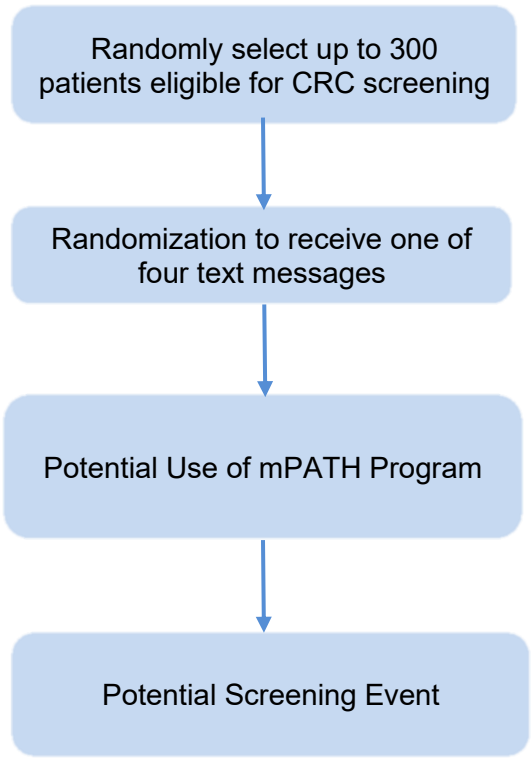
SCHEMA


Randomly select up to 300 patients eligible for CRC screening
Randomization to receive one of four text messages
Potential Use of mPATH Program
Potential Screening Event

1.0 Introduction and Background

Screening for colorectal cancer is widely recommended but underused. Colorectal cancer (CRC) screening is cost-effective and reduces both CRC mortality and incidence by detecting and removing pre-cancerous polyps.1–4 Regular screening for CRC beginning at age 45 is widely recommended by several groups, including the United States Preventive Services Task Force.5–7 Nonetheless, over 30% of Americans are unscreened.8

Screening rates are even lower among underserved populations, contributing to health disparities.9,10 Individuals who are Black, Hispanic/Latinx, have less education, limited income, or rural residences are less likely to be screened, and thus more likely to present with advanced-stage CRC and die from it.11–16 Limited health literacy, which affects over 33% of American adults, further interferes with patients' ability to access and use health information.17–21

Our mPATH™ (mobile PAtient Technology for Health) digital health navigator program overcomes the multilevel barriers to CRC screening. Barriers to CRC screening include patient factors (lack of knowledge, low self-efficacy, fears, negative attitudes)23–29 and provider/system factors (lack of time, failure to offer screening options, lack of patient support).30–34 mPATH™ addresses these barriers by determining if patients are due for screening, educating patients about screening options, and letting patients request a test directly via the program. mPATH™ also sends patients supportive text messages to help them complete their chosen test.

In a rigorous randomized controlled trial of 450 patients, an iPad version of mPATH™ for CRC screening (mPATH™-CRC) doubled CRC screening rates in a population prone to health disparities and was well accepted.35–37 Patients used mPATH™-CRC immediately before a scheduled primary care visit at one of six community-based practices. Compared to patients randomized to usual care, twice as many patients completed a CRC screening test (30% vs 15%, p=0.0001).35 Patients in this study faced significant barriers to care; over 50% reported annual household incomes less than $20,000 and over one-third had limited health literacy. Almost all patients rated the user-friendliness of the program as "excellent"(82%) or "good"(16%).36

Incorporating patient decision aids like mPATH™ in clinical care is challenging. We are currently conducting a hybrid implementation-effectiveness study of the mPATH™-CRC iPad app in which office staff hand mPATH™ to patients as part of routine care. As of August 2022, mPATH™ has identified over 3600 patients who are overdue for CRC screening, but nursing staff have given the mPATH™-CRC app to less than 20% of these patients, resulting in tremendous missed opportunities. While our implementation study is still ongoing, we have already identified several important variables (time pressures, staff turnover, and the COVID19 pandemic) significantly hampering clinics' ability to implement mPATH™.

Delivering mPATH™ to patients at home on their own devices via the cloud is a promising strategy. Over 90% of American adults have internet access at home, including 85% who own a smartphone.38 While home broadband access shows a digital divide, smartphone ownership is similar across racial/ethnic groups.38 Even among rural residents, those with a high school education or less, and individuals with annual household incomes less than $30,000, smartphone ownership exceeds 75%.38 The growing ownership of smartphone and tablet devices offers new opportunities to reach broadly into patient populations. We previously

developed and pilot tested a cloud-based version of mPATH™ for lung cancer (mPATH™-Lung). In a highly pragmatic feasibility study, we sent 1000 patients electronic invitations to use mPATH™-Lung, and 41% (410) visited the mPATH™-Lung Web App and 85% of all visitors (365) completed the program. Therefore, a cloud-based version of mPATH™-CRC has great potential to reach patients and increase CRC screening independent of a medical visit, which is especially important for the 15% of adults who have not seen a doctor in the last year.39 We hypothesize that at least 25% of patients who are overdue for CRC screening and use a cloud-based version of mPATH™-CRC will request a screening test via the program, demonstrating the feasibility of this strategy.

2.0 Objectives

2.1 Primary Objective

2.1.1 Evaluate the feasibility of the cloud-based version of mPATH-CRC in a large health system.

2.2 Exploratory Objective

2.2.1 Examine the response rates to different versions of the outreach invitation messages created with community member input.

3.0 Study Population

3.1 Inclusion Criteria

3.1.1 Meet the U.S. Preventive Services Task Force (USPSTF) criteria for colorectal cancer screening.

3.1.1.1 Age 45 to 75 years.

3.1.1.2 No record of current colorectal cancer screening.

3.1.2 Have a cell phone number listed in the electronic health record.

3.1.3 Language preference of English in the electronic health record.

3.2 Exclusion Criteria

3.2.1 Prior diagnosis of colorectal cancer.

3.2.2 Prior diagnosis of inflammatory bowel disease.

3.2.3 Have a record of completing a colonoscopy within the last 10 years, a FIT-DNA test in the last 3 years, or a FIT in the last 1 year based on the electronic health record.

3.2.4 Patients who may be inappropriate candidates for colorectal screening based on comorbidities (electronic Charlson Comorbidity Index > 2).

3.3 Inclusion of Women and Minorities

Participants of all races and ethnicities who meet the above-described eligibility criteria are eligible to participate in this study.

Based on WFBCCC population estimates, we expect approximately 55% of participants to be women. We will oversample for non-white patients with the goal of creating a final study sample that is approximately 50% non-Hispanic white, at least 20% Black, and at least 20% Hispanic/Latinx. We anticipate 2% or less of our sample will identify as American Indian, Asian, Hawaiian/Pacific Islanders, or more than one race, reflecting the low prevalence of these races/ethnicities in the health system's older patient population. Translating this to our sample size estimate of 240, we plan to enroll at least 132 women. Similarly, we expect approximately 20% of study participants to be Hispanic/Latino (N = 48). We plan to enroll at least 20% Black or African American (N = 48), 2% or less will be American Indian, Asian, Hawaiian/Pacific Islanders, or more than one race (N = 4). Should we not meet or exceed these estimates, the PI will engage the Office of Cancer Health Equity to discuss strategies to enhance recruitment in these target populations.

3.4 Registration Procedures

The intervention will be developed with input from focus groups. We will hold two focus groups of 8 – 12 patients each (one English speakers and one Spanish speakers) to review the animated "core content" of the video and the collected video clips of patient testimonials. We will give these participants a study information sheet explaining the purpose of the study, the nature of the data to be collected, and the voluntary nature of their participation.

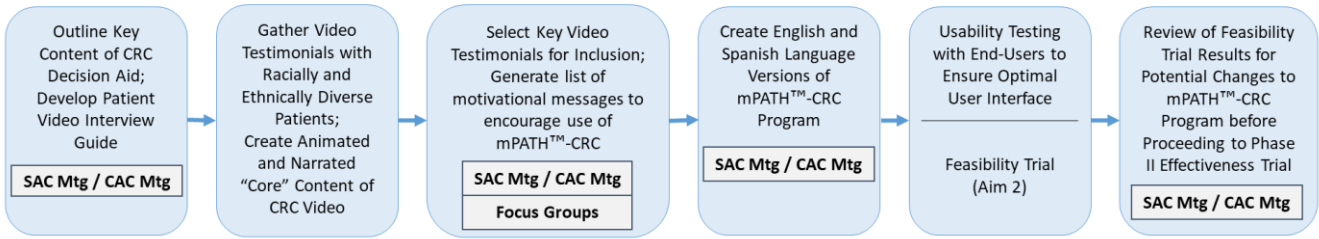
After the intervention is finalized, patients will be participating in a pragmatic trial in which patient data collection will occur by retrospective electronic chart review. All patients will receive current guideline-recommended care, and we will request a waiver of patient Informed Consent. Therefore, it is impractical to register patients with the Cancer Center, and any such registration would jeopardize patient confidentiality.

4.0 Methods for Intervention Creation

4.1 Formation of Scientific and Community Advisory Committees

To ensure the intervention is culturally appropriate and addresses relevant barriers to screening, we will form a Scientific Advisory Committee and a Community Advisory Committee to guide our work. The Scientific Advisory Committee (SAC) will be comprised of nationally-known researchers with deep expertise examining and addressing barriers to CRC screening in racial and ethnic subgroups. The Community Advisory Committee (CAC) will have 6 members that include leaders of organizations that serve the Black/African American and Hispanic/LatinX communities and members of those communities. We will form the CAC in collaboration with the Wake Forest Maya Angelou Center for Health Equity and the CTSI Program in Community Engagement. Both groups have deep ties to the community. The SAC and CAC will meet at key points in the development of the revised mPATH™-CRC decision aid (**Figure 2**). At the initial meeting, the SAC and CAC will review and provide input on: 1) our outline for key content to include in the revised mPATH™-CRC decision aid, and 2) the semistructured interview guide that will be used to capture patient testimonials to ensure that appropriate questions are asked to reveal potential screening barriers and garner culturally appropriate information.

Figure 2. Overview of process for revising mPATH-CRC program



4.2 Video Testimonial Recruitment

We will query the EHR to identify patients aged 45 to 75 with a preferred language of Spanish or English who: 1) were seen at one of three Atrium Health Wake Forest Baptist primary care practices, and 2) completed a screening colonoscopy or FIT in the past 6 months. To help us recruit a diverse sample, we will abstract patient gender, race/ethnicity, age, health insurance status, preferred language, phone number, date of colonoscopy, date of FIT, screening test results. We will give the primary care providers in these three practices a list of their patients who met our EHR inclusion criteria, and we will ask the providers to nominate patients who they think may be interested in participating in a video interview. A study team member will then call the nominated patients to inform them of the study, and if interested, administer a brief eligibility questionnaire. Based on responses to the questionnaire, we will exclude patients with a history of CRC or inflammatory bowel disease.

Our goal is to interview up to 18 patients, selected to reflect diversity in age, race/ethnicity, gender, and type of screening test completed. We will schedule each participant for an individual 20-30 video interview held in a private location. Interviews will be conducted in the patient's preferred language, either English or Spanish. A trained interviewer will conduct each interview using a semi-structured interview guide. We will select clips from these interviews for potential inclusion in the revised CRC video decision aid.

4.3 Focus Group Recruitment

We will query the EHR to identify patients aged 45 to 75 with a preferred language of Spanish or English who are seen at one of four Atrium Health Wake Forest Baptist primary care practices and serve a racially/ethnically and socioeconomically diverse population. We will exclude patients who have a prior diagnosis of CRC or inflammatory bowel disease. We will selectively

recruit patients by phone and patient portal messages to ensure good representation of age, gender, race, insurance status, and screening status. We plan include between 16-24 participants in total for these focus groups.

4.4 Focus Group Sessions

A trained moderator will lead each focus group using a moderator's guide developed by the study team. Each focus group will first review the animated core content of the CRC screening video decision aid. Questions from the moderator's guide will probe to determine if any parts of the video could be improved for clarity or acceptability. Participants will then review the patient testimonial clips grouped by theme (motivators, barriers, rationale). We will ask participants to identify which testimonials they feel should be included in the final video and why. Next, each focus group will be presented with the sample outreach messages generated with the input from the Scientific Advisory Committee (SAC) and Community Advisory Committee (CAC). The moderator's guide will explore participants' reactions to the messages, content/language that is viewed favorably or unfavorably, and suggestions for improving the messages. Additionally, focus groups will be asked to suggest their own messages that would motivate others to use mPATH™. Each participant will receive a $50 gift card. Results from the focus groups will be used to finalize the CRC screening decision aid video and outreach messages for the pragmatic trial.

The full moderator's guide will be submitted to the IRB for review and approval prior to being used.

4.5 Usability Testing

Patients will be recruited from Atrium Health Wake Forest Baptist Family Medicine – Bermuda Run, by flyer as well as community-based sampling. Patients may be eligible to participate if they are aged 45 to 75 and have a smartphone. Patients who are interested in participating will be asked to use the web app on their own smartphone. They will be asked questions about the web app's usability. Results from the interviews will be used to finalize the program. Patients will receive a $50 gift card as a thank you. The study team will interview up to 25 patients.

5.0 Methods for Pragmatic Trial

5.1 Participant Recruitment

We will request a waiver of informed consent from the Wake Forest IRB to allow our highly pragmatic testing since the mPATH™-CRC web application delivers guideline recommended care and not experimental care.

Each week we will query the EHR to randomly select 240 potentially eligible patients who have no record of current CRC screening. We will oversample by race and ethnicity. We will then randomize these 240 patients, to receive one of four outreach messages with equal probability.

Patients will receive the invitation message as a HIPAA-compliant text message. Each invitation message includes an embedded hyperlink to the web app appended with an anonymous study identifier that allows us to track who visits mPATH™. A reminder message will be sent once weekly for two weeks (no more than 3 messages total). We will continue to send weekly outreach messages until 120 patients who are overdue for CRC screening complete the mPATH™-CRC web app.

Low socioeconomic status individuals are more likely to suffer health disparities from colorectal cancer. Therefore, it is critically important to include low income participants in colorectal cancer screening studies. To avoid coercion, participant incentives will not exceed $50.

5.2 mPATH™-CRC Intervention

The mPATH™ homepage will inform visitors that by using the program, their deidentified data may be used in research. The mPATH™-CRC Web App takes approximately 8 to 10 minutes to complete. It begins with a brief overview of the importance of CRC screening. Then the Web App confirms patients are due for routine CRC screening and have no risk factor that would necessitate specialized screening considerations. Patients with a risk factor will be informed of their risk status and encouraged to discuss screening with their primary care provider. Patients who are confirmed due for CRC screening and are at average risk will then be shown our updated animated and narrated CRC screening decision aid video that reviews the CRC screening tests offered by each healthcare organization: colonoscopy, FIT-DNA, and FIT. Lastly, patients can request a CRC screening test directly through the mPATH™ program. mPATH™ automatically transmits test requests to the appropriate personnel (patient navigators or clinical staff) at our partnering healthcare organizations via its secure referral dashboard. These personnel then ensure requested home-based testing is delivered or colonoscopies are scheduled. Patients who request a screening test have the option to sign up for automated text message reminders to help them complete their chosen test, as we used in our prior study.[35]

5.3 Usual Care

Patients who are not randomly selected to receive an invitation will receive usual care, which includes the organizations' standard procedures for addressing CRC screening. At AHWFB, the EHR flags patients who are overdue for CRC screening as a "care gap" that is visible to all primary care providers.

6.0 Outcomes Measures

6.1 Primary Outcome

6.1.1 Proportion of patients who are confirmed eligible for CRC screening and request a CRC screening test within the mPATH-CRC Web App.

6.2 Exploratory Outcome

6.2.1 Proportion of participants who complete the CRC screening eligibility questions within 4 weeks of the initial invitation using the mPATH-CRC Web App.

7.0 Analytic Plan

7.1 Sample Size and Power

We will consider that the cloud-based mPATH™-CRC program is feasible for increasing CRC screening uptake if at least 25% of patients who complete the app request a screening test via

the program. We chose 25% as our threshold because we acknowledge that patients may not complete screening tests they request. If only half of patients complete their requested test (which is what we observed in our prior trial), a 25% test-request rate would increase overall screening rates by 12.5%, a clinically meaningful effect for a low cost intervention.

In our ongoing study of the iPad-version of mPATH™-CRC, 38% of patients who complete the program are requesting a screening test. Conservatively assuming the actual rate of requesting a screening test in the cloud-based version is 30%, a sample size of 120 patients will result in a 90% probability of demonstrating feasibility by observing a rate of at least 25%. Therefore, messages will be sent until 120 patients have completed the app in order to evaluate feasibility. Full operating characteristics of this feasibility design for a sample size of 120 are included in table below.

Table. Feasibility operating characteristics for a sample size of 120

True Rate of Requesting a Screening Test	Probability of Demonstrating Feasibility
10%	<0.001
15%	0.003
20%	0.107
25%	0.535
30%	**0.904**
35%	0.993
40%	>0.999

In our ongoing trial of the iPad version of mPATH™, 50% of patients who have no record of current CRC screening in the EHR report current screening in the mPATH™ app. Based on this experience, we will conservatively estimate that 25% of patients will respond to our invitations and 50% of patients who use mPATH™ will meet our inclusion criteria of being due for CRC screening (with no risk factors) resulting in an overall weekly accrual rate of 30 patients (25% x 50% x 240). Therefore, while the sample size for our main feasibility outcome of screening decisions is 120 patients, approximately 1000 (250 per message) patients will receive an invitation for our exploratory analysis of message response rates. With a sample size of 250, the proportion who use the web app can be estimated to +/- 6.4% based on a 95% confidence interval. Based on oversampling for race/ethnicity, we anticipate that at least 50 patients from each race/ethnicity group will receive each message. With a sample size of 50, the proportion who use the web app can be estimated to +/- 14.5% based on a 95% confidence interval. The precision estimates are based on a 50% response rate as this gives the maximum half-width of a confidence interval, and therefore provides the most conservative estimate around precision.

7.2 Analysis of Primary Outcome

Feasibility will be claimed if at least 25% of patients who complete the app (regardless of randomization group) request a screening test via the program. Completion of the app is defined as using the program to a point of indicating their screening decision. This proportion will be reported along with a 95% confidence interval.

7.3 Analysis of Exploratory Outcome

Use of the web app will be defined as completing the web app's eligibility questions for CRC screening. For each of the four messages, we will calculate the proportion who use the web app

with a 95% confidence interval. We will also calculate the proportion who use the web app with a 95% confidence interval separately for each race/ethnic group for each of the four messages. We will assess for differences in response rates between messages using chi-square tests or Fisher's exact tests as appropriate. All tests will be 2-sided with a significance level of 0.05.

7.4 Estimated Accrual Rate

Based on our ongoing trial experience, we will conservatively estimate that 25% of patients will respond to our invitations and 50% of patients who use mPATH will meet our inclusion criteria of being due for CRC screening without any risk factors resulting in an overall weekly accrual rate of 30 patients (25% x 50% x 240). We plan to closely monitor the accrual rate and will discontinue sending messages once 120 patients have used the app.

7.5 Estimated Study Length

Activity / Month	1	2	3	4	5	6	7	8	9	10	11	12
mPATH tech stack transfer / development	X	X	X									
Develop video interview guide; SAC/CAC meeting #1	X											
Gather CRC screening patient video testimonials		X	X									
Focus groups and SAC/CAC meeting #2 to select content for revised video and draft outreach messages				X	X							
Create final English and Spanish language videos; SAC/CAC meeting #3					X	X						
Usability testing and refinement of mPATH™ cloud app							X	X				
Feasibility testing of mPATH™-CRC cloud app									X	X	X	
SAC/CAC meeting #4 to review results												X

8.0 Confidentiality and Privacy

Confidentiality will be protected by collecting only information needed to assess study outcomes, minimizing to the fullest extent possible the collection of any information that could directly identify subjects, and maintaining all study information in a secure manner. To help ensure subject privacy and confidentiality, only a unique study identifier will appear on the data collection form. Any collected patient identifying information corresponding to the unique study identifier will be maintained on a linkage file, store separately from the data. The linkage file will be kept secure, with access limited to designated study personnel. The linkage file will be kept secure, with access limited to designated study personnel. An honest broker will mediate the electronic health record data queries to limit the exposure of patient identifying information. All personal identifiers (other than dates of service and patient zip code) will be removed from the study datasets and only the study ID included. One year after publication of the main study findings, the linkage file will be destroyed (electronically deleted or shredded in the case of paper forms). Data access will be limited to study staff. Data and records will be kept locked and

secured, with any computer data password protected. No reference to any individual participant will appear in reports, presentations, or publications that may arise from the study.

9.0 Data Safety and Monitoring

The principal investigator will be responsible for the overall monitoring of the data and safety of study participants. The principal investigator will be assisted by other members of the study staff.

The only anticipated risks specific to this study are loss of data confidentiality. The research team will form an internal Data and Safety Monitoring committee, comprised of the PI from DHN Solutions, Site Lead Investigator from Wake Forest, Wake Forest Project Manager, and study statistician (Snavely). DHN Solutions' cloud platform uses Microsoft Azure. Azure has enabled the physical, technical, and administrative safeguards required by HIPAA and the HITECH Act inside the in-scope Azure services, and offers a HIPAA BAA as part of the Microsoft Product Terms to all customers who are covered entities or business associates under HIPAA for use of such in-scope Azure services. In the BAA, Microsoft makes contractual assurances about data safeguarding, reporting (including breach notifications), data access in accordance with HIPAA and the HITECH Act, and many other important provisions. Microsoft adheres to the HIPAA Security Rule requirements in its capacity as a business associate. Microsoft Azure is an official partner of the NIH STRIDES initiative.

All of DHN Solutions devices will have encrypted storage. The DHN Solutions PI will convene the Data and Safety Monitoring committee if any security breaches are detected. Data quality reports will be run weekly to assure fidelity to the study protocol and integrity of the data. The PI and Wake Forest Site Lead Investigator will promptly review any participant or other-reported concerns regarding the study. The PI will report any loss of data confidentiality or other adverse event to the Wake Forest IRB and the NIH within 2 business days of the discovery the event.

10.0 Reporting of Unanticipated Problems, Adverse Events or Deviations

Any unanticipated problems, deviations or protocol changes will be promptly reported by the principal investigator or designated member of the research team to the IRB and sponsor or appropriate government agency if appropriate.

References