Improving Colorectal Cancer Screening in Racially Diverse Zip Codes Using Navigation and Machine Learning (PCSNaP)

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PA-20-272 "Administrative Supplements to Existing Grants and Cooperative Agreements (Parent Admin Supplement)": **A Feasibility Study to Improve Colorectal Cancer Screening among Racially Diverse Zip Codes in a Persistent Poverty County using Navigation and Machine Learning Predictive Algorithms**

Abstract

The overarching goals of this Administrative Supplement to Existing NIH Grants and Cooperative Agreements (PA-20-272, Parent Admin Supplement) is to support the Abramson Cancer Center (ACC) of the University of Pennsylvania in carrying out its mission to increase colorectal cancer (CRC) screening completion among high-risk individuals living in a persistent poverty county by designing, conducting, disseminating and evaluating an electronic health record-based automated identification program to target effective, culturally-sensitive CRC screening navigation to individuals who have not completed an ordered colonoscopy or fecal immunochemical test (FIT).

Specifically, the goals of this supplement are to: 1) Adapt a previously validated electronic health record (EHR)-based machine learning algorithm to predict CRC detection by retraining the model using data from patients seen in primary care clinics serving zip codes with a high proportion of racial and ethnic minorities living in Philadelphia County, a persistent poverty county; and 2) Implement and evaluate the feasibility and effectiveness of an algorithm-based CRC navigation program to increase colorectal cancer screening among patients in Philadelphia county who are at high risk of CRC and have uncompleted colonoscopies.

Together, these novel projects aim to be the first to combine use machine learning algorithms and patient navigation to increase guideline-based cancer screening in order to reduce the burden of CRC among high-risk individuals living in a persistent poverty county through targeted, culturally-sensitive navigation that addresses social factors that prevent CRC screening. This study will generate preliminary data in support of an R01 application to scale algorithm-informed cancer screening navigation in persistent poverty areas.

Specific Aims

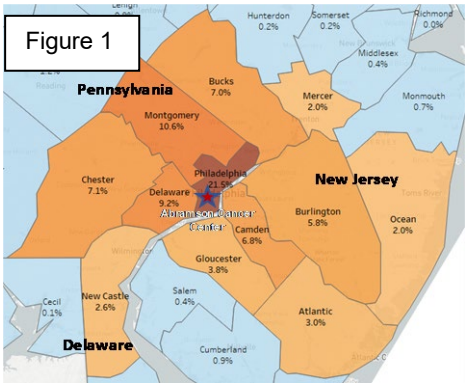
Aim 1: Adapt a previously validated machine learning algorithm to predict risk of colorectal cancer or adenoma among a retrospective cohort of Penn Medicine patients living in vulnerable zip codes within Philadelphia County. We will improve upon a previously validated machine learning algorithm[1] to predict risk of colorectal cancer by (1) re-training the model to predict both cancer and adenoma detection; (2) integrating additional clinical and socioeconomic risk factors for colorectal cancer risk; and (3) retraining the model in a cohort of individuals living in Philadelphia County zip codes that are minority-predominant and have lowest median incomes in the county. We will compare algorithm performance to existing criteria, based on age and prior colon cancer screening history, which are currently used to stratify colorectal cancer risk among Penn Medicine patients. We hypothesize that machine learning models will maintain good performance in predicting CRC risk among a community living in a persistent poverty area.

Aim 2. Test the feasibility, usability, and effectiveness of algorithm-informed navigation on colorectal cancer screening rates and adenoma detection rates among Penn Internal Medicine and Family Medicine patients residing in racially and ethnically diverse zip codes. We will use the machine learning algorithm developed in Aim 1 to inform the CRC screening navigation program process and evaluate its impact on the identification of Penn Internal Medicine and Family Medicine patients with adenomas and CRC. We will generate automated monthly lists of Penn Medicine Internal and Family Medicine patients from diverse communities ranked by predicted cancer risk. High-risk patients will be prioritized for navigation of socioeconomic and financial barriers to colonoscopy through an existing navigation program created and managed by our team at the University of Pennsylvania.[2] In addition to assessing feasibility and usability, we will evaluate the effectiveness of the program on rates of completed colonoscopies and rates of CRC/adenoma detection, compared to historical rates prior to the intervention. We hypothesize that algorithm-informed navigation will improve CRC screening rates and cancer/adenoma detection rates.

Need for Cancer Control Program in Philadelphia County

Nearly 150,000 individuals will be diagnosed with colorectal cancer in 2020 in the United States, with incidence and cancer-associated mortality higher for African-Americans and other minorities.[3,4] The ACC's 12-county catchment area is comprised of urban and suburban counties in southeastern Pennsylvania (Bucks, Chester, Delaware, Montgomery, Philadelphia), southern New Jersey (Atlantic, Burlington, Camden, Gloucester, Mercer, Ocean), and Delaware (New Castle) (**Fig. 1**). These 12 counties have a population of 7,015,781 residents and capture the residences of 81.4% of the patients seen at ACC.

Figure 1



There is greater incidence and mortality from CRC in the ACC catchment area compared to the general US population. (**Table 1**). **Philadelphia County, which contributes 21.5% of the patients seen at ACC, has an even higher CRC incidence and mortality compared to the rest of the catchment area and the US. Furthermore, Philadelphia County is a persistent poverty county,** with 23% of patients living in poverty (90% confidence interval 21.8-24.2%).[5] Philadelphia County has the second highest poverty rate in the state of Philadelphia, with over 352,748 residents living in poverty. In 25 of the city's 46 residential zip codes, more than 1 in 5 individuals are living below the poverty line.[6] In Philadelphia, the poverty rate is roughly 19% among whites and 29%

Table 1. Age-adjusted rates per 100,000 for colorectal cancer incidence and mortality by race and geography

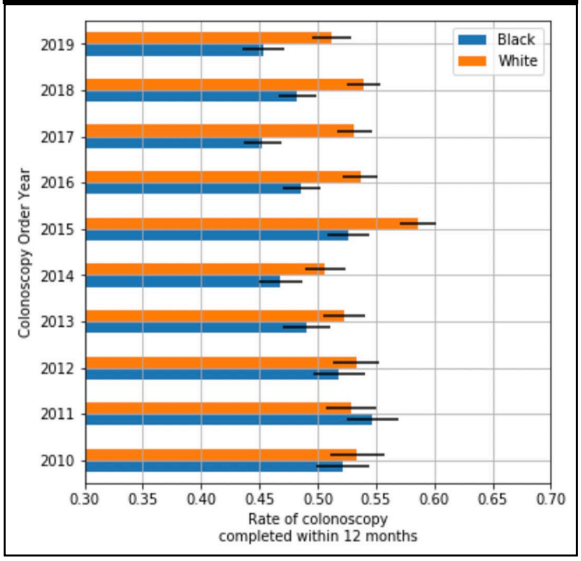
	Entire ACC catchment area				Philadelphia County				non-Philadelphia catchment area				United States			
Colorectal	Incidence		Mortality		Incidence		Mortality		Incidence		Mortality		Incidence		Mortality	
	W†	B	W	B	W	B	W	B	W	B	W	B	W	B	W	B
	41.8	45.0	14.4	17.5	46.8	47.1	15.1	20.4	41.1	43.2	14.3	14.7	38.4	45.7	14.1	19.4

Sources: PA, NJ and DE state cancer registries, SEER; 2011-2015.*ages 0-14; †W - White; B - Black; red shade > US, green shade < US (non-overlapping 95% CIs and > 10% difference)

among African-Americans. Poverty is strongly associated with CRC incidence and with minority communities.[7–9] Furthermore, there are racial inequities in CRC incidence and mortality in all of the geographic areas analyzed**: African-American residents consistently have a higher incidence and mortality from CRC compared to White residents.**

While colorectal cancer screening may reduce cancer-associated mortality, African-Americans in Philadelphia County are over 10 percentage-points less likely to be adherent to colorectal cancer screening guidelines compared to Whites. Despite the proven benefit of regular colonoscopy, CRC screening adherence rates remain only around 50% for Penn Medicine primary care patients. Furthermore, screening rates are consistently worse for African-Americans than White individuals – and this disparity is widening at Penn Medicine (**Fig. 2**). **For this reason, Penn Medicine, a safety net provider for low income, underserved patients in Philadelphia, has instituted a system-wide goal of improving CRC screening for African-American patients.**

Figure 2. CRC screening in Philadelphia county



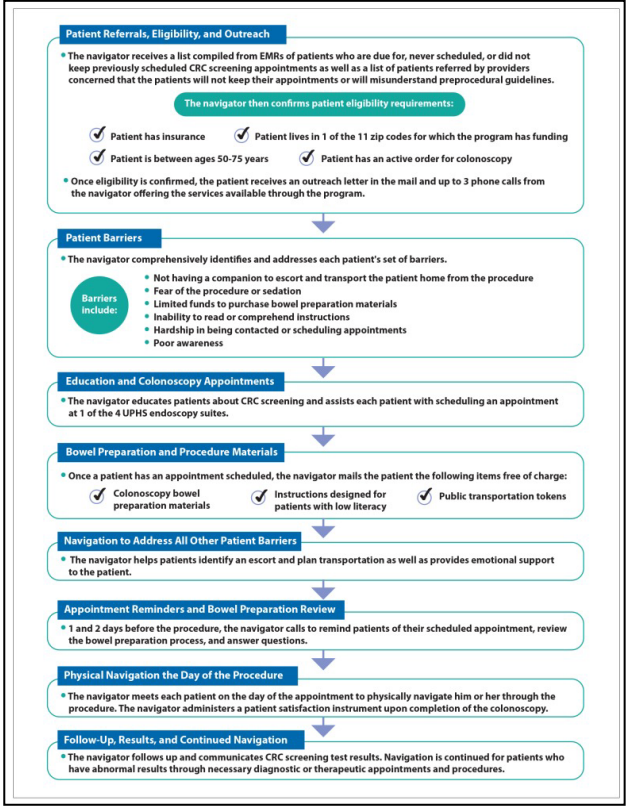
Existing Services

Colorectal cancer screening navigator program: Adverse social determinants of health such as lack of transportation access contribute to CRC screening nonadherence disproportionately for African-American and other minority communities. Recognizing this, in 2011, Penn Medicine created a navigation program to address poor CRC screening rates and increase access to screening colonoscopies for patients in underserved areas of West, South, and Southwest Philadelphia.[2] The navigation program provides services to address barriers to cancer screening; these include transportation assistance, detailed instructions on bowel prep, or mailed FIT test for average-risk patients who refuse colonoscopy (see **Fig. 3**). Eligible patients have had a colonoscopy order placed in the past six months and have not scheduled, cancelled, or no-showed to their colonoscopy. Among eligible patients contacted by the navigator program, 50% agree to a colonoscopy over the phone. Of those patients, 80% complete a colonoscopy. The CRC screening navigator program is currently staffed by 1.5 FTE staff, including the nurse lead of the navigator program **Diann Boyd**, BSN, RN, OCN (see attached **Letter of Support**) and a part-time clinical assistant. Our prior research has shown that navigated patients have a high rate of colorectal cancer screening completion (79%) and a significantly lower rate of cancelled and/or skipped appointments.[2] In addition, those who were screened as a result of the program had a much higher

adenoma detection rate (40%). An adenoma detection rate of 40% is an increase of at least 15 percentage points, or a 60% increase, over the national benchmark of 15% to 25%.

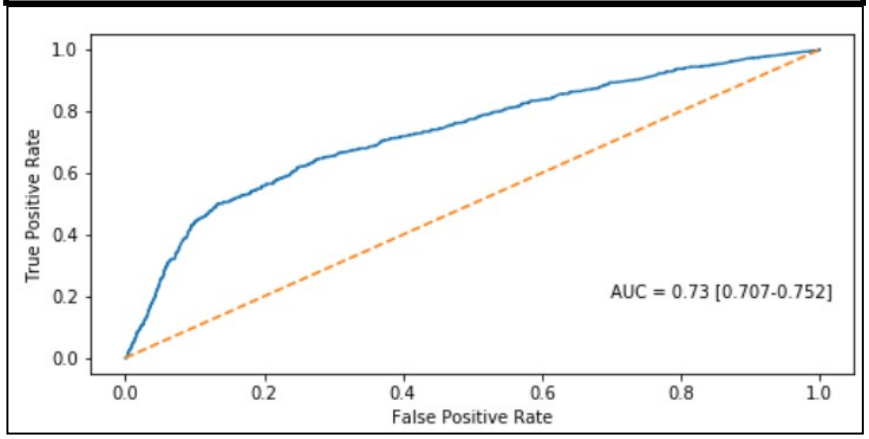
Patients and clinics served: Currently the On July 1, 2015, the program was enlarged and institutionalized by Penn Medicine with expansion from 5 to 11 zip codes to include Southwest and South Philadelphia. On January 1, 2021, the program expanded from 11 to 18 zip codes throughout Philadelphia County. Currently patients receiving care at one of 4 Internal Medicine practices located in Philadelphia County participate in the program. Another key goal of Penn Medicine is to expand navigation services beyond Internal Medicine to other types of primary care practices, including 3 Family Medicine practices in Philadelphia County. **As part of the resulting expansion of patients requiring navigation, additional FTE navigation staff will be needed and are requested as part of this Administrative Supplement.** Additionally, a key challenge in scaling this navigation program is identifying patient populations at increased risk of CRC, who may benefit most from timely navigation. While risk stratification guidelines exist to determine who should be prioritized for colonoscopy[10], these require time-consuming chart review and may not be adequately sensitive. Automated machine learning algorithms based on routine EHR data accurately estimate a patient's relative risk of CRC in multi-institutional studies.[1,11,12]

Figure 3. CRC navigator workflow



CRC risk algorithm: The Penn Predictive Healthcare Group is a Penn Medicine-employed team of data and human factors scientists. Their objective is to use EHR data to develop real-time, automated predictive models for use in inpatient and outpatient care settings to inform clinical care delivery. In collaboration with the Predictive Healthcare Group, we have adapted a previously published EHR-based ML algorithm[1] based on complete blood count records from EHR data, adding additional variables of significance including age, gender, BMI, alcohol and smoking status, and relevant comorbidities to generate a model with good discrimination (AUC 0.73), sensitivity (44%), and specificity (90%) in identifying future risk of CRC or adenoma (**see Fig. 4**). During the period of this award, the Data Science Team will retrain the algorithm in a racially and ethnically diverse subgroup residing and receiving care within Penn Medicine Internal and Family Medicine clinics located in Philadelphia County.

Figure 4. ML algorithm performance in unselected Penn Medicine cohort



Strategies to Elicit Needs

Given that we are utilizing a central navigator program that exists outside of the clinic and does not require additional clinic staff, in addition to the fact that outcomes will be identified from routine EHR records and not from dedicated research staff within clinics, we do not anticipate that there will be issues implementing this program into our target clinics given our preexisting infrastructure. However, we will take several steps to ensure clinics' feedback prior to Aim 2.

Focus groups: First, to ensure buy-in and feedback of the additional clinics participating in this program, we will conduct focus groups with relevant leadership from each of the 3 new clinics and each of the 4 older clinics.

The focus group will garner feedback about the intervention and strategies to integrate automated navigation services into routine workflow. This intervention will occur without physician referral; however, given that some automated predictions may be incorrect, we will display results from an algorithm that predicts both CRC and adenoma vs. a model that predicts CRC alone. We will elicit perspectives from these clinic groups about which algorithm they agree with the most, in order to determine which algorithm to proceed with for Aim 2.

PDSA cycles: After training the algorithm, we will conduct a 3-month pilot using patients from one primary care practice, using the Plan-Do-Study-Act (PDSA) Framework[13] to identify patient and clinic barriers to this research program. In the "Plan" stage, the critical elements are: (1) integrating flags for algorithm-predicted high-risk patients into existing automated lists given to the navigator program; (2) selection, training and defining the functions of the new CRC screening navigator; and (3) establishment of a network of clinic partners serving patients in the high poverty navigation program. The "Do" stage is focused on the implementation of an algorithm-facilitated navigation process to address the clinical and social barriers to CRC screening. The "Study" stage is defined by tracking enrolled patients and evaluating program measures that include completion of screening and adenoma detection rates and, then, in the "Act" stage, optimizing the program to expand the reach of the program to serve a broader population of patients, potentially even outside of Penn Medicine.

Approach

Aim 1. Validation of ML algorithm to predict colon cancer and adenoma risk

Study Design. Retrospective cohort study

Cohort. 60,270 unique patients without a prior CRC diagnosis who had a colonoscopy order placed by a Penn Internal Medicine or Family Medicine provider living in one of 18 minority-predominant zip codes in Western and Southwestern Philadelphia County; completed a colonoscopy at Penn between January 1st, 2010 and December 31st, 2019; and were seen by a Penn primary care physician in the preceding year. We will split the cohort into training (70%) and validation (30%) sets at the patient-level so that patients are represented in either the training or validation set only.

Outcome. The primary outcome will be biopsy-proven CRC or adenoma, based on (1) diagnostic or procedural codes for CRC or adenoma using previously published administrative code mappings[14,15]; and (2) internal datasets on Adenoma Detection Rate (ADR), generated by the Data Analytics Center using Provation and Clarity pathology data. Preliminary data suggest that 4,210 cases of CRC or adenomas exist in our cohort.

Predictors. We will use PennChart Clarity data form the 6 months prior to the colonoscopy as predictors in the model. Predictors will be adapted from prior literature and will include demographic (e.g. age, gender, EtOH history), comorbidity (e.g. anemia, inflammatory bowel disease), laboratory (e.g. hemoglobin, BUN), utilization (e.g. prior colonoscopy orders), and socioeconomic (e.g. area-level income and education) data.[1,11,12] Additionally, we will use the EPIC social determinants of health tool to extract features such as income, education level, and homelessness that may be association with CRC risk. .

Modelling strategy. We will compare the cross-validation predicted performance of several ML strategies, including logistic regression, random forest, gradient boosting, and recurrent neural networks, to identify the model with optimal predictive performance. We will report algorithm performance on the hold-out validation set, specifically testing for performance differences between the algorithms. Finally, we will compare performance of the best ML algorithm against an existing PennChart risk stratification model that uses only age and prior colorectal cancer screening utilization as predictors.

Performance metrics. Primary performance metrics will include area under the receiver operating characteristic curve (AUC), area under the precision-recall curve (AUPRC), and sensitivity.

Limitations. Administrative codes and internal ADR data may underestimate the true outcome rate, although the number of cases and event rate (7.0%) should still allow adequate model development.

Aim 2. Pilot testing of ML-facilitated colon cancer screening navigation

Study Design. Prospective cohort study with 3-month enrollment period and 3-month follow-up.

Cohort. The cohort will consist of patients residing in 18 zip codes in Western and Southwestern Philadelphia who have primary care providers in 4 Penn Medicine Internal Medicine practices and 3 Penn Medicine Family Medicine Practices. Patients will have had a colonoscopy order placed in the past 6 months and have not scheduled, cancelled, or no-showed to their colonoscopy.

Intervention. This intervention will utilize the existing Penn Medicine CRC patient navigation program; administrative supplement funding will be used to expand the staff from 1.5 FTE to 2.5 FTE. In the revised intervention, we will provide a monthly list of ~300 patients with unfilled colonoscopies, risk-stratified according

the ML algorithm and select high-risk criteria.[10] The navigation team will prioritize timely outreach and navigation to high-risk patients according to a script that communicates risk.

Outcome. The co-primary outcomes, measured within 3 months of enrollment, will be (1) enrollment in navigator program (feasibility); (2) completion of colonoscopy or FIT testing; and (3) adenoma detection rate.

Analysis Plan. We will use an intention-to-treat analysis. We will use propensity score matching using clinical and sociodemographic characteristics to create matched cohorts of patients between the intervention participants and historical controls from the same clinics in the year prior. We will then use logistic regression to assess the association between the intervention and the two primary outcomes, adjusted for age, gender, comorbidity, and area-level socioeconomic status.

Statistical Power. A sample of 344 participants (172 per group) will provide >90% power, assuming Type I error rate with a 2-sided α 0.05 and 50% dropout/refusal to participate to navigation, to detect a 20 percentage-point (pp) increase in colon cancer screening completion (40 → 60%, SD 20%) in the intervention group.

Work plan and timeline

As seen in our Gantt chart, we plan to complete all Aims within one year. This feasibility study will generate preliminary data within 1 year that will lead to an R-level grant application to support a well-powered cluster-randomized controlled trial that tests the impact of ML-guided patient navigation services on colorectal cancer screening rates and detection among Penn Medicine primary care practices within and outside of Philadelphia County serving underserved, high poverty areas. This R-level funding application will also be used support additional patient navigators to support this trial.

Tasks	Q1	Q2	Q3	Q4
Aim 1: Algorithm development				
Data cleaning and feature extraction	■			
Algorithm validation	■			
Algorithm IT integration	■			
Preparation of Manuscripts		■		
Aim 2: Feasibility study				
Focus groups		■		
PDSA cycles		■		
Recruitment for feasibility study			■	
Analyze data and post-study questionnaires				■
Preparation of manuscripts				■
R01 preparation				■

Sustainability

Our team maintains strong working relationship with the Colorectal Cancer Alliance (CCA) and Get Your Rear in Gear (GYRIG), both which are 501(c)3 nonprofit organizations whose mission is to reduce the burden of CRC in communities. The CCA and GYRIG have generous supported the Penn Medicine CRC screening navigation program with through their community health partnerships grant program for over eight years. We believe that our continued engagement with the CCA and GYRIG, in addition to planned R01 level funding, could lead to the organization expanding the navigator program to additional underserved communities and practices in zip codes beyond Philadelphia County. Additionally, future funding will help to support a dedicated data science specialist to improve the algorithm by mining unstructured clinical notes and pathology reports in order to better target the navigator program towards high-risk individuals.

Qualifications of program leads

The multidisciplinary team members proposed are: **Dr. Robert Vonderheide**, Director of the ACC at the University of Pennsylvania, Vice Dean for Cancer Programs for the Perelman School of Medicine at the University of Pennsylvania, and Vice President for Cancer Programs for the University of Pennsylvania Health System will serve as PI. **Dr. Ravi B. Parikh,** Assistant Professor of Medicine and Medical Ethics and Health Policy, is proposed as PD and will work with Dr. Guerra to oversee all aspect of the proposed work including design, implement and evaluation of the proposed work. **Dr. Carmen Guerra**, **MD, MSCE,** Associate Professor of Medicine, practicing general internist and Associate Director of Diversity and Outreach and co-leader of COE at the ACC is proposed as co-investigator and will work with Dr. Parikh to oversee all aspects of the proposed work including design, implement and evaluation of the proposed work. We will hire a **research coordinator** senior at the ACC, who will work with Drs. Vonderheide, Parikh, and Guerra to expand the reach of the navigator program; integrate algorithm output into the workflow of the navigator program; solicit feedback from patients, clinics, and navigators via regular questionnaires; assist in navigation of patients under supervision of Ms. Boyd; create the database and collect data; conduct analyses for the program evaluation; and present the results. In this application, the team will collaborate with **Michael Draugelis, MS** (see **Letter of Support**), Chair of the Penn Medicine Predictive Healthcare group, in order to integrate algorithm output into the navigator workflow.