



## Multi-component interventions and change in screening rates in primary care clinics in the Colorectal Cancer Control Program

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### ABSTRACT

Colorectal cancer (CRC) screening has been shown to decrease CRC mortality. Implementation of evidence-based interventions (EBIs) increases CRC screening. The purpose of this analysis is to determine which combinations of EBIs or strategies led to increases in clinic-level screening rates among clinics participating in CDC's Colorectal Cancer Control Program (CRCCP). Data were collected from CRCCP clinics between 2015 and 2018 and the analysis was conducted in 2020. The outcome variable was the annual change in clinic level CRC screening rate in percentage points. We used first difference (FD) estimator of linear panel data regression model to estimate the associations of outcome with independent variables, which include different combinations of EBIs and intervention strategies. The study sample included 486 unique clinics with 1156 clinic years of total observations. The average baseline screening rate was 41 % with average annual increase of 4.6 percentage points. Only two out of six combinations of any two EBIs were associated with increases in screening rate (largest was 6.5 percentage points,  $P < 0.001$ ). Any combinations involving three EBIs or all four EBIs were significantly associated with the outcome with largest increase of 7.2 percentage points ( $P < 0.001$ ). All interventions involving 2–3 strategies led to increases in rate with largest increase associated with the combination of increasing community demand and access (6.1 percentage points,  $P < 0.001$ ). Clinics implementing combinations of these EBIs, particularly those including three or more EBIs, often were more likely to have impact on screening rate change than those implementing none.

### 1. Introduction

Colorectal cancer (CRC) screening has been shown to decrease CRC mortality. (Mandel et al., 1993) The U.S. Preventive Services Task Force (USPSTF) recommends that adults aged 45–75 years receive CRC screening (until May 2021 the recommendation included adults aged 50–75) (United States Preventive Services Task Force) through stool-based tests or direct visualization tests, however as of 2018, only 69.6 % of U.S. adults aged 50–75 were up-to-date for CRC screening. (Centers for Disease Control and Prevention NCCDPHP, Division of Population Health, 2015) Racial and ethnic minority groups, such as those who are Black, as well as those who are uninsured, living under poverty, and living in rural areas suffer disproportionately from CRC, due in part to

lower guideline-concordant screening. (Printz, 2011; Singh and Jemal A., 2017; Singh et al., 2011; Joseph, 2016; Siegel et al., 2017; de Moor et al., 2018; Joseph et al., 2012; Demb and Gupta, 2020; Centers for Disease Control and Prevention).

Implementation of evidence-based interventions (EBIs) increases adherence to CRC screening, and use of those EBIs in settings that provide care to underserved populations has great promise to increase CRC screening. (Joseph, 2016; Community Preventive Services Task Force, 2021; Maxwell et al., 2014) EBIs for CRC screening include patient and provider-level interventions (e.g., patient and provider reminders, and provider assessment and feedback) and interventions that reduce healthcare access-related barriers (e.g., expanding clinic hours, offering transportation, providing language interpreters). Research has indicated

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that individual EBIs differ in the extent of their effectiveness; for example, studies have shown that provider assessment and feedback, client and provider reminders, and interventions that reduce structural barriers were more effective in increasing screening rates than EBIs, such as client reminders or SAs, such as patient navigators and small media. (Sharma et al., 2019) Research also suggests that multi-component interventions (i.e., implementation of multiple EBIs) are more effective in increasing CRC screening rates. (Joseph, 2016; Sharma et al., 2019; Davis et al., 2018; Adams et al., 2018) However, evidence regarding which combinations of EBIs are most effective in bolstering screening rates is limited.

Federally Qualified Health Centers (FQHCs) provide primary care for a significant proportion of underserved populations and, therefore, are important sites to implement EBIs to increase CRC screening and reduce CRC morbidity and mortality. Yet, as of 2019, only 45.6 % of the eligible FQHC patient population was screened for CRC. (Health Resources and Services Administration, 2019) The Centers for Disease Control and Prevention’s (CDC) Colorectal Cancer Control Program (CRCCP) aims to increase screening rates in primary care clinics serving high-need populations, including FQHCs. (Maxwell et al., 2014; Hannon et al., 2013; Joseph et al., 2011) Under CDC’s DP15-1502, 30 CRCCP state, tribal, and university awardees were funded for five years (2015–2020) to partner with primary care clinics, to implement (i.e., if not already in place) or enhance (i.e., improve implementation if already in place) four EBIs recommended by the Community Preventive Services Task Force to promote CRC screening. In *The Community Guide*, the CPSTF groups these EBIs into 3 types of strategy (e.g., community demand) (Table 1). (Community Preventive Services Task Force, 2021) Awardees could also implement or enhance supporting activities (SAs) that include patient navigation, small media, and provider education. CRC screening rates have increased in CRCCP clinics implementing EBIs. (Joseph, 2016; Maxwell et al., 2014) However, which combinations of EBIs are associated with the greatest increases in CRC screening remains unanswered.

The purpose of this analysis was to determine which combinations of EBIs or strategies (e.g., community demand) may effect the greatest increases in clinic-level screening rates among CRCCP clinic patient populations. Results were expected to inform how to best to invest resources to leverage the greatest gains in CRC screening among safety net populations with the goal of reducing CRC incidence and mortality. In this study, we utilized data collected from participating CRCCP clinics over the first three program years to assess which CRCCP components and strategies were associated with improvements in screening rates.

**2. Methods**

**2.1. Study population and data**

Data for this study were drawn from primary care clinics that participated in the CRCCP DP15-1502. The clinics in this study, most of which are FQHCs or Community Health Centers (CHCs), provided care primarily to low income, medically underserved populations. Beginning at baseline—the 12-month period prior to the clinic’s recruitment into the CRCCP—and then annually for each year of participation, clinic self-reported data on clinic characteristics, use of CRCCP resources towards newly implementing or enhancing existing EBIs and SAs, and CRC screening rates. This study reports on clinics recruited in the first program year and includes data reported at baseline and Program Years 1, 2, and 3, which coincided with calendar years 2015 to 2018. The analysis was conducted in 2020.

**2.2. Measures**

We used the following variables to describe the study population: clinic type (e.g., FQHC, CHC), clinic size (size of the patient population aged 50–75 years), percent of the patient population aged 50–75 years that is uninsured, primary CRC screening test type used (e.g., fecal

**Table 1**

EBIs and SAs supported by the CRCCP, by Community Guide strategies.

Strategy	EBI or SA	Description* and examples
Increasing Community Demand	Patient reminders (EBI)	Textual (letter, postcard, e-mail) or telephone messages advising people that they are due (reminder) or overdue (recall) for screening. Reminder messages might be general to address an overall priority population or tailored to specific individuals.
	Small media (SA)	Includes videos and printed materials such as letters, brochures, and newsletters. These materials can be used to inform and motivate people to be screened for cancer. They can provide information tailored to specific individuals or targeted to general audiences.
Increasing Community Access	Reducing structural barriers (EBI)	Structural barriers are non-economic burdens or obstacles that impede access to screening. Interventions designed to reduce these barriers might facilitate access to cancer screening services by reducing time or distance between service delivery settings and target populations, modifying hours of service to meet patient needs, offering services in alternative or non-clinical settings or eliminating or simplifying administrative procedures and other obstacles.
	Patient navigation (SA)	Individualized assistance offered to patients to help overcome healthcare system barriers and facilitate timely access to quality screening and follow-up as well as initiation of treatment services for persons diagnosed with cancer. Patient navigation includes assessment of patient barriers, patient education, resolution of barriers, and patient tracking and follow-up. Patient navigators might be professional (e.g., nurse) or lay workers.
Increasing Provider Delivery	Provider reminders (EBI)	Interventions that inform healthcare providers it is time for a patient’s cancer screening test (reminder) or that the patient is overdue for screening (recall). The reminders can be provided in different ways, such as patient charts or by e-mail.
	Provider assessment and feedback (EBI)	Interventions that both evaluate provider performance in offering and/or delivering screening to patients (assessment) and present providers with information about their performance in providing screening services (feedback). Feedback might describe the performance of a group of providers or an individual provider and might be compared with a goal or standard.

\*Mostly based on the definitions from *The Guide to Community Preventive Services* (Community Preventive Services Task Force, 2021) with added elaboration. Abbreviations: EBI - Evidence Based Intervention; SA - Supporting Activity; CRCCP - Colorectal Cancer Control Program.

immunochemical test, colonoscopy), and clinics’ distribution of free fecal kits. These variables were not part of the statistical model described below as the model eliminates the effect of fixed factors on screening rate.

The outcome variable for this study was the annual change in CRC screening rate (unweighted) at the clinic level, calculated in absolute terms (percentage points). The clinic-level screening rate is defined as

the percentage of clinic patients aged 50–75 years (i.e., all individuals with at least one visit to the clinic during the year) that are up-to-date with CRC screening (i.e., not overdue for screening tests) according to USPSTF guidelines. (Bibbins-Domingo et al., 2016) The predictor variables were all dichotomized and include newly implemented or enhanced CRCCP-supported EBIs (provider reminders, provider assessment and feedback, client reminders, reducing structural barriers), SAs (small media, patient navigation, provider education), and strategies (increasing community demand for screening, increasing community access to screening, increasing provider delivery of screening) within which these four EBIs are grouped, as defined in Table 1. An EBI or SA was considered newly implemented if it was in place and operational at the end of the current year but not in place and operational in the previous year. Similarly, an EBI or SA was considered enhanced if it was in place and operational in the previous year and clinics allocated CRCCP resources towards the EBI or SA in the current year, presumably to improve the quality, reach or intensity of the EBI/SA. An EBI or SA newly implemented or enhanced in the current year was also considered newly implemented or enhanced in the following year if it was still in place the next year. We assumed that the effect of any newly implemented/enhanced EBI lasts for another program year. Our assumption was based on the fact that clinics can implement EBIs at any point in time during the program year. This means the average time of implementation of any new EBI was only six months during the first year which we thought was too short to have the full impact. We used two sets of variables defined differently in our regression models. The first set of variables included whether clinics newly implemented or enhanced CRCCP-supported EBIs and SAs. The second set of variables included grouping the EBIs into the three strategies. EBIs and SAs supported by CRCCP, and the strategies they comprise are listed and defined in Table 1.

2.3. Statistical analysis

This study used a retrospective observational and longitudinal design. Data were structured in a panel form in which clinics had up to three measurements of change over a 4-year period. We used first difference (FD) estimator (Wooldridge, 2010) of linear panel data regression model to estimate the associations of independent variables with the outcome (i.e., annual percentage point change in clinic screening rate). FD estimation is chosen to eliminate the confounding effect of fixed factors in a regression model. To implement FD estimator, all independent and dependent variables were first differenced. First differencing eliminated all time invariant variables (e.g., clinic type). Consequently, only the time dependent variables remained as independent variables in the model while all other fixed variables typically used as controls were dropped. Variables representing clinic type, clinic size, percent uninsured patients, primary test type, and distribution of free fecal kits were collected at baseline only and remained fixed through the intervention period. The estimation equation was implemented without a constant, ruling out the presence of a secular time trend, i.e., annual rate change without an intervention. We used generalized estimating equations (GEE) technique for the estimation. (Zeger et al., 1988) Because data included repeated measures of clinics, GEE technique was suitable for the longitudinal data (Zeger et al., 1988). Regression analysis for the multi-component intervention was performed by using a full factorial of variables for four EBIs as well as for three strategies as described in Table 1. A full factorial ensures that all possible combinations of variables are included and are used as independent variables. All analyses were performed using STATA software (Version 14) by StataCorp LLC, Cary, NC.

The study sample included 486 unique clinics with each clinic contributing up to four years of data (Table 2). With repeated measures, these clinics contributed 1156 clinic years of total observations. Of the total observations, 72 % of the clinic years were FQHCs and 76 % were either medium sized (500–1500 patients) or large sized (>1,500

**Table 2**  
Summary statistics for clinics included in the study sample.

Clinic variables (Unique Clinics: n, %)	Freq (clinic years)	%	Baseline CRC screening rate (%)	Yearly increase in CRC screening rate (percentage points)
<b>All clinics</b> (486, 100 %)	1156	100	41.0	4.6
<b>Clinic type</b>				
CHC/FQHC (345, 72.0)	831	71.9	39.7	5.0
Health system/ Hospital owned (65, 13.4)	157	13.6	49.3	4.1
Private/Physician owned (31, 6.4)	61	5.3	54.6	1.1
Health department (45, 9.3)	107	9.3	31.3	4.6
<b>Clinic size</b>				
Small: <500 patients (122, 25.1)	276	23.9	36.0	6.5
Medium: 500–1,500 patients (178, 36.6)	441	38.1	40.5	4.7
Large: >1500 patients (186, 38.3)	439	38.0	44.7	3.3
<b>Uninsured patients</b>				
<5 % (134, 27.6)	328	28.4	44.0	4.7
5–20 % (127, 26.1)	307	26.6	40.8	5.3
More than 20 % (163, 33.5)	405	35.0	38.7	4.8
Unknown (62, 12.8)	116	10.0	41.5	2.2
<b>Clinic location</b>				
Metro (355, 74.3)	848	74.6	42.0	4.7
Urban (91, 19.0)	211	18.6	39.0	5.0
Rural (32, 6.7)	77	6.8	38.2	3.0
<b>Primary test type</b>				
FOBT/FIT (254, 52.3)	623	53.9	37.7	5.3
Colonoscopy (156, 32.1)	347	30.0	45.6	3.5
Varies (62, 12.8)	157	13.6	43.3	5.1
Unknown (14, 2.9)	29	2.5	25.3	11.5
<b>Clinic distributes free fit kit</b> (162, 33.3)	388	33.6	39.4	5.0
<b>Newly implemented or enhanced EBIs</b>				
Patient reminder (328, 67.5)	792	68.5	42.2	5.0
Provider reminder (265, 54.5)	688	57.8	42.5	5.0
Provider assessment & feedback (322, 66.3)	821	71.0	42.5	5.2
Reducing structural barrier (252, 51.8)	710	61.4	41.1	5.2
<b>Newly implemented or enhanced supporting activities</b>				
Small media (289, 59.5)	733	63.4	41.4	5.1
Provider education and development (211, 43.4)	495	42.8	43.0	5.6
Patient navigator (142, 29.2)	318	27.5	42.5	5.9
<b>Number of newly implemented or enhanced EBIs</b>				
None (54, 11.1)	86	7.4	36.0	2.4
One EBI (67, 13.8)	158	13.7	40.4	2.1
Two EBIs (106, 21.8)	249	21.5	39.7	4.9
Three EBIs (148, 30.4)	317	27.4	39.4	6.3

(continued on next page)

**Table 2 (continued)**

Clinic variables (Unique Clinics: n, %)	Freq (clinic years)	%	Baseline CRC screening rate (%)	Yearly increase in CRC screening rate (percentage points)
Four EBIs (111, 22.8)	346	29.9	45.0	4.7
<b>Number of newly implemented or enhanced SAs</b>				
None (102, 21.0)	207	17.9	38.6	2.7
One SA (174, 35.8)	473	40.9	40.7	4.0
Two SAs (162, 33.3)	355	30.7	41.0	6.5
Three SAs (48, 9.9)	121	10.5	46.1	5.0

**Note:** The observations include the repeated measures of clinics (or clinic years) for up to 3 timepoints.

Abbreviations: EBI - Evidence Based Intervention; SA - Supporting Activity. CRCCP - Colorectal Cancer Control Program; CRC - Colorectal Cancer; CHC - Community Health Center; FQHC - Federally Qualified Health Centers; FIT - Fecal Immunochemical Test; FOBT - Fecal Occult Blood Test; EBI - Evidence Based Intervention.

patients) clinics. Thirty-five percent of clinic years were from clinics where more than 20 % of their patients are aged 50–75 and uninsured. A vast majority of clinics (>74 %) were located in metro areas while a just about 7 % were rural clinics. The majority (54 %) of clinic years were from clinics using FOBT/FIT as their primary screening test type and 33.6 % distributed free FIT kits to patients. Each new or enhanced EBI was implemented in clinics contributing more than 57 % of the clinic years. Among SAs, only 27.5 % and 42.8 % of clinic years were contributed by clinics that newly implemented or enhanced patient navigation and provider education and development, respectively. In contrast, 63.4 % of clinic years were contributed by clinics that newly implemented small media. More than 57 % of clinic years were contributed by clinics that newly implemented or enhanced 3–4 EBIs while 7.4 % were contributed by clinics that neither newly implemented nor enhanced any EBIs. Two to three SAs were newly implemented or enhanced by clinics contributing 41.1 % of clinic years.

The average clinic CRC screening rate at baseline was 41.0 % and the

average annual rate increase was 4.6 percentage points (Table 2). Across clinic characteristics, both the average baseline rates and the increases in screening rates varied. Average clinic CRC screening rates generally increased when clinics implemented or enhanced any number EBIs or SAs compared to clinics that did not newly implement or enhance any EBIs/SAs. Note that clinic level screening rates were unweighted.

Table 3 presents the full factorial regression results involving four EBIs with the inclusion of new implementation or enhancement of three SAs as independent control variables. Clinics with no new implementation or EBI enhancement were used as the reference. Clinics implementing or enhancing a single EBI had no significant association with the annual rate change except for provider assessment and feedback which was associated with a 1.9 percentage point average annual increase in screening rate (p-value < 0.05). There were six different combinations of two EBIs. Combination-3 (client reminders + reducing structural barriers) and combination-4 (provider reminders and provider assessment and feedback) were associated with 4.5 percentage points (p-value < 0.001) and 6.5 percentage point (p-value < 0.001) increase in screening rates, respectively. All combinations involving any three EBIs or all four EBIs were significantly associated with increase in clinic screening rate. The combination involving client reminders, provider assessment and feedback and reducing structural barriers was associated with largest increase (7.2 percentage points, p-value = 0.00) in screening rate. EBI categories that were not significant generally had small n's, i.e. number of clinics years. Among SAs, only provider education and development was significantly associated with an increase in the rate (1.9 percentage points, p-value = 0.001).

Table 4 shows the results for EBI strategies. Compared to no strategy in place, clinics newly implementing or enhancing interventions related to increasing provider delivery alone had a 4.3 percentage point higher rate (p-value < 0.001). Interventions related to increasing community demand and increasing community access alone were not significantly associated with a change in clinic screening rates. All interventions involving 2–3 strategies were associated with positive rate change with statistical significance at p < 0.01. Among them, interventions involving increasing community demand and increasing community access had

**Table 3**  
Regression results of clinic screening rate change and EBIs (N = 1,156 clinic years).

	Client Reminders	Provider Reminders	Provider Assessment and Feedback	Reducing Structural Barriers	Clinic Years (%)	Coeff.	P-Value	95 % Confidence Interval
<b>Interventions</b>								
No EBIs	0	0	0	0	86 (7.4)	Reference		
Client reminders alone	1	0	0	0	18 (1.6)	1.37	0.563	-3.28 6.03
Provider reminders alone	0	1	0	0	20 (1.7)	3.00	0.157	-1.15 7.15
Provider assessment and feedback alone	0	0	1	0	87 (7.5)	1.91 *	0.049	0.01 3.82
Reducing structural barriers alone	0	0	0	1	33 (2.8)	-0.22	0.894	-3.37 2.94
Combination 1 (2 EBIs)	1	1	0	0	34 (2.9)	2.68	0.109	-0.60 5.96
Combination 2 (2 EBIs)	1	0	1	0	53 (4.6)	2.07	0.119	-0.53 4.67
Combination 3 (2 EBIs)	1	0	0	1	65 (5.6)	<b>4.54</b> ***	<b>0.000</b>	2.26 6.83
Combination 4 (2 EBIs)	0	1	1	0	52 (4.5)	<b>6.53</b> ***	<b>0.000</b>	3.79 9.27
Combination 5 (2 EBIs)	0	1	0	1	14 (1.2)	3.98	0.106	-0.85 8.82
Combination 6 (2 EBIs)	0	0	1	1	31 (2.7)	2.26	0.209	-1.26 5.78
Combination 7 (3 EBIs)	1	1	1	0	96 (8.3)	<b>3.27</b> **	<b>0.006</b>	0.93 5.61
Combination 8 (3 EBIs)	1	1	0	1	65 (5.6)	<b>2.84</b> *	<b>0.027</b>	0.32 5.35
Combination 9 (3 EBIs)	1	0	1	1	115 (9.9)	<b>7.17</b> ***	<b>0.000</b>	5.04 9.30
Combination 10 (3 EBIs)	0	1	1	1	41 (3.5)	<b>5.96</b> ***	<b>0.000</b>	2.84 9.08
Combination 11 (4 EBIs)	1	1	1	1	346 (29.9)	<b>3.20</b> ***	<b>0.000</b>	1.54 4.87
<b>Supporting activities</b>								
Small Media					733 (63.4)	0.07	0.923	-1.32 1.46
Provider Ed. & Development					494 (42.8)	<b>1.86</b> **	<b>0.001</b>	0.73 2.98
Patient Navigators					318 (27.5)	1.17	0.064	-0.07 2.41

boldface indicates statistical significance (p < 0.05).

\* p < 0.05, \*\* < 0.01, \*\*\* p < 0.001.

Abbreviations: EBI - Evidence Based Intervention.



**Table 4**  
Regression results of clinic screening rate change and intervention strategies (N = 1,156 clinic years).

	Strategy to Increase Community Demand	Strategy to Increase Community Access	Strategy to Increase Provider Delivery	n (%)	Coeff.	P-Value	95 % CI	
<b>Interventions Strategies<sup>1</sup></b>								
No strategy	0	0	0	67 (5.8)				
Single Strategy	1	0	0	5 (0.4)	2.08	0.639	-6.61	10.76
Single Strategy	0	1	0	15 (1.3)	-1.02	0.671	-5.70	3.67
Single Strategy	0	0	1	113 (9.8)	<b>4.31</b> ***	<b>0.000</b>	2.63	5.99
Two Strategies	1	1	0	59 (5.1)	<b>6.13</b> ***	<b>0.000</b>	3.83	8.44
Two Strategies	1	0	1	188 (16.3)	<b>4.85</b> ***	<b>0.000</b>	3.51	6.19
Two Strategies	0	1	1	71 (6.1)	<b>2.98</b> **	<b>0.007</b>	0.80	5.17
Three Strategies	1	1	1	638 (55.2)	<b>5.19</b> ***	<b>0.000</b>	4.51	5.87

Boldface indicates statistical significance (p < 0.05).

\* p < 0.05, \*\* p < 0.01, \*\*\* p < 0.001.

<sup>1</sup>Strategies included EBIs and two of the SAs (small media, patient navigation) to increase community demand, community access, and provider delivery.

the highest association with increase in screening rate (6.1 percentage points, p-value < 0.001) followed by interventions involving all three strategies (5.2 percentage points, p-value < 0.001).

### 3. Discussion

This study was unique in using data from a large number of clinics across 30 states, largely FQHCs/CHCs, serving high need populations with low CRC screening rates. This study found that many multicomponent interventions were associated with significant increases in CRC screening. Except for provider assessment and feedback, EBIs did not show any significant relationships with CRC screening rates if they were implemented in isolation. However, interventions had significant associations with the outcome when multiple EBIs were combined. The greatest increase in CRC screening rates (7.2 percentage points) was associated with a combination of 3 EBIs (client reminders, provider assessment and feedback, and reducing structural barriers), each representing a different Community Guide strategy (community demand, provider delivery, community access). These findings support studies that found positive associations between use of multiple EBIs and cancer screening. Feldman and colleagues reported an increase in CRC screening rate from 59 % to 70 % when they implemented a multifaceted intervention involving patient reminders, audit and feedback and automated clinic reminders (Feldman et al., 2017). A study of the first CRCCP from 2009 to 2015 found that many clinics were more likely to put in place EBIs that were easier to implement, and thus opportunities may exist to further increase screening uptake by facilitating implementation of other EBIs. (Hannon et al., 2013) Organizational readiness has been identified within the field of implementation science as important to change management. (Weiner, 2020) Support and technical assistance may be necessary to assist health systems to effect health system change through the implementation of multiple EBIs targeting patients, providers, and access. To determine appropriate EBIs and ensure clinic capacity to implement them, programs can conduct readiness assessments of clinics prior to implementation. However, clinics may lack resources to implement all available interventions, and may strategically choose EBIs that are less resource intensive. Costs of implementing different interventions including their cost-effectiveness in the context of CRCCP are also becoming increasingly available (Subramanian et al., 2020; Kim et al., 2020) and they can inform similar programs in the future.

This study also adds to the literature in showing that particular EBIs, specifically the combination of provider reminder and provider assessment and feedback, were consistently associated with a significant

increase in CRC screening rates. These two EBIs were focused on organizational changes that intend to reach all providers in a clinic or health system and, subsequently, impacted patients. In contrast, we found that provider reminder alone was not associated with the rate change. This may be due to the ways clinics implement or enhance provider reminders and their organizational commitment to improving screening rate. Of interest, interventions involving all four EBIs or all strategies were not associated with the largest increases in CRC screening rates. Reasons for this could be diminishing returns of adding EBIs or a ceiling effect as clinics newly implementing or enhancing all EBIs or all strategies may have had higher baseline screening rates than those that newly implemented or enhanced fewer EBIs or SAs. Further, the quality of implementation may have been compromised when clinics are implementing multiple EBIs at the same time.

There are several studies, including randomized controlled trials, examining multiple strategies and associated interventions to increase CRC screening rates. The CPSTF systematically reviewed 56 studies of multicomponent interventions in various settings and varying timespans of interventions and found a median increase in CRC screening rates of 15.4 percentage points. Our study examined the annual change in screening rate and the association of EBIs (including multiple component EBIs) and found that screening rate change is about a third of what the CPSTF found. This difference may have been due to differences in eligible populations, interventions and their duration, methods and analytical approaches, and other factors. For example, our study may have differed in the unique nature of the clinics included as well as differences in implementation quality and intervention exposure or dose. In addition, the intervention timespan and the set of interventions or their variation in this study was not the same as in CPSTF studies. The CRCCP is a public health program implemented in real world settings, not a research study. The CRCCP clinics varied significantly regarding setting, context, population, and EBI implementation quality which could not be fully adjusted for in the analysis due to data limitations. This contrasted with most other studies that were done in controlled environments with greater control over implementation quality. EBIs may have been more effective in such circumstances.

As noted, the CRCCP involved clinics in practice environments and covered three years of program delivery. Given that the study included diverse patient populations, context and geography, the generalizability of our study findings is stronger than studies with a more limited scope. Further, we examined multi-component interventions in two different ways. One of our approaches was to use the conceptual framework for multi-component interventions developed by CPSTF with interventions grouped into three distinct strategies. We believe this is the first study to

use the Community Guide strategies as a testable hypothesis. Our second approach to examine multi-component interventions is even more novel and useful from a practice point of view. By examining all four EBIs in isolation and in all possible combinations (16 in total), we were able to examine the results for every possible scenario. Finally, our study clinics were mostly FQHCs that served populations with lower than average screening rates. These clinics can be put in a primary focus for future intervention to increase CRC screening rates. Our study build on previous work related to implementation strategies regarding the choices of interventions by generating good insights that are more practical and informative. Findings from our studies, if combined with cost data from other studies, can be more useful for programs to inform future interventions.

#### 4. Limitations

There are some limitations to this study. Data were based on self-report and quality of EBI/SA implementation or enhancement is unknown and effects of any new EBIs can last for more than two years assumed in this study. Future research could explore not only reports of EBI implementation but also elements of their implementation such as fidelity (quality) and intensity. Additionally, study is needed to assess potential leveling of screening rates across clinics over time (i.e., the duration of intervention effect) and the effect of baseline screening rate on the rate change. For some interventions or groups, the number of clinics was too small to produce effect sizes that are statistically significant. Finally, our study may have suffered from omitted variable bias as the data do not capture all the variables, including any other interventions not included in our analysis, for the model to produce unbiased estimates.

#### 5. Conclusion

Our study examined the implementation of client or provider reminders, provider assessment and feedback, and reducing structural barriers in the context of SAs to promote CRC screening among clinics involved in the CRCPP, a public health program for underserved communities. Clinics implementing combinations of these EBIs, particularly those including three or more EBIs, often were more likely to have impact on screening rate change than those implementing none.

#### 6. Disclaimer

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

#### 7. Financial disclosure

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#### Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence

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