BMJ open

Physician-linked mailed invitation to be screened improves uptake in an organized colorectal cancer screening program: Two linked cohort studies.

Journal:	*BMJ Open*
Manuscript ID:	bmjopen-2013-004494
Article Type:	Research
Date Submitted by the Author:	18-Nov-2013
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Primary Subject Heading:	Gastroenterology and hepatology
Secondary Subject Heading:	Oncology, Public health, General practice / Family practice, Health services research
Keywords:	Gastrointestinal tumours < GASTROENTEROLOGY, PREVENTIVE MEDICINE, PRIMARY CARE, PUBLIC HEALTH

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TITLE PAGE

Title: Physician-linked mailed invitation to be screened improves uptake in an organized colorectal cancer screening program: Two linked cohort studies.

Short tile: Physician-linked invitations for colorectal cancer screening

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Word count: 2637 (main text),   242 (abstract)

Number of Tables: 4

Number of Figures: 1

Number of References: 40

Key words: Mailed invitations, colorectal cancer, organized screening

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Physician-linked mailed invitations for colorectal cancer screening

ABSTRACT

Objectives: A central tenet of organized cancer screening is that all persons in a target

population are invited. The aims of this study are to identify patient and physician factors

associated with response to mailed physician-linked invitations (Study 1) and to evaluate

their effectiveness in an organized colorectal (CRC) screening program (Study 2).

Design and setting: Two linked cohort studies conducted in context of Ontario's

organized province-wide CRC screening program.

Participants: 102 family physicians and 11,302 associated eligible patients participating

in a technical evaluation ("the Pilot") of large scale mailed invitations for CRC screening

were included. Matched controls were randomly selected using propensity scores from

among eligible patients associated with family physicians in similar practice types as the

Pilot physicians.

Intervention: Physician-linked mailed invitation to have CRC screening.

Outcomes: Uptake of FOBT within 6 months of mailed invitation (primary) and uptake of

FOBT or colonoscopy within 6 months of mailed invitation (secondary).

Results: Factors significantly associated with uptake of FOBT included prior FOBT use,

older patient age, greater patient co-morbidity and having a female physician. In the

matched analysis, Pilot patients were more likely to complete an FOBT (22% vs. 8%,

p<0.0001) or an FOBT or colonoscopy (25% vs. 11%, p <0.0001) within 6 months of

mailed invitation than matched controls. The number needed to invite to screen one

additional person was 7.

Conclusions: Centralized large scale mailing of physician-linked invitations is both

feasible and effective in an organized CRC screening program.

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ARTICLE SUMMARY

Strengths and limitations of this study:

- Implementation and effectiveness of physician-linked invitations in an organized colorectal screening program have not yet been reported
- We have shown that centralized large scale mailing of physician-linked invitations is feasible
- We found that physician linked mailed invitations improve CRC screening participation by 14% such that 7 physician-linked invitations need to be mailed to screen one additional person
- We were limited to data found in Ontario health administrative databases; for example, we were not able to determine family history
- Findings are promising but require appropriate infrastructure in order to be implemented in other jurisdictions

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INTRODUCTION

Colorectal cancer (CRC) is the 3rd most common cancer and the 4th leading cause of

cancer-related death worldwide.[1] FOBT[2-4] and flexible sigmoidoscopy[5-7] have

been shown to decrease CRC mortality in randomized controlled trials.

Given these data, organized CRC screening programs[8] are being implemented

worldwide.[9]   On April 1 2008, Ontario launched Canada's first organized province-

wide CRC screening program, ColonCancerCheck (CCC).[10] CCC has a dual strategy:

through the primary care physician, FOBT is offered to people at average risk for CRC

and colonoscopy to those at increased risk based on family history. The CCC program

uses a non-rehydrated guaiac FOBT (Hema-Screen, Immmunostics, Inc., NJ, USA)

requiring 3 stool samples from separate stools. The only recommended dietary

restriction is to avoid vitamin C for 3 days prior to and during the collection period.

A central tenet of organized screening programs is that all persons in the target

population be invited to participate.[8] Operationalization of this strategy can vary:

invitations may be sent with an FOBT kit, can include physician recommendation or may

incorporate tailored messaging.[11 ,12] Some of these approaches, such as

incorporation of physician recommendation, present significant implementation

challenges for organized screening programs such as Ontario's.

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In 2009, the CCC program conducted the CCC Invitation Pilot (the "Pilot"), an evaluation

that tested the technical feasibility of a centralized approach to sending physician-linked

mailed invitations for CRC screening.   In this paper, we describe the structure and the

implementation of the Pilot. In addition, we report on patient and physician factors

associated with response to mailed physician-linked invitations and on the effectiveness

of these invitations in an organized CRC screening program.

METHODS

The CCC Invitation Pilot – Implementation and Evaluation

The Pilot was conducted by CCC in November 2009 in order to develop and test the

technical infrastructure required for large scale centralized physician-linked mailed

invitations in Ontario. For the Pilot, invitation letters were generated by the CCC

program on behalf of 102 family physicians and sent to all their eligible enrolled patients.

Just over 11,000 patients received mailed invitations requesting they visit their family

physician to obtain an FOBT kit or, if appropriate based on family history, a referral for

colonoscopy. In this paper, we report on the 2 linked quantitative studies done using this

cohort. Ethics approval was obtained from the research ethics boards at Sunnybrook

Health Sciences Centre and the Institute for Clinical Evaluative Sciences (ICES) and

permission to use the Pilot data was obtained from Cancer Care Ontario's Data Access

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Committee. All analyses were conducted using SAS v.9 (SAS Institute, Cary, NC). A p-

value of 0.05 was used to determine statistical significance.

Data Sources

The quantitative Pilot study was conducted at ICES which holds the administrative

health records for all 12.4 million Ontarians. CCC program databases were linked to the

ICES administrative databases using an encrypted version of the provincial health

insurance number.

The ICES databases used include the Canadian Institute of Health Information (CIHI)

databases, the Ontario Health Insurance Program (OHIP) Claims History Database, the

Registered Persons Database (RPDB), the Ontario Cancer Registry, the ICES Physician

Database, and the Client Agency Program Enrollment (CAPE) registry. The CIHI, OHIP,

RPDB and the Ontario Cancer Registry and the ICES Physician Database have been

previously described.[13 ,14] The CAPE registry tracks patients registered to a specific

physician in patient enrolled models (PEMs) of care. PEMs comprise family physicians

who provide enrolled patients with comprehensive health care and extended hours; PEM

physicians receive incentives for the use of preventive care measures such as CRC

screening.[15] PEMs vary in terms of structure, services provided and remuneration

(varying from enhance fee-for-service to blended capitation). It is estimated that 75% of

Ontario residents received their care via a PEM in 2009.[16]

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The CCC program has collected data on CRC screening since its inception using

Laboratory Reporting Tool (LRT) and comprises data related to the FOBT kits

administered by the CCC program, including the results of these tests.

Study 1: Factors associated with response to the mailed invitation

Cohort Definition: For the Pilot, a convenience sample of physicians participating in PEM

practices was recruited via Cancer Care Ontario's Provincial Primary Care Cancer

Network. Prior to the Pilot mailing, CCC generated lists of patients eligible for CRC

screening for each participating physician using CAPE, Ontario Cancer Registry, OHIP,

CIRT and LRT. Patients aged 50 to 74 years without a history of CRC and who were

due for CRC screening (without a record of recent FOBT (previous two years) or lower

GI investigation including flexible sigmoidoscopy and colonoscopy (previous 5 years))

were eligible.

The Mailing: Invitations were mailed in November 2009. The date of mailing was the

index date. The letters were compiled centrally by the CCC program but were physician-

linked; patients received a letter from their own physician, as indicated by their name at

the bottom of the letter in an italicized font (Figure 1). The letter asked patients to visit

their family physician for screening; it did not include an FOBT kit. They were

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accompanied by an CRC screening information brochure and sent in an envelope with

the family physician name in the front upper left corner.

Response to Mailed Invitation: We defined response to the mailed invitation as a record

of FOBT in OHIP or in LRT within 6 months of the index date. We were not able to

measure response in persons at increased risk of CRC as we do not have family history

data available in the administrative databases.

Patient and Physician Factors: We characterized patients by age group, sex, co-

morbidity, median neighborhood income[17 ,18], health region[19], immigration status,

and prior FOBT. Comorbidity was measured by counting the number of Aggregated

Diagnosis Groups (ADGs) in the prior 12 months according to the Johns Hopkins ACG

Case-Mix System.[20] This system has been shown to accurately predict mortality in a

general population ambulatory cohort in Ontario.[21] We used date of registration in the

RPDB as a proxy measure for immigration status; patients were considered recent

immigrants if their date of registration was within 5 years of the index date.[22]

Physicians were characterized according to age, sex, training location (attended

Canadian medical school vs. outside of Canada), practice type, size of practice, age-

eligible rate of colonoscopy or FOBT over prior 2 years as well as the age-eligible rate of

annual physical exams or influenza vaccinations in the prior year. All physicians were in

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PEMs; practice types included family health groups (FHGs, enhanced fee-for-service

models), family health organizations or networks (FHO/FHNs, blended capitation

models), FHO/FHN with family health team (FHO/FHN-FHT, interprofessional team

model with a blended capitation fee structure) and other PEMs.[23] We measured

practice size as the number of enrolled patients stratified in a binary fashion (≤1800 vs.

>1800 enrolled patients) as larger practice sizes have been shown to be associated with

poorer preventative care.[24] For the remaining physician characteristics, we identified

all enrolled and non-enrolled patients aged 50-74 years in their practices as of the index

date. Age-eligible FOBT and colonoscopy rates were obtained for each Pilot physician

by calculating the proportion of their age-eligible patients who had had an FOBT or

colonoscopy in the 2 years prior to the index date. Similarly, we calculated their rates of

age-eligible annual physical exams or influenza vaccine in the year prior to the index

date. These variables were derived in order to estimate physician adherence to CRC

screening and preventive medicine practices at baseline.

Analysis: The number and proportion of persons in the cohort who responded to the

mailed invitation within 6 months was determined overall and by patient and physician

characteristics. Multivariate logistic regression modeling was used to identify patient and

physician factors associated with response to the mailed invitation. In order to account

for potential clustering of patients within physicians, Generalized Estimating Equations

(GEE) were used in the model.

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Study 2: Evaluation of the effectiveness of mailed invitations

Overview and study participants: This was a matched double cohort analysis, comparing

uptake of FOBT in those who received a mailed invitation (Pilot cohort) to a matched

control group who were not sent a mailed invitation. The Pilot cohort comprised all

members of the cohort described in Study 1 for whom a matched control could be

identified. We identified potential patient controls as follows: 1) Pilot physicians were

matched to non-Pilot physicians practicing in PEMs in a 1:5 ratio using physician age,

sex, size and practice type; 2) enrolled patients belonging to the selected control

physicians were retained if they met the same inclusion/exclusion criteria as those in the

intervention cohort (aged 50 to 74 years with no prior CRC who were due for CRC

screening). Propensity scores that modeled the probability of belonging to the Pilot

group were calculated for each patient. The variables in this model included age (as a

continuous measure), sex, co-morbidity, median neighborhood income quintile, health

region, immigration status, and FOBT from 2 to 5 years prior.[25 ,26] Pilot patients were

matched to controls in a 1:1 fashion based on propensity scores using a caliper width of

0.25. This methodology was implemented to balance the distribution of patient-level

variables between the Pilot and control groups.

Response to mailed invitation: For our primary outcome, we defined response to the

mailed invitation as above, FOBT within 6 months of the index date. For our secondary

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outcome, response was defined as a record of either FOBT or colonoscopy (in OHIP) within 6 months of the index date. For the purposes of this study, controls were assigned the same index date as their matched counterpart in the Pilot group.

Analysis: Standard differences between the Pilot participants and controls were calculated for the variables included in the propensity score. Important differences between the 2 groups were defined by a standardized difference exceeding 0.1.[26 ,27] In the primary analysis, we compared the number and proportion in the Pilot and control groups responding to the mailed invitation with FOBT using McNemar's test.[26] We determined the number of invitations mailed in order to screen one additional person with FOBT. We repeated the above analyses using our secondary outcome in order to determine if observed differences in FOBT uptake could be attributed to a differences in colonoscopy uptake (i.e., patients had CRC screening but chose colonoscopy over FOBT). As the matching only accounted for patient level variables, we repeated our analyses using conditional logistic regression in order to adjust for physician covariates (age, sex, practice type and size).

RESULTS

Study 1: Factors associated with response to the mailed invitation

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There were 11,311 eligible patients associated with the 102 family physicians in the Pilot

cohort. Nine patients were excluded as we were unable to determine their health region

and/or income quintile; this left 11,302 patients for the analysis. The majority of patients

were 50 to 59 years of age, 52% were women, 48% had no or low co-morbidity and 14%

had completed an FOBT from 2 to 5 years prior to the mailing. Two thirds of patients had

a male physician, approximately half were part of a primary care team reimbursed via an

enhanced fee-for-service arrangement and just under half were enrolled in larger

practices (>1800 enrolled patients) (Table 1).

2503 (22%) completed an FOBT within 6 months of mailing. In the multivariate

regression, the strongest patient factor associated with FOBT completion was prior

FOBT use (2 to 5 years prior vs. > 5 years or never: OR 2.8, 95% C.I.: 2.5 to 3.3, p <

0.0001). Other significant factors associated with FOBT completion included older

patient age, greater co-morbidity, and having a female physician (Table 2).

Study 2: Evaluation of the effectiveness of mailed invitations

Of the 11,302 patients in Study 1, 10,652 patients were successfully matched to 10,652

controls using propensity scores. Standardized differences for the patient

characteristics included in the propensity score were all <0.1, indicating that the two

cohorts were well matched for measurable potential confounders (Table 3).

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Pilot patients were significantly more likely than controls to complete FOBT alone (2387

(22%) versus 854 (8%), p<0.0001) and FOBT or colonoscopy (2664 (25%) vs. 1191

(11%), p<0.0001) within 6 months of mailing. The association between the mailed

invitation and CRC screening participation (either FOBT alone or FOBT or colonoscopy)

remained after adjusting for physician level characteristics (Table 4).

DISCUSSION

In the current study, we have demonstrated that physician-linked mailed invitations are

both feasible and effective in the context of a large organized, population-based

screening program; only 7 letters would need to be sent in order to screen one additional

person. Furthermore, we have found that older patients, those with greater co-morbidity,

those who have previously been screened and patients of female physicians were more

likely to respond to this type of invitation. Our findings are of particular interest to other

jurisdictions planning or who already have organized CRC screening.

In other published studies of mailed invitations, an FOBT kit is often included. Three

studies done outside organized screening programs have found physician-linked

invitations superior to non-linked invitations; 2 studies of invitations included an FOBT

kit,[28 ,29] and the third study did not.[30] Other studies have examined mailed

invitations with FOBT kits in the context of primary care practices in the USA.[31-33]

While the results from these trials were largely supportive of mailed invitations, kit

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inclusion can make it difficult to separate the convenience of receiving the FOBT kit

directly by mail from the impact of an invitation from one's own physician.

Our study demonstrates the effectiveness and feasibility of physician-linked invitations in

the context of a large organized CRC screening program with an estimated target

population of over 3 million persons. Implementation in this context confers challenges in

terms of technological infra-structure, privacy and regulatory issues. There are 2 studies

(from the United Kingdom[34] and Italy[35]) that have reported on mailed invitations in

the context of organized colorectal cancer screening programs and found them to be

effective. Both studies included FOBT kits and one studied the impact of physician

endorsement specifically.[34] Our findings are important because they support a

potentially more cost-effective approach that avoids wasting kits that are mailed but not

used.

Our results highlight the critical role of physician recommendation, a finding supported

by others. For example, in the NHS Bowel Cancer Screening Programme (BCSP)

currently, the primary care physician receives the result but is not directly involved in the

mailed invitation or the actual screening. Recently, a randomized controlled trial

conducted in the context of the BCSP showed that an endorsement letter from the

primary care provider increased participation by 6%.[34]   In 2 studies from Australia,

endorsement improved initial participation[28 ,29] and over 4 successive screening

rounds.[29]

Our study has several limitations. As mentioned above, we are unable to determine

family history using Ontario administrative data. A second limitation is that a single

generic letter was used. Tailored letters with key messages for specific subgroups may

be more effective,[12] a finding that may be relevant in Ontario as we did find that

response to the letter appeared to differ in various subgroups. Finally, while our findings

are promising, there are challenges to widespread implementation in other population-

based screening programs, including the requirement for a centralized database that

links patients and physicians. Finally, implementation of this strategy in population

based screening is predicated on physician acceptability and agreement. While we

have found that this approach is acceptable in principle to many Ontario physicians,[36]

processes to determine physician agreement have not been worked out for the entire

CCC program which comprises an estimated 7000 primary care physicians.

CONCLUSIONS

In summary, we have demonstrated that physician-linked mailed invitations for CRC

screening, even without the inclusion of an FOBT kit, can have substantial effect on

participation in an organized CRC screening program and that it is technically feasible to

centrally organize and mail physician-linked invitations on a large scale. Organized

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screening programs, which often use unlinked invitations, should consider adopting this

approach given its demonstrated effectiveness and feasibility.

COMPETING INTERESTS STATEMENT

Dr. Tinmouth is the Lead Scientist for the ColonCancerCheck program and Dr.

Rabeneck oversees the ColonCancerCheck program in her capacity as the Vice-

President, Cancer Prevention and Control at Cancer Care Ontario. None of the other

authors have any conflicts of interest to report.

AUTHOR CONTRIBUTION:

Authors contributed substantially to each of the following areas:

-conception and design (JT, LFP, LR) or analysis and interpretation of data (JT, NB,

LFP, LR, RS, LY)

-drafting the article (JT) or revising it critically for important intellectual content (JT, NB,

LFP, LR, RS, LY)

-final approval of the version to be published (JT, NB, LFP, LR, RS, LY)

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Tables.

Table 1. Patient and physician characteristics for Pilot participants in Study 1

	FOBT within 6 months	No FOBT within 6 months	Total
	(n=2,503)	(n=8,799)	(n=11,302)
Patients			
Age group in years, No. (%)			
50-59	1,279 (51%)	5,384 (61%)	6,663 (59%)
60-69	894 (36%)	2,637 (30%)	3,531 (31%)
70-74	330 (13%)	778 (9%)	1,108 (10%)
Sex, No. (%)			
Female	1,299 (52%)	4,554 (52%)	5,853 (52%)
Male	1,204 (48%)	4,245 (48%)	5,449 (48%)
Co-morbidity*, No. of ADGs (%)			
0	257 (10%)	1,279 (15%)	1,536 (14%)
1-2	828 (33%)	3,044 (35%)	3,872 (34%)
3-4	712 (28%)	2,241 (25%)	2,953 (26%)
5-6	393 (16%)	1,224 (14%)	1,617 (14%)
7+	313 (13%)	1,011 (11%)	1,324 (12%)
Median neighborhood income quintile, No. (%)			
Rural	394 (16%)	1,431 (16%)	1,825 (16%)
Low Urban	360 (14%)	1,375 (16%)	1,735 (15%)
2	402 (16%)	1,418 (16%)	1,820 (16%)
3	429 (17%)	1,430 (16%)	1,859 (16%)
4	432 (17%)	1,552 (18%)	1,984 (18%)
High Urban	486 (19%)	1,593 (18%)	2,079 (18%)
Health region, No. (%)			
Erie St.Clair	125 (5%)	337 (4%)	462 (4%)
South West	284 (11%)	823 (9%)	1,107 (10%)
Waterloo Wellington	76 (3%)	251 (3%)	327 (3%)
Hamilton Niagara	289 (12%)	976 (11%)	1,265 (11%)
Central West	138 (6%)	482 (5%)	620 (5%)
Mississauga Halton	22 (1%)	120 (1%)	142 (1%)
Toronto Central	111 (4%)	392 (4%)	503 (4%)
Central	24 (1%)	177 (2%)	201 (2%)
Central East	361 (14%)	1,282 (15%)	1,643 (15%)
South East	162 (6%)	697 (8%)	859 (8%)
Champlain	219 (9%)	676 (8%)	895 (8%)
North Simcoe-Muskoka	77 (3%)	188 (2%)	265 (2%)
North East	291 (12%)	1,118 (13%)	1,409 (12%)
North West	324 (13%)	1,280 (15%)	1,604 (14%)

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Recent immigrant, No. (%)	23 (1%)	88 (1%)	111 (1%)
FOBT 2 to 5 years prior to mailing, No. (%)	643 (26%)	905 (10%)	1,548 (14%)
Physician			
Median age in years (IQR)	52 (45-59)	53 (46-59)	52 (45-59)
Sex, No. (%)			
Female	936 (37%)	3,044 (35%)	3,980 (35%)
Male	1,567 (63%)	5,755 (65%)	7,322 (65%)
Training location, No. (%)			
Outside Canada	312 (12%)	1,196 (14%)	1,508 (13%)
In Canada	2,191 (88%)	7,603 (86%)	9,794 (87%)
Practice type, No. (%)			
FHG	1,082 (43%)	4,266 (48%)	5,348 (47%)
FHO/FHN	432 (17%)	1,456 (17%)	1,888 (17%)
FHO/FHN-FHT	881 (35%)	2,620 (30%)	3,501 (31%)
Other PEM	108 (4%)	457 (5%)	565 (5%)
Practice size (enrolled patients), No. (%)			
>1800 patients	1,105 (44%)	4,104 (47%)	5,209 (46%)
Age-eligible rate of colonoscopy quintile, No. (%)			
Low	485 (19%)	1,619 (18%)	2,104 (19%)
2	548 (22%)	1,940 (22%)	2,488 (22%)
3	637 (25%)	2,279 (26%)	2,916 (26%)
4	477 (19%)	1,696 (19%)	2,173 (19%)
High	356 (14%)	1,265 (14%)	1,621 (14%)
Age-eligible rate of FOBT quintile, No. (%)			
Low	487 (19%)	1,888 (21%)	2,375 (21%)
2	504 (20%)	1,886 (21%)	2,390 (21%)
3	533 (21%)	1,890 (21%)	2,423 (21%)
4	522 (21%)	1,680 (19%)	2,202 (19%)
High	457 (18%)	1,455 (17%)	1,912 (17%)
Age-eligible rate of annual physical exams quintile, No. (%)			
Low	496 (20%)	2,009 (23%)	2,505 (22%)
2	490 (20%)	1,625 (18%)	2,115 (19%)
3	472 (19%)	1,638 (19%)	2,110 (19%)
4	509 (20%)	1,686 (19%)	2,195 (19%)
High	536 (21%)	1,841 (21%)	2,377 (21%)

Age-eligible rate of influenza vaccine quintile, No. (%)			
Low	548 (22%)	1,997 (23%)	2,545 (23%)
2	549 (22%)	1,765 (20%)	2,314 (20%)
3	435 (17%)	1,930 (22%)	2,365 (21%)
4	485 (19%)	1,770 (20%)	2,255 (20%)
High	486 (19%)	1,337 (15%)	1,823 (16%)

*Co-morbidity scored using number of Aggregated Diagnosis Groups (ADGs) using the Johns Hopkins Case Mix System

FHG = family health group

FHO/FHN = family health organizations or networks

Other PEM = other patient enrolled model of care

FOBT = fecal occult blood test

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Table 2. Multivariate logistic regression analysis using Generalized Estimating Equations for the

characteristics of patients and physicians associated with completing an FOBT within 6 months of the

mailing date.

Patients	Odds ratio (95% C.I.)	P-value
Age group, years		
50-59	0.6 (0.5, 0.8)	<.0001
60-69	0.8 (0.7, 1.0)	NS
70-74	Reference	N/A
Sex		
Female	0.9 (0.9, 1.0)	NS
Male	Reference	N/A
Co-morbidity*, No. of ADGs		
0	0.7 (0.6, 0.8)	0.0002
1-2	0.9 (0.7, 1.0)	NS
3-4	1.0 (0.9, 1.2)	NS
5-6	1.0 (0.9, 1.2)	NS
7+	Reference	N/A
Median neighborhood income quintile		
Rural	0.9 (0.7, 1.1)	NS
Low Urban	0.9 (0.7, 1.0)	NS
2	1.0 (0.8, 1.1)	NS
3	1.0 (0.9, 1.1)	NS
4	0.9 (0.8, 1.1)	NS
High Urban	Reference	N/A
Health region		
Erie St.Clair	1.3 (0.9, 1.8)	NS
South West	0.9 (0.6, 1.4)	NS
Waterloo Wellington	0.8 (0.6, 1.2)	NS
Hamilton Niagara	0.9 (0.6, 1.2)	NS
Central West	1.0 (0.7, 1.4)	NS
Mississauga Halton	0.6 (0.3, 1.2)	NS
Toronto Central	0.8 (0.6, 1.2)	NS
Central	0.5 (0.4, 0.7)	0.0004
South East	0.8 (0.4, 0.7)	NS
Champlain	1.0 (0.7, 1.4)	NS
North Simcoe-Muskoka	0.9 (0.6, 1.4)	NS
North East	1.1 (0.7, 1.5)	NS
North West	0.7 (0.5, 1.0)	0.03
Central East	Reference	N/A
Recency of immigration		
Remote or non-immigrant	1.0 (0.6, 1.6)	NS
Recent immigrant	Reference	N/A
Prior FOBT Use		
2 to 5 years prior to mailing	2.8 (2.5, 3.3)	<.0001

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> 5 years or never	Reference	
Physician		
Increasing age (per year)	1.0 (1.0, 1.0)	NS
Sex		
Female	1.3 (1.0, 1.5)	0.02
Male	Reference	N/A
Training location		
In Canada	0.9 (0.7, 1.2)	NS
Outside Canada	Reference	N/A
Practice type		
FHG	0.9 (0.7, 1.1)	NS
FHO/FHN	0.8 (0.6, 1.1)	NS
Other PEM	0.7 (0.4, 1.0)	0.05
FHO/FHN-FHT	Reference	N/A
Practice size (enrolled patients)		
≤ 1800 patients	1.1 (0.9, 1.3)	NS
> 1800 patients	Reference	N/A
Age-eligible rate of colonoscopy quintile		
Low	1.1 (0.8, 1.5)	NS
2	1.2 (1.0, 1.6)	NS
3	1.0 (0.8, 1.2)	NS
4	1.0 (0.8, 1.3)	NS
High	Reference	N/A
Age-eligible rate of FOBT quintile		
2	0.9 (0.6, 1.3)	NS
3	0.9 (0.7, 1.2)	NS
4	1.1 (0.8, 1.4)	NS
High	0.9 (0.7, 1.3)	NS
Low	Reference	N/A
Age-eligible rate of annual physical exams quintile		
2	1.4 (0.9, 2.0)	NS
3	1.3 (0.9, 1.8)	NS
4	1.3 (0.9, 1.8)	NS
High	1.1 (0.8, 1.5)	NS
Low	Reference	N/A
Age-eligible rate of influenza vaccine quintile		
2	1.0 (0.8, 1.2)	NS
3	0.8 (0.6, 1.0)	0.02
4	0.9 (0.7, 1.2)	NS
High	1.3 (1.0, 1.7)	NS
Low	Reference	N/A

*Co-morbidity scored using number of Aggregated Diagnosis Groups (ADGs) using the Johns Hopkins Case Mix System
FHG = family health group
FHO/FHN = family health organizations or networks

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Other PEM = other patient enrolled model of care
NS = not significant
N/A - not applicable
FOBT = fecal occult blood test

Table 3. Characteristics of the 2 cohorts matched by propensity score in Study 2

	Pilot participants (n=10,652)	Control patients (n=10.652)	Standardized Difference*
Patients			
Age group in years, No. (%)			
50-59	6,248 (59%)	6,324 (59%)	0.01
60-69	3,342 (31%)	3,316 (31%)	0.01
70-74	1,062 (10%)	1,012 (10%)	0.02
Sex, No. (%)			
Female	5548 (52%)	5477 (51%)	0.01
Male	5,104 (48%)	5,175 (49%)	0.01
Co-morbidity**, No. of ADGs (%)			
0	1,462 (14%)	1,425 (13%)	0.01
1-2	3,647 (34%)	3,716 (35%)	0.01
3-4	2,764 (26%)	2,835 (27%)	0.02
5-6	1,536 (14%)	1,473 (14%)	0.02
7+	1,243 (12%)	1,203 (11%)	0.01
Median neighborhood income quintile, No. (%)			
Rural	1,825 (17%)	1,889 (18%)	0.02
Low Urban	1,628 (15%)	1,699 (16%)	0.02
2	1,698 (16%)	1,728 (16%)	0.01
3	1,728 (16%)	1,681 (16%)	0.01
4	1,831 (17%)	1,753 (16%)	0.02
High Urban	1,942 (18%)	1,902 (18%)	0.01
Health region, No. (%)			
Erie St.Clair	462 (4%)	423 (4%)	0.02
South West	1,107 (10%)	1,114 (10%)	0
Waterloo Wellington	327 (3%)	343 (3%)	0.01
Hamilton Niagara	1,265 (12%)	1,290 (12%)	0.01
Central West	620 (6%)	580 (5%)	0.02
Mississauga Halton	142 (1%)	144 (1%)	0
Toronto Central	503 (5%)	478 (4%)	0.01
Central	201 (2%)	209 (2%)	0.01
Central East	1,643 (15%)	1,702 (16%)	0.02
South East	859 (8%)	891 (8%)	0.01
Champlain	895 (8%)	904 (8%)	0
North Simcoe-Muskoka	265 (2%)	242 (2%)	0.01
North East	1,409 (13%)	1,378 (13%)	0.01
North West	954 (9%)	954 (9%)	0
Recent immigrant, No. (%)	111 (1%)	105 (1%)	0.01
FOBT 2 to 5 years prior to mailing, No. (%)	1,476 (14%)	1,240 (12%)	0.07
Physician			

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Median age in years (IQR)	52 (45-59)	52 (47-58)	N/A
Sex, No. (%)			
Female	3,875 (36%)	3,335 (31%)	N/A
Male	6,777 (64%)	7,317 (69%)	
Practice type, No. (%)			
FHG	4,854 (46%)	4,885 (46%)	
FHO/FHN	1,859 (17%)	1,718 (16%)	N/A
FHO/FHN-FHT	3,374 (32%)	3,027 (28%)	
Other PEM	565 (5%)	1,022 (10%)	
Practice size (enrolled patients), No. (%)			
>1800 patients	5,366 (50%)	5,026 (47%)	N/A

*Standardized differences for physician level variables not reported as propensity scores were estimated using patient level characteristics only
**Co-morbidity scored using number of Aggregated Diagnosis Groups (ADGs) using the Johns Hopkins Case Mix System
FHG = family health group
FHO/FHN = family health organizations or networks
Other PEM = other patient enrolled model of care
FOBT = fecal occult blood test

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Table 4. Association between mailed invitation and FOBT completion or mailed invitation and FOBT or colonoscopy completion after adjusting for physician factors.

	FOBT completion		FOBT or Colonoscopy completion	
	Odds ratio (95% C.I.)	P-value	Odds ratio (95% C.I.)	P-value
Mailed invitation				
Yes (Pilot)	3.3 (3.1, 3.6)	<.0001	2.7 (2.5, 2.9)	<.0001
No (Controls)	Reference	N/A	Reference	N/A
Increasing age (per year)	1.0 (1.0, 1.0)	NS	1.0 (1.0, 1.0)	0.03
Sex, No. (%)				
Female	1.0 (0.9, 1.1)	NS	1.0 (0.9, 1.1)	NS
Male	Reference	N/A	Reference	N/A
Practice type, No. (%)				
FHG	0.7 (0.6, 0.8)	<.0001	0.7 (0.7, 0.8)	<.0001
FHO/FHN	0.8 (0.7, 0.9)	<.0001	0.8 (0.7, 0.9)	<.0001
Other PEM	0.8 (0.7, 1.0)	0.03	0.8 (0.7, 1.0)	NS
FHO/FHN-FHT	Reference	N/A	Reference	N/A
Practice size (enrolled patients)				
≤ 1800 patients	1.2 (1.1, 1.3)	0.0004	1.2 (1.1, 1.3)	<.0001
> 1800 patients	Reference	N/A	Reference	N/A

FHG = family health group

FHO/FHN = family health organizations or networks

Other PEM = other patient enrolled model of care

FOBT = fecal occult blood test

Figure Legends

Figure 1. Mock-up of physician-linked invitation used in the Pilot.

ColonCancerCheck | ContrôleCancerColorectal   cancer care ontario | action cancer ontario

From the office of Dr. George Black

June 1, 2009

Lawren Harris
456 Superior Street
Lindsay ON K2L 3M4

Dear Lawren Harris:

You have received this letter because it is time to be screened for colon cancer. Our records as of April 1st, 2009 show that you have never had a fecal occult blood test (FOBT) or we do not know when you had your last FOBT. All adults between the ages of 50 and 74 years who are at average risk for colon cancer should do a FOBT every two years.

If your parent, brother, sister or child has had colon cancer, your risk is higher and you should have a colonoscopy.

Please call my office to set up an appointment to talk about your risk for colon cancer and which test is right for you.

If you have recently completed colon cancer screening, please disregard this letter.

I look forward to hearing from you soon.

Dr. George Black
705-555-1212

GET THE FACTS. GET CHECKED.

- Colon cancer is the second most common cause of cancer death in Ontario
- Colon cancer can develop without any early warning signs.
- If it is caught early enough, 9 out of every 10 people can be cured.
- Regular screening is the best way to catch colon cancer early.
- The FOBT is a simple test that can be done at home.

For more information please visit www.coloncancercheck.ca

This letter has been sent on my behalf by ColonCancerCheck (CCC), Ontario's colorectal cancer screening program. CCC is a collaborative initiative of the Ministry of Health and Long-Term Care and Cancer Care Ontario. If for any reason you do not wish to receive future correspondence from the program, simply call the ColonCancerCheck Information Line at 1-866-662-9233 during business hours.

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	Item No	Recommendation	Page	Comment
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1, 3	
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	3	
Introduction				
Background/ratio nale	2	Explain the scientific background and rationale for the investigation being reported	07-Jun	
Objectives	3	State specific objectives, including any prespecified hypotheses	7, first paragraph	
Methods				
Study design	4	Present key elements of study design early in the paper	7, paragraph 2	
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	7, paragraph 2	
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	9, paragraph 2, 10, paragraph 2 & 12, first paragraph	
		Case-control study—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls	n/a	
		Cross-sectional study—Give the eligibility criteria, and the sources and methods of selection of participants	n/a	
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed	12, first paragraph	
		Case-control study—For matched studies, give matching criteria and the number of controls per case	n/a	
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	9, 10 & 11	
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	8, 9, 10 & 11	
Bias	9	Describe any efforts to address potential sources of bias	11, paragraph 2 & 13, paragraph	
Study size	10	Explain how the study size was arrived at	5, paragraph 1	
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why		
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	11, paragraph 2 & 13, paragraph	
		(*b*) Describe any methods used to examine subgroups and interactions	n/a	
		(*c*) Explain how missing data were addressed	14, first paragraph	
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed	n/a	all patients followed through administrative data, therefore no loss to f/u
		Case-control study—If applicable, explain how matching of cases and controls was addressed	n/a	
		Cross-sectional study—If applicable, describe analytical methods taking account of sampling strategy	n/a	
		(*e*) Describe any sensitivity analyses	n/a	
Results				
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	14, first & last paragraphs	
		(b) Give reasons for non-participation at each stage	14, first & last paragraphs	

		(c) Consider use of a flow diagram	n/a
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	Table 1 & Table 3
		(b) Indicate number of participants with missing data for each variable of interest	15, first paragraph
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)	all followed up for 6 months
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time	15, 2nd paragraph & 16, 1st paragraph
		Case-control study—Report numbers in each exposure category, or summary measures of exposure	n/a
		Cross-sectional study—Report numbers of outcome events or summary measures	n/a
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	15, 2nd paragraph, Tables 2 & 4
		(*b*) Report category boundaries when continuous variables were categorized	Tables 2 & 4
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	n/a
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	n/a
Discussion			
Key results	18	Summarise key results with reference to study objectives	16, paragraph 1
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	18, 2nd paragraph
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	17 & 18
Generalisability	21	Discuss the generalisability (external validity) of the study results	18, last paragraph
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	19, 20

Physician-linked mailed invitations to be screened in an organized colorectal cancer screening program: effectiveness and factors associated with response.

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TITLE PAGE

Title: Physician-linked mailed invitations to be screened in an organized colorectal cancer screening program: effectiveness and factors associated with response..

Short tile: Physician-linked invitations for colorectal cancer screening

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Word count: 3211 (main text),   262 (abstract)

Number of Tables: 4

Number of Figures: 1

Number of References: 40

Key words: Mailed invitations, colorectal cancer, organized screening

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ABSTRACT

Objectives: A central tenet of organized cancer screening is that all persons in a target population are invited. The aims of this study were to identify participant and physician factors associated with response to mailed physician-linked invitations (Study 1) and to evaluate their effectiveness in an organized colorectal (CRC) screening program (Study 2).

Design and setting: Two studies (Study 1 – cohort design and Study 2 – matched cohort design of Study 1 participants and a matched control group) conducted in context of Ontario's organized province-wide CRC screening program.

Participants: 102 family physicians and 11,302 associated eligible patients from a technical evaluation ("the Pilot") of large scale mailed invitations for CRC screening were included. Matched controls were randomly selected using propensity scores from among eligible patients associated with family physicians in similar practice types as the Pilot physicians.

Intervention: Physician-linked mailed invitation to have CRC screening.

Outcomes: Uptake of fecal occult blood test (FOBT) within 6 months of mailed invitation (primary) and uptake of FOBT or colonoscopy within 6 months of mailed invitation (secondary).

Results: Factors significantly associated with uptake of FOBT included prior FOBT use, older participant age, greater participant co-morbidity and having a female physician. In

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the matched analysis, Pilot participants were more likely to complete an FOBT (22% vs. 8%, p<0.0001) or an FOBT or colonoscopy (25% vs. 11%, p <0.0001) within 6 months of mailed invitation than matched controls. The number needed to invite to screen one additional person was 7.

Conclusions: Centralized large scale mailing of physician-linked invitations is both feasible and effective in an organized CRC screening program.

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ARTICLE SUMMARY

Strengths and limitations of this study:

- We describe the implementation of physician-linked invitations in an organized colorectal screening program that is characterized by a high level of primary care physician involvement and that operates in a context where opportunistic screening with colonoscopy is possible
- We have shown that centralized large scale mailing of physician-linked invitations is feasible and effective in this context
- We found that physician linked mailed invitations improve CRC screening participation by 14% such that 7 physician-linked invitations need to be mailed to screen one additional person
- We were limited to data found in Ontario health administrative databases; for example, we were not able to determine family history
- Findings are promising but require appropriate infrastructure in order to be implemented in other jurisdictions

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INTRODUCTION

Colorectal cancer (CRC) is the 3rd most common cancer and the 4th leading cause of cancer-related death worldwide.[1] Fecal occult blood testing (FOBT)[2-4] and flexible sigmoidoscopy[5-7] have been shown to decrease CRC mortality in randomized controlled trials.

Given these data, organized CRC screening programs[8] are being implemented worldwide.[9] On April 1 2008, Ontario launched Canada's first organized province-wide CRC screening program, ColonCancerCheck (CCC).[10] CCC has a dual strategy: through the primary care physician, FOBT is offered to people at average risk for CRC and colonoscopy to those at increased risk based on family history. The CCC program uses a non-rehydrated guaiac FOBT (Hema-Screen, Immmunostics, Inc., NJ, USA) requiring 3 stool samples from separate stools. The only recommended dietary restriction is to avoid vitamin C for 3 days prior to and during the collection period.

Approximately 75% of Ontario residents received their care via a patient enrolled model (PEMs) of care at the time of the study (2009).[11] PEMs comprise teams of family physicians who provide their enrolled patients with comprehensive health care and extended hours.[12] PEMs vary in terms of structure, services provided and remuneration (varying from enhance fee-for-service to blended capitation). All Ontario physicians are remunerated for preventive care such as CRC screening however, PEM

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physicians are incented to a greater degree than those who are not in PEMs.

Specifically, PEM physicians receive a $7/patient fee for FOBT Distribution and

Counseling, a $6.86/patient fee for CRC Screening Management and an annual

Colorectal Cancer Screening Preventive Care Bonus ($220 to $4000) depending on the

proportion of enrolled patients who are up-to-date with FOBT (15-70%). The physician

is entitled to the CRC Screening Management fee if the enrolled patient attends an

appointment to discuss CRC screening, has declined the test verbally or in writing or

there has been no response after 2 written notices and a telephone call from the

physician.[13]

A central tenet of organized screening programs is that all persons in the target

population be invited to participate.[8] Implementation of this aspect of organized

screening vary: invitations may be sent with an FOBT kit, can include physician

recommendation or may incorporate tailored messaging.[14 ,15] Some of these

approaches, such as incorporation of physician recommendation, present significant

implementation challenges for organized screening programs such as Ontario's.

In 2009, the CCC program conducted the CCC Invitation Pilot (the "Pilot"), an evaluation

that tested the technical feasibility of a centralized approach to sending physician-linked

mailed invitations for CRC screening. In this paper, we describe the structure and the

implementation of the Pilot. In addition, we report on participant and physician factors

associated with response to mailed physician-linked invitations and on the effectiveness

of these invitations in an organized CRC screening program.

METHODS

The CCC Invitation Pilot – Implementation and Evaluation

The Pilot was conducted by CCC in November 2009 in order to develop and test the

technical infrastructure required for large scale centralized physician-linked mailed

invitations in Ontario. For the Pilot, invitation letters were generated by the CCC

program on behalf of 102 family physicians and sent to all their eligible enrolled patients.

Just over 11,000 eligible patient participants were sent mailed invitations requesting they

visit their family physician to obtain an FOBT kit or, if appropriate based on family

history, a referral for colonoscopy. In this paper, we report on 2 studies using this cohort.

Study 1 examines participant and physician factors associated with response to the

mailed invitation among those who were sent the mailed invitation. Study 2 evaluates

the effectiveness of the mailed invitation by comparing uptake of CRC screening among

Study 1 participants compared to a matched control group. Ethics approval was

obtained from the research ethics boards at Sunnybrook Health Sciences Centre and

the Institute for Clinical Evaluative Sciences (ICES) and permission to use the Pilot data

was obtained from Cancer Care Ontario's (CCO) Data Access Committee. All analyses

were conducted using SAS v.9 (SAS Institute, Cary, NC). A p-value of 0.05 was used to

determine statistical significance.

Data Sources

The Pilot study was conducted at ICES, which houses the administrative health records

for all 12.4 million Ontarians. CCC program databases were linked to the ICES

administrative databases using an encrypted version of the provincial health insurance

number.

The ICES databases used include the Canadian Institute of Health Information (CIHI)

databases, the Ontario Health Insurance Program (OHIP) Claims History Database, the

Registered Persons Database (RPDB), the Ontario Cancer Registry, the ICES Physician

Database, and the Client Agency Program Enrollment (CAPE) registry. The CIHI, OHIP,

RPDB and the Ontario Cancer Registry and the ICES Physician Database have been

previously described.[16 ,17] The CAPE registry tracks patients enrolled to physicians

who participate in PEMs and is a centralized electronic record of the linkage between

specific patients and their physicians.,

The CCC program has collected data on CRC screening since its inception using

Laboratory Reporting Tool (LRT) and comprises data related to the FOBT kits

administered by the CCC program, including the results of these tests.

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Study 1: Factors associated with response to the mailed invitation

Cohort Definition: For the Pilot, a convenience sample of physicians participating in

PEM-type practices was recruited via CCO's Provincial Primary Care Cancer Network.

Patients enrolled to these physicians, aged 50 to 74 years without a history of CRC and

who were due for CRC screening (without a record of recent FOBT (previous two years)

or lower GI investigation including flexible sigmoidoscopy and colonoscopy (previous 5

years)), were eligible. For the Pilot mailing, CCC generated lists of patient participants

eligible for CRC screening for each participating physician using CAPE, Ontario Cancer

Registry, OHIP, CIRT and LRT. All persons who were sent an invitation were included in

the cohort, regardless of whether the letter was returned to the sender.

The Mailing: Invitations were mailed in November 2009. The date of mailing was the

index date. The letters were compiled centrally by the CCC program but were physician-

linked; patient participants were sent a letter from their own physician, as indicated by

their name at the bottom of the letter in an italicized font (Figure 1). The letter asked

participants to visit their family physician for screening; it did not include an FOBT kit.

The letter was accompanied by a CRC screening information brochure and sent in an

envelope with the family physician name in the front upper left corner. For the purposes

of the study, Pilot physicians were compensated an equivalent amount to the CRC

Screening Management fee ($6.86 per eligible enrolled patient) as Ontario PEM

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physicians are eligible for this fee for contacting the patient by mail regarding CRC

screening.

Response to Mailed Invitation: We used a broad definition of response to the mailed

invitation: any record of FOBT in either OHIP or in LRT within 6 months of the index

date, regardless of result (including rejected kits). Up to 10% of FOBT done in the

province are captured only through OHIP, which does not have data on test results. We

were not able to measure response in persons at increased risk of CRC as we do not

have family history data available in the administrative databases.

Participant and Physician Factors: We characterized participants by age group, sex, co-

morbidity, median neighborhood income[18 ,19], health region[20], immigration status,

and prior FOBT. Comorbidity was measured by counting the number of Aggregated

Diagnosis Groups (ADGs) in the prior 12 months according to the Johns Hopkins ACG®

Case-Mix System.[21] This system has been shown to accurately predict mortality in a

general population ambulatory cohort in Ontario.[22] We used date of registration in the

RPDB as a proxy measure for immigration status; participants were considered recent

immigrants if their date of registration was within 5 years of the index date.[23]

Physicians were characterized according to age, sex, training location (attended

Canadian medical school vs. outside of Canada), practice type, size of practice, age-

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eligible rate of colonoscopy or FOBT over prior 2 years as well as the age-eligible rate of

annual physical exams or influenza vaccinations in the prior year. All physicians were in

PEMs; practice types included family health groups (FHGs, enhanced fee-for-service

models), family health organizations or networks (FHO/FHNs, blended capitation

models), FHO/FHN with family health team (FHO/FHN-FHT, interprofessional team

model with a blended capitation fee structure) and other PEMs.[24] We measured

practice size as the number of enrolled patients stratified in a binary fashion (≤1800 vs.

>1800 enrolled patients) as larger practice sizes have been shown to be associated with

poorer preventative care.[25] For the remaining physician characteristics, we identified

all enrolled and non-enrolled patients aged 50-74 years in their practices as of the index

date. Age-eligible FOBT and colonoscopy rates were obtained for each Pilot physician

by calculating the proportion of their age-eligible patients who had had an FOBT or

colonoscopy in the 2 years prior to the index date. Similarly, we calculated their rates of

age-eligible annual physical exams or influenza vaccine in the year prior to the index

date. These variables were derived in order to estimate physician adherence to CRC

screening and preventive medicine practices at baseline.

Analysis: The number and proportion of persons in the cohort who responded to the

mailed invitation within 6 months were determined overall and by participant and

physician characteristics. Multivariate logistic regression modeling was used to identify

participant and physician factors associated with response to the mailed invitation. In

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order to account for potential clustering of participants within physicians, Generalized

Estimating Equations (GEE) were used in the model.

Study 2: Evaluation of the effectiveness of mailed invitations

Overview and study participants: This was a matched double cohort analysis, comparing

uptake of FOBT in those who were sent a mailed invitation (Pilot cohort) to a matched

control group who were not sent a mailed invitation. The control group comprised

patients who were enrolled to PEM physicians who had not participated in the Pilot.

Control participants received "usual care" for the CCC program in terms of screening

promotion. As such, they received screening via their primary care physician who were

eligible for the same financial incentives as Pilot physicians. Control participants were

not sent a centralized physician-linked invitation from the CCC program although their

physicians could send them a mailed invitation at their own discretion.

The Pilot cohort comprised all members of the cohort described in Study 1 for whom a

matched control could be identified. We identified potential controls as follows: 1) Pilot

physicians were matched to non-Pilot physicians who were also practicing in PEMs in a

1:5 ratio using physician age, sex, size and practice type; 2) individuals enrolled to the

selected control physicians were retained if they met the same inclusion/exclusion

criteria as those in the intervention cohort (aged 50 to 74 years with no prior CRC who

were due for CRC screening). As with the identification of eligible participants in the

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Pilot, we used CAPE, Ontario Cancer Registry, OHIP, CIRT and LRT to determine

eligibility of potential control participants.

Propensity scores that modeled the probability of belonging to the Pilot group were

calculated for each participant in the entire group (Pilot and control). The variables in this

model included age (as a continuous measure), sex, co-morbidity, median neighborhood

income quintile, health region, immigration status, and FOBT from 2 to 5 years prior.[26

,27] Pilot participants were matched to controls in a 1:1 fashion based on propensity

scores using a caliper width of 0.25. This methodology was implemented to balance the

distribution of participant-level variables between the Pilot and control groups.

Response to mailed invitation: For our primary outcome, we defined response to the

mailed invitation as in Study 1, a record of FOBT regardless of result, within 6 months of

the index date. For our secondary outcome, response was defined as a record of either

FOBT or colonoscopy within 6 months of the index date. For the purposes of this study,

controls were assigned the same index date as their matched counterpart in the Pilot

group.

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Analysis: Standard differences between the Pilot participants and controls were

calculated for the variables included in the propensity score. Important differences

between the 2 groups were defined by a standardized difference exceeding 0.1.[27 ,28]

In the primary analysis, we compared the number and proportion in the Pilot and control

groups responding to the mailed invitation with FOBT using McNemar's test.[27] We

determined the number of invitations mailed in order to screen one additional person

with FOBT. We repeated the above analyses using our secondary outcome in order to

determine if observed differences in FOBT uptake could be attributed to differences in

colonoscopy uptake (i.e., participants had CRC screening but chose colonoscopy over

FOBT). As the matching only accounted for participant-level variables, we repeated our

analyses using conditional logistic regression in order to adjust for physician covariates

(age, sex, practice type and size).

RESULTS

Study 1: Factors associated with response to the mailed invitation

There were 11,311 eligible patient participants associated with the 102 family physicians

in the Pilot cohort. Nine participants were excluded as we were unable to determine

their health region and/or income quintile; this left 11,302 participants for the analysis.

The majority of participants were 50 to 59 years of age, 52% were women, 48% had no

or low co-morbidity and 14% had completed an FOBT from 2 to 5 years prior to the

mailing. Two thirds of participants had a male physician, approximately half were part of

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a primary care team reimbursed via an enhanced fee-for-service arrangement and just

under half were enrolled in larger practices (>1800 enrolled patients) (Table 1).

2503 (22%) completed an FOBT within 6 months of mailing. In the multivariate

regression, the strongest participant factor associated with FOBT completion was prior

FOBT use (2 to 5 years prior vs. > 5 years or never: OR 2.8, 95% C.I.: 2.5 to 3.3, p <

0.0001). Other significant factors associated with FOBT completion included older

participant age, greater co-morbidity, and having a female physician (Table 2).

Study 2: Evaluation of the effectiveness of mailed invitations

Of the 11,302 participants in Study 1, 10,652 were successfully matched to 10,652

controls using propensity scores. Standardized differences for the participant

characteristics included in the propensity score were all <0.1, indicating that the two

cohorts were well matched for measurable potential confounders (Table 3).

Pilot participants were significantly more likely than controls to complete FOBT alone

(2387 (22%) versus 854 (8%), p<0.0001) and FOBT or colonoscopy (2664 (25%) vs.

1191 (11%), p<0.0001) within 6 months of mailing. The association between the mailed

invitation and CRC screening participation (either FOBT alone or FOBT or colonoscopy)

remained after adjusting for physician level characteristics (Table 4).

DISCUSSION

In the current study, we have demonstrated that physician-linked mailed invitations are

both feasible and effective in the context of a large organized, population-based

screening program; only 7 letters would need to be sent in order to screen one additional

person. Furthermore, we have found that older participants, those with greater co-

morbidity, those who have previously been screened and those with female physicians

were more likely to respond to this type of invitation. Our findings are of particular

interest to other jurisdictions planning or who already have organized CRC screening.

In other published studies of mailed invitations, an FOBT kit is often included with the

invitation. Three studies done outside organized screening programs have found

physician-linked invitations superior to non-linked invitations; 2 of these studies included

an FOBT kit,[29 ,30] and the third study did not.[31] Other studies have examined mailed

invitations with FOBT kits in the context of primary care practices in the USA.[32-34]

While the results from these trials were largely supportive of mailed invitations, kit

inclusion can make it difficult to separate the convenience of receiving the FOBT kit

directly by mail from the impact of an invitation from one's own physician.

Our study demonstrates the effectiveness and feasibility of physician-linked invitations in

the context of a large organized CRC screening program with an estimated target

population of over 3 million persons. Implementation in this context confers challenges in

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terms of technological infra-structure, privacy and regulatory issues. There are 2 studies

(from the United Kingdom[35] and Italy[36]) that have reported on mailed invitations in

the context of organized colorectal cancer screening programs and found them to be

effective. Both studies included FOBT kits and one studied the impact of physician

endorsement specifically.[35] Our findings are important because they support a

potentially more cost-effective approach that avoids wasting kits that are mailed but not

used.

Our results highlight the critical role of physician recommendation, a finding supported

by others. For example, in the NHS Bowel Cancer Screening Programme (BCSP)

currently, the primary care physician receives the result but is not directly involved in the

mailed invitation or the actual screening. Recently, a randomized controlled trial

conducted in the context of the BCSP showed that an endorsement letter from the

primary care provider increased participation by 6%.[35]   In 2 studies from Australia,

endorsement improved initial participation[29 ,30] and over 4 successive screening

rounds.[30]

Uptake of FOBT in Ontario is lower than some organized CRC screening programs in

other countries. For example, 30% of Ontarians were up-to-date with FOBT in 2008-

9[37] compared to 52% participation in the United Kingdom program by October

2008,[38] 54% in the Italian program in 2007,[39] and 54% in the New Zealand pilot

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program in 2012.[40] However, in the latter countries, there is very little, if any,

opportunistic CRC screening using colonoscopy whereas Ontario's program operates in

a hybrid environment where opportunistic colonoscopy is available as the initial

screening test in persons at average risk. It has been noted that uptake of FOBT may

be lower in settings, such as Ontario's or Australia's,[41] where opportunistic screening

is available.[42] The findings from the current study indicate that physician-linked

invitations for CRC screening can be effective in increasing uptake of FOBT in programs

that operate in the context of opportunistic colonoscopy for average risk screening.

Our study has several limitations. As mentioned above, we are unable to determine

family history using Ontario administrative data. A second limitation is that a single

generic letter was used. Tailored letters with key messages for specific subgroups may

be more effective,[15] an approach that may be relevant in Ontario as we did find that

response to the letter appeared to differ in various subgroups. Additionally, while our

findings are promising, there are challenges to widespread implementation in other

population-based screening programs, including the requirement for a centralized

database that links patients to their physicians. Finally, implementation of this strategy in

population based screening is predicated on physician acceptability and agreement.

While we have found that this approach is acceptable in principle to many Ontario

physicians,[43] processes to confirm individual physician agreement have not been

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determined for the entire CCC program which comprises an estimated 7000 primary

care physicians.

CONCLUSIONS

In summary, we have demonstrated that physician-linked mailed invitations for CRC

screening, even without the inclusion of an FOBT kit, can have substantial effect on

participation in an organized CRC screening program and that it is technically feasible to

centrally organize and mail physician-linked invitations on a large scale. Organized

screening programs, which often use unlinked invitations, should consider adopting this

approach given its demonstrated effectiveness and feasibility.

ACKNOWLEDGEMENTS

COMPETING INTERESTS STATEMENT

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Dr. Tinmouth is the Lead Scientist for the ColonCancerCheck program and Dr.

Rabeneck oversees the ColonCancerCheck program in her capacity as the Vice-

President, Cancer Prevention and Control at CCO. None of the other authors have any

conflicts of interest to report.

FUNDING STATEMENT

AUTHOR CONTRIBUTION:

Authors contributed substantially to each of the following areas:

-conception and design (JT, LFP, LR) or analysis and interpretation of data (JT, NB,

LFP, LR, RS, LY)

-drafting the article (JT) or revising it critically for important intellectual content (JT, NB,

LFP, LR, RS, LY)

-final approval of the version to be published (JT, NB, LFP, LR, RS, LY)

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Tables.

Table 1. Patient participant and physician characteristics for Study 1

	FOBT within 6 months	No FOBT within 6 months	Total
	(n=2,503)	(n=8,799)	(n=11,302)
Patient participants			
Age group in years, No. (%)			
50-59	1,279 (51%)	5,384 (61%)	6,663 (59%)
60-69	894 (36%)	2,637 (30%)	3,531 (31%)
70-74	330 (13%)	778 (9%)	1,108 (10%)
Sex, No. (%)			
Female	1,299 (52%)	4,554 (52%)	5,853 (52%)
Male	1,204 (48%)	4,245 (48%)	5,449 (48%)
Co-morbidity*, No. of ADGs (%)			
0	257 (10%)	1,279 (15%)	1,536 (14%)
1-2	828 (33%)	3,044 (35%)	3,872 (34%)
3-4	712 (28%)	2,241 (25%)	2,953 (26%)
5-6	393 (16%)	1,224 (14%)	1,617 (14%)
7+	313 (13%)	1,011 (11%)	1,324 (12%)
Median neighborhood income quintile, No. (%)			
Rural	394 (16%)	1,431 (16%)	1,825 (16%)
Low Urban	360 (14%)	1,375 (16%)	1,735 (15%)
2	402 (16%)	1,418 (16%)	1,820 (16%)
3	429 (17%)	1,430 (16%)	1,859 (16%)
4	432 (17%)	1,552 (18%)	1,984 (18%)
High Urban	486 (19%)	1,593 (18%)	2,079 (18%)
Health region, No. (%)			
Erie St.Clair	125 (5%)	337 (4%)	462 (4%)
South West	284 (11%)	823 (9%)	1,107 (10%)
Waterloo Wellington	76 (3%)	251 (3%)	327 (3%)
Hamilton Niagara	289 (12%)	976 (11%)	1,265 (11%)
Central West	138 (6%)	482 (5%)	620 (5%)
Mississauga Halton	22 (1%)	120 (1%)	142 (1%)
Toronto Central	111 (4%)	392 (4%)	503 (4%)
Central	24 (1%)	177 (2%)	201 (2%)
Central East	361 (14%)	1,282 (15%)	1,643 (15%)
South East	162 (6%)	697 (8%)	859 (8%)
Champlain	219 (9%)	676 (8%)	895 (8%)
North Simcoe-Muskoka	77 (3%)	188 (2%)	265 (2%)
North East	291 (12%)	1,118 (13%)	1,409 (12%)
North West	324 (13%)	1,280 (15%)	1,604 (14%)

Recent immigrant, No. (%)	23 (1%)	88 (1%)	111 (1%)
FOBT 2 to 5 years prior to mailing, No. (%)	643 (26%)	905 (10%)	1,548 (14%)
Physician			
Median age in years (IQR)	52 (45-59)	53 (46-59)	52 (45-59)
Sex, No. (%)			
Female	936 (37%)	3,044 (35%)	3,980 (35%)
Male	1,567 (63%)	5,755 (65%)	7,322 (65%)
Training location, No. (%)			
Outside Canada	312 (12%)	1,196 (14%)	1,508 (13%)
In Canada	2,191 (88%)	7,603 (86%)	9,794 (87%)
Practice type, No. (%)			
FHG	1,082 (43%)	4,266 (48%)	5,348 (47%)
FHO/FHN	432 (17%)	1,456 (17%)	1,888 (17%)
FHO/FHN-FHT	881 (35%)	2,620 (30%)	3,501 (31%)
Other PEM	108 (4%)	457 (5%)	565 (5%)
Practice size (enrolled patients), No. (%)			
>1800 patients	1,105 (44%)	4,104 (47%)	5,209 (46%)
Age-eligible rate of colonoscopy quintile, No. (%)			
Low	485 (19%)	1,619 (18%)	2,104 (19%)
2	548 (22%)	1,940 (22%)	2,488 (22%)
3	637 (25%)	2,279 (26%)	2,916 (26%)
4	477 (19%)	1,696 (19%)	2,173 (19%)
High	356 (14%)	1,265 (14%)	1,621 (14%)
Age-eligible rate of FOBT quintile, No. (%)			
Low	487 (19%)	1,888 (21%)	2,375 (21%)
2	504 (20%)	1,886 (21%)	2,390 (21%)
3	533 (21%)	1,890 (21%)	2,423 (21%)
4	522 (21%)	1,680 (19%)	2,202 (19%)
High	457 (18%)	1,455 (17%)	1,912 (17%)
Age-eligible rate of annual physical exams quintile, No. (%)			
Low	496 (20%)	2,009 (23%)	2,505 (22%)
2	490 (20%)	1,625 (18%)	2,115 (19%)
3	472 (19%)	1,638 (19%)	2,110 (19%)
4	509 (20%)	1,686 (19%)	2,195 (19%)
High	536 (21%)	1,841 (21%)	2,377 (21%)

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Age-eligible rate of influenza vaccine quintile, No. (%)			
Low	548 (22%)	1,997 (23%)	2,545 (23%)
2	549 (22%)	1,765 (20%)	2,314 (20%)
3	435 (17%)	1,930 (22%)	2,365 (21%)
4	485 (19%)	1,770 (20%)	2,255 (20%)
High	486 (19%)	1,337 (15%)	1,823 (16%)

*Co-morbidity scored using number of Aggregated Diagnosis Groups (ADGs) using the Johns Hopkins Case Mix System

FHG = family health group

FHO/FHN = family health organizations or networks

Other PEM = other patient enrolled model of care

FOBT = fecal occult blood test

Table 2.   Multivariate logistic regression analysis using Generalized Estimating Equations for the characteristics of participants and physicians associated with completing an FOBT within 6 months of the mailing date.

Participants	Odds ratio (95% C.I.)	P-value
Age group, years		
50-59	0.6 (0.5, 0.8)	<.0001
60-69	0.8 (0.7, 1.0)	NS
70-74	Reference	N/A
Sex		
Female	0.9 (0.9, 1.0)	NS
Male	Reference	N/A
Co-morbidity*, No. of ADGs		
0	0.7 (0.6, 0.8)	0.0002
1-2	0.9 (0.7, 1.0)	NS
3-4	1.0 (0.9, 1.2)	NS
5-6	1.0 (0.9, 1.2)	NS
7+	Reference	N/A
Median neighborhood income quintile		
Rural	0.9 (0.7, 1.1)	NS
Low Urban	0.9 (0.7, 1.0)	NS
2	1.0 (0.8, 1.1)	NS
3	1.0 (0.9, 1.1)	NS
4	0.9 (0.8, 1.1)	NS
High Urban	Reference	N/A
Health region		
Erie St.Clair	1.3 (0.9, 1.8)	NS
South West	0.9 (0.6, 1.4)	NS
Waterloo Wellington	0.8 (0.6, 1.2)	NS
Hamilton Niagara	0.9 (0.6, 1.2)	NS
Central West	1.0 (0.7, 1.4)	NS
Mississauga Halton	0.6 (0.3, 1.2)	NS
Toronto Central	0.8 (0.6, 1.2)	NS
Central	0.5 (0.4, 0.7)	0.0004
South East	0.8 (0.4, 0.7)	NS
Champlain	1.0 (0.7, 1.4)	NS
North Simcoe-Muskoka	0.9 (0.6, 1.4)	NS
North East	1.1 (0.7, 1.5)	NS
North West	0.7 (0.5, 1.0)	0.03
Central East	Reference	N/A
Recency of immigration		
Remote or non-immigrant	1.0 (0.6, 1.6)	NS
Recent immigrant	Reference	N/A
Prior FOBT Use		
2 to 5 years prior to mailing	2.8 (2.5, 3.3)	<.0001

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> 5 years or never	Reference	
Physician		
Increasing age (per year)	1.0 (1.0, 1.0)	NS
Sex		
Female	1.3 (1.0, 1.5)	0.02
Male	Reference	N/A
Training location		
In Canada	0.9 (0.7, 1.2)	NS
Outside Canada	Reference	N/A
Practice type		
FHG	0.9 (0.7, 1.1)	NS
FHO/FHN	0.8 (0.6, 1.1)	NS
Other PEM	0.7 (0.4, 1.0)	0.05
FHO/FHN-FHT	Reference	N/A
Practice size (enrolled patients)		
≤ 1800 patients	1.1 (0.9, 1.3)	NS
> 1800 patients	Reference	N/A
Age-eligible rate of colonoscopy quintile		
Low	1.1 (0.8, 1.5)	NS
2	1.2 (1.0, 1.6)	NS
3	1.0 (0.8, 1.2)	NS
4	1.0 (0.8, 1.3)	NS
High	Reference	N/A
Age-eligible rate of FOBT quintile		
2	0.9 (0.6, 1.3)	NS
3	0.9 (0.7, 1.2)	NS
4	1.1 (0.8, 1.4)	NS
High	0.9 (0.7, 1.3)	NS
Low	Reference	N/A
Age-eligible rate of annual physical exams quintile		
2	1.4 (0.9, 2.0)	NS
3	1.3 (0.9, 1.8)	NS
4	1.3 (0.9, 1.8)	NS
High	1.1 (0.8, 1.5)	NS
Low	Reference	N/A
Age-eligible rate of influenza vaccine quintile		
2	1.0 (0.8, 1.2)	NS
3	0.8 (0.6, 1.0)	0.02
4	0.9 (0.7, 1.2)	NS
High	1.3 (1.0, 1.7)	NS
Low	Reference	N/A

*Co-morbidity scored using number of Aggregated Diagnosis Groups (ADGs) using the Johns Hopkins Case Mix System
FHG = family health group
FHO/FHN = family health organizations or networks

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Other PEM = other patient enrolled model of care
NS = not significant
N/A - not applicable
FOBT = fecal occult blood test

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Table 3. Characteristics of the 2 cohorts matched by propensity score in Study 2

	Pilot participants (n=10,652)	Control participants (n=10.652)	Standardized Difference*
Participants			
Age group in years, No. (%)			
50-59	6,248 (59%)	6,324 (59%)	0.01
60-69	3,342 (31%)	3,316 (31%)	0.01
70-74	1,062 (10%)	1,012 (10%)	0.02
Sex, No. (%)			
Female	5548 (52%)	5477 (51%)	0.01
Male	5,104 (48%)	5,175 (49%)	0.01
Co-morbidity**, No. of ADGs (%)			
0	1,462 (14%)	1,425 (13%)	0.01
1-2	3,647 (34%)	3,716 (35%)	0.01
3-4	2,764 (26%)	2,835 (27%)	0.02
5-6	1,536 (14%)	1,473 (14%)	0.02
7+	1,243 (12%)	1,203 (11%)	0.01
Median neighborhood income quintile, No. (%)			
Rural	1,825 (17%)	1,889 (18%)	0.02
Low Urban	1,628 (15%)	1,699 (16%)	0.02
2	1,698 (16%)	1,728 (16%)	0.01
3	1,728 (16%)	1,681 (16%)	0.01
4	1,831 (17%)	1,753 (16%)	0.02
High Urban	1,942 (18%)	1,902 (18%)	0.01
Health region, No. (%)			
Erie St.Clair	462 (4%)	423 (4%)	0.02
South West	1,107 (10%)	1,114 (10%)	0
Waterloo Wellington	327 (3%)	343 (3%)	0.01
Hamilton Niagara	1,265 (12%)	1,290 (12%)	0.01
Central West	620 (6%)	580 (5%)	0.02
Mississauga Halton	142 (1%)	144 (1%)	0
Toronto Central	503 (5%)	478 (4%)	0.01
Central	201 (2%)	209 (2%)	0.01
Central East	1,643 (15%)	1,702 (16%)	0.02
South East	859 (8%)	891 (8%)	0.01
Champlain	895 (8%)	904 (8%)	0
North Simcoe-Muskoka	265 (2%)	242 (2%)	0.01
North East	1,409 (13%)	1,378 (13%)	0.01
North West	954 (9%)	954 (9%)	0
Recent immigrant, No. (%)	111 (1%)	105 (1%)	0.01
FOBT 2 to 5 years prior to mailing, No. (%)	1,476 (14%)	1,240 (12%)	0.07
Physician			

Median age in years (IQR)	52 (45-59)	52 (47-58)	N/A
Sex, No. (%)			
Female	3,875 (36%)	3,335 (31%)	N/A
Male	6,777 (64%)	7,317 (69%)	
Practice type, No. (%)			
FHG	4,854 (46%)	4,885 (46%)	
FHO/FHN	1,859 (17%)	1,718 (16%)	N/A
FHO/FHN-FHT	3,374 (32%)	3,027 (28%)	
Other PEM	565 (5%)	1,022 (10%)	
Practice size (enrolled patients), No. (%)			
>1800 patients	5,366 (50%)	5,026 (47%)	N/A

*Standardized differences for physician level variables not reported as propensity scores were estimated using patient level characteristics only

**Co-morbidity scored using number of Aggregated Diagnosis Groups (ADGs) using the Johns Hopkins Case Mix System

FHG = family health group

FHO/FHN = family health organizations or networks

Other PEM = other patient enrolled model of care

FOBT = fecal occult blood test

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Table 4. Association between mailed invitation and FOBT completion or mailed invitation and FOBT or colonoscopy completion after adjusting for physician factors.

	FOBT completion		FOBT or Colonoscopy completion	
	Odds ratio (95% C.I.)	P-value	Odds ratio (95% C.I.)	P-value
Mailed invitation				
Yes (Pilot)	3.3 (3.1, 3.6)	<.0001	2.7 (2.5, 2.9)	<.0001
No (Controls)	Reference	N/A	Reference	N/A
Increasing age (per year)	1.0 (1.0, 1.0)	NS	1.0 (1.0, 1.0)	0.03
Sex, No. (%)				
Female	1.0 (0.9, 1.1)	NS	1.0 (0.9, 1.1)	NS
Male	Reference	N/A	Reference	N/A
Practice type, No. (%)				
FHG	0.7 (0.6, 0.8)	<.0001	0.7 (0.7, 0.8)	<.0001
FHO/FHN	0.8 (0.7, 0.9)	<.0001	0.8 (0.7, 0.9)	<.0001
Other PEM	0.8 (0.7, 1.0)	0.03	0.8 (0.7, 1.0)	NS
FHO/FHN-FHT	Reference	N/A	Reference	N/A
Practice size (enrolled patients)				
≤ 1800 patients	1.2 (1.1, 1.3)	0.0004	1.2 (1.1, 1.3)	<.0001
> 1800 patients	Reference	N/A	Reference	N/A

FHG = family health group

FHO/FHN = family health organizations or networks

Other PEM = other patient enrolled model of care

FOBT = fecal occult blood test

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Figure Legends

Figure 1. Mock-up of physician-linked invitation used in the Pilot.

TITLE PAGE

Title: Physician-linked mailed invitations ~~to be screened~~ to be screened improves uptake in an organized colorectal cancer screening program: effectiveness and factors associated with response. ~~Two linked cohort studies~~.

Short tile: Physician-linked invitations for colorectal cancer screening

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Word count: ~~2637~~ 3211 (main text),   2~~6~~42 (abstract)

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Number of Tables: 4

Number of Figures: 1

Number of References: 40

Key words: Mailed invitations, colorectal cancer, organized screening

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ABSTRACT

Objectives: A central tenet of organized cancer screening is that all persons in a target population are invited. The aims of this study ~~we~~are to identify ~~patient~~participant and physician factors associated with response to mailed physician-linked invitations (Study 1) and to evaluate their effectiveness in an organized colorectal (CRC) screening program (Study 2).

Design and setting: Two ~~linked cohort~~ studies (Study 1 – cohort design and Study 2 – matched cohort design of Study 1 participants and a matched control group) conducted in context of Ontario's organized province-wide CRC screening program.

Participants: 102 family physicians and 11,302 associated eligible patients ~~participating~~ from~~in~~ a technical evaluation ("the Pilot") of large scale mailed invitations for CRC screening were included. Matched controls were randomly selected using propensity scores from among eligible patients associated with family physicians in similar practice types as the Pilot physicians.

Intervention: Physician-linked mailed invitation to have CRC screening.

Outcomes: Uptake of fecal occult blood test (FOBT) within 6 months of mailed invitation (primary) and uptake of FOBT or colonoscopy within 6 months of mailed invitation (secondary).

Results: Factors significantly associated with uptake of FOBT included prior FOBT use, older ~~patient~~participant age, greater ~~patient~~participant co-morbidity and having a female

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physician. In the matched analysis, Pilot ~~patient~~participants were more likely to

complete an FOBT (22% vs. 8%, p<0.0001) or an FOBT or colonoscopy (25% vs. 11%,

p <0.0001) within 6 months of mailed invitation than matched controls. The number

needed to invite to screen one additional person was 7.

Conclusions: Centralized large scale mailing of physician-linked invitations is both

feasible and effective in an organized CRC screening program.

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ARTICLE SUMMARY

Strengths and limitations of this study:

- We describe the iImplementation and effectiveness of physician-linked invitations in an organized colorectal screening program that is characterized by a high level of primary care physician involvement and that operates in a context where opportunistic screening with colonoscopy is possible have not yet been reported
- We have shown that centralized large scale mailing of physician-linked invitations is feasible and effective in this context
- We found that physician linked mailed invitations improve CRC screening participation by 14% such that 7 physician-linked invitations need to be mailed to screen one additional person
- We were limited to data found in Ontario health administrative databases; for example, we were not able to determine family history
- Findings are promising but require appropriate infrastructure in order to be implemented in other jurisdictions

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INTRODUCTION

Colorectal cancer (CRC) is the 3rd most common cancer and the 4th leading cause of cancer-related death worldwide.[1] Fecal occult blood testing (FOBT)[2-4] and flexible sigmoidoscopy[5-7] have been shown to decrease CRC mortality in randomized controlled trials.

Given these data, organized CRC screening programs[8] are being implemented worldwide.[9] On April 1 2008, Ontario launched Canada's first organized province-wide CRC screening program, ColonCancerCheck (CCC).[10] CCC has a dual strategy: through the primary care physician, FOBT is offered to people at average risk for CRC and colonoscopy to those at increased risk based on family history. The CCC program uses a non-rehydrated guaiac FOBT (Hema-Screen, Immmunostics, Inc., NJ, USA) requiring 3 stool samples from separate stools. The only recommended dietary restriction is to avoid vitamin C for 3 days prior to and during the collection period.

Approximately 75% of Ontario residents received their care via a patient enrolled model (PEMs) of care at the time of the study (2009).[11] PEMs comprise teams of family physicians who provide their enrolled patients with comprehensive health care and extended hours.[12] PEMs vary in terms of structure, services provided and remuneration (varying from enhance fee-for-service to blended capitation). All Ontario physicians are remunerated for preventive care such as CRC screening however, PEM

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physicians are incented to a greater degree than those who are not in PEMs.

Specifically, PEM physicians receive a $7/patient fee for FOBT Distribution and

Counseling, a $6.86/patient fee for CRC Screening Management and an annual

Colorectal Cancer Screening Preventive Care Bonus ($220 to $4000) depending on the

proportion of enrolled patients who are up-to-date with FOBT (15-70%). The physician

is entitled to the CRC Screening Management fee if the enrolled patient attends an

appointment to discuss CRC screening, has declined the test verbally or in writing or

there has been no response after 2 written notices and a telephone call from the

physician.[13]

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A central tenet of organized screening programs is that all persons in the target

population be invited to participate.[8] Operationalization Implementation of this strategy

aspect of organized screening can vary: invitations may be sent with an FOBT kit, can

include physician recommendation or may incorporate tailored messaging.[14 ,15] Some

of these approaches, such as incorporation of physician recommendation, present

significant implementation challenges for organized screening programs such as

Ontario's.

In 2009, the CCC program conducted the CCC Invitation Pilot (the "Pilot"), an evaluation

that tested the technical feasibility of a centralized approach to sending physician-linked

mailed invitations for CRC screening. In this paper, we describe the structure and the

implementation of the Pilot. In addition, we report on patientparticipant and physician

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factors associated with response to mailed physician-linked invitations and on the

effectiveness of these invitations in an organized CRC screening program.

METHODS

The CCC Invitation Pilot – Implementation and Evaluation

The Pilot was conducted by CCC in November 2009 in order to develop and test the

technical infrastructure required for large scale centralized physician-linked mailed

invitations in Ontario. For the Pilot, invitation letters were generated by the CCC

program on behalf of 102 family physicians and sent to all their eligible enrolled patients.

Just over 11,000 eligible patient patients participants received were sent mailed

invitations requesting they visit their family physician to obtain an FOBT kit or, if

appropriate based on family history, a referral for colonoscopy. In this paper, we report

on the 2 linked quantitative studies done using this cohort. Study 1 examines participant

and physician factors associated with response to the mailed invitation among those

who were sent the mailed invitation. Study 2 evaluates the effectiveness of the mailed

invitation by comparing uptake of CRC screening among Study 1 participants compared

to a matched control group. Ethics approval was obtained from the research ethics

boards at Sunnybrook Health Sciences Centre and the Institute for Clinical Evaluative

Sciences (ICES) and permission to use the Pilot data was obtained from Cancer Care

Ontario's (CCO) Data Access Committee. All analyses were conducted using SAS v.9

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(SAS Institute, Cary, NC). A p-value of 0.05 was used to determine statistical

significance.

Data Sources

The ~~quantitative~~ Pilot study was conducted at ICES, which ~~holds~~ houses the

administrative health records for all 12.4 million Ontarians. CCC program databases

were linked to the ICES administrative databases using an encrypted version of the

provincial health insurance number.

The ICES databases used include the Canadian Institute of Health Information (CIHI)

databases, the Ontario Health Insurance Program (OHIP) Claims History Database, the

Registered Persons Database (RPDB), the Ontario Cancer Registry, the ICES Physician

Database, and the Client Agency Program Enrollment (CAPE) registry. The CIHI, OHIP,

RPDB and the Ontario Cancer Registry and the ICES Physician Database have been

previously described.[16 ,17] The CAPE registry tracks patients enrolled to physicians

who participate in PEMs and is a centralized electronic record of the linkage between

specific patients and their physicians. ~~registered to a specific physician in patient~~

~~enrolled models (PEMs) of care. PEMs comprise family physicians who provide enrolled~~

~~patients with comprehensive health care and extended hours; PEM physicians receive~~

~~incentives for the use of preventive care measures such as CRC screening.[15] PEMs~~

~~vary in terms of structure, services provided and remuneration (varying from enhance~~

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fee for service to blended capitation). It is estimated that 75% of Ontario residents received their care via a PEM in 2009.[16].

The CCC program has collected data on CRC screening since its inception using Laboratory Reporting Tool (LRT) and comprises data related to the FOBT kits administered by the CCC program, including the results of these tests.

Study 1: Factors associated with response to the mailed invitation

Cohort Definition: For the Pilot, a convenience sample of physicians participating in PEM-type -practices was recruited via Cancer Care OntarioCCO's Provincial Primary Care Cancer Network. Prior to the Pilot mailing, CCC generated lists of patients eligible for CRC screening for each participating physician using CAPE, Ontario Cancer Registry, OHIP, CIRT and LRT. PatientPatients enrolled to these physicians,s aged 50 to 74 years without a history of CRC and who were due for CRC screening (without a record of recent FOBT (previous two years) or lower GI investigation including flexible sigmoidoscopy and colonoscopy (previous 5 years)). were eligible. For the Pilot mailing, CCC generated lists of patient participants eligible for CRC screening for each participating physician using CAPE, Ontario Cancer Registry, OHIP, CIRT and LRT. All persons who were sent an invitation were included in the cohort, regardless of whether the letter was returned to the sender.

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The Mailing: Invitations were mailed in November 2009. The date of mailing was the index date. The letters were compiled centrally by the CCC program but were physician-linked; ~~patient~~patient participants ~~received~~ were sent a letter from their own physician, as indicated by their name at the bottom of the letter in an italicized font (Figure 1). The letter asked ~~patient~~participants to visit their family physician for screening; it did not include an FOBT kit. The letter was~~y were~~ accompanied by a~~n~~ CRC screening information brochure and sent in an envelope with the family physician name in the front upper left corner. For the purposes of the study, Pilot physicians were compensated an equivalent amount to the CRC Screening Management fee ($6.86 per eligible enrolled patient) as Ontario PEM physicians are eligible for this fee for contacting the patient by mail regarding CRC screening.

Response to Mailed Invitation: We ~~defined~~ used a broad definition of response to the mailed invitation: ~~as~~ any record of FOBT in either OHIP or in LRT within 6 months of the index date~~,~~ regardless of result (including rejected kits). Up to 10% of FOBT done in the province are captured only through OHIP, which does not have data on test results. We were not able to measure response in persons at increased risk of CRC as we do not have family history data available in the administrative databases.

~~Patient~~Participant and Physician Factors: We characterized ~~patient~~participants by age group, sex, co-morbidity, median neighborhood income[18 ,19], health region[20],

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immigration status, and prior FOBT. Comorbidity was measured by counting the

number of Aggregated Diagnosis Groups (ADGs) in the prior 12 months according to the

Johns Hopkins ACG® Case-Mix System.[21] This system has been shown to accurately

predict mortality in a general population ambulatory cohort in Ontario.[22] We used date

of registration in the RPDB as a proxy measure for immigration status;

patientparticipants were considered recent immigrants if their date of registration was

within 5 years of the index date.[23]

Physicians were characterized according to age, sex, training location (attended

Canadian medical school vs. outside of Canada), practice type, size of practice, age-

eligible rate of colonoscopy or FOBT over prior 2 years as well as the age-eligible rate of

annual physical exams or influenza vaccinations in the prior year. All physicians were in

PEMs; practice types included family health groups (FHGs, enhanced fee-for-service

models), family health organizations or networks (FHO/FHNs, blended capitation

models), FHO/FHN with family health team (FHO/FHN-FHT, interprofessional team

model with a blended capitation fee structure) and other PEMs.[24] We measured

practice size as the number of enrolled patients stratified in a binary fashion (≤1800 vs.

>1800 enrolled patients) as larger practice sizes have been shown to be associated with

poorer preventative care.[25] For the remaining physician characteristics, we identified

all enrolled and non-enrolled patients aged 50-74 years in their practices as of the index

date. Age-eligible FOBT and colonoscopy rates were obtained for each Pilot physician

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by calculating the proportion of their age-eligible patients who had had an FOBT or colonoscopy in the 2 years prior to the index date. Similarly, we calculated their rates of age-eligible annual physical exams or influenza vaccine in the year prior to the index date. These variables were derived in order to estimate physician adherence to CRC screening and preventive medicine practices at baseline.

Analysis: The number and proportion of persons in the cohort who responded to the mailed invitation within 6 months wereas determined overall and by patientparticipant and physician characteristics. Multivariate logistic regression modeling was used to identify patientparticipant and physician factors associated with response to the mailed invitation. In order to account for potential clustering of patientparticipants within physicians, Generalized Estimating Equations (GEE) were used in the model.

Study 2: Evaluation of the effectiveness of mailed invitations

Overview and study participants: This was a matched double cohort analysis, comparing uptake of FOBT in those who received were sent a mailed invitation (Pilot cohort) to a matched control group who were not sent a mailed invitation. The control group comprised patients who were enrolled to PEM physicians who had not participated in the Pilot. Control participants received "usual care" for the CCC program in terms of screening promotion. As such, they received screening via their primary care physician who were eligible for the same financial incentives as Pilot physicians. Control

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participants were not sent a centralized physician-linked invitation from the CCC program although their physicians could send them a mailed invitation at their own discretion.

The Pilot cohort comprised all members of the cohort described in Study 1 for whom a matched control could be identified. We identified potential ~~patient~~ controls as follows: 1) Pilot physicians were matched to non-Pilot physicians who were also practicing in PEMs in a 1:5 ratio using physician age, sex, size and practice type; 2) individuals enrolled ~~patients belonging~~ to the selected control physicians were retained if they met the same inclusion/exclusion criteria as those in the intervention cohort (aged 50 to 74 years with no prior CRC who were due for CRC screening). As with the identification of eligible participants in the Pilot, we used CAPE, Ontario Cancer Registry, OHIP, CIRT and LRT to determine eligibility of potential control participants.

Propensity scores that modeled the probability of belonging to the Pilot group were calculated for each ~~patient~~participant in the entire group (Pilot and control). The variables in this model included age (as a continuous measure), sex, co-morbidity, median neighborhood income quintile, health region, immigration status, and FOBT from 2 to 5 years prior.[26 ,27] Pilot ~~patient~~participants were matched to controls in a 1:1 fashion based on propensity scores using a caliper width of 0.25. This methodology was

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implemented to balance the distribution of ~~patient~~participant-level variables between the

Pilot and control groups.

Response to mailed invitation: For our primary outcome, we defined response to the

mailed invitation as ~~above~~in Study 1, a record of FOBT regardless of result, within 6

months of the index date. For our secondary outcome, response was defined as a

record of either FOBT or colonoscopy ~~(in OHIP)~~ within 6 months of the index date. For

the purposes of this study, controls were assigned the same index date as their matched

counterpart in the Pilot group.

Analysis: Standard differences between the Pilot participants and controls were

calculated for the variables included in the propensity score. Important differences

between the 2 groups were defined by a standardized difference exceeding -0.1.[27 ,28]

In the primary analysis, we compared the number and proportion in the Pilot and control

groups responding to the mailed invitation with FOBT using McNemar's test.[27] We

determined the number of invitations mailed in order to screen one additional person

with FOBT. We repeated the above analyses using our secondary outcome in order to

determine if observed differences in FOBT uptake could be attributed to ~~a~~ differences in

colonoscopy uptake (i.e., ~~patient~~participants had CRC screening but chose colonoscopy

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over FOBT). As the matching only accounted for ~~patient~~participant- level variables, we

repeated our analyses using conditional logistic regression in order to adjust for

physician covariates (age, sex, practice type and size).

RESULTS

Study 1: Factors associated with response to the mailed invitation

There were 11,311 eligible patient ~~patient~~participants associated with the 102 family

physicians in the Pilot cohort. Nine ~~patient~~participants were excluded as we were

unable to determine their health region and/or income quintile; this left 11,302

~~patient~~participants for the analysis. The majority of ~~patient~~participants were 50 to 59

years of age, 52% were women, 48% had no or low co-morbidity and 14% had

completed an FOBT from 2 to 5 years prior to the mailing. Two thirds of

~~patient~~participants had a male physician, approximately half were part of a primary care

team reimbursed via an enhanced fee-for-service arrangement and just under half were

enrolled in larger practices (>1800 enrolled patients) (Table 1).

2503 (22%) completed an FOBT within 6 months of mailing. In the multivariate

regression, the strongest ~~patient~~participant factor associated with FOBT completion was

prior FOBT use (2 to 5 years prior vs. > 5 years or never: OR 2.8, 95% C.I.: 2.5 to 3.3, p

< 0.0001). Other significant factors associated with FOBT completion included older

~~patient~~participant age, greater co-morbidity, and having a female physician (Table 2).

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Study 2: Evaluation of the effectiveness of mailed invitations

Of the 11,302 ~~patient~~participants in Study 1, 10,652 ~~patients~~ were successfully matched

to 10,652 controls using propensity scores. Standardized differences for the

~~patient~~participant characteristics included in the propensity score were all <0.1,

indicating that the two cohorts were well matched for measurable potential confounders

(Table 3).

Pilot ~~patient~~participants were significantly more likely than controls to complete FOBT

alone (2387 (22%) versus 854 (8%), p<0.0001) and FOBT or colonoscopy (2664 (25%)

vs. 1191 (11%), p<0.0001) within 6 months of mailing. The association between the

mailed invitation and CRC screening participation (either FOBT alone or FOBT or

colonoscopy) remained after adjusting for physician level characteristics (Table 4).

DISCUSSION

In the current study, we have demonstrated that physician-linked mailed invitations are

both feasible and effective in the context of a large organized, population-based

screening program; only 7 letters would need to be sent in order to screen one additional

person. Furthermore, we have found that older ~~patient~~participants, those with greater

co-morbidity, those who have previously been screened and ~~patients of~~those with

female physicians were more likely to respond to this type of invitation. Our findings are

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of particular interest to other jurisdictions planning or who already have organized CRC

screening.

In other published studies of mailed invitations, an FOBT kit is often included with the

invitation. Three studies done outside organized screening programs have found

physician-linked invitations superior to non-linked invitations; 2 of these studies of

invitations included an FOBT kit,[29 ,30] and the third study did not.[31] Other studies

have examined mailed invitations with FOBT kits in the context of primary care practices

in the USA.[32-34] While the results from these trials were largely supportive of mailed

invitations, kit inclusion can make it difficult to separate the convenience of receiving the

FOBT kit directly by mail from the impact of an invitation from one's own physician.

Our study demonstrates the effectiveness and feasibility of physician-linked invitations in

the context of a large organized CRC screening program with an estimated target

population of over 3 million persons. Implementation in this context confers challenges in

terms of technological infra-structure, privacy and regulatory issues. There are 2 studies

(from the United Kingdom[35] and Italy[36]) that have reported on mailed invitations in

the context of organized colorectal cancer screening programs and found them to be

effective. Both studies included FOBT kits and one studied the impact of physician

endorsement specifically.[35] Our findings are important because they support a

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potentially more cost-effective approach that avoids wasting kits that are mailed but not used.

Our results highlight the critical role of physician recommendation, a finding supported by others. For example, in the NHS Bowel Cancer Screening Programme (BCSP) currently, the primary care physician receives the result but is not directly involved in the mailed invitation or the actual screening. Recently, a randomized controlled trial conducted in the context of the BCSP showed that an endorsement letter from the primary care provider increased participation by 6%.[35]   In 2 studies from Australia, endorsement improved initial participation[29 ,30] and over 4 successive screening rounds.[30]

Uptake of FOBT in Ontario is lower than some organized CRC screening programs in other countries. For example, 30% of Ontarians were up-to-date with FOBT in 2008-9 [37] compared to 52% participation in the United Kingdom program by October 2008,[38] 54% in the Italian program in 2007,[39] and 54% in the New Zealand pilot program in 2012.[40] However, in the latter countries, there is very little, if any, opportunistic CRC screening using colonoscopy whereas Ontario's program operates in a hybrid environment where opportunistic colonoscopy is available, as the initial screening test in persons at average risk. It has been noted that uptake of FOBT may be lower in settings, such as Ontario's or Australia's,[41] where opportunistic screening is

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available.[42] The findings from the current study indicate that physician-linked invitations for CRC screening can be effective in increasing uptake of FOBT in programs that operate in the context of opportunistic colonoscopy for average risk screening.

Our study has several limitations. As mentioned above, we are unable to determine family history using Ontario administrative data. A second limitation is that a single generic letter was used. Tailored letters with key messages for specific subgroups may be more effective,[15] an approach finding that may be relevant in Ontario as we did find that response to the letter appeared to differ in various subgroups. FinallyAdditionally, while our findings are promising, there are challenges to widespread implementation in other population-based screening programs, including the requirement for a centralized database that links patients and to their physicians. Finally, implementation of this strategy in population based screening is predicated on physician acceptability and agreement. While we have found that this approach is acceptable in principle to many Ontario physicians,[43] processes to determine confirm individual physician agreement have not been worked outdetermined for the entire CCC program which comprises an estimated 7000 primary care physicians.

CONCLUSIONS

In summary, we have demonstrated that physician-linked mailed invitations for CRC screening, even without the inclusion of an FOBT kit, can have substantial effect on

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participation in an organized CRC screening program and that it is technically feasible to centrally organize and mail physician-linked invitations on a large scale. Organized screening programs, which often use unlinked invitations, should consider adopting this approach given its demonstrated effectiveness and feasibility.

COMPETING INTERESTS STATEMENT

Dr. Tinmouth is the Lead Scientist for the ColonCancerCheck program and Dr. Rabeneck oversees the ColonCancerCheck program in her capacity as the Vice-President, Cancer Prevention and Control at Cancer Care OntarioCCO. None of the other authors have any conflicts of interest to report.

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AUTHOR CONTRIBUTION:

Authors contributed substantially to each of the following areas:

-conception and design (JT, LFP, LR) or analysis and interpretation of data (JT, NB, LFP, LR, RS, LY)

-drafting the article (JT) or revising it critically for important intellectual content (JT, NB, LFP, LR, RS, LY)

-final approval of the version to be published (JT, NB, LFP, LR, RS, LY)

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Tables.

Table 1. ~~Patient~~Patient participant and physician characteristics for ~~Pilot participants in~~ Study 1

	FOBT within 6 months (n=2,503)	No FOBT within 6 months (n=8,799)	Total (n=11,302)
~~Patient~~Patient participants			
Age group in years, No. (%)			
50-59	1,279 (51%)	5,384 (61%)	6,663 (59%)
60-69	894 (36%)	2,637 (30%)	3,531 (31%)
70-74	330 (13%)	778 (9%)	1,108 (10%)
Sex, No. (%)			
Female	1,299 (52%)	4,554 (52%)	5,853 (52%)
Male	1,204 (48%)	4,245 (48%)	5,449 (48%)
Co-morbidity*, No. of ADGs (%)			
0	257 (10%)	1,279 (15%)	1,536 (14%)
1-2	828 (33%)	3,044 (35%)	3,872 (34%)
3-4	712 (28%)	2,241 (25%)	2,953 (26%)
5-6	393 (16%)	1,224 (14%)	1,617 (14%)
7+	313 (13%)	1,011 (11%)	1,324 (12%)
Median neighborhood income quintile, No. (%)			
Rural	394 (16%)	1,431 (16%)	1,825 (16%)
Low Urban	360 (14%)	1,375 (16%)	1,735 (15%)
2	402 (16%)	1,418 (16%)	1,820 (16%)
3	429 (17%)	1,430 (16%)	1,859 (16%)
4	432 (17%)	1,552 (18%)	1,984 (18%)
High Urban	486 (19%)	1,593 (18%)	2,079 (18%)
Health region, No. (%)			
Erie St.Clair	125 (5%)	337 (4%)	462 (4%)
South West	284 (11%)	823 (9%)	1,107 (10%)
Waterloo Wellington	76 (3%)	251 (3%)	327 (3%)
Hamilton Niagara	289 (12%)	976 (11%)	1,265 (11%)
Central West	138 (6%)	482 (5%)	620 (5%)
Mississauga Halton	22 (1%)	120 (1%)	142 (1%)
Toronto Central	111 (4%)	392 (4%)	503 (4%)
Central	24 (1%)	177 (2%)	201 (2%)
Central East	361 (14%)	1,282 (15%)	1,643 (15%)
South East	162 (6%)	697 (8%)	859 (8%)
Champlain	219 (9%)	676 (8%)	895 (8%)
North Simcoe-Muskoka	77 (3%)	188 (2%)	265 (2%)
North East	291 (12%)	1,118 (13%)	1,409 (12%)
North West	324 (13%)	1,280 (15%)	1,604 (14%)

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Recent immigrant, No. (%)	23 (1%)	88 (1%)	111 (1%)
FOBT 2 to 5 years prior to mailing, No. (%)	643 (26%)	905 (10%)	1,548 (14%)
Physician			
Median age in years (IQR)	52 (45-59)	53 (46-59)	52 (45-59)
Sex, No. (%)			
Female	936 (37%)	3,044 (35%)	3,980 (35%)
Male	1,567 (63%)	5,755 (65%)	7,322 (65%)
Training location, No. (%)			
Outside Canada	312 (12%)	1,196 (14%)	1,508 (13%)
In Canada	2,191 (88%)	7,603 (86%)	9,794 (87%)
Practice type, No. (%)			
FHG	1,082 (43%)	4,266 (48%)	5,348 (47%)
FHO/FHN	432 (17%)	1,456 (17%)	1,888 (17%)
FHO/FHN-FHT	881 (35%)	2,620 (30%)	3,501 (31%)
Other PEM	108 (4%)	457 (5%)	565 (5%)
Practice size (enrolled patients), No. (%)			
>1800 patients	1,105 (44%)	4,104 (47%)	5,209 (46%)
Age-eligible rate of colonoscopy quintile, No. (%)			
Low	485 (19%)	1,619 (18%)	2,104 (19%)
2	548 (22%)	1,940 (22%)	2,488 (22%)
3	637 (25%)	2,279 (26%)	2,916 (26%)
4	477 (19%)	1,696 (19%)	2,173 (19%)
High	356 (14%)	1,265 (14%)	1,621 (14%)
Age-eligible rate of FOBT quintile, No. (%)			
Low	487 (19%)	1,888 (21%)	2,375 (21%)
2	504 (20%)	1,886 (21%)	2,390 (21%)
3	533 (21%)	1,890 (21%)	2,423 (21%)
4	522 (21%)	1,680 (19%)	2,202 (19%)
High	457 (18%)	1,455 (17%)	1,912 (17%)
Age-eligible rate of annual physical exams quintile, No. (%)			
Low	496 (20%)	2,009 (23%)	2,505 (22%)
2	490 (20%)	1,625 (18%)	2,115 (19%)
3	472 (19%)	1,638 (19%)	2,110 (19%)
4	509 (20%)	1,686 (19%)	2,195 (19%)
High	536 (21%)	1,841 (21%)	2,377 (21%)

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Age-eligible rate of influenza vaccine quintile, No. (%)			
Low	548 (22%)	1,997 (23%)	2,545 (23%)
2	549 (22%)	1,765 (20%)	2,314 (20%)
3	435 (17%)	1,930 (22%)	2,365 (21%)
4	485 (19%)	1,770 (20%)	2,255 (20%)
High	486 (19%)	1,337 (15%)	1,823 (16%)

*Co-morbidity scored using number of Aggregated Diagnosis Groups (ADGs) using the Johns Hopkins Case Mix System

FHG = family health group

FHO/FHN = family health organizations or networks

Other PEM = other patient enrolled model of care

FOBT = fecal occult blood test

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Table 2.   Multivariate logistic regression analysis using Generalized Estimating Equations for the characteristics of ~~patient~~participants and physicians associated with completing an FOBT within 6 months of the mailing date.

~~Patient~~Participants	Odds ratio (95% C.I.)	P-value
Age group, years		
50-59	0.6 (0.5, 0.8)	<.0001
60-69	0.8 (0.7, 1.0)	NS
70-74	Reference	N/A
Sex		
Female	0.9 (0.9, 1.0)	NS
Male	Reference	N/A
Co-morbidity*, No. of ADGs		
0	0.7 (0.6, 0.8)	0.0002
1-2	0.9 (0.7, 1.0)	NS
3-4	1.0 (0.9, 1.2)	NS
5-6	1.0 (0.9, 1.2)	NS
7+	Reference	N/A
Median neighborhood income quintile		
Rural	0.9 (0.7, 1.1)	NS
Low Urban	0.9 (0.7, 1.0)	NS
2	1.0 (0.8, 1.1)	NS
3	1.0 (0.9, 1.1)	NS
4	0.9 (0.8, 1.1)	NS
High Urban	Reference	N/A
Health region		
Erie St.Clair	1.3 (0.9, 1.8)	NS
South West	0.9 (0.6, 1.4)	NS
Waterloo Wellington	0.8 (0.6, 1.2)	NS
Hamilton Niagara	0.9 (0.6, 1.2)	NS
Central West	1.0 (0.7, 1.4)	NS
Mississauga Halton	0.6 (0.3, 1.2)	NS
Toronto Central	0.8 (0.6, 1.2)	NS
Central	0.5 (0.4, 0.7)	0.0004
South East	0.8 (0.4, 0.7)	NS
Champlain	1.0 (0.7, 1.4)	NS
North Simcoe-Muskoka	0.9 (0.6, 1.4)	NS
North East	1.1 (0.7, 1.5)	NS
North West	0.7 (0.5, 1.0)	0.03
Central East	Reference	N/A
Recency of immigration		
Remote or non-immigrant	1.0 (0.6, 1.6)	NS
Recent immigrant	Reference	N/A
Prior FOBT Use		
2 to 5 years prior to mailing	2.8 (2.5, 3.3)	<.0001

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> 5 years or never	Reference	
Physician		
Increasing age (per year)	1.0 (1.0, 1.0)	NS
Sex		
Female	1.3 (1.0, 1.5)	0.02
Male	Reference	N/A
Training location		
In Canada	0.9 (0.7, 1.2)	NS
Outside Canada	Reference	N/A
Practice type		
FHG	0.9 (0.7, 1.1)	NS
FHO/FHN	0.8 (0.6, 1.1)	NS
Other PEM	0.7 (0.4, 1.0)	0.05
FHO/FHN-FHT	Reference	N/A
Practice size (enrolled patients)		
≤ 1800 patients	1.1 (0.9, 1.3)	NS
> 1800 patients	Reference	N/A
Age-eligible rate of colonoscopy quintile		
Low	1.1 (0.8, 1.5)	NS
2	1.2 (1.0, 1.6)	NS
3	1.0 (0.8, 1.2)	NS
4	1.0 (0.8, 1.3)	NS
High	Reference	N/A
Age-eligible rate of FOBT quintile		
2	0.9 (0.6, 1.3)	NS
3	0.9 (0.7, 1.2)	NS
4	1.1 (0.8, 1.4)	NS
High	0.9 (0.7, 1.3)	NS
Low	Reference	N/A
Age-eligible rate of annual physical exams quintile		
2	1.4 (0.9, 2.0)	NS
3	1.3 (0.9, 1.8)	NS
4	1.3 (0.9, 1.8)	NS
High	1.1 (0.8, 1.5)	NS
Low	Reference	N/A
Age-eligible rate of influenza vaccine quintile		
2	1.0 (0.8, 1.2)	NS
3	0.8 (0.6, 1.0)	0.02
4	0.9 (0.7, 1.2)	NS
High	1.3 (1.0, 1.7)	NS
Low	Reference	N/A

*Co-morbidity scored using number of Aggregated Diagnosis Groups (ADGs) using the Johns Hopkins Case Mix System

FHG = family health group

FHO/FHN = family health organizations or networks

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Other PEM = other patient enrolled model of care
NS = not significant
N/A - not applicable
FOBT = fecal occult blood test

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Table 3. Characteristics of the 2 cohorts matched by propensity score in Study 2

	Pilot participants (n=10,652)	Control ~~patients~~ participants (n=10.652)	Standardized Difference*
ParticipantsPatients			
Age group in years, No. (%)			
50-59	6,248 (59%)	6,324 (59%)	0.01
60-69	3,342 (31%)	3,316 (31%)	0.01
70-74	1,062 (10%)	1,012 (10%)	0.02
Sex, No. (%)			
Female	5548 (52%)	5477 (51%)	0.01
Male	5,104 (48%)	5,175 (49%)	0.01
Co-morbidity**, No. of ADGs (%)			
0	1,462 (14%)	1,425 (13%)	0.01
1-2	3,647 (34%)	3,716 (35%)	0.01
3-4	2,764 (26%)	2,835 (27%)	0.02
5-6	1,536 (14%)	1,473 (14%)	0.02
7+	1,243 (12%)	1,203 (11%)	0.01
Median neighborhood income quintile, No. (%)			
Rural	1,825 (17%)	1,889 (18%)	0.02
Low Urban	1,628 (15%)	1,699 (16%)	0.02
2	1,698 (16%)	1,728 (16%)	0.01
3	1,728 (16%)	1,681 (16%)	0.01
4	1,831 (17%)	1,753 (16%)	0.02
High Urban	1,942 (18%)	1,902 (18%)	0.01
Health region, No. (%)			
Erie St.Clair	462 (4%)	423 (4%)	0.02
South West	1,107 (10%)	1,114 (10%)	0
Waterloo Wellington	327 (3%)	343 (3%)	0.01
Hamilton Niagara	1,265 (12%)	1,290 (12%)	0.01
Central West	620 (6%)	580 (5%)	0.02
Mississauga Halton	142 (1%)	144 (1%)	0
Toronto Central	503 (5%)	478 (4%)	0.01
Central	201 (2%)	209 (2%)	0.01
Central East	1,643 (15%)	1,702 (16%)	0.02
South East	859 (8%)	891 (8%)	0.01
Champlain	895 (8%)	904 (8%)	0
North Simcoe-Muskoka	265 (2%)	242 (2%)	0.01
North East	1,409 (13%)	1,378 (13%)	0.01
North West	954 (9%)	954 (9%)	0
Recent immigrant, No. (%)	111 (1%)	105 (1%)	0.01
FOBT 2 to 5 years prior to mailing, No. (%)	1,476 (14%)	1,240 (12%)	0.07
Physician			

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Median age in years (IQR)	52 (45-59)	52 (47-58)	N/A
Sex, No. (%)			
Female	3,875 (36%)	3,335 (31%)	N/A
Male	6,777 (64%)	7,317 (69%)	
Practice type, No. (%)			
FHG	4,854 (46%)	4,885 (46%)	
FHO/FHN	1,859 (17%)	1,718 (16%)	N/A
FHO/FHN-FHT	3,374 (32%)	3,027 (28%)	
Other PEM	565 (5%)	1,022 (10%)	
Practice size (enrolled patients), No. (%)			
>1800 patients	5,366 (50%)	5,026 (47%)	N/A

*Standardized differences for physician level variables not reported as propensity scores were estimated using patient level characteristics only

**Co-morbidity scored using number of Aggregated Diagnosis Groups (ADGs) using the Johns Hopkins Case Mix System

FHG = family health group

FHO/FHN = family health organizations or networks

Other PEM = other patient enrolled model of care

FOBT = fecal occult blood test

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Table 4. Association between mailed invitation and FOBT completion or mailed invitation and FOBT or colonoscopy completion after adjusting for physician factors.

	FOBT completion		FOBT or Colonoscopy completion	
	Odds ratio (95% C.I.)	P-value	Odds ratio (95% C.I.)	P-value
Mailed invitation				
Yes (Pilot)	3.3 (3.1, 3.6)	<.0001	2.7 (2.5, 2.9)	<.0001
No (Controls)	Reference	N/A	Reference	N/A
Increasing age (per year)	1.0 (1.0, 1.0)	NS	1.0 (1.0, 1.0)	0.03
Sex, No. (%)				
Female	1.0 (0.9, 1.1)	NS	1.0 (0.9, 1.1)	NS
Male	Reference	N/A	Reference	N/A
Practice type, No. (%)				
FHG	0.7 (0.6, 0.8)	<.0001	0.7 (0.7, 0.8)	<.0001
FHO/FHN	0.8 (0.7, 0.9)	<.0001	0.8 (0.7, 0.9)	<.0001
Other PEM	0.8 (0.7, 1.0)	0.03	0.8 (0.7, 1.0)	NS
FHO/FHN-FHT	Reference	N/A	Reference	N/A
Practice size (enrolled patients)				
≤ 1800 patients	1.2 (1.1, 1.3)	0.0004	1.2 (1.1, 1.3)	<.0001
> 1800 patients	Reference	N/A	Reference	N/A

FHG = family health group

FHO/FHN = family health organizations or networks

Other PEM = other patient enrolled model of care

FOBT = fecal occult blood test

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8   Figure Legends
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11   Figure 1. Mock-up of physician-linked invitation used in the Pilot.
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ColonCancerCheck | ContrôleCancerColorectal

cancer care | action cancer
ontario | ontario

From the office of Dr. George Black

June 1, 2009

Lawren Harris
456 Superior Street
Lindsay ON K2L 3M4

Dear Lawren Harris:

You have received this letter because it is time to be screened for colon cancer. Our records as of April 1st, 2009 show that you have never had a fecal occult blood test (FOBT) or we do not know when you had your last FOBT. All adults between the ages of 50 and 74 years who are at average risk for colon cancer should do a FOBT every two years.

If your parent, brother, sister or child has had colon cancer, your risk is higher and you should have a colonoscopy.

Please call my office to set up an appointment to talk about your risk for colon cancer and which test is right for you.

If you have recently completed colon cancer screening, please disregard this letter.

I look forward to hearing from you soon.

Dr. George Black
705-555-1212

GET THE FACTS. GET CHECKED.

- Colon cancer is the second most common cause of cancer death in Ontario
- Colon cancer can develop without any early warning signs.
- If it is caught early enough, 9 out of every 10 people can be cured.
- Regular screening is the best way to catch colon cancer early.
- The FOBT is a simple test that can be done at home.

For more information please visit www.coloncancercheck.ca

This letter has been sent on my behalf by ColonCancerCheck (CCC), Ontario's colorectal cancer screening program. CCC is a collaborative initiative of the Ministry of Health and Long-Term Care and Cancer Care Ontario. If for any reason you do not wish to receive future correspondence from the program, simply call the ColonCancerCheck Information Line at 1-866-662-9233 during business hours.

Tinmouth et al., Physician-linked mailed invitation to be screened improves uptake in an organized colorectal cancer screening program.

	Item No	Recommendation	Page	Comment
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1, 3	
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	3	
Introduction				
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	07-Jun	
Objectives	3	State specific objectives, including any prespecified hypotheses	7, first paragraph	
Methods				
Study design	4	Present key elements of study design early in the paper	7, paragraph 2	
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	7, paragraph 2	
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	9, paragraph 2, 10, paragraph 2 & 12, first paragraph	
		Case-control study—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls	n/a	
		Cross-sectional study—Give the eligibility criteria, and the sources and methods of selection of participants	n/a	
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed	12, first paragraph	
		Case-control study—For matched studies, give matching criteria and the number of controls per case	n/a	
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	9, 10 & 11	
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	8, 9, 10 & 11	
Bias	9	Describe any efforts to address potential sources of bias	11, paragraph 2 & 13, paragraph	
Study size	10	Explain how the study size was arrived at	5, paragraph 1	
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why		
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	11, paragraph 2 & 13, paragraph	
		(*b*) Describe any methods used to examine subgroups and interactions	n/a	
		(*c*) Explain how missing data were addressed	14, first paragraph	
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed	n/a	all patients followed through administrative data, therefore no loss to f/u
		Case-control study—If applicable, explain how matching of cases and controls was addressed	n/a	
		Cross-sectional study—If applicable, describe analytical methods taking account of sampling strategy	n/a	
		(*e*) Describe any sensitivity analyses	n/a	
Results				
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	14, first & last paragraphs	
		(b) Give reasons for non-participation at each stage	14, first & last paragraphs	

		(c) Consider use of a flow diagram	n/a
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	Table 1 & Table 3
		(b) Indicate number of participants with missing data for each variable of interest	15, first paragraph
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)	all followed up for 6 months
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time	15, 2nd paragraph & 16, 1st paragraph
		Case-control study—Report numbers in each exposure category, or summary measures of exposure	n/a
		Cross-sectional study—Report numbers of outcome events or summary measures	n/a
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	15, 2nd paragraph, Tables 2 & 4
		(*b*) Report category boundaries when continuous variables were categorized	Tables 2 & 4
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	n/a
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	n/a
Discussion			
Key results	18	Summarise key results with reference to study objectives	16, paragraph 1
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	18, 2nd paragraph
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	17 & 18
Generalisability	21	Discuss the generalisability (external validity) of the study results	18, last paragraph
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	19, 20

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Using physician-linked mailed invitations in an organized colorectal cancer screening program: effectiveness and factors associated with response.

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TITLE PAGE

Title: Using physician-linked mailed invitations in an organized colorectal cancer screening program: effectiveness and factors associated with response.

Short tile: Physician-linked invitations for colorectal cancer screening

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Word count: 3159 (main text),   263 (abstract)

Number of Tables: 4

Number of Figures: 1

Number of References: 45

Key words: Mailed invitations, colorectal cancer, organized screening

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ABSTRACT

Objectives: A central tenet of organized cancer screening is that all persons in a target population are invited. The aims of this study were to identify participant and physician factors associated with response to mailed physician-linked invitations (Study 1) and to evaluate their effectiveness in an organized colorectal (CRC) screening program (Study 2).

Design and setting: Two studies (Study 1 – cohort design and Study 2 – matched cohort design, comprising Study 1 participants and a matched control group) conducted in context of Ontario's organized province-wide CRC screening program.

Participants: 102 family physicians and 11,302 associated eligible patients from a technical evaluation ("the Pilot") of large scale mailed invitations for CRC screening were included. Matched controls were randomly selected using propensity scores from among eligible patients associated with family physicians in similar practice types as the Pilot physicians.

Intervention: Physician-linked mailed invitation to have CRC screening.

Outcomes: Uptake of fecal occult blood test (FOBT) within 6 months of mailed invitation (primary) and uptake of FOBT or colonoscopy within 6 months of mailed invitation (secondary).

Results: Factors significantly associated with uptake of FOBT included prior FOBT use, older participant age, greater participant co-morbidity and having a female physician. In

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the matched analysis, Pilot participants were more likely to complete an FOBT (22% vs.

8%, p<0.0001) or an FOBT or colonoscopy (25% vs. 11%, p <0.0001) within 6 months of

mailed invitation than matched controls. The number needed to invite to screen one

additional person was 7.

Conclusions: Centralized large scale mailing of physician-linked invitations is both

feasible and effective in the context of organized CRC screening.

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ARTICLE SUMMARY

Strengths and limitations of this study:

- We describe the implementation of physician-linked invitations in an organized colorectal screening program that is characterized by a high level of primary care physician involvement and that operates in a context where opportunistic screening with colonoscopy is possible
- We have shown that centralized large scale mailing of physician-linked invitations is feasible and effective in this context
- We found that physician linked mailed invitations improve CRC screening participation by 14% such that 7 physician-linked invitations need to be mailed to screen one additional person
- We were limited to data found in Ontario health administrative databases; for example, we were not able to determine family history
- Findings are promising but require appropriate infrastructure in order to be implemented in other jurisdictions

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INTRODUCTION

Colorectal cancer (CRC) is the second leading cause of cancer-related death among

men and the third among women in Canada.[1] Fecal occult blood testing (FOBT)[2-4] and

flexible sigmoidoscopy[5-7] have been shown to decrease CRC mortality in randomized

controlled trials.

Given these data, organized CRC screening programs[8] are being implemented

worldwide.[9]   On April 1 2008, Ontario launched ColonCancerCheck (CCC), Canada's

first organized province-wide CRC screening program.[10] Through the primary care

physician, FOBT is offered to people at average risk for CRC and colonoscopy to those

at increased risk based on family history. The CCC program uses a non-rehydrated

guaiac FOBT (Hema-Screen, Immmunostics, Inc., NJ, USA) requiring samples from 3

separate stools. While there is data to suggest that dietary restriction may be

unnecessary,[11] the program recommends avoiding vitamin C for 3 days prior to and

during the collection period in order to minimize false negative results.

Approximately 75% of Ontario residents received their care via a patient enrolled model

(PEM) of care at the time of the study (2009).[12] PEMs comprise teams of family

physicians who provide their enrolled patients with comprehensive health care and

extended hours.[13] PEMs vary in terms of structure, services provided and remuneration

(varying from enhance fee-for-service to blended capitation). All Ontario physicians are

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remunerated for preventive care such as CRC screening however, PEM physicians are

incented to a greater degree than those who are not in PEMs. Specifically, PEM

physicians receive a $7/patient fee for "FOBT distribution and counseling", a

$6.86/patient fee for "CRC screening management" and an annual "Colorectal cancer

screening preventive care bonus" ($220 to $4000) depending on the proportion of

enrolled patients who are up-to-date with FOBT (15-70%). The physician is entitled to

the CRC screening management fee if the enrolled patient attends an appointment to

discuss CRC screening, has declined the test verbally or in writing or if there has been

no response after 2 written notices and a telephone call from the physician.[14]

A central tenet of organized screening programs is that all persons in the target

population be invited to participate.[8] Implementation of this aspect of organized

screening varies: invitations may be sent with an FOBT kit, can include physician

recommendation or may incorporate tailored messaging.[15][16] Some of these approaches,

such as incorporation of physician recommendation, present significant implementation

challenges for organized screening programs such as Ontario's.

In 2009, the CCC program undertook the CCC Invitation Pilot (the "Pilot"), an evaluation

that tested the technical feasibility of a centralized approach to sending physician-linked

mailed invitations for CRC screening. In this paper, we describe the structure and the

implementation of the Pilot. In addition, we report on participant and physician factors

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associated with response to mailed physician-linked invitations and on the effectiveness

of these invitations in Ontario's organized CRC screening program.

METHODS

The CCC Invitation Pilot – Implementation and Evaluation

The CCC program conducted the Pilot in November 2009. Invitation letters were

generated by the CCC program on behalf of 102 family physicians and sent to all their

eligible enrolled patients. Just over 11,000 eligible patient participants were sent mailed

invitations requesting they visit their family physician to obtain an FOBT kit or, if

appropriate based on family history, a referral for colonoscopy. In this paper, we report

on 2 studies using this cohort. Study 1 examines participant and physician factors

associated with response to the mailed invitation among those who were sent the mailed

invitation. Study 2 evaluates the effectiveness of the mailed invitation by comparing

uptake of CRC screening among Study 1 participants compared to a matched control

group. Ethics approval was obtained from the research ethics boards at Sunnybrook

Health Sciences Centre and the Institute for Clinical Evaluative Sciences (ICES) and

permission to use the Pilot data was obtained from Cancer Care Ontario's (CCO) Data

Access Committee. All analyses were conducted using SAS v.9 (SAS Institute, Cary,

NC). A p-value of 0.05 was used to determine statistical significance.

Data Sources

The Pilot study was conducted at ICES, which houses the administrative health records for all 13.5 million Ontarians. CCC program databases were linked to the ICES administrative databases using an encrypted version of the provincial health insurance number.

The ICES databases used include the Canadian Institute of Health Information (CIHI) databases, the Ontario Health Insurance Program (OHIP) Claims History Database, the Registered Persons Database (RPDB), the Ontario Cancer Registry, the ICES Physician Database, and the Client Agency Program Enrollment (CAPE) registry. The CIHI, OHIP, RPDB and the Ontario Cancer Registry and the ICES Physician Database are described elsewhere.[17] [18] The CAPE registry tracks patients enrolled to physicians who participate in PEMs and is a centralized electronic record of the linkage between specific patients and their physicians.

Since its inception, the CCC program has collected data related to the FOBT kits administered by the CCC program, including the results of these tests, using Laboratory Reporting Tool (LRT) .

Study 1: Factors associated with response to the mailed invitation

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Cohort Definition: For the Pilot, a convenience sample of physicians participating in

PEM-type practices was recruited via CCO's Provincial Primary Care Cancer Network.

Patients enrolled to these physicians, aged 50 to 74 years without a history of CRC and

who were due for CRC screening (without a health administrative data record of recent

FOBT (previous two years) or lower GI investigation including flexible sigmoidoscopy

and colonoscopy (previous 5 years)), were eligible. For the Pilot mailing, CCC

generated lists of patient participants eligible for CRC screening for each participating

physician using CAPE, Ontario Cancer Registry, OHIP, CIRT and LRT. All persons who

were sent an invitation were included in the cohort, regardless of whether the letter was

returned to the sender.

The Mailing: Invitations were mailed in November 2009. The date of mailing was the

index date. The letters were compiled centrally by the CCC program but were physician-

linked; patient participants were sent a letter from their own physician, as indicated by

their name at the bottom of the letter in an italicized font (Figure 1). The letter asked

participants to visit their family physician for screening; it did not include an FOBT kit.

The letter was accompanied by a CRC screening information brochure and sent in an

envelope with the family physician name in the front upper left corner. Pilot physicians

were not compensated for study participation, however, they were able to apply the

letter towards meeting the requirements for the CRC screening management fee ($6.86

per eligible enrolled patient).

<u>Response to Mailed Invitation</u>: We used a broad definition of response to the mailed invitation: any record of FOBT in either OHIP or in LRT within 6 months of the index date, regardless of result (including rejected kits). Up to 10% of FOBT done in the province are captured only in OHIP, which does not have data on test results. We were not able to measure response in persons at increased risk of CRC as we do not have family history data available in the administrative databases.

<u>Participant and Physician Factors</u>: We characterized participants by age group, sex, co-morbidity, median neighborhood income,[19] [20] health region,[21] immigration status, and prior FOBT. We measured comorbidity by counting the number of Aggregated Diagnosis Groups (ADGs) using the Johns Hopkins ACG® Case-Mix System in the prior 12 months.[22] Mortality in a general population ambulatory cohort in Ontario was accurately predicted using this system.[23] We used date of registration in the RPDB as a proxy measure for immigration status; participants were considered recent immigrants if their date of registration was within 5 years of the index date.[24]

Physicians were characterized according to age, sex, training location (Canada vs. outside of Canada), practice type, size of practice, age-eligible rate of colonoscopy or FOBT over prior 2 years as well as the age-eligible rate of annual physical exams or influenza vaccinations in the prior year. All participating physicians were in PEMs;

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practice types included family health groups (FHGs, enhanced fee-for-service models),

family health organizations or networks (FHO/FHNs, blended capitation models),

FHO/FHN with family health team (FHO/FHN-FHT, interprofessional team model with a

blended capitation fee structure) and other PEMs.[25] We measured practice size as the

number of enrolled patients stratified in a binary fashion (≤1800 vs. >1800 enrolled

patients) as larger practice sizes have been shown to be associated with poorer

preventative care.[26] For the remaining physician characteristics, we identified all enrolled

and non-enrolled patients aged 50-74 years in their practices as of the index date. Age-

eligible FOBT and colonoscopy rates were obtained for each Pilot physician by

calculating the proportion of their age-eligible patients who had had an FOBT or

colonoscopy in the 2 years prior to the index date. Similarly, we calculated their rates of

age-eligible annual physical exams or influenza vaccine in the year prior to the index

date. These variables were derived in order to estimate physician adherence to CRC

screening and preventive medicine practices at baseline.

Analysis: The number and proportion of persons in the cohort who responded to the

mailed invitation within 6 months were determined overall and by participant and

physician characteristics. Multivariate logistic regression modeling was used to identify

participant and physician factors associated with response to the mailed invitation. In

order to account for potential clustering of participants within physicians, Generalized

Estimating Equations (GEE)[27] were used in the model.

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Study 2: Evaluation of the effectiveness of mailed invitations

Overview and study participants: This was a matched double cohort analysis, comparing

uptake of FOBT in those who were sent a mailed invitation (Pilot cohort) to a matched

control group who were not sent a mailed invitation. The control group comprised

patients who were enrolled to PEM physicians who had not participated in the Pilot.

Control participants received "usual care" from the CCC program in terms of screening

promotion. As such, they were eligible for screening via their primary care physician

who was eligible for the same financial incentives as the Pilot physicians. Control

participants were not sent a centralized physician-linked invitation from the CCC

program although their physicians could send them a mailed invitation at their own

discretion.

The Pilot cohort comprised all members of the cohort described in Study 1 for whom a

matched control could be identified. We identified potential controls as follows: 1) Pilot

physicians were matched to non-Pilot physicians who were also practicing in PEMs in a

1:5 ratio using physician age, sex, size and practice type; 2) individuals enrolled to the

selected control physicians were retained if they met the same inclusion/exclusion

criteria as those in the intervention cohort (aged 50 to 74 years with no prior CRC who

were due for CRC screening). As with the identification of eligible participants in the

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Pilot, we used CAPE, Ontario Cancer Registry, OHIP, CIRT and LRT to determine

eligibility of potential control participants.

Propensity scores that modeled the probability of belonging to the Pilot group were

calculated for each participant in the entire group (Pilot and control). The variables in this

model included age (as a continuous measure), sex, co-morbidity, median neighborhood

income quintile, health region, immigration status, and FOBT from 2 to 5 years prior.[28 29]

Pilot participants were matched to controls in a 1:1 fashion based on propensity scores

using a caliper width of 0.25. This methodology was implemented to balance the

distribution of participant-level variables between the Pilot and control groups.

Response to mailed invitation: For our primary outcome, we defined response to the

mailed invitation as in Study 1, a record of FOBT regardless of result, within 6 months of

the index date. For our secondary outcome, response was defined as a record of either

FOBT or colonoscopy within 6 months of the index date. For the purposes of this study,

controls were assigned the same index date as their matched counterpart in the Pilot

group.

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Analysis: Standard differences between the Pilot participants and controls were

calculated for the variables included in the propensity score. Important differences

between the 2 groups were defined by a standardized difference exceeding 0.1.[29] [30] In

the primary analysis, we compared the number and proportion in the Pilot and control

groups responding to the mailed invitation with FOBT using McNemar's test.[29] We

determined the number of invitations mailed in order to screen one additional person

with FOBT. We repeated the above analyses using our secondary outcome in order to

determine if observed differences in FOBT uptake could be attributed to differences in

colonoscopy uptake (i.e., participants had CRC screening but chose colonoscopy over

FOBT). As the matching only accounted for participant-level variables, we repeated our

analyses using conditional logistic regression in order to adjust for physician covariates

(age, sex, practice type and size).

RESULTS

Study 1: Factors associated with response to the mailed invitation

There were 11,311 eligible patient participants associated with the 102 family physicians

in the Pilot cohort. Nine participants were excluded, as we were unable to determine

their health region and/or income quintile; this left 11,302 participants for the analysis.

The majority of participants were 50 to 59 years of age, 52% were women, 48% had no

or low co-morbidity and 14% had completed an FOBT from 2 to 5 years prior to the

mailing. Two thirds of participants had a male physician, approximately half were part of

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a primary care team reimbursed via an enhanced fee-for-service arrangement and just

under half were enrolled in larger practices (>1800 enrolled patients) (Table 1).

2503 (22%) completed an FOBT within 6 months of mailing. In the multivariate

regression, the strongest participant factor associated with FOBT completion was prior

FOBT use (2 to 5 years prior vs. > 5 years or never: OR 2.8, 95% C.I.: 2.5 to 3.3, p <

0.0001). Other significant factors associated with FOBT completion included older

participant age, greater co-morbidity, and having a female physician (Table 2).

Study 2: Evaluation of the effectiveness of mailed invitations

Of the 11,302 participants in Study 1, 10,652 were successfully matched to 10,652

controls using propensity scores. Standardized differences for the participant

characteristics included in the propensity score were all <0.1, indicating that the two

cohorts were well matched for measurable potential confounders (Table 3).

Pilot participants were significantly more likely than controls to complete FOBT alone

(2387 (22%) versus 854 (8%), p<0.0001) and FOBT or colonoscopy (2664 (25%) vs.

1191 (11%), p<0.0001) within 6 months of mailing. The association between the mailed

invitation and CRC screening participation (either FOBT alone or FOBT or colonoscopy)

remained after adjusting for physician level characteristics (Table 4).

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DISCUSSION

In the current study, we have demonstrated that physician-linked mailed invitations are

both feasible and effective in the context of a large organized, population-based

screening program; only 7 letters would need to be sent in order to screen one additional

person. Furthermore, we have found that older participants, those with greater co-

morbidity, those who have previously been screened and those with female physicians

were more likely to respond to this type of invitation. Our findings are of particular

interest to other jurisdictions planning or who already have organized CRC screening.

In other published studies of mailed invitations, an FOBT kit is often included with the

invitation. Three studies done outside organized screening programs have found

physician-linked invitations superior to non-linked invitations; 2 of these studies included

an FOBT kit,[31] [32] and the third study did not.[33] Other studies have examined mailed

invitations with FOBT kits in the context of primary care practices in the USA.[34-36] While

the results from these trials were largely supportive of mailed invitations, kit inclusion

can make it difficult to separate the convenience of receiving the FOBT kit directly by

mail from the impact of an invitation from one's own physician.

Our study demonstrates the effectiveness and feasibility of physician-linked invitations in

the context of a large organized CRC screening program with an estimated target

population of over 3 million persons. Implementation in this context confers challenges in

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terms of technological infra-structure, privacy and regulatory issues. There are 2 studies

(from the United Kingdom[37] and Italy[38]) that have reported on mailed invitations in the

context of organized colorectal cancer screening programs and found them to be

effective. Both studies included FOBT kits and one studied the impact of physician

endorsement specifically.[37] Our findings are important because they support a

potentially more cost-effective approach that avoids wasting kits that are mailed but not

used.

Our results highlight the critical role of physician recommendation, a finding supported

by others. For example, in the NHS Bowel Cancer Screening Programme (BCSP)

currently, the primary care physician receives the result but is not directly involved in the

mailed invitation or the actual screening. Recently, a randomized controlled trial

conducted in the context of the BCSP showed that an endorsement letter from the

primary care provider increased participation by 6%.[37] In 2 studies from Australia,

endorsement improved initial participation[31 32] and over 4 successive screening

rounds.[32]

Uptake of FOBT in Ontario is lower than some organized CRC screening programs in

other countries. For example, 30% of Ontarians were up-to-date with FOBT in 2008-9[39]

compared to 52% participation in the United Kingdom program by October 2008,[40] 54%

in the Italian program in 2007,[41] and 54% in the New Zealand pilot program in 2012.[42]

However, in the latter countries, there is very little, if any, opportunistic CRC screening

using colonoscopy whereas Ontario's program operates in a hybrid environment where

opportunistic colonoscopy is available as the initial screening test in persons at average

risk. It has been noted that uptake of FOBT may be lower in settings, such as Ontario's

or Australia's,[43] where opportunistic screening is available.[44] The findings from the

current study indicate that physician-linked invitations for CRC screening can be

effective in increasing uptake of FOBT in programs that operate in the context of

opportunistic colonoscopy for average risk screening.

Our study has several limitations. First, we are unable to determine family history using

Ontario administrative data. A second limitation is that a single generic letter was used.

Tailored letters with key messages for specific subgroups may be more effective[16] – an

approach that may be relevant in Ontario as we did find that response to the letter

appeared to differ in various subgroups. Additionally, while our findings are promising,

there are challenges to adoption by other population-based screening programs,

including the need for a centralized database that links patients to their physicians.

Finally, implementation of this strategy in population-based screening is predicated on

physician acceptability and agreement. While we have found that this approach is

acceptable in principle to many Ontario physicians,[45] processes to confirm individual

physician agreement have not been determined for the entire CCC program which

comprises an estimated 7000 primary care physicians.

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CONCLUSIONS

In summary, we have demonstrated that physician-linked mailed invitations for CRC

screening, even without the inclusion of an FOBT kit, can have substantial effect on

participation in an organized CRC screening program and that it is technically feasible to

centrally organize and mail physician-linked invitations on a large scale. Organized

screening programs, which often use unlinked invitations, should consider adopting this

approach given its demonstrated effectiveness and feasibility.

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Physician-linked mailed invitations for colorectal cancer screening

AUTHOR CONTRIBUTION:

Authors contributed substantially to each of the following areas:

-conception and design (JT, LFP, LR) or analysis and interpretation of data (JT, NB,

LFP, LR, RS, LY)

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-drafting the article (JT) or revising it critically for important intellectual content (JT, NB,

LFP, LR, RS, LY)

-final approval of the version to be published (JT, NB, LFP, LR, RS, LY)

COMPETING INTERESTS STATEMENT

Dr. Tinmouth is the Lead Scientist for the ColonCancerCheck program and Dr.

Rabeneck oversees the ColonCancerCheck program in her capacity as the Vice-

President, Cancer Prevention and Control at CCO. None of the other authors have any

conflicts of interest to report.

DATA SHARING STATEMENT

Under Ontario's privacy legislation, neither Cancer Care Ontario nor ICES are permitted
to share individual level data from the submitted work.

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Tables.

Table 1. Patient participant and physician characteristics for Study 1

	FOBT within 6 months	No FOBT within 6 months	Total
	(n=2,503)	(n=8,799)	(n=11,302)
Patient participants			
Age group in years, No. (%)			
50-59	1,279 (51%)	5,384 (61%)	6,663 (59%)
60-69	894 (36%)	2,637 (30%)	3,531 (31%)
70-74	330 (13%)	778 (9%)	1,108 (10%)
Sex, No. (%)			
Female	1,299 (52%)	4,554 (52%)	5,853 (52%)
Male	1,204 (48%)	4,245 (48%)	5,449 (48%)
Co-morbidity*, No. of ADGs (%)			
0	257 (10%)	1,279 (15%)	1,536 (14%)
1-2	828 (33%)	3,044 (35%)	3,872 (34%)
3-4	712 (28%)	2,241 (25%)	2,953 (26%)
5-6	393 (16%)	1,224 (14%)	1,617 (14%)
7+	313 (13%)	1,011 (11%)	1,324 (12%)
Median neighborhood income quintile, No. (%)			
Rural	394 (16%)	1,431 (16%)	1,825 (16%)
Low Urban	360 (14%)	1,375 (16%)	1,735 (15%)
2	402 (16%)	1,418 (16%)	1,820 (16%)
3	429 (17%)	1,430 (16%)	1,859 (16%)
4	432 (17%)	1,552 (18%)	1,984 (18%)
High Urban	486 (19%)	1,593 (18%)	2,079 (18%)
Health region, No. (%)			
Erie St.Clair	125 (5%)	337 (4%)	462 (4%)
South West	284 (11%)	823 (9%)	1,107 (10%)
Waterloo Wellington	76 (3%)	251 (3%)	327 (3%)
Hamilton Niagara	289 (12%)	976 (11%)	1,265 (11%)
Central West	138 (6%)	482 (5%)	620 (5%)
Mississauga Halton	22 (1%)	120 (1%)	142 (1%)
Toronto Central	111 (4%)	392 (4%)	503 (4%)
Central	24 (1%)	177 (2%)	201 (2%)
Central East	361 (14%)	1,282 (15%)	1,643 (15%)
South East	162 (6%)	697 (8%)	859 (8%)
Champlain	219 (9%)	676 (8%)	895 (8%)
North Simcoe-Muskoka	77 (3%)	188 (2%)	265 (2%)
North East	291 (12%)	1,118 (13%)	1,409 (12%)
North West	324 (13%)	1,280 (15%)	1,604 (14%)

Recent immigrant, No. (%)	23 (1%)	88 (1%)	111 (1%)
FOBT 2 to 5 years prior to mailing, No. (%)	643 (26%)	905 (10%)	1,548 (14%)
Physician			
Median age in years (IQR)	52 (45-59)	53 (46-59)	52 (45-59)
Sex, No. (%)			
Female	936 (37%)	3,044 (35%)	3,980 (35%)
Male	1,567 (63%)	5,755 (65%)	7,322 (65%)
Training location, No. (%)			
Outside Canada	312 (12%)	1,196 (14%)	1,508 (13%)
In Canada	2,191 (88%)	7,603 (86%)	9,794 (87%)
Practice type, No. (%)			
FHG	1,082 (43%)	4,266 (48%)	5,348 (47%)
FHO/FHN	432 (17%)	1,456 (17%)	1,888 (17%)
FHO/FHN-FHT	881 (35%)	2,620 (30%)	3,501 (31%)
Other PEM	108 (4%)	457 (5%)	565 (5%)
Practice size (enrolled patients), No. (%)			
>1800 patients	1,105 (44%)	4,104 (47%)	5,209 (46%)
Age-eligible rate of colonoscopy quintile, No. (%)			
Low	485 (19%)	1,619 (18%)	2,104 (19%)
2	548 (22%)	1,940 (22%)	2,488 (22%)
3	637 (25%)	2,279 (26%)	2,916 (26%)
4	477 (19%)	1,696 (19%)	2,173 (19%)
High	356 (14%)	1,265 (14%)	1,621 (14%)
Age-eligible rate of FOBT quintile, No. (%)			
Low	487 (19%)	1,888 (21%)	2,375 (21%)
2	504 (20%)	1,886 (21%)	2,390 (21%)
3	533 (21%)	1,890 (21%)	2,423 (21%)
4	522 (21%)	1,680 (19%)	2,202 (19%)
High	457 (18%)	1,455 (17%)	1,912 (17%)
Age-eligible rate of annual physical exams quintile, No. (%)			
Low	496 (20%)	2,009 (23%)	2,505 (22%)
2	490 (20%)	1,625 (18%)	2,115 (19%)
3	472 (19%)	1,638 (19%)	2,110 (19%)
4	509 (20%)	1,686 (19%)	2,195 (19%)
High	536 (21%)	1,841 (21%)	2,377 (21%)

Age-eligible rate of influenza vaccine quintile, No. (%)			
Low	548 (22%)	1,997 (23%)	2,545 (23%)
2	549 (22%)	1,765 (20%)	2,314 (20%)
3	435 (17%)	1,930 (22%)	2,365 (21%)
4	485 (19%)	1,770 (20%)	2,255 (20%)
High	486 (19%)	1,337 (15%)	1,823 (16%)

*Co-morbidity scored using number of Aggregated Diagnosis Groups (ADGs) using the Johns Hopkins Case Mix System

FHG = family health group

FHO/FHN = family health organizations or networks

Other PEM = other patient enrolled model of care

FOBT = fecal occult blood test

Table 2. Multivariate logistic regression analysis using Generalized Estimating Equations for the characteristics of participants and physicians associated with completing an FOBT within 6 months of the mailing date.

Participants	Odds ratio (95% C.I.)	P-value
Age group, years		
50-59	0.6 (0.5, 0.8)	<.0001
60-69	0.8 (0.7, 1.0)	NS
70-74	Reference	N/A
Sex		
Female	0.9 (0.9, 1.0)	NS
Male	Reference	N/A
Co-morbidity*, No. of ADGs		
0	0.7 (0.6, 0.8)	0.0002
1-2	0.9 (0.7, 1.0)	NS
3-4	1.0 (0.9, 1.2)	NS
5-6	1.0 (0.9, 1.2)	NS
7+	Reference	N/A
Median neighborhood income quintile		
Rural	0.9 (0.7, 1.1)	NS
Low Urban	0.9 (0.7, 1.0)	NS
2	1.0 (0.8, 1.1)	NS
3	1.0 (0.9, 1.1)	NS
4	0.9 (0.8, 1.1)	NS
High Urban	Reference	N/A
Health region		
Erie St.Clair	1.3 (0.9, 1.8)	NS
South West	0.9 (0.6, 1.4)	NS
Waterloo Wellington	0.8 (0.6, 1.2)	NS
Hamilton Niagara	0.9 (0.6, 1.2)	NS
Central West	1.0 (0.7, 1.4)	NS
Mississauga Halton	0.6 (0.3, 1.2)	NS
Toronto Central	0.8 (0.6, 1.2)	NS
Central	0.5 (0.4, 0.7)	0.0004
South East	0.8 (0.5, 1.3)	NS
Champlain	1.0 (0.7, 1.4)	NS
North Simcoe-Muskoka	0.9 (0.6, 1.4)	NS
North East	1.1 (0.7, 1.5)	NS
North West	0.7 (0.5, 1.0)	0.03
Central East	Reference	N/A
Recency of immigration		
Remote or non-immigrant	1.0 (0.6, 1.6)	NS
Recent immigrant	Reference	N/A
Prior FOBT Use		
2 to 5 years prior to mailing	2.8 (2.5, 3.3)	<.0001

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> 5 years or never	Reference	
Physician		
Increasing age (per year)	1.0 (1.0, 1.0)	NS
Sex		
Female	1.3 (1.0, 1.5)	0.02
Male	Reference	N/A
Training location		
In Canada	0.9 (0.7, 1.2)	NS
Outside Canada	Reference	N/A
Practice type		
FHG	0.9 (0.7, 1.1)	NS
FHO/FHN	0.8 (0.6, 1.1)	NS
Other PEM	0.7 (0.4, 1.0)	0.05
FHO/FHN-FHT	Reference	N/A
Practice size (enrolled patients)		
≤ 1800 patients	1.1 (0.9, 1.3)	NS
> 1800 patients	Reference	N/A
Age-eligible rate of colonoscopy quintile		
Low	1.1 (0.8, 1.5)	NS
2	1.2 (1.0, 1.6)	NS
3	1.0 (0.8, 1.2)	NS
4	1.0 (0.8, 1.3)	NS
High	Reference	N/A
Age-eligible rate of FOBT quintile		
2	0.9 (0.6, 1.3)	NS
3	0.9 (0.7, 1.2)	NS
4	1.1 (0.8, 1.4)	NS
High	0.9 (0.7, 1.3)	NS
Low	Reference	N/A
Age-eligible rate of annual physical exams quintile		
2	1.4 (0.9, 2.0)	NS
3	1.3 (0.9, 1.8)	NS
4	1.3 (0.9, 1.8)	NS
High	1.1 (0.8, 1.5)	NS
Low	Reference	N/A
Age-eligible rate of influenza vaccine quintile		
2	1.0 (0.8, 1.2)	NS
3	0.8 (0.6, 1.0)	0.02
4	0.9 (0.7, 1.2)	NS
High	1.3 (1.0, 1.7)	NS
Low	Reference	N/A

*Co-morbidity scored using number of Aggregated Diagnosis Groups (ADGs) using the Johns Hopkins Case Mix System
FHG = family health group
FHO/FHN = family health organizations or networks

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Other PEM = other patient enrolled model of care
NS = not significant
N/A - not applicable
FOBT = fecal occult blood test

Table 3. Characteristics of the 2 cohorts matched by propensity score in Study 2

	Pilot participants (n=10,652)	Control participants (n=10.652)	Standardized Difference*
Participants			
Age group in years, No. (%)			
50-59	6,248 (59%)	6,324 (59%)	0.01
60-69	3,342 (31%)	3,316 (31%)	0.01
70-74	1,062 (10%)	1,012 (10%)	0.02
Sex, No. (%)			
Female	5548 (52%)	5477 (51%)	0.01
Male	5,104 (48%)	5,175 (49%)	0.01
Co-morbidity**, No. of ADGs (%)			
0	1,462 (14%)	1,425 (13%)	0.01
1-2	3,647 (34%)	3,716 (35%)	0.01
3-4	2,764 (26%)	2,835 (27%)	0.02
5-6	1,536 (14%)	1,473 (14%)	0.02
7+	1,243 (12%)	1,203 (11%)	0.01
Median neighborhood income quintile, No. (%)			
Rural	1,825 (17%)	1,889 (18%)	0.02
Low Urban	1,628 (15%)	1,699 (16%)	0.02
2	1,698 (16%)	1,728 (16%)	0.01
3	1,728 (16%)	1,681 (16%)	0.01
4	1,831 (17%)	1,753 (16%)	0.02
High Urban	1,942 (18%)	1,902 (18%)	0.01
Health region, No. (%)			
Erie St.Clair	462 (4%)	423 (4%)	0.02
South West	1,107 (10%)	1,114 (10%)	0
Waterloo Wellington	327 (3%)	343 (3%)	0.01
Hamilton Niagara	1,265 (12%)	1,290 (12%)	0.01
Central West	620 (6%)	580 (5%)	0.02
Mississauga Halton	142 (1%)	144 (1%)	0
Toronto Central	503 (5%)	478 (4%)	0.01
Central	201 (2%)	209 (2%)	0.01
Central East	1,643 (15%)	1,702 (16%)	0.02
South East	859 (8%)	891 (8%)	0.01
Champlain	895 (8%)	904 (8%)	0
North Simcoe-Muskoka	265 (2%)	242 (2%)	0.01
North East	1,409 (13%)	1,378 (13%)	0.01
North West	954 (9%)	954 (9%)	0
Recent immigrant, No. (%)	111 (1%)	105 (1%)	0.01
FOBT 2 to 5 years prior to mailing, No. (%)	1,476 (14%)	1,240 (12%)	0.07
Physician			

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Median age in years (IQR)	52 (45-59)	52 (47-58)	N/A
Sex, No. (%)			
Female	3,875 (36%)	3,335 (31%)	N/A
Male	6,777 (64%)	7,317 (69%)	
Practice type, No. (%)			
FHG	4,854 (46%)	4,885 (46%)	
FHO/FHN	1,859 (17%)	1,718 (16%)	N/A
FHO/FHN-FHT	3,374 (32%)	3,027 (28%)	
Other PEM	565 (5%)	1,022 (10%)	
Practice size (enrolled patients), No. (%)			
>1800 patients	5,366 (50%)	5,026 (47%)	N/A

*Standardized differences for physician level variables not reported as propensity scores were estimated using patient level characteristics only

**Co-morbidity scored using number of Aggregated Diagnosis Groups (ADGs) using the Johns Hopkins Case Mix System

FHG = family health group

FHO/FHN = family health organizations or networks

Other PEM = other patient enrolled model of care

FOBT = fecal occult blood test

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Table 4. Association between mailed invitation and FOBT completion or mailed invitation and FOBT or colonoscopy completion after adjusting for physician factors.

	FOBT completion		FOBT or Colonoscopy completion	
	Odds ratio (95% C.I.)	P-value	Odds ratio (95% C.I.)	P-value
Mailed invitation				
Yes (Pilot)	3.3 (3.1, 3.6)	<.0001	2.7 (2.5, 2.9)	<.0001
No (Controls)	Reference	N/A	Reference	N/A
Increasing age (per year)	1.0 (1.0, 1.0)	NS	1.0 (1.0, 1.0)	0.03
Sex, No. (%)				
Female	1.0 (0.9, 1.1)	NS	1.0 (0.9, 1.1)	NS
Male	Reference	N/A	Reference	N/A
Practice type, No. (%)				
FHG	0.7 (0.6, 0.8)	<.0001	0.7 (0.7, 0.8)	<.0001
FHO/FHN	0.8 (0.7, 0.9)	<.0001	0.8 (0.7, 0.9)	<.0001
Other PEM	0.8 (0.7, 1.0)	0.03	0.8 (0.7, 1.0)	NS
FHO/FHN-FHT	Reference	N/A	Reference	N/A
Practice size (enrolled patients)				
≤ 1800 patients	1.2 (1.1, 1.3)	0.0004	1.2 (1.1, 1.3)	<.0001
> 1800 patients	Reference	N/A	Reference	N/A

FHG = family health group

FHO/FHN = family health organizations or networks

Other PEM = other patient enrolled model of care

FOBT = fecal occult blood test

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Figure Legends

Figure 1. Mock-up of physician-linked invitation used in the Pilot.

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TITLE PAGE

Title: ~~Using p~~Physician-linked mailed invitations ~~to be screened~~ in an organized colorectal cancer screening program: effectiveness and factors associated with response~~.~~.

Short title: Physician-linked invitations for colorectal cancer screening

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Word count: ~~3211~~ 3159 (main text),   263~~2~~ (abstract)

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Physician-linked mailed invitations for colorectal cancer screening

Number of Tables: 4

Number of Figures: 1

Number of References: 4045

Formatted: Highlight

Key words: Mailed invitations, colorectal cancer, organized screening

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4   Tinmouth et al.
5   Physician-linked mailed invitations for colorectal cancer screening
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7
8   **ABSTRACT**
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11   Objectives: A central tenet of organized cancer screening is that all persons in a target
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13   population are invited. The aims of this study were to identify participant and physician
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15   factors associated with response to mailed physician-linked invitations (Study 1) and to
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17   evaluate their effectiveness in an organized colorectal (CRC) screening program (Study
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19   2).
20
21   Design and setting: Two studies (Study 1 – cohort design and Study 2 – matched cohort
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23   design, ~~of~~ comprising Study 1 participants and a matched control group) conducted in
24
25   context of Ontario's organized province-wide CRC screening program.
26
27   Participants: 102 family physicians and 11,302 associated eligible patients from a
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29   technical evaluation ("the Pilot") of large scale mailed invitations for CRC screening were
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31   included. Matched controls were randomly selected using propensity scores from among
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33   eligible patients associated with family physicians in similar practice types as the Pilot
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35   physicians.
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37   Intervention: Physician-linked mailed invitation to have CRC screening.
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39   Outcomes: Uptake of fecal occult blood test (FOBT) within 6 months of mailed invitation
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41   (primary) and uptake of FOBT or colonoscopy within 6 months of mailed invitation
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43   (secondary).
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45   Results: Factors significantly associated with uptake of FOBT included prior FOBT use,
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47   older participant age, greater participant co-morbidity and having a female physician. In
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the matched analysis, Pilot participants were more likely to complete an FOBT (22% vs.

8%, p<0.0001) or an FOBT or colonoscopy (25% vs. 11%, p <0.0001) within 6 months of

mailed invitation than matched controls. The number needed to invite to screen one

additional person was 7.

Conclusions: Centralized large scale mailing of physician-linked invitations is both

feasible and effective in an the context of organized CRC screening program.

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ARTICLE SUMMARY

Strengths and limitations of this study:

- We describe the implementation of physician-linked invitations in an organized colorectal screening program that is characterized by a high level of primary care physician involvement and that operates in a context where opportunistic screening with colonoscopy is possible
- We have shown that centralized large scale mailing of physician-linked invitations is feasible and effective in this context
- We found that physician linked mailed invitations improve CRC screening participation by 14% such that 7 physician-linked invitations need to be mailed to screen one additional person
- We were limited to data found in Ontario health administrative databases; for example, we were not able to determine family history
- Findings are promising but require appropriate infrastructure in order to be implemented in other jurisdictions

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INTRODUCTION

Colorectal cancer (CRC) is ~~the 3rd most common cancer and the 4th~~the second leading cause of cancer-related death among men and the third among women ~~worldwide~~in Canada.[1]~~REF.~~ Fecal occult blood testing (FOBT)[2-4] and flexible sigmoidoscopy[5-7] have been shown to decrease CRC mortality in randomized controlled trials.

Given these data, organized CRC screening programs[8] are being implemented worldwide.[9] On April 1 2008, Ontario launched ColonCancerCheck (CCC), Canada's first organized province-wide CRC screening program~~, ColonCancerCheck (CCC)~~.[10] ~~CCC has a dual strategy: t~~Through the primary care physician, FOBT is offered to people at average risk for CRC and colonoscopy to those at increased risk based on family history. The CCC program uses a non-rehydrated guaiac FOBT (Hema-Screen, Immmunostics, Inc., NJ, USA) requiring ~~3 stool~~ samples from 3 separate stools. While there is data to suggest that dietary restriction may be unnecessary,[11] ~~T~~the program recommends avoiding ~~only recommended dietary restriction is to avoid~~ vitamin C for 3 days prior to and during the collection period in order to minimize false negative results.

Approximately 75% of Ontario residents received their care via a patient enrolled model (PEM~~s~~) of care at the time of the study (2009).[12] PEMs comprise teams of family physicians who provide their enrolled patients with comprehensive health care and extended hours.[13] PEMs vary in terms of structure, services provided and remuneration

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(varying from enhance fee-for-service to blended capitation). All Ontario physicians are remunerated for preventive care such as CRC screening however, PEM physicians are incented to a greater degree than those who are not in PEMs. Specifically, PEM physicians receive a $7/patient fee for "FOBT dDistribution and cCounseling", a $6.86/patient fee for "CRC sScreening mManagement" and an annual "Colorectal cCancer sScreening pPreventive cCare bBonus" ($220 to $4000) depending on the proportion of enrolled patients who are up-to-date with FOBT (15-70%). The physician is entitled to the CRC sScreening mManagement fee if the enrolled patient attends an appointment to discuss CRC screening, has declined the test verbally or in writing or if there has been no response after 2 written notices and a telephone call from the physician.[14]

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A central tenet of organized screening programs is that all persons in the target population be invited to participate.[8] Implementation of this aspect of organized screening varyvaries: invitations may be sent with an FOBT kit, can include physician recommendation or may incorporate tailored messaging.[15 16] Some of these approaches, such as incorporation of physician recommendation, present significant implementation challenges for organized screening programs such as Ontario's.

In 2009, the CCC program conducted undertook the CCC Invitation Pilot (the "Pilot"), an evaluation that tested the technical feasibility of a centralized approach to sending physician-linked mailed invitations for CRC screening. In this paper, we describe the

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structure and the implementation of the Pilot. In addition, we report on participant and physician factors associated with response to mailed physician-linked invitations and on the effectiveness of these invitations in ~~an~~ Ontario's organized CRC screening program.

METHODS

The CCC Invitation Pilot – Implementation and Evaluation

The ~~Pilot was conducted by CCC~~ CCC program conducted the Pilot in November 2009 ~~in order to develop and test the technical infrastructure required for large scale centralized physician-linked mailed invitations in Ontario~~. ~~For the Pilot, i~~Invitation letters were generated by the CCC program on behalf of 102 family physicians and sent to all their eligible enrolled patients. Just over 11,000 eligible patient participants were sent mailed invitations requesting they visit their family physician to obtain an FOBT kit or, if appropriate based on family history, a referral for colonoscopy. In this paper, we report on 2 studies using this cohort. Study 1 examines participant and physician factors associated with response to the mailed invitation among those who were sent the mailed invitation. Study 2 evaluates the effectiveness of the mailed invitation by comparing uptake of CRC screening among Study 1 participants compared to a matched control group. Ethics approval was obtained from the research ethics boards at Sunnybrook Health Sciences Centre and the Institute for Clinical Evaluative Sciences (ICES) and permission to use the Pilot data was obtained from Cancer Care Ontario's (CCO) Data

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Access Committee. All analyses were conducted using SAS v.9 (SAS Institute, Cary,

NC). A p-value of 0.05 was used to determine statistical significance.

Data Sources

The Pilot study was conducted at ICES, which houses the administrative health records

for all 12.43.5 million Ontarians. CCC program databases were linked to the ICES

administrative databases using an encrypted version of the provincial health insurance

number.

The ICES databases used include the Canadian Institute of Health Information (CIHI)

databases, the Ontario Health Insurance Program (OHIP) Claims History Database, the

Registered Persons Database (RPDB), the Ontario Cancer Registry, the ICES Physician

Database, and the Client Agency Program Enrollment (CAPE) registry. The CIHI, OHIP,

RPDB and the Ontario Cancer Registry and the ICES Physician Database have beenare

previously described elsewhere.[17] [18] The CAPE registry tracks patients enrolled to

physicians who participate in PEMs and is a centralized electronic record of the linkage

between specific patients and their physicians.,

Since its inception, tThe CCC program has collected data related to the FOBT kits

administered by the CCC program, including the results of these tests, on CRC

screening since its inception using Laboratory Reporting Tool (LRT) and comprises data

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related to the FOBT kits administered by the CCC program, including the results of these tests.

Study 1: Factors associated with response to the mailed invitation

Cohort Definition: For the Pilot, a convenience sample of physicians participating in PEM-type practices was recruited via CCO's Provincial Primary Care Cancer Network. Patients enrolled to these physicians, aged 50 to 74 years without a history of CRC and who were due for CRC screening (without a health administrative data record of recent FOBT (previous two years) or lower GI investigation including flexible sigmoidoscopy and colonoscopy (previous 5 years)), were eligible. For the Pilot mailing, CCC generated lists of patient participants eligible for CRC screening for each participating physician using CAPE, Ontario Cancer Registry, OHIP, CIRT and LRT. All persons who were sent an invitation were included in the cohort, regardless of whether the letter was returned to the sender.

The Mailing: Invitations were mailed in November 2009. The date of mailing was the index date. The letters were compiled centrally by the CCC program but were physician-linked; patient participants were sent a letter from their own physician, as indicated by their name at the bottom of the letter in an italicized font (Figure 1). The letter asked participants to visit their family physician for screening; it did not include an FOBT kit. The letter was accompanied by a CRC screening information brochure and sent in an

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envelope with the family physician name in the front upper left corner. ~~For the purposes of the study,~~ Pilot physicians were not compensated for study participation, however, they were able to apply the letter towards meeting the requirements for the ~~an equivalent amount to the~~ CRC ~~s~~Screening ~~m~~Management fee ($6.86 per eligible enrolled patient) ~~as Ontario PEM physicians are eligible for this fee for contacting the patient by mail regarding CRC screening~~.

Response to Mailed Invitation: We used a broad definition of response to the mailed invitation: any record of FOBT in either OHIP or in LRT within 6 months of the index date, regardless of result (including rejected kits). Up to 10% of FOBT done in the province are captured only ~~through~~ in OHIP, which does not have data on test results. We were not able to measure response in persons at increased risk of CRC as we do not have family history data available in the administrative databases.

Participant and Physician Factors: We characterized participants by age group, sex, co-morbidity, median neighborhood income,[19 20] health region,[21] immigration status, and prior FOBT. ~~C~~We measured comorbidity ~~was measured~~ by counting the number of Aggregated Diagnosis Groups (ADGs) using ~~in the prior 12 months according to~~ the Johns Hopkins ACG® Case-Mix System in the prior 12 months.[22] ~~This system has been shown to~~M~~ accurately predict m~~ortality in a general population ambulatory cohort in Ontario was accurately predicted using this system.[23] We used date of registration in

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the RPDB as a proxy measure for immigration status; participants were considered recent immigrants if their date of registration was within 5 years of the index date.[24]

Physicians were characterized according to age, sex, training location (~~attended Canadian medical school~~Canada vs. outside of Canada), practice type, size of practice, age-eligible rate of colonoscopy or FOBT over prior 2 years as well as the age-eligible rate of annual physical exams or influenza vaccinations in the prior year. All participating physicians were in PEMs; practice types included family health groups (FHGs, enhanced fee-for-service models), family health organizations or networks (FHO/FHNs, blended capitation models), FHO/FHN with family health team (FHO/FHN-FHT, interprofessional team model with a blended capitation fee structure) and other PEMs.[25] We measured practice size as the number of enrolled patients stratified in a binary fashion (≤1800 vs. >1800 enrolled patients) as larger practice sizes have been shown to be associated with poorer preventative care.[26] For the remaining physician characteristics, we identified all enrolled and non-enrolled patients aged 50-74 years in their practices as of the index date. Age-eligible FOBT and colonoscopy rates were obtained for each Pilot physician by calculating the proportion of their age-eligible patients who had had an FOBT or colonoscopy in the 2 years prior to the index date. Similarly, we calculated their rates of age-eligible annual physical exams or influenza vaccine in the year prior to the index date. These variables were derived in order to

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estimate physician adherence to CRC screening and preventive medicine practices at baseline.

Analysis: The number and proportion of persons in the cohort who responded to the mailed invitation within 6 months were determined overall and by participant and physician characteristics. Multivariate logistic regression modeling was used to identify participant and physician factors associated with response to the mailed invitation. In order to account for potential clustering of participants within physicians, Generalized Estimating Equations (GEE)[27] were used in the model.

Study 2: Evaluation of the effectiveness of mailed invitations

Overview and study participants: This was a matched double cohort analysis, comparing uptake of FOBT in those who were sent a mailed invitation (Pilot cohort) to a matched control group who were not sent a mailed invitation. The control group comprised patients who were enrolled to PEM physicians who had not participated in the Pilot. Control participants received "usual care" from the CCC program in terms of screening promotion. As such, they were eligible for screening via their primary care physician who was eligible for the same financial incentives as the Pilot physicians. Control participants were not sent a centralized physician-linked invitation from the CCC program although their physicians could send them a mailed invitation at their own discretion.

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The Pilot cohort comprised all members of the cohort described in Study 1 for whom a matched control could be identified. We identified potential controls as follows: 1) Pilot physicians were matched to non-Pilot physicians who were also practicing in PEMs in a 1:5 ratio using physician age, sex, size and practice type; 2) individuals enrolled to the selected control physicians were retained if they met the same inclusion/exclusion criteria as those in the intervention cohort (aged 50 to 74 years with no prior CRC who were due for CRC screening). As with the identification of eligible participants in the Pilot, we used CAPE, Ontario Cancer Registry, OHIP, CIRT and LRT to determine eligibility of potential control participants.

Propensity scores that modeled the probability of belonging to the Pilot group were calculated for each participant in the entire group (Pilot and control). The variables in this model included age (as a continuous measure), sex, co-morbidity, median neighborhood income quintile, health region, immigration status, and FOBT from 2 to 5 years prior.[28 29] Pilot participants were matched to controls in a 1:1 fashion based on propensity scores using a caliper width of 0.25. This methodology was implemented to balance the distribution of participant-level variables between the Pilot and control groups.

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<u>Response to mailed invitation</u>: For our primary outcome, we defined response to the mailed invitation as in Study 1, a record of FOBT regardless of result, within 6 months of the index date. For our secondary outcome, response was defined as a record of either FOBT or colonoscopy within 6 months of the index date. For the purposes of this study, controls were assigned the same index date as their matched counterpart in the Pilot group.

<u>Analysis</u>: Standard differences between the Pilot participants and controls were calculated for the variables included in the propensity score. Important differences between the 2 groups were defined by a standardized difference exceeding 0.1.[29 30] In the primary analysis, we compared the number and proportion in the Pilot and control groups responding to the mailed invitation with FOBT using McNemar's test.[29] We determined the number of invitations mailed in order to screen one additional person with FOBT. We repeated the above analyses using our secondary outcome in order to determine if observed differences in FOBT uptake could be attributed to differences in colonoscopy uptake (i.e., participants had CRC screening but chose colonoscopy over FOBT). As the matching only accounted for participant-level variables, we repeated our analyses using conditional logistic regression in order to adjust for physician covariates (age, sex, practice type and size).

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RESULTS

Study 1: Factors associated with response to the mailed invitation

There were 11,311 eligible patient participants associated with the 102 family physicians

in the Pilot cohort. Nine participants were ~~excluded~~excluded, as we were unable to

determine their health region and/or income quintile; this left 11,302 participants for the

analysis. The majority of participants were 50 to 59 years of age, 52% were women,

48% had no or low co-morbidity and 14% had completed an FOBT from 2 to 5 years

prior to the mailing. Two thirds of participants had a male physician, approximately half

were part of a primary care team reimbursed via an enhanced fee-for-service

arrangement and just under half were enrolled in larger practices (>1800 enrolled

patients) (Table 1).

2503 (22%) completed an FOBT within 6 months of mailing. In the multivariate

regression, the strongest participant factor associated with FOBT completion was prior

FOBT use (2 to 5 years prior vs. > 5 years or never: OR 2.8, 95% C.I.: 2.5 to 3.3, p <

0.0001). Other significant factors associated with FOBT completion included older

participant age, greater co-morbidity, and having a female physician (Table 2).

Study 2: Evaluation of the effectiveness of mailed invitations

Of the 11,302 participants in Study 1, 10,652 ~-~were successfully matched to 10,652

controls using propensity scores. Standardized differences for the participant

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characteristics included in the propensity score were all <0.1, indicating that the two

cohorts were well matched for measurable potential confounders (Table 3).

Pilot participants were significantly more likely than controls to complete FOBT alone

(2387 (22%) versus 854 (8%), p<0.0001) and FOBT or colonoscopy (2664 (25%) vs.

1191 (11%), p<0.0001) within 6 months of mailing. The association between the mailed

invitation and CRC screening participation (either FOBT alone or FOBT or colonoscopy)

remained after adjusting for physician level characteristics (Table 4).

DISCUSSION

In the current study, we have demonstrated that physician-linked mailed invitations are

both feasible and effective in the context of a large organized, population-based

screening program; only 7 letters would need to be sent in order to screen one additional

person. Furthermore, we have found that older participants, those with greater co-

morbidity, those who have previously been screened and those with female physicians

were more likely to respond to this type of invitation. Our findings are of particular

interest to other jurisdictions planning or who already have organized CRC screening.

In other published studies of mailed invitations, an FOBT kit is often included with the

invitation. Three studies done outside organized screening programs have found

physician-linked invitations superior to non-linked invitations; 2 of these studies included

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an FOBT kit,[31] [32] and the third study did not.[33] Other studies have examined mailed

invitations with FOBT kits in the context of primary care practices in the USA.[34-36] While

the results from these trials were largely supportive of mailed invitations, kit inclusion

can make it difficult to separate the convenience of receiving the FOBT kit directly by

mail from the impact of an invitation from one's own physician.

Our study demonstrates the effectiveness and feasibility of physician-linked invitations in

the context of a large organized CRC screening program with an estimated target

population of over 3 million persons. Implementation in this context confers challenges in

terms of technological infra-structure, privacy and regulatory issues. There are 2 studies

(from the United Kingdom[37] and Italy[38]) that have reported on mailed invitations in the

context of organized colorectal cancer screening programs and found them to be

effective. Both studies included FOBT kits and one studied the impact of physician

endorsement specifically.[37] Our findings are important because they support a

potentially more cost-effective approach that avoids wasting kits that are mailed but not

used.

Our results highlight the critical role of physician recommendation, a finding supported

by others. For example, in the NHS Bowel Cancer Screening Programme (BCSP)

currently, the primary care physician receives the result but is not directly involved in the

mailed invitation or the actual screening. Recently, a randomized controlled trial

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conducted in the context of the BCSP showed that an endorsement letter from the

primary care provider increased participation by 6%.[37] —In 2 studies from Australia,

endorsement improved initial participation[31 32] and over 4 successive screening

rounds.[32]

Uptake of FOBT in Ontario is lower than some organized CRC screening programs in

other countries. For example, 30% of Ontarians were up-to-date with FOBT in 2008-9[39]

compared to 52% participation in the United Kingdom program by October 2008,[40] 54%

in the Italian program in 2007,[41] and 54% in the New Zealand pilot program in 2012.[42]

However, in the latter countries, there is very little, if any, opportunistic CRC screening

using colonoscopy whereas Ontario's program operates in a hybrid environment where

opportunistic colonoscopy is available as the initial screening test in persons at average

risk. It has been noted that uptake of FOBT may be lower in settings, such as Ontario's

or Australia's,[43] where opportunistic screening is available.[44] The findings from the

current study indicate that physician-linked invitations for CRC screening can be

effective in increasing uptake of FOBT in programs that operate in the context of

opportunistic colonoscopy for average risk screening.

Our study has several limitations. ~~As mentioned above~~First, we are unable to determine

family history using Ontario administrative data. A second limitation is that a single

generic letter was used. Tailored letters with key messages for specific subgroups may

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be more effective,[16] – an approach that may be relevant in Ontario as we did find that

response to the letter appeared to differ in various subgroups. Additionally, while our

findings are promising, there are challenges to ~~widespread implementation~~adoption by ~~in~~

other population-based screening programs, including the ~~requirement~~ need for a

centralized database that links patients to their physicians. Finally, implementation of

this strategy in population-based screening is predicated on physician acceptability and

agreement. While we have found that this approach is acceptable in principle to many

Ontario physicians,[45] processes to confirm individual physician agreement have not

been determined for the entire CCC program which comprises an estimated 7000

primary care physicians.

CONCLUSIONS

In summary, we have demonstrated that physician-linked mailed invitations for CRC

screening, even without the inclusion of an FOBT kit, can have substantial effect on

participation in an organized CRC screening program and that it is technically feasible to

centrally organize and mail physician-linked invitations on a large scale. Organized

screening programs, which often use unlinked invitations, should consider adopting this

approach given its demonstrated effectiveness and feasibility.

ACKNOWLEDGEMENTS

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COMPETING INTERESTS STATEMENT

Dr. Tinmouth is the Lead Scientist for the ColonCancerCheck program and Dr.
Rabeneck oversees the ColonCancerCheck program in her capacity as the Vice-
President, Cancer Prevention and Control at CCO. None of the other authors have any
conflicts of interest to report.

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AUTHOR CONTRIBUTION:

Authors contributed substantially to each of the following areas:

-conception and design (JT, LFP, LR) or analysis and interpretation of data (JT, NB,

LFP, LR, RS, LY)

-drafting the article (JT) or revising it critically for important intellectual content (JT, NB,

LFP, LR, RS, LY)

-final approval of the version to be published (JT, NB, LFP, LR, RS, LY)

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Field Code Changed

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Tables.

Table 1. Patient participant and physician characteristics for Study 1

	FOBT within 6 months (n=2,503)	No FOBT within 6 months (n=8,799)	Total (n=11,302)
Patient participants			
Age group in years, No. (%)			
50-59	1,279 (51%)	5,384 (61%)	6,663 (59%)
60-69	894 (36%)	2,637 (30%)	3,531 (31%)
70-74	330 (13%)	778 (9%)	1,108 (10%)
Sex, No. (%)			
Female	1,299 (52%)	4,554 (52%)	5,853 (52%)
Male	1,204 (48%)	4,245 (48%)	5,449 (48%)
Co-morbidity*, No. of ADGs (%)			
0	257 (10%)	1,279 (15%)	1,536 (14%)
1-2	828 (33%)	3,044 (35%)	3,872 (34%)
3-4	712 (28%)	2,241 (25%)	2,953 (26%)
5-6	393 (16%)	1,224 (14%)	1,617 (14%)
7+	313 (13%)	1,011 (11%)	1,324 (12%)
Median neighborhood income quintile, No. (%)			
Rural	394 (16%)	1,431 (16%)	1,825 (16%)
Low Urban	360 (14%)	1,375 (16%)	1,735 (15%)
2	402 (16%)	1,418 (16%)	1,820 (16%)
3	429 (17%)	1,430 (16%)	1,859 (16%)
4	432 (17%)	1,552 (18%)	1,984 (18%)
High Urban	486 (19%)	1,593 (18%)	2,079 (18%)
Health region, No. (%)			
Erie St.Clair	125 (5%)	337 (4%)	462 (4%)
South West	284 (11%)	823 (9%)	1,107 (10%)
Waterloo Wellington	76 (3%)	251 (3%)	327 (3%)
Hamilton Niagara	289 (12%)	976 (11%)	1,265 (11%)
Central West	138 (6%)	482 (5%)	620 (5%)
Mississauga Halton	22 (1%)	120 (1%)	142 (1%)
Toronto Central	111 (4%)	392 (4%)	503 (4%)
Central	24 (1%)	177 (2%)	201 (2%)
Central East	361 (14%)	1,282 (15%)	1,643 (15%)
South East	162 (6%)	697 (8%)	859 (8%)
Champlain	219 (9%)	676 (8%)	895 (8%)
North Simcoe-Muskoka	77 (3%)	188 (2%)	265 (2%)
North East	291 (12%)	1,118 (13%)	1,409 (12%)
North West	324 (13%)	1,280 (15%)	1,604 (14%)

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Recent immigrant, No. (%)	23 (1%)	88 (1%)	111 (1%)
FOBT 2 to 5 years prior to mailing, No. (%)	643 (26%)	905 (10%)	1,548 (14%)
Physician			
Median age in years (IQR)	52 (45-59)	53 (46-59)	52 (45-59)
Sex, No. (%)			
Female	936 (37%)	3,044 (35%)	3,980 (35%)
Male	1,567 (63%)	5,755 (65%)	7,322 (65%)
Training location, No. (%)			
Outside Canada	312 (12%)	1,196 (14%)	1,508 (13%)
In Canada	2,191 (88%)	7,603 (86%)	9,794 (87%)
Practice type, No. (%)			
FHG	1,082 (43%)	4,266 (48%)	5,348 (47%)
FHO/FHN	432 (17%)	1,456 (17%)	1,888 (17%)
FHO/FHN-FHT	881 (35%)	2,620 (30%)	3,501 (31%)
Other PEM	108 (4%)	457 (5%)	565 (5%)
Practice size (enrolled patients), No. (%)			
>1800 patients	1,105 (44%)	4,104 (47%)	5,209 (46%)
Age-eligible rate of colonoscopy quintile, No. (%)			
Low	485 (19%)	1,619 (18%)	2,104 (19%)
2	548 (22%)	1,940 (22%)	2,488 (22%)
3	637 (25%)	2,279 (26%)	2,916 (26%)
4	477 (19%)	1,696 (19%)	2,173 (19%)
High	356 (14%)	1,265 (14%)	1,621 (14%)
Age-eligible rate of FOBT quintile, No. (%)			
Low	487 (19%)	1,888 (21%)	2,375 (21%)
2	504 (20%)	1,886 (21%)	2,390 (21%)
3	533 (21%)	1,890 (21%)	2,423 (21%)
4	522 (21%)	1,680 (19%)	2,202 (19%)
High	457 (18%)	1,455 (17%)	1,912 (17%)
Age-eligible rate of annual physical exams quintile, No. (%)			
Low	496 (20%)	2,009 (23%)	2,505 (22%)
2	490 (20%)	1,625 (18%)	2,115 (19%)
3	472 (19%)	1,638 (19%)	2,110 (19%)
4	509 (20%)	1,686 (19%)	2,195 (19%)
High	536 (21%)	1,841 (21%)	2,377 (21%)

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Age-eligible rate of influenza vaccine quintile, No. (%)			
Low	548 (22%)	1,997 (23%)	2,545 (23%)
2	549 (22%)	1,765 (20%)	2,314 (20%)
3	435 (17%)	1,930 (22%)	2,365 (21%)
4	485 (19%)	1,770 (20%)	2,255 (20%)
High	486 (19%)	1,337 (15%)	1,823 (16%)

*Co-morbidity scored using number of Aggregated Diagnosis Groups (ADGs) using the Johns Hopkins Case Mix System

FHG = family health group

FHO/FHN = family health organizations or networks

Other PEM = other patient enrolled model of care

FOBT = fecal occult blood test

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Table 2.   Multivariate logistic regression analysis using Generalized Estimating Equations for the characteristics of participants and physicians associated with completing an FOBT within 6 months of the mailing date.

Participants	Odds ratio (95% C.I.)	P-value
Age group, years		
50-59	0.6 (0.5, 0.8)	<.0001
60-69	0.8 (0.7, 1.0)	NS
70-74	Reference	N/A
Sex		
Female	0.9 (0.9, 1.0)	NS
Male	Reference	N/A
Co-morbidity*, No. of ADGs		
0	0.7 (0.6, 0.8)	0.0002
1-2	0.9 (0.7, 1.0)	NS
3-4	1.0 (0.9, 1.2)	NS
5-6	1.0 (0.9, 1.2)	NS
7+	Reference	N/A
Median neighborhood income quintile		
Rural	0.9 (0.7, 1.1)	NS
Low Urban	0.9 (0.7, 1.0)	NS
2	1.0 (0.8, 1.1)	NS
3	1.0 (0.9, 1.1)	NS
4	0.9 (0.8, 1.1)	NS
High Urban	Reference	N/A
Health region		
Erie St.Clair	1.3 (0.9, 1.8)	NS
South West	0.9 (0.6, 1.4)	NS
Waterloo Wellington	0.8 (0.6, 1.2)	NS
Hamilton Niagara	0.9 (0.6, 1.2)	NS
Central West	1.0 (0.7, 1.4)	NS
Mississauga Halton	0.6 (0.3, 1.2)	NS
Toronto Central	0.8 (0.6, 1.2)	NS
Central	0.5 (0.4, 0.7)	0.0004
South East	0.8 (0.54, 1.30.7)	NS
Champlain	1.0 (0.7, 1.4)	NS
North Simcoe-Muskoka	0.9 (0.6, 1.4)	NS
North East	1.1 (0.7, 1.5)	NS
North West	0.7 (0.5, 1.0)	0.03
Central East	Reference	N/A
Recency of immigration		
Remote or non-immigrant	1.0 (0.6, 1.6)	NS
Recent immigrant	Reference	N/A
Prior FOBT Use		
2 to 5 years prior to mailing	2.8 (2.5, 3.3)	<.0001

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> 5 years or never	Reference	
Physician		
Increasing age (per year)	1.0 (1.0, 1.0)	NS
Sex		
Female	1.3 (1.0, 1.5)	0.02
Male	Reference	N/A
Training location		
In Canada	0.9 (0.7, 1.2)	NS
Outside Canada	Reference	N/A
Practice type		
FHG	0.9 (0.7, 1.1)	NS
FHO/FHN	0.8 (0.6, 1.1)	NS
Other PEM	0.7 (0.4, 1.0)	0.05
FHO/FHN-FHT	Reference	N/A
Practice size (enrolled patients)		
≤ 1800 patients	1.1 (0.9, 1.3)	NS
> 1800 patients	Reference	N/A
Age-eligible rate of colonoscopy quintile		
Low	1.1 (0.8, 1.5)	NS
2	1.2 (1.0, 1.6)	NS
3	1.0 (0.8, 1.2)	NS
4	1.0 (0.8, 1.3)	NS
High	Reference	N/A
Age-eligible rate of FOBT quintile		
2	0.9 (0.6, 1.3)	NS
3	0.9 (0.7, 1.2)	NS
4	1.1 (0.8, 1.4)	NS
High	0.9 (0.7, 1.3)	NS
Low	Reference	N/A
Age-eligible rate of annual physical exams quintile		
2	1.4 (0.9, 2.0)	NS
3	1.3 (0.9, 1.8)	NS
4	1.3 (0.9, 1.8)	NS
High	1.1 (0.8, 1.5)	NS
Low	Reference	N/A
Age-eligible rate of influenza vaccine quintile		
2	1.0 (0.8, 1.2)	NS
3	0.8 (0.6, 1.0)	0.02
4	0.9 (0.7, 1.2)	NS
High	1.3 (1.0, 1.7)	NS
Low	Reference	N/A

*Co-morbidity scored using number of Aggregated Diagnosis Groups (ADGs) using the Johns Hopkins Case Mix System

FHG = family health group

FHO/FHN = family health organizations or networks

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Other PEM = other patient enrolled model of care
NS = not significant
N/A - not applicable
FOBT = fecal occult blood test

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Table 3. Characteristics of the 2 cohorts matched by propensity score in Study 2

	Pilot participants (n=10,652)	Control participants (n=10.652)	Standardized Difference*
Participants			
Age group in years, No. (%)			
50-59	6,248 (59%)	6,324 (59%)	0.01
60-69	3,342 (31%)	3,316 (31%)	0.01
70-74	1,062 (10%)	1,012 (10%)	0.02
Sex, No. (%)			
Female	5548 (52%)	5477 (51%)	0.01
Male	5,104 (48%)	5,175 (49%)	0.01
Co-morbidity**, No. of ADGs (%)			
0	1,462 (14%)	1,425 (13%)	0.01
1-2	3,647 (34%)	3,716 (35%)	0.01
3-4	2,764 (26%)	2,835 (27%)	0.02
5-6	1,536 (14%)	1,473 (14%)	0.02
7+	1,243 (12%)	1,203 (11%)	0.01
Median neighborhood income quintile, No. (%)			
Rural	1,825 (17%)	1,889 (18%)	0.02
Low Urban	1,628 (15%)	1,699 (16%)	0.02
2	1,698 (16%)	1,728 (16%)	0.01
3	1,728 (16%)	1,681 (16%)	0.01
4	1,831 (17%)	1,753 (16%)	0.02
High Urban	1,942 (18%)	1,902 (18%)	0.01
Health region, No. (%)			
Erie St.Clair	462 (4%)	423 (4%)	0.02
South West	1,107 (10%)	1,114 (10%)	0
Waterloo Wellington	327 (3%)	343 (3%)	0.01
Hamilton Niagara	1,265 (12%)	1,290 (12%)	0.01
Central West	620 (6%)	580 (5%)	0.02
Mississauga Halton	142 (1%)	144 (1%)	0
Toronto Central	503 (5%)	478 (4%)	0.01
Central	201 (2%)	209 (2%)	0.01
Central East	1,643 (15%)	1,702 (16%)	0.02
South East	859 (8%)	891 (8%)	0.01
Champlain	895 (8%)	904 (8%)	0
North Simcoe-Muskoka	265 (2%)	242 (2%)	0.01
North East	1,409 (13%)	1,378 (13%)	0.01
North West	954 (9%)	954 (9%)	0
Recent immigrant, No. (%)	111 (1%)	105 (1%)	0.01
FOBT 2 to 5 years prior to mailing, No. (%)	1,476 (14%)	1,240 (12%)	0.07
Physician			

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Median age in years (IQR)	52 (45-59)	52 (47-58)	N/A
Sex, No. (%)			
Female	3,875 (36%)	3,335 (31%)	N/A
Male	6,777 (64%)	7,317 (69%)	
Practice type, No. (%)			
FHG	4,854 (46%)	4,885 (46%)	
FHO/FHN	1,859 (17%)	1,718 (16%)	N/A
FHO/FHN-FHT	3,374 (32%)	3,027 (28%)	
Other PEM	565 (5%)	1,022 (10%)	
Practice size (enrolled patients), No. (%)			
>1800 patients	5,366 (50%)	5,026 (47%)	N/A

*Standardized differences for physician level variables not reported as propensity scores were estimated using patient level characteristics only

**Co-morbidity scored using number of Aggregated Diagnosis Groups (ADGs) using the Johns Hopkins Case Mix System

FHG = family health group

FHO/FHN = family health organizations or networks

Other PEM = other patient enrolled model of care

FOBT = fecal occult blood test

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Table 4. Association between mailed invitation and FOBT completion or mailed invitation and FOBT or colonoscopy completion after adjusting for physician factors.

	FOBT completion		FOBT or Colonoscopy completion	
	Odds ratio (95% C.I.)	P-value	Odds ratio (95% C.I.)	P-value
Mailed invitation				
Yes (Pilot)	3.3 (3.1, 3.6)	<.0001	2.7 (2.5, 2.9)	<.0001
No (Controls)	Reference	N/A	Reference	N/A
Increasing age (per year)	1.0 (1.0, 1.0)	NS	1.0 (1.0, 1.0)	0.03
Sex, No. (%)				
Female	1.0 (0.9, 1.1)	NS	1.0 (0.9, 1.1)	NS
Male	Reference	N/A	Reference	N/A
Practice type, No. (%)				
FHG	0.7 (0.6, 0.8)	<.0001	0.7 (0.7, 0.8)	<.0001
FHO/FHN	0.8 (0.7, 0.9)	<.0001	0.8 (0.7, 0.9)	<.0001
Other PEM	0.8 (0.7, 1.0)	0.03	0.8 (0.7, 1.0)	NS
FHO/FHN-FHT	Reference	N/A	Reference	N/A
Practice size (enrolled patients)				
≤ 1800 patients	1.2 (1.1, 1.3)	0.0004	1.2 (1.1, 1.3)	<.0001
> 1800 patients	Reference	N/A	Reference	N/A

FHG = family health group

FHO/FHN = family health organizations or networks

Other PEM = other patient enrolled model of care

FOBT = fecal occult blood test

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Figure Legends

Figure 1. Mock-up of physician-linked invitation used in the Pilot.

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ColonCancerCheck | ContrôleCancerColorectal   cancer care | action cancer
                                                                ontario | ontario

From the office of Dr. George Black

                                                                June 1, 2009

Lawren Harris
456 Superior Street
Lindsay ON K2L 3M4

Dear Lawren Harris:

You have received this letter because it is time to be screened for colon cancer. Our records as of April 1st, 2009 show that you have never had a fecal occult blood test (FOBT) or we do not know when you had your last FOBT. All adults between the ages of 50 and 74 years who are at average risk for colon cancer should do a FOBT every two years.

If your parent, brother, sister or child has had colon cancer, your risk is higher and you should have a colonoscopy.

Please call my office to set up an appointment to talk about your risk for colon cancer and which test is right for you.

If you have recently completed colon cancer screening, please disregard this letter.

I look forward to hearing from you soon.

Dr. George Black
705-555-1212

GET THE FACTS. GET CHECKED.

- Colon cancer is the second most common cause of cancer death in Ontario
- Colon cancer can develop without any early warning signs.
- If it is caught early enough, 9 out of every 10 people can be cured.
- Regular screening is the best way to catch colon cancer early.
- The FOBT is a simple test that can be done at home.

For more information please visit www.coloncancercheck.ca

This letter has been sent on my behalf by ColonCancerCheck (CCC), Ontario's colorectal cancer screening program. CCC is a collaborative initiative of the Ministry of Health and Long-Term Care and Cancer Care Ontario. If for any reason you do not wish to receive future correspondence from the program, simply call the ColonCancerCheck Information Line at 1-866-662-9233 during business hours.

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Tinmouth et al., Physician-linked mailed invitation to be screened improves uptake in an organized colorectal cancer screening program.

	Item No	Recommendation	Page	Comment
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1, 3	
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	3	
Introduction				
Background/ratio nale	2	Explain the scientific background and rationale for the investigation being reported	07-Jun	
Objectives	3	State specific objectives, including any prespecified hypotheses	7, first paragraph	
Methods				
Study design	4	Present key elements of study design early in the paper	7, paragraph 2	
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	7, paragraph 2	
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	9, paragraph 2, 10, paragraph 2 & 12, first paragraph	
		Case-control study—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls	n/a	
		Cross-sectional study—Give the eligibility criteria, and the sources and methods of selection of participants	n/a	
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed	12, first paragraph	
		Case-control study—For matched studies, give matching criteria and the number of controls per case	n/a	
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	9, 10 & 11	
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	8, 9, 10 & 11	
Bias	9	Describe any efforts to address potential sources of bias	11, paragraph 2 & 13, paragraph	
Study size	10	Explain how the study size was arrived at	5, paragraph 1	
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why		
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	11, paragraph 2 & 13, paragraph	
		(*b*) Describe any methods used to examine subgroups and interactions	n/a	
		(*c*) Explain how missing data were addressed	14, first paragraph	
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed	n/a	all patients followed through administrative data, therefore no loss to f/u
		Case-control study—If applicable, explain how matching of cases and controls was addressed	n/a	
		Cross-sectional study—If applicable, describe analytical methods taking account of sampling strategy	n/a	
		(*e*) Describe any sensitivity analyses	n/a	
Results				
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	14, first & last paragraphs	
		(b) Give reasons for non-participation at each stage	14, first & last paragraphs	

		(c) Consider use of a flow diagram	n/a
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	Table 1 & Table 3
		(b) Indicate number of participants with missing data for each variable of interest	15, first paragraph
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)	all followed up for 6 months
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time	15, 2nd paragraph & 16, 1st paragraph
		Case-control study—Report numbers in each exposure category, or summary measures of exposure	n/a
		Cross-sectional study—Report numbers of outcome events or summary measures	n/a
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	15, 2nd paragraph, Tables 2 & 4
		(*b*) Report category boundaries when continuous variables were categorized	Tables 2 & 4
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	n/a
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	n/a
Discussion			
Key results	18	Summarise key results with reference to study objectives	16, paragraph 1
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	18, 2nd paragraph
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	17 & 18
Generalisability	21	Discuss the generalisability (external validity) of the study results	18, last paragraph
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	19, 20