Ontario’s ColonCancerCheck: Results from Canada’s First Province-Wide Colorectal Cancer Screening Program

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Abstract

Background: ColonCancerCheck (CCC), Canada’s first province-wide colorectal cancer screening program, was publicly launched in Ontario in April 2008. The objective of this article is to report on key indicators of CCC Program performance since its inception.

Methods: The CCC Program recommends biennial guaiac-based fecal occult blood test (gFOBT) for persons 50 to 74 years of age at average risk for colorectal cancer and colonoscopy for those at increased risk (having one or more first-degree relatives with a diagnosis of colorectal cancer). Opportunistic screening with colonoscopy is available in Ontario. Five data sources were used to compute indicators of program performance during 2008 to 2011. The indicators computed were FOBT participation, overdue for screening, FOBT positivity, positive predictive value (PPV) of FOBT for colorectal cancer, diagnostic follow-up, and colorectal cancer detection rate.

Results: In 2011, FOBT participation was 29.8% and 46.8% of the target population was overdue for screening. FOBT positivity was higher among men (5.1%) than women (3.5%), and the PPV of FOBT for cancer was 4.3% in 2011. Follow-up colonoscopy within 6 months of a positive FOBT was completed by 74.6% of Program participants in 2011. The cancer detection rates for FOBT and for colonoscopy in those with a family history were 1.3 per 1,000 and 4.0 per 1,000, respectively, in 2011.

Conclusion: These results provide an early indication of Program performance and provide findings relevant to other organized colorectal cancer screening programs.

Impact: The greater cancer detection rate in those at increased risk due to family history who undergo colonoscopy screening suggests that a strategy of risk stratification will enhance the impact of FOBT-based screening programs.

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Introduction

The incidence of colorectal cancer in Canada is among the highest in the world (1). Colorectal cancer is the second leading cause of cancer deaths and the third most commonly diagnosed cancer in the country (2, 3). Results from four randomized controlled trials (RCT) have shown that screening for colorectal cancer using guaiac-based fecal occult blood test (gFOBT) and follow-up colonoscopy in those with a positive test can reduce colorectal cancer mortality by at least 16% (4, 5). In 2001, the Canadian Task Force on Preventive Health Care recommended annual or biennial FOBT for average risk individuals as the initial screening test for colorectal cancer (6). In 2002, Health Canada’s National Committee on Colorectal Cancer Screening also endorsed these recommendations, stating that “screening be offered to a target population of adults aged 50 to 74 years of age, using unrehydrated Hemoccult II or equivalent” and that “individuals be screened at least every two years” (7). Since then, organized colorectal cancer screening programs with fecal testing have been introduced in most Canadian provinces, as a pilot, via a phased implementation or full province-wide implementation from the outset (8).

In January 2007, the Ministry of Health and Long-Term Care (MOHLTC) announced funding for a provincial colorectal cancer screening program in Ontario. In April 2008, Cancer Care Ontario (CCO) and the MOHLTC launched ColonCancerCheck (CCC), Canada’s first province-wide colorectal cancer screening program. The goals of the CCC Program are to reduce colorectal cancer mortality and to support primary care providers (PCP) to deliver colorectal cancer screening. The CCC Program has a dual strategy and recommends biennial gFOBT for persons 50 to 74 years of age at average risk for colorectal cancer and colonoscopy for those at increased risk (having...
one or more first-degree relative with a diagnosis of colorectal cancer).

Ontario is the largest province in Canada, with a population of 13.5 million (9). Briefly, healthcare in the province is publicly funded and all permanent residents and refugees are entitled to coverage under the Ontario Health Insurance Plan (OHIP). Primary care is central to care in the province as the PCP is the main point of entry for patients into the healthcare system. Under OHIP, a referral from a PCP is required to receive coverage of specialty services. The choice of PCP ultimately rests with the patient.

The Program was launched province-wide from the outset, with several components (e.g., invitation to screen) introduced in a phased implementation. Before and after launch of the Program, screening colonoscopy is available as the initial test in persons at average risk for colorectal cancer in opportunistic screening. During several years of planning leading up to the funding announcement and launch of the Program, the evidence base to support the use of the fecal immunochemical test (FIT) was increasing, but FIT was not then endorsed by screening guidelines (6). This explains the decision to implement gFOBT.

The objective of this article is to report on key indicators of CCC Program performance since its inception in 2008.

Materials and Methods

Data sources

The five data sources used were the Registered Persons Database (RPDB), the OHIP Claims History Database (CHDB), the Ontario Cancer Registry (OCR), the Laboratory Reporting Tool (LRT), and the Colonoscopy Interim Reporting Tool (CIRT).

The RPDB, OHIP CHDB, and the OCR have been previously described (10, 11). Briefly, the RPDB provides demographic information, including age, sex, and location of residence for those with a valid health card in Ontario. All Canadian citizens, permanent residents, and refugees are eligible for coverage by the OHIP under the publicly funded healthcare system. The RPDB contains more than 12 million records and is updated regularly. Illegal migrants are the only group excluded from the RPDB.

The OHIP CHDB provides information on all FOBT, flexible sigmoidoscopy, and colonoscopy services provided in the province. Because every resident is covered by OHIP, the data are representative of health services use in Ontario. Ontario physicians are paid on a fee-for-service basis and submit claims to OHIP. The private sector is limited to cosmetic surgery, some MRI and positron emission tomography scans without clinical indication.

The OCR registers all new diagnosed cases of cancer in Ontario residents since 1964 and receives over 95% of pathology reports relating to cancer in Ontario (10).

The LRT includes information on CCC Program FOBT kit results. The CIRT provides information on all colonoscopies performed at collaborating hospitals, including date of procedure, indication for the colonoscopy, and gross findings. Approximately 70 collaborating hospitals (varying in size and capacity) are provided funding to perform additional colonoscopies for the Program. Approximately 65% of colonoscopies in Ontario are performed at the collaborating hospitals.

Program design

FOBT kits (Hemascreen; Immunostics Inc.) are distributed by PCPs. The Program advises that Vitamin C, and citrus fruits and juices be discontinued three days before and during stool collection (12). Three stool cards with two samples each are collected from three consecutive spontaneously passed stools. For those with a positive FOBT, defined as one or more positive samples out of six, colonoscopy is recommended. In persons with an increased risk of colorectal cancer, the Program recommends colonoscopy, beginning at age of 50 years, or 10 years earlier than the age at which the relative was diagnosed, whichever occurs first.

Target population identification

At launch, the CCC Program relied on PCPs to identify eligible patients in their practices, and to recommend screening, either with FOBT or colonoscopy, depending on the patient’s risk. Screen-eligible individuals include asymptomatic Ontarians ages 50 to 74 years of age. The Program also relied on a public awareness campaign for individuals to self-identify as eligible and to visit their PCPs to discuss screening. The small proportion (<5%) of individuals without a PCP could obtain an FOBT kit from a pharmacist or call a 1-800-number (INFOline) to have a kit mailed to him/her. Individuals without a PCP are queried about large bowel symptoms and family history to determine risk status. This is done by the pharmacist or trained INFOline staff. If individuals have symptoms (e.g., unexplained weight loss, unexplained change in bowel habits, rectal bleeding, persistent urge to evacuate the rectum or unexplained stool incontinence), they are referred for diagnostic work-up. If an individual has no symptoms of colorectal cancer and has one or more first-degree relatives with colorectal cancer, she or he is referred to the CCC Program in which she or he is assigned a PCP who has been identified as willing to accept new patients. Finally, individuals are considered average risk if they have no symptoms or signs of colorectal cancer and no affected first-degree family member.

Invitations to screen

Beginning in late 2010, mailed invitation letters were launched as part of a planned phased implementation of correspondence. These were sent to those newly eligible turning 50 years of age, advising them to contact their PCPs to discuss colorectal cancer screening. The Program does not send invitations to individuals who have had a FOBT in the prior 2 years, a flexible sigmoidoscopy in the prior 5 years, or a colonoscopy in the prior 10 years. Also beginning in 2010, mailed recall letters were launched;
these are sent to those who had a negative FOBT and are due for repeat screening.

**Screening**

PCPs conduct risk assessments, discuss the importance of screening, and arrange colorectal cancer screening. For those at average risk, the PCPs dispense gFOBT kits that contain instructions, stool cards, privacy information, and a postage-paid mail back envelope. For those at increased risk, the PCPs make referrals for colonoscopy. If an individual without a PCP is at increased risk for colorectal cancer, she or he is assigned a PCP who has been identified as willing to accept new patients specifically for the Program.

**Healthcare provider and public awareness campaign**

A PCP awareness campaign was developed in partnership with the Ontario College of Family Physicians and begun in September 2007, preceding the Program launch in April 2008. The campaign included information kits, patient counseling materials, journal articles, regional forums, a dedicated website, and continuing education events.

A multifaceted public campaign was launched in March 2008 (which is colorectal cancer Awareness Month) to educate the public and increase awareness about colorectal cancer screening. The campaign consisted of innovative television advertisements broadcast in many languages. Other aspects of the public campaign included a new website, an INFOline, print advertisements, posters, information pamphlets, and street teams that distributed program literature and information.

**FOBT processing and results notification**

Seven community laboratories process CCC Program FOBT kits and follow requirements outlined in CCO’s gFOBT Laboratory Standards (12). All results are reported to the respective PCPs and to the Program. The Program notifies participants by mail of their FOBT results. Participants without a PCP who have a positive FOBT are referred by the Program to a PCP who is responsible for arranging colonoscopy. All participants with an inadequate test result (FOBT card could not be read or an inconclusive result) are advised to obtain another kit.

**Colonoscopy**

The CCC Program arranged for additional colonoscopies (for those with a positive FOBT and those at increased risk for colorectal cancer) at approximately 70 collaborating hospitals across Ontario, before the Program launch. These collaborating hospitals, through contracts with CCO, are provided incremental funding for the additional colonoscopies. These hospitals are guided by CCO’s Colonoscopy Standards (13) and report detailed information on all colonoscopies performed monthly using the CIRT. Persons who are FOBT positive or who have a family history of colorectal cancer are not restricted to undergo their colonoscopies at collaborating hospitals. For colonoscopies that occur outside a collaborating hospital, detailed information is not captured in CIRT, but the date of the procedure is recorded in OHIP.

**Performance indicators**

The Canadian Partnership Against Cancer has outlined a quality determinants framework for colorectal cancer screening programs (14). The Program has adapted this framework to report on program indicators for participation, screening, diagnostic follow-up, and outcomes.

**Participation**

FOBT participation is the percentage of screen-eligible Ontario men and women in the 50- to 74-age group who have completed an FOBT in a 2-year period. Overdue for screening is the percentage of Ontario men and women of screen-eligible age who have not had an FOBT in the prior 2 years, or a flexible sigmoidoscopy or colonoscopy in the prior 5 years. These indicators are computed using the OHIP CHDB, which records all services in Ontario and includes those screened with a non-Program FOBT kit and all large bowel endoscopy.

**Screening**

FOBT positivity is the percentage of individuals ages 50 to 74 years who completed a CCC Program FOBT and had a positive test result during the calendar year. A positive sample of one out of six flaps is considered positive. PPV of FOBT for cancer is the percentage of persons who completed a CCC Program FOBT who had a positive result and subsequently underwent large bowel endoscopy (flexible sigmoidoscopy or colonoscopy) or surgery within the subsequent 183 days and who were diagnosed with colorectal cancer. The LRT database provides detailed information, including test result for all individuals who completed a CCC Program FOBT, and OHIP is used to capture all subsequent large bowel endoscopy procedures.

**Diagnostic follow-up**

Diagnostic follow-up is the percentage of individuals with a positive CCC Program FOBT who had a follow-up colonoscopy within 6 months. Participants are not restricted to undergo their colonoscopies at collaborating hospitals. Detailed information on colonoscopies performed outside a collaborating hospital is not captured in CIRT, but the date of the procedure is recorded in OHIP, so the ascertainment of colonoscopies performed is complete.

**Outcomes**

The Program computes cancer detection rates for the two risk groups. For those at average risk, the cancer detection rate is the number of cancers detected per 1,000 persons ages 50 to 74 years who were screened with a CCC Program FOBT kit. For those at increased risk, it is the number of cancers detected per 1,000 persons ages 20 to 74 years who were screened with colonoscopy because of a family history of the disease, as recorded in CIRT.
Data analysis
A descriptive analysis of computed indicators was done for each calendar year from Program launch in 2008 to 2011. FOBT participation was computed for each 2-year period. Individuals were counted only once regardless of the number of tests or procedures (FOBT, colonoscopy, flexible sigmoidoscopy) received in each calendar year or time period (2-year period for FOBT participation). If multiple FOBT results were available, the date of the first result was selected. Where applicable, 95% confidence intervals (95% CI) are provided in the text, tables, and figures.

Results
Participation
In 2010, the Ontario target population ages 50 to 74 years of age was 3,491,067. In 2010 to 2011, 2,612,382 persons in the target population were eligible for screening and 29.8% (95% CI, 29.7%–29.9%) of these persons completed an FOBT in the 2-year period. This is almost double the 2004 and 2005 FOBT participation (Fig. 1). Figure 2 shows the percentage of the target population who were overdue for screening from 2008 to 2011 by age group. Since Program launch, the percent overdue for screening has decreased from 51.9% (95% CI, 51.9%–52.0%) to 46.8% (46.6%–46.8%) of the 3,384,138 eligible persons in 2011. Those in the younger age groups were less likely to get screened.

Screening
In 2011, FOBT positivity was 5.1% for men and 3.5% for women, showing very little change from the results observed in 2008 for men (5.3%) and women (3.5%). Overall, FOBT positivity did not vary widely across age groups (data not shown). The PPV of FOBT for cancer was 4.3% (95% CI, 4.0%–4.6%) in 2011. Those in the oldest age group had the highest PPV for cancer (Table 1).

Diagnostic follow-up
In 2008, only 62.6% (95% CI, 60.9%–64.2%) of 8,799 individuals who had a positive FOBT had a follow-up colonoscopy within 6 months compared with 74.6% (95% CI, 73.4%–75.8%) of the 20,740 persons with a positive FOBT in 2011. This increasing trend holds true for each year and age group (data not shown).

Outcomes
Tables 2 and 3 show the colorectal cancer detection rates for average risk and increased risk individuals in 2011. For every 1,000 persons ages 50 to 74 years screened with FOBT, the cancer detection rate was 1.3 (95% CI, 1.2–1.4). For every 1,000 persons ages 20 to 74 years at increased risk for colorectal cancer who were screened with colonoscopy, the cancer detection rate was 4.0 (95% CI, 3.3–4.7). Cancer detection rates increased with age in both risk groups.

Discussion
We report here the early performance results from Ontario’s province-wide colorectal cancer screening program, launched in 2008. FOBT participation was 29.8% (2010–2011) and 46.8% of the target population was overdue for screening in 2011. FOBT positivity was higher among men (5.1%) and the PPV of FOBT for cancer was 4.3% in 2011. Follow-up colonoscopy within 6 months of a positive FOBT was completed by 74.6% of participants in 2011. In 2011, the cancer detection rates for FOBT and for colonoscopy in those with a family history were 1.3 per 1,000 and 4.0 per 1,000, respectively.

How do these results compare with other organized colorectal cancer screening programs? Few programs...
have published early results. Results from the phased implementation of the Bowel Cancer Screening Programme (BCSP) launched in 2006 in England showed FOBT participation of 52% in 2008 after the first 1.08 million tests (15), whereas Finland’s phased implementation with individual level randomization to screening versus control based on age and municipality reported FOBT participation of 70.8% in 2004 to 2006 with a population of 52,998 in the screening arm (16). In 2008 and 2009, France’s national screening program reported FOBT participation of 34.3% in a target population of over 9.7 million people in 46 out of 99 districts (17). Our results for FOBT participation are somewhat lower in comparison. However, there are two important differences between the results from these three European programs and the Ontario Program. First, in the BCSP and the Finnish program, kits are mailed to all potential participants, removing the need for a PCP visit. Second, these three programs were launched in the context of very limited or virtually no prior or ongoing opportunistic colorectal cancer screening, whereas in Ontario, opportunistic screening colonoscopy is available as an initial screening test in persons at average risk. Previous work in Ontario demonstrates an increase in colonoscopy use during 1996 to 2001, well before CCC Program launch (18). Moss and colleagues state that “in a setting where opportunistic screening (for example colonoscopy) has been taking place for some time, the uptake and performance of an organized programme may differ markedly from those in a setting where no such screening has been taking place” (19). However, in Ontario, when use of flexible sigmoidoscopy and colonoscopy for all indications (i.e., screening or other) is considered, 46.8% of the target population was overdue for screening in 2011. This may be a more

### Table 1. PPV of FOBT for cancer, by age group, Ontario, 2011

<table>
<thead>
<tr>
<th>Age group (y)</th>
<th>Number of cancers diagnosed&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Number of persons with a positive FOBT&lt;sup&gt;b&lt;/sup&gt;</th>
<th>PPV (%); 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>50–74</td>
<td>671</td>
<td>15,556</td>
<td>4.3 (4.0–4.6)</td>
</tr>
<tr>
<td>50–54</td>
<td>84</td>
<td>4,109</td>
<td>2.0 (1.6–2.5)</td>
</tr>
<tr>
<td>55–59</td>
<td>113</td>
<td>3,220</td>
<td>3.5 (2.9–4.2)</td>
</tr>
<tr>
<td>60–64</td>
<td>135</td>
<td>3,214</td>
<td>4.2 (3.5–5.0)</td>
</tr>
<tr>
<td>65–69</td>
<td>171</td>
<td>2,756</td>
<td>6.2 (5.3–7.2)</td>
</tr>
<tr>
<td>70–74</td>
<td>168</td>
<td>2,257</td>
<td>7.4 (6.4–8.6)</td>
</tr>
</tbody>
</table>

<sup>a</sup>Number of persons who completed a CCC Program FOBT kit who had a positive FOBT who subsequently underwent large bowel endoscopy or surgery within the subsequent 183 days and who were diagnosed with colorectal cancer.

<sup>b</sup>Number of persons who completed a CCC Program FOBT kit who had a positive FOBT who subsequently underwent large bowel endoscopy or surgery within the subsequent 183 days.
appropriate measure of the extent of screening, as it describes the unmet need in Ontario.

FOBT positivity reported here was higher (4.2%) than the results from the BCSP (2.0%; ref. 15) or France’s national screening program (2.8%; ref. 17). However, the BCSP uses more stringent criteria for defining FOBT positivity (five or more positive windows out of six, or one or more positive windows out of six on the second FOBT after a result of one to four positive windows on the first FOBT). In addition, because of the CCC Program’s dual screening strategy, those at increased risk are recommended to undergo colonoscopy and are removed from the Ontario target population for FOBT, which is therefore at lower risk than the BCSP target population. On the other hand, Ontario results are comparable with pooled data from organized screening programs identified by the International Colorectal Cancer Screening Network (ICCSN) in 2008, which reported gFOBT positivity of 4.6% for first screens and 3.7% for subsequent screens (20). FOBT positivity reported here was higher in men (5.1%) than women (3.5%), consistent with results from other programs (15–17) and reflecting the epidemiology of colorectal cancer (19).

The PPV of FOBT for colorectal cancer in the BCSP program was higher at 10.1% than that observed in the CCC Program (4.3%; ref. 15). This difference may again be a result of the more stringent criteria used to determine FOBT positivity in the BCSP and the lower risk target population for FOBT screening in the CCC Program.

An area of concern is the low (74.6%) follow-up colonoscopy use reported here for participants with a positive FOBT. The BCSP reported colonoscopy compliance of 83% in 2008 (15). An important aspect of the BCSP is that participants with a positive FOBT are provided a pre-booked appointment date for colonoscopy when they are notified of their result by mail. On the other hand, in France, where participants with a positive FOBT are referred for colonoscopy through their PCPs, follow-up colonoscopy compliance was 88% in 2008 and 2009 (17). Clearly, further efforts are needed to improve follow-up colonoscopy in those with a positive FOBT in the CCC Program.

The cancer detection rate for those screened with FOBT in the CCC Program was comparable with the French program (1.3 and 1.9 per 1,000 screened, respectively; ref. 17). The European guidelines for quality assurance in colorectal cancer screening report an expected cancer detection rate for first screens in FOBT population-based programs of 1.2 to 2.3 per 1,000 screened (19). Our results are within this range.

The results reported here must be considered in light of the study limitations. For colonoscopies that occur outside

Table 2. CCC Program average risk participants screened with FOBT, who were diagnosed with colorectal cancer, by age group, Ontario, 2011

<table>
<thead>
<tr>
<th>Age group (y)</th>
<th>Number of cancers diagnosed</th>
<th>Number screened</th>
<th>Cancer detection rate (per 1,000; 95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>50–74</td>
<td>657</td>
<td>510,630</td>
<td>1.3 (1.2–1.4)</td>
</tr>
<tr>
<td>50–54</td>
<td>81</td>
<td>125,655</td>
<td>0.6 (0.5–0.8)</td>
</tr>
<tr>
<td>55–59</td>
<td>113</td>
<td>111,618</td>
<td>1.0 (0.8–1.2)</td>
</tr>
<tr>
<td>60–64</td>
<td>132</td>
<td>110,749</td>
<td>1.2 (1.0–1.4)</td>
</tr>
<tr>
<td>65–69</td>
<td>168</td>
<td>91,842</td>
<td>1.8 (1.6–2.1)</td>
</tr>
<tr>
<td>70–74</td>
<td>163</td>
<td>70,766</td>
<td>2.3 (2.0–2.7)</td>
</tr>
</tbody>
</table>

*Number of persons who completed a CCC Program FOBT kit (regardless of FOBT test result) and were diagnosed with colorectal cancer.

Table 3. The CCC Program increased risk participants screened with colonoscopy at a collaborating hospital, who were diagnosed with colorectal cancer, by age group, Ontario, 2011

<table>
<thead>
<tr>
<th>Age group (y)</th>
<th>Number of cancers diagnosed</th>
<th>Number screened</th>
<th>Cancer detection rate (per 1,000; 95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–74</td>
<td>132</td>
<td>33,157</td>
<td>4.0 (3.3–4.7)</td>
</tr>
<tr>
<td>20–49</td>
<td>14</td>
<td>8,309</td>
<td>1.7 (0.9–2.8)</td>
</tr>
<tr>
<td>50–54</td>
<td>17</td>
<td>6,919</td>
<td>2.5 (1.4–3.8)</td>
</tr>
<tr>
<td>55–59</td>
<td>20</td>
<td>6,057</td>
<td>3.3 (2.0–5.0)</td>
</tr>
<tr>
<td>60–64</td>
<td>24</td>
<td>5,317</td>
<td>4.5 (2.9–6.6)</td>
</tr>
<tr>
<td>65–69</td>
<td>28</td>
<td>3,969</td>
<td>7.1 (4.7–10.0)</td>
</tr>
<tr>
<td>70–74</td>
<td>29</td>
<td>2,586</td>
<td>11.2 (7.5–15.9)</td>
</tr>
</tbody>
</table>
a collaborating hospital, detailed information is not captured in CIRT. On the other hand, we are able to identify the occurrence of these procedures as they are recorded in OHIP.

Taken together, our results suggest several important lessons relevant to other jurisdictions as they implement organized colorectal cancer screening programs. First, a PCP-driven FOBT-based program may have limited uptake, particularly in areas where opportunistic screening colonoscopy is available. Alternate approaches, including sending invitation letters to those who are overdue for screening and mailing test kits may be considered. Second, a prebooked appointment for those with a positive FOBT may increase attendance for follow-up colonoscopy. Third, a dual strategy, recommending colonoscopy for those at increased risk of colorectal cancer may enhance the impact of FOBT screening programs.

Ontario, with a target population of over 3.4 million, was the first province in Canada to introduce an organized colorectal cancer screening program that was implemented province-wide from the outset. The results reported here provide an early indication of Program performance. The 3-fold increase in cancer detection rate for those at increased risk who undergo colonoscopy compared with those who undergo FOBT screening is encouraging, as it should enhance the impact of the program on colorectal cancer mortality. Two areas that need attention are FOBT participation and follow-up colonoscopy in those with a positive FOBT. Changes in program design and/or interventions to address performance gaps are needed to maximize the quality and effectiveness of colorectal cancer screening in Ontario.

Disclosure of Potential Conflicts of Interest
No potential conflicts of interest were disclosed.

Authors’ Contributions
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Writing, review, and/or revision of the manuscript: L. Rabeneck, J.M. Tinmouth, L.F. Paszat, N.N. Baxter, L.D. Marrett, A. Ruco, N. Lewis, J. Gao
Administrative, technical, or material support (i.e., reporting and organizing data, constructing databases): L. Rabeneck, A. Ruco, J. Gao
Study supervision: L. Rabeneck

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