Risks associated with colonoscopy in a population-based colon screening program: an observational cohort study

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Abstract

Background: The risks associated with colonoscopy performed through the British Columbia Colon Screening Program (BCCSP) are not known. We aimed to determine the rate of colonoscopy-related serious adverse events within this program.

Methods: For this prospective observational study, we used the BCCSP database to identify participants 50 to 74 years of age who had a positive result on fecal immunochemical testing (FIT) between Nov. 15, 2013, and Dec. 31, 2017, followed by colonoscopy. Unplanned medical events were recorded at the time of colonoscopy and 14 days later. We reviewed the unplanned events and defined them as serious adverse events if they resulted in death, hospital admission or intervention; we also classified them as probably, possibly or unlikely related to the colonoscopy. The primary outcome was the overall rate of serious adverse events; the secondary outcomes were 14-day post-colonoscopy rates of perforation, bleeding and death.

Results: During the study period, a total of 96 192 colonoscopies were performed by 308 physicians at 50 sites. The median age of patients was 62 (10th–90th percentile 52–71) years, and 56% were male. Of these, 78 831 patients were contacted after the colonoscopy. Serious adverse events were deemed to have occurred in 350 colonoscopies (44 per 10 000, 95% confidence interval [CI] 39–50 per 10 000), with a number needed to harm of 225. Of the 332 (94.9%) serious adverse events that were probably or possibly related to colonoscopy, perforation occurred in 6 (95% CI 5–8) per 10 000 colonoscopies, bleeding in 26 (95% CI 22–30) per 10 000 colonoscopies and death in 3 (95% CI 1–10) per 100 000 colonoscopies.

Interpretation: The rate of serious adverse events associated with colonoscopy in the BCCSP was in keeping with previous publications and met accepted benchmarks. The findings of this study inform stakeholders of the risks associated with colonoscopy in an FIT-based colon screening program.

Background: The Canadian Task Force on Preventive Health Care has recommended colorectal cancer screening for individuals 50 to 74 years of age with either a fecal occult blood test every 2 years or flexible sigmoidoscopy every 10 years. All Canadian provinces and 1 territory have commenced or intend to commence provincial colon screening programs using fecal occult blood testing. Apart from Manitoba, all are using a fecal immunochemical test (FIT) as the primary screening test, with follow-up colonoscopy for those with abnormal results.

There are risks associated with undergoing colonoscopy, primarily bleeding after removal of a precancerous polyp and perforation, but there is also a risk of death after colonoscopy. A recent systematic review and meta-analysis of 21 studies, which included 3 Canadian studies, reported the risks of perforation and bleeding as about 6 per 10 000 colonoscopies and 24 per 10 000 colonoscopies, respectively, and the risk of colonoscopy-related death as 3 per 100 000 procedures. Monitoring and reviewing post-colonoscopy adverse events has become standard of care to identify performance gaps and continuously improve the safety of colonoscopy.

Programs that use colonoscopy screening following FIT involve an enriched patient population with a high prevalence of precancerous polyps. The risks associated with colonoscopy in this population are not well understood and may differ.

Competing interests: The following authors are currently (or were, at the time of the study) employed with the British Columbia Cancer Screening Programs: Laura Gentile as operations director, Jeremy Hamm as a biostatistician, Nazanin Azari-Razm as a former data coordinator, Dmitriy Bykov as data and analytics manager and Jennifer Telford as medical director. No other competing interests were declared.

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from the published risks that have been the basis for the widely accepted expert consensus benchmarks: less than 1 perforation per 500 colonoscopies performed for any indication, less than 1 perforation per 1000 screening colonoscopies and less than 1 episode of bleeding per 100 colonoscopies.8

The British Columbia Colon Screening Program (BCCSP) is a population-based program enrolling 50- to 74-year-old average-risk adults for biennial FIT. The rate of serious adverse events is an important quality metric of the program and, once established, will improve the informed consent discussion with screening participants who undergo colonoscopy. Our objective was to determine the overall rate of serious adverse events related to colonoscopy, as well as the specific rates of death, perforation and bleeding after colonoscopy.

Methods

Study design

This prospective observational cohort study included all patients who had an abnormal FIT result in the BCCSP from Nov. 15, 2013, to Dec. 31, 2017, and subsequently underwent colonoscopy. We identified individuals who had a serious adverse event related to their colonoscopy. In preparing this article, we followed the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) reporting guidelines.10

Setting and participants

The BCCSP is a provincial colorectal cancer screening program that was available throughout the province of British Columbia until 2015, at which time the Northern Health Authority, one of the 5 geographic regions in the province, ceased participating. The Northern Health Authority extends from the city of Quesnel to the northern border of the province and is home to 5.5% of the age-eligible population. The program continues to operate in the other 4 regions of the province.

Primary care providers in BC perform initial risk stratification of potential screening participants. High-risk patients, defined as those having either a first-degree relative with a diagnosis of colorectal cancer before age 60 years, 2 or more first-degree relatives with a diagnosis of colorectal cancer at any age, or a personal history of precancerous polyps, undergo primary colonoscopy within the program and were not included in this analysis. Patients 50 to 74 years of age are otherwise classified as having average risk and undergo biennial FIT (NS-Plus test kits, Alfresa Pharma Corporation, Japan), with a test cut-off (defining a positive result) of at least 50 ng hemoglobin per millilitre of feces. Exclusion criteria are patient refusal to undergo colonoscopy, a personal history of colorectal cancer, a personal history of ulcerative colitis or Crohn disease, and medical comorbidities contraindicating colonoscopy.

Colonoscopy is performed by a local physician in the patient’s community. Physicians performing BCCSP colonoscopies are general surgeons; gastroenterologists; and internists, general practitioners and family physicians with additional training in colonoscopy. Trainees do not perform program colonoscopies.

Data sources

BC Cancer is responsible for BCCSP operations and maintains the electronic platform housing the BCCSP data. Data are prospectively collected from various sources and entered into the BCCSP platform by a trained registry clerk (Figure 1). Participants are registered in the BCCSP when they obtain their FIT kit from their local laboratory, and the following data are recorded (then or subsequently): name, address, date of birth, gender, ordering physician, date FIT kit was distributed, date FIT kit was returned and FIT value. If the FIT result is abnormal, the BCCSP refers the participant to their local health authority for assessment for colonoscopy.

At the time of colonoscopy, the physician performing the procedure completes a standardized colonoscopy report form (Appendix 1, available at www.cmajopen.ca/content/9/4/ E940/suppl/DC1) for submission to BCCSP; this form includes colonoscopy quality indicators such as bowel preparation quality and completeness of the procedure, as well as details on each polyp removed, including location within the colon, size (with large polyps defined as those with diameter ≥ 10 mm11) and method of removal. The form also documents any unplanned events that occurred during the colonoscopy and whether the patient required admission to hospital. The BCCSP receives copies of the pathology reports.

Trained health authority registered nurses, known as patient coordinators, contact patients 14 days after the colonoscopy to determine whether an unplanned medical event occurred the day before (i.e., during bowel preparation) or in the 14 days after the colonoscopy.9 Unplanned events are defined as those leading to additional medical care. A standardized follow-up form is completed by the patient coordinator and submitted to BCCSP indicating whether the patient was contacted and whether any unplanned event occurred. If so, then an unplanned event form is completed (Appendix 2, available at www.cmajopen.ca/content/9/4/ E940/suppl/DC1), with further description of the event and any interventions that were performed; this form is submitted to BCCSP. Any unplanned event recorded on the colonoscopy report form or on an unplanned event form is extracted for review by the BCCSP Quality Management Committee (Appendix 3, available at www.cmajopen.ca/content/9/4/ E940/suppl/DC1).

Review of unplanned events

An unplanned event met the criteria for review if the event was a perforation or a cardiovascular or respiratory event, or if it resulted in death, hospital admission or important intervention, such as repeat colonoscopy; interventional radiology, surgery, blood transfusion or cardioversion.

The colonoscopy lead for each health authority conducted the detailed review of the electronic chart to confirm and supplement the review completed by the nurse. The colonoscopy lead presented the case to the other colonoscopy leads and the
operations director (L.G.) and medical director (J.T.) of the BCCSP. Decisions were made by consensus, and any disagreements were resolved through discussion.

We defined unplanned events as serious adverse events if they resulted in death, hospital admission or important intervention, and we subclassified them (by consensus) as probably, possibly or unlikely related to the colonoscopy. We included in the analysis only events that occurred the day before or within the 14 days after the colonoscopy was performed as follow-up to the abnormal FIT result.

We defined perforation by cross-sectional imaging showing gas outside the colon lumen in a patient with abdominal pain. We defined bleeding as blood per rectum.12 We attributed serious adverse events to bowel preparation if onset

Figure 1: Flow diagram showing activities related to colonoscopy and subsequent follow-up to identify serious adverse events.
occurred during the preparation, before the colonoscopy. We documented resolution of the unplanned event and recorded death resulting from a serious adverse event regardless of how long after the colonoscopy the death occurred.

Statistical analysis
We used descriptive statistics to describe the patient population. The primary outcome was the overall rate of serious adverse events. The secondary outcomes were 14-day post-colonoscopy rates of perforation, bleeding and death. We calculated point estimates with 95% confidence intervals (CIs). We derived the CIs using general estimating equations to account for possible clustering of serious adverse events to individual physicians performing BCCSP colonoscopies.

We used SAS software, version 9.4 (SAS Institute, Inc.).

Ethics approval
Application of a Project Ethics Community Consensus Initiative screening tool determined that the project fell within the category of quality improvement and evaluation projects. As a result, the BC Cancer Research Ethics Board waived review (reference H19-02975).

Results
A total of 96,192 colonoscopies were performed at 50 sites by 308 physicians. Of these physicians, 194 (63.0%) were surgeons, 62 (20.1%) were gastroenterologists, 43 (14.0%) were internists, and 9 (2.9%) were general practitioners or family physicians. The patient characteristics are shown in Table 1 and serious adverse events in Table 2. During 62,647 (65.1%) of the colonoscopies, at least 1 polyp was removed, with 15,143 (15.7%) of all procedures having removal of a large precancerous polyp.

Serious adverse events
Overall, for 78,831 (82.0%) of the colonoscopies, the patients were successfully contacted afterward (Figure 2). Among those contacted, serious adverse events were reported for 44 (95% CI 39–50) per 10,000 colonoscopies, which generated a number needed to harm of 225. Of the 350 serious adverse events in Table 2. During 62,647 (65.1%) of the colonoscopies, at least 1 polyp was removed, with 15,143 (15.7%) of all procedures having removal of a large precancerous polyp.

Table 1: Patient characteristics (n = 92,461)

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Data value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, yr, median (10th–90th percentile)</td>
<td>62 (52–71)</td>
</tr>
<tr>
<td>Sex, male, no. (%) of participants</td>
<td>51,466 (56)</td>
</tr>
<tr>
<td>No. of colonoscopies performed</td>
<td>96,192</td>
</tr>
<tr>
<td>No. (%) with removal of polyps</td>
<td>62,647 (65.1)</td>
</tr>
<tr>
<td>No. (%) with removal of precancerous polyps</td>
<td>51,150 (53.2)</td>
</tr>
<tr>
<td>No. (%) with removal of large precancerous polyps*</td>
<td>15,143 (15.7)</td>
</tr>
</tbody>
</table>

*Precancerous polyp ≥ 10 mm in diameter.

Serious adverse events during or after colonoscopy occurred in 16 patients; these included acute coronary syndrome, atrial fibrillation (requiring cardioversion in 1 case), bradycardia and an abdominal aortic aneurysm dissection during the colonoscopy. There were 2 ischemic cerebrovascular events in patients whose antithrombotic medications had been held for the colonoscopy. Two additional patients whose antithrombotic medications were held experienced thromboembolic events that necessitated surgery.

Serious adverse events during bowel preparation occurred in 12 patients. Six patients were admitted to hospital with emesis that began while consuming the bowel preparation; 2 of these patients underwent esophagogastroduodenoscopy for hematemesis, with diagnosis of Mallory-Weiss tears. One patient was admitted to hospital with a seizure due to hypotension. One patient required surgery for acute diverticulitis with symptom onset after ingestion of the preparation. One patient had a syncopal event and sustained a laceration that required sutures. One patient had worsening of chronic kidney disease leading to dependence on hemodialysis. One patient was admitted with paroxysmal atrial fibrillation, managed medically. Finally, 1 patient had symptomatic and endoscopic findings consistent with ischemic colitis.

There were 3 respiratory events, which consisted of 2 cases of hypoxia secondary to medication administered for sedation (which required completion of colonoscopy at a later date) and 1 case in which the patient was admitted with aspiration pneumonia.

Two deaths occurred after colonoscopy (for a rate of 3 [95% CI 1–10] per 100,000 colonoscopies). One death occurred several weeks after surgical treatment of a post-polypectomy perforation with a complicated postoperative course. The other death occurred at home 3 days after colonoscopy in a patient with substantial comorbid medical conditions; this death was determined to be possibly related to colonoscopy, although the exact cause was unknown.

Interpretation
We determined the rate of colonoscopy-related serious adverse events in the BCCSP using prospective data collection and formal review of unplanned medical events. The risk of a serious adverse event occurring 14 days after colonoscopy was 44 per 10,000 colonoscopies, including a 6 per 10,000 risk of perforation, a 26 per 10,000 risk of bleeding and a 3 per 100,000 risk of death. As such, the BCCSP has a colonoscopy-related rate of serious adverse events that meets accepted benchmarks, particularly given the high proportion...
Research

Few studies have evaluated colonoscopy-related complications in FIT-based screening programs, and it is difficult to interpret our findings in relation to other programs because of different processes and timing of data collection (Table 3). The Basque and Danish screening programs reported serious adverse event rates that were higher than those in the current study, perhaps due in part to a longer window of data collection after colonoscopy. In addition, both of those studies used administrative databases rather than contacting participants directly. In the Basque study, which did not involve chart review, it is possible that some hospital admissions were misclassified as colonoscopy-related complications. Alternatively, unplanned events self-reported by participants may result in underestimation of colonoscopy risk. However, the process of contacting participants to ascertain adverse events has been validated by the English NHS Bowel Cancer Screening Programme. Finally, the Slovenian FIT-based screening program reported very low rates of adverse events. Data on adverse events were collected by means of a standard form initiated by physicians or patients, and it is unlikely that such methodology captured all events. There are high-quality publications on colonoscopy-related complications in screening programs using guaiac-based fecal occult blood tests (Table 3), but the rates of adverse events varied widely in those studies as well.

Two strengths of this study were the large number of colonoscopies included in the analysis and the population-based design. In addition, systematic, prospective data

Table 2: Serious adverse events probably or possibly related to colonoscopy and their outcomes

<table>
<thead>
<tr>
<th>Serious adverse event</th>
<th>No. of patients with event*</th>
<th>Repeat colonoscopy</th>
<th>Surgery</th>
<th>Death</th>
</tr>
</thead>
<tbody>
<tr>
<td>Perforation†</td>
<td>48</td>
<td>1</td>
<td>41</td>
<td>1</td>
</tr>
<tr>
<td>Bleeding</td>
<td>203</td>
<td>102</td>
<td>4</td>
<td>0</td>
</tr>
<tr>
<td>Post-polypectomy syndrome‡</td>
<td>15</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Bowel preparation§</td>
<td>12</td>
<td>2</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Splenic injury</td>
<td>4</td>
<td>0</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Cardiovascular¶</td>
<td>16</td>
<td>0</td>
<td>4</td>
<td>0</td>
</tr>
<tr>
<td>Respiratory**</td>
<td>3</td>
<td>1</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Other††</td>
<td>31</td>
<td>2</td>
<td>9</td>
<td>1</td>
</tr>
<tr>
<td>Total</td>
<td>332</td>
<td>108</td>
<td>60</td>
<td>2</td>
</tr>
</tbody>
</table>

*In each row, the sum of values for outcomes is less than the number of patients with the event because some patients had no or multiple interventions related to the adverse event.
†Includes 1 patient with post-polypectomy bleeding who sustained a perforation as a complication of endoscopic therapy during repeat colonoscopy.
‡Abdominal pain, fever, peritoneal signs without perforation following colonoscopy and polypectomy.
§Serious adverse events that occurred during preparation, before colonoscopy: vomiting (n = 6), hematemesis (n = 2), arrhythmia (n = 1), fall (n = 1), seizure (n = 1), worsening renal function requiring dialysis (n = 1).
¶Cardiac event (acute coronary syndrome [n = 7] or arrhythmia [n = 4], cerebrovascular event [n = 2], thromboembolic event [n = 2], abdominal aortic dissection [n = 1]).
**Pneumonia (n = 1), hypoxia (n = 2).
††Includes infection (n = 6), small-bowel obstruction (n = 3), fall (n = 2), diverticulitis (n = 2), acute kidney injury (n = 2), appendicitis (n = 1), large-bowel obstruction (n = 1), hemorrhoids (n = 1), seizure (n = 1), hospital admission for various other symptoms and no clear diagnosis (n = 11). In addition, 1 patient died at home.

of colonoscopies with polyp removal, a known risk factor for perforation and bleeding. Kothari and colleagues recently performed a systematic review and meta-analysis assessing the rates of colonoscopy-related serious adverse events among 21 population-level studies, including 3 Canadian studies. Among 10 328 360 colonoscopies included, the pooled rate of perforation was 6 per 10 000 with significant heterogeneity across studies due to the inclusion of all patient ages and all indications for colonoscopy. After adjustment for age and gender, polypectomy was not significantly associated with a risk of perforation. In contrast, Rabeneck and colleagues, who also found that cardiopulmonary events or sequelae of bowel perforation were the most commonly reported causes of death, consistent with our findings.
gathering, event reporting and assessment enhanced the quality of the results. Furthermore, the indication for all colonoscopies was follow-up of an abnormal FIT result. Physicians performing colonoscopy within the BCCSP have varied training backgrounds and practice settings. As a result, the data should be generalizable to other population-based screening programs with a similar mixture of physicians, as is the case in Canadian provinces and territories.5

![Flow diagram of study cohort](image-url)

*Figure 2:* Flow diagram of study cohort. *Transcription errors: an unplanned event was recorded, but none occurred.*
serious adverse events may occur between 14 and 30 days.21 included follow-up for 30 days after colonoscopy showed that (100 ng/mL in Saskatchewan, New Brunswick, Nova Scotia, these results in the context of their respective FIT cut-offs. may have decreased the proportions of colonoscopies with polyps and larger polyps removed, with removal being a risk fac- ership Against Cancer. 9 However, a recent study that was the follow-up time recommended by the Canadian Part- database, these data have been neither validated nor published. The accuracy of data collected from the chart review was not validated by a second reviewer; however, the data were not contacted had a different rate of serious adverse events than the study cohort and whether their inclusion would have changed the rates presented here. Planned future studies include data linkage to hospital administrative databases to vali- date our ascertainment process for serious adverse events. The accuracy of data collected from the chart review was not validated by a second reviewer; however, the data were collected by experienced colonoscopists (the respective health authority colonoscopy leads). Although there are regular quality checks of the BCCSP database, these data have been neither validated nor published. The FIT positivity cut-off in the BCCSP is 50 ng/mL, which is lower than in other provincial programs in Canada2 (100 ng/mL in Saskatchewan, New Brunswick, Nova Scotia, and Newfoundland and Labrador; 175 ng/mL in Quebec). This may have decreased the proportions of colonoscopies with polyps and larger polyps removed, with removal being a risk factor for serious adverse events. These data (Table 2) have been included in the current analysis to assist other programs in using these results in the context of their respective FIT cut-offs.

### Table 3: Risks associated with colonoscopy in FOBT-based screening programs for colorectal cancer

<table>
<thead>
<tr>
<th>Study location</th>
<th>No. of patients</th>
<th>Ascertainment</th>
<th>FOBT</th>
<th>Polyp removal, %</th>
<th>Follow-up</th>
<th>Event; rate, per 10 000</th>
</tr>
</thead>
<tbody>
<tr>
<td>British Columbia</td>
<td>96 192</td>
<td>Phone call 14 d after colonoscopy</td>
<td>FIT</td>
<td>65</td>
<td>14 d</td>
<td>All 44; Perforation 6; Bleeding 26; Death 0.3</td>
</tr>
<tr>
<td>Basque, Spain</td>
<td>39 254</td>
<td>Hospital admission data</td>
<td>FIT</td>
<td>NR</td>
<td>30 d</td>
<td>All 100; Perforation 27; Bleeding 62; Death NR</td>
</tr>
<tr>
<td>Denmark</td>
<td>14 671</td>
<td>Chart review of cases identified through hospital admission data</td>
<td>FIT</td>
<td>55</td>
<td>14 d for bleeding 30 d for other SAEs 90 d for death</td>
<td></td>
</tr>
<tr>
<td>Slovenia</td>
<td>13 919</td>
<td>Physician and/or patient had option of mailing standardized form to program</td>
<td>FIT</td>
<td>NR</td>
<td>NR</td>
<td>All 8; Perforation 8; Bleeding 3; Death NR</td>
</tr>
<tr>
<td>England</td>
<td>130 831</td>
<td>Mailed questionnaire 30 d after colonoscopy</td>
<td>Guaiac FOBT</td>
<td>53</td>
<td>30 d</td>
<td>All 142; Perforation 6; Bleeding 65; Death 0</td>
</tr>
<tr>
<td>Alsace, France</td>
<td>10 277</td>
<td>Phone call 1 d after and mailed questionnaire 30 d after colonoscopy</td>
<td>Guaiac FOBT</td>
<td>49</td>
<td>30 d</td>
<td>All 243; Perforation 10; Bleeding 30; Death 0</td>
</tr>
<tr>
<td>Gotland, Sweden</td>
<td>2984</td>
<td>Hospital admission data</td>
<td>Guaiac FOBT</td>
<td>40</td>
<td>30 d</td>
<td>All 100; Perforation 10; Bleeding 140; Death 0</td>
</tr>
</tbody>
</table>

Note: FIT = fecal immunochemical test, FOBT = fecal occult blood test, NR = not reported, SAE = serious adverse event.

### Limitations
This study may have been limited by the duration of follow-up after colonoscopy. The BCCSP used 14-day follow-up to capture serious adverse events related to colonoscopy, as this was the follow-up time recommended by the Canadian Partnership Against Cancer.9 However, a recent study that included follow-up for 30 days after colonoscopy showed that serious adverse events may occur between 14 and 30 days.21

It was not possible to contact all patients who underwent colonoscopy through the BCCSP. It is unknown whether those not contacted had a different rate of serious adverse events than the study cohort and whether their inclusion would have changed the rates presented here. Planned future studies include data linkage to hospital administrative databases to validate our ascertainment process for serious adverse events.

### Conclusion
The BCCSP colonoscopy-related rate of serious adverse events is in keeping with previous publications and meets accepted benchmarks. This study will help BCCSP, and other provincial screening programs, to improve the informed consent process for screening participants who undergo colonoscopy in an FIT-based colon screening program.

### References


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**Contributors:** David Sanders, Laura Gentile, Nazanin Azari-Razm, Dimitriy Bykov and Jennifer Telford designed the study. Marcel Tomaszewski, Robert Enns, Laura Gentile, Scott Cowie, Carla Nash, Denis Petrunia, Paul Mullins, Jeremy Hamm, Nazanin Azari-Razm, Dimitriy Bykov and Jennifer Telford acquired, analyzed and interpreted the data. Marcel Tomaszewski, David Sanders and Jennifer Telford drafted the manuscript. All of the authors revised the manuscript for important intellectual content, approved the final version to be published and agreed to be accountable for the work.

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**Data sharing:** The data are not available for use by other researchers.

**Supplemental information:** For reviewer comments and the original submission of this manuscript, please see [www.cmajopen.ca/content/9/4/E940/suppl/DC1](http://www.cmajopen.ca/content/9/4/E940/suppl/DC1).