Rates of polypectomy in screening and non-screening colonoscopies classified by patient and endoscopist reports

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ABSTRACT

Background: Polypectomy rate may be related to indicators of quality assurance for screening colonoscopy. However, it is difficult to identify screening colonoscopies in provincial health databases.

Objective: To estimate polypectomy rates for screening colonoscopy according to patient and endoscopist reported indications and to compare them to published quality indicators.

Methods: A retrospective cohort study was conducted of staff endoscopists at 7 Montreal hospitals and their patients aged 50-75 who underwent colonoscopy. Consecutive patients were interviewed by a research assistant in the waiting room prior to colonoscopy. Patient reported indication was defined in 4 ways: 1) perceived screening (routine screening, family history, age); 2) perceived non-screening (follow-up); 3) medical history indicating non-screening; 4) combination of the 3 indications. Endoscopist indication was derived from a questionnaire completed immediately after colonoscopy. Polypectomy status was obtained from Quebec provincial physician billing records. Polypectomy rates were computed, while accounting for physician and hospital level clustering, using all 4 patient indications, endoscopist indication, and the agreement between patient and endoscopist indications. Polypectomy rates were adjusted for the accuracy of provincial databases.

Results: 2143 patients (mean age=61, 50% female) were included. Adjusted polypectomy rates ranged between 22.6-26.2% for screening colonoscopy and between 27.1-30.8% for non-screening. Polypectomy rates for screening colonoscopy were 16.3-19.6 % in women and 29.1-34.2% in men. These rates fall below the published benchmarks for polypectomy rates of 30% in women and 40% in men.

Conclusion: Polypectomy rates calculated from the different screening definitions were similar and fall below quality benchmarks.

RÉSUMÉ

Mise en contexte: Le taux de polypectomie est lié à des indicateurs d'assurance qualité de la coloscopie de dépistage. Toutefois, il est difficile d'identifier les coloscopies de dépistage des bases de données de santé provinciaux.

Objectif: estimer les taux de polypectomie pour la coloscopie de dépistage en fonction des indications selon le patient et l'endoscopiste et de les comparer aux indicateurs de qualité publiés.

Méthodes: Une étude de cohorte rétrospective des endoscopists dans 7 hôpitaux de Montréal et leurs patients âgés de 50-75 qui ont eu subi une coloscopie. Des patients consécutifs ont été interviewés par un assistant de recherche dans la salle d'attente avant la coloscopie. L'indication de patient a été définie de 4 façons: 1) le dépistage perçu (dépistage systématique, les antécédents familiaux, l'âge); 2) perçue non-dépistage (suivi), 3) les antécédents médicaux indiquant non-dépistage; 4) la combinaison des 3 indications. L'indication d'endoscopiste a été dérivée à partir d'un questionnaire rempli immédiatement après la coloscopie. Le statut de polypectomie a été obtenu des archives de demandes de paiement des médecins. Le taux de polypectomie a été calculés, tout en tenant compte du niveau des médecins et des hôpitaux de regroupement, en utilisant les 4 indications de patient, l'indication d'endoscopiste, et l'accord entre les deux. Les taux de polypectomie ont été ajustés de l'exactitude des bases de données provinciales.

Résultats: 2143 patients (âge moyen = 61, 50% de femmes) ont été inclus. Les taux de polypectomie ajusté compris entre coloscopie de dépistage de 22,6 à 26,2% et de 27,1 à 30,8% entre les cas de non-dépistage. Les taux de polypectomie pour la coloscopie de dépistage ont été de 16,3 à 19,6% parmi des femmes et de 29,1 à 34,2% pour les hommes. Ces taux sont inférieurs de référence publié de 30% pour les femmes et 40% pour les hommes.

Conclusion: Les taux de polypectomie calculés à partir des différentes définitions de dépistage ont été similaires, mais ils sont inférieurs de référence de qualité publié.

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LIST OF ABBREVIATIONS

ACG	American College of Gastroenterology
ADR	Adenoma detection rate
ASGE	American Society for Gastrointestinal Endoscopy
CAG	Canadian Association of Gastroenterology
CDHF	Canadian Digestive Health Foundation
CI	(Bayesian) credible interval
CRC	Colorectal cancer
CT	Computed tomography
CTFPHC	Canadian Task Force on Preventive Health Care
DCBE	Double contrast barium enema
FIT	Fecal immunochemical test
FOBT	Fecal occult blood test
gFOBT	Guaiac fecal occult blood test
OR	Odds ratio
RA	Research assistant
RAMQ	Régie de l'assurance maladie du Québec
RCT	Randomized controlled trial

1. RATIONALE

Colorectal cancer (CRC) is a leading cause of cancer mortality in Canada, responsible for 11.9% of all cancer deaths. It also accounts for 12.9% of all cancer cases, making it the third most common cancer among Canadian men and women [1]. Screening for CRC in healthy asymptomatic people reduces the incidence and mortality from the disease. A number of CRC screening tests are available and have been recommended by U.S. and Canadian guidelines on CRC screening. These include colonoscopy, sigmoidoscopy, CT colonography, double contrast barium enema (DCBE) and various fecal tests. Colonoscopy is considered a crucial screening test in any CRC screening program because it allows for the visualization and removal of polyps (polypectomy) throughout the entire colon. Screening colonoscopy is the use of colonoscopy as a first-line screening test, rather than as a follow-up to other tests, and has been endorsed as the preferred screening strategy by some U.S. guidelines.

As the use of colonoscopy has increased in the past 10 years, the rates of both polypectomy and complications from colonoscopies have also increased. The polypectomy rate is the proportion of people in whom polyps are removed among those who undergo colonoscopic examination. The polypectomy rate is strongly correlated with the adenoma detection rate (ADR), as adenomas are identified in a subset of polyps removed during colonoscopy. ADR in screening colonoscopies is an important quality indicator for endoscopist competence, as established by the American Society for Gastrointestinal Endoscopy and the American College of Gastroenterology (ASGE-ACG) [2, 3]. The quality of colonoscopy has significant implications for any population based CRC screening programs as the goal of such programs is the removal of precancerous and early cancerous lesions.

However, it is unclear what proportion of polypectomies and adenomas detected result from screening colonoscopies. Presently, it is difficult to distinguish

between screening and other indications for colonoscopy (non-screening) in Quebec provincial health databases. Aside from screening, indications for colonoscopy include those for surveillance, diagnostic, and confirmatory purposes. Although database codes for screening colonoscopies exist, they are infrequently used. It is worthwhile to estimate the rates of polypectomy in screening colonoscopy to improve our understanding of the risks and benefits of CRC screening.

The primary aim of this study is to estimate polypectomy rates in screening and non-screening colonoscopy using different definitions for screening. The study involved endoscopists and their patients at seven Montreal hospitals. The indications for screening were derived from patient and endoscopist questionnaire responses. Our novel approach to identifying screening colonoscopies would enable us to provide the first estimates of polypectomy rates in screening and non-screening colonoscopies in Quebec. The outcome, polypectomy status – whether or not one or more polyps were removed – was obtained from provincial physician billing records. The advantage of our method of outcome ascertainment is that the accuracy of physician billing records for polypectomy status has been previously assessed using medical chart review as the reference. Thus, we were able to adjust the estimated polypectomy rates for the imperfect accuracy of physician billing records.

A secondary objective was to estimate the sex-specific polypectomy rates in screening colonoscopies because the quality benchmarks for ADRs have been defined for asymptomatic men and women. Given that polypectomy rates are highly correlated with ADRs, analogous benchmarks have been established for polypectomy rates. The sex-specific rates in our study were compared to the polypectomy benchmarks to determine whether quality targets are met.

A third objective was to estimate the extent to which indication (screening or non-screening) independently predicts polypectomy, while adjusting for other risk

factors for CRC. This assesses whether the rate of polypectomy differs substantially between screening and non-screening colonoscopies.

The potential impacts of our findings are three-fold. First, we will provide the first estimates of polypectomy rate in screening colonoscopies in Quebec, which will inform decision and policy-makers. The findings will be especially timely, since the development of a Quebec CRC screening program is currently underway and the Canadian Association of Gastroenterology (CAG) is in the process of updating its CRC screening guidelines. Second, sex-specific polypectomy rate estimates in screening colonoscopy relative to quality benchmarks will speak to the quality of colonoscopy services provided at the participating hospitals. Finally, previous studies of screening colonoscopy vary in their definitions of screening, which are based on patient inclusion and exclusion criteria. We will demonstrate how different definitions for screening affect the proportion of screening colonoscopies and polypectomy rates that, in turn, will inform health services research in CRC screening.

In this thesis, I will first review the literature on CRC, CRC screening guidelines, and various screening modalities. Emphasis will be placed on colonoscopy quality indicators and evidence for the accuracy, safety, efficacy, and cost-effectiveness of screening colonoscopy. The specific study objectives and how they were addressed will be discussed in detail in chapters 3 and 4. Finally I will present and discuss the findings and share my conclusions in chapters 5 to 7.

2. LITERATURE REVIEW

2.1 COLORECTAL CANCER

2.1.1 ETIOLOGY

Most colorectal carcinomas develop from benign adenomatous polyps (also referred to as adenomas) [4]. The development from normal colonic epithelium to adenoma and then to carcinoma is mediated by multiple mutations. The most common mutations in colorectal carcinomas are found in the APC (adenomatous polyposis coli), K-ras, and p53 genes [5]. Inactivation of the APC gene typically permits the development of benign adenomas. K-ras mutations are associated with but not necessary for the growth into advanced carcinomas. Inactivation of p53 is associated with advancement into malignant carcinoma [5].

Polyps other than adenomatous polyps are present in the colon, the most common being hyperplastic polyps, which are not typically considered to be CRC precursors [6].

2.1.2 RISK FACTORS

The biggest risk factor for CRC is age. The incidence of CRC increases dramatically after the age of 50 [Figure 2-1]. Guidelines for CRC screening usually target people aged 50 or over, however, some also recommend screening for those 40-49 with a family history of CRC [7].

Other risk factors for CRC include sex (more common in males than in females). The age-adjusted incidence rate in Canada is 62 per 100,000 for males and 41 per 100,000 for females [1]. About one third of CRCs are related to familial risk and genetic diseases, such as familial adenomatous polyposis and Lynch syndrome, which significantly increase the risks for CRC [8]. Bowel diseases such as Crohn's disease and ulcerative colitis are also associated with increased CRC risk [9]. Family history of CRC increases the risk for CRC; a prospective study found

that individuals with one or more first-degree relatives with CRC have a 1.7 fold increase in risk of developing CRC [10].

Modifiable risk factors for CRC include dietary patterns, smoking, alcohol consumption, physical activity, medication use, and sedentary lifestyle [11].

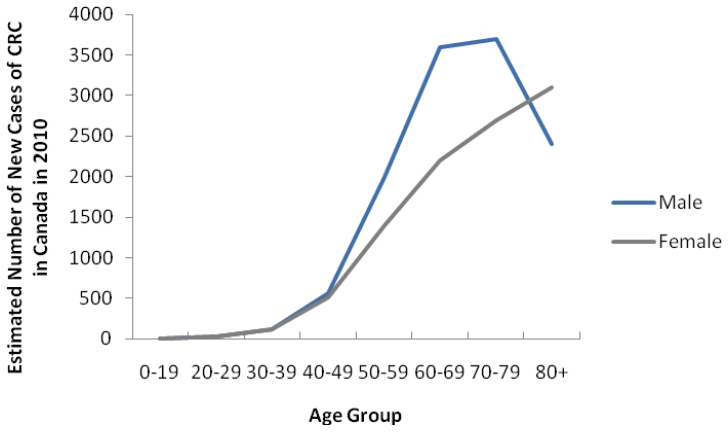

Figure 2-1: 2010 estimates of incident cases of CRC in Canada by sex and age groups. Based on data from Canadian Cancer Statistic 2010 [1].

2.2 COLONOSCOPY

2.2.1 OVERVIEW

Colonoscopy is generally recognized as the optimal screening, diagnostic, and surveillance procedure for CRC as it enables complete visualization of the colon as well as concomitant biopsy and polypectomy [12, 13]. The procedure involves the insertion of a colonoscope - a flexible tube with a fiber optic video camera - from the anal canal through to the cecum. Examination of the colon by the endoscopist occurs during the withdrawal of the colonoscope.

Polypectomy is the removal of polyps during colonoscopy, typically achieved by electrocauterization for smaller polyps and snare polypectomy for small or large polyps [14].

2.2.2 QUALITY INDICATORS

In 2006, the American Society for Gastrointestinal Endoscopy and the American College of Gastroenterology (ASGE-ACG) published a list of quality indicators for colonoscopy – objective measures which allow physicians to assess and continually improve their performance [3].

Among the 14 quality indicators, the highest level of evidence for the recommendations exists for: having an appropriate indication for colonoscopy, appropriate postpolypectomy and postcancer resection surveillance intervals, cecal intubation rates (visualization and photograph of the cecum), adenoma detection rate in asymptomatic individuals, biopsy samples in ulcerative colitis and Crohn's surveillance, and postpolypectomy bleeding management [3].

2.2.2.1 ADENOMA DETECTION RATE

Adenoma detection rate (ADR) is a benchmark of particular interest to this thesis. It first appeared in the 2002 recommendations of the U.S. Multi-Society Task Force on Colorectal Cancer on technical performance of colonoscopy, where it was defined as the adenoma prevalence rate in persons undergoing *first-time colonoscopies* [2]. However, in the 2006 formulation it was defined as the proportion of asymptomatic individuals aged 50 and over who undergo *screening colonoscopies* in whom adenomas are detected [3]. First-time colonoscopies and colonoscopies in asymptomatic individuals are two distinct concepts. Patients undergoing a first-time colonoscopy need not be asymptomatic, and asymptomatic patients are not necessarily undergoing colonoscopy for the first time. Most studies on ADR in screening colonoscopies use the second definition, judging by their inclusion and exclusion criterion that are based on GI symptoms [15-17]. However, some experts still insist that the correct interpretation is first-time colonoscopy definition [18]. The ADR benchmarks cited by both publications are 25% in men and 15% in women [2, 3]. The rationale for selecting

these quality targets is that adenoma detection rates found in the literature are consistently above these figures [2, 3].

Increasing patient age and male sex, as well as the endoscopist performing the procedure are important predictors of ADR, while indication for colonoscopy is not [19, 20].

2.2.2.2 ENDOSCOPIST VARIATION

The quality of colonoscopy is operator dependent. Adenoma detection is a function of both the patient's risk for developing adenomas and the performance of the endoscopist. Several studies have reported important variation in endoscopists' adenoma detection rates. Barclay et al. examined 2053 screening colonoscopies by 12 endoscopists and found substantial differences in adenoma detection rate between endoscopists, varying from 9.4 to 32.7% [21]. In addition, withdrawal times were found to be associated with adenoma detection rates. However, patient risk factors were not considered in this analysis. Chen et al. studied the variation among 9 endoscopists who performed 10,034 colonoscopies while adjusting for patient age and sex. Detection rates for at least one adenoma ranged between 15.5–41.1% [20]. Using summary level data, Imperiale et al. found 7% to 44% range of adenoma detection rate among 46 endoscopists who performed 2664 screening colonoscopies. In multiple linear regression, mean procedure time was found to account for 36-56% of all variation in detection rates [22].

2.2.2.3 POLYPECTOMY RATE

Polypectomy rates are expected to be higher than ADRs because hyperplastic or other types of polyps, which cannot always be distinguished visually from adenomatous polyps by the endoscopist, may be removed during polypectomy [23]. Adenomas are ascertained through histological examination following surgical removal. Although polypectomy rate has not been typically used as a

quality benchmark, it has been found to be highly correlated with ADR. Williams et al. found a correlation of 0.86 between the two using 2706 screening colonoscopies performed by 15 endoscopists [24]. Chen et al. found the correlation between non-adenomatous polyp removal and adenoma detection to be 0.84 for patients aged 50 or over [25].

The advantages of using polypectomy rates as opposed to ADRs as a quality indicator are 1) their availability at the time of the colonoscopy and 2) they can be easily extracted from hospital-based electronic endoscopy reporting systems and billing records. In many institutions histologic and endoscopic findings are not linked electronically, making ADRs difficult to calculate and susceptible to misclassification. Using linear regression, Williams et al. found that to achieve ADRs of 25% in men and 15% in women, endoscopists needed polypectomy rates of 40% in men and 30% in women [24]. Francis et al. proposed another approach – calculating a conversion factor for estimating ADRs from polypectomy rates using the ratio between the average ADR and polypectomy rate in their sample of endoscopists. They calculated the conversion ratio to be 0.64, and found the correlation between the estimated and the true ADRs to be 0.85 [26]. However, this study included colonoscopies for all indications, not just screening. A limitation for both this and the Williams study is that the approaches developed were based on the correlation between ADRs and polypectomy rates in their samples, and generalizability to other samples is unknown.

2.3 COLORECTAL CANCER SCREENING

2.3.1 GUIDELINE RECOMMENDATIONS

2.3.1.1 CANADIAN GUIDELINES

The Canadian Task Force on Preventive Health Care's (CTFPHC) recommendation statement for CRC screening from 2001 endorses annual to biennial fecal occult blood test (FOBT) or periodic sigmoidoscopy for average

risk individuals over the age of 50 [27]. The task force concluded that there was insufficient evidence for the effectiveness of colonoscopy as a primary screening strategy. Concerns over the feasibility of a colonoscopy-based screening program include problems with compliance and resource-intensiveness, however, high effectiveness may prevail over these concerns [27].

Recommendations for population-based screening from The National Committee on Colorectal Cancer Screening in 2002 support annual to biennial FOBT in particular, as it is the only initial screening strategy for which evidence from randomized controlled trials (RCTs) is available [28].

The 2004 guidelines from the Canadian Association of Gastroenterology and Canadian Digestive Health Foundation (CAG-CDHF) recognize several screening strategies for average-risk individuals aged 50 or over. Recommended strategies include: FOBT every 2 years, flexible sigmoidoscopy with or without FOBT every 5 years, double contrast barium enema every 5 years, or colonoscopy every 10 years [29]. Access to gastroenterology specialty care varies across Canada, and the choice of screening strategy is influenced by availability of resources as well as physician and patient preferences [29].

2.3.1.2 U.S. GUIDELINES

Guidelines published by the American Society of Gastrointestinal Endoscopy in 2006 endorse colonoscopy as the preferred method of screening but also recommend sigmoidoscopy every 5 years and annual FOBT alone or in combination as alternative strategies [30].

Recommendations from the 2008 joint guidelines from the American Cancer Society, US Multi-Society Task Force on Colorectal Cancer, and the American College of Radiology are similar to those from CAG-CDHF. The guidelines emphasize CRC prevention as the primary goal of CRC screening; noting that fecal tests are less likely to prevent cancer than the structural exams [12].

The 2008 guidelines from the American College of Gastroenterology, like its recommendations in 2000, continue to endorse colonoscopy every 10 years as the preferred CRC screening strategy and support the distinction between cancer detection and cancer prevention screening strategies [13, 31].

2.3.2 PREVALENCE OF SCREENING IN CANADA

Despite the endorsement of CRC screening by Canadian professional and governmental organizations, adherence to the guidelines is low. Rabeneck et al. followed a cohort of Ontarians aged 50-59 from the beginning of 1995 to the end of 2000. During the 6 years of follow up, less than 20.5% of the subjects underwent any screening test for CRC according to data obtained from 3 provincial health databases. The most common screening procedure was FOBT at 9.3% compared to endoscopy at only 6% [32]. In a 2004 telephone survey of average-risk individuals aged 50-74 in Alberta, 11.9% of respondents reported having had FOBT in the past 2 years, 3% had endoscopy in the past 5 years. Overall only 14.3% of respondents were up-to-date on CRC screening [32]. Using the 2003 Canadian Community Health Survey data, Sewitch et al. estimated the screening rate for FOBT to be 7.7% in the past year, and the rate for endoscopy in the past 5 years to be 8.8% [33].

2.4 SCREENING COLONOSCOPY

2.4.1 ACCURACY

Accuracy of screening tests is usually assessed by sensitivity and specificity of the test in relation to disease status as determined by a reference standard. Sensitivity is defined as the proportion of people who test positive among those who truly have the disease. Specificity is defined as the proportion of people who test negative among those who are disease free. Colonoscopy is usually used as a reference standard to assess the accuracy of other screening tests that detect

polyps or CRC. Thus, it is difficult to assess the sensitivity of screening colonoscopy itself due to the lack of an independent gold standard.

However, comparative studies suggest that polyps, especially smaller ones, can be missed by colonoscopy. Miss rate is defined as the proportion of lesions missed by a single examination that are detected by another examination or a re-examination. It is akin to the rate of false negatives, however, no independent gold standard is used in determining miss rate. Using back-to-back same day colonoscopies to compare findings from two examinations, Rex et al. reported an overall miss rate for adenomas to be 24%; 27% for adenomas 5 mm or smaller, 13% for those between 6 and 9 mm, and 6% for those 1 cm or bigger [34]. Other studies have used segmental unblinding, where CT colonography is performed prior to colonoscopy and the findings for each section of the colon just examined are revealed to the endoscopist, who may then re-examine that section of the colon. Pickhardt reported miss rates of 10% for adenomas at least 6 mm and 12% for those 10 mm or greater [35]. Postic et al. used colon resection specimens as a reference standard by comparing the number of lesions in sections of surgically removed colons to those found in colonoscopies conducted up to 5 months prior. The sensitivity of colonoscopy was determined to be 76.7% [36].

2.4.2 DIAGNOSTIC YIELD

The extent to which screening colonoscopy can prevent CRC can be described by its diagnostic yield – the proportion of people in whom adenomas or carcinomas are detected among those who undergo the test [19]. According to a 1995 review of 5 studies evaluating screening colonoscopy in average risk individuals, the detection rate was 0.7% for cancer and 29% for adenomatous polyps [19]. It is worth noting that in 4 of the 5 studies, subjects were prescreened with FOBT, and those with a positive result were excluded; therefore, colonoscopy was performed on truly asymptomatic individuals (free of occult blood in the stool). The highest yield was found in males aged 60 years or older, with a prevalence of 1.6% for

cancer, and 38% for adenomas [19]. This was not, however, a systematic review, the methods on literature searches and pooling results were not clearly described.

In 2008, Niv et al. published a meta-analysis of 10 cohort studies on screening colonoscopy. The pooled rate of CRC was 0.78% and ADR was 19% [37]. However, this meta-analysis suffers from methodological issues: poorly defined search terms and a lack of information regarding the study selection process [38].

The studies in the previous two reviews included mostly colonoscopies performed by gastroenterologists. In 2009, Wilkins et al. published a meta-analysis reporting a 28.9% ADR for screening colonoscopies performed by family physicians [39]. Although the methods of this study were thoroughly described, it becomes clear upon closer examination that many of the studies included were not restricted to colonoscopies performed in asymptomatic patients and were not truly screening colonoscopies

Although ADR in screening colonoscopies has been cited as one of the most important quality indicators for colonoscopy, there has been no high-quality, up-to-date meta-analysis on this topic.

2.4.3 COMPLICATIONS

Complications, though relatively rare, do occur with colonoscopy. The most common complications include colonic perforation and bleeding. Perforations in colonoscopy result from excessive wall pressure, mechanical trauma from the colonoscope, or polypectomy-related perforations [40]. Bleeding occurs more frequently than perforation and is often associated with polypectomy. Other complications include severe abdominal pain, sedation-related events, and more rarely: pneumothorax, mesenteric tears, colonic volvulus, appendicitis, diverticulitis, splenic trauma, and death [40].

According to the meta-analysis of screened cohorts by Niv et al., perforation occurred in 0.01% of individuals and bleeding in 0.05% [37]. In the community

setting, Whitlock et al. reported the rate of serious complications resulting from screening colonoscopies to be 2.8 in 1,000 pooled over 12 studies using a random effects model [41]. Eighty-five percent of complications arose from colonoscopies that involved polypectomies. Pateris et al. reported a perforation rate of 1 in 1,400 for colonoscopies overall, and 1 in 1,000 for therapeutic colonoscopies involving polypectomy [42]. Compared to sigmoidoscopy, where the complication rate is 3.4 in 10,000, the risk for complications from colonoscopy is much higher [41].

2.4.4 EFFECT ON INCIDENCE AND MORTALITY

There are no RCTs evaluating the effectiveness of screening colonoscopy in reducing CRC incidence and mortality, however, evidence from observational studies and inferences from RCTs of other screening tests are often drawn upon to support the efficacy of colonoscopy in CRC prevention [12, 30]. In the National Polyp Study, CRC incidence during follow-up in patients who underwent polypectomy during colonoscopy and surveillance was reduced by 76-90% compared to three independent reference groups [43]. Kahi et al. compared CRC incidence and mortality in asymptomatic individuals who underwent screening colonoscopy to expected rates from the SEER database, and reported a standardized incidence ratio of 0.33 and standardized mortality ratio of 0.35 [44]. The reduction in incidence was significant, while the mortality reduction was of borderline significance due to few deaths – 2.9 per 1000 person-years. An RCT on FOBT showed a 20% reduction in CRC incidence in the screened groups compared to the control group, which can be attributed to more opportunities for polyp removal in screened groups since colonoscopy was performed for 83-84% of patients with positive FOBT slides [45]. Case-control studies demonstrating significant reduction in CRC mortality with sigmoidoscopy and polypectomy have been cited as indirect evidence for colonoscopy due to the similarity between the two exams [12, 30].

2.4.5 PATIENT COMPLIANCE

Low patient compliance is often cited as a drawback of screening colonoscopy [27]. Evidence from population-wide screening programs is available from Australia and Europe. In an Australian study where average-risk subjects aged 50-55 and 65-70 randomly selected from the electoral roll were invited to participate in screening colonoscopy, CT colonography, or their choice of the 2 tests. The participation rate was 18% overall [46] and did not differ between the 3 groups. Another Australian study comparing 6 different screening strategies found the participation rate for colonoscopy to be 17.8%, significantly lower than FOBT at 27.4% [47]. In an Italian population-based randomized trial comparing FIT (fecal immunochemical test), flexible sigmoidoscopy and total colonoscopy, the participation rates were 32.3% for FIT and flexible sigmoidoscopy and 26.5% for colonoscopy [48].

2.4.6 COST-EFFECTIVENESS

Cost-effectiveness analyses of screening colonoscopy and other screening tests have reached varied conclusions due to different assumptions that are made. In an analysis by Frazier et al., colonoscopy every 10 years was less cost effective than annual FOBT with sigmoidoscopy every 5 years. Colonoscopy compliance rate was assumed to be 60% for the initial screen and 80% for surveillance. 100% compliance is assumed for FOBT with sigmoidoscopy. The authors note that compliance rates significantly impact cost-effectiveness; 60% compliance for a 5 year program is equivalent to 100% compliance for a 10 year program. Cost-effectiveness of CRC screening appears to be comparable to that of other cancer screening programs [49]. In a study comparing colonoscopy every 10 years, annual FOBT, and sigmoidoscopy every 5 years, Sonnenberg et al. found that sigmoidoscopy was less cost-effective than the other 2 tests using life years saved as a measure of effectiveness. A sensitivity analysis was performed by varying the compliance rate to repeated screening. FOBT was more sensitive to reductions in

compliance rate than colonoscopy, leading the authors to conclude that colonoscopy is the preferred screening method [50]. The sensitivity analysis also included varying other assumptions of the tests' accuracy and incidence reduction rates, but these had less effect on the difference in cost-effectiveness between the tests. A recent analysis by Telford et al. compared 3 screening strategies currently used in Canadian provinces: annual low-sensitivity gFOBT (guaiac-based stool test), annual FIT, and colonoscopy every 10 years. Colonoscopy had the greatest impact on incidence and mortality, followed by FIT. Annual FIT had the lowest incremental cost-effectiveness ratio (incremental cost per incremental quality adjusted life year) [51].

2.5 OTHER SCREENING TESTS

2.5.1 FLEXIBLE SIGMOIDOSCOPY

Flexible sigmoidoscopy is an endoscopic structural exam similar to total colonoscopy; however, it permits visualization and polypectomy in only the distal part of the colon and it does require bowel preparation. The review by Whitlock et al. reported the sensitivity of sigmoidoscopy in the community setting to be 58 – 75% for adenomas and 86% for advanced neoplasia. However, the results are from studies that used colonoscopy to simulate sigmoidoscopy by assuming that all lesions in the regions within the reach of the sigmoidoscope would have been detected by sigmoidoscopy [41]. In the baseline report of an RCT of sigmoidoscopy vs. no screening in the UK, the detection rate was 12.1% for distal adenomas and 0.3% for carcinoma. Participants in whom high-risk polyps were identified by sigmoidoscopy were referred to colonoscopy, and adenomas were found in the proximal colon in 18.8% of these cases, and proximal carcinoma in 0.4% [52]. The complication rate pooled from 6 studies was 0.34 per 1000, lower than that of total colonoscopy [41].

2.5.2 CT COLONOGRAPHY

CT colonography is a virtual colonoscopy emerging in recent years as a CRC screening exam that is recommended by the American Cancer Society. The procedure requires bowel preparation similar to colonoscopy but sedation is typically not required. 3D images of the colon are generated by computed tomography allowing abnormalities to be visualized. Resection of detected colorectal lesions is not possible, so patients with positive scans need to undergo colonoscopy, usually scheduled in the same day [53]. Studies show the accuracy for the detection of large polyps (> 10 mm) is similar to that of colonoscopy. Whitlock et al. reported a pooled sensitivity of 92%. However, estimates of sensitivity of CT colonography for smaller adenomas (> 6 mm) have been between 78 – 88.7%, lower than that of colonoscopy. If patients with polyps 6 mm or greater are referred to colonoscopy, it is expected that 1 in 3 to 1 in 8 patients will be referred to colonoscopy [41]. One of the advantages of CT colonography is that it is non-invasive, thus the risk for complications is minimal. However, the cancer risk from radiation exposure, that is not minimal, has not been fully assessed [41]. Currently, studies comparing the cost-effectiveness of CT colonography and colonoscopy usually favour colonoscopy. However, these findings may be flawed due to unrealistic assumptions about compliance and test characteristics [54].

2.5.3 DOUBLE CONTRAST BARIUM ENEMA (DCBE)

Double contrast barium enema is an older radiologic colon exam developed in the 1960s. It involves the introduction of a barium suspension into colon, which enables the capture of x-ray images [55]. Its usage had declined in recent years due to the emergence of CT colonography. It is no longer recommended as a screening test in the 2008 American College of Gastroenterology guidelines [13]. Results from the National Polyp Study brought the effectiveness of DCBE as a screening test into question. In this study, patients followed for post-polypectomy

surveillance underwent both DCBE and colonoscopy. DCBE detected only 35% of the polyps found during colonoscopy [56].

2.5.4 FECAL SCREENING TESTS

2.5.4.1 GUAIAC FECAL OCCULT BLOOD TEST (GFOBT)

gFOBTs are designed to detect heme in occult blood in the stool, which could arise from CRC or large polyps. The test is non-invasive and does not require bowel preparation. Typically, samples from 3 consecutive bowel movements are collected for improved sensitivity of tests [12]. Most guidelines recommend annual or biennial FOBT, and that positive FOBT be followed up with colonoscopy. The latest American guidelines emphasize that while FOBT can detect cancer, it is not adequate for detecting adenomas and therefore cannot prevent cancer [12, 13]. The sensitivity and specificity of gFOBTs vary by product as well as by technique of carrying out the tests.

gFOBT is the only CRC screening test for which there is direct evidence from RCTs for reducing CRC mortality. The Cochrane review on the topic found a significant reduction of 16% in CRC mortality across 4 large RCTs based on intention to screen. When adjusted for actual attendance to screening, the reduction in mortality risk was 25% for those who were screened at least once compared to the unscreened [57].

2.5.4.2 FECAL IMMUNOCHEMICAL TEST (FIT)

FIT is very similar to gFOBT, except it detects human globin in blood as opposed to heme. It picks up only blood from the lower GI tract, and is thus potentially more specific to CRC than gFOBT [13]. A study by Levi et al. suggested that the sensitivity of FIT is higher than that of gFOBT. Average-risk individuals aged 50-75 were randomized to FIT or gFOBT; sensitivity and specificity of the tests were assessed using cancer registry data 2 years after the study as a reference standard.

Sensitivity for FIT and gFOBT respectively is 100% and 61.5%, and specificity is 85.9% for the former and 96.4% for the latter [58].

2.5.4.3 FECAL DNA TEST

The rationale for fecal DNA test is based on the molecular genetics of CRC. Genetic abnormalities that are associated with CRC are used to for its detection [59]. In a study by Imperiale et al., stool samples from asymptomatic individuals 50 years or older were analyzed using both fecal DNA panel and gFOBT. Using results from colonoscopy as a reference standard, fecal DNA panel detected 51.6% of the 31 invasive cancers and gFOBT detected only 12.9%. The DNA panel was positive in 18.2% of the cases with advanced neoplasia, while gFOBT detected only 10.8% [59]. Further research is needed to determine the optimal testing interval [60].

2.6 SUMMARY

As a structural exam, colonoscopy is a preferred screening exam for CRC recommended by several guidelines. It has been shown to have acceptably low complication rates and there is indirect evidence for its effectiveness in reducing CRC incidence and mortality. In terms of accuracy, it is the gold standard exam to which other screening tests are compared. However, studies have shown that adenomas could be missed during colonoscopy. Endoscopist performance with respect to adenoma detection also varies considerably. Although there is no high quality meta-analysis on ADR to date, quality benchmarks for ADR in screening colonoscopies have been promoted to reduce missed lesions. Polypectomy rates have been shown to be highly correlated with ADRs, and analogous quality benchmarks have been established for polypectomy rates. To our knowledge, there are no published estimates of polypectomy rates in screening colonoscopies in Quebec.

3. OBJECTIVES & HYPOTHESES

3.1 MAIN OBJECTIVE

The main objective of this project is to estimate rates of polypectomy in screening and non-screening colonoscopy according to different definitions of screening based on patient and endoscopist reports.

We hypothesize that polypectomy rates would be higher in non-screening colonoscopies than screening colonoscopies as non-screening patients are likely to be a higher-risk for adenomatous polyps. We also expect polypectomy rate to vary depending on the definition of screening.

3.2 SECONDARY OBJECTIVES

3.2.1 OBJECTIVE 2

To compare study sex-specific polypectomy rates in screening colonoscopies with published quality benchmarks for colonoscopy.

We expect the rate of polypectomy to be higher in men than women as men are at higher risk for developing adenomatous polyps.

3.2.2 OBJECTIVE 3

To estimate the effect of indication (screening or non-screening) on polypectomy, adjusted for age, sex, and family history of CRC.

We hypothesize that indication would not be an important predictor of polypectomy since previous studies have suggested that the indication for colonoscopy is not a predictor of adenoma detection rate [19, 20].

4. METHODS

4.1 STUDY DESIGN OVERVIEW

This study combines data from two prospective cohort studies. The purpose of the first cohort study was to develop a database classification scheme to discern screening and non-screening colonoscopies. Data on the second cohort were collected to provide additional power for the purposes of the present study. Participants were endoscopists at seven Montreal hospitals and their patients who underwent a colonoscopy. Data collection took place between January 2007 to March 2007 for the first cohort and between January 2008 and December 2009 for the second cohort.

4.2 PROCEDURE

4.2.1 RECRUITMENT

4.2.1.1 STUDY SITES

Endoscopists and patients were recruited from seven teaching hospitals in Montreal: Royal Victoria Hospital, Montreal General Hospital, St. Mary's Hospital Centre, Jewish General Hospital, Hôpital Maisonneuve-Rosemont, Hôpital Fleury, and Hôpital Hôtel Dieu. All seven institutions were represented in both cohorts.

4.2.1.2 ENDOSCOPISTS

For the first cohort study, all staff endoscopists at each institution were contacted by research assistants (RAs) who explained the study and obtained informed consent from those who were willing to participate. In order to be eligible, the endoscopist had to have Régie de l'assurance maladie du Québec (RAMQ) colonoscopy billing rights. RAMQ is the body responsible for public health insurance in Quebec. Endoscopists who participated in the first cohort study were

contacted for their willingness to participate for cohort 2. In addition endoscopists who were new staff at the institutions were recruited using the same procedure as described for cohort 1.

4.2.1.3 PATIENTS

Patient recruitment followed the same procedure for both cohorts. On selected days, RAs received a list of patients scheduled to undergo colonoscopy with participating endoscopists. In the endoscopy waiting room, consecutive patients were approached by RAs who explained the study and asked eligible patients to participate. Inclusion criteria were: 1) aged 50 to 75; 2) scheduled for colonoscopy with a participating endoscopist. Exclusion criteria were: 1) not eligible for provincial health insurance coverage; 2) not eligible for provincial health insurance coverage during the previous year; 3) unable to provide informed consent. Informed consent was obtained from eligible patients agreeing to participate.

4.2.2 DATA COLLECTION

Data collection for both cohorts followed the same procedures.

4.2.2.1 ENDOSCOPISTS AND CLINIC STAFF

Endoscopists were asked to complete a brief 2-item questionnaire per patient immediately after completing the colonoscopy [Appendix A]. The questionnaire was attached by RAs to the outside of a participating patient's medical file. The questionnaire assessed the specialty of the endoscopist and the indication for colonoscopy (screening, follow-up, diagnostic, surveillance, other). If a patient did not have a complete colonoscopy as scheduled, the RA would be alerted by the clinic staff.

4.2.2.2 PATIENTS

Prior to the colonoscopy, the RA administered an 11-item questionnaire to patients [Appendix B]. Questions included socio-demographics, perceived reason for colonoscopy, history of gastrointestinal conditions, gastrointestinal symptoms, previous CRC screening tests, and family history of CRC.

Patients were also asked to provide their health care card number so that their data could be retrieved from the provincial health database.

4.2.2.3 PHYSICIAN BILLING RECORDS

Patient health care card numbers were sent to RAMQ, where they were linked with patient records in the RAMQ database. Extracted from the RAMQ database were data on patient age group and sex, and all medical acts performed on the date of the index colonoscopy and up to 1 year prior to the index date.

4.3 VARIABLES

Polypectomy status is a binary outcome variable indicating whether or not at least one polyp was removed during the colonoscopy. Polypectomy status for each patient's colonoscopy was extracted from the RAMQ physician billing records by matching the date of the colonoscopy with the date of polypectomy billing code "0794". If the polypectomy billing code appeared on the date of the colonoscopy, polypectomy status took the value of 1, otherwise it was 0. Polypectomy rate was defined as the proportion of colonoscopies where at least 1 polyp was removed. All data manipulations and descriptive analyses were performed with SAS 9.2. Other variables used in our analyses are summarized in Table 4-1.

Table 4-1: Description of variables and the data sources

VARIABLE	TYPE (LEVELS)	DATA SOURCE
Date of colonoscopy	Date	Patient questionnaire
Institution	ID	Patient questionnaire
Endoscopist	ID	Endoscopist questionnaire
Endoscopist Specialty	Nominal (gastroenterologist/ surgeon/ internist/family physician)	Endoscopist questionnaire
Patient age group	Ordinal (50-54/55-59/ 60-64/65-70/70-75)	RAMQ database
Patient sex	Binary (male/female)	RAMQ database
Patient perceived reason for colonoscopy		
Family history	Binary (yes/no)	Patient questionnaire
Routine screening		
Aging		
Follow-up to a problem		
Follow-up to a test		
Don't know		
History of gastrointestinal conditions		
Ulcerative colitis	Binary (yes/no)	Patient questionnaire
Crohn's disease		
Colon polyps		
Colon cancer		
Colon/bowel surgery		
Gastrointestinal symptoms in past 6 months		
Rectal bleeding	Binary (yes/no)	Patient questionnaire
Unintentional weight loss		
Change in bowel habits		
Lower abdominal pain		
Anemia in past 12 months	Binary (yes/no)	Patient questionnaire
Positive FOBT in past 12 months	Binary (yes/no)	Patient questionnaire
Family history of CRC	Binary (yes/no)	Patient questionnaire
Endoscopist indication for colonoscopy	Binary (screening/ non-screening)	Endoscopist questionnaire

4.4 STATISTICAL ANALYSES

4.4.1 MODEL SPECIFICATION

Polypectomy rates were calculated using hierarchical logistic regression to account for potential clustering by physicians and by hospitals. All modelling was conducted with WinBUGS 1.4.3 using diffuse or wide prior distributions [see Appendix C for a sample hierarchical logistic model in WinBUGS]. Ninety-five percent CIs represent Bayesian credible intervals.

There is *a priori* evidence that polypectomy rates would be clustered by endoscopists, however, the extent of hospital-level clustering is unknown. To investigate the extent of clustering by hospital, a 3-tier intercepts only model using polypectomy status as the outcome was run on all patients' colonoscopies. The 3 tiers consist of patients nested in physicians, who were, in turn, nested in hospitals. Since physicians must be nested with hospitals and physician level clustering is expected to be stronger than hospital level clustering, physicians who worked at more than one hospital have all their patients analyzed under their primary workplace. At the first level, an intercept only logistic model was fitted for patients from each endoscopist. The model was

$$logit(p_{ijk}) = \alpha_{ij}$$

where p_{ijk} is the probability of polypectomy for patient k seen by endoscopist j at hospital i. α_{ij} is the endoscopist-specific intercept. At the second level, the endoscopist specific intercepts were modeled to be normally distributed around a hospital specific mean as below

$$\alpha_{ij} \sim N(\mu_i, \sigma_i)$$

where μ_i and σ_i represent the mean of endoscopist-specific intercepts and the variation around this mean respectively for the ith hospital. At the third level, the hospital means were allowed to vary normally around an overall mean.

$$\mu_i \sim N(\mu, \sigma)$$

Diffuse prior distributions were used for μ, σ, and σ_i.

The 2-tier model was very similar to the 3-tier model at the first level. The second level consisted of the endoscopist-specific intercepts being normally distributed around the overall mean.

$$\alpha_j \sim N(\mu, \sigma)$$

Hence there is no hospital level clustering in the two-tier model.

The two models were compared and the clinical significance of the variation between hospitals was used to assess whether or not there was clustering by hospital and to determine whether a 3-tier model was necessary.

4.4.2 MAIN OBJECTIVE: POLYPECTOMY RATES BY INDICATION

Nine different ways to define a colonoscopy as screening or non-screening were devised. Patient reported indication was defined in 4 ways [61].

Indication 1: Perceived screening (screening is defined as when patients perceived reason for their colonoscopy is routine screening, family history, or aging)

Indication 2: Perceived non-screening (non-screening is defined as when patient perceived reason for their colonoscopy is to follow-up on a previous test or problem)

Indication 3: Medical history indicating non-screening (non-screening is defined as when patients report a GI symptom or a history of GI diseases or anemia or a positive FOBT)

Indication 4: Combination of the 3 indications (screening is defined as when all 3 indications indicate screening)

Endoscopist indication (Indication 5) for screening was a binary variable derived from the endoscopist questionnaire item (asymptomatic people or those with family history of CRC). Screening was defined as when only screening was indicated as the reason for the colonoscopy by the endoscopist. Non-screening was defined as when one or more other indications were selected.

Four additional indications were defined based on the agreement between patient and endoscopist indications. The agreement between endoscopist indication and each of the four patient indications were assessed in a previous study using cohort 1 data. Concordance for the indications ranged from 0.79 to 0.85 and kappa ranged between 0.58 and 0.70 [61]. Screening was defined as when both patient and endoscopist agree that the colonoscopy was screening. Non-screening was when both patient and endoscopist agree that the colonoscopy was not for screening.

Indication 6: Patient indication 1 × Endoscopist indication
Indication 7: Patient indication 2 × Endoscopist indication
Indication 8: Patient indication 3 × Endoscopist indication
Indication 9: Patient indication 4 × Endoscopist indication

Using the hierarchical model chosen, polypectomy rates were calculated for colonoscopies identified as screening by each of the 9 indications, and similarly for those identified as non-screening. Polypectomy rates were computed from the overall intercept mean by taking the inverse logit using equation 1.

$$P_{RAMQ} = 1 / [1 + exp(-\mu)] \qquad [1]$$

The polypectomy rates calculated by the models were adjusted by the sensitivity and specificity of RAMQ polypectomy status relative to polypectomy status from medical chart. The adjusted polypectomy rates represent the polypectomy rate that one would find by chart review. Calculated from cohort 1 data in a previous study, the sensitivity of polypectomy reporting in RAMQ was 84.7%, (95% CI:

79, 89) and specificity was 99.0%, (95% CI: 98, 100) [62]. The adjustment was done within the WinBUGS model, where the adjusted rate was calculated from the rate estimated from the logistic model by using equation 2. The uncertainties of the sensitivity and specificity estimates were taken into account by converting the CIs into beta distributions Beta(174.77, 31.57) and Beta(391.05, 3.95), which were used as priors for sensitivity and specificity respectively.

$$P_{chart\ review} = (P_{RAMQ} + Specificity - 1) / (Sensitivity + Specificity - 1) \quad [2]$$

4.4.3 OBJECTIVE 2: SEX-SPECIFIC POLYPECTOMY RATES

Polypectomy rates were calculated using the model of choice, separately for each sex, for colonoscopies identified as screening by each of the 9 indication variables. Polypectomy rates adjusted for RAMQ accuracy were also calculated using the approach described in section 4.4.2.

4.4.4 OBJECTIVE 3: EFFECT OF INDICATION ON POLYPECTOMY

A 2-tier model was constructed where the first level was a logistic model of patients' probability of polypectomy as a function of the endoscopist-specific intercept and patient-level covariates. Three covariates were adjusted for based on substantive grounds. Age and sex are known predictors of CRC risk and ADR. Family history is a predictor of CRC risk.

Age was categorized into 5 groups (50-54/55-59/60-64/65-70/70-75), and indicators for the latter 4 age groups were entered into the model. Age was entered as categorical variables as it is known that the effect of age on CRC risk is not linear (see section 2.1.2). The first level of the model is as follows

$$logit(p_{jk}) = \alpha_j + \beta_1 * agecategory1_{jk} + \beta_2 * agecategory2_{jk} + \beta_3 * agecategory3_{jk} + \beta_4 * agecategory4_{jk} + \beta_5 * sex_{jk} + \beta_6 * familyhistory_{jk}$$

where β_1 to β_6 are logistic regression parameters for the covariates, and they are not endoscopist specific. The second level of this model was similar to that of the basic 2-tier model, where endoscopist-specific intercepts were defined as normally distributed around μ. Diffuse priors were assigned to all parameters including the βs.

5. RESULTS

5.1 RECRUITMENT STATISTICS

5.1.1 INSTITUTIONS

Institutions varied in the number of endoscopists and patients recruited [Figure 5-1]. Four endoscopists performed colonoscopies at more than one institution.

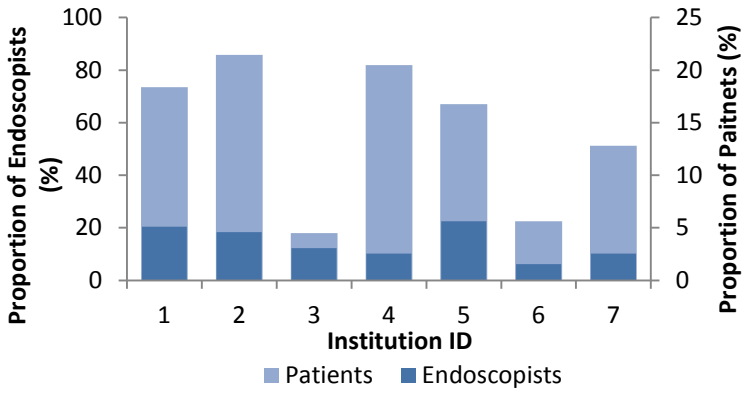

Figure 5-1: Proportion of endoscopists and patients recruited from each institution. The left axis represents the proportion of all endoscopists who were recruited from each institution, and the right axis represents the proportion of all participating patients who were recruited from each institution.

5.1.2 ENDOSCOPISTS

Thirty-eight endoscopists agreed to participate in cohort 1. Cohort 2 consisted of 45 endoscopists: 35 of the ones in cohort 1 as well as 10 additional ones. In total 48 endoscopists were recruited. However 3 endoscopists who participated in both cohorts were unable to bill to RAMQ, therefore, they and their 45 patients were excluded from the study for protocol violation. Hence, 45 endoscopists were included in our analyses.

5.1.3 PATIENTS

Of a total of 2614 patients who were approached, 2216 (84.8%) were eligible and consented to participate [Figure 5-2]. Reasons for non-eligibility were: aged under

50 or over 75, and not covered by RAMQ. Twelve patients were excluded due to protocol violations including: wrong questionnaire administered by RAs, colonoscopy not performed by a participating endoscopist, colonoscopy was not completed as scheduled. One patient withdrew consent after enrollment and 45 patients were excluded due to protocol violations regarding their endoscopists.

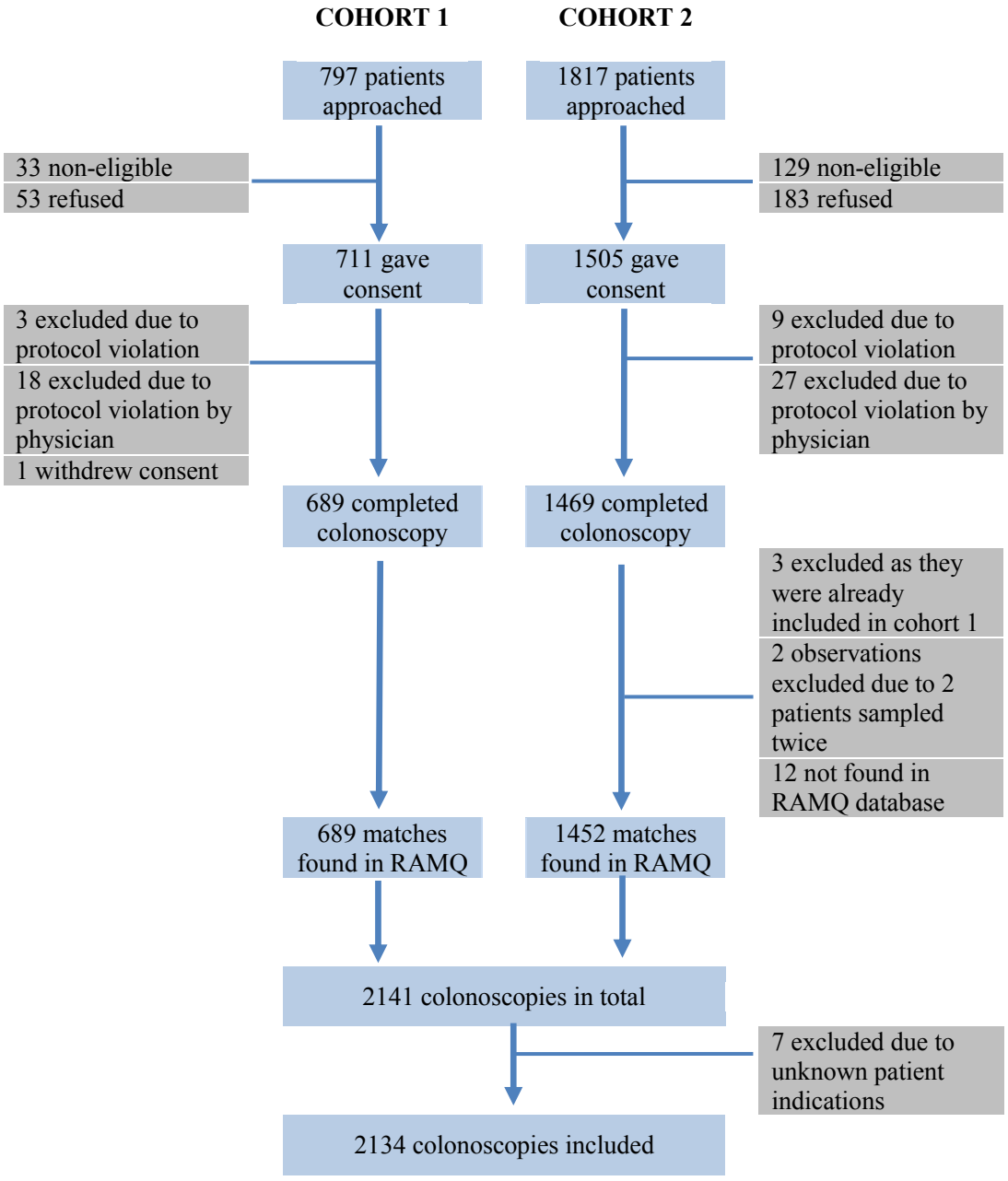

Figure 5-2: Flowchart for recruitment and exclusion of patients.

From cohort 2, 3 patients were excluded because they had previously participated in cohort 1. Two patients underwent colonoscopy twice during the recruitment period, so only their first visits were included. Twelve patients provided RAMQ numbers that were not matched with insured persons in the RAMQ database.

From the remaining 2141 colonoscopies, 7 were excluded for the purposes of our analyses due to missing patient colonoscopy indication because patients reported that they did not know the reason for their colonoscopy in the patient questionnaire. Patient indication is an important component of most of our analyses. Although it would be interesting to examine polypectomy rates among these patients, such a small sample would not yield meaningful inferences.

Thus, 2134 unique patients (81.6% of all those approached) who underwent colonoscopy were included in our analyses.

5.2 PARTICIPANT CHARACTERISTICS

5.2.1 ENDOSCOPIST CHARACTERISTICS

Of all colonoscopies, 89.3% were performed by 38 gastroenterologists, 9.7% by 6 surgeons, and 0.1% by 1 internist. Descriptively, polypectomy rates were 26.9% (95% CI: 24.9-28.9) for gastroenterologists, 15.5% (95% CI: 10.3-20.6) for surgeons, and 19.1% (95% CI: 0-38.2) for the internist.

5.2.2 PATIENT CHARACTERISTICS

Table 5-1: Patient characteristics

Patient Characteristics	Count	Proportion (%)
Age group		
50-54	500	23.4
55-59	489	22.9
60-64	456	21.4
65-69	373	17.5
70-75	316	14.8
Male	1070	50.1

Patient Characteristics	Count	Proportion (%)
History of gastrointestinal conditions	627	29.4
Ulcerative colitis	67	3.1
Crohn's disease	38	1.8
Colon polyps	480	22.7
Colon cancer	78	3.7
Colon/bowel surgery	131	6.1
Gastrointestinal symptoms in past 6 months	853	40.0
Rectal bleeding	429	20.1
Unintentional weight loss	109	5.1
Change in bowel habits	391	18.3
Lower abdominal pain	344	16.1
Anemia in past 12 months	227	10.7
Positive FOBT in past 12 months	60	2.8
Family history of colon cancer	505	23.8

5.3 MODEL SPECIFICATION

5.3.1 THREE-TIER MODEL

In the three tier model, the overall unadjusted polypectomy rate was 22.8% (95% CI: 16.9, 28.7). The standard deviation of hospital intercepts around the overall mean on the logit scale was 0.208 (95% CI: 0.005, 0.664). The standard deviation of endoscopist intercepts around the hospital means was 0.745, (95% CI: 0.531, 1.024). Hospital-specific rates are shown in Table 5-2.

Table 5-2: Unadjusted institution-specific polypectomy rates

Institution ID	Polypectomy rate	95% CI Lower Limit	95% CI Upper Limit
1	22.6	15.7	29.6
2	24.7	18.5	34.8
3	21.8	13.0	29.0
4	22.7	15.4	30.3
5	22.3	15.6	28.8
6	22.7	14.1	32.6
7	22.8	15.3	30.9

The point estimates of institution-specific rates are similar. However, the CIs are somewhat wide due to reduced sample sizes. Increased complexity of the model,

in terms of the number of levels may also contribute to increased CI widths. Comparisons between the institutions show small differences accompanied by relatively wide CIs [Table 5-3].

Table 5-3: Differences in unadjusted institution-specific polypectomy rates

Institutions Compared	Difference In Rate	95% CI Lower Limit	95% CI Upper Limit
1-2	-1.4	-14.1	4.7
1-3	0.4	-7.3	10.9
1-4	0.0	-9.2	8.7
1-5	0.1	-7.7	9.1
1-6	0.0	-11.0	9.6
1-7	-0.1	-9.9	8.7
2-3	2.1	-4.1	17.3
2-4	1.4	-5.2	14.5
2-5	1.7	-4.2	14.8
2-6	1.2	-6.6	15.3
2-7	1.2	-5.7	14.3
3-4	-0.4	-11.9	7.6
3-5	-0.3	-10.4	7.9
3-6	-0.4	-13.3	8.0
3-7	-0.5	-12.6	7.3
4-5	0.1	-8.0	9.7
4-6	0.0	-11.3	10.1
4-7	0.0	-10.2	9.4
5-6	-0.1	-11.5	8.9
5-7	-0.1	-10.4	7.9
6-7	0.0	-10.5	10.9

5.3.2 TWO-TIER MODEL

The two-tier model involving only patients nested within physicians yielded an overall unadjusted polypectomy rate of 22.7% (95% CI: 18.2, 27.4). This was very close to the estimate from the three-tier model, but the CI was narrower in the two-tier model. The standard deviation of endoscopist intercepts around the overall mean on the logit scale was 0.738 (95% CI: 0.530, 1.008), which is very

similar to the variation of endoscopists around the hospital means in the three-tier model.

The two models yielded very similar results. Although the CIs for some of the between hospital differences may be of clinical concern, for parsimony subsequent models were fitted without the hospital level.

5.4 MAIN OBJECTIVE: POLYPECTOMY RATES BY INDICATION

5.4.1 PROPORTION OF SCREENING COLONOSCOPY BY INDICATION

The proportion of colonoscopies defined as screening differed considerably among the different indications, the highest proportion defined as screening by indication 1 at 70.9% and the lowest defined by indication 9 at 32.2% [Tables 5-4 and 5-5]. Proportion of colonoscopies defined as non-screening range from 23.2% to 64.5%.

Table 5-4: Proportion of screening and non-screening colonoscopies as classified by indications 1-5

Type of Colonoscopy	Indication	Proportion (%)	95% CI Lower Limit	95% CI Upper Limit
Non-screening	1	29.1	27.2	31.0
	2	46.3	44.2	48.4
	3	59.8	57.7	61.8
	4	64.5	62.5	66.6
	5	44.9	42.8	47.1
Screening	1	70.9	69.0	72.9
	2	53.7	51.6	55.8
	3	40.3	38.2	42.4
	4	35.5	33.4	37.5
	5	55.1	52.9	57.2

Table 5-5: Proportion of screening and non-screening colonoscopies as classified by indications 6-9

Type of Colonoscopy	Indication	Proportion (%)	95% CI Lower Limit	95% CI Upper Limit
Non-screening (by both patient and endoscopist)	6	23.2	21.4	25.0
	7	33.2	31.2	35.2
	8	39.8	37.8	41.9
	9	41.7	39.6	43.8
Screening (by both patient and endoscopist)	6	49.2	47.0	51.3
	7	41.9	39.8	44.1
	8	35.2	33.1	37.2
	9	32.2	30.2	34.2
Screening by patient but not endoscopist	6	21.7	20.0	23.5
	7	11.8	10.4	13.2
	8	5.1	4.2	6.1
	9	3.3	2.5	4.1
Screening by endoscopist but not patient	6	5.9	4.9	6.9
	7	13.1	11.7	14.6
	8	19.9	18.2	21.6
	9	22.9	21.1	24.7

5.4.2 POLYPECTOMY RATES BY INDICATION

Unadjusted polypectomy rates in screening colonoscopies were similar among the indications, ranging from 20% for indication 6 to 22.9% for indication 2 [Figure 5-3]. The median among the indications was indication 8 at 21.3%. Polypectomy rates were slightly higher in non-screening compared to screening colonoscopies. Unadjusted polypectomy rates in non-screening colonoscopies were also similar among indications, ranging from 23.7% for indication 2 to 26.8% for indication 5. The median was 26.0% [Figure 5-4]. Adjusting for the accuracy of RAMQ physician billing records increased the polypectomy rate estimates slightly. The median adjusted rates were 24.2% (range: 22.6-26.2%) for screening, and 29.9% (range: 27.1-30.8%) for non-screening. Indications 1-4 produced higher polypectomy estimates for screening and lower estimates for non-screening compared to indications 5-6.

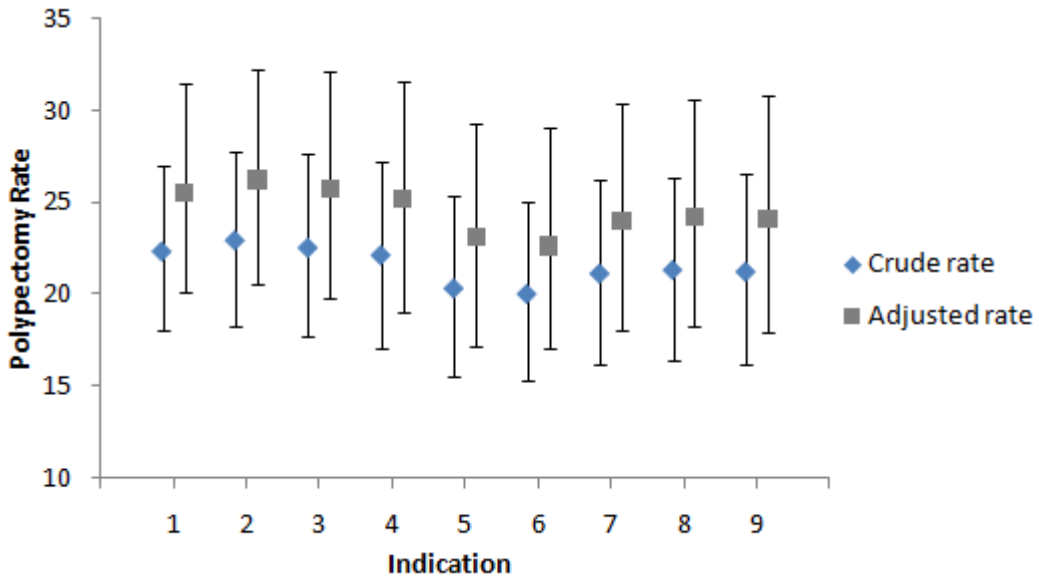

Figure 5-3: Polypectomy rates in screening colonoscopies. Error bars represent 95% CIs.

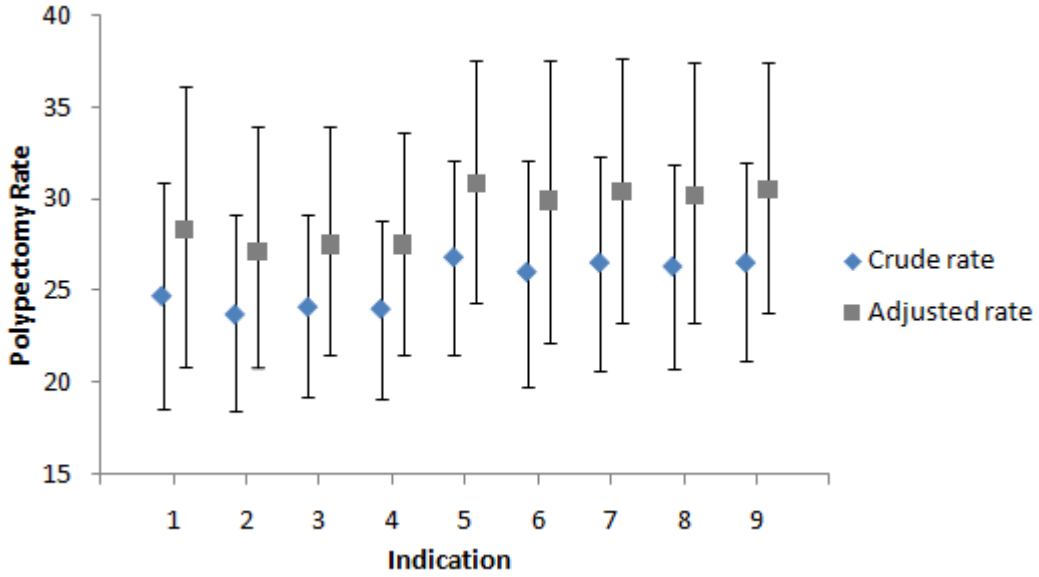

Figure 5-4: Polypectomy rates in non-screening colonoscopies. Error bars represent 95% CIs.

5.5 OBJECTIVE 2: SEX-SPECIFIC POLYPECTOMY RATES

The overall model polypectomy rate estimates, regardless of indication, were 18.1% (95% CI: 13.9, 22.6) for women and 28.6% (95% CI: 23.1, 34.4) for men.

The adjusted overall rates were 20.4 (95% CI: 15.1, 26.1) and 33.0% (95% CI: 26.2, 40.4) in women and men respectively.

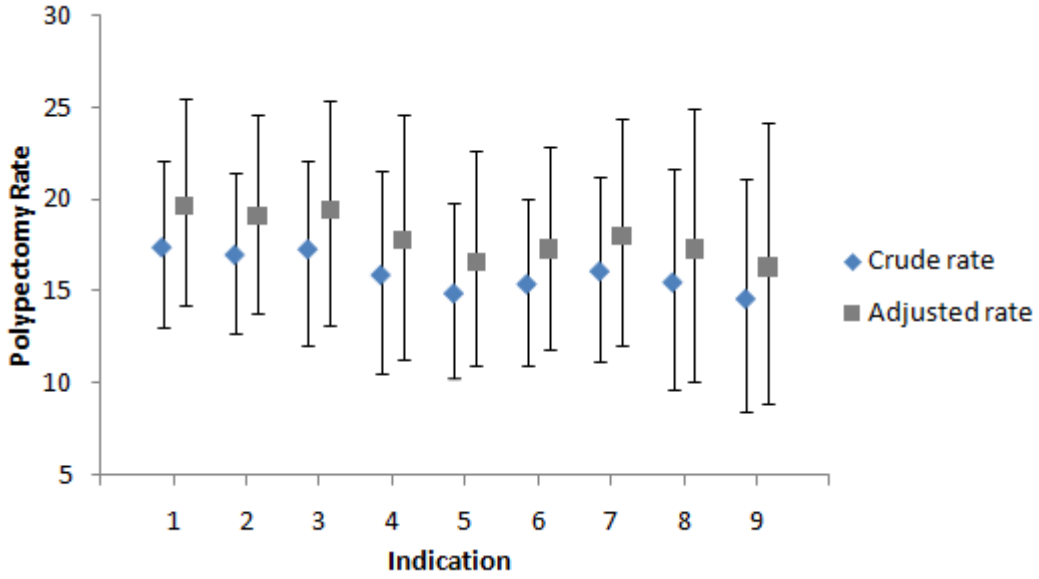

Figure 5-5: Polypectomy rates in screening colonoscopies among women. Error bars represent 95% CIs.

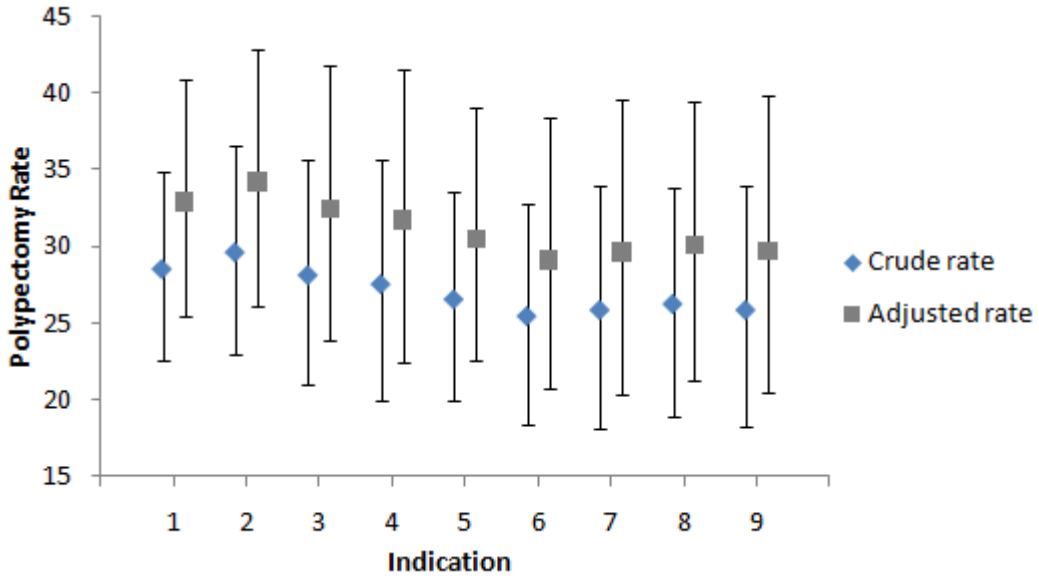

Figure 5-6: Polypectomy rates in screening colonoscopies among men. Error bars represent 95% CIs.

In women undergoing screening colonoscopies, the median estimated polypectomy rate was 15.9% (range: 14.6-17.4%) and the median adjusted rate was 17.8% (range: 16.3-19.6%) [Figure 5-5]. For men undergoing screening colonoscopies, the median estimated rate was 26.5% (range: 25.4-29.6%) and the median adjusted rate was 30.5% (range: 29.1-34.2%) [Figure 5-6].

5.6 OBJECTIVE 3: EFFECT OF INDICATION

To estimate the effect of indication on polypectomy status, multiple logistic regression was performed with age, sex, and family history of CRC as covariates. The OR estimates for indication range from 0.74 to 0.94 [Table 5-6].

Table 5-6: Odds ratios for the effect of the indications

Indication	OR	95% CI Lower Limit	95% CI Upper Limit
1	0.89	0.70	1.13
2	0.92	0.74	1.14
3	0.94	0.76	1.18
4	0.90	0.72	1.12
5	0.75	0.60	0.92
6	0.74	0.59	0.91
7	0.83	0.67	1.04
8	0.86	0.69	1.08
9	0.86	0.68	1.08

Estimates for the remaining covariates were very similar across all models [Figure 5-7]. All age groups had significantly higher risk for polypectomy compared to the reference age group (50-54). Median OR was 1.66 (95% CI: 1.20, 2.3) for the 55-59 age category, 1.62 (95% CI: 1.17, 2.26) for age 60-64, 1.99 (95% CI: 1.42-2.81) for age 65-69, and 1.91 (95% CI: 1.35, 2.74) for age 70-75. Male sex was also a significant predictor of polypectomy status with a median OR of 1.9 (95% CI: 1.53, 2.34). Family history of CRC, in contrast, was not a strong predictor in any of the models with a median OR of 1.15 (95% CI: 0.89, 1.48).

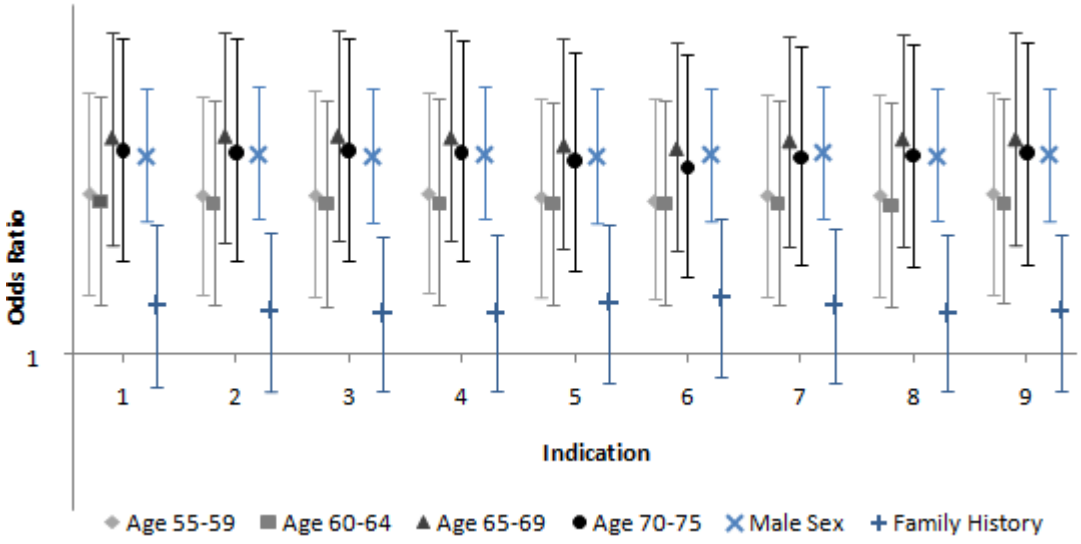

Figure 5-7: Odds ratios of covariates across models. Error bars represent 95% CIs. The reference group for age, sex, and family history are the 50-54 age group, female sex, and no family history.

6. DISCUSSION

6.1 FINDINGS

6.1.1 POLYPECTOMY RATES BY INDICATION

The proportion of colonoscopies identified as screening by the different indications varied widely from 32.2% (indication 9) to 70.9% (indication 1). The endoscopist indication (indication 5) identified 55.1% screening colonoscopies. Indications with stringent criteria for screening identified fewer colonoscopies as screening compared to less stringent indications. Indications 1 (patient perceived screening) used the most relaxed criterion for screening, while 2 (perceived non-screening) and 3 (GI history) were progressively more stringent. Indication 3 is most consistent with the asymptomatic definition of screening used by the guidelines. Indeed, most recent studies of screening colonoscopies based their inclusion and exclusion criteria on patient reported history of GI diseases and GI symptoms [15-17]. Indication 4, which required all of indications 1-3 to be screening, was the strictest of all patient criterions. Indications 6-9 were more restrictive than their counterparts in 1-4 because they required both patient and endoscopist to agree on screening.

Despite the variation in identifying screening colonoscopies, the polypectomy rate estimates from the various indications were similar, ranging from 20.0% to 22.9% for screening and 23.7% to 27.5% for non-screening. As expected, polypectomy rates in non-screening colonoscopies tended to be higher compared screening colonoscopies since such non-screening patients are likely to be at higher risk for adenomas. The similarity of the indication estimates is probably due to the fact that the rates for screening and non-screening were close to one another. The median estimate among all indications was 21.3% (95% CI: 16.4, 26.3) for screening and 26.0% (95% CI: 19.8, 32.1) for non-screening. Given that the screening and non-screening rates were fairly close, shifting some colonoscopies from the screening group to the non-screening and vice versa may not have

altered the rate estimates considerably. Hence the polypectomy rate estimates were relatively insensitive to the indication used. However, it is worth noting that the less stringent indications (1-4) tended to result in higher estimates for screening and lower rates for non-screening compared to more restrictive indications, likely by including some non-screening colonoscopies as screening.

Adjusting for the sensitivity and specificity of the polypectomy procedure code in RAMQ physician billing records relative to medical records boosted the polypectomy rate estimates. The median adjusted polypectomy rate was 24.2% (95% CI: 18.2, 30.6) for screening, and 29.9% (95% CI: 22.2, 37.6) for non-screening.

6.1.2 SEX-SPECIFIC POLYPECTOMY RATES

As expected, polypectomy rate estimates for women were lower than those for men. Again, all indications produced similar estimates and adjusting for RAMQ accuracy increased the estimates slightly. The median adjusted rate was 17.8% (95% CI: 11.3, 24.6) for women and 30.5% (95% CI: 22.5, 39.1) for men and fall below the published polypectomy benchmarks of 30% for women and 40% for men. For women, none of the upper CI limits were above 30%, while for men, the upper limits for indications 1-4 were just above 40%. Therefore, we are fairly certain that the polypectomy rate for women in our study falls below the benchmark. There remains a possibility that the benchmark was met for men as the confidence interval encompasses the benchmark, however, the median adjusted rate of 30.5% is considerably lower than the targeted 40%.

It is possible that men, compared to women, under report their GI symptoms or are more likely to perceive the procedure as screening rather than non-screening. This would result in more high-risk individuals being classified as screening by many of the indications, leading to an inflated polypectomy rate for screening colonoscopies. Thus, the estimates for men may need to be interpreted more conservatively.

6.1.3 EFFECT OF INDICATION

In the logistic models, age and male sex emerged as strong predictors of polypectomy status, as expected. Age categories 65-69 and 70-75 had higher ORs than age categories 55-59 and 60-64, suggesting that risk increases with age. Family history was positively associated with polypectomy, although it was not an important predictor.

OR estimates for the indications are all below 1, suggesting that screening colonoscopy tends to be associated with reduced risk for polypectomy compared to non-screening as expected. Indications 1-4 and 7-9 did not seem like important predictors. The lower CI limits of indications 5 and 6 suggest there could be as much as 40% lower odds of polypectomy in colonoscopies for screening as non-screening. Indication 6 is likely very similar to indication 5 because it requires a combination of indications 1 and 5, however, indication 1 is a very relaxed criterion and is likely to be non-informative in forming indication 6. Lower odds of up to 40% may be of clinical relevance. However, there are several caveats. Firstly, it is important to note that the odds ratio will be exaggerated in this case compared to risk ratio, because the outcome rate is more than 20%. Second of all, the meaning of this finding suggests that colonoscopies reported as screening by the endoscopist are less likely to result in polypectomy than those reported as non-screening. However, it does not tell us whether or not endoscopist reports are accurate indications of whether or not the colonoscopies are truly screening procedures. Lastly, and perhaps most importantly, the endoscopist indication was collected as part of a questionnaire that was completed by the endoscopist immediately after the colonoscopy and polypectomy performance may have biased the endoscopist's assessment of whether or not the exam was a screening colonoscopy. Thus, caution should be used in interpreting results arising from indication 5 as well as those that rely on it (indications 6-9).

6.2 IMPLICATIONS

Among our findings, there is a lack of evidence that indication is an important predictor of polypectomy status, given that the screening and non-screening polypectomy rates are similar and that the findings from the logistic models are, for the most part, non-significant. This prompts the question as to why the quality benchmarks refer only to screening colonoscopies, as if screening and non-screening polypectomy or ADRs would be very different. If they are not that different, as our findings and those of others suggest, it may suffice to merely define benchmarks for all colonoscopies. Moreover, given the difficulty in defining and identifying screening colonoscopy in health administrative databases and hospital records, it would be much easier for endoscopists and institutions to try to adhere to benchmarks if they could simply calculate the ADRs, or even easier yet – polypectomy rates, for all colonoscopies without having to distinguish between screening and non-screening,

Our findings indicate that the polypectomy rates, and thus likely the ADRs, in our study population fall below the published quality benchmarks for screening colonoscopy. However, it is unclear from the guidelines how one should interpret this. Does falling below the benchmark mean that the polypectomy rate in our study population was below average? Or below what was acceptable? The basis for the benchmarks was merely that most published studies on screening colonoscopy had rates that were above those numbers, which may be biased upwards as endoscopists in academic institutions may have higher than average ADRs.

The proportion of patients who have been previously screened is unknown. Polypectomy rates would be expected to be higher among first-time screenees than those previously screened. Thus it is uncertain how our study findings compared to the benchmarks if we use the first-time screening definition. This further illustrates the difficulty in implementing the benchmarks. Moreover,

identifying first-time screening procedures is even more challenging and susceptible to misclassification compared to identifying screening procedures.

6.3 LIMITATIONS

6.3.1 SELECTION BIAS

Patient recruitment occurred on selected days in endoscopy waiting rooms. If patients with certain risk profiles were systematically scheduled for colonoscopy on certain days, then our sample may not be representative of the endoscopist's practice. However, secretaries at the study endoscopist clinics have assured us that this was generally not the case.

In addition, patients were recruited from large academic tertiary institutions in Montreal, thus findings may not be generalizable to small, rural practices.

6.3.2 INFORMATION BIAS

Two sources of potential information bias have already been discussed. Firstly, men may be more likely misclassified as screening by some of the indications due to their tendency to under-report medical problems. Secondly, the endoscopist indication and indications related to it may be subject to reporting bias, due the indication being reported after the outcome (polypectomy) was already known to the endoscopist.

6.3.3 BENCHMARKS

Our finding that the study polypectomy rates fall below the benchmark suggests that the ADRs would also fail to meet the targets. The benchmarks for polypectomy, 30% in women and 40% in men, are based on a study by Williams et al. which found that these proportions were correlated with the published ADR benchmarks of 15% in women and 25% in men [24]. This finding depends on the correlation between endoscopists' polypectomy rates and ADRs in their study,

which may differ from that of the endoscopists in our study. There is much evidence to suggest that polypectomy rates and ADRs are correlated and that this correlation tends to be around 0.85 [see section 2.2.2.3]. Nonetheless, the validity with which we can extend the interpretation of our results to ADRs relies on the untestable assumption that the correlation in our sample of endoscopist is similar to that in the study by Williams et al.

7. CONCLUSION

In conclusion, our study provides the first estimates of polypectomy rates in screening and non-screening colonoscopies in Montreal and shows that these rates do differ substantially depending on the definitions for screening and non-screening exams. Our findings on polypectomy rates suggest that established colonoscopy quality benchmarks are not being met. Our findings also point to possible limitations with current colonoscopy quality benchmarks. First, the distinction between screening and non-screening colonoscopies may be unnecessary and its removal may, in fact, facilitate uptake of quality monitoring. Second, guidelines need to be provided on the interpretation of endoscopist performance relative to published benchmarks. These findings may be informative to the ongoing development of a CRC screening program in Quebec.

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APPENDIX A: ENDOSCOPIST QUESTIONNAIRE

ENDOSCOPIST QUESTIONNAIRE

Understanding Outcomes of Colonoscopy

PID : _____ **Date:** ____/____/____
dd mm yyyy

MD ID: _____

1. Please specify the REASON for performing this colonoscopy:

☐ **Screening** Performed in **asymptomatic** people at **average-risk** for developing colorectal cancer
OR
Performed in people **with a family history of colorectal cancer**

☐ **Surveillance** Performed in patients with **history of either**:
colon polyps
colorectal cancer
ulcerative colitis
Crohn's disease

☐ **Diagnostic** Performed in patients **with large bowel symptoms** (in order to confirm or rule out disease)

☐ **Confirmatory** Performed in patients **for a follow-up to a positive screen** (in order to confirm or rule out disease)

☐ **Other ⇒** **Please specify:** _____

2. Polypectomy performed: ☐ **YES** ☐ **NO**

If YES, how many Polyps were removed: _____

APPENDIX B: PATIENT QUESTIONNAIRE

PID: _____ **Date:** ____/____/____ (dd mm yyyy)

Development and validation of a method to differentiate screening from surveillance, diagnostic and confirmatory colonoscopy in health administrative databases in three Canadian provinces

1. **Age:** _____ years

2. What is the **highest level of schooling** you completed?

- ☐ Primary school: grade: _____
- ☐ Attended high school: grade _____
- ☐ High school graduate
- ☐ Attended college/ CEGEP/ technical school
- ☐ College/ CEGEP/ technical school graduate
- ☐ Attended University
- ☐ University graduate

3. Have you ever been told by a doctor that you have one of the following medical conditions:

   a. **Ulcerative colitis** ..... ☐ Yes ☐ No

   b. **Crohn's disease** ..... ☐ Yes ☐ No

   c. **Colon polyps** (non-cancerous growths)..... ☐ Yes ☐ No

   d. **Colon cancer** ..... ☐ Yes ☐ No

   e. Did you ever have **colon/bowel surgery** ..... ☐ Yes ☐ No

4. Has anyone in your immediate family, meaning your **parents, sisters, brothers or children,** ever had colon cancer (please consider only blood relatives)?..... ☐ Yes ☐ No

5. In the **past 12 months**, did you have a **positive stool blood test (or FOBT)**..... ☐ Yes ☐ No

6. In the **past 12 months**, did your doctor tell you that your **blood is low in iron** or that you have **anemia** ..... ☐ Yes ☐ No

7. In the **past 10 years**, have you had any of the following colon / bowel exams:

   a. **Sigmoidoscopy ....** ☐ Yes ☐ No

   b. **Colonoscopy .....** ☐ Yes ☐ No

   c. **Barium enema ....** ☐ Yes ☐ No

PID: _____ **Date:** ____/____/____
dd mm yyyy

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8. In the **past 6 months**, have you experience any of the following symptoms:

   a. **Rectal bleeding / blood in your stools or in the toilet water** on more than one occasion ..... ☐ Yes ☐ No

   b. Unintentional weight loss of more than 10 pounds or 4-5 Kg ..... ☐ Yes ☐ No

   c. Marked change in bowel habits (diarrhea / constipation) ..... ☐ Yes ☐ No

   d. Lower abdominal pain / rectal pain that required medical attention ..... ☐ Yes ☐ No

9. Why are you having a colonoscopy today?

   ☐ **Family history of colon cancer**

   ☐ **Part of regular check-up / routine screening**

   ☐ **Age**

   ☐ **Follow-up to a previous problem**

   ☐ **Follow-up to a previous screening test**
   (stool blood test, sigmoidoscopy, barium enema, virtual colonoscopy)

   ☐ **Other,** please specify _____

   ☐ **Don't know / remember**

10. **SITE OF RECRUITMENT:** _____

11. **Sex:** ☐ Male ☐ Female

THANK YOU

APPENDIX C: SAMPLE WINBUGS MODEL

```
model {

        for (j in 1:45) {


                        for (k in indexa[j]:indexb[j]) {

                                logit(p[k]) <-alpha[j]
                                polypectomy[k] ~ dbern(p[k])

                        }

                        alpha[j]~dnorm(mu,tau)

        }


        tau<- 1/(sigma*sigma)
        mu~dnorm(0, 0.001)
        sigma~dunif(0,2)

}
```