Factors Effecting Adenoma Detection During Screening Colonoscopy

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ABSTRACT

Background. Adenoma detection rate (ADR) has been associated with the incidence of interval colorectal cancer (CRC) in patients undergoing screening colonoscopy.

Objective. This study aimed to identify factors that effect adenoma detection during screening colonoscopy.

Methods. A retrospective cross sectional study was conducted of patients who underwent screening colonoscopy between June 1st and August 25th 2009 at the McGill University Health Center. Variables were abstracted from two electronic databases: Endoworks (for colonoscopy reports) and OACIS (for pathology reports for polyps removed). Multivariable logistic regression analysis was performed using the software R to determine the association between patient, colonoscopy, endoscopist related variables, and adenoma detection.

Results. 430 sequentially performed colonoscopies met eligibility criteria and were included. In univariable analysis, higher likelihood of detecting adenomas was associated with male patients, increasing patient age, prior polyp removal, photo-documentation of the cecum, and increasing number of polyps detected; a lower likelihood of detecting adenomas was associated with average risk for CRC, colonoscopy performed by surgeon, increasing number of endoscopies and colonoscopies before the index colonoscopy, and increasing duration of time in the endoscopy unit. In multivariable analysis, increased likelihood of adenoma detection was

associated with increasing patient age (in years) OR 1.04 (95%CI, 1.02 to 1.07), the more polyps detected the higher the odds of detecting an adenoma (OR 3.71 (95%CI, 2.70 to 5.10), while lower likelihood for detecting adenoma was increased time (in hours) from the beginning of the endoscopy session till the index colonoscopy (OR 0.51 (95%CI, 0.31 to 0.79).

Conclusions. In addition to patient characteristics, operator fatigue, as evidenced by a decrease in adenoma detection as time progresses from the start of the endoscopy session, is an important factor that should be considered in endoscopy scheduling. Further research is required to evaluate factors that would optimize the adenoma detection and performance of colonoscopy as a screening tool for CRC.

RÉSUMÉ

Contexte. Le taux de détection d'adénome (TDA) a été associé avec l'incidence intervalle subséquente du cancer colorectal (CRC) chez les patients subissant une coloscopie de dépistage.

Objectif. Cette étude visait à identifier les facteurs affectant la détection d'adénome au cours d'une coloscopie de dépistage.

Méthodes Une étude rétrospective transversale a été menée chez les patients ayant subi une coloscopie de dépistage entre le 1er Juin et 25 août 2009 au Centre universitaire de Santé McGill. Les variables ont été extraites à partir de deux bases de données électroniques Endoworks (pour les rapports de coloscopie) et OACIS (rapports de pathologie pour les polypes enlevés). Une analyse multivariable de régression logistique a été effectuée en utilisant le logiciel R.

Résultats. 430 coloscopies effectuées successivement rencontrèrent les critères d'admissibilité et ont été incluses. En analyse univariable, une probabilité de détection d' adénomes accrue a été notée chez les patients de sexe masculin, plus âgés, ayant eu une ablation de polypes antécédente, s'il y avait eu photo-documentation du caecum, et avec la présence d'un nombre de polypes plus élevés. La probabilité de détecter un adénome était affaiblie chez les patients à risque moyen de CCR, si la coloscopie était effectuée par un chirurgien, et avec un nombre croissant d'endoscopies et coloscopies complétées avant la coloscopie le même jour, ainsi qu'en augmentant la durée de temps passé ce jour-là dans

l'unité d'endoscopie. En analyse multivariable, une augmentation de la probabilité de détection d'adénome a été associée avec l' augentation de l'âge du patient (en années) (OR=1,04 (IC 95% (1,02 à 1,07)), un nombre accru de polypes détectés (OR = 3,71 (95% IC, 2,70 à 5,10), tandis qu'une plus faible probabilité de détection d'adénome était associée avec une augmentation du temps (en heures) passé depuis le début de la session endoscopie jusqu'à la coloscopie de dépistage donnée (OR 0,51 (IC 95%: 0,31 à 0,79).

Conclusions. En plus des caractéristiques de patients reconnus, la fatigue de l'endoscopiste, telle que reflétée par le temps écoulé depuis le début de la session d'endoscopie est associée avec une diminution significative du taux de détection d' adénomes. Ce facteur important doit donc être pris en compte dans la planification de la liste d'endoscopie dans un contexte de dépistage. D'autres recherches sont nécessaires pour évaluer les facteurs qui permettent d'optimiser la détection des adénomes et la performance de la coloscopie comme outil de dépistage pour le CCR.

ABBREVIATIONS

ADR	Adenoma detection rate
CI	Confidence interval
CRC	Colorectal cancer
CT	Computerized tomography
CTC	Computed tomographic colonography
GI	Gastroenterologist
FIT	Fecal immunochemical test
FAP	Familial adenomatous polyposis
FICE	Fujinon intelligent chromoendoscopy
FIT	Fecal immunochemical test
HR	Hazard ratio
HNPCC	Hereditary non-polyposis colorectal cancer
MGH	Montreal General Hospital
MUHC	McGill University Health Center
NA	Not applicable
OR	Odds ratio

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CHAPTER I: INTRODUCTION

Colorectal cancer (CRC) is a malignant growth in the lining of the large intestine; it ranks third in cancer incidence and mortality for males and females alike with an estimated 142,000 new cases and more than 51,000 deaths in the United States in 2010[1]. CRC represents 10% of all incident cancers and 8 to 9% of all cancer related mortality[1]. Recent trends demonstrate declining incidence and mortality from CRC[1, 2] and screening, defined as "the identification of asymptomatic disease or risk factors"[3], is thought to play a major role in these declines[1, 2].

CRC develops from colonic polyps (Figure 1.1 and 1.2), which are projections of tissue that develop on the lining of the colon; these polyps could harbor tissue, adenomas, which predisposes to CRC (Figure 1.3). The intent of CRC screening is to intervene in the natural progression of adenoma to carcinoma (Figure 1.4) by performing a polypectomy (removal of the polyp) (Figure 1.5). Polypectomy removes the tissue believed to be causal in the development of CRC[4] (Figure 1.6), thereby decreasing the incidence of CRC[5] and improving survival[2, 6-9].

The preferred method of screening is colonoscopy (examining the colon with a colonoscope)[10] as it allows for the simultaneous examination of the colon and removal of any polyps that are detected. Colonoscopy requires a number of steps that will be discussed in the following chapter.

Figure 1.1. A broad based polyp

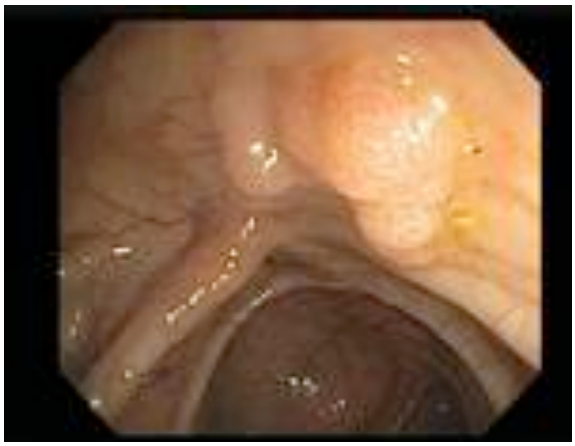


Figure 1.2. A colonoscopy demonstrating a large polyp

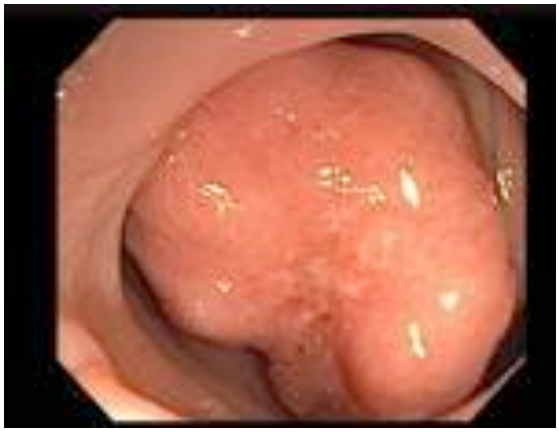


Figure 1.3 CRC develop from polyps that contain adenomatous tissue within them.

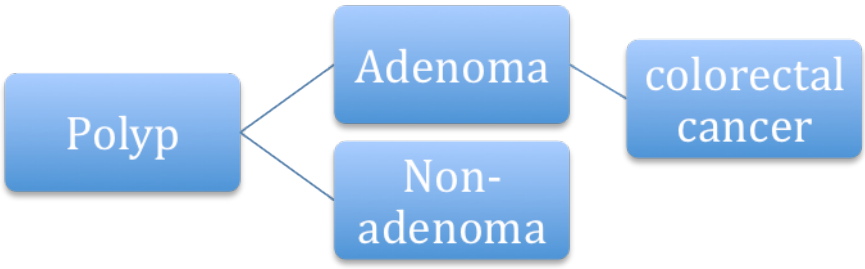


Figure 1.4 The aim of CRC screening is to intervene in the natural progression of adenoma to CRC.

Figure 1.5. A colonoscopy demonstrating the polyp in figure 1.2 after polypectomy (being removed).

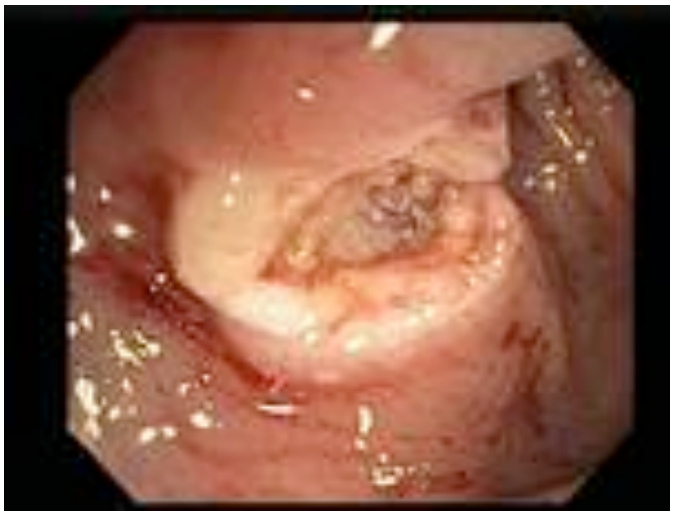
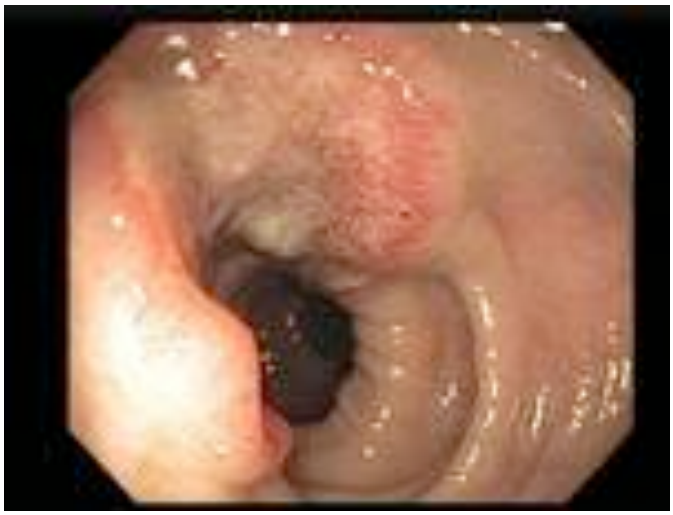


Figure 1.6 A colonoscopy demonstrating CRC.



The launching of regional and provincial CRC screening programs in Canada has led to an increase in the number of annual colonoscopies. Although current CRC screening programs reach only one fifth of the eligible population[11], numbers will increase because of efforts to boost CRC screening rates. Colonoscopy-related quality measures (i.e. withdrawal time, cecal intubation rate, polyp detection rate, adenoma detection rate (ADR) and polypectomy) have been put forth because of the need to establish standards.

The quality of a colonoscopy is a complex construct that incorporates the appropriateness of the reason for performing the colonoscopy, the diagnostic accuracy (the ability of the test to correctly classify the presence or absence of the target disorder[12]) and the safety of the colonoscopy. Over the last 10 years, endpoints in colonoscopy performance have been refined from conducting a full examination of the colon[13-15] to more specific targets[16] that have come to be known as quality indicators[17-20]. These quality indicators or benchmarks strive to achieve a common standard of practice across endoscopy centers with the main goal of maximizing the detection of adenomas during screening colonoscopy and the prevention of progression to CRC.

CRC is a relatively common disease that requires allocation of significant resources to provide CRC screening programs. Improving the performance of colonoscopy is a major concern. Thus, we sought to identify factors that effect adenoma detection during screening colonoscopy. Identifying factors that either augment or dampen adenoma detection could be targeted in the future with the aim of increasing the effectiveness of colonoscopy as a screening instrument.

The overall study objective is to identify factors that are associated with adenoma detection.
Specifically, we will examine the relationships between the adenoma detection rate and factors that likely impact it, including: hours, endoscopies (gastroscopies and colonoscopies) and colonoscopies the endoscopist worked/performed prior to the index colonoscopy on the day of the procedure and adenoma detection.

In this thesis, we will first review the literature on the known factors that affect the ADR, and then present the study methodology and results. We used an endoscopy report database at the Montreal General Hospital (MGH), Montreal, Canada and included consecutive individuals who had undergone screening colonoscopies. We obtained variables related to patients including the patients age, sex, family history of CRC, previous colonoscopy, prior polyp removal, and CRC risk. Variables related to the colonoscopy were obtained as well as the pathology reports of the polyps removed. Finally we discuss and interpret the findings, and provide concluding remarks.

CHAPTER II: Literature review

2.1 Epidemiology of CRC

CRC is the third leading cause of cancer deaths in North America[1], with an estimated 142,000 new cases and 51,000 deaths in 2010 in the USA[1], CRC constitutes 10% of all new cancers and 8% to 9% of cancer-related mortality[1]. The age standardized CRC incidence and death rates over the last two decades have been declining,[2, 21] but the absolute number of CRC cases are increasing due to aging of the population[22]. At the time of screening colonoscopy, 1% of screenees are found to have invasive cancer[23], and 7.9% have advanced adenoma (an adenoma with an increased risk of transforming to CRC)[23].

2.2 CRC screening

Screening is defined as "the presumptive identification of unrecognized disease or defect by the application of tests, examinations or other procedures which can be applied rapidly"[12]. Another definition is "the identification of asymptomatic disease or risk factors"[3].

For a screening test to be effective, it has to fulfill the following conditions:

1- Early detection of the disease being screened should improve prognosis.

2- The disease should be detectable at a preclinical stage.

3- The benefit that early treatment conveys should exceed the cost of screening[24].

CRC screening fulfils these conditions, it is performed on asymptomatic individuals, has a lengthy preclinical stage (10 to 15 years) [25] during which polyps can be detected and removed (polypectomy) thereby decreasing the incidence of CRC[5] and improving survival[6-9]. Benefits of CRC screening have been demonstrated in several long-term cohort studies[26-29] and, not surprisingly, professional and governmental organizations

advocate for CRC screening; these include the American Cancer Society, the U.S. Multi-Society Task Force on Colorectal cancer, the American College of Radiology, the U.S. Preventive Services Task Force [30, 31], the American College of Gastroenterology[10], the Canadian Association of Gastroenterology and the Canadian Digestive Health Foundation[32], as well as the Canadian Task Force on Preventive Health Care[33].

CRC screening is recommended for individuals aged 50 to 75 years, who do not have complaints or manifest findings on physical examination or other investigations that could be attributed to CRC. CRC screening outside this age range should be on an individual basis and only up to the age of 85 years [31]; it can be performed prior to the age of 50 years in people who are at high risk for developing CRC as stated by U.S. Agency for Health Care Policy and Research[34], such as patients with a family history of an inherited polyposis syndrome or inflammatory bowel disease[34, 35], although in the literature these cases are referred to as screening people at high risk for CRC, these might be classified as surveillance colonoscopy as per prior guidelines that dated to 1997[5]. The U.S. Multi-Society Task Force on Colorectal Cancer[36] stated that colonoscopy may be performed for the purpose of screening in people with complaints such as abdominal pain and altered bowel habit (a change in the individuals bowel movements to diarrhea or constipation) with no evidence of bleeding depending on the patients age and family history.

The sequence of events that precede and follow a colonoscopy are demonstrated in figure 2.1

Figure 2.1 The sequence of events prior and following the colonoscopy

2.3 CRC screening modalities

Several modalities for CRC screening (Table 1) have been endorsed by the various soceties[30-32, 35] including: fecal testing, flexible sigmoidoscopy, colonoscopy, or computed tomographic colonography (CTC or virtual colonoscopy). These modalities can be divided into those that depend on fecal testing and those that structurally assess the colon.

Table 2.1 Screening exams for CRC

Fecal tests	Guaiac test, fecal occult blood test (FOBT)
	Fecal immunochemical test (FIT)
	Stool deoxyribonucleic acid (DNA) test
Structural tests	Double contrast barium enema
	Flexible sigmoidoscopy
	Colonoscopy
	Computed tomographic colonography (CTC)

2.4 Importance of colonoscopy

Colonoscopy is the examination of the lining of the colon using a camera on a flexible tube that is inserted through the anus and advanced to the cecum (Figure 2.2). Colonoscopy is used to examine the colon and to remove polyps; its use as a screening tool for CRC has increased over the years[37] as it is the most accurate test compared to other screening tools . However, with a risk of 3.1 complications per 1000 colonoscopies performed[38], colonoscopy also has the highest risk of complications compared to other screening tools[38]. These complications are not non-significant and include perforation of the colon, bleeding and death as well as complications from the sedative medications used during the colonoscopy.

2.5 Accuracy of colonoscopy in detecting CRC

Accuracy is defined as "the ability of a diagnostic test to correctly classify the presence or absence of the target disorder"[12] and is usually measured by the sensitivity and specificity of the test. Sensitivity is " the probability that a diseased person (case) in the population tested will be correctly identified as diseased by the test", while specificity is "the probability that a person without the disease (non-case) will be correctly identified as non-diseased by the test"[12]. Colonoscopy has a sensitivity of 85% to 95% [39-41] and a specificity of 99% to 100%[42-44].

Adenoma detection is the entire process of identifying and removing polyps during colonoscopy that are subsequently found to be adenomatous (a precursor for CRC) on examination by a pathologist. It is believed that hyperplastic polyps have no potential to evolve into CRC. Variation in ADR between endoscopists has been of interest with recent studies suggesting that colonoscopy is protective for CRC on the left as opposed to right side of the colon[9, 44, 45]. Factors that affect adenoma detection include polyp size, where the sensitivity of colonoscopy

decreased as the polyp size decreased with an overall miss rate of 20% to 24%[46, 47] and a tendency to miss adenomas in the right colon compared to the left side, 27% and 21% respectively. This has also been reproduced in studies comparing CTC to colonoscopy and found that the miss rate of colonoscopy for polyps greater than 10mm in size was from 2% to 12% [39, 40, 48]. This miss rate is a compound of different factors that will be discussed.

The optimal polyp detection rate for colonoscopy is 44%[49] and the ADR, defined as the proportion of patients undergoing colonoscopy and found to have adenomas on histological examination, is 22% to 25% [50-52] based on large cohort studies.

2.6 Instruments and techniques for colonoscopy

Multiple technologies and techniques have been added to colonoscopy with the intent of improving the sensitivity of colonoscopy (Table 2.2). However, when compared to conventional colonoscopy [53-63], they either had no impact on the ADR or had limitations that rendered them impractical; these included extra time spent performing these advanced colonoscopic techniques or the costs and specialized expertise needed.

Table 2.2 Colonoscopy image-enhancing techniques

Colonoscopy image enhancing techniques
Wide angle viewing scope
Fujinon intelligent chromoendoscopy (FICE) system
Chromoendoscopy
Narrow band imaging
Tissue spectroscopy
Magnifying colonoscopy
Third eye retroscope

2.7 Impact of screening on CRC incidence

In 1993 The National Polyp Study[26] found that colonoscopy reduced the incidence of CRC by up to 90%. Although other studies demonstrated a reduction in the incidence of CRC with the use of colonoscopy[28, 64-66] none replicated the magnitude of the National polyp study[67, 68]. Reasons for the discrepancies might be related to methodological issues as the investigators in the National polyp study had used historical control groups, where the intervention group (polypectomy) was conducted between 1980 and 1990 while the reference groups were from the mayo clinic (1965 to 1970), St. Mark's hospital (1957 to 1980), and the Surveillance, Epidemiology, and End Results (SEER) program (1983 to 1987)[26]. A decrease in mortality rates from CRC has been associated with the increase in the utilization of colonoscopy services[69]. On a population basis, one ecologic study found that every 1% increase in the rate of screening colonoscopy was associated with a 3% decrease in risk of death from CRC [70].

Two Canadian studies from Ontario[9] and Manitoba[71] demonstrated that although there was a reduced risk of dying of CRC in patients undergoing attempted colonoscopy, this reduction in death rate was from left- as opposed to right-sided CRC, which might be due to incomplete colonoscopies or poor bowel preparation quality on the right side compared to the left.

Evaluating the impact of colonoscopy on CRC incidence and mortality has been hampered by the lack of randomized controlled trials that compare colonoscopy to either other CRC screening modalities or no screening[72].

2.8 Adenoma detection rates (ADR)

ADR is defined as the proportion of all patients undergoing colonoscopy who are found to have adenomas on histological examination and is the definition we used in this study. Advanced adenomas are defined as those that are ≥ 10 mm in size, or that are histologically described as villous or

have high grade dysplasia[73], these are all features that the adenoma is at high risk of becoming a cancer.

The ADR for the individual endoscopist was found to be inversely related incidence of interval CRC, that is the development of CRC in the period between the initial colonoscopy and the scheduled repeat colonoscopy[74].

2.9 Variability in colonoscopy performance

Colonoscopy as a screening tool for detecting pre-cancerous and cancerous lesions is variable as evidenced by the incidence of CRC in patients who had undergone screening colonoscopies and were deemed free from polyps and were supposed to have a repeated screening colonoscopy at a latter date[9, 67, 75]. The factors leading to these "failures", or what has been called "interval CRC", are numerous and will be elaborated on.

A common issue in a number of these studies is that colonoscopy is used as its own reference standard; this has been challenged when colonoscopy is compared to CTC[76].

2.10 Quality indicators in screening colonoscopy

With the aim of establishing a standardized system for colonoscopy performance, the Quality Assurance Task Group of the National Colorectal Cancer Roundtable[77] set forth a number of benchmarks that have been collectively called "Quality Indicators" (Table 2.3). In the United States, some of these benchmarks, such as the ADR and cecal intubation rate, are being advocated as endpoints that should be reported for colonoscopy reimbursement purposes[78].

2.11 What affects the ADR?

Several variables related to the colonoscopy are identified in the literature as impacting the ADR (Table 2.4)

Table 2.3 Quality indicators endorsed by the Quality Assurance Task Group of the National Colorectal Cancer Roundtable [77]

Colonoscopy report
Patient demographics and history
Assessment of patient risk and comorbidity
Procedure indication(s)
Procedure technical description
Colonoscopic finding
Assessment
Intervention/unplanned events
Follow-up plan
Pathology
Benchmarks that are used in quality audits
Bowel preparation quality: percent adequate to detect polyps > 5 mm
Cecal intubation rate
Rate of photodocumentation of cecal landmarks
Mean colonoscopic withdrawal time in patients without polypectomy or biopsy
Adenoma detection rate in first time screening examination based on patients sex
Adverse or unplanned events occurring within 24 hours of colonoscopy
Rates of: hospitalization, bleeding requiring transfusion, bleeding requiring unplanned endoscopic intervention, perforation, and surgery.
Rate of documentation of recommendations for follow up

Table 2.4 Factors affecting the adenoma detection rate

Factors affecting the adenoma detection rate	
Patient	Age
	Sex
	Family history of CRC
	Lifestyle (obesity and diet)
	Socioeconomic status
	Smoking
	Dietary habits
	Primary care physician
Colonoscopy	Level of difficulty of the colonoscopy
	Quality of the bowel preparation
	Cecal intubation
	Withdrawal time
	Size and position of the polyp
	Specialty of the endoscopist
	Experience of the assisting nurse
	Timing of the colonoscopy
	Level of sedation
Physician	Specialty
	Age
	Sex
Nurse	Experience in assisting in the colonoscopy

2.11.1 Patient factors

Numerous risk factors are associated with an increased risk for developing adenomas. Increasing age and male gender[51, 79] are associated with increased risks for adenomas with males having double the rate compared to females[80] . Other risk factors include, family history of CRC (OR 1.62, 95% CI 1.16-2.26)[81], increased abdominal visceral adipose tissue (central obesity) or increased body mass index[79, 82, 83], cigarette smoking [83-85], dietary habits (amount of fiber intake, energy percentage from fat, red and processed meat, and fruits and vegetables)[83].

Colonoscopy factors

2.11.2 Level of sedation

Colonoscopy in North America is performed under conscious sedation, defined as a level of sedation between being conscious and unconscious. Medications are administered intravenously prior to the start of the colonoscopy with the aim of decreasing discomfort; additional medication is administered intra-procedurally at the discretion of the endoscopist. The administration of conscious sedation is associated with an increased rate of cecal intubation and polyp detection [86].

2.11.3 Level of difficulty of the colonoscopy

Each endoscopist subjectively assesses the level of difficulty in performing the colonoscopy. Assessments are confounded by other factors including adequacy of sedation and quality of the bowl preparation prior to colonoscopy.

2.11.4 Quality of the bowel preparation

The quality of the bowel preparation is gauged by the endoscopist's ability to visualize the lining of the colon. When the quality of the bowel preparation is poor, visualization of the colonic mucosa is impaired by the

colonic contents. It has been demonstrated that the quality of the bowel preparation affects the ADR[87-89] although it seems to affect detection of smaller polyps (≤ 9mm) as opposed to larger ones (OR 1.23 95% CI, 1.19 - 1.28)[88]. Poor quality preparations are more often encountered in elderly and hospitalized patients[89]. The quality of the bowel preparation is commonly described by the endoscopist using a scoring system described in table 2.5[90]

Table 2.5 The "Boston Bowel Preparation Scale" scoring system used for the description of the quality of the bowel preparation during colonoscopy[90].

Score	Description
0	Unprepared colon segment with mucosa not seen due to solid stool that cannot be cleared.
1	Portion of mucosa of the colon segment seen, but other areas of the colon segment not well seen due to staining, residual stool and/or opaque liquid.
2	Minor amount of residual staining, small fragments of stool and/or opaque liquid, but mucosa of colon segment seen well.
3	Entire mucosa of colon segment seen well with no residual staining, small fragments of stool or opaque liquid

2.11.5 Cecal intubation

Cecal intubation is defined as passing the colonoscope beyond the iliocecal valve and visualizing the cecum. Reaching the cecum implies completion of the colonoscopy. A complete colonoscopy is achieved in 97%[23, 91] of patients undergoing screening colonoscopy.

2.11.6 Photo-documentation of the cecum

A photographic still image of the cecum provides good evidence that a complete examination of the colon was performed.

2.11.7 Withdrawal time

The withdrawal time is defined as the number of minutes it takes to withdraw the colonoscope from the cecum to the anal verge and calculated as the mean number of minutes per colonoscopy. Withdrawal time has been studied extensively[49, 50, 92-94],and found to be associated with the ADR with those taking on average more than 6 minutes detecting adenomas more than those with a mean time of less than 6 minutes (28.3% vs. 11.8%)[50].

Although withdrawal time was associated with an increased ADR, this was not associated with a decreased incidence of advanced neoplasia or cancer, in the following 5 years[95].

2.11.8 The size, shape, and position of the polyps

A meta-analysis that had included studies where two colonoscopies were performed on the same individuals on the same day found that miss rate for polyps of any size was 22% (Table 2.6)[96].

A study utilizing a new enhancing visual accessory (third eye retroscope) increased the adenomas detected by 11%[97], this increase in adenoma detection is thought to be because of polyps and adenomas on the proximal side of colonic folds that are difficult to examine by conventional colonoscopy, this is supported by the finding of a 12% miss rate by colonoscopy for adenomas when compared to CTC[76], the majority of these were on the proximal side of colonic folds. Flat polyps are more difficult to identify and at the same time might have a different biology[98].

Table 2.6 the sensitivity of colonoscopy decreases as the size of the polyps decrease

Size of adenoma	Miss rate OR (95%CI)
Any size	22% (19% to 26%)
1-5 mm	26% (27% to 35%)
5-10 mm	13% (8% to 18%)
≥ 1 cm	2.1% (0.3% to 7.3%)

Physician factors

2.11.9 Endoscopist characteristics

Endoscopists vary widely in their ADR[80, 99-102] and rates of complications from performing a lower endoscopy[103, 104]. Variation might be related to age and sex of the endoscopist[100]. Specialty may also influence the ADR since the incidence of CRC following a negative colonoscopy was higher in colonoscopies performed by non-gastroenterologist compared to gastroenterologist[105]. The rate for subsequent CRC was higher when the index colonoscopy was performed by a surgeon (the hazard ratio (HR) 1.39, (95%CI, 1.16 to 1.67) [106].

2.11.10 The nurse assisting the endoscopist during the colonoscopy

Number of years of experience for endoscopy nurses assisting with the colonoscopy effects the colonoscopy quality and even polyp detection rates but not ADR[52].

2.11.11 The timing and sequence of colonoscopies performed

There is a higher probability of incomplete colonoscopies OR 1.64 (95%CI, 1.11 to 2.44) and inadequate bowl preparation in screening colonoscopies performed in the afternoon compared to those performed in the morning [108, 109]. The ADR also has been found to be higher in colonoscopies performed in the morning OR 1.2 (95% CI, 1.06 - 1.4) with a trend in decreasing ADR with each hour [110], these finding were

reproduced in a second study[111]. In a study where endoscopists performed endoscopies on a three shift per day pattern, the timing of the colonoscopy had no impact on the polyp detection rate[112]. These findings might imply that the timing of the endoscopy session does not have an effect on polyp detection but rather the length of the endoscopy session, and that endoscopists start to fatigue with increased time spent performing endoscopic procedures.

2.12 Summary

Although CRC carries significant morbidity and mortality and affects a large segment of the population, screening may prevent it. Colonoscopy has emerged as the preferred CRC screening modality given its diagnostic and therapeutic potential and impact on the incidence of CRC but it is associated with non-negligible risks for complications related to the bowel cleansing preparation, the colonoscopy itself and the medication administered during colonoscopy. Furthermore, many factors affect its diagnostic accuracy and in particular the ADR. For these reasons quality indicators have been proposed by gastrointestinal societies with the aim of achieving a common standard for the test performance of colonoscopy.

Thus, we aimed to evaluate the influence of different factors on adenoma detection during screening colonoscopy and to examine the relationship between the numbers of: hours, endoscopies (gastroscopies and colonoscopies) and colonoscopies the endoscopist worked/performed prior to the index colonoscopy and adenoma detection.

CHAPTER III: METHODS

3.1 Objectives

The objectives of the present study were:

1) The overall study objective is to identify variables that are associated with adenoma detection (Table 3.1).
2) More specifically, we sought to examine the relationships between the adenoma detection rate and factors that likely impact it including: hours worked and number of procedures performed by the endoscopist on the day of the procedure prior to the index colonoscopy and adenoma detection.

3.2 Hypothesis

We hypothesized that increasing the number of hours worked and number of procedures performed prior to the index colonoscopy time per endoscopy session would be associated with decreased adenoma detection.

3.3 Study design and site

A retrospective cohort study was conducted using an endoscopy report database of individuals seen at the Montreal General Hospital (MGH) campus of the McGill University Health Center (MUHC), Montreal, Canada, a major tertiary care hospital in Montreal. Both surgeons and gastroenterologists staff the endoscopy service. On average, 11,000 colonoscopies and gastroscopies are performed annually, of which 75% were colonoscopies in 2008.

3.4 Study population

The study population included consecutive individuals who underwent CRC screening colonoscopy from June 1st until August 25th 2009. For the

purposes of this study, only individuals with Endoworks-generated colonoscopy reports were included. Excluded were individuals who underwent flexible sigmoidoscopy or colonoscopy where the indication was not CRC screening (e.g. bleeding, anemia, weight loss).

3.5 Endoscopy database

Endoworks is a computerized system that generates endoscopy reports and is capable of capturing endoscopic still images and videos (Endoworks, Olympus Corporation, Center valley, PA, USA); it is used for colonoscopies that are performed during regular working hours, Monday to Friday, from 8 am till 4 pm. Endoworks allows for capture of the immediate intra-colonoscopy unplanned events but not the down stream complications such as post polypectomy bleeding that can occur a few days after the colonoscopy.

Each endoscopist upon completion of the colonoscopy, enters data into the computer report that is electronically transmitted to a central data repository housed at the MUHC-MGH where it is kept secure. The endoscopy report has default fields that the endoscopist may either approve or choose from alternative options by drop down menu or by entering free text. Data include the patient's medical history as well as colonoscopy details including the type and amount of sedation administered, the comfort level of the patient during the colonoscopy, the quality of the colonoscopy preparation and the details of the colonoscopy (any abnormal findings, therapeutic or diagnostic interventions performed).

3.6 Pathology reports

Pathologists specialized in gastrointestinal pathology examined the histology of tissue/polyps obtained during colonoscopy and generated electronic reports that were stored in OACIS is an institutional electronic reporting data system.

3.7 Data abstraction

Three trained research assistants abstracted data from the Endoworks-generated colonoscopy reports of procedures that were performed during the study period as well as from the corresponding OACIS pathology reports. The research assistants entered the abstracted data into an electronic database (Microsoft Access).

3.8 Data sources and variables of interest

From the Endoworks generated endoscopy reports we obtained patient age, sex, family history of CRC, previous colonoscopy, prior polyp removal, CRC risk based on the endoscopist's judgment and knowledge of the patient's history. Events related to the colonoscopy were obtained including the number of polyps detected. The location and shape of polyps. In addition to cecal intubation, photo-documentation of the cecum, and incomplete colonoscopies. For incomplete colonoscopy (a procedure that fails to reach the cecum), the reason and the level of the colon reached were included. Quality of the bowel preparation was based on the endoscopist's subjective evaluation and was selected from a drop down menu in Endoworks; no scoring system was used although at least two are described in the litrature[90, 113]. In addition the time spent by the endoscopist performing endoscopies (gastroscopies and colonoscopies) from the start of the endoscopy session and until the index colonoscopy, the number of colonoscopies, and the number of endoscopic procedures prior to the index colonoscopy were recorded. Colonoscopies that were performed between 8:00 and 12:00 were considered morning and those performed after 12:00 were considered afternoon.

From OACIS, data were obtained on whether the polyp removed was an adenoma or not.

Table 3.1 Variables of interest.

	Source of data	Variables of interest	Category	Values
Patient	Endoworks	Sex	Binary	Male Female
		Age	Continuous	Years
		Previous colonoscopy	Binary	Yes No
		Prior polyp removal	Binary	Yes No
		Average risk for CRC	Binary	Yes No
		Family history of CRC	Nominal	Yes No HNPCC FAP
Colonoscopy		Incomplete colonoscopy	Binary	Yes No
		Cecal intubation	Binary	Yes No
		Photo-documentation of the cecum	Binary	Yes No
		Level reached	Ordinal	Sigmoid Descending Transverse Ascending Not mentioned
		Reason for an incomplete exam	Nominal	Inadequate preparation

		Technical difficulty Poor patient tolerance Not mentioned
Quality of the bowel preparation	Ordinal	Good Fair Poor Not mentioned
Number of polyps detected	Continuous	Discrete
Location of polyps removed	Nominal	Rectum Recto-sigmoid Sigmoid Descending Splenic flexure Transverse Hepatic flexure Ascending Cecum Ileocecal valve Not mentioned
Shape of the polyps detected	Nominal	Sessile Pedunculated Not mentioned
Number of tattoos performed to mark sites of suspicious polyps	Continuous	Discrete
Specialty of the endoscopist	Binary	Gastroenterology Surgery
Number of	Continuous	Discrete

		minutes to the beginning of the index colonoscopy		
		Number of endoscopies prior to index colonoscopy	Continuous	Discrete
		Number of colonoscopies prior to index colonoscopy	Continuous	Discrete
		Colonoscopy occurence	Nominal	Morning Afternoon Not mentioned
	OACIS	Number of adenomas detected	Continuous	Discrete
		Number of advanced adenomas	Continuous	Discrete
		Number of cancers detected	Continuous	Discrete

3.9 Outcome variable

Adenoma detection, a binary variable, was based on the pathology report, and defined as a colonoscopy where at least one adenoma was detected i.e. if a single adenoma was detected during a screening colonoscopy that would be as a positive outcome.

3.10 Sample size calculation

Sample size calculation was based on a baseline adenoma occurrence in the population of 25%, an *a priori* set confidence interval width of +/- 4%, and a 95%confidence level. We used the formula below:

Sample size = $(Z^2 \times P \times (1-P)/C^2$

Where Z = 1.96 for a confidence level 95%

P = proportion of the outcome variable of interest (adenoma)

C = confidence interval width (here +/- 0.04)

We calculated a needed sample size of 450 patients.

3.11 Institution approval

The Institutional Review Board at the McGill University Health Center approved the study.

3.12 Method of data analysis

Descriptive statistics were computed for continuous variables, means, standard deviations and minimum and maximum values were used; for categorical variables frequencies and interquartile ranges were used. Descriptive plots were used to illustrate bivariate relationships between selected independent variables and adenoma detection. Univariable and multivariable logistic regression were used to examine the association between independent variables and adenoma detection. Odds ratios (OR) and 95% confidence intervals (CI) were estimated. We examined how odds ratios changed as terms were added or subtracted from the model in order to identify any confounding between variables. We used the software R[114] in our analysis.

A secondary analysis restricted to average risk individuals was performed to compare our results to those in the literature.

CHAPTER IV: RESULTS

Over the 12-week period from June 1st and until August 25th 2009, we identified 450 consecutive eligible patients who underwent screening colonoscopy. There were 20 duplicate entries that were excluded leaving a final sample size of 430 colonoscopy reports.

4.1 Descriptive statistics

The characteristics of the 430 patients included in this study are displayed in Table 4.1. Mean age was 63.4 (SD= 10.9) years, there was a higher proportion of males compared to females 56.3% (95%CI, 51.4 to 61.0) vs. 43.7% (95%CI, 39.0 to 48.6) respectively, and 18.6% (95%CI, 15.0 to 22.6) had a prior colonoscopy of whom 71.3% had a prior polypectomy. In total, 49.3% (95%CI, 44.5 to 54.1) of patients were at average risk for CRC while 50.7% (95%CI, 45.9 to 55.5) were at increased risk, 16% (95%CI, 12.7 to 19.9) had a family history of CRC, 3 (0.7%) individuals with hereditary nonpolyposis CRC (HNPCC), and 4 (0.9%) patients with familial adenomatous polyposis (FAP).

The mean time from the beginning of the endoscopy session to the index colonoscopy was 164 minutes (95%CI, 151.8 to 175.6) (range 0 to 450 minutes), the mean number of endoscopic procedures (gastroscopies and colonoscopies) prior to the index colonoscopy was 5.3 (95%CI, 4.9 to 5.7) endoscopies and 3.8 (95%CI, 3.4 to 4.10) colonoscopies. The majority of the colonoscopies were performed in the morning 70.9% (95%CI, 66.4 to 75.2).

Over the study period the total number of colonoscopies performed by each physician ranged from 7 to 76 with a mean of 43 colonoscopies and the ADR varied from 15% to 48.5% with a mean of 27% (Table 4.2).

Table 4.1 Patient and colonoscopy characteristics

Variable	Frequency (N=430)	Percentage/mean (95%CI)
Gender of patients		
Male	242	56.3 (51.4 to 61.0)
Female	188	43.7 (39.0 to 48.6)
Age in years (mean)	NA	63.4 (62.4 to 64.4)
Previous colonoscopy		
Yes	80	18.6 (15.0 to 22.6)
No	350	81.4 (77.4 to 85.0)
Previous polyp removal		
Yes	57	13.3 (10.2 to 16.8)
No	373	86.7 (83.2 to 89.8)
Average risk		
Yes	212	49.3 (44.5 to 54.1)
No	218	50.7 (45.9 to 55.5)
Family history of CRC		
Yes	69	16.0 (12.7 to 19.9)
No	361	84.0 (80.1 to 87.3)
HNPCC	3	0.7 (0.1 to 2.0)
FAP	4	0.9 (0.3 to 2.4)
Colonoscopy variables		
Minutes to the beginning of the index colonoscopy (mean)	NA	163.7 (151.8 to 175.6)
Number of endoscopies prior to index colonoscopy (mean)	NA	5.3 (4.9 to 5.7)
Number of colonoscopies prior to index colonoscopy (mean)	NA	3.8 (3.4 to 4.10)

NA= Not applicable

Table 4.2 Description of colonoscopies per physician

Physician	Physician sex	Number of colonoscopies	Number of adenomas detected	Adenoma detection rate* (95%CI)
MD 1	Male	58	18	31.0 (19.5 to 44.5)
MD 2	Male	76	14	18.4 (10.5 to 29.0)
MD 3	Male	33	16	48.5 (30.8 to 66.5)
MD 4	Male	33	5	15.2 (1.9 to 24.3)
MD 5	Female	7	2	28.6 (3.7 to 71.0)
MD 6	Male	51	12	23.5 (12.8 to 37.5)
MD 7	Male	75	19	25.3 (16.0 to 36.7)
MD 8	Male	40	6	15 (5.7 to 29.8)
MD 9	Female	24	6	25 (9.8 to 46.7)
MD 10	Male	33	13	39.4 (22.9 to 57.9)

* Defined as the number of colonoscopies where an adenoma was detected divided by the number of colonoscopies performed (these numbers are not adjusted according to age, sex, or previous colonoscopy).

The completion rate of colonoscopies was 96.3% (95%CI, 94.0 to 97.9); cecal intubation occurred in 95.8% (95%CI, 93.5 to 97.5), although photodocumentation was available for only 72.1% (95%CI, 67.6 to 76.3). The bowel preparation quality was rated as good in 86.3% (95%CI, 82.7 to 89.4) of procedures, fair in 9.1% (95%CI, 6.5 to 12.2), poor in 3.7% (95%CI, 2.1 to 6.0), and missing in 0.9% (95%CI, 0.3 to 2.4).
Among all patients, the adenoma detection rate was 25.8% (95%CI, 21.7 to 30.2), polyp shape 83.2% (95%CI, 79.3 to 86.6), and location 68.7% (95%CI, 64.1 to 73.1) were often not described (Table 4.3).

Table 4.3 Characteristics and findings of screening colonoscopies based on Endoworks.

Variable	Frequency (N=430)	Percentage (95%CI)
Incomplete colonoscopy [a]		
Yes	16	3.7 (2.1 to 6.0)
No	414	96.3 (94.0 to 97.9)
Cecal Intubation		
Yes	412	95.8 (93.5 to 97.5)
No	18	4.2 (2.5 to 6.5)
Photo-documentation of the cecum		
Yes	310	72.1 (67.6 to 76.3)
No	120	27.9 (23.7 to 32.4)
Bowel preparation quality		
Good	371	86.3 (82.7 to 89.4)
Fair	39	9.1 (6.5 to 12.2)
Poor	16	3.7 (2.1 to 6.0)
Don't know	4	0.9 (0.3 to 2.4)
Total number of polyps	428	NA
Adenoma detected on current colonoscopy		
Yes	111	25.8 (21.7 to 30.2)
No	319	74.2 (69.8 to 78.3)
Polyp shape		
Pedunculated	17	4.0 (2.3 to 6.3)
Sessile	55	12.8 (9.8 to 16.4)
Don't know	356	83.2 (79.3 to 86.6)
Location of the polyp [b]		
Rectum	19	4.4 (2.7 to 6.8)
Recto-sigmoid junction	12	2.8 (1.5 to 4.8)
Sigmoid	32	7.5 (5.2 to 10.4)
Descending colon	13	3.0 (1.6 to 5.1)
Splenic flexure	0	0
Transverse colon	23	5.4 (3.4 to 8.0)
Hepatic flexure	4	0.9 (0.3 to 2.4)
Ascending colon	19	4.4 (2.7 to 6.8)
cecum	11	2.6 (1.3 to 4.6)
Ileocecal valve	1	0.2 (0.0 to 1.3)
Don't know	294	68.7 (64.1 to 73.1)
Tattoo	0	0
Adenomas	111	25.9 (21.8 to 30.4)
Cancer	1	0.2 (0.0 to 1.3)
Advanced adenoma	45	10.5 (7.8 to 13.8)
Timing of colonoscopy		
Morning	305	70.9 (66.4 to 75.2)
Afternoon	124	28.8 (24.6 to 33.4)
Don't know	1	0.2 (0.0 to 1.3)

a. The discrepancy between the cecal intubation rate and the colonoscopy completion rate might be related incomplete documentation.
b. The percentage is from the 428 polyps detected. Location of only 134 polyps was described.

The reasons for incomplete colonoscopies as well as the level reached are displayed in table 4.4.
Table 4.5 shows the tabulations of different variables with respect to the presence or absence of adenomas on colonoscopies.
There was a trend of increased adenoma detection in males (30.6% vs. 19.7%), in patients who were at an increased risk for CRC (30.7% vs. 20.8%), in those who had a prior polypectomy (36.8 vs. 24.1%), those who had a complete colonoscopy (26.2%, vs. 16.7%), picture documentation of the cecum (29.4% vs. 16.7%), in those who had a good quality of bowel preparation compared to those with a fair or poor quality (27.5%, 15.4%, and 12.5% respectively), colonoscopies performed in the morning (27.9% vs. 20.1%), colonoscopies performed by female endoscopist (37.5 vs. 24.6), as well as colonoscopies performed by a gastroenterologist (29.0% vs. 18.0%). But all of these findings were inconclusive as the 95% confidence intervals overlapped.
We noticed that the percentage of adenomas detected increased with the increasing number of polyps detected per-colonoscopy (Figure 4.1), and decreased abruptly after 5.5 hours from the beginning of the endoscopy session (Figure 4.2), after 9 colonoscopies (Figure 4.3), and 12 endoscopies (Figure 4.4).

Table 4.4 Reasons for an incomplete colonoscopy and the level reached in that exam.

Incomplete colonoscopy	Frequency (N= 16)	Mean (95%CI)
Level reached in the exam		
Ascending colon	6	37.5 (15.2 to 64.6)
Transverse colon	2	12.5 (1.6 to 38.3)
Sigmoid	6	37.5 (15.2 to 64.6)
Unknown	2	12.5 (1.6 to 38.3)
Reason		
Inadequate preparation quality	2	12.5 (1.6 to 38.3)
Technical difficulty	6	37.5 (15.2 to 64.6)
Poor patient tolerance	3	18.8 (4.0 to 45.6)
Not mentioned	5	31.3 (11.0 to 58.7)

Table 4.5 Variables with regard to adenoma detection and the percentage of adenomas detected.

	Adenoma (N=111)	No adenoma (N=319)	Percentage of adenomas (95%CI)
Patient sex			
Male	74	168	30.6 (24.8 to 36.8)
Female	37	151	19.7 (14.2 to 26.1)
History of colonoscopy			
Previous colonoscopy	22	58	27.5 (18.1 to 38.6)
No previous colonoscopy	89	261	25.4 (20.9 to 30.3)
Risk of CRC			
Average risk	44	168	20.8 (15.5 to 26.8)
Increased risk	67	151	30.7 (24.7 to 37.3)
Family history of CRC			
Family history	18	51	26.1 (16.3 to 38.1)
No family history	93	268	25.8 (21.3 to 30.6)
History of prior polypectomy			
Previous polypectomy	21	36	36.8 (24.4 to 50.7)
No previous polypectomy	90	283	24.1 (19.9 to 28.8)
Colonoscopy extent			
Complete colonoscopy	108	304	26.2 (22.0 to 30.7)
Incomplete colonoscopy	3	16	18.8 (4.0 to 45.6)
Preparation quality			
Good	102	269	27.5 (23.0 to 32.3)
Fair	6	33	15.4 (5.8 to 30.5)
Poor	2	14	12.5 (1.6 to 38.3)
Don’t know	1	3	25 (0.6 to 80.6)

Picture documentation of the cecum			
Documented	91	219	29.4 (24.3 to 34.8)
Not documented	20	100	16.7 (10.5 to 24.6)
Shape of the polyp			
Pedunculated polyp	15	2	88.2 (63.6 to 98.5)
Sessile polyp	29	26	52.7 (38.8 to 66.3)
Not described	67	291	18.7 (14.8 to 23.1)
Timing of endoscopy			
Morning session	85	220	27.9 (22.9 to 33.3)
Afternoon session	25	99	20.1 (13.5 to 28.3)
Unknown	1	0	NA
Endoscopist sex			
Male	96	294	24.6 (20.4 to 29.2)
Female	15	25	37.5 (22.7 to 54.2)
Specialty of endoscopist			
Gastroenterology	91	223	29.0 (24.0 to 34.3)
Surgery	20	91	18.0 (11.4 to 26.4)

Figure 4.1 The percentage of adenomas detected increases as the number of polyps detected increases

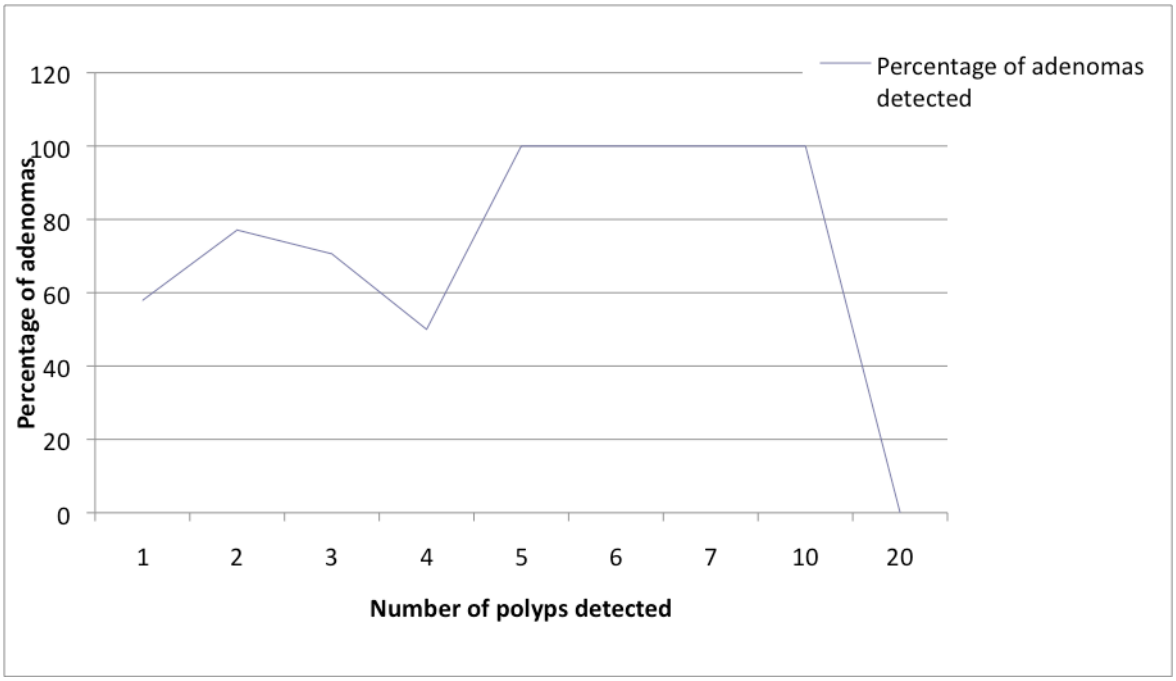


Figure 4.2 The percentage of adenomas detected decreases as the time (in hours) from the beginning of the endoscopy session increases

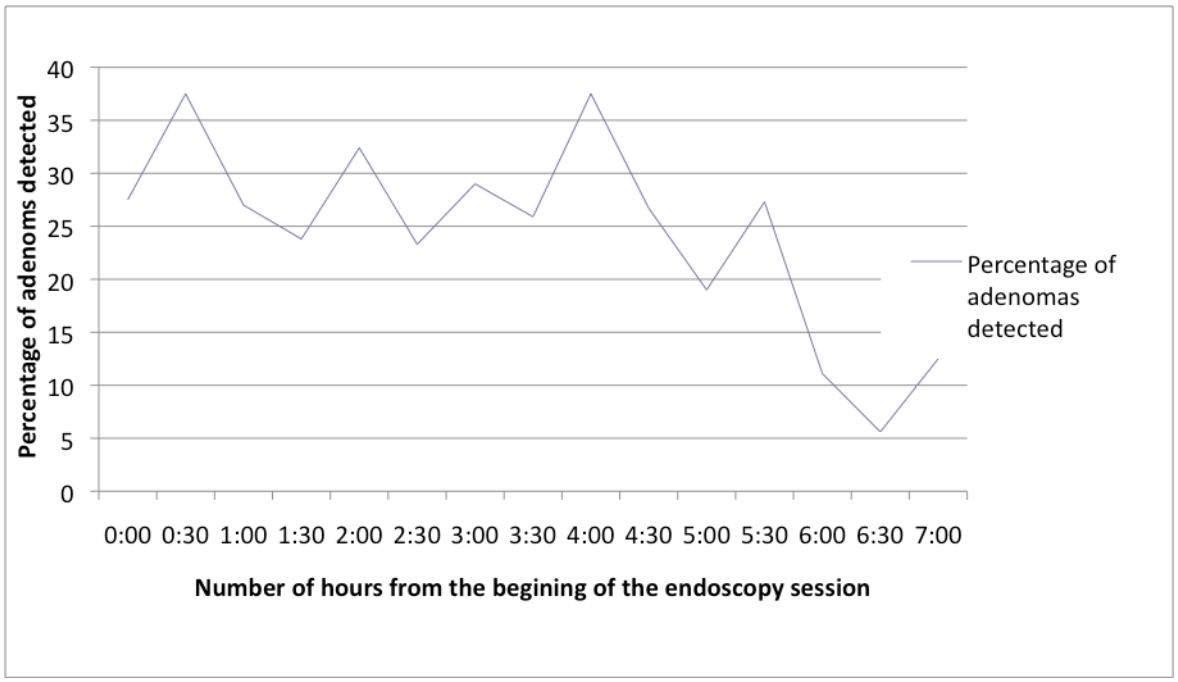


Figure 4.3 Percentage of adenomas detected in relation to the sequence of index colonoscopy in relation to the number of colonoscopies

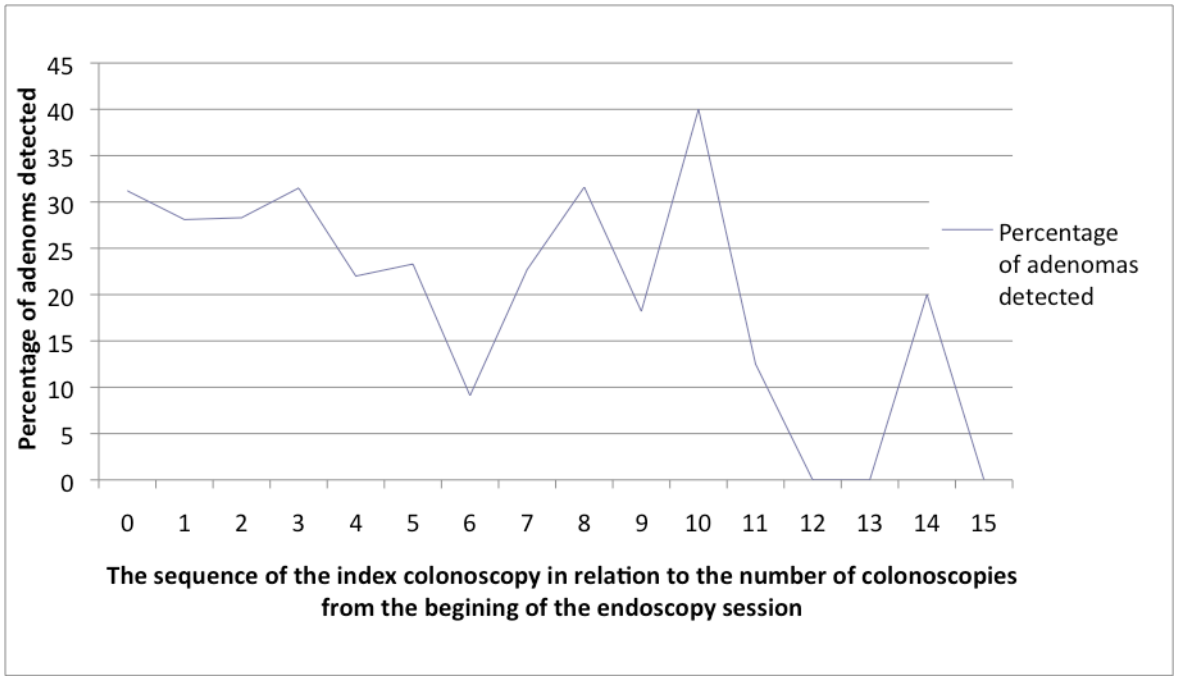
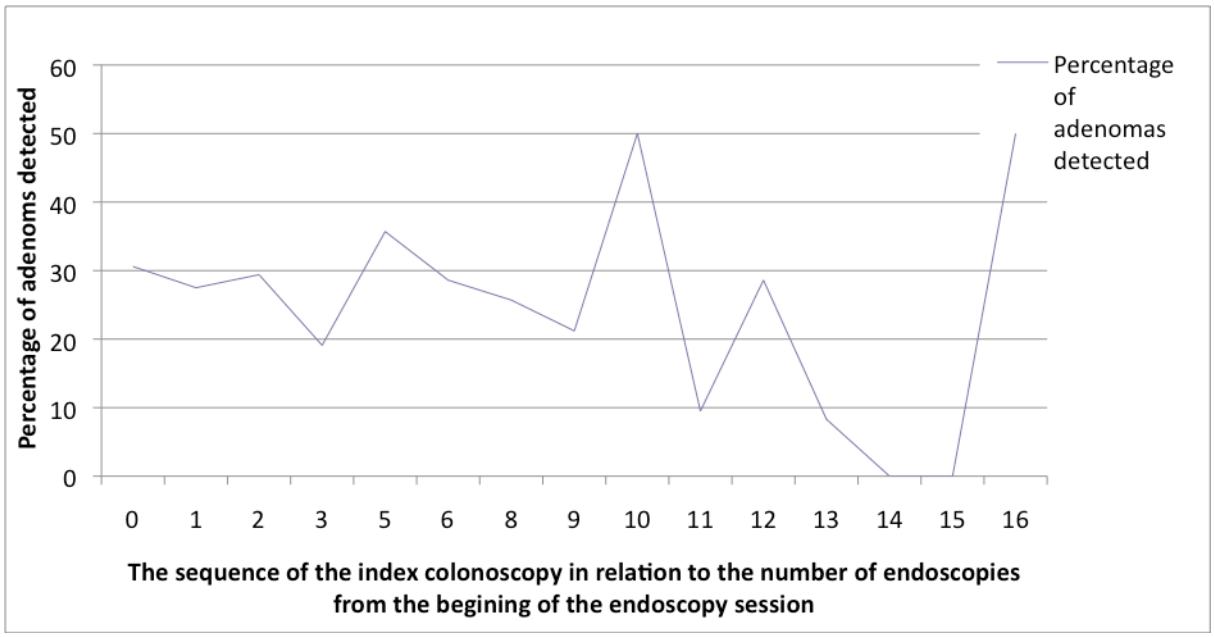


Figure 4.4 Percentage of adenomas detected in relation to the sequence of index colonoscopy in relation to the number of endoscopies


Percentage of adenoms detected
60
50
40
30
20
10
0
0 1 2 3 5 6 8 9 10 11 12 13 14 15 16
Percentage of adenomas detected
The sequence of the index colonoscopy in relation to the number of endoscopies from the begining of the endoscopy session

4.2 Examining descriptive graphs

The age of the patients who underwent screening colonoscopies was normally distributed (Figure 4.5). Male endoscopists performed colonoscopies on a population with a much broader age span compared to female endoscopists (figure 4.6).

As the quality of the bowel preparation decreased the number of polyps detected decreased (figure 4.7). Comparing the good and poor quality of bowel preparation, the poor quality preparation colonoscopies tended to start later in the endoscopy session compared to the good quality bowel preparation (figure 4.8). Numerous other descriptive graphs are included in the appendix (chapter VI).

Using the pairs function in R (figure 4.9), we notice collinearity between minutes to endoscopy, sequence of colonoscopy in relation to all endoscopies as well as in relation to colonoscopies, which occurred because these variables are measuring a similar construct. Thus we will only use minutes to endoscopy in the following segments.

Figure 4.5 Age distribution of the patients who underwent screening colonoscopy.

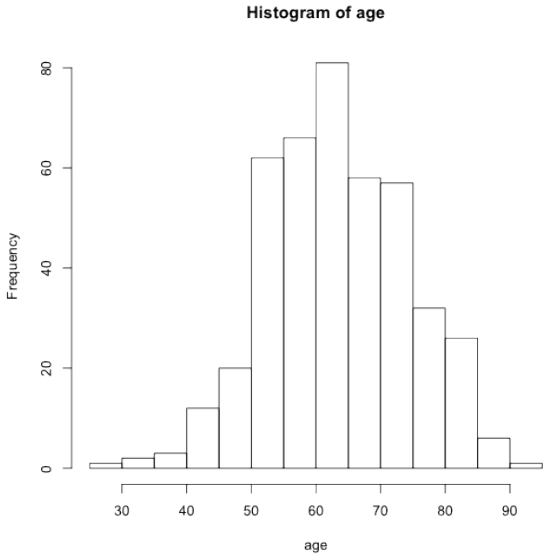


Figure 4.6 Box plot of age of patients based on the gender of the endoscopist

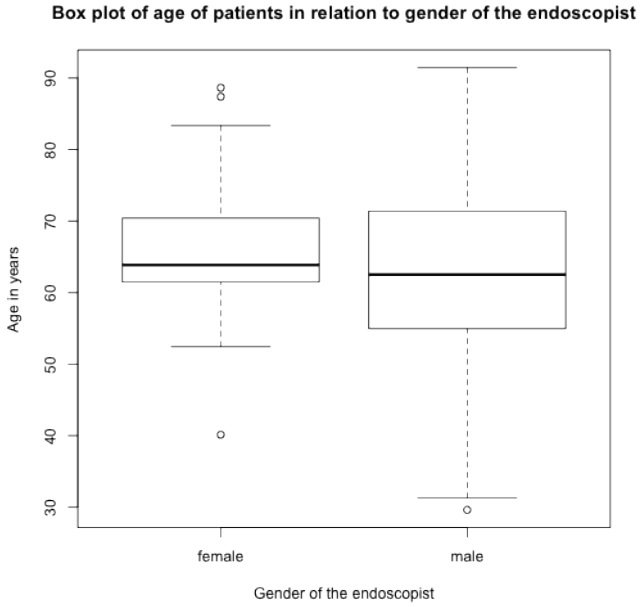


Figure 4.7 Box plot of the number of polyps detected in relation to the quality of the bowel preparation.

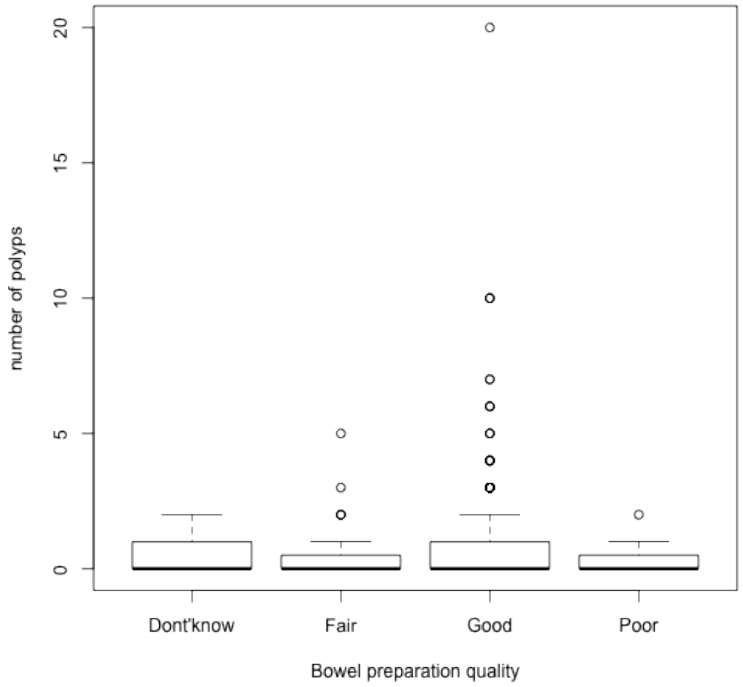


Figure 4.8 Box plot of the quality of the bowel preparation in relation to the time till the start of the index colonoscopy from the beginning of the endoscopy session.

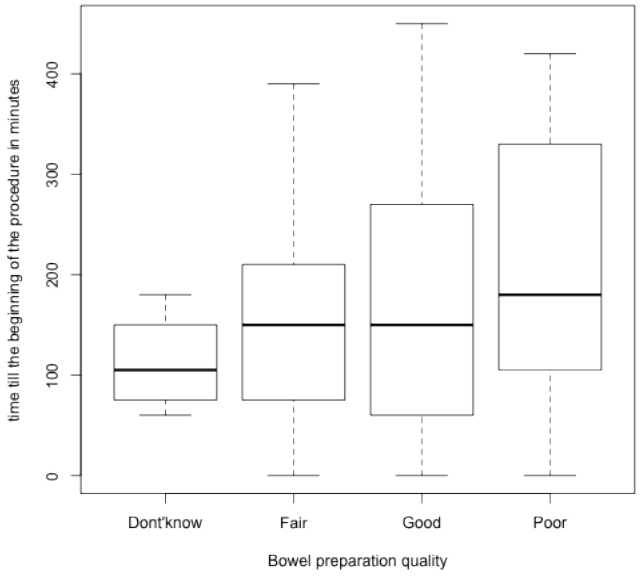
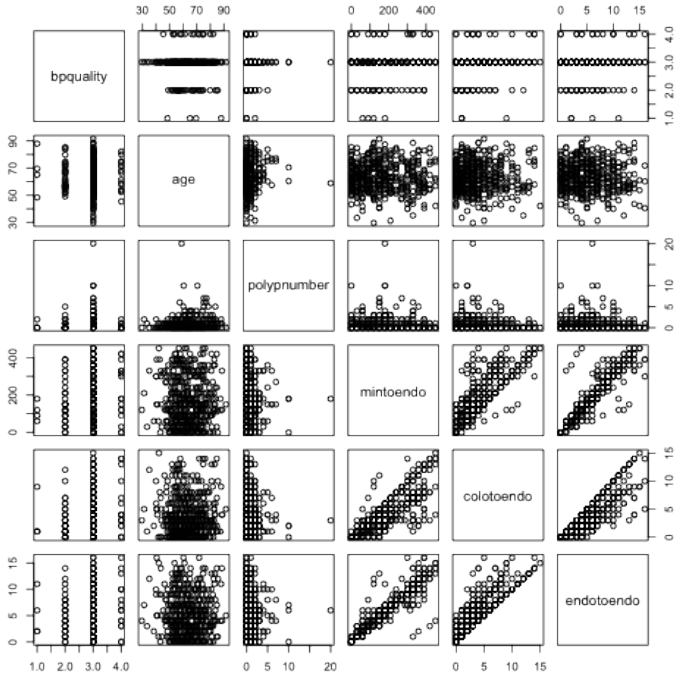


Figure 4.9 Pairs function in R to investigate confounding.



4.3 Univariable and multivariable model

Results of the univariable analysis are shown in table 4.6.

The evidence was inconclusive for the effect of prior colonoscopy (OR 1.11, 95%CI, 0.64 to 1.92), family history of CRC (OR 1.02, 95%CI, 0.57 to 1.83), incomplete colonoscopy (OR 1.44, 95%CI, 0.13 to 16.05), cecal intubation (OR 1.78, 95%CI, 0.50 to 6.26), quality of the bowel preparation, and endoscopist sex (OR 0.54, 95%CI, 0.28 to 1.07) on the detection of adenomas. There was an increased odds of detecting adenomas when the patient was male (OR 1.80, 95%CI, 1.14 to 2.82), for every 1-year increase in age (OR 1.04, 95%CI, 1.02 to 1.06), previous polyp removal (OR 1.83, 95%CI, 1.02 to 3.30), photo-documentation of the cecum (OR 2.08, 95%CI, 1.21 to 3.56), and with increasing number of polyps (OR 3.74, 95%CI, 2.76 to 5.06). The detection of adenomas was decreased in patients who were at average risk for CRC (OR 0.59, 95%CI,

0.38 to 0.92), with each increased hour from the beginning of the endoscopy session to the index colonoscopy (OR 0.87, 95%CI, 0.78 to 0.97), with each colonoscopy performed prior to the index colonoscopy (OR 0.93, 95%CI, 0.87 to 0.99), with each endoscopy (colonoscopy and gastroscopy) prior to the index colonoscopy (OR 0.95, 95%CI, 0.90 to 1.00), and when the colonoscopy was performed by a surgeon (OR 0.51, 95%CI, 0.30 to 0.88).

When multivariable modeling was conducted all the point estimates as well as the confidence intervals changed and in general got substantially wider suggesting confounding (table 4.6).

We used the BIC command in R to create formatted output to compare coefficients between different models and found confounding between:

1- Male gender and family history.
2- Male gender and average risk.
3- Age and polyp number.
4- Age and family history.

When the analysis was limited to average risk patients only (212), there was an increased odds of detecting adenomas when the patient was male (OR 2.74, 95%CI, 1.27 to 5.91), for every 1-year increase in age (OR 1.06, 95%CI, 1.02 to 1.11), and with increasing number of polyps (OR 2.14, 95%CI, 1.56 to 2.93). The detection of adenomas was decreased with every colonoscopy performed prior to the index colonoscopy (OR 0.84, 95%CI, 0.74 to 0.95), with each endoscopy (colonoscopy and gastroscopy) prior to the index colonoscopy (OR 0.88, 95%CI, 0.80 to 0.97), and with each increased hour from the beginning of the endoscopy session to the index colonoscopy (OR 0.80, 95%CI, 0.67 to 0.95).

When the analysis is restricted to average risk individuals on multivariate analysis, male gender was associated with increased adenoma detection OR 3.52 (95%CI, 1.31 to 9.42) and the risk associated with increasing number of polyps detected was less pronounced OR 2,14 (95%CI, 1.44 to

3,19) and the effect of the number of hours till the index colonoscopy was inconclusive OR 0.67 (95%CI, 0.33 to 1.27) (table 4.7).

Table 4.6 Results of univariable and multivariable modeling for detection of at least one adenoma on screening colonoscopy. (N= 430)

Variable	Univariable models Odds ratios	Multivariate model Adjusted odds ratios
Male patient	1.80 (1.14 to 2.82)	1.67 (0.91 to 3.04)
Age	1.04 (1.02 to 1.06)	1.04 (1.02 to 1.07)
Prior colonoscopy	1.11 (0.64 to 1.92)	0.67 (0.28 to 1.59)
Average risk	0.59 (0.38 to 0.92)	0.71 (0.33 to 1.50)
Family history	1.02 (0.57 to 1.83)	1.89 (0.72 to 4.89)
Incomplete colonoscopy	1.44 (0.13 to 16.05)	1.36 (0.03 to 57.86)
Previous polyp removed	1.83 (1.02 to 3.30)	1.60 (0.58 to 4.43)
Cecum intubated	1.78 (0.50 to 6.26)	1.10 (0.20 to 5.99)
Bowel preparation quality		
Good	1.14 (0.12 to 11.06)	2.17 (0.07 to 67.48)
Fair	0.55 (0.05 to 6.16)	1.31 (0.04 to 47.08)
Poor	0.43 (0.03 to 6.41)	1.21 (0.03 to 57.07)
Photo-documentation of the cecum	2.08 (1.21 to 3.56)	0.92 (0.39 to 2.19)
Polyp number	3.74 (2.76 to 5.06)	3.71 (2.70 to 5.10)
Time to colonoscopy		
Hours to colonoscopy	0.87 (0.78 to 0.97)	0.51 (0.31 to 0.79)
Number of colonoscopies to the index colonoscopy	0.93 (0.87 to 0.99)	0.99 (0.81 to 1.21)
Number of endoscopic procedures to the index colonoscopy	0.95 (0.90 to 1.00)	1.18 (0.91 to 1.52)
Endoscopy in the morning	4.96 e-07 (0 to Inf)	0.32 (0.10 to 1.04)
Male endoscopist	0.54 (0.28 to 1.07)	0.65 (0.25 to 1.65)
Surgical specialty of endoscopist	0.51 (0.30 to 0.88)	0.89 (0.38 to 2.06)

Table 4.7 Results of univariable and multivariable modeling for detection of an adenoma on screening colonoscopy when the analysis was restricted to average risk patients (N= 212).

Variable	Univariable models Odds ratios	Multivariate model Adjusted odds ratios
Male patient	2.74 (1.27 to 5.91)	3.52 (1.31 to 9.42)
Age	1.06 (1.02 to 1.11)	1.10 (1.04 to 1.16)
Prior colonoscopy	1.40 (0.55 to 3.56)	1.09 (0.29 to 4.09)
Previous polyp removed	8275680 (0 to Inf)	1.11 e+6 (0 to Inf)
Cecum intubated	1.19 (0.25 to 5.71)	0.70(0.06 to 7.65)
Bowel preparation quality		
Good	6.04 (0.79 to 46.37)	2.94 (0.34 to 25.38)
Poor	2.22 (0.12 to 39.63)	2.74 (0.10 to 76.97)
Photo-documentation of the cecum	2.02 (0.88 to 4.64)	2.25 (0.57 to 8.91)
Polyp number	2.14 (1.56 to 2.93)	2.14 (1.44 to 3.19)
Time to colonoscopy		
Hours to colonoscopy	0.80 (0.67 to 0.95)	0.67 (0.33 to 1.27)
Number of colonoscopies to the index colonoscopy	0.84 (0.74 to 0.95)	0.92 (0.64 to 1.32)
Number of endoscopic procedures to the index colonoscopy	0.88 (0.80 to 0.97)	0.93 (0.65 to 1.35)
Endoscopy in the morning	1.94 (0.87 to 4.32)	0.23 (0.03 to 1.65)
Male endoscopist	0.41 (0.16 to 1.05)	0.43 (0.11 to 1.59)
Surgical specialty of endoscopist	0.76 (0.35 to 1.65)	2.76 (0.76 to 10.00)

CHAPTER V: DISCUSSION

5.1 Discussion

Gastrointestinal endoscopy is essential to digestive health care and CRC screening is a large component of that care with significant resources allocated to it. This study aimed to identify variables related to adenoma detection on screening colonoscopy in order to optimize the detection of adenomas and, thereby, improve colonoscopy as a screening tool for CRC. The age range of patients included in our study was wider than that recommended for average risk screening due to including patients at increased risk for CRC.

We found that fewer polyps and adenomas were detected as the time to the index colonoscopy increased, this might be due to operator fatigue, pressure for keeping the procedure scheduling on time, poorer bowel preparation or a combination of these factors. Our results are in keeping with those of prior studies showing that the polyp detection rate decreased with time[111]. For example, in one study insertion time, defined as time spent from the introduction of the colonoscope through the anus until reaching the end of the colon, increased as time progressed from the beginning of the endoscopy session[115], suggesting endoscopist fatigue. Because the majority of the patients in our study received conscious sedation, we did not evaluate this factor because of the lack of variability.

A study found that deep sedation was associated with an increased detection of polyps > 9 mm in size, the calculated number needed to screen for the detection of an advanced lesion would be 141 patients under deep sedation, which was not clinically acceptable given the risks associated with the administration of deep sedation by the endoscopist, or the cost associated with the involvement of an anesthesiologist[116]. We could not evaluate the level of sedation achieved throughout the colonoscopy due to the retrospective nature of the study.

A variant definition of the ADR is the proportion of adenomas detected per patient[117]. Our definition of the ADR does not account for the presence of more than one adenoma per patient, which might be a shortcoming; nonetheless, we opted to use the definition we had stated because of its broad adoption in the literature which permitted comparing our results with other studies[110, 118]. The ADR in our study was comparable to others[50-52], however it varied greatly between endoscopists, but by the same token so did the patient characteristics they screened (age, risk for the development of CRC, previous colonoscopy…), and the number of procedures they performed. We found that male endoscopists performed colonoscopies on a population with a much broader age range compared to female endoscopists. This might have inflated the ADR for female endoscopists as their patients were expected to have a higher prevalence of adenomas as adenomas increase with age.

More adenomas were detected in male patients, those with a prior history of a polypectomy, and in those with good quality of bowel preparation; all of these factors are known to be associated with an increased ADR[51, 87-89]. In addition, there was increased adenomas detection in the colonoscopies with photo-documentation of the cecum, for which we have no explanation; this would require further investigation. One possible explanation might be the personality of the endoscopist with those who photo-document the cecum may be more meticulous. We cannot, however, exclude other explanations dependent on variables that we did not account for in our study.

On univariable analysis, adenoma detection was higher in patients that were judged by the endoscopist to be at increased risk but the evidence was inconclusive on the multivariable analysis. Although the adenoma detection rate has been advocated as a quality indicator for colonoscopies we think that using a cut-off value is an oversimplification. This is due to that even when we limit this indicator to average risk patients the detection of adenomas varies with age, and varies even between the index

colonoscopy and individuals who had already had one or two prior colonoscopies.

There are numerous studies that have demonstrated that increased withdrawal time is associated with an increased ADR[49, 50, 95]. We did not have withdrawal times for the colonoscopies for most endoscopists, as time recording has not yet been implemented in a standardized way. In a recent retrospective study where time recording was implemented there was a statistically non-significant increase in polyps detected, and these were mostly small non-adenomatous polyps with no cancer potential[120]. We think that the withdrawal times represents a characteristic of the endoscopist and the degree of care and scrutiny that he/she takes in examining the colon, definitely taking less time in the examination will not aid in detecting more adenomas, but by merely increasing the time without other associated procedural characteristics we do not expect that the ADR would increase in a predictable fashion. Furthermore, the effect of the withdrawal time is expected to be variable when the time is spent on examining a segment of the colon as opposed to the whole colon[121]. Other issues raised about withdrawal times include the subjective threshold of 6 minutes that has become the cutoff value used in these studies[122, 123]. In addition it seems that the slower, more patient and meticulous the endoscopist is, the higher the ADR and rather than a dichotomized variable the withdrawal time is more likely a continues one[117].

One of the limitations of the study is that we did not have the date of the prior colonoscopy in patients with prior procedures, thus, those who had a colonoscopy a year prior to the current exam and had a repeated colonoscopy due to a suboptimal cleansing bowel preparation might have exhibited a lower probability for adenoma when compared to a person who had undergone colonoscopy 10 years prior.

On univariable analysis there was a higher probability of detecting adenomas in male patients, with increasing age, in those who had a prior polyp removed, when there was photo-documentation of the cecum, and

as the number of polyps detected during a colonoscopy increases. In contrast, there was a lesser probability of detecting adenomas in those at average risk for CRC, when the colonoscopy was performed by a surgeon, and with an increasing number of endoscopies and colonoscopies before the index colonoscopy, and as the time from the beginning of the endoscopy session till the index colonoscopy increased. The results for other variables were inconclusive.

On multivariable analysis almost all the variables point estimates and confidence intervals changed, reflecting confounding. The finding of confounding is not unexpected as these variables are correlated, for example adenomas increase with age, those with a family history of CRC have an increased risk for developing adenomas, and older subjects are more likely to have had a colonoscopy with or without polyps being removed.

After multivariable analysis, variables that were associated with increased adenoma detection were increasing age of the patients (in years) OR 1.04 (95%CI, 1.02 to 1.07), increased polyp number OR 3.71 (95%CI, 2.70 to 5.10), while there was a decreased probability of detecting an adenoma with greater elapsed time (in hours) from the beginning of the endoscopy session till the index colonoscopy OR 0.51 (95%CI, 0.31 to 0.79).

When the analysis was limited to average risk individuals, similar variables were associated with the detection of adenomas apart from on univariable analysis there was a decreased probability of detecting an adenoma with the increased number of endoscopies prior to the index colonoscopy.

While the association between adenoma detection and photo-documentation of the cecum as well as prior polyp removal was inconclusive. While on multivariable analysis the association between the number of hours prior to the index colonoscopy was inconclusive, this is most probably due to the small number of individuals when the analysis was limited to average risk individuals.

The retrospective nature of the study eliminated the possibility of a Hawthorne effect but also was a limiting factor, for instance some of the variables known to effect the adenoma formation like the metabolic syndrome [124-126], smoking [127-129], body mass index[79], and socioeconomic status[11] were not available

Some of the concerns raised with using ADR as a benchmark for colonoscopy quality is that it is a multifaceted variable, meaning that an adenoma has to be visualized, then be identified as an abnormality[130], be excised or biopsied, and subsequently retrieved for pathological examination[117]. Thus ADR could be affected at each stage by a number of variables and be confounded by any factor that affects the sequence of adenoma removal.

Alternatively, if endoscopists are going to be benchmarked according to ADRs as is currently recommended, they most probably will be more meticulous in their exams, and would have a low threshold for repeating the exam in cases of suboptimal cleansing preparation as “unclean” colons may obscure adenomas that are flat or small.

Our study was inconclusive with regards to the detection of adenomas in those where the cecum was intubated, but other studies found that the cecal intubation rate was not associated with decreased interval CRC (incidence of CRC between the initial colonoscopy and the follow up colonoscopy).[131] Perhaps because of more difficult detection of flatter polyps in the right colon (or poorer preps affecting the ascending colon), or even, a differential growth rate of adenomas in that colonic segment[44, 132].

Also the results that we obtained might be of limited generalizability as the patient population referred to a tertiary care center might differ in many aspects from those seen on a community level.

5.2 Conclusion

In conclusion, patient characteristics as well as, increased time from the start of the endoscopy session until the index colonoscopy was associated with decreased adenoma detection. This finding, which suggests operator fatigue, implies that there might be an optimal length of time for endoscopy sessions. This would be an important factor that should be taken into account in endoscopy scheduling. Further research is required to evaluate the effect of prolonged endoscopy sessions, as is commonly performed, on the detection of adenomas during screening colonoscopy.

CHAPTER VI: REFERENCES

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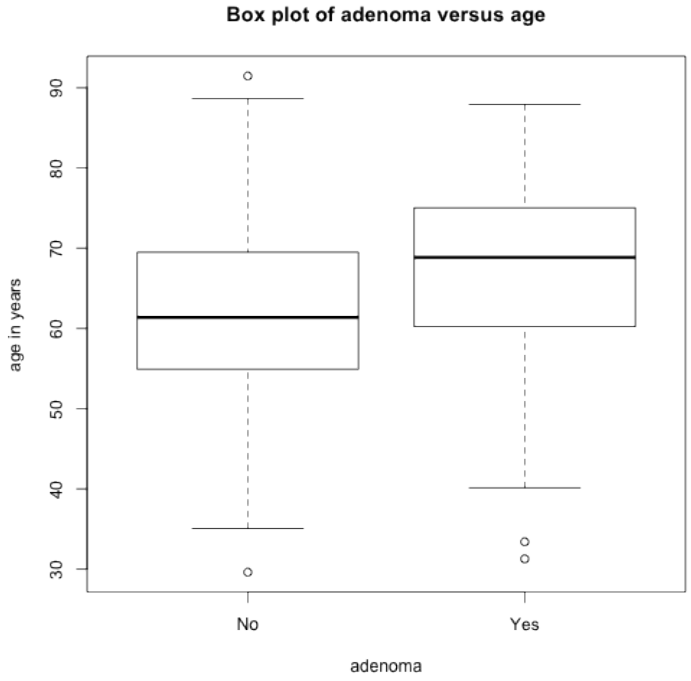
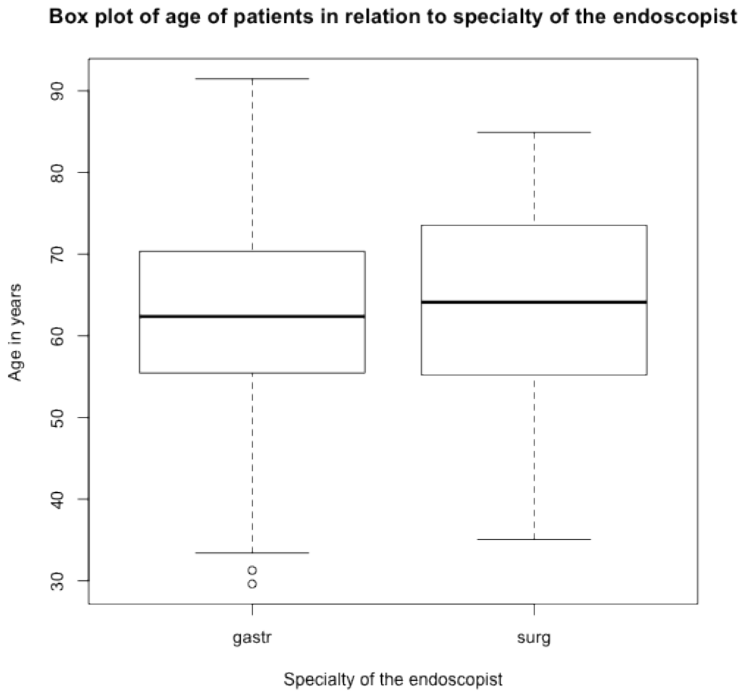
CHAPTER VII: APENDICIES

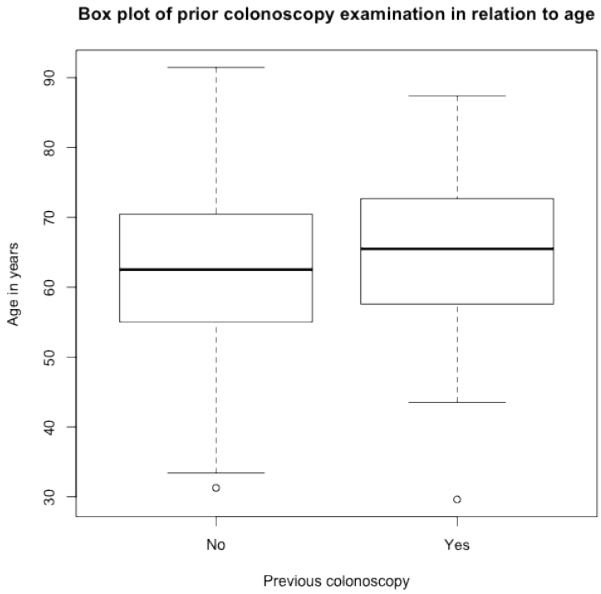
Box plot of age of patients based on adenoma detection



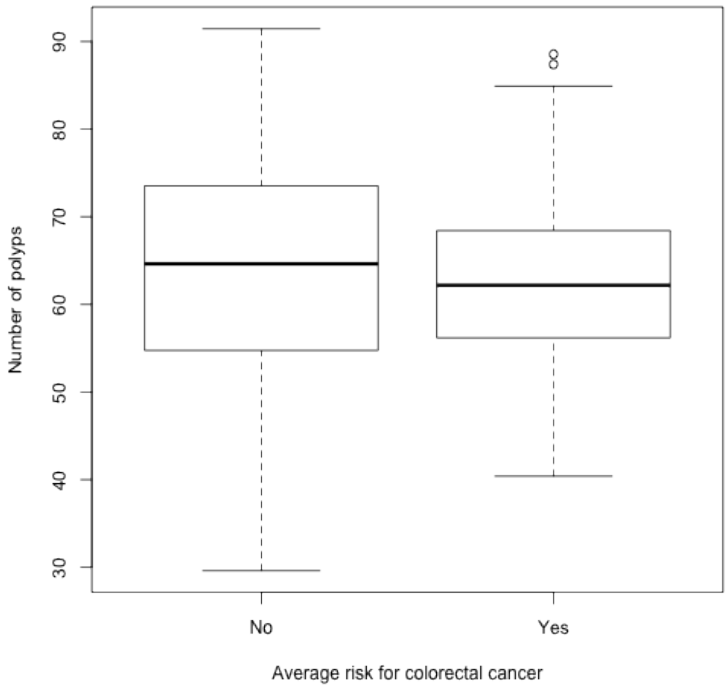
Box plot of age of patients based on the specialty of the endoscopist



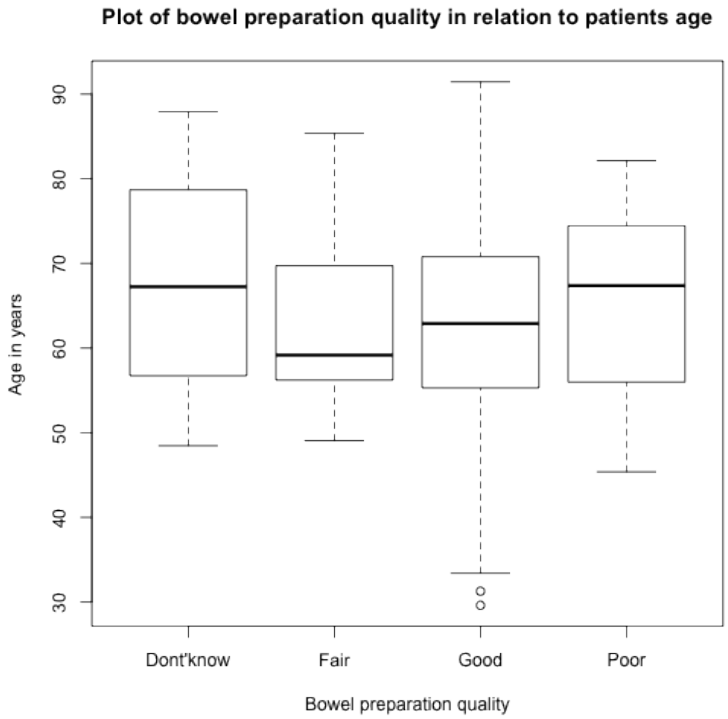
Box plot of age of patients based on the exposure to a prior colonoscopy



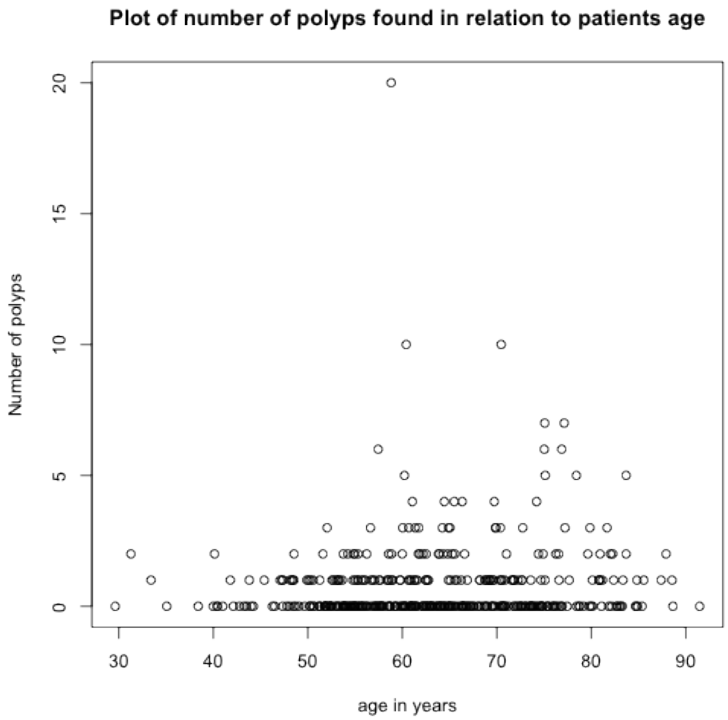
Box plot of age of patients based on the risk for the development of colorectal cancer.



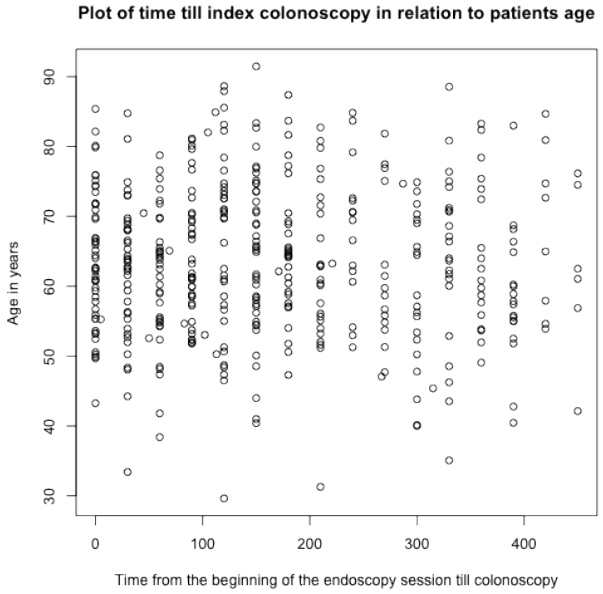
Box plot of age of patients based on the quality of the bowel preparation.



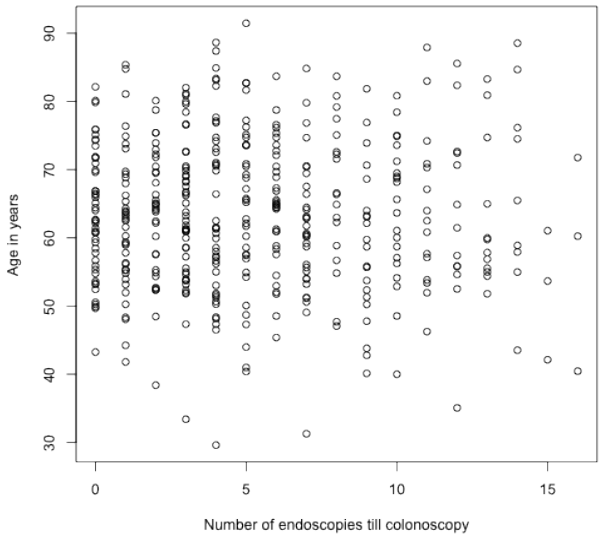
Scatter plot of age and the number of polyps detected.



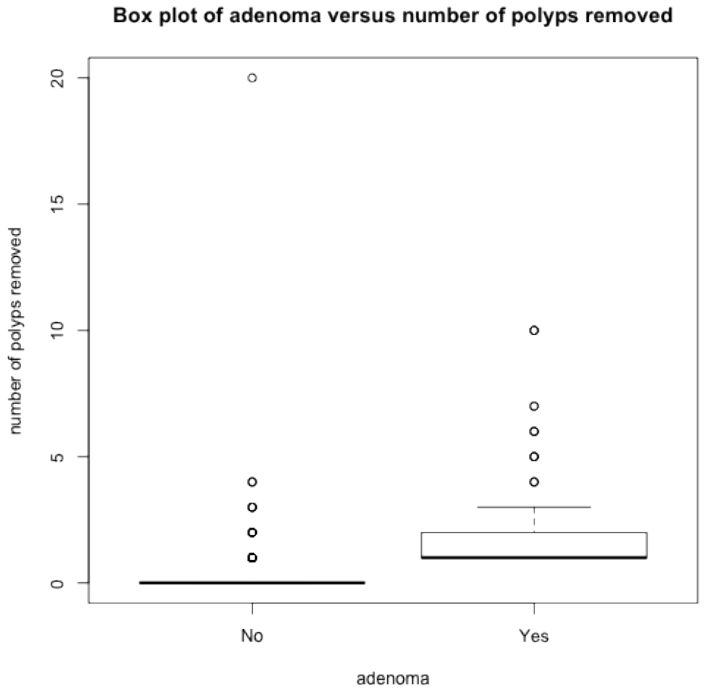
Scatter plot of age and the timing till the beginning of the index colonoscopy.



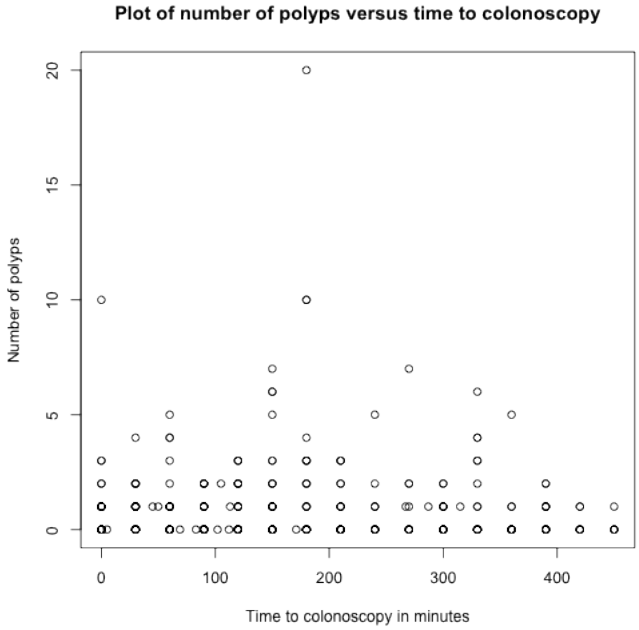
Scatter plot of age and the number of endoscopies till the index colonoscopy.



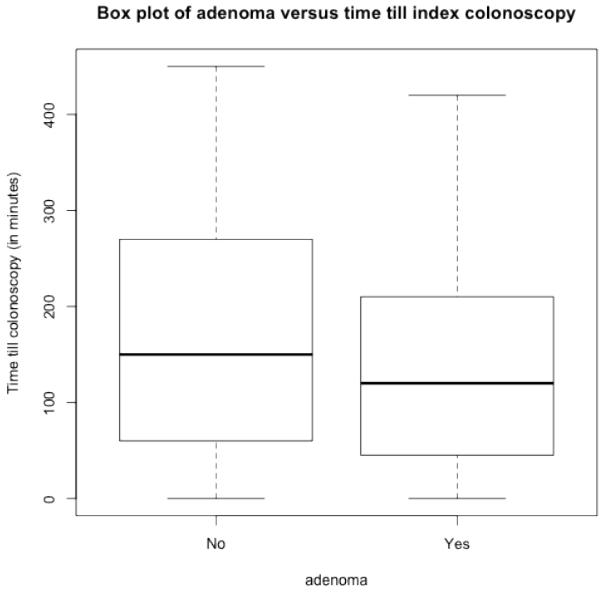
Box plot of adenomas and the number of polyps removed.



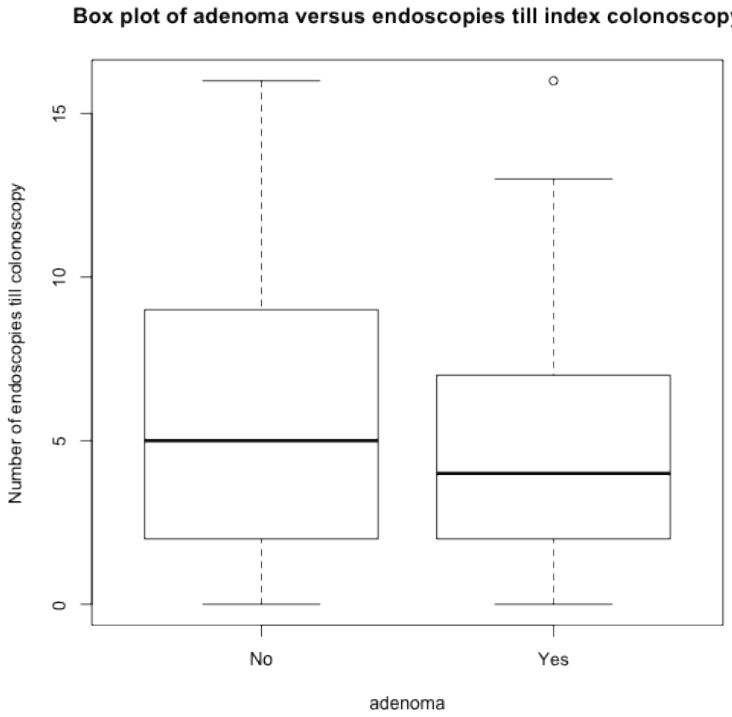
Scatter plot of the number of polyps detected and time till the start of the index colonoscopy.



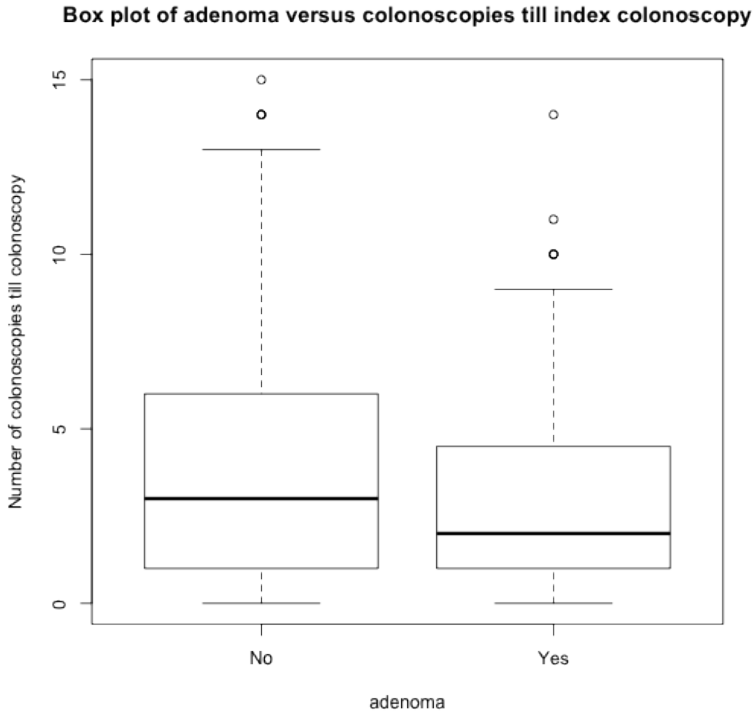
Box plot of adenomas and the time till index colonoscopy from the beginning of the endoscopy session.



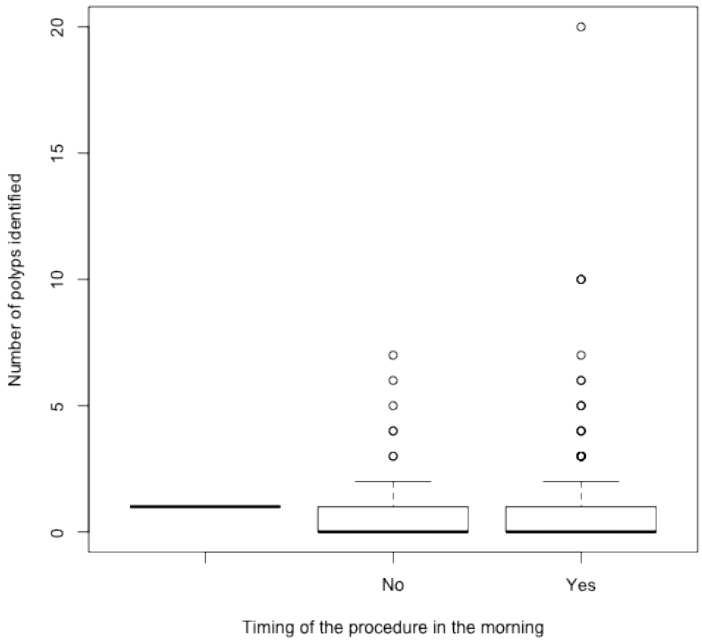
Box plot of adenomas and the number of endoscopies till index colonoscopy from the beginning of the endoscopy session.



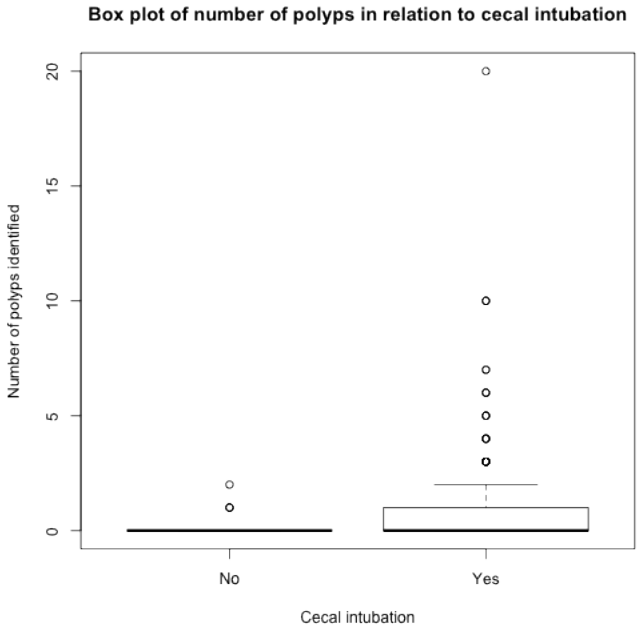
Box plot of adenomas and the number of colonoscopies till index colonoscopy from the beginning of the endoscopy session.



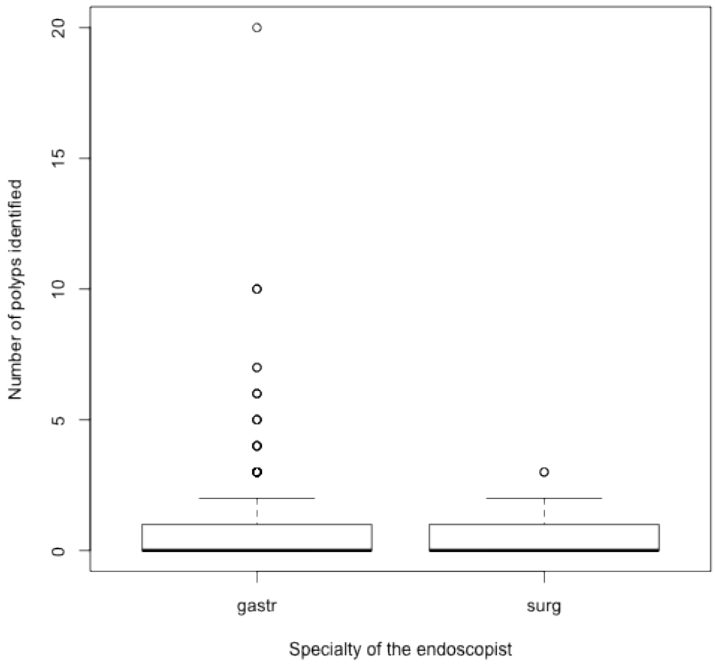
Box plot of adenomas in relation to the timing of endoscopy (am vs. pm)



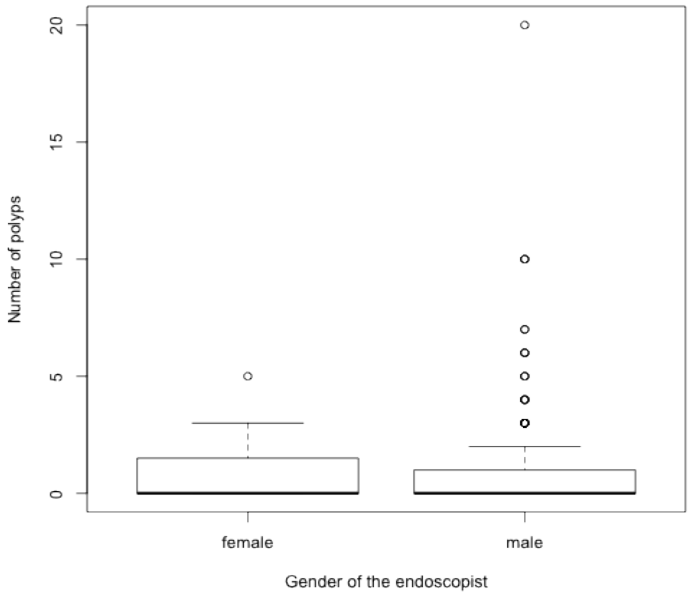
Box plot of the number of polyps detected in relation to cecal intubation.



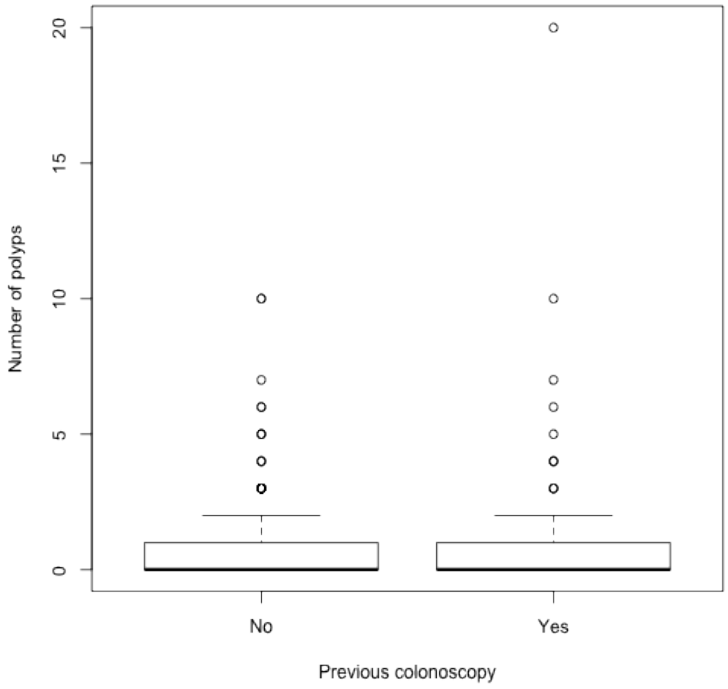
Box plot of the number of polyps detected in relation to the specialty of the endoscopist.



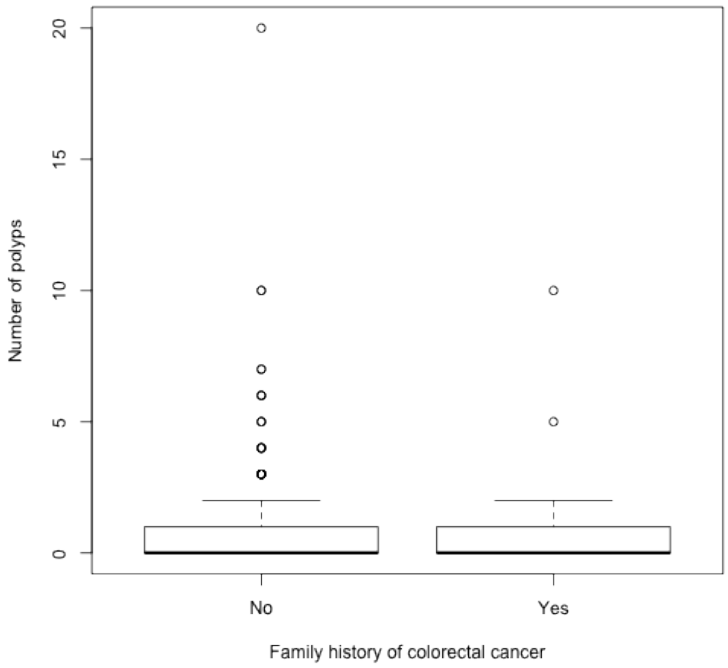
Box plot of the number of polyps detected in relation to the gender of the endoscopist.



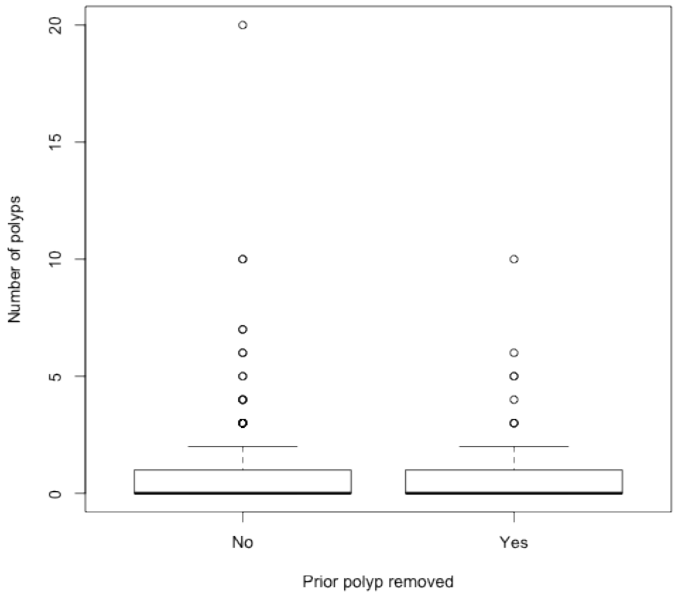
Box plot of the number of polyps detected in relation to the patient having a prior colonoscopy.



Box plot of the number of polyps detected in relation to the patient having a family history of colorectal cancer.



Box plot of the number of polyps detected in relation to the patient having a prior polyp removed



Box plot of the quality of the bowel preparation in relation to the number of colonoscopies from the beginning of the endoscopy session till the start of the index colonoscopy.