Understanding Outstanding
- Quality assurance in colonoscopy -

V. de Jonge en J. Sint Nicolaas

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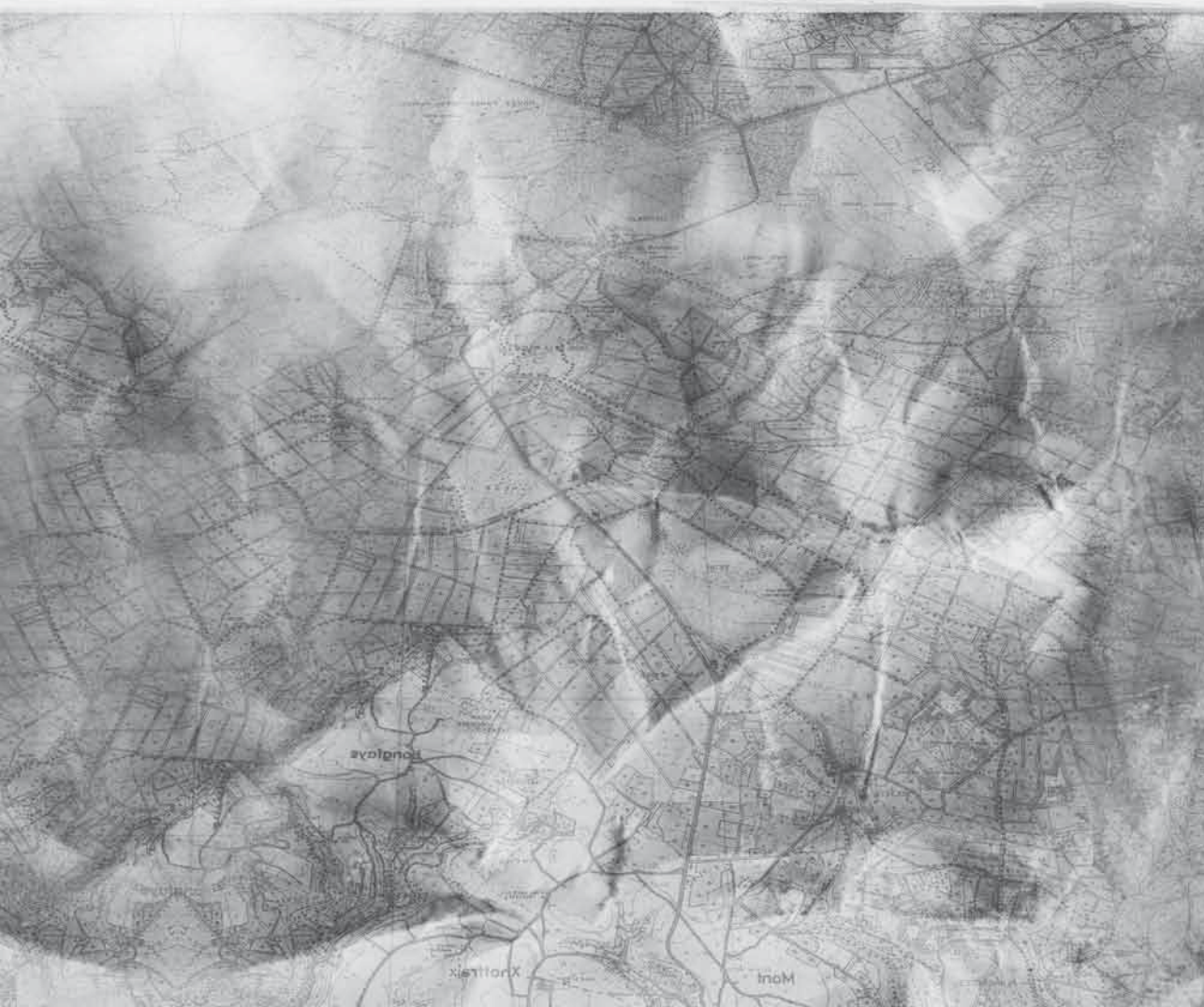
Chapter 1

Introduction and outline of this thesis



INTRODUCTION

Since a couple of years, quality assurance (QA) stands at the core of the attention in the healthcare sector. Especially after the publication in 2000 of the Institute of Medicine's report 'To err is human' the interest in QA has taken a quantum leap and many quality initiatives have been developed.[1] This report revealed that every year in the United States approximately 98,000 patients died because of medical errors. Following this report, within the healthcare sector the awareness arose that the quality of the service had to improve, with special attention to safety and patient experiences.[2] Since then the healthcare sector has learned some important lessons in QA from other industries such as the airline industry and energy sector, which are generally classified as ultra-safe organizations.[3]

Gastrointestinal endoscopy has been one of the medicine specialties which enrolled important quality initiatives.[4, 5] Especially since the introduction of colorectal cancer (CRC) screening programs, many efforts have been undertaken to better understand the concept of high quality endoscopy.[6] CRC screening has been proven to decrease the incidence of CRC, and CRC related mortality.[7, 8] Therefore many institutions and societies recommend to screen asymptomatic individuals by fecal occult blood tests, flexible sigmoidoscopy, or colonoscopy.[9-11] As these screening programs involve healthy individuals, the cost-effectiveness of such programmatic screening approaches is highly dependent on the quality of the procedure, but also on pre- and post-procedure quality aspects to improve screenee experiences and thereby the uptake of and adherence to screening modalities.

In the Netherlands, CRC screening is about to start in 2013 by means of biennial fecal immunochemical testing.[12] To attain the highest effect a comprehensive QA program should be enrolled with major focus on endoscopy as secondary screening method, as is recommended now by the European Union.[13] The other diagnostic and therapeutic services provided by the endoscopy units will benefit simultaneously from such an initiative.

Structured QA

Effective QA is dependent on several aspects. First, the culture of an organization is of paramount importance.[14] To ascertain that quality and safety are integrated in the way an organization and its members work, the opinion of the personnel should be reflected in the quality program enrolled. Thus, taking into account the priorities and preferences of endoscopy personnel in developing a QA program is necessary in order to successfully implement a QA program.

An example of a successful and comprehensive QA program in endoscopy can be found in the English endoscopy sector, called the Global Rating Scale (GRS).[15, 16] In 2005, this program was developed by guidance of a task force including all stakeholders in endoscopy for the National Health Service endoscopy service. This effort was undertaken following poor out-

comes both in clinical performance and patient experiences in large colonoscopy audits, just prior the start of the English National Bowel Cancer Screening Program.[17] A large prospective study showed for example a cecal intubation rate of 77%, and low rates of supervised training and attendance of training courses by endoscopists (17% and 39% respectively). Since the implementation of the GRS in 2005, it achieved major successes throughout the whole of England and it is now receiving international attention. Although international interest is growing (i.e. Canada, New Zealand) for this program, the applicability of the system in other health systems, such as the Dutch, has not been assessed. Further, it is uncertain whether the program complies to the wishes of the Dutch endoscopy departments.

Quality outcomes in endoscopy

In order to structurally monitor quality over time, quality measures that reflect the efficacy of prevention or treatment in patients must be evaluated. Such clinical quality indicators have been extensively studied for colonoscopy, and can be described as qualitative (quality of reporting) or quantitative indicators (endoscopic performance).[18] In daily clinical practice, the use of standardized endoscopy reports makes quality assessment straight-forward. As a result of standardized endoscopy reports case-mix adjustments can also be performed, giving in-depth insight in the results and enabling comparison between individual centers and endoscopists. Which aspects are most relevant for continuous quality assessment remains at question.

The occurrence of interval CRC has been regarded as the ultimate quality indicator for colonoscopy. As colonoscopy is the gold standard in detecting and removing precursor lesions (adenomas) and CRC generally develops via the adenoma-carcinoma sequence, a high quality colonoscopy prevents the development of CRC in the years after the procedure. This was already shown in the National Polyp Study in the United States in 1993 as colonoscopy with polypectomy resulted in a significant lower than expected incidence of CRC, with a 76 to 90% incidence reduction.[19] However, CRC does occur within a few years after a clearing baseline colonoscopy in a proportion of patients.[20] A proportion of these CRCs are missed neoplastic lesions on the initial colonoscopy, as the general adenoma-carcinoma sequence has a time span in the order of 10 to 20 years. Some data suggest that at least 1 in 13 CRCs occurring after screening colonoscopy may be a missed lesion. Risk factors for missed cancers include female gender, proximal location, and the endoscopist being a general physician, internist, or surgeon.[21, 22] CRC after colonoscopy (so-called interval CRC) occurs at different rates. The single most important reason for the variability is the quality of the baseline colonoscopy. As the quality has been shown to be highly variable, not every colonoscopy performed by every physician offers the same protection. Thus, the quality of colonoscopy and the incidence of interval CRC are inversely associated. Adding to the evidence of the influence of the quality of a baseline colonoscopy, the effectiveness of colonoscopy seems to differ for left-sided and

right-sided colorectal neoplasia. A Canadian case-control study showed that the protective effect of a complete colonoscopy was strong for mortality from left-sided lesions (OR: 0.33), but not associated with mortality from right- sided lesions (OR=0.99).[23] This was supported by a German study.[24] This is likely related to quality issues such as bowel preparation, completeness of colonoscopy, and skills of the endoscopist, besides potential differences in biology of left- and right-sided lesions.

Unfortunately, interval CRC is labor-intensive to measure, patients are lost to follow-up, and data only become available after several years and thus may not reflect current quality of performance. One of the most promising surrogate quality indicators for colonoscopy is the adenoma detection rate (ADR) which is also inversely related with the risk of interval colorectal cancer. In a primary colonoscopy screening program, the risk for interval CRC was significantly higher for patients who had been treated by endoscopists with adenoma detection rates <20% compared to endoscopists with an ADR ≥20% (HR= 10.94; 95%CI: 1.37–87.01).[22] Following this, considerable variance in the ADR between endoscopists and departments has been reported in several studies. The majority of these studies are performed in screening populations and single center studies, thus it may be questionable whether the ADR can also be used for colonoscopy procedures in daily practice (including symptomatic patients). In a large community-based gastroenterology practice from the United States a variance in the ADR between endoscopists was observed that ranged from 9 to 33%.[25] Besides the technical aspects of endoscopic procedures, QA has in recent years also focused on patient-centered service in the last years.[5] It has been shown that poor patient experience leads to 'doctor shopping' and makes patients more prone to engage in litigation.[26, 27] Further, an aversive patient experiences may negatively influence the patients´ willingness to undergo surveillance colonoscopy. This may affect the efficacy of CRC screening and surveillance programs, as patient adherence is a key factor for efficacy. However, quality indicators in patient experiences are difficult to define or assess on a uniform level, as no quantitative standard is readily available as to what an acceptable patient experience is. Benchmarking using a uniform assessment may provide the solution. With benchmarking, the standard for a particular outcome is set by the best performers, without setting a standard, as is the case with quantitative quality indicators. Results in benchmarking give insight in how a department performs in comparison to others, and will motivate to continuously strive for the best performance within an audit.

Complications of endoscopic procedures are another important aspect in quality of the service. Colonoscopy is in general a safe procedure, but serious adverse events do occur. A Canadian population-based cohort study showed that colonoscopy-related mortality within 30 days after the procedure was 0.007%.[28] The incidence of other perforation was approximately 0.09%, while post-polypectomy bleeding was reported in 0.16%.[29] The most common adverse events are sedation related, in particular cardiopulmonary events. Another study showed that these adverse events may occur in up to >1% of colonoscopies.[30] It has been

shown that complications do occur more often in endoscopies performed by endoscopists who perform <300 procedures per year (RR: 2.0), again signifying that quality issues may play a pivotal role.[28, 31] Although complications cannot always be prevented, the balance between the benefits and harm of colonoscopy is even more delicate in CRC screening, which focuses on healthy individuals. There are two approaches for complication registration. The first assesses direct adverse event during the endoscopic procedure itself by means of endoscopy reports. The other assesses the adverse events in the 30-day period following the procedure. A caveat in assessing adverse events and complications in the first approach lies in differences in reporting of adverse events between endoscopists or endoscopy departments, as not everyone agrees with uniform definitions what a complication or adverse event should be. A problem with the second approach is that complication registries are less likely to capture those adverse events for which a patient is not admitted or is admitted to another hospital. Last, few data are available on minor long-term adverse events which do have influence on the patient experiences. In one prospective study, the most common minor adverse events reported by patients were abdominal discomfort (5.4%) and rectal bleeding (2.1%), but this study was performed in a single center.[32]

Quality of guidelines

As mentioned above, screening for CRC has been shown effective in reducing the CRC incidence and CRC-related mortality by removing adenomas and detection of CRC in an early stage. However, during surveillance by colonoscopy of these patients, adenomas are still commonly found due to recurrence or missed adenomas. The prevalence of advanced adenoma (with characteristics such as high-grade dysplasia, ≥10 mm, ≥3 adenomas, villous histology) or any adenoma on the first surveillance colonoscopy have been reported to be 7% respectively 33%.[33] The RR for patients with high-risk adenomas at baseline was 1.76 (95%CI: 1.26-2.46). Therefore, surveillance colonoscopy guidelines recommend that patients undergo regular surveillance colonoscopy to detect metachronous adenomas.[11, 34] These guidelines now often tailor the surveillance time interval to the initial baseline endoscopic findings such as high grade dysplasia and villous histology. This patient-tailored approach requires a more vigilant control of the surveillance program. As new evidence on this theme is emerging quickly, revising the guidelines is necessary on a regular basis.

Physicians do not always adhere to guidelines, which undermines the cost-efficiency of programs.[35] A previous study using a Markov-model found that more vigilant surveillance would result in considerable higher costs with comparable benefits compared to strategies recommended by the guidelines.[36] Besides, unnecessary endoscopic procedures have the potential to harm the patient and shift the balance between benefits and harms in the wrong direction. Although there may be several reasons to deviate from recommended surveillance time intervals for repeat procedures (i.e. incomplete index examination, piecemeal resection

of polyps, or poor quality of bowel preparation), the question arises whether a proportion of (early) follow-up procedures may be prevented or postponed to lower the burden for the endoscopic capacity. Another intriguing reason for deviation might be that physicians are insufficiently familiar with the guidelines.[37] On a patient-level, interest has grown in the attendance of patients for follow-up colonoscopies, which is suboptimal. Non-attendance rates have been described up to 30% for surveillance colonoscopy.[38, 39] In this context little is known what patients actually know about their results and follow-up policy after removal of colorectal neoplasia and whether raising the patient awareness in these aspects may result in increased attendance rates for surveillance procedures.

Current CRC surveillance guidelines from a variety of societies recommend more intensive screening by means of colonoscopy in patients with higher risk for developing CRC (i.e. a family history for CRC) compared to the general population.[11] It is hypothesized that patients undergoing organ transplantation may also have an increased risk of developing malignancies such as CRC, amongst others due to the long-term use of immunosuppressive medicines.[40] Due to the better survival of transplant recipients, long-term complications such as post-transplant malignancy now become more apparent in this population. This is in particularly the case for post-transplant lymphomas, skin malignancies and Kaposi's sarcoma. Controversies have been reported for the risk of CRC in the post-transplant setting. One study found an increased risk for CRC in liver transplants compared to an age- and gender matched general population (RR: 12.5, 95%CI 2.5-36.6).[41] This was in contrast with a study from the US that reported a standardized incidence ratio (SIR) for CRC in liver transplants of 1.01 (95%CI: 0.27-2.59) compared to the US National Cancer Institutes' SEER database.[42] The question arises whether liver transplant recipients should undergo intensified screening by colonoscopy in the post-transplant period. As post-transplant screening programs have been proposed in order to detect a variety of malignancies in these patients, the issue whether colonoscopy should be adopted in such programs is debatable due to inconclusive evidence of the risk for CRC post liver transplantation.

AIM OF THIS THESIS

As outlined above, many different aspects determine the quality of a colonoscopy. The aim of this thesis is to give a 360º view of the current status of colonoscopy in the Netherlands.

The results provide a starting point from where future quality initiatives can be initiated. This thesis aims to set priorities for coming quality initiatives and establishes the content for comprehensive QA in the near future internationally. It can thereby be used as a guide for comprehensive QA.

Part I: QA in endoscopy: how to start?

The first part of this thesis starts with an overview of the general principles of QA in health care. Before starting to enroll comprehensive QA projects it is important to acknowledge what is already known in this area. Moreover the attitude of the target population should be assessed to guide research and QA initiatives.

Therefore, at first we performed a review of the history of QA in health care (**Chapter 2**) to describe basic principles. The health care sector has learned lessons from other industries such as the airline industry, nuclear energy industry, and oil and gas industry. By evaluating the processes these industries went through to become considered as ultra-safe, health care quality improvement can be better understood and faster applied with greater success.

A lot of the quality improvement projects in medicine have taken place in the context of colorectal cancer screening programs. The inclusion of healthy individuals forces endoscopy departments to assure an excellent care. Therefore, we reviewed the QA initiatives needed to take place in the complete journey of patients undergoing CRC screening (**Chapter 3**).

From the literature review two important aspects became apparent that improve the chance of success of QA projects: the extent to which it addresses the wishes and concerns of the people working with the program, and the team culture. Therefore, we assessed the opinion of gastroenterologists towards QA (**Chapter 4**). Additionally, we assessed the opinion of other endoscopy personnel (nurses and assistants) towards QA and the team culture that exists on the endoscopy department (**Chapter 5**). These data help to understand the issues that need to be addressed both in the enrollment and design of a QA program.

In order to propose a comprehensive QA program we tested an adapted QA program from England: the Global Rating Scale (**Chapter 6**). Using this program, the endoscopy departments in England have raised the status of their units significantly. We assessed whether such a program would be feasible and applicable to Dutch endoscopy departments.

Part II: QA in colonoscopy: where do we stand?

The second part of this thesis focuses on the current quality of colonoscopy. This can be defined from different point of views. Physicians and patients may have different expectations and thoughts about the delivered care. Both the quality from the endoscopist's view (clinical quality) and from the patient's view (quality of patient experiences) were assessed.

The clinical quality of the procedure was first assessed in a baseline quality evaluation in daily clinical practice. As a quality evaluation of colonoscopy in daily practice is dependent on the compliance to reporting certain variables we first assessed the quality of colonoscopy reports, based on guidelines from the American Society of Gastrointestinal Endoscopy (**Chapter 7**). Based on these reports we also assessed the quality of colonoscopy performance (**Chapter 7**). As adenoma detection rates are currently accepted as one of the most important

quality indicators in colonoscopy, we further brought this quality indicator into focus, by evaluating differences in adenoma detection rates between endoscopy departments and endoscopists (**Chapter 8**).

The quality of patient experiences was evaluated in an international setting. We developed a survey based on the items of the Global Rating Scale. This survey was used first in a Canadian multicenter setting to assess the quality of patient experiences (**Chapter 9**). After this research, a uniform survey instrument was used in a larger multicenter setting to investigate the quality of patient experiences in the Netherlands (**Chapter 10**). These two studies provided for the first time some insight in benchmark principles in patient satisfaction at an international level.

As the quality of colonoscopy exists of a complete, thorough, and safe procedure, this last aspect was also investigated. We assessed the occurrence of adverse events in the 30 days following a colonoscopy by interviewing patient by telephone (**Chapter 11**).

Part III: QA in colorectal cancer screening and surveillance: how to guide?

With colorectal cancer screening and surveillance procedures demanding an increasing amount of the endoscopic resources, it is important that colonoscopy is performed appropriately. The third part of this thesis evaluated the appropriateness of surveillance colonoscopy in daily practice. We investigated in at what intervals surveillance colonoscopies are currently performed in Canada (**Chapter 12**), and what the yield in appropriate versus non-appropriate colonoscopies was.

We furthermore investigated how much of the current endoscopy resources are used by repeat colonoscopies, and what their yield is (**Chapter 13**).

As the guidelines for surveillance colonoscopy after polypectomy in the Netherlands are outdated, and recent years have shown an abundant amount of studies investigating the risk for adenoma recurrence, we performed a meta-analysis to further emphasize the need for revision of the current post-polypectomy guidelines (**Chapter 14**). As updated guidelines are already used in Canada, we performed a study to assess the knowledge and adherence to these guidelines by Canadian endoscopists in a survey study (**Chapter 15**). In current health care, the patient has great influence on his or her care. Therefore, the awareness of patients of their colonoscopy findings and follow up advises could also be important to increase the proportion of patients that receive surveillance at the appropriate intervals. Therefore we performed a study to assess how well patients are familiar with the outcome of colonoscopy and the interval at which they should undergo surveillance colonoscopy (**Chapter 16**).

The last part of this thesis deals with a different aspect of QA: delivering the optimal care to specific subgroups of patients with tailored screening and surveillance for colorectal cancer. We first retrospectively investigated whether liver-transplant recipients are at increased risk of developing colorectal cancer (**Chapter 17**). We then performed a meta-analysis to answer

this question (**Chapter 18**). To summarize this evidence and provide an overview of the available literature a short overview is provided with current perspectives for the future in this topic (**Chapter 19**).

Finally, we conclude with a general discussion and conclusion based on the results we presented in this thesis (**Chapter 20**).

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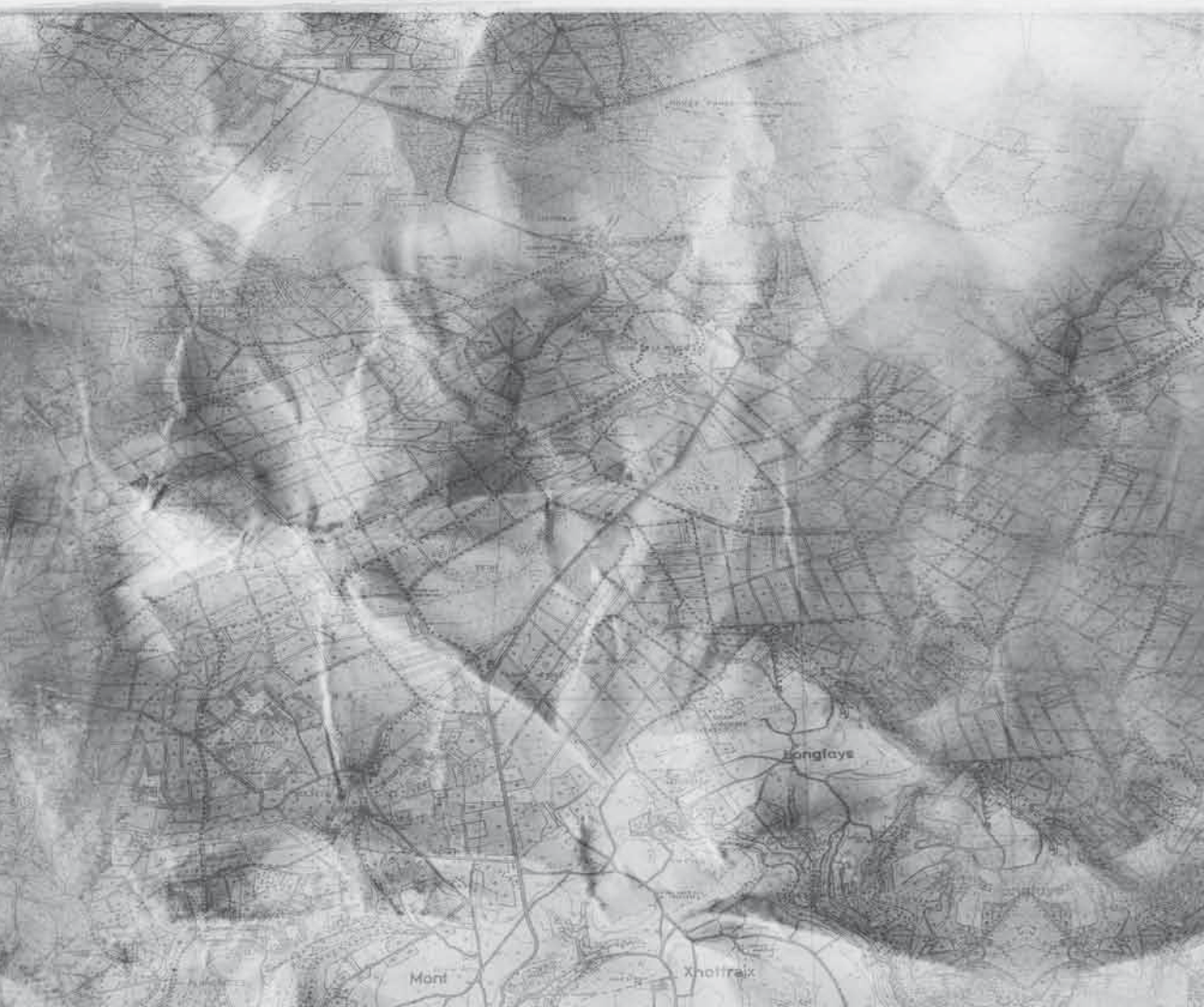
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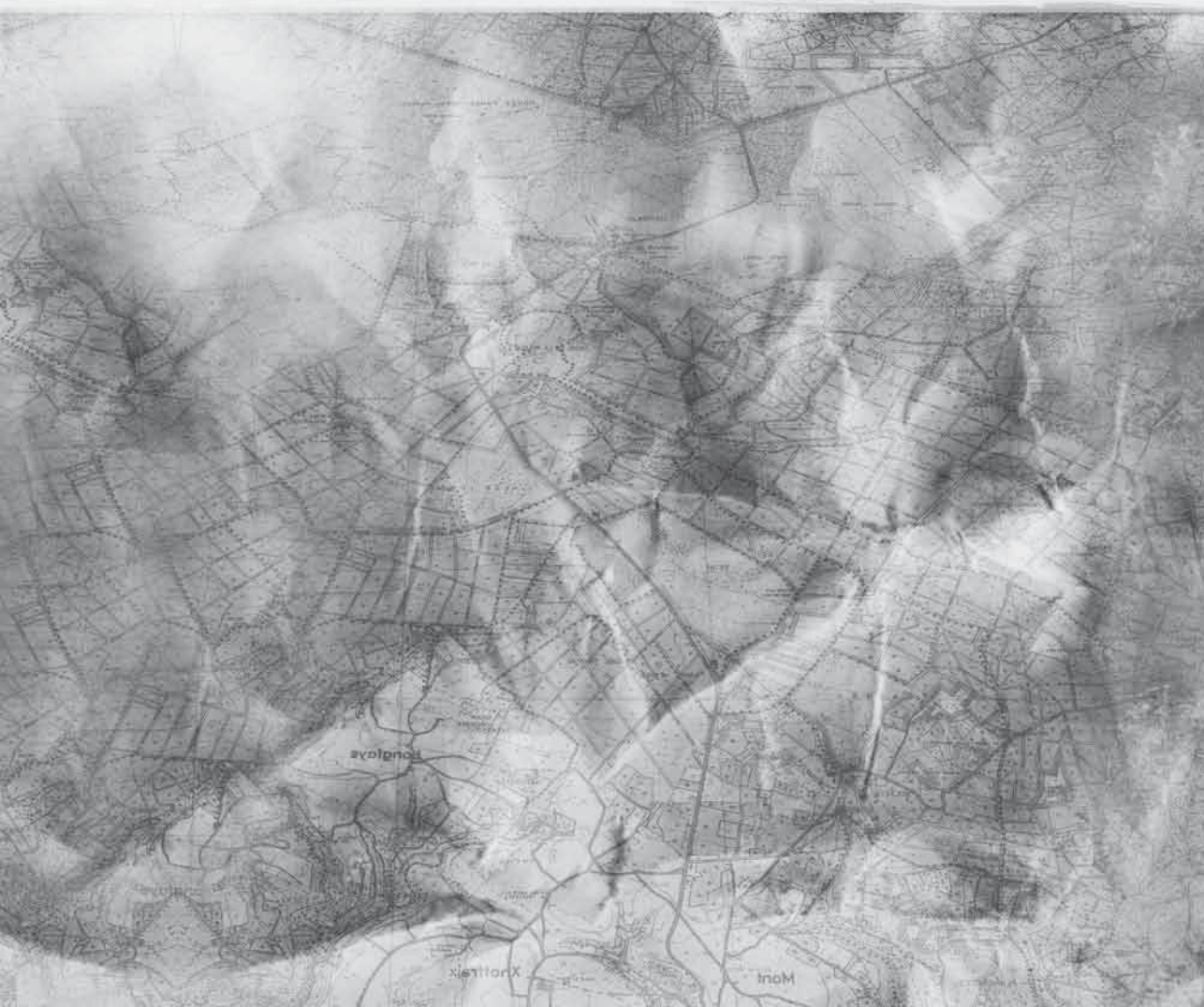
PART I

Quality assurance in endoscopy: how to start?



Chapter 2

Overview of the quality assurance movement in health care

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ABSTRACT

This chapter aims to describe the origin and current status of quality assurance (QA) in health care and to provide a background of similar developments in other industries, which have provided a major impetus for QA initiatives in health care. The interest in quality and safety in the health care sector has rapidly risen over the past decade. Without important lessons learnt from other industries, the interest and obtained improvements would have been far less fast. Knowledge on basic principles and challenges faced by other industries like the airline, car, and nuclear energy industry, that drove quality improvement projects, is of major relevance to understand the evolutions taking place in health care. To fully appreciate the QA movement, and design or implement quality improvement projects, its basic principles need to be understood. This chapter aims to give insights in basic principles underlying QA, and to discuss historical lessons that have been learnt from other industries. Furthermore, it discusses how to implement and assure a sustainable QA program.

INTRODUCTION

QA in health care – Where do we come from?

Quality improvement in medical practice has been sought ever since Hippocrates' school changed the way people looked at illnesses. Hippocrates was the first to describe and diagnose diseases in a systematic way and is generally referred to as the 'Father of Western Medicine'.[1] Ever since his ancient work, the medical world has gone through a series of changes that every time had significant impact on the way medicine was practised. Ultimately, this led to the culture of evidence-based medicine we live in nowadays, in which the medical world, supported by numerous other fields such as biochemistry, information technology, pharmacology, and medical technology, tries to find the optimal care for each individual patient.[2] All the efforts from these stakeholders in health care aim to achieve an identical goal: to ensure the highest quality of care for each patient, without losing societal aspects such as cost control, and accessibility of care, out of sight. Thereby, it becomes clear that quality is deeply embedded in the health care system. The risk of the on-going evolution of medical practice initiated by all the involved sectors is that the patient focus is easily lost, and replaced by a focus on diagnostics and therapeutics. This is enhanced by continuous rapid technical developments. Thus, comprehensive QA is of paramount importance to achieve and guarantee excellent service for each patient with each provider.

QA in health care – Where do we stand?

Until recently, quality of care was hard to describe, measure, or report. A landmark in the quality movement in health care has been the publication of the Institute of Medicine's (IoM) report 'To err is human: building a safer health system' in 1999.[3] Since the publication of this report, QA in health care has steadily become a top priority for health care providers. It was shown that up to 98,000 deaths per year occurred in the United States (US) because of medical errors, thereby being among the top 10 causes of deaths. Emphasising on medical errors, either human or systematic, an abundant amount of protocols, projects, and legislation have been studied and implemented since the IoM publication. Since then, specific outcome measures have been proposed as quality indicators for provided care. For example, the hospital standardised mortality ratio has been in use in England and The Netherlands since 1999.[4] In the US, the Health Care Financing Administration (HCFA) has developed a set of quality indicators to assess the quality of care delivered to Medicare beneficiaries.[5] Many other institutions have made their own set of quality indicators. It has led to a huge number of quality initiatives and thereby, to a complete new field in health care research. A couple of months after the first report, the IoM released a second report, 'Crossing the quality chasm'.[6]

Herein it was proposed that the necessary changes should be translated into six dimensions of health care: safety, effectiveness, patient-centeredness, timeliness, efficiency, and equity.[7]

All these six domains are a direct reflection of top priorities in other sectors, such as the airline industry, oil and gas industry, nuclear power industry, and car industry.[8, 9] These industries have thus been used as exemplars for quality improvements in health care. Although obvious differences between those industries and the health care sector exist, on-going lessons can be learnt from them. With help from the extensive experience in other sectors, the health care sector has taken a big step forward in the quality of care since the reports of the Institute of Medicine. Both safety and patient-centred care have been at the core of these developments. To fully appreciate the QA movement, and design or implement quality improvement projects, its basic principles need to be understood. This chapter will be far from a complete overview of all aspects concerned with QA in health care and other industries. It aims to give insights in basic principles underlying QA, and to discuss historical lessons that have been learnt from other industries. Furthermore, it discusses how to implement and assure a sustainable QA program.

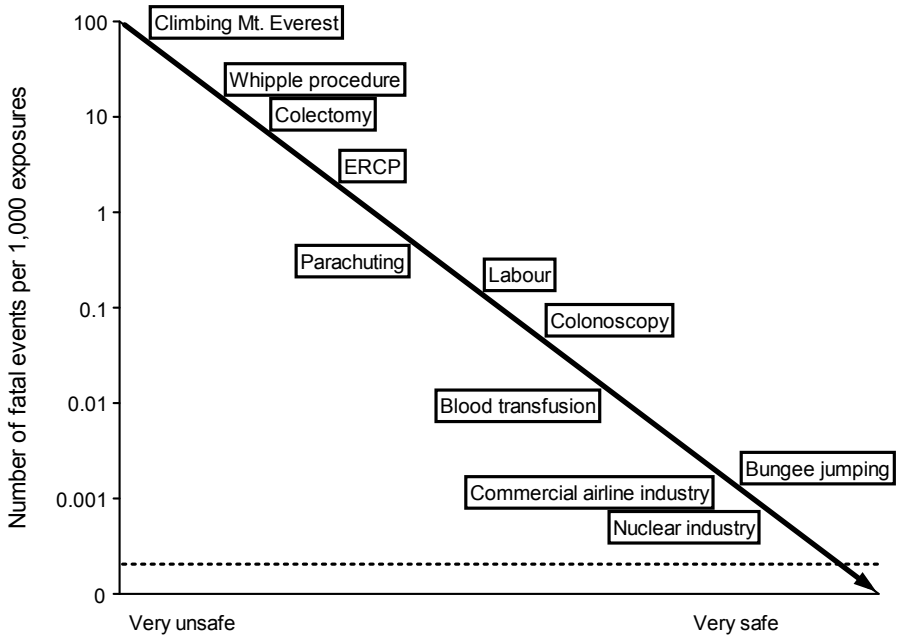
QUALITY AND SAFETY

When talking about quality, one of the first things that comes to mind is safety, which has been the core driver in many industries for quality improvement projects. Some of these industries are now regarded as very safe, amongst others because of a change in culture from solely aimed at economic profit to a system which embed and embrace safety protocols and challenges itself Figure 1. Besides safety, customer-service has been a top priority since decades in various industries, especially in the airline industry. As a bad reputation in customer-service directly influences the financial status of airline companies, many action plans have taken place to ensure a client-centred approach. Customer-service in health care may be translated to patient-centeredness. Since several years, patient experiences and patient satisfaction have become part of the accepted quality indicators of provided care.[10, 11] This chapter will mainly focus on safety issues. However these principles are applicable to patient satisfaction as well.

Safety and quality are closely intertwined, as optimal patient safety can only be achieved with high quality of care throughout the complete patient journey. When the quality of all processes of a patient's journey are ensured, possible threats for patient safety will be recognised early to prevent the threat becoming an accident. This will be further discussed later on.

Several industries which due to the character of their practice require major emphasis on safety have been taken as example for the health care sector.[8] Especially, in the airline industry and nuclear power industry, safety issues are a top priority because of strict regula-

Figure 1. Safety based on number of fatal events.



Adopted from Amalberti R. Five system barriers to achieving ultrasafe health care. Ann Intern Med 2005; 142:756–764.

tions followed after major fatal events with high impact, and public and media attention. Historic aeroplane crashes and nuclear accidents like the Three Mile Island partly meltdown in the US in 1979 and the Chernobyl' nuclear power plant explosion in the Ukraine in 1986 had such a large impact, that these industries were forced to come up with strict regulations and protocols both by themselves, as well as by governments and international organisations. The recent nuclear disaster in Japan, which is now the second worst nuclear power plant accident in human history, already within months has an impact on nuclear industry and politics worldwide.

SYSTEM THINKING

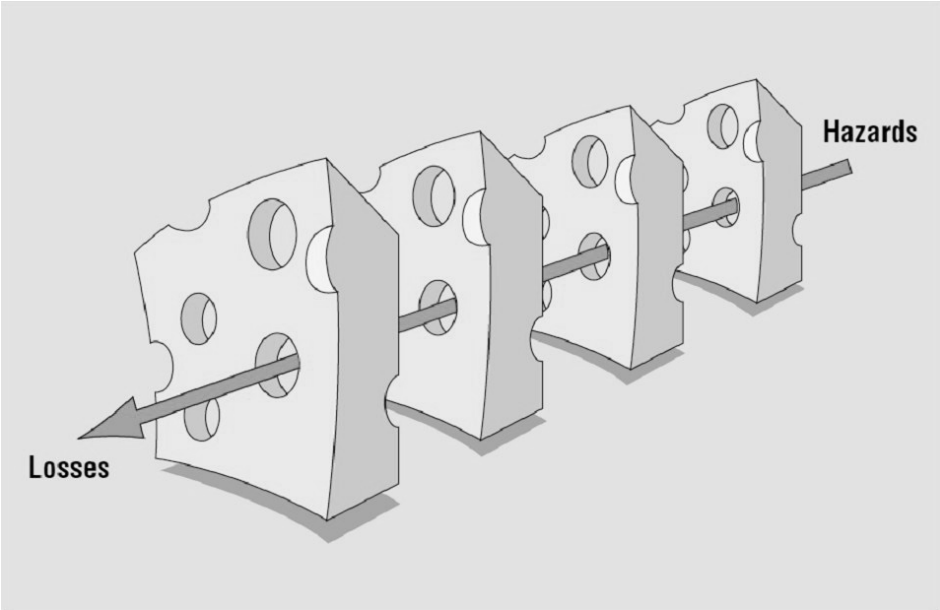
One of the most important lessons to be learnt from other industries is that most (although not all, as shown in the nuclear accident in Japan) errors occur from system errors. Thinking of system errors instead of human errors implies that wherever humans work, errors can be made, as it recognises the limitations human beings face in their abilities for multitasking, concentration, and prolonged attention. This was already acknowledged by Florence Nightingale, when she tried to standardise nursing practice in 1854.[12] The IoM report again emphasized this theory.[13] The system approach is opposite to the person approach which

blames errors on individuals because of inattention, forgetfulness, or negligence.[14] The system approach recognizes that most errors occur due to system errors. It should not be ignored that individuals do make mistakes for whatever reason, so-called active failures.[15] However, by investigating the complete system in the evaluation of errors, further active failures can often be prevented and the impact and occurrence of human errors can be minimised if latent conditions in the system are identified. Latent conditions are characteristics of the organisation or design of a system where individuals work in. These latent conditions are often the result of the policy of the organisation, and include problems for example in staff mix, understaffing, work pressure, multiple software systems, unworkable procedures, or unreliable checklists, backups, and alarm systems.

The system approach implies that care consists of connected processes that influence each other, and the ultimate patient outcome. An error occurring in one of these processes does not necessarily lead to a fatal event as it can be identified both in downstream and upstream processes leading to early recognition or intervention, with either full prevention or down staging of detrimental results. This theory led James Reason in 2000 to propose the Swiss Cheese model.[14] This model was first designed for the oil industry, but was soon embraced by the airline industry as well.[16] In this model hazards on one side, and losses on the other side, are separated by different kind of barriers. All these barriers are developed in different process stages. The model assumes that every single barrier itself is not perfect and can be penetrated because of latent conditions or active failures. However, a next barrier is designed in such a way that the error that penetrated through the former barrier is put to a hold in the next. Designing different barriers at different stages of the process, with different weaknesses, makes it more difficult and thus less likely for a hazard to lead to a loss. In the Swiss cheese model, each barrier is depicted as a single slice of cheese with its well-known holes at different points in every slice, so that a straight line from the hazard to the loss does not exist figure 2.[14]

Application of this theory to health care and the link between patient safety and the quality of the entire system makes clear that a comprehensive QA program is needed to ensure quality and safety in all processes of patient care. This ultimately results in a safer patient journey. Until recently, comprehensive QA programs were not available in the health care sector, and many quality initiatives stood and stand alone. Nowadays the theory of comprehensiveness is more accepted, and besides individual quality indicators, more extensive QA programs become available. An example is the Global Rating Scale, currently in use on the National Health Services' endoscopy departments in England.[17] Following its success, international attention has been drawn to this comprehensive QA program which focuses on both process and structure outcomes evaluation in order to optimalise the patient experience.[18]

Figure 2. Swiss Cheese model.



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BASIC PRINCIPLES OF QUALITY IMPROVEMENT

For a QA program to efficiently address all processes in the industry, and continuously ensure the quality of these processes, it is important that all aspects of the business are covered and that on-going evaluation of performance is guaranteed. The former aspect is being described as total quality management (TQM), the latter is grounded in the Plan-Do-Check–Act cycle (PDCA-cycle). Both aspects will be discussed below.

TQM has first been developed in the Japanese industry and was later adopted by the US Navy. Companies such as Toyota, Motorola, and Ford do have extensive experience with TQM programs, which require standardisation in processes, training and equipment, and strict management of resources, delivery lines, and infrastructure.[19] TQM aims at an integral approach on quality improvement, at management, personnel, client, organisational, and resource level. Donald Berwick, a paediatrician in the US, acknowledged the success of this theory and applied the theory to the health care sector in the US. He tested the TQM approach of industry in twenty-one hospitals in the National Demonstration Project, in which the hospitals were supposed to collaborate with industrial quality assurance professionals.[20] Together they applied the TQM concept to their health care settings. Major successes that were not considered possible were achieved in the health care sector. Basic principles of TQM applied in this study led to patient-centeredness, improvement of processes of care, cooperation between professionals, and structural methods and measurements. The importance of

dedicated leadership was also emphasized. Thanks to the great success of this project and many other quality initiatives, Donald Berwick is now appointed by the American government to serve as Administrator of the Centres for Medicare and Medicaid Services.

A more advanced approach of TQM is known as the '(Lean) Six Sigma' strategy, which incorporates advanced statistical tools to reduce the waste and failure of resources.[21, 22] Six Sigma was first used by Motorola in 1986 as an advancement of the TQM model. Where TQM focuses on internal requirements, the emphasis of Six Sigma is put on continuously reducing the number of errors and is more data driven.[23] Compared to the TQM model, Six Sigma also has a stronger focus on financial aspects, and the usage of advanced metrics. The system requires the availability of intensely trained Six Sigma specialists within the organisation.[24, 25] This strategy is still not fully explored and supported in the medical literature, although some radiology and pathology departments in hospitals have reported on several improvement initiatives using Six Sigma with promising results.[26, 27]

CONTINUOUS QUALITY ASSURANCE

As stated above, the comprehensive nature of QA should be matched by continuous monitoring with persistent feedback whether adopted improvements have been effective. A commonly observed quality principle is defined as the PDCA-cycle. The PDCA framework was proposed in the 1950s by Dr. W. Edward Deming in order to perform continuous quality management. His concept was adapted from Shewhart's Plan-Do-Study-Act. As a matter of fact Deming kept calling his PDCA-cycle the Shewhart's cycle. Deming proposed this concept of continuous QA to the Japanese car industry, after the Second World War had destroyed much of the Japanese industry. Deming was a teacher and consultant to the Japanese industry, through the Union of Japanese Scientists and Engineers from 1950 till 1965. He acknowledged that QA is a continuous process. His proposed PDCA-cycle has four stages; 'Plan' means that an organisation is actively planning improvements. 'Do' refers to the actual implementation of the planned activity. 'Check' corresponds with monitoring, e.g. an audit, with analysis of the results. Lastly, 'Act' means that an action plan is being formulated if results or standards are not reached. One of the important aspects in this cycle is the real-time feedback of results. The PDCA-methodology has been used in many industry sectors. At first, the Japanese industry greatly benefitted from these quality initiatives after the complete destruction during the Second World War although much of the work mentioned above was already developed before the Second World War in the United Stated. After the major economic success in Japan, it was incorporated in US industries as well.

QUALITY MEASURES

One of the main challenges of QA initiatives in health care is the issue of quality measurement, given the range of outcome parameters that can be selected, the difficulty with which reliable data are often obtained, and the wide variation in populations served by different health care providers both between, and within certain specialties. In general, quality of care can be measured and defined on three different levels; the structural level, the process level, and the (clinical) outcome level.[10, 28]

Quality aspects on the first level, the structural level, deal with the organisation of a health care system. Structural indicators can be found in both physical and staff characteristics. Physical characteristics of structure indicators include for example the available resources (buildings, equipment). Staff characteristics cover for example skill mix and team culture.[29] Indicators on structural level evaluate whether certain facilities are present or offered, but do not assess whether the care is optimally carried out.

The second level covers indicators that are associated with processes of care. It evaluates the interaction between the health care providers and the health care users (patients). Two aspects are important in process of care indicators, namely the interpersonal interaction and the actual provided clinical care. The latter describes the medical aspects of delivered care to an individual patient. An example of such an indicator is the amount of patients that has received a certain therapy. It is thus an extension of the structural level as it assesses whether the required care is indeed carried out.

The third level, clinical outcomes, is directly associated with the patient's health status or patient satisfaction.[29] It should be noticed that variation in clinical outcome does not necessarily mean difference in quality of care. Four explanations have been mentioned that can attribute to observed differences between hospitals concerning clinical outcomes. First, the patients managed by different health care providers may differ in socio-demographic aspects, severity of their disease, or presence of co-morbidity. It is important to adjust for these confounders, also known as case-mix adjustment. Second, variance in outcome indicators can be due to differences in measurement methods, in particular in the absence of clear definitions or standards. This is often the case in measuring patient satisfaction. Benchmarking, which will be discussed in more detail later on, with a uniform instrument is a way to address this. Thirdly, observed differences can have occurred just by random variation between providers. This relates to the number of cases, the expected frequency of events, and time of follow-up. Finally, a fourth reason for differences in outcome reflects the real variation in quality between health care settings or providers.[30]

It has been discussed extensively whether process or clinical outcome indicators should be obtained in order to measure and monitor quality.[31] Although clinicians primarily tend to focus on clinical outcomes as most important parameters to reflect quality, they are difficult to measure, whereas process indicators can give a more concise picture. Strategies to

improve processes of care are easier translated to the work floor, especially if one aims to change practice in health care provision as processes can be controlled by the health professional itself. Clinical outcomes are more prone to case-mix, require more follow-up data or a larger number of patients in order to detect differences between interventions and evaluate if improvements have been effective (for example in decreasing the rate of rare but serious complications). In other words, improvements in process indicators are easier to observe in daily practice.

For some quality measures, no quantitative standard can easily be formulated. In this case, quality cannot be grasped by indicators but is rather formulated in terms of auditable outcomes. Quality of care is easily assessed by quality indicators, as standards are available.[17] Thus, when these standards are not reached, improvement is clearly needed. It is more difficult to determine at which level the quality of care is or should be for auditable outcomes. As mentioned before, patient satisfaction is a good example in this case. To interpret auditable outcomes, a principle known as benchmarking is one of the strategies receiving increasing attention. The Xerox Company is generally credited to have been the first company applying benchmarking in its organisation. Following rumours that the production of their copy machines was much more expensive compared to production costs in Asia, they gained insights in the processes and designs of products of other comparable companies, improved the way they worked, and ultimately decreased their expenses.[32] Over time, other industries such as the car industry have implemented similar strategies.[33] In benchmarking, quality improvement is sought by evaluation of the variance in performance between different providers, where the standard is determined by the best performers.[34, 35] Benchmarking is defined as a continuous, systematic process for evaluating the products, services and work processes of organisations that are recognized as representing best-practices for the purpose of organisational improvement.[36] Although benchmarking is becoming increasingly popular in health care, there is a still a shortage of peer-reviewed research on the use of benchmarking in health organisations.[37] This is unfortunately the case with many quality initiatives.[38]

A SUSTAINABLE QA PROGRAM

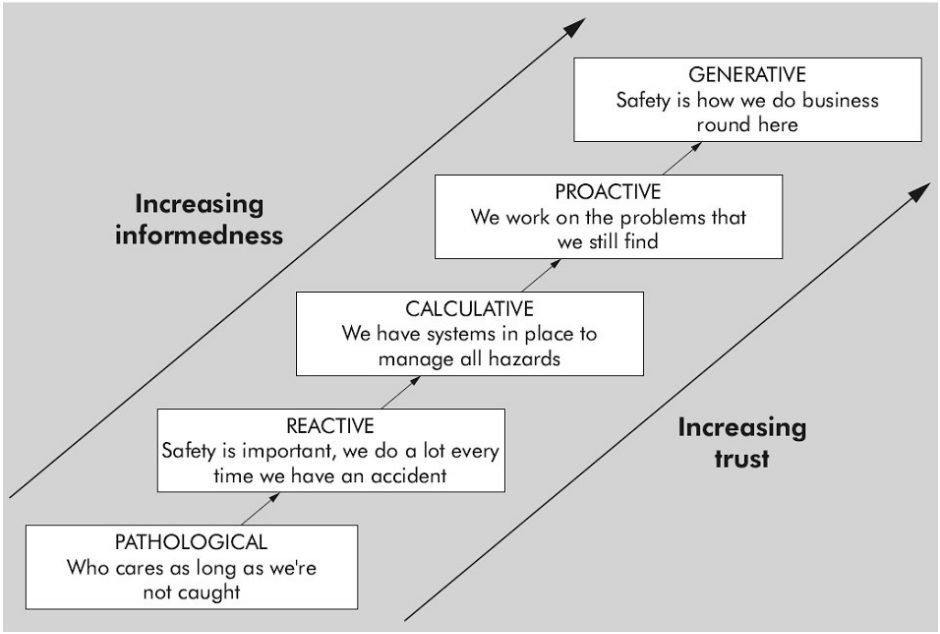
Implementing a QA program is regarded as a long-term process. The implementation strategy begins with the establishment of the right culture and awareness of the proposed change, followed by search for background information, followed by acceptance of the change and adoption in practice.

QA and improvement starts with the appropriate attitude. This has been underlined many times. And although different starting points can ultimately lead to the same quality improvement, general principles can be identified to indicate the phase of evolution a certain industry is in.[16] The development of a safety culture in hazardous industries can start from

very different points. For example, the airline industry was acknowledged to be dangerous from the start in 1903 with the first 12-second/37-metre flight by the brothers Wright and even before this moment, as until then all flights attempts had ended in accidents. Thus the need for quality improvement was obvious. On the other hand, the oil industry was more of a macho culture in which the need for profits easily overtook the safety issues. However, as the effects of errors in the oil industry proved to be far more extensive, with long-term local and global environmental effects, the oil industry ultimately turned itself into the same quality-eager industry as the airline industry.

The evolution of a safety culture within a sector has been described by Westrum et al.[39] His theory showed that in most organisations the first phase is the 'pathological' phase. From that point on, an organisation has to work its way up on the cultural ladder to improve on the safety culture Figure 3. This workup goes from 'reactive', to 'calculative', to 'proactive', and ends with a 'generative' culture. At this point, an organisation is informed at all levels, exhibits trust by all, is adaptable to change, and it worries or is wary.[16] It is stated that the medical world is somewhere around the second phase: a 'reactive' culture exists, but is developing to a more 'calculative' culture in the recent years.

Figure 3. Evolution of a safety culture model by Westrum.



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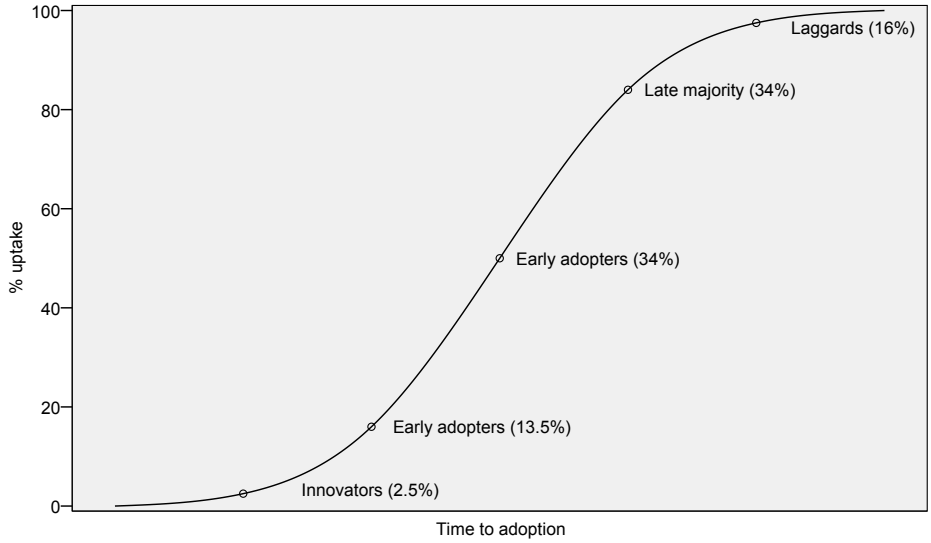
GETTING THE QA PROGRAM RUNNING

In the context of the suitable culture to become a generative organization, another important lesson from the past deals with the dissemination of innovations through an industry.[40] Studies have shown that for instance compliance to guidelines in health care is at best moderate, despite the fact that they incorporate the best-available evidence and are often developed by experts in the field.[41, 42] Moreover does it take several years for guidelines or new best-practice evidence to be common-practice.[43] This hampers the impact of quality initiatives. The way innovations (including quality initiatives) disseminate through a sector can be described by an S-curve Figure 4.[44] This means that it all starts with a small number of innovators (2.5%), the innovation is then adopted by a small number of early adopters (13.5%), who are followed by the early majority (34%). At this stage the innovation becomes common-practice and the late majority (34%) adopts the innovation as well. At last, it takes some extra time to get the laggards (16%) on board. Resistance can exist either because of the loss of control by the participating or target populations, or in distrust in the persons that are proposing these innovations. It is important to keep in mind for the first innovators that it may be hard to get quality initiatives off the ground, but as the past learnt from other industries, a change is forced with time. An important role in the dissemination of quality initiatives throughout health care is for 'clinical champions' or leaders. Without dedicated leadership from renowned experts within a certain area, it will be much harder to achieve a true improvement in culture and ultimately quality.

Figure 4. Dissemination of innovations over time.



Adapted from Berwick D.M. Disseminating innovations in health care. JAMA 2003; 289:1969–1975.

The right team culture is a key element in QA. Following an aeroplane accident with a Pan American 747 and a KLM 747 on Tenerife, Spain, on March 27, 1977, the airline industry became more aware of the importance of the team culture in their industry.[45] During this accident, the air traffic control tower provided the KLM 747 with information meant for the Pan American 747. One of the copilots knew that the information was not intended for the KLM flight, but did not dare to speak-up out of fear to undermine the authority of the senior captain. With 583 fatalities, one of the largest aeroplane accidents in the aviation history made clear how important shared responsibility and team culture is. Hierarchical relations were downplayed and a stronger emphasis was put on teamwork after the accident.

The Federal Aviation Administration (FAA) from the United States has mandated Crew Resource Management (CRM) as training for aviation industry personnel since 2006 in order to further improve quality in the airline industry. CRM can be described as a methodology to improve utilisation of the available resources such as optimal human performance with equipment and teamwork with communication between personnel.[46] CRM techniques have been reported to be achievable in the health care industry, again just as in the aviation industry professionals in health care are dedicated, skilled and highly educated in order to perform their job. Two core principles in CRM are referred to as cross-sectional monitoring and situational awareness.[45] Cross-sectional monitoring is a double check, to verify certain information. Situational awareness has everything to do with the larger purpose of your work. The awareness what type of actions are required at the moment and in due time in order to reach your objective. Central in CRM is the attitude to speak-up freely against the supervisor, as has been shown to be very important in the Tenerife aeroplane crash. CRM methodology works because a predetermined set of actions is formulated and being adhered to. CRM methodology seems to work especially in the acute care setting, because the principles are most easily translated into the work environment. Several studies have evaluated whether CRM Training enforces teamwork within health services using different approaches. In a survey study among hospital staff in the United States, positive findings were found in ratings by participants about CRM in a pre- and post-training design (8 hours of CRM training) for departments situated in acute care delivery.[47] However, in a large study performed in a neuro- and cardiac surgery department, only 60% of staff was compliant in adhering to the CRM principles after specific training.[48] This finding underlines the difficulty in maintaining a quality improvement after the implementation.

The Institute for Health care Improvement (IHI) has developed the Situation-Background-Assessment-Recommendations (SBAR) instrument based on CRM methods for critical situations and the urgent needed conversations between health care professionals.[49, 50] 'Situation' is a concise description of your own situation, 'background' of relevant information of the patient, 'assessment' why the patient is in danger at that moment and 'recommendation' describing what you are actually planning to do in agreement with your colleague. The SBAR instrument has been adopted from the military army.[50]

Besides the right team culture, dedicated leadership has been associated with improvement.[51] Excellent leadership provides the opportunity for implementation and sustainability. Additionally, the introduction of a learning environment by the management team has been shown to be effective on the work floor.[52] A good leader will realise improvements on a short timescale by engaging staff, quick implementation, and the use of appropriate methods to show whether interventions were effective. Involvement of physicians is reckoned as one of the most important parts in engagement, as support of them is needed in order to achieve a successful implementation.[53, 54]

Some barriers for the implementation of a QA program are based on financial constraints or the absence of motivated and supportive leadership, which is mandatory for successful engagement of staff in adopting a quality-centered attitude. Barriers for innovations were clearly observed in the National Demonstration Project in the USA, where three of the twenty included hospitals did not comply with implementation of QA policies due to financial problems.[20] Besides such constraints, another interesting observation is the resistance against changes that are often encountered in health care when implementing new changes or policies in organisations. Additionally, workload or other efforts associated with the implementation can be expected to increase. Results from the past can have a negative influence on implementation if they have not succeeded in a positive way for the parties concerned. The accessibility to high qualitative data for QA has also been mentioned as barrier for a physician to be involved in quality improvement initiatives.[55]

QA IN DAILY PRACTICE

Besides the application of theories derived from other industries, the health care sector has learnt a lot from those industries in more practical solutions and should strive for continuous learning from these interventions. To briefly touch this in the context of quality improvement in health care, the application of simulators in training and accreditation of physicians serves as example. Extensive experience exists with the use of simulators in the airline and naval industry and military army.[56, 57] Simultaneously, a large computer-gaming industry has arisen. The use of simulators has found its way through health care sectors in recent years as well, which for instance in endoscopy makes use of techniques such as forced feedback which were originally developed by the gaming industry. With these simulators in endoscopy, it has been shown that colonoscopic skills are at least as efficiently learnt on colonoscopy simulators as on patients.[58] Especially in surgery extensive research has shown similar results in different subspecialties.[59]

The use of checklists is recently receiving more attention as practical solution as well. Where comprehensive checklists are used in the airline industry before the aeroplane can proceed with the take-off procedure, the use of checklists are now getting more common-practice

in the medical world as well. A recent study from the Netherlands showed that the use of these checklists did significantly lower the number of surgical complications and mortality.[60] Thereby, more and more evidence is gathered for the usefulness of quality improvements project in health care derived from other industries.

CONCLUSIONS

This chapter aimed to provide an overview of aspects to keep in mind when working on quality in health care. We have learnt important lessons from the past and especially from other industries. Hereby we tried to give some insight in methodological approaches developed from other industries, which are more and more applied in health care. It is clear that in health care, tremendous efforts have been undertaken to raise the quality of delivered health care, and that this continuous urge for quality improvement for the patient is deeply rooted in the sector. Working, in close collaboration with all stakeholders in health care, from the discussed principles on would clear the way for further quality initiatives.

PRACTICE POINTS

- Quality assurance is deeply rooted in the way clinicians practice and has made a significant improvement since the last decade
- Important lessons can be learnt from industries outside the health care sector and can have tremendous implications for the way health care is delivered
- Applying and acknowledging these practice points from others will enable the health care sector to further improve, and achieve maximum benefit from the on-going quality initiatives

RESEARCH AGENDA

- Associations between structure, process, and clinical outcomes should be established to get everyone aboard
- Comprehensive quality assurance programs should be developed, implemented, and evaluated for this effect on different outcome of health care
- Uniform and comprehensive quality indicators should be developed to assess the patient satisfaction with delivered health care

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Chapter 3

Quality assurance of endoscopy in colorectal cancer screening

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ABSTRACT

This chapter explores the concept of quality assurance of colorectal cancer screening. It argues that effective quality assurance is critical to ensure that the benefits of screening outweigh the harms. The three key steps of quality assurance, definition of standards, measurement of standards and enforcement of standards, are explained. Quality is viewed from the perspective of the patient and illustrated by following the path of patients accessing endoscopy within screening services. The chapter discusses the pros and cons of programmatic versus non-programmatic screening and argues that quality assurance of screening can and should benefit symptomatic services. Finally, the chapter emphasises the importance of a culture of excellence underpinned by continuous quality improvement and effective service leadership.

INTRODUCTION

Background

It has been shown that colorectal cancer (CRC) screening leads to benefit in terms of decreased CRC related mortality.[1, 2] However, screening may also have harmful effects, such as psychological distress from false positive tests or false reassurance, or in a physical way from rare, but serious complications.[3, 4] Screening can thus cause both benefit as well as harm. This is particularly the case for CRC screening because the recommended final step in the diagnostic pathway will almost always be an invasive test such as a colonoscopy.[5] A key part of this procedure is removal of polyps, which carries additional risks.

If the quality of the screening process, including the selection and invitation of the target population, the screening procedure itself or the aftercare is poor, then the benefit of screening will be less. A point can be reached where the harm outweighs the benefit and screening will be of no value for the population nor the individual.[6] The problem of low quality and high harm is compounded by the observation that there is a finite amount of benefit that can occur in a screening programme as the intensity of screening increases (diminishing returns of benefit) but the harm continues in a linear fashion.

Screening invites healthy people with no symptoms, in good faith that the process will benefit them. Thus screening programmes have the responsibility to ensure quality is optimised: the patient has a high quality and safe procedure, and has a satisfactory experience.

Endoscopy in screening

Endoscopy has two roles in screening: as a primary screening test or as a test following another primary screening test such as a positive faecal occult blood test (FOBT) or flexible sigmoidoscopy (FS). The primary endoscopy screening test is either a colonoscopy or FS. Invariably this second diagnostic work-up test is a colonoscopy but in some circumstances it might be appropriate to use other techniques such as CT-colography. The aim of the two approaches is quite different.

The aim of endoscopy, when used as a primary screening tool, is to prevent CRC by detecting and removing pre-cancerous lesions (polyps). This effect has been proven with FS screening in an RCT and it is assumed that colonoscopy will have an equally positive effect.[1] However, there is no RCT evidence of the efficacy of colonoscopy for screening and several studies have now shown that colonoscopy does not 'protect' the colon from cancer.[7, 8] Furthermore, the UK FS Trial showed no difference in right sided cancer between the control and intervention groups.[1]

The principal aim of colonoscopy when used as a work-up test (after a previous positive screening such as FOBT or FS) is to reduce mortality by detecting early cancer.[1, 9] Five-year

survival has been shown to decrease from over 90% in localised disease to less than 10% when metastases are present. FOBT screening has been shown in several RCTs to reduce mortality from CRC but not to reduce overall mortality.[10]

Whatever the timing or impact of the endoscopic investigation, it is essential that it is of the highest quality otherwise the potential for preventing or curing CRC will be much diminished, and harm from the invasive diagnostic test or therapy will be very much greater. In a poor quality screening programme harm might outweigh the benefit, at both a population as well as patient level. This chapter will be primarily concerned with the quality of an endoscopy service in the context of screening and not distinguish the issues when endoscopy is used as a primary or secondary screening tool, or the differences between FS and colonoscopy.

Programmatic versus non-programmatic screening

Programmatic screening refers to screening that is organised centrally, either on a national or regional basis. A designated (usually by age criteria) portion of the population is invited according to a defined protocol and screen positives follow a prescribed pathway. Critically, organised screening programmes are quality assured against defined indicators in a rigorous way. In contrast, non-programmatic screening is done on an ad hoc basis and there is no formal quality assurance (QA) process.

The advantages of programmatic screening are that it maximises the chance of public involvement, reduces inequality of access and it is able to reassure patients and commissioners that screening is doing more good than harm. The disadvantages of programmatic screening are that there is an opportunity cost related to the organisational process itself (money spent on organisation cannot be spent on patient care) and programmatic screening is complicated to set up.

The advantages and disadvantages of non-programmatic or opportunistic screening are generally the flip side of programmatic screening. Screening can begin immediately with minimal set up or organisational costs. The individuals start gaining from screening immediately and all resource goes into patient care, with none or very little on organisation. The principal disadvantage is the lack of quality control. There is an abundant evidence base of highly variable endoscopy quality thus if there is no control of who does what, it is virtually impossible to know whether screening is benefiting the population.[11, 12] Because the event rate of complications is low, some time can elapse before it is known there is a problem if monitoring of outcomes is occurring on a local basis. Even when there is excellent local monitoring of outcomes the sample size may be too small to be sure there is a problem. In contrast systematic data collection in programme-based screening can identify problems and rectify them at an earlier stage. In opportunistic, non-programmatic screening resources are wasted with inappropriate testing (too young, excessively short intervals between tests), and higher marginal cost of low volume activity. Thus in non-programmatic screening considerable

resource might be wasted and, worse still, patients may be harmed unnecessarily because corrective processes cannot be put in place if there is no way of identifying there is a problem through regional or national QA.

Impact of screening on symptomatic services

It is possible to organise screening in isolation but in most circumstances screening will be integrated into symptomatic services. Screening creates a significant demand on endoscopy services and may disrupt symptomatic care and, in particular, cause lengthening waiting times. In 2002, it was shown that almost half of all colonoscopies and sigmoidoscopies in the US were performed for screening purposes, when approximately half of the eligible population receives appropriate screening.[13] In the near future, screening will increase the demand on endoscopy further as new screening programmes come on line in different countries, as age criteria for eligible populations are extended, as new methods of screening are introduced (such as FS were FOBT screening is the current method) and as we become more sophisticated in the way we invite the population for screening.

The primary responsibility of an endoscopy service should be for those presenting with symptoms. Because of the likely disruption that screening will cause to symptomatic services a key component of QA in CRC screening should be monitoring of its effect on the symptomatic service, particularly waiting times. On the other hand screening can enhance symptomatic services by introducing stricter QA mechanisms and by the knock on effect of the development of a 'culture' of quality improvement and QA. Wherever possible endoscopy services should look explicitly at how the introduction of screening can improve their symptomatic service.

QUALITY ASSURANCE

Quality assurance of screening is a process that is intended to reassure patients and programme organisers that the maximum benefit is achieved from the screening programme with minimum harm. QA is an essential part of screening and should be at the core of any screening programme. The emphasis of this chapter will be on the endoscopic aspects of the screening pathway as this has the greatest potential for both benefit and harm.

What is quality?

Defining quality in CRC screening is less straightforward than it might seem and will often mean something different to different stakeholders. From the endoscopist's view, doing a complete procedure, seeing everything there is to see and removing all polyps safely are par-

amount.[14] However, if the patient has a bad experience because he is not treated with dignity, or if he finds the procedure very uncomfortable, then he is less likely to return for follow-up or recommend screening to his family, friends and work colleagues, as is suggested in the PLCO Cancer Screening Trial in screening FS.[15] This will reduce the overall impact of a screening programme, making it less efficient and less cost-effective, because cost-effectiveness of CRC screening is dependent on uptake.[16] So the quality of the patient experience in the screening process is also very important.

Besides the endoscopist's expertise, the eventual outcome for the patient is a product of teamwork, the right equipment and facilities, and appropriate back-up processes when things go wrong. Thus quality monitoring systems need a wider view that look at the entire endoscopy unit, including its team, processes and facilities, as well as procedure outcomes. Quality monitoring also needs to include the entire screening pathway and systematic capture of the patient experience.

Measuring and monitoring quality

A key component of QA and quality improvement is measuring important outcomes.[17] Measuring have different functions at different levels in the health care system: at programme or regional level we need high level outcomes, preferably ones that clearly impact on the patient. Every screening programme has its own main outcomes and decreased cancer incidence of, and mortality from, cancer are the most important ones for cancer screening. As these outcomes are only apparent many years in the future, surrogate indicators are used to measure the impact of screening on these outcomes, such as cancer staging and adenoma detection rates.[18, 19] However, while these outcomes might tell us there is a problem and where the problem is, it does not tell us the cause of the problem. Thus, quality indicators need to capture outcomes that give an indication of the success of CRC screening in the long term, but also inform about the cause of problems in the short and medium term.

Another key aspect of QA is the importance of continuous quality improvement. This is best encapsulated in continuous audit programmes or the so called Plan-Do-Study-Act cycle (PDSA).[17] Continuous evaluation of performance ensures continuous improvement and ultimately the highest quality.

Another important aspect of QA is the handling of harmful events. Harmful events in CRC screening rates are fortunately rare. However, sometimes harmful events occur, even with optimal technique. When event rates are low it will often be difficult to know whether there is a correctable problem because the confidence intervals around the event rate will be wide. To monitor risk we need surrogate markers of safety that are immediately apparent and, in particular, look at what a service is doing to minimise risk, such as its pre-assessment processes and its response to minor adverse events. The occurrence and response to minor adverse events is very important because every fatal event will be underpinned by a series of

near-fatal events and these will be underpinned by an even larger number of minor adverse events. Diagnosing and correcting the cause(s) of minor adverse events will lead to a reduction in 'near misses' and eventually fatal events.

The airline industry does not wait for a plane crash to know whether it is has the appropriate safety checks and processes in place. Quite the reverse: it goes to extraordinary lengths to prevent things going wrong. Because plane crashes are fortunately very rare it is not possible to choose your airline on the basis of plane crashes. If you have concerns about safety you are best advised to look for processes that tell you the airline is doing all it can to prevent a problem. Likewise with an endoscopy service, a robust approach to safety will reassure you that serious events will be kept well within acceptable margins.

Quality indicators and auditable outcomes

Quality assurance requires a process of creating measurable standards for both the benefit as well as the possible harms, monitoring them reliably and then reviewing them on a regular basis. For those standards for which a target can be set (such as caecal intubation rates) a good QA programme will continually raise the target when the majority have achieved the standard. Obviously there is a limit to this process and a point will arise when it is impractical, or indeed unsafe, to raise the bar further.

Many things which we would like to measure are difficult to capture (such as missed CRC) and for others it is difficult to apply a target to (such as comfort during the procedure). On the other hand it might be quite possible to capture an outcome with a clear numerical measure but we have no idea of what is acceptable and therefore cannot, in the first instance, assign a target. Interval cancers appearing in surveillance programmes would be a good example of this.

It has been proposed that the term auditable outcome is used to describe a measure which is categorical rather than a continuous variable, or a measure for which a target level cannot be set. On the other hand those measures for which a target level can be set should be called quality indicators or quality standards.

THE PATIENT JOURNEY

The patient journey and multidisciplinary collaboration

With these issues in mind this chapter will focus on the patient journey through an endoscopy service and look at some of the peripheral factors that affect quality, as well as the more obvious determinants. Ultimately, a high quality CRC screening programme is dependent on effective teamwork underpinned by a culture of the entire team to achieve high quality;

things that are difficult to assess and compare objectively. Thus the themes of the chapter will be patient focus and multidisciplinary collaboration.

Patient information and consent

A high quality screening programme ensures that the population is well informed about the screening test offered, including its benefits and associated risks. Proper information provision has two main objectives.

Firstly, information provision should increase the awareness of the health problem associated with CRC and the possibility to diminish the burden of CRC by screening. This increased awareness will lead to increased attendance, higher uptake and thereby increased cost-effectiveness.

Several studies have addressed whether information provision influences the uptake of screening.[20-26] Results are somewhat conflicting. In a Swiss screening program, the majority of screenees indicated that participation in the screening program was influenced by more than one type of information, including written public and personal information and a discussion with their general practitioner (GP).[21] However, despite an extensive public awareness campaign, only 12% of the target population registered for the screening programme. An observational study in a Veterans Affairs setting found that informed decision-making decreased the chance of completing CRC screening.[20] On the other hand, a recent Italian study found that among the factors associated with participation in screening by FOBT or FS, a GP consult and an information letter and/or leaflet increased the odds ratio for participation.[25] Another recent RCT showed that higher intention scores were reached to participate in CRC screening among participants who received a decision aid.[24] Additionally, in the UK FS Trial psycho-educational interventions seemed to increase the attendance somewhat, because of less negative attitude.[26] Although increase in attendance was small (3.6%) this difference can have a big impact at the population level.

Secondly, a high quality information system ensures that patients can make an objective decision on participation based on the balance between perceived benefits and risks associated with the screening test. This leads to a high quality informed consent process in which patients understand every aspect of the screening, including necessary work-up after positive test results. This might be important in the context of litigation as it is known that litigation is less likely if robust consent processes are followed. In a Japanese study, it was found that when patients were informed about all the risks of colonoscopy, a minority changed their preferences for screening.[27] The authors concluded that the majority of patients was able to judge the balance of effectiveness and risk. This was emphasised by another study from the Netherlands, which showed that patients wished to be informed of all information, with more severe complications considered to be more important.[28] The authors concluded that a

stepwise approach in informing the patient about the complications would achieve the best balance between ethical considerations, good care, and practicality.

Finally, information provision for minority groups is very important. Several studies have shown that CRC screening uptake is lower in different ethnic groups.[29, 30] Barriers to screening include limited awareness, and anxiety.[31] By addressing these barriers among non-whites, awareness of screening and screening uptake was increased when doctors recommended screening.[32] Different approaches have been described in several studies to increase the enrolment of ethnic minority groups.[33-36] Overall, identifying the barriers and addressing them improves screening uptake.

In summary, the patient journey begins at the point they are notified of, or invited to attend for screening. At this point they need clear information about the procedure, what will happen to them, and what work-up might be necessary in the case of positive findings. They should have early access to the endoscopic service so that they can ask questions and eventually be consented for the procedure. They need clear instructions of how to perform and prepare for the procedure. All this will impact on the likelihood of them turning up for the procedure and being properly prepared. This will prevent waste of endoscopic resources, and ensure patients have a satisfactory experience. Ultimately their satisfaction will be determined by the extent to which their experience matches their expectations. Thus a comprehensive QA program should make sure that the information provided from the point of invitation until the patient is no longer eligible for, or part of the screening programme, is sufficient, that it is adjusted for the target population and routinely reviewed for effectiveness and acceptability.

Preparing for the procedure

During the pre-procedural phase it is essential to identify potential risk factors for complications during the procedure such as the use of anticoagulants or pre-morbid conditions such as heart disease or renal failure. These factors have been shown to increase the likelihood of adverse events in endoscopy.[37, 38] Thus, the patient needs to be interviewed, preferably face-to-face and using a check list, by a health professional for pre-assessment.

Another important aspect in the pre-procedure phase is the bowel preparation. Poor bowel preparation significantly affects the quality and safety of the procedure: it prolongs procedure time and decreases adenoma detection rate.[39, 40] Moreover, if poor bowel preparation leads to repeat procedures, it wastes endoscopic resources which are invariably already under pressure.[41] It has been shown that failure to adequately follow bowel instructions is significantly associated with the risk of an inadequate bowel preparation.[42] It emphasises the need for services to have clear instructions, and procedures in place to optimise bowel preparation. While no intervention trials have shown significant improvement in the quality of the bowel preparation by education, patients who followed the correct dietary instructions were more likely to have adequate bowel preparation.[43, 44]

It is recommended that the adequacy of bowel preparation is monitored on a continuous basis and that there should be a process of continuous improvement whereby factors leading to poor preparation are identified and corrected.[45]

Patient experience of the procedure

On the day of the procedure the patient is likely to be nervous and worried about their privacy and dignity, the procedure itself and what it might find. The environment, the attitude of staff and efficiency of process can have an important impact on these things by reassuring patients: it has been shown that patient satisfaction is highly dependent on doctors' and nurses' personal manner and the physical environment.[46] Moreover, realistic information about what an endoscopy involves also reduces anxiety.[47]

During the procedure the patient will be concerned about their comfort and a combination of sedation and professional support will ensure their discomfort is minimised. There are big differences between countries, and between institutions within countries, in sedation practice ranging from no sedation to anaesthesia.[48] This highly varying practice indicates that there is no approach which is superior. This is reflected in contradicting findings in the literature on the benefit of different approaches on the quality of the patient experience, the quality of the procedure and the efficiency of the process.[49, 50] Much depends on the expectation of the local public, the location and nature of the facilities and the attitude and experience of the endoscopist.[46]

Capturing the patient experience during the procedure is clearly important; however, if the patient has been sedated their recollection of events may be indistinct. Nurses are probably best placed to assess patient discomfort as they are the only individuals who can benchmark performance as they are usually the only persons who observe many endoscopists. Nurses should be empowered to ask an endoscopist to stop if they have concerns about the patient's safety or comfort. If the endoscopist ignores the nurse then this should be recorded as an adverse event.

Quality of the procedure

Broadly speaking there are two key components to colonoscopy: examining the colon to the caecum completely, safely, comfortably and within a reasonable time and second the detection of adenomas and their successful removal. In recent years much attention has been focussed on the first component. However, as caecal intubation rates and tolerance of colonoscopy improve, and as an evidence base has emerged of colonoscopy missing polyps and failing to 'protect' proximal cancer, the second component is becoming more important. Successful removal of polyps impact on the ultimate rate of CRC in the years following a colonoscopy.[51] Studies have shown that the CRC rates after colonoscopy range from 1 to

6% in different study settings.[52-54] There is no certainty of whether CRC appearing after a colonoscopy are 'missed' cancers or cancers that show more aggressive behaviour and rapid growth. However, the substantial variation in post-colonoscopy CRC, strongly suggests that these are truly missed cancers or cancers arising from incompletely excised benign lesions.

The rate of CRC after colonoscopy is a difficult indicator to measure, because of the need for long-term follow-up and a link between endoscopy and pathology reports, or cancer registry databases (which are unavailable in some countries). In view of this we need surrogate markers of quality. The most commonly adopted quality indicators of colonoscopy are those of the American Society of Gastrointestinal Endoscopy.[45] However, few studies have looked at the correlation of these indicators with the important outcome of CRC. In a recent study from Poland, it was found that among the suggested quality indicators, only the adenoma detection rate was significantly correlated with the risk of interval cancer.[51] In another study it was found that the type of specialist performing the colonoscopy was also associated with the risk of new or missed CRC, within three years of colonoscopy, with internists and GP's having higher rates of newly diagnosed or missed cancers.[52]

Thus where the post-colonoscopy cancer rate is difficult to obtain, or when a more immediate indication of quality is required, surrogate outcomes such as caecal intubation rates and adenoma detection rates are used as surrogate markers for quality of colonoscopy.

A caecal intubation rate is the most commonly used indicator of the quality of colonoscopy and 90% caecal intubation for symptomatic patients and 95% for patients having a screening colonoscopy are the generally accepted standards.[45] These rates allow for some adjustment for poor bowel preparation, stricture or severe colitis. In the UK there is one standard (90%) which refers to unadjusted rates. Unadjusted rates have been chosen to avoid confusion and 'gaming'. The rates are on an intention to scope basis and allowance is made if an individual has an unusually high occurrence of failure to complete because of known stricture, poor bowel preparation or severe colitis. Most standard frameworks require photo-documentation of completion with at least still, and preferably video images. However, there is good evidence that it is difficult to reliably confirm completion with still images and various audits have shown that photo-documentation is still poorly done.[55, 56]

Determining accurate adenoma detection rates is also not without problems. To get accurate estimates of adenoma detection rate requires linkage between endoscopy and pathology databases, which is not always straightforward to achieve. Adenoma detection rates have been shown to range from 15 to 36% in asymptomatic average risk populations over 50 years of age.[57] Differences in detection rates have been observed between males and females, and non-whites versus whites. A systematic review to determine the pooled miss rates for adenomas using tandem colonoscopy studies (two colonoscopies performed in the same patient by different endoscopists) have shown that miss rates for adenomas are as high as 22% (95%CI: 15–32%).[58]

If it is not possible to document adenoma detection rates, withdrawal times are a good but not perfect proxy.[59] Use of withdrawal times of >6 minutes as an outcome measure is popular in the United States but it can be subject to misuse, for example withdrawing quickly to the rectum and then waiting for the required time to elapse. However, while withdrawal time may have limitations as an outcome measure it may be useful to explain low adenoma detection rates and help correct technique.

Safety of the procedure

Several complications can present before, during or after an endoscopic procedure. Death, perforation and bleeding are the most important. Fortunately, death after screening colonoscopy has been reported in very few cases. A Canadian population-based cohort study reported that colonoscopy-related mortality30 days after the procedure was <0.01% (1 out of 14,000 procedures).[60] A prospective cohort from the US identified three deaths in 21,375 patients 30 days after the procedure.[37]

In this same cohort study, there was a perforation rate of 0.19 per 1,000 screenees. The generally accepted rate of perforation is less than 1 in 1,000 screening colonoscopies (<0.1%), while for FS perforation rates should occur in less than 25,000 to 50,000 screening exams.[18, 45] A recent review has shown that in some screening settings accepted colonoscopic perforation rates are exceeded.[61] The authors suggested that the prospective design of the screening trials, which leads to more comprehensive and reliable data about perforations compared to retrospective cohort studies, might be the reason for the high rates. On the other hand, studies have shown perforation rates below the target.[37, 62, 63] There is also increasing evidence from studies of colonoscopy outside the screening setting that a more acceptable target for perforation secondary to diagnostic colonoscopy is less than 1 in 5,000. Clearly, we would expect different rates of perforation in diagnostic procedures versus therapeutic colonoscopy, and this is evident in the systematic review mentioned previously.[61] Rates of perforation for diagnostic colonoscopies range from 0.03 to 0.8%, while perforation occurred in 0.15–3% in therapeutic colonoscopies. Therefore, it is appropriate to set different standards for diagnostic and therapeutic colonoscopies.

Contradicting results from different studies in complication rates also reflect the additional problem of underreporting. Perforation may only be apparent after the patient has been discharged and sometimes the patient will be admitted and treated at a different location. Unless there are linked databases it is very difficult to capture this type of event unless endoscopy teams routinely contact their patients a few days after the procedure. The majority of complications identified in the CORI database in the United States occurred within 7 days of the endoscopic procedure.[37] However, a significant proportion of serious complications occurred much later than this, with the majority being bleeding and diverticulitis with or without hospitalisation. Furthermore, risk factors for complications following colonoscopy

were use of warfarin (Odds Ratio (OR) 2.88; 95% CI 1.18–7.04 for directly adverse events) and polypectomy with cautery (OR 6.71; 95%CI 2.79–16.10).

To acquire an accurate estimate of the harm of colonoscopy requires a more rigorous approach to capture complications after the patient has left the endoscopy department, using established techniques such as 8 day unplanned readmission and 30 day mortality rates, otherwise harm will always be underestimated. Clearly many readmissions or deaths after colonoscopy will not be attributed to the procedure underlying the importance of case review as well as capture of delayed events. One study found that a standard telephone interview 30 days after an outpatient colonoscopy identified more complications than was previously known about.[64] Only 15% of all complications captured by interview were being discussed in mortality and morbidity conferences and physicians were unaware of half the emergency admissions that had occurred after colonoscopy.

Capturing and reporting of quality and safety indicators

Documentation of outcomes is critical for QA and it is very difficult to systematically capture and review outcomes without an information technology (IT) system.[65] Thus services are strongly recommended to have an IT system (usually in the form of an endoscopy reporting system) for standardised endoscopy reporting. These systems should have mandated fields to ensure there is 100% capture of key outcomes. In other words it should not be possible to complete the report until all key data fields have been captured.

Many commercial endoscopy reporting systems are able to capture the required data but are not very good at presenting it in a digestible form. Be sure when purchasing reporting systems to be satisfied with the data output as well as the data input. A second problem is one of data robustness. Before data is presented back to endoscopists great care should be taken to ensure the data is accurate. Doctors are exceptionally good at identifying flaws in data. Once inaccurate data is detected it will be difficult to win the confidence of the endoscopists about future data. Thus it is especially important to make sure the data is accurate first time round.

Post procedure aftercare

The care of patients following an endoscopy is critical for a good patient experience and for safety and quality reasons. Patients want to know what has been diagnosed and treated in terms they understand. They need to know what is happening next, what problems they might encounter and what they should do if a problem arises. Therefore, it is recommended to include a follow-up plan in each endoscopy report and provide them with a copy.[65, 66]

Many patients will need repeat procedures, often many years in the future. Reasons and plans for such surveillance must be clearly communicated to the patient, including a clear

description of the process by which they will be recalled. It has been shown in an RCT that patients had better recall of follow-up recommendations when an endoscopy report was combined with a verbal report of the endoscopist, compared to the verbal results alone.[66] Therefore, endoscopy services should consider providing all patients with a written report, unless deemed inappropriate.

Identifying problems with aftercare processes and correcting them can only be achieved if patients are systematically asked for feedback and if outcomes such as timelines for results and compliance with surveillance recommendations are measured. A good QA programme will include such processes.

Surveillance endoscopy

It is known that patients with adenomas are at higher risk of adenoma recurrence and development of CRC. In recognition of this, most countries will recommend surveillance colonoscopy at intervals that are related to the level of risk. Risk of adenoma recurrence has been shown to be dependent on several patient and adenoma characteristics, among which patient age and adenomas size, and number of adenomas on index colonoscopy are considered to be the most important.[67] Incomplete excision of polyps is a recognised reason for development of CRC and an additional reason to repeat colonoscopy. If the endoscopist recognises he has incompletely excised a polyp the site should be tattooed and re-inspected within a few months according to local protocols.

Every endoscopy service should ensure there are processes in place to inform patients of surveillance plans which should include an explanation of who is responsible for recalling the patient. If the endoscopy service takes responsibility for recall it needs a robust booking system supported by clear processes. Some endoscopy reporting systems have an automated system that supports the process of selecting and recalling patients for surveillance colonoscopy.

To maximise efficiency, reduce no show rates and avoid the harm of unnecessary colonoscopy these processes should include a clerical and clinical validation of the need for colonoscopy a few weeks or months before the surveillance procedure is due. Clerical validation refers to a clerical check on whether the patient has moved, had a colonoscopy done recently or died. Clerical validation should precede clinical validation which is a review of the appropriateness (need and timing) and of the fitness of the patient to undergo the procedure. For example, a surveillance procedure may be unnecessary because the patient had a colonoscopy for another reason in the recent past, or he may have developed an intercurrent illness that now makes colonoscopy inappropriate. Finally, guidelines for surveillance change periodically and patients should be warned that the guidance might change before the next procedure and that their case will be reviewed in the light of new guidance just before it is

due. If they are not warned then some patients will find it more difficult to accept a change in plan and be less satisfied.

Monitoring endoscopists' compliance with recommended intervals is necessary because there is abundant evidence that endoscopists schedule repeat procedures too soon and this is wasteful of resource and puts patients at unnecessary risk.[68, 69] Monitoring patients' compliance is equally important because poor compliance may indicate inadequate information and/or poor recall procedures.

Surveillance programmes offer an excellent opportunity to monitor the quality of endoscopy and benchmark colonoscopy practice because the next procedure is effectively a check on the previous one in a relatively controlled situation: a defined risk group over a fixed period. The adenomas and CRC found at the next procedure will be either new lesions, or missed or incompletely removed lesions. New lesions should occur at a stable rate in a defined population over a fixed period. Therefore the development of adenomas and cancers following an optimal baseline colonoscopy in each risk group should be predictable. Thus variation seen at the surveillance colonoscopy will reflect the quality of the previous procedure. It should be emphasised that for the indicators to be an accurate reflection of quality it is essential for the patient to be allocated to the correct risk group and the colonoscopy to occur at the correct interval. We do not have good enough data currently to set a target for the incidence of adenomas and CRC in each risk group but this will change and services are highly recommended to monitor these indicators.

Further treatment of screen detected CRC

The potential of screening to impact on mortality of CRC is partly dependent on optimising treatment of screen detected cancers. A detailed review of QA of treatment of screen detected cancers is beyond the remit of this chapter. However, it should be emphasised that it is the responsibility of endoscopy teams to ensure that patients are handed over to colorectal cancer multidisciplinary teams as smoothly and expeditiously as possible, and to provide surgeons with sufficient information to plan treatment. While small delays and clumsy processes may not impact on cancer outcome, they can have a huge negative effect on the patient experience. Endoscopy services are strongly recommended to include transfer of responsibility to CRC treatment teams in the audits of the patient experience to optimise hand over of care.

Endoscopy teams should work closely with surgical teams to ensure that inadequate information about the site and nature of cancers does not constrain planning of surgery. The tattooing of tumours and polyps is particularly important (and sometimes contentious). There are no fixed guidelines on tattooing and it is recommended endoscopists agree tattooing protocols with local surgeons and monitor compliance with these protocols by continuous audit of agreed outcomes.

QUALITY IMPROVEMENT

Quality assurance versus quality improvement

Quality assurance ensures a programme, service or an individual has achieved a standard of care or performance. Quality improvement refers to a cycle of monitoring of performance, making continuous refinements to improve performance and then further monitoring to ensure the refinements have been effective and to look for further opportunities to improve care. Quality improvement is underpinned by robust and reliable methods of data collection and reporting that are not excessively burdensome.

Endoscopy services should have in place regular meetings when key outcome data is reviewed. If there are concerns about performance a plan of action (with timelines) should be agreed with the individual(s) concerned and this plan should be reviewed for effectiveness at a later date. Similarly programmes should regularly review data and act on problems as they arise. As has been indicated at several points, certain indicators which are infrequent are best reviewed at service or programme, rather than individual level. Table 1 illustrates what indicators might be best monitored at which level.

Table 1. Levels at which performance should be monitored. Frequently occurring events are monitored and acted upon at a local level, while infrequently occurring events can only be monitored at the service or programme level. However, ultimately they need to be acted upon at a local level.

Proposed indicator	Indicator rate	Actual frequency of occurrence	Level at which indicator should be monitored		
			Individual	Service	Programme
Withdrawal time	6+	High	++++	-	-
Adenoma detection	20%	High	+++	+	+
Incomplete excision of polyps	5%	Low	+++	+	-
Complications	0.5%	Low	+	+++	++
'Missed' cancer	1-5%	Very low	±	+++	++++

Leadership of an endoscopy service

Effective quality improvement depends as much on the culture of the service as processes, because the strong desire to continually improve is essential to motivate staff and to make processes effective. Endoscopy staff 'going through the motions' and 'ticking the boxes' will not deliver the best care. Ultimately the culture of a service is determined by its leaders. Running an endoscopy department has become a complicated business and endoscopy services should appoint leaders (usually a clinician, nurse and manager) to manage the service effectively and to create a culture of patient centeredness and high quality care. Leading a service requires bespoke leadership skills and leaders will benefit from leadership training like endoscopists will benefit from endoscopy skills training.

Team competencies, equipment, decontamination and infrastructure

Continuous training, equipment and infrastructure are essential components of a high quality endoscopy service. A detailed description of what is required and how this might be delivered is beyond the scope of this chapter. Every country will have its own approach to the registration and training of professionals, and guidelines on infrastructure especially standards for decontamination facilities. The Endoscopy Global Rating Scale (GRS) and the Joint Advisory Group on Gastrointestinal Endoscopy (the JAG) provide a detailed description of what a patient centred high quality endoscopy service needs to have in place in terms of process, equipment, staff and training.[70, 71] It might be used as a template for others to adopt.

SUMMARY

Quality assurance of endoscopy is an essential component of any CRC screening programme. Without it there is a risk of doing more harm than good and of wasting valuable health care resource. Screening has the potential to harm and help symptomatic services and the impact of screening on the symptomatic service should form part of a CRC screening QA framework. Quality is a multi-dimensional concept that requires continuous monitoring of a variety of indicators and a culture of excellence supported by effective clinical and managerial leadership. Finally, the patient must be at the heart of quality assurance and services should be delivered around the needs of the patient and not health care systems or those that deliver the service.

PRACTICE POINTS

- Comprehensive quality assurance of colorectal cancer screening is essential to ensure the benefits of screening outweigh the risks by a considerable margin
- Quality assurance of the entire patient journey is necessary to ensure an excellent patient experience
- An excellent quality patient experience of CRC screening will enhance the reputation of screening thereby encouraging others to partake in screening
- Organised screening programmes enable comprehensive quality assurance which is not possible with opportunistic or non-organised screening
- The culture of quality assurance of CRC screening programmes integrated into symptomatic endoscopy services will accelerate improvements in quality assurance of those services

RESEARCH AGENDA

- Determine the frequency of interval cancers appearing in different risk groups in surveillance programmes
- Determine the modifiable reasons for the wide variations in post colonoscopy colorectal cancer
- Determine optimal bowel preparation cleansing regimens and ways of assessing them
- Determine target rates of early and late complications following diagnostic and therapeutic colonoscopy
- Determine what factors predict a high quality endoscopy service

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Chapter 4

Opinion of gastroenterologists towards quality assurance in endoscopy

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ABSTRACT

Background: Quality assurance has become an important issue. Many societies are adopting quality assurance programs in order to monitor and improve quality of care.

Aim: To assess the opinion of gastroenterologists towards quality assurance on the endoscopy department.

Methods: A survey was sent to all gastroenterologists (n = 319) in the Netherlands. It assessed their opinion on a quality assurance program for endoscopy units, including its design, logistics, and content.

Results: 200 gastroenterologists (63%) completed the questionnaire. 95% had a positive opinion towards quality assurance and 67% supposed an increase in quality. 28% assumed a negative impact on the time available for patient contact by introducing a quality assurance program and 35% that the capacity would decrease. A negative attitude towards disclosure of results to insurance companies (23%) and media (53%) was reported. Female gastroenterologists were less positive to share the results with other stakeholders ($p < 0.05$).

Most important quality measurements were assessment of complications (97%), standardised reporting (96%), and adequate patient information (95%).

Conclusion: Gastroenterologists have a positive attitude towards quality assurance. However, concerns do exist about time investment and disclosure of results to others. Information provision and procedure characteristics were considered the most important aspects of quality assurance.

INTRODUCTION

Quality assurance (QA) has become a very important aspect of endoscopy during the last decade.[1, 2] In recent years, several quality indicators for endoscopy and QA programs have been tested in practice and proven to be effective to improve specific quality indicators over time.[3-7] Provision of endoscopy thus seems to be perfectly suitable for a QA program with specified quality indicators and quality improvement by training and feedback.

QA is of paramount importance in the present health care. First of all, rising costs in health care emphasized the attention to quality of care in order to justify the money expenditures. Secondly, the increasing demand for endoscopic procedures can put the quality of procedures under pressure, while in the same context appropriate and well-performed endoscopies are required in busy daily clinical practice to prevent inappropriate and unnecessary repeated procedures. The demand of endoscopic procedures will further increase in the coming years, especially because of the implementation of colorectal cancer (CRC) screening programs in many countries and the accompanied surveillance procedures.[8-10] Moreover, successful implementation of a CRC screening program is highly dependent on high quality procedures.[11]

The success of a QA program depends on the willingness of the physicians to adopt the program in their practice.[12] Without the endoscopists properly reporting about their procedures, giving feedback about quality indicators and incorporating the QA program in their clinical practice, a QA initiative will fail. Additionally, in order to spread an innovative QA program it has to be compatible with the values, beliefs, and needs of the individuals working with it.[13, 14] Therefore, it is necessary to acknowledge the ideas of gastroenterologists (GE) working with a QA program beforehand.

So far, no study has addressed the opinion of GE about a QA program for the endoscopy department and how such a program should be designed. In other health care specialties, few studies have addressed the attitude of physicians towards QA. Barriers identified in the literature are the lack of time to perform QA and fear of assessment and critics.[15] In order to assess the attitude of GE towards a QA program we performed a study to evaluate the opinion and concerns of Dutch GE about a QA program on the endoscopy department in general and about its design.

MATERIALS AND METHODS

A questionnaire was sent to all registered GE (n = 320) in the Netherlands in May 2009. The recipients were offered a choice to complete the questionnaire online, or send it back by mail in a stamped, pre-addressed envelope. A reminder was sent after 5 weeks to all respondents who did not return the questionnaire. At the end of the study, the registry of the Dutch

Society of Gastroenterology was used to obtain demographic information about the non-respondents.

The first part of the questionnaire addressed the characteristics of the respondent, including age, gender, type of hospital they were employed at (academic vs. general hospital), and years in endoscopy practice.

The second part assessed the general opinion towards the implementation of a QA program on the endoscopy department. The questionnaire asked about the assumed effect of a QA program on capacity, time, and quality and about the disclosure of results to different stakeholders.

In the third part, questions about how important the respondent deemed several design aspects of a QA program, such as the role of patient experiences, clinical quality, involvement of nurses and managers, the comparison between hospitals, and the availability of the data for research were asked.

The last part of the questionnaire contained questions about the importance of specific quality indicators in a QA program, i.e. length of waiting lists, appropriateness of procedures, number of interventions, use of sedation, and completeness of reports.

For all responses a 5-point Likert-scale was used to score the opinion of the respondent, corresponding from a very positive to a very negative attitude towards a QA program or a specific indicator.

Statistical analyses were performed using SPSS 17.0.2. Chi-Square tests were used to compare categorical data between subgroups and Student's t-tests were used for numerical data. Associations between gender, employment at an academic or general hospital, and years of endoscopy experience and a positive attitude towards QA were assessed using univariate and multivariate ordinal regression models. The association between those variables and the willingness to share results with different stakeholders of endoscopy, and the perceived effects of a QA program were also assessed. A two-sided p-value <0.05 was considered statistically significant.

RESULTS

A total of 202 GE (63%) completed the questionnaire. Their characteristics are shown in Table 1. The respondents did not differ significantly from the non-respondents in their demographic data, although there was a strong trend towards a higher response from male GE compared to female GE (Table 1). The mean age of the respondents was 47.0 years (SD: 8.6 years), 79% was male. Mean endoscopy experience was 15.5 years (range: 0–39 years, SD: 9.4 years), 43% of the respondents had >15 years of experience in performing endoscopy. All respondents were affiliated with a hospital, 24% was employed at an academic hospital, and 76% worked in a general hospital.

Table 1. Demographic characteristics of respondents

	Respondents n (%)		Non-respondents n (%)		p-value
Gender					
Male	160	(79.2)	82	(69.5)	
Female	42	(20.8)	36	(30.5)	0.051
Mean age (yrs, SD)	47.0	(8.6)	47.7	(8.8)	0.570
Years of board certification (yrs, SD)	12.5	(8.5)	14.0	(8.2)	0.147
Employed at					
Academic hospital	49	(24.3)	33	(28.0)	
General hospital	153	(75.7)	85	(72.0)	0.404

Yrs: years; SD: standard deviation

A total of 93% of the respondents reported that they kept active track of complications, 78% had local initiatives to monitor and improve clinical quality of endoscopic procedures, and 70% regularly monitored patient satisfaction.

Quality assurance program, opinion and results

The attitude of GE towards a QA program and its results are shown in Table 2. The general opinion about the implementation of a QA program was positive among 95% of the respondents, while 1% of the respondents had a negative attitude towards the implementation of a QA program and 5% had a neutral opinion about it.

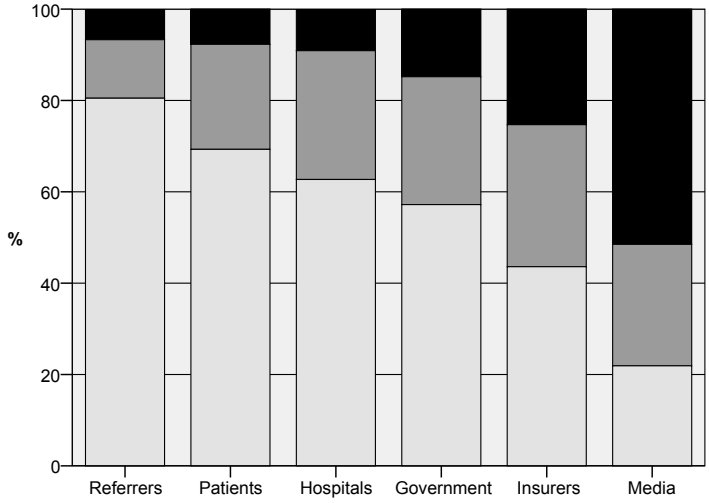
Table 2. Opinion of gastroenterologists towards a quality assurance program and the results.

	(Very) positive (%)	Neutral (%)	(Very) negative (%)
Overall attitude	94.5	4.5	1.0
Feasibility of implementation	72.6	21.4	6.0
Time available for patient contact	19.5	53.0	27.5
Endoscopy capacity	11.0	54.5	34.5
Endoscopic quality	66.2	33.3	0.5
Publicity around endoscopy department	57.7	41.3	1.0

When implementing a QA program, 20% of the GE thought this would positively influence the time they would have available for the patient, 28% thought the time would be negatively affected. Additionally, 11% thought the capacity of the endoscopy department would increase, while 35% thought this would decrease.

Figure 1 shows the opinion of the GE towards the disclosure of the results of a QA program to several stakeholders. Respondents had a negative attitude towards disclosing the results to the media (53%), insurance companies (23%), and the government (16%). Respondents were less negative towards sharing the results with referrers (7.0%), patients (8.0%), and other hospitals (8.5%).

Figure 1. Attitude of gastroenterologists towards the disclosure of results of a QA program to different stakeholders of endoscopy.



Quality assurance program, design

The possibility of comparing the quality of endoscopy departments within the Netherlands with a QA program was deemed to be important by 84%, while 4% thought this was unimportant. Comparing the quality of Dutch endoscopy departments to endoscopy departments from abroad was deemed to be important by 51% and not important by 21%.

A QA program should place clinical quality of the procedures central according to 93%, as well as patient centered care according to 90%.

Involvement of nurses in the quality assessment was deemed to be important by 73% and unimportant by 6%. Additionally, involving the managers of the endoscopy department in quality assessment was deemed to be important by 60% and unimportant by 17%. At last, 58% found it important to include patients in the quality assessment and 9% found this not important.

Quality assurance program, content

Table 3 lists the importance which the responding GE assigned to specific aspects of a QA program. Most important aspects to be included in a QA program were number and character of complications (97%), completeness of reporting (96%), adequate patient information (95%), and sufficient aftercare (94%). Of the respondents, 66% found the amount of sedation used during endoscopic procedures to be important, 65% the time that a patient had to wait on the endoscopy department, and 66% considered waiting lists a relevant QA issue to take into account.

Table 3. Importance of aspects to assess quality of the endoscopy department

Variable	(Very) important (%)	Neutral (%)	(Absolutely) not important (%)
Complications	96.5	3.0	0.5
Completeness of reporting	95.5	4.5	0.0
Sufficient patient information	95.0	5.0	0.0
Sufficient aftercare	93.5	6.5	0.0
Appropriate FU-recommendations	92.5	7.5	0.0
Complete procedures	92.0	8.0	0.0
Appropriateness of indication	90.0	9.0	1.0
Patient experiences	86.5	12.5	1.0
Findings during endoscopy	81.8	14.6	3.5
Use of IC	78.5	19.0	2.5
Length waiting list	66.0	22.5	13.5
Amount of sedation	65.8	24.6	9.5
Waiting time on the endoscopy department	65.0	26.5	8.5

FU: follow-up; IC: informed consent

Predictors of positive opinion towards QA

The results of the univariate and multivariate ordinal regression models are shown in Table 4. In the multivariate ordinal regression model, years of endoscopy experience was found to be of influence on an overall positive attitude towards QA. GE with <5 years of experience (OR: 3.76, 95%CI: 1.08–13.08) had a more negative attitude towards QA than GE with ≥15 years of experience, whereas gender and type of hospital (academic vs. general hospital) were not associated.

No factors were found to be correlated with the perceived feasibility of implementation of a QA program nation-wide ($p > 0.2$).

Female GE had a more reserved attitude towards the disclosure of the outcomes of a QA program than male GE to both health insurers (OR: 2.13, 95%CI: 1.10–4.13), other hospitals (OR: 2.23, 95%CI: 1.13–4.41), and patients (OR: 2.01, 95%CI: 1.02–3.96). There were no differences between males and females with respect to sharing the results with other stakeholders. Disclosure of results was not influenced by years of endoscopy experience and type of hospital (academic vs. general hospital).

No factors were found to be significant associated with the perceived effect of a QA program on the overall quality of the endoscopy department ($p > 0.4$), endoscopic capacity ($p > 0.1$), and publicity ($p > 0.1$).

Table 4. Results of the ordinal regression models

		Univariate regression OR (95%CI)	Multivariate regression OR (95%CI)
A negative attitude towards QA			
Gender	Male	0.69 (0.35-1.33)	0.86 (0.42-1.77)
	Female	1.0	1.0
Type of hospital	Academic center	0.60 (0.32-1.14)	0.57 (0.29-1.10)
	General hospital	1.0	1.0
Endoscopy experience	<5 years	3.71 (1.08-12.70)	3.76 (1.08-13.08)
	≥15 years	1.0	1.0
Implementation of a nationwide QA program feasible			
Gender	Male	1.13 (0.59-2.18)	1.19 (0.59-2.39)
	Female	1.0	1.0
Type of hospital	Academic center	1.10 (0.59-2.06)	1.11 (0.59-2.08)
	General hospital	1.0	1.0
Endoscopy experience	<5 years	0.97 (0.30-3.07)	1.0 (0.31-3.23)
	≥15 years	1.0	1.0
Willing to disclose QA results to government			
Gender	Male	0.70 (0.37-1.29)	0.74 (0.38-1.43)
	Female	1.0	1.0
Type of hospital	Academic center	0.70 (0.37-1.23)	0.70 (0.38-1.27)
	General hospital	1.0	1.0
Endoscopy experience	<5 years	1.56 (0.53-4.63)	1.41 (0.47-4.25)
	≥15 years	1.0	1.0
Willing to disclose QA results to media			
Gender	Male	0.56 (0.30-1.04)	0.53 (0.27-1.03)
	Female	1.0	1.0
Type of hospital	Academic center	1.17 (0.65-2.09)	1.12 (0.62-2.02)
	General hospital	1.0	1.0
Endoscopy experience	<5 years	1.48 (0.50-4.34)	1.20 (0.40-3.59)
	≥15 years	1.0	1.0
Willing to disclose QA results to health insurers			
Gender	Male	2.13 (1.14-3.96)	2.13 (1.10-4.13)
	Female	1.0	1.0
Type of hospital	Academic center	0.75 (0.42-1.33)	0.71 (0.39-1.29)
	General hospital	1.0	1.0
Endoscopy experience	<5 years	0.62 (0.21-1.81)	0.75 (0.25-2.23)
	≥15 years	1.0	1.0
Willing to disclose QA results to patients			
Gender	Male	2.09 (1.10-3.94)	2.01 (1.02-3.96)
	Female	1.0	1.0
Type of hospital	Academic center	0.81 (0.47-2.27)	0.78 (0.43-1.45)
	General hospital	1.0	1.0
Endoscopy experience	<5 years	0.95 (0.31-2.92)	1.14 (0.37-3.54)
	≥15 years	1.0	1.0
Willing to disclose QA results to other hospitals			
Gender	Male	2.26 (1.19-4.27)	2.23 (1.13-4.41)
	Female	1.0	1.0
Type of hospital	Academic center	1.06 (0.57-1.94)	1.06 (0.57-1.98)
	General hospital	1.0	1.0
Endoscopy experience	<5 years	0.91 (0.30-2.77)	1.09 (0.35-3.36)
	≥15 years	1.0	1.0

Table 4. Results of the ordinal regression models (continued)

		Univariate regression OR (95%CI)	Multivariate regression OR (95%CI)
Willing to disclose QA results to referrers			
Gender	Male	0.55 (0.28-1.07)	0.57 (0.28-1.15)
	Female	1.0	1.0
Type of hospital	Academic center	1.10 (0.59-2.07)	1.13 (0.60-2.13)
	General hospital	1.0	1.0
Endoscopy experience	<5 years	1.04 (0.33-3.30)	0.92 (0.29-2.98)
	≥15 years	1.0	1.0
Positive perceived effect of QA program on capacity			
Gender	Male	0.89 (0.46-1.72)	0.67 (0.33-1.37)
	Female	1.0	1.0
Type of hospital	Academic center	0.61 (0.32-1.15)	0.62 (0.33-1.19)
	General hospital	1.0	1.0
Endoscopy experience	<5 years	0.60 (0.19-1.95)	0.56 (0.85-3.09)
	≥15 years	1.0	1.0
Positive perceived effect of QA program on quality			
Gender	Male	1.11 (0.57-2.18)	1.05 (0.51-2.16)
	Female	1.0	1.0
Type of hospital	Academic center	1.10 (0.58-2.09)	1.14 (0.60-2.17)
	General hospital	1.0	1.0
Endoscopy experience	<5 years	1.23 (0.38-3.96)	1.24 (0.38-4.06)
	≥15 years	1.0	1.0
Positive perceived effect of QA program on publicity			
Gender	Male	1.05 (0.54-2.01)	0.91 (0.45-1.84)
	Female	1.0	1.0
Type of hospital	Academic center	1.31 (0.70-2.45)	1.43 (0.76-2.71)
	General hospital	1.0	1.0
Endoscopy experience	<5 years	0.95 (0.30-3.00)	0.90 (0.28-2.88)
	≥15 years	1.0	1.0

OR: odds ratio; CI: confidence interval; QA: quality assurance

DISCUSSION

In this study we assessed the opinion of Dutch GE about the implementation and design of a QA program for the endoscopy department. In order to get an innovative QA program disseminated on the endoscopy department and be effective nation-wide, it should address the needs and beliefs of the individuals working with it.[13] The most important determinant of rapid spreading of health care innovations is the perceived benefit of the change accompanied with it. Our study shows that the GE do have a positive perception of the results of the implementation of a QA program. Almost all (>95%) GE have a positive attitude towards the implementation of a QA program and 66% assumed that the quality of the endoscopy department would increase. However, almost 30% doubted whether it would be feasible to implement a QA program nation-wide.

Additionally, concerns were raised about the time involved with quality assessment, i.e. 28% feared that the time for patient contact would decrease and another 35% were afraid

that the capacity would decline. Furthermore, disclosure of the results to media, government, and insurance companies were received with some reserve by 16–53% of the respondents.

These concerns are in line with previous research.[15, 16] In a Dutch study among general practitioners the most frequently mentioned barriers were the extra time concerned with QA, fear of assessment, and criticism from colleagues.[15] In the 2003 Commonwealth Fund National Survey of Physicians and Quality of Control among US physicians, only 29% answered in a national survey that they were willing to share the results with the general public, while more than half of them were willing to share the results with their own patients and medical leaders.[16]

Our survey shows that GE value the same quality indicators for a QA program. It is important that an innovation is compatible with the needs and values of the physicians.[13] Clinical quality, measured in number of complications, standardized reporting, and completeness of procedures, was deemed to be important by more than 90%. International literature and guidelines have underlined the importance of these quality indicators and many studies have addressed these indicators.[1, 17] Additionally, GE were well aware of the importance of a good experience for patients. Satisfied patients are more likely to be compliant with medical care.[18, 19] More than 90% of the respondents answered that patient centered care should be included in a QA program and especially adequate patient information and good aftercare were deemed to be of importance.

A limitation of this study was the use of a questionnaire, which may not reflect willingness to participate in clinical practice. Furthermore, the response rate was 63%, which means that one third of the registered GE did not respond. A reason for not completing the questionnaire could be a negative attitude towards a QA program leading to selection bias and overestimation of the positive attitude towards QA. The respondents and non-respondents did not differ with respect to age and endoscopy experience. However, a trend towards less response amongst female GE was seen. In this context it should be emphasized that we also observed a more negative attitude among female GE with respect to disclosure of QA results towards some of the stakeholders of endoscopy (especially insurers, patients, and other hospitals). However, no differences were found in overall attitude towards QA, the feasibility of the implementation of a QA program, and the perceived effect of a QA program. Reasons for the differences in disclosure viewpoints are unknown. The results do underline the importance of the role of innovators and early adopters to convince other individuals to achieve the maximum effect of a QA program.[13] In this case, there might be special attention from health authorities implementing QA programs towards female GE. A last concern could be the fact that we only addressed gastroenterologists in our study, and did not focus on internists and surgeons. This was done because more than 80 percent of gastroenterology procedures in the Netherlands are performed by gastroenterologists, who also run all endoscopy units with exception of some units in small rural hospitals.

This study was performed in a Western setting, with no comprehensive QA program available yet and took place as part of an exploration of the current climate for QA on endoscopy units in the Netherlands. Individual hospitals are paying attention to improving quality of patient experiences, and most individual GE work on the clinical quality of their procedures by visiting congresses and training sessions and discuss new developments within their (professional) networks. Additionally, until now, no CRC screening program has been implemented in the Netherlands, although recently the National Health Council of the Netherlands recommended starting CRC screening based on results of pilot screening programs.[20-22] In the context of this situation, GE are likely to pay increasing attention to quality assessment and improvement in advance of the coming changes.

In other countries, QA programs for endoscopy have been tested and implemented successfully.[6, 23] Financial consequences of such implementation are an important, underexposed, issue as the implementation and enforcement of quality monitoring and improvement will take time. Financial incentives can work positive by rewarding institutions that reach certain quality thresholds, or negative by limiting allowed procedures. However, no financial incentives have been proposed as part of the implementation of an endoscopy QA program in the Netherlands. Unfortunately, we did not capture any data on this issue and therefore, future studies need to explore the possible influences of finances on attitude and cooperation in quality initiatives.

In conclusion, this study shows that GE are aware of the importance of QA and are willing to work on a comprehensive QA program. Although some concerns need to be adequately addressed, like the time needed for adequate ongoing QA, and the handling of results, the implementation of a QA program will be possible and GE are willing to monitor and improve their quality.

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Chapter 5

Quality assurance in the endoscopy unit; the view of the endoscopy personnel

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ABSTRACT

Introduction: Quality of health services depend on the entire medical team. A supportive team culture, and effective leadership is required for successful quality assurance (QA). The opinion of endoscopy personnel towards QA is unknown, while they have to collaborate in many quality projects.

Methods: A survey was send to all endoscopy nurses, assistants, and managers. It focused on the implementation of a QA program. Further, a team assessment was included, focusing on leadership and team functioning, using scores on 5-point Likert-scales, with 1 being a very positive opinion, and 5 being a very negative opinion towards the item.

Results: 294 persons completed the questionnaire (44%). Eighty-seven percent expressed a positive attitude towards a QA program, and 54% thought that the implementation of a nationwide QA program for endoscopy would be feasible. Positive effects of QA were expected on publicity (62%) and overall quality (70%). Most important QA aspects were patient-related factors, such as aftercare (97%) and patient experiences (96%). Concerns were raised about the time QA would cost (18%), and about disclosure of results towards media (24%). Team assessment showed good scores on 'Team working' with a mean score of 1.97. Lower scores were given to the 'Wider organization' (3.00) and 'Team process' (2.42).

Conclusion: Endoscopy personnel have a positive attitude towards a QA programme. Besides, the team culture and its leadership are ready for the implementation of a QA programme. Efforts should be made to improve team processes and the relation with the wider organization to ensure an optimal team culture, aimed at quality improvement.

INTRODUCTION

Quality assurance (QA) in endoscopy is of utmost importance.[1, 2] The rising expenditures in health care and the increasing demand for endoscopic procedures both stress the need for continuous QA.[3, 4] Furthermore, in colorectal cancer (CRC) screening programs, comprehensive monitoring of the quality of the endoscopy service is essential as healthy individuals are invited and may receive an invasive endoscopic procedure. Therefore, during the implementation of a CRC screening program, a comprehensive QA program should be enrolled as well.

QA in endoscopy consists of various aspects.[5, 6] First and foremost, the clinical quality of the procedure is important. A high quality endoscopic procedure consists of a safe, thorough, and complete inspection of the gastrointestinal tract. However, the complete journey of a patient through the endoscopy department is important in optimizing the benefits of endoscopy, providing maximal clinical benefit at minimal risk, and at maximal patients' satisfaction and willingness to return. This, in turn, enhances the uptake and thereby the cost-effectiveness of CRC screening.[7]

The attitudes and behavior of health care personnel appears to have a major impact on patient experiences.[8] Every endoscopy team member influences the quality of the endoscopy department. Therefore, it is crucial that there is a team culture aimed at providing excellent care with well-organized collaboration both between and within teams. In recent years the team culture within health care departments has increasingly become of interest, following developments in the airline industry.[9, 10] Within a team culture aimed at quality improvement, personnel should know the targets of their department, feel responsible to achieve these targets, and feel free to speak up. It should be stressed that QA is a team responsibility. Dedicated leadership is a key factor to realize this.

In an earlier study, we assessed the opinion of gastroenterologists with respect to QA in endoscopy.[11] Gastroenterologists were well aware of the need of QA and were prepared to work on the quality of the endoscopy department. However, as outlined above, the opinion of the other team members is as important to successfully improve the quality of the service. Therefore, the aim of this study was to assess the opinion about QA of endoscopy personnel other than gastroenterologists. Additionally, a team assessment was performed to explore the team´s leadership and team´s performance to determine what organizational areas need attention to enforce a culture aimed at quality improvement.

METHODS

A survey was sent to all endoscopy nurses, assistants, and managers registered at the Dutch Society of Endoscopy Nurses and Assistants (n=670).[12] In a former study, the opinion of gastroenterologists was investigated. As we were interested whether there were differences

between their opinion and the opinion of the other endoscopy personnel, we performed this current study and did not send a new survey to the gastroenterologists making part of the endoscopy team. In the Netherlands, officially trained endoscopy nurses, as well as general nurses and assistants can be employed on the endoscopy department. The specialism of endoscopy nurse is an expanding expertise, which requires additional training, besides the general nurse training. Nearly all Dutch hospitals employ trained endoscopy nurses for the direct assistance of endoscopists. Other personnel like endoscopy assistants provide support on the department in patient care, service maintenance, and administrative work.

The first part of the survey contained questions inquiring the attitude of the endoscopy personnel towards QA in endoscopy. This part was utilized before in a former study about the attitude of gastroenterologists towards QA.[11] In short, the first part of the questionnaire assessed the overall attitude towards a QA program, its design, content, the handling of results, and the perceived effects of a comprehensive QA program.

The second part of the survey was a previously used team assessment tool from the United Kingdom. The team assessment is an evaluation of the team functioning and leadership and was designed as part of a Team Leadership Program in endoscopy in the United Kingdom. The team assessment was translated into Dutch by a certified translation company. The team assessment tool contained 43 statements subdivided in six separate domains, called: 'Communication' (four questions about the communication within the team), 'Recognition and reward' (four questions about how team members feels their contributions are rewarded), 'Team culture' (nine questions about whether team members enjoy working in the team), 'Team process' (nine questions about planning), 'Team working' (eight questions about responsibilities within the team), and 'Wider organization' (nine questions about the relation with the high managerial levels within the hospital).

All answers were given on a 5-point Likert-scale, with 1 being a very positive opinion, and 5 being a very negative opinion towards the particular item. Nurses and assistants were given the possibility to complete the questionnaire online or send it back by mail. All non-respondents were sent a reminder five weeks after the first mailing. The completed questionnaires were anonymously entered into a database. Statistical analyses were performed using the SPSS statistical package version 17.0.2. Descriptive statistical analyses were performed using Chi-Square tests for categorical data, and Student's t-tests for continuous data.

Multivariate ordinal logistic regression was performed to assess correlations between overall attitude towards QA, perceived effects, and the willingness to disclose QA results with gender, age, and type of hospital where the respondent was employed at.

The data from the items of the team assessment were transformed in a summary score for each domain. The higher the summary score, the less positive participants judged about a certain domain. Beforehand, it was decided arbitrarily that scores between 1 and 2 would be regarded as positive, scores between 2 and 3 as reassuring scores, although improvements in these areas should be sought, while scores of 3 and higher would be regarded as insufficient,

delineating high priority areas of attention. The summary scores were then used in multivariate regression analyses to assess correlation with age, gender, type of hospital where the respondent was employed at, and overall attitude towards QA.

RESULTS

Study population

Of the 670 questionnaires, a total of 295 (44%) were returned. Table 1 shows the available demographic data of the respondents and the non-respondents. Respondents were significantly more often employed at a general hospital, compared to non-respondents (93 vs. 85%, p = 0.003).

Table 1. Demographic data

	Responders n (%)	Non-responders n %	p
Total	294 (44.0)	376 (56.3)	-
Female gender	269 (91.5)	346 (92.0)	0.774
Mean age (years, SD)	46.5 (8.7)	NA	-
Employed at			
Academic hospital	22 (7.5)	56 (15.1)	0.003
General hospital	271(92.5)	315 (84.9)	
Median years of experience on the endoscopy department (interquartile range)	10.0 (6.0-17.0)	NA	-

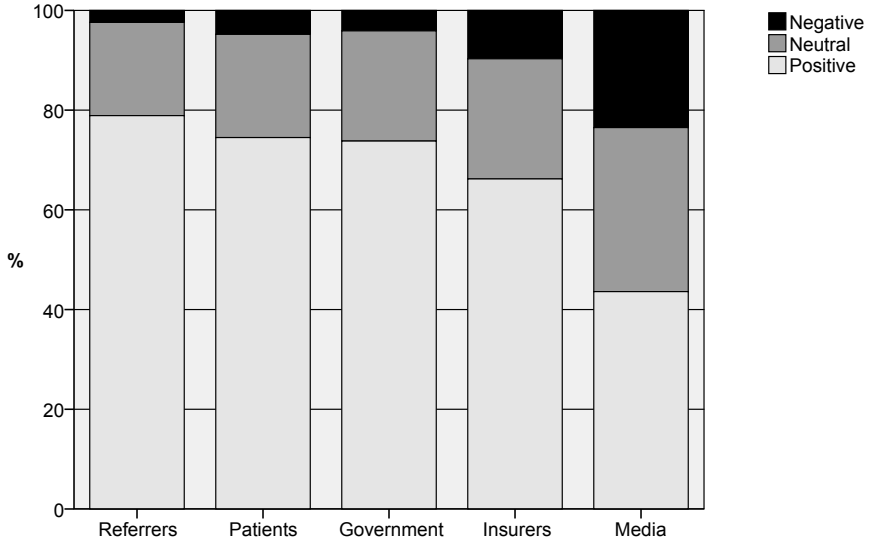
SD: Standard Deviation; NA: Not Available

Attitude towards quality assurance

The majority of the respondents (87%) expressed a positive attitude towards the implementation of a nationwide QA program on the endoscopy department. Only one person reported a negative attitude towards it, while 12% of the respondents were neutral. When asked about the feasibility of implementation, 54% of the respondents perceived that it would be feasible to implement a QA program nationwide. Thirty-eight percent had no clear opinion, while 8% expected it to be unfeasible.

Figure 1 shows the results of the respondents with respect to the disclosure of QA results towards different stakeholders in endoscopy. The nurses and assistants on the endoscopy department were especially reserved towards disclosure of the results to media (24%) and insurers (9%), while a less negative perception was reported to share the results with patients (5%), government (4%), and referrers (2%).

Figure 1. Attitude of endoscopy personnel towards the disclosure of quality assurance results to different stakeholders



Eighteen percent of the respondents were afraid that a comprehensive QA program on the endoscopy department would lead to reduction of the available time for patient contact, 50% thought there would be no impact on the time, while 33% thought that more time would come available.

The endoscopic capacity would increase according to 33% of the respondents, the quality would increase according to 70%, and 62% of the respondents expected that the publicity around the endoscopy department would be positively influenced.

Table 2 shows the priority ranking of different quality aspects according to the endoscopy personnel. Optimal provision of patient information (99%), attentive aftercare (97%), and optimal patient experiences (96%) were regarded to be the most important aspects to consider in a QA program on the endoscopy department. Least important were the diagnostic findings (77%), use of sedation (78%), and completeness of procedures (80%).

In the multivariate analyses, older age was significantly associated with a less positive general attitude towards QA (OR: 1.04, 95%CI: 1.00-1.08), whereas type of hospital and gender were not.

Older age was also a significant predictor of a less positive attitude towards sharing the results with the government (OR: 0.97, 95%CI: 0.94-0.99) and other hospitals (OR: 0.95, 95%CI: 0.92-0.98), while the type of hospital and gender were not associated with the attitude to disclose results. Willingness to disclose the results to other stakeholders in endoscopy and the perceived effects of a QA program were not significant associated with age, gender, and type of hospital.

Table 2. Importance of different quality parameters

Parameter	(Very) important (%)	Neutral (%)	(Absolutely) not important (%)
Length of waiting list	85.3	12.7	2.1
Proper patient information	98.6	1.4	0.0
Use of informed consent	84.2	15.8	0.0
Waiting time on the department	87.6	11.4	1.0
Appropriate indication	93.5	6.2	0.3
Monitoring of use of sedation	78.1	18.8	3.0
Findings	77.0	19.6	3.4
Completeness of procedures	79.6	18.0	2.4
Patient experiences	96.2	3.4	0.3
Aftercare	96.9	3.1	0.0
Complications	88.3	11.7	0.0
Correct follow-up advice	89.3	10.0	0.7
Complete reporting	92.8	6.9	0.3

Team assessment

Table 3 shows the mean scores for the six different domains regarding the team assessment. Employees of academic hospitals in comparison with those working in general hospitals scored significantly less favorable for the domains of 'Team culture' (2.07 vs. 2.39, p = 0.02) and 'Recognition and reward' (2.13 vs. 2.40, p = 0.048)

Within the domain 'Communication', team members were most positive about the ability of the team to negotiate solutions when problems arise (mean score: 1.78, SD: 0.72), while a considerable number of team members were unsatisfied with the freedom to speak out their mind within the team (mean score: 2.49, SD: 1.03).

The domain 'Recognition and reward' showed that team members feel appreciated by other team members for the work they do (mean score: 1.71, SD: 0.66). Less favorable scores were given to the team incentives to generate financial savings (mean scores: 2.50, SD: 0.86).

Endoscopy team members were positive about the flexibility and willingness of colleagues to go the extra mile when needed (mean score: 1.66, SD: 0.80) within the 'Team culture' do-

Table 3. Team assessment scores

Domain	Mean domain score	Academic vs. general hospital	Range of item scores	Cronbach's alpha
Communication	2.05	2.19-2.04	1.78-2.49	0.78
Recognition and reward	2.15	2.40-2.13 *	1.71-2.50	0.56
Team culture	2.09	2.39-2.07 *	1.66-2.80	0.86
Team process	2.42	2.59-2.40	2.08-2.88	0.89
Team working	1.97	2.12-1.95	1.63-2.38	0.79
Wider organization	3.00	3.00-3.00	2.66-3.75	0.86

5-point Likert-scale: 1 – Very positive; 2 – Positive; 3 – Neutral; 4 - Negative; 5 – Very negative

* $p < 0.05$

main. On the other hand, a considerable number of respondents indicated that there was a 'blame culture' in the endoscopy team (mean score: 2.80, SD: 1.04).

Team members judged the most negative about the larger organization. A mean score of 3.75 (SD: 1.00) was given to the statement whether the team has influence on higher levels in the organization, while the best score within this domain was given for the statement that the teams' goodwill was not abused (mean score: 2.65, SD: 1.05).

Multivariate regression analyses showed that older age was the only variable significantly associated with more positive scores within the domains 'Team work' (OR: 0.99, 95%CI: 0.98-1.00) and 'Team culture' (OR: 0.99, 95%CI: 0.98-1.00). No other correlations between the variables age, gender, or type of hospital, and one of the domains were found.

DISCUSSION

This study shows that endoscopy nurses and assistants generally have a positive attitude towards QA on the endoscopy department and expect that a QA program would have a positive effect on the overall quality of the department. However, concerns were raised about the time required for structured QA resulting in less time for patient care and a decreased capacity. Additionally, only half of the respondents expected the implementation of a QA program nationwide would be feasible. Respondents indicated that the most important quality parameters were patient-related aspects like patient information provision, patient experiences, and aftercare. The results from the team assessment showed that the endoscopy personnel were in general satisfied about their team culture, and indicated that attention is needed for the relation with the wider organization.

Before health care innovations such as continuous quality assessment and quality improvement projects can be disseminated throughout a health care system, it should be assured that the project is compatible with the beliefs, values and needs of the people who should work with it.[13] The results of the first part of this study showed that the majority of the endoscopy teams supports introduction of a QA program. These results are in line with a previous study in the same setting, among gastroenterologists.[11] Although there were small differences, gastroenterologists expressed the same attitude towards, and perceived the same benefits from a comprehensive, nationwide QA program.

An important finding is that gastroenterologists and nurses prioritize different quality parameters. In the current study, nurses prioritize patient aspects of care, with especially waiting lists (85%), patient information (99%), and patient experiences (96%) as important quality indicators. In the previous study among endoscopists, these parameters were deemed important by less respondents (66%, 95%, and 87%, respectively).[11] On the other hand, the clinical aspects of the procedure, like completeness (92%), diagnostic yield (82%), and complications (97%), deemed to be more important by the gastroenterologists, while

less nurses and assistants rated these parameters important (79%, 77%, 88%, respectively). The differences in priorities of QA might be explained by the important role nurses play in patient satisfaction. Over 60% of patients' satisfaction is determined by nurse interaction, as they have the most intense patient contact.[14, 15] Moreover, several studies have shown that nurses' personal manner is an important factor in patient satisfaction in endoscopy.[8, 16] Nurses might be well aware of their ability to influence patients' satisfaction and know they are well suited in addressing these quality parameters that directly influence the patient experiences.

Besides their role in patient satisfaction it has been suggested that nurses are probably best equipped to identify department strengths, as well as weaknesses, as they are present on the endoscopy department the entire working day.[17] Therefore, their knowledge and commitment in QA should be mobilized. Dedicated leadership is a key factor to pursue the right team culture aimed at continuous quality improvement. Our team assessment indicates that the team is motivated and willing to collaborate to actively work on the departments' service. However, low scores on the domain 'Team process' indicate that improvement should be sought in setting and planning common targets. This is important as the endoscopy team should agree on common goals to provide excellent care and these goals should be understood by everyone in the team.

Our study showed that endoscopy personnel feel that there is a satisfactory presence of skill and knowledge mix. There is evidence that the skill mix of the team, and the number of nurses available in the hospital, influences clinical outcomes. In several studies it has been shown that factors of influence on hospital mortality outcomes are level of experience and number of registered nurses, as well as ratios between nurses to unqualified staff, or nurses to patients.[18, 19]

Improvement can be achieved within the domain 'Wider organizations', which indicates that the communication with higher management levels should be improved. As QA programs are often designed and controlled by managers, these results emphasize that the management should stay in close contact with the people working with their interventions in order to be effective.[13] The implementation of a QA program should not be a top-down process, but more a close collaboration between the different levels, as is also underlined by the differences in priorities in quality indicators between gastroenterologists and nurses and assistants.

The results of this study should be appreciated in the context of its setting. Currently no comprehensive QA program for endoscopy is available in the Netherlands. In the coming years, while a CRC screening program will be enrolled throughout the country, it is expected that a QA program will become available. Results of the studies discussed above are incorporated in the development of this program, and it will be interesting to see how satisfied the personnel will be in a couple of years with the proposed QA program. In this context there is also a lot to learn from the United Kingdom, where many developments in QA have taken place a couple of years ago. The success in the United Kingdom in raising the quality

of endoscopy has depended greatly on the efforts of the nurses and assistants. Therefore it is recommended to seek their input in developing a QA program in order to achieve the maximum benefit from the efforts.

A limitation of our study is that the response rate is low despite the fact that the survey was brought to the attention on different occasions. No additional data are available on the non-responders. In the context of the above mentioned setting of this study, the low uptake might reflect the fact that currently QA is not a general accepted part of the work of the endoscopy personnel other than gastroenterologists. As in the United Kingdom nurses have taken a leading role in QA at the endoscopy department, all efforts should be sought to incorporate the nurses and assistants in the development of a QA program to increase the probability of success of a QA program.

In conclusion, the implementation of a QA program in endoscopy is supported by endoscopy nurses, assistants, and managers. Moreover it seems that the current team culture suffices to create an optimal team culture to improve the quality of the endoscopy department. The results emphasize the need for close collaboration with all levels within an organization to design such a QA program, to properly address all their concerns. QA will only successfully lead to quality improvement as the entire endoscopy team will be dedicated to collaborate in the quality initiatives.

What is already known on this subject:

- For successful quality assurance (QA), the entire medical team should be motivated and support the programme
- In the implementation of a QA programme, all stakeholders should be heard

What this study adds

- Endoscopy personnel feel positive about the implementation of a QA programme
- Endoscopy personnel prioritize different aspects of QA compared to gastroenterologists
- The team culture on the endoscopy department and its leadership seems to be sufficient to implement a QA program successfully, although the communication to the wider organization and within the team may need some attention

How might it impact on clinical practice in the forseeable future

- Endoscopy personnel other than gastroenterologists should be actively engaged in the process of developing a QA programme
- Successful QA needs the support of the entire health care team working with it

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Chapter 6

The Global Rating Scale in clinical practice: a comprehensive quality assurance program for endoscopy departments

Submitted

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ABSTRACT

Introduction: The Global Rating Scale (GRS) is a quality assurance (QA) program, successfully implemented in endoscopy departments throughout England. It is uncertain whether it is applicable in another health care setting. We aimed to assess the applicability and validity of the GRS as a benchmarking tool in an international context.

Methods: Eleven Dutch endoscopy departments were included for a GRS-census. Two GRS-dimensions – 'clinical quality' and 'quality of patient experience' – were assessed across six items using a range of levels: from level-D (basic care) to level-A (excellent service). Construct validity was assessed by comparing department-specific colonoscopy audit data to GRS-levels.

Results: For 'clinical quality', variable scores were achieved in the items *'safety'* (9%=B, 27%=C, 64%=D) and *'communicating results'* (46%=A, 18%=C, 36%=D). All departments achieved a basic score in '*quality assessment procedure'* (100%=D).

For 'quality of patient experience', variable scores were achieved in *'timeliness'* (18%=A, 9%=B and 73%=D) and *'booking & choice'* (36%=B, 46%=C, and 18%=D). All departments achieved a basic score in '*equality'* (100%=D).

Departments obtaining level-C or above in *'information', 'comfort', 'communicating results'*, *'timeliness'* and *'aftercare',* achieved significantly better audit outcomes compared to those obtaining level-D (all correlations $p<0.05$).

Conclusion: The GRS is an appropriate QA benchmarking tool for a context outside England. There was significant variance across departments in the GRS-dimensions. Most GRS-levels were in line with departments' clinical audit outcomes, indicating construct validity.

INTRODUCTION

With increasing recognition of variability in the quality, safety and patient experiences of endoscopy, there is a growing need for comprehensive quality assurance (QA) programs that assess all aspects of care. Quality of care can be evaluated using structural, procedural and (clinical) outcomes.[1] Thus far the literature in endoscopic quality has centered primarily upon procedural indicators, such as the adenoma detection rate for colonoscopy, and procedural indicators, such as guidelines in standardized endoscopy reporting.[2, 3] Structural indicators concern whether certain facilities, such as an appropriate endoscopy reporting system, are available in the endoscopy practice. A recent Italian study acknowledged the importance of these in combination with procedural indicators.[4] A comprehensive QA program should incorporate indicators from all three areas, in order to ensure quality across all aspects of endoscopy.

A comprehensive QA program, the Global Rating Scale (GRS), containing the abovementioned features has been implemented in endoscopy departments throughout England. The development of the GRS was prompted by the introduction of a colorectal cancer (CRC) screening program and by shortcomings in the quality of endoscopy.[5, 6] The GRS achieved such excellent results in England, that it is now part of the accreditation process of the national CRC screening program.[7, 8] Currently, the GRS has received international attention.[9-12] However, data is lacking about the application and validity of the GRS in an international context.

The primary aim of this study is to evaluate whether the GRS is applicable as QA tool for endoscopy departments outside England, and to assess its reliability as benchmark tool. Secondary objectives are to establish the validity of the GRS in assessing patient-centered care, and to assess the endoscopy staff's experience of the GRS.

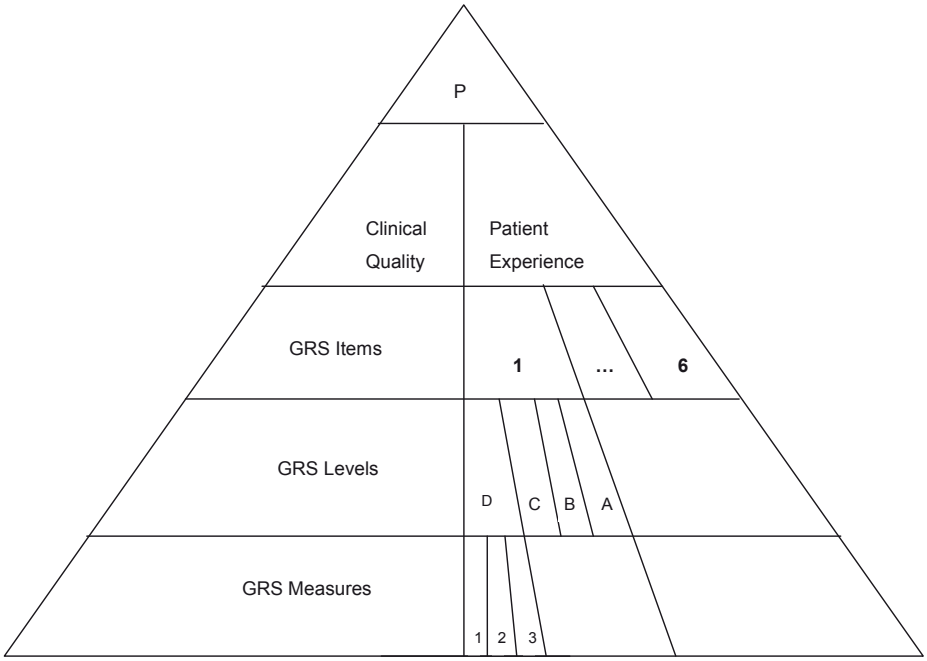
METHODS

Concept of the GRS framework

The GRS is a web-based QA program to assess the patient-centered care. The GRS consists of different layers, the so-called dimensions, items, levels and measures (Figure 1).[6]

The first layer consists of dimensions: 'clinical quality', 'quality of patient experience', 'workforce' and 'training'. Each dimension is then divided into several items. Different levels can be achieved for each item, ranging from basic (level D) to excellent (level A). The levels are subdivided into several measures: statements that are intended to be unambiguous (achieved or not achieved/ available or not available). The tool thus works as a web-based checklist to

Figure 1. Design of the GRS with the evaluation of 'Clinical Quality and 'Quality of Patient Experience' dimensions



P= Patient as central key element

evaluate the service. The levels achieved by an endoscopy unit provide a summary of the service for that particular item.

We decided beforehand to focus the study on evaluating 'clinical quality' and 'quality of patient experience' dimensions; 'workforce' and 'training' were not assessed.

Evaluation of the English GRS for Dutch applicability

The content of the GRS items was evaluated for the Dutch endoscopy setting by two Dutch and two English investigators, who were experienced in the development and implementation of the GRS.

A Dutch certified translation agency experienced in health-care translated the GRS checklist, which was then translated back into English by another translation agency. The transcripts were compared by the investigators and any differences resolved by consensus.

A Dutch expert panel consisting of health-care professionals (five gastroenterologists and one endoscopy department manager) reviewed the translated GRS to adapt it to the Dutch setting. Appropriate government policies, procedures and existing guidelines were incorporated. Table 1 shows the final list of GRS items used in this study.

Table 1. GRS items for 'Clinical Quality' and 'Quality of Patient Experience' dimensions

Clinical Quality	Description	Number of measures	Audit outcomes
Information & Consent	Evaluation of the consent procedure and pre-procedure information provision	n=10	Complications (perforation and bleeding) discussed with health care professional
Safety	The availability of complication management systems within an endoscopy department	n=14	Not applicable
Comfort	Processes are in place to monitor patient comfort before, during, and after endoscopic procedures	n=10	Comfort
Quality assessment of procedure	Assessment whether audit programs for clinical outcomes in performance of procedures are available	n=12	Not applicable
Appropriateness endoscopic procedures	Evaluation of processes to ensure the appropriateness of (surveillance) indications policies for endoscopies	n=15	Not applicable
Communication to the referrer	Assessment of communication of results, follow-up policy, and advise to referrer in the discharge pathway of the patient	n=10	Follow-up policy mentioned in endoscopy report
Quality of Patient Experience			
Equality and Equity	Processes of care for the needs for minority populations (ethnic, disabled, etc.)	n=13	Not applicable
Timeliness	Targets in waiting times for patients who need to undergo an endoscopic procedure	n=14	Estimated waiting time by patients
Booking and Choice	The planning of endoscopy programs and whether patients are given a choice in scheduling procedures	n=11	Opportunity to have a choice in scheduling a procedure
Privacy and Dignity	Optimization of the patients' privacy within the endoscopy department	n=19	Privacy recovery room endoscopy unit
Aftercare	Assessment of aftercare protocols (discharge instructions, communication of results, for endoscopic procedures	n=16	Aftercare pamphlet
Ability to provide feedback	Evaluation whether patient feedback is available assuring continuous input by the patients	n=9	Not applicable

Data collection

GRS-census

To address the objective whether the GRS is applicable as a QA program in the Dutch endoscopy service, we carried out a baseline census in 11 Dutch endoscopy departments (Table 2). These departments represent approximately 10% of all endoscopy departments in the Netherlands. Six of them were teaching endoscopy departments (including one university hospital) and five were non-teaching. For each department, a gastroenterologist, an endoscopy nurse and/or an endoscopy unit manager, together with the two Dutch investigators, completed the GRS online.

Table 2. Baseline characteristics of the endoscopy departments (n=11)

Department	1	2	3	4	5	6	7	8	9	10	11
Teaching / Non-teaching setting	T	T	T	N	N	T	N	N	T	N	T
Total number of endoscopists (n)	8	5	25	8	9	11	5	5	15	5	9
Gastroenterologists (n)	6	5	10	4	4	6	5	5	9	2	6
Total endoscopies annually performed	8569	6493	8078	5549	5406	6522	4985	8470	7416	3100	7676
Colonoscopy	2568	2914	2030	2073	2111	3043	1747	3152	3072	1042	3965
Gastroscopy	4054	2877	4448	2682	2290	2919	2589	3617	3681	1279	3158
Flexible sigmoidoscopy	1727	526	726	671	718	291	490	1515	298	690	289
ERCP	220	176	874	123	287	269	159	186	365	89	264
Number of endoscopy rooms	4	3	8	3	5	3	3	4	4	2	4

Construct validity

The GRS measures indicate whether structural and procedural quality indicators are in place in a department. It may therefore be argued that the GRS is not a valid system for measuring patient satisfaction and clinical outcomes. To assess the validity of the program, we evaluated whether the GRS levels scored by the different departments (as recorded by the endoscopy staff) correlated with actual patient reported and clinical outcomes. For this purpose, GRS results were compared to data from a colonoscopy quality project taking place in the same departments during the same study period, described elsewhere.[13, 14] The quality of colonoscopy was assessed by two separate studies: a patient satisfaction study using a pre-and post-colonoscopy GRS-questionnaire, and a colonoscopy performance study (both studies obtained ethical approval). Endoscopy personnel were at the time of completing the GRS-census unaware of the results from the colonoscopy audit in their department.

A total of 1,391 patients who participated and responded in the patient satisfaction survey for colonoscopy were collected from the 11 departments.[13] The colonoscopy performance study evaluated the quality of colonoscopy reporting and performance from 4,400 colonoscopy reports (400 per unit), based on quality indicators from the American Society of Gastrointestinal Endoscopy (ASGE).[14] For the 'clinical quality' three out of six GRS items could be correlated to the audit results; and for 'quality of patient experiences', four out of six could be correlated (Table 1).

Experiences of endoscopy personnel of the GRS

After the GRS-census, a survey was completed by members of staff that had been involved in the study. The survey contained questions about the characteristics of the staff respondent, and about the perception of the GRS in terms of applicability, usefulness, quality content in endoscopy, overall satisfaction, and willingness to work with it again (5-point Likert scaling).

Statistical analysis

GRS-census

Descriptive statistics were used to report the overall results of endoscopy departments within the two dimensions.

As it is often argued that (larger) teaching endoscopy departments have more resources for quality improvement than non-teaching departments, the levels achieved by both groups were compared using the Fisher's exact test.

Construct validity

Differences in continuous variables between departments achieving level D and departments achieving level C, B, or A in the same item were tested using the Mann-Whitney *U* test, as level D is regarded as basic care. For categorical outcomes, the Chi-squared test was used.

Experiences of endoscopy personnel regarding the GRS

Questions on a five point-Likert scale were first converted to a three-point scale for interpretability and presented as positive, neutral and negative ratings. Statistical analyses were performed using SPSS PASW, version 17. A two-sided p-value of <0.05 was considered significant.

RESULTS

GRS-census

The results for the 'clinical quality' dimension are depicted in Figure 2. The scores within this dimension showed large variation between departments for the items *'safety'* and *'communicating results'*. For *'safety'*, one department scored level B, and the other departments scored level C (n=3) or D (n=7). Five hospitals reached level A for *'communicating results'*, and the others achieved level C (n=2) or D (n=4).

Scores for other items within the 'clinical quality' dimension were more uniform and basic-level: Nine departments scored level D for '*appropriateness',* and all 11 departments scored a level D for *'quality assessment of procedure'*.

The results for the 'quality of patient experience' dimension are depicted in Figure 3. The scores for individual items within this dimension showed a large variation between departments for the items *'booking & choice'* and *'timeliness'*. Four departments scored level B in *'booking & choice'*, and the others obtained level C (n=5) or D (n=2). For *'timeliness'*, two

Figure 2. 'Clinical Quality' dimension percentages of GRS levels of all 11 departments

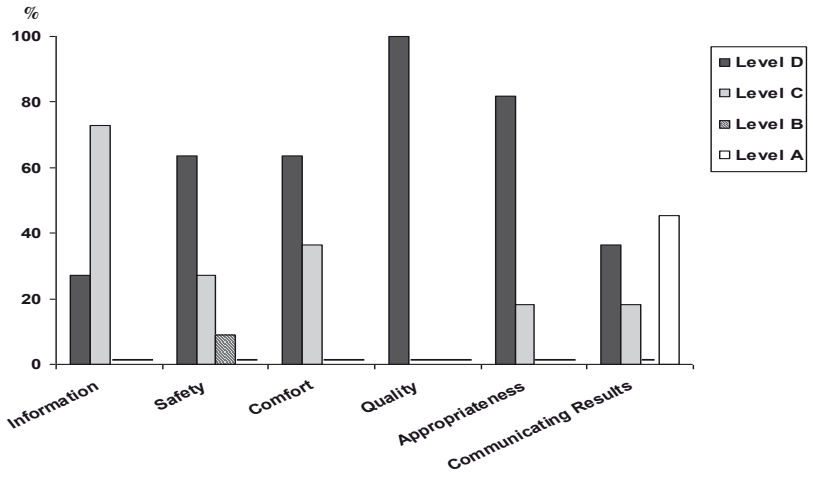
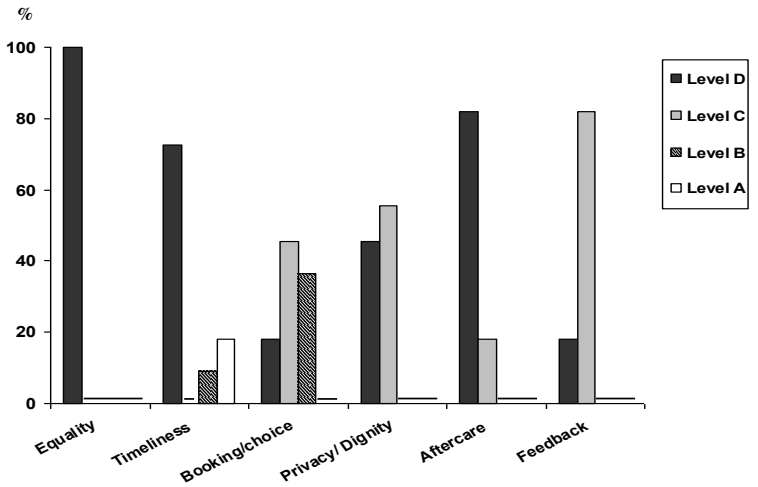


Figure 3. 'Quality of Patient Experience' dimension percentages of GRS levels of all 11 departments



departments (18%) reached level A, one department level B (9%), and the remaining departments level D (73%). The results for the item '*equality*' were uniform and low-level, with all departments scoring level D.

No significant differences were observed between teaching (n=6) and non-teaching departments (n=5) in obtaining a level B (50 vs. 40%, p=1.0) or a level A (83% vs. 60%, p=0.55) for any item in either dimension.

Construct validity

To assess the validity of the GRS, we compared the GRS scores given by the endoscopy staff to the department-specific patient satisfaction and clinical practice data derived from the colonoscopy quality project.

Fewer patients in departments that obtained level D in the item *'information'* (32 vs. 52%, p<0.001) stated that the risk of colon perforation was discussed than in departments that achieved level C or above. For the risk of bleeding the same findings were observed (44% vs. 53%, p<0.01).

The proportion of patients that experienced discomfort during their colonoscopy was significantly higher in departments that obtained level D in the item *'comfort'* than in those that achieved level C or above (23 vs. 11%, p<0.001).

For *'communicating results'* the proportion of reported follow-up policies in the colonoscopy report was used as an audit indicator. Departments that obtained level D were found to provide a follow-up policy significantly less often than those that achieved level C or above (50 vs. 80%, p<0.001).

Patients reported significantly longer waiting times in the departments that obtained level D in *'timeliness'* than in departments that achieved level C or above (mean estimated waiting time 4.6 vs. 4.0 weeks, p<0.01).

For *'booking & choice'*, the choice of dates and times available for scheduling a colonoscopy was evaluated. Unusually, the proportion of patients that reported that they were given the opportunity to choose a date and a time was significantly higher in endoscopy departments that obtained level D than in departments that achieved level C or above (63 vs. 52%, p<0.001).

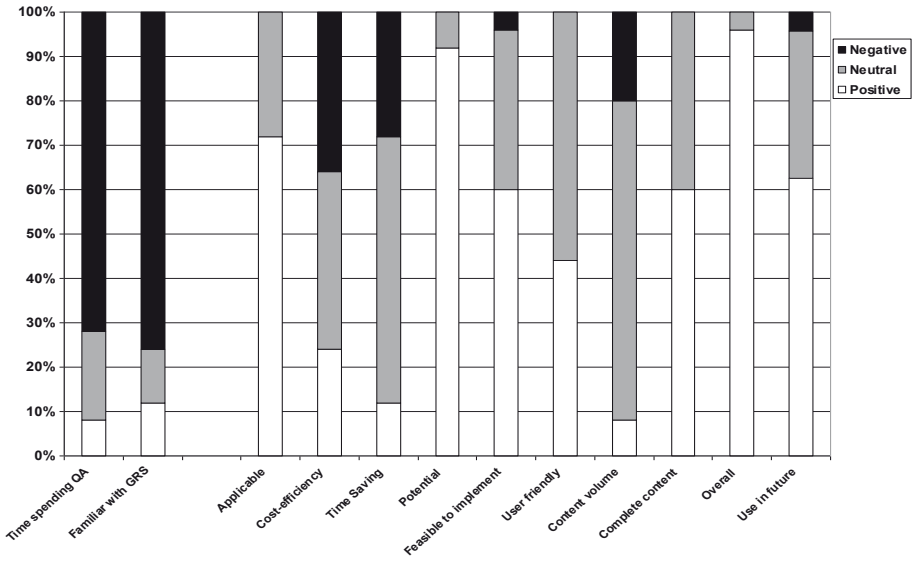
To evaluate *'privacy & dignity'*, patient ratings of privacy in the recovery room of the endoscopy department were assessed. The proportion of patients that were satisfied with the recovery area did not vary significantly between departments that obtained level D and departments that achieved level C or above (77 vs. 76%, p=0.63).

For *'aftercare',* the proportion of patients that received an aftercare information leaflet was significantly lower in departments that obtained level D than in departments that achieved level C (60 vs. 70%, p<0.001).

Experiences of endoscopy personnel regarding the GRS

Overall, 86% of staff members completed the survey evaluating the GRS. Eleven respondents were gastroenterologists, seven were endoscopy nurses, and seven were managers. The mean years in endoscopy practice was 10 (SD=8). Figure 4 shows the results. Staff were negative about the 'cost efficiency' (36%) and 'time burden' (28%) of using the GRS as QA program. 'Content' and 'potential as standardized QA program in endoscopy' were rated satisfactory in

Figure 4. Endoscopy personnel survey regarding the GRS



60% and 92% respectively. The majority (96%) was positive about using the GRS. Overall, 63% were willing to use it again in the future.

DISCUSSION

Comprehensive QA in endoscopy has gradually received more structured attention since the introduction of CRC screening programs. In the Netherlands, programmatic CRC screening is expected to start in 2013. Besides a quality audit system for endoscopy services by external auditors every 5 years from the Dutch society of Gastroenterology, no comprehensive QA system does exist yet.

A potential QA program is the Global Rating Scale (GRS), successfully implemented to accredit English endoscopy departments for CRC screening.[6] Since 2005, excellent results have been achieved in improving the performance of endoscopy in focusing on patient-centered care.[8] Despite its international interest, there has been no data available about the applicability and validity of this program as a QA tool in other countries.

Our study shows that the GRS is applicable as a QA program outside England. The GRS-census identified important service deficiencies in the Netherlands. For some GRS items large variance was seen in levels, but for other items all departments scored level D. The majority of English departments also had level D in certain items when the system was first implemented in 2005 (3% of NHS departments in England obtained level B or A for *'quality of the procedure'*).

However, since then large improvements were realized in England in most departments.[8, 12] The results of this study show that it could easily be used to achieve similar results in the Netherlands.

Most departments achieved only basic levels in this GRS-census. This is not necessarily because they provide a poor service; it could be that they are simply unable to demonstrate that they provide a good one. One advantage of the GRS is that departments are able to identify how 'quick wins' can be achieved. In the item *'safety',* the majority of departments (n=7) did not complete measure 3 for level D and C ("Adverse events review by the endoscopy unit team on a regular basis (at least 2x/year)"). Thus, by implementing an adverse events meeting of all endoscopy staff members, the department could improve from level D to C for the entire item, with reassurance that there is a process in place to learn from adverse events. 'Quick wins' have the further positive effect of engaging staff by making quality improvements visible.

In order to achieve continuous quality improvement, departments must continually challenge the bar by raising their standards. This can be done by means of benchmarking, where the bar is set by exemplary best-in-field organizations.[15] Benchmarking also provides the opportunity for collaboration because departments can share solutions to particular service deficiencies. The opportunity to benchmark between departments is illustrated in our results, showing significant variability in GRS items between departments. It is often argued that teaching departments achieve higher GRS levels more easily than those in non-teaching departments as they have more resources available. We did not observe this difference, which strengthens our opinion that the GRS is applicable to all types of practice. Alternatively, floor effects may also be attributable, as in every item basic scores were apparent.

Some of the basic scores deserve further discussion such as *'quality assessment of procedure'* (100% D). This can be explained by the fact that it is not currently obligatory for endoscopy quality indicators to be monitored in Dutch endoscopy departments; they lack formal audit systems, a prerequisite for this item. In the future, it is expected that quality indicators will be implemented in the Dutch setting, and scores will thus improve for this item. Dutch endoscopy departments also achieved basic scores for the item *'equality'*. This might reflect the different priorities of Dutch and English society and health-care systems. In conclusion, the GRS should be critically reviewed before being fully implemented in any health-care system.

The construct validity of the GRS may be questioned as the GRS statements were established during consensus meetings in England. There may be concern that improvement in GRS levels does not always reflect better patient outcomes. This underlines the importance of our study, which validated the GRS by linking the underlying structural and process indicators in measures to the clinical outcomes found in clinical practice and reported by patients. When the structural and process indicators are properly addressed, patient satisfaction is expected to be higher. In the item *'comfort'*, for example, where one of the GRS measures is 'patients are given a realistic expectation of discomfort prior to the procedure', the propor-

tion of patients that experienced discomfort during their colonoscopy was significantly lower in departments that obtained GRS level C or above than in departments that scored level D. This finding suggests that the incorporation of process measures as proposed by the GRS does produce better clinical outcomes. In this study, this was the case for the majority of the investigated items, although it was not possible to correlate all of them. This was due to uniform basic scores such as *'quality assessment of procedure'*. Previous work yielded significant variation in cecal intubation- and adenoma detection rates between departments in the colonoscopy performance audit.[14]

Interestingly, the relationship between GRS level scores in *'booking & choice'* and the patient experience was inversely correlated: more patients reported that they had a choice in scheduling the procedure in level D departments than in level C departments. Possible explanations include that the GRS does not reflect the patient experience for this item or that the questions asked of patients were not the most appropriate ones.

The GRS was deemed to be applicable as a QA tool that encompassed all aspects of endoscopy and therefore provided a comprehensive QA framework for endoscopy in England. The rationale for the content has been discussed in previous studies, as has the importance of the incorporation of *'information'*.[16, 17] Patients prefer to be informed about possible risks even if these are small or rare.[17] Furthermore, a valid complication registration or safety management system must be operational within each department in order to record complications over time.[18] The quality of the endoscopic procedure has been studied intensively.[3, 19] Running audit programs should be available to monitor these indicators, which are reflected in *'quality assessment of procedure'*. For this item, the GRS does not set specific outcomes itself but refers to the latest published society guidelines. It thus remains flexible in practice and enforces adherence to guidelines.

Appropriateness criteria are important to ensure resources are used appropriately and to protect patients from unnecessary risks. The importance of referral criteria in controlling demand has been observed in several studies, particularly demand for surveillance colonoscopy.[20, 21] Close monitoring of adherence to guidelines, established in the item *'appropriateness'* is therefore essential for effective utilization of resources.

The evaluation of waiting times has been acknowledged in patient-centered care as the association between perceived waiting time by patients and dissatisfaction has been established in studies.[22] Our results showed that patients perceived shorter waiting times for procedures in departments that achieved higher GRS levels for *'timeliness'*. Long waiting times have been a problem worldwide.[23] It is therefore necessary to monitor waiting lists and booking procedures, and implement improvement plans to ensure acceptable waiting times are achieved (measures of the item *'booking & choice'*).

This study does have some limitations. Although the instrument was carefully reviewed prior to use by an expert panel, some items need to be adapted further in order to accord with protocols in the Dutch health-care system. Second, for a sustainable QA program barriers

must be addressed, where wide support is needed. In this study, the majority of participants responded that they felt they spent insufficient time on QA on a daily basis. However, a previous survey held just before this study showed that Dutch endoscopists are willing to work on the quality of their endoscopy department.[24] Last, only department-specific colonoscopy audit data was used for correlations between GRS levels and clinical outcomes.

In conclusion, this study shows that the GRS is applicable in an alternative health-care setting, and that it was able to identify service gaps in the Dutch endoscopy service. Our study indicates that the framework has construct validity: the majority of the GRS items correlated with department specific data originating from both the patient and clinical outcomes. Therefore, we consider the GRS to be an effective framework for quality assurance, which can be used, with slight adjustments, outside its original setting. The GRS may form the basis of quality initiatives in other countries enabling international benchmarking of endoscopy services.

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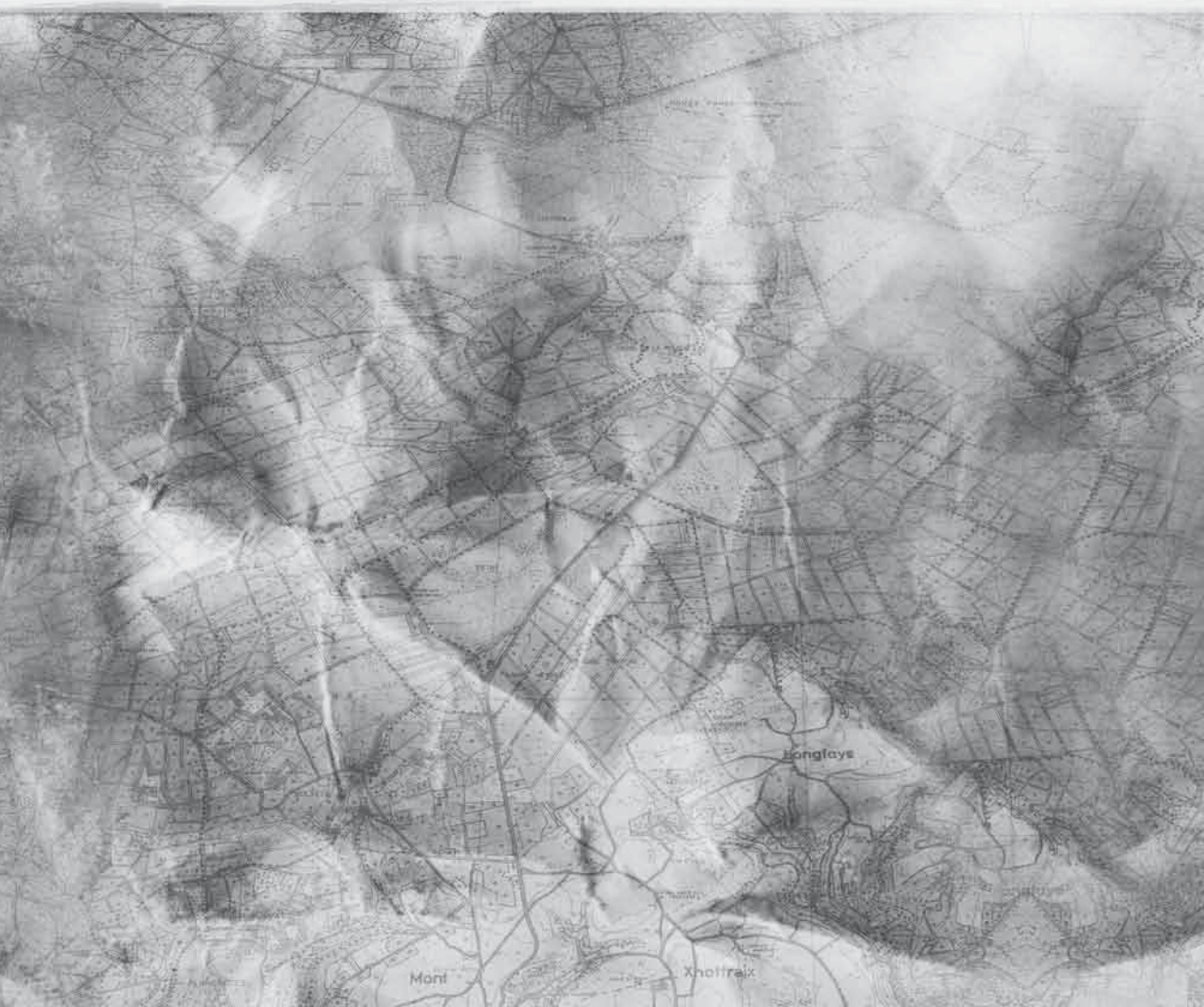
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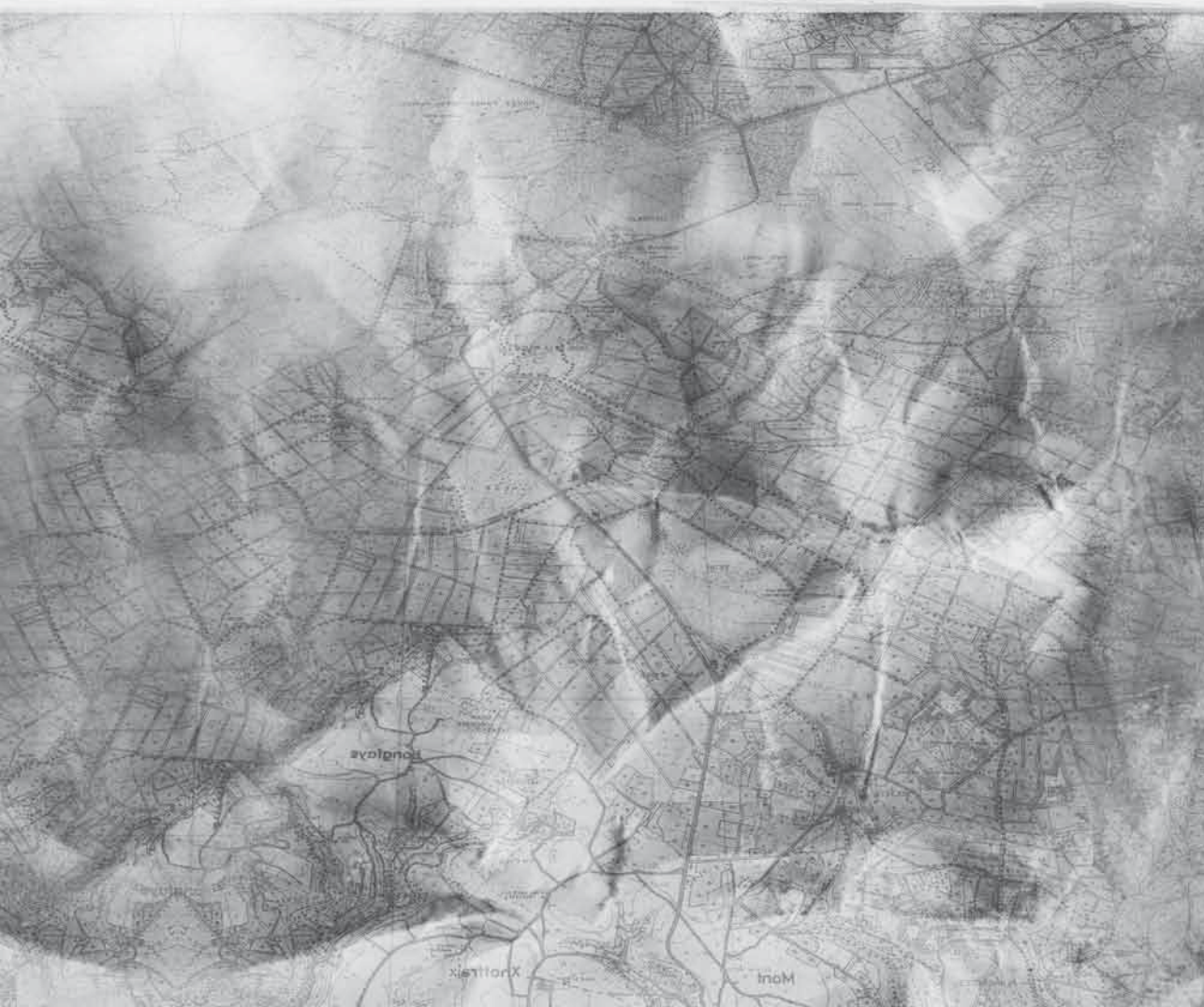
PART II

Quality assurance in colonoscopy: where do we stand?



Chapter 7

Quality evaluation of colonoscopy reporting and colonoscopy performance in daily clinical practice

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ABSTRACT

Background: Comprehensive monitoring of colonoscopy quality requires complete and accurate colonoscopy reporting.

Objective: This study aimed to assess the compliance with colonoscopy reporting and to assess the quality of colonoscopy performance.

Design: Consecutive colonoscopy reports were reviewed by hand. Four hundred reports were included from each department.

Setting: Daily clinical practice in 12 Dutch endoscopy departments.

Patients: Consecutive patients undergoing scheduled colonoscopy procedures.

Main Outcome Measurements: Quality of reporting was assessed by using the American Society for Gastrointestinal Endoscopy criteria for colonoscopy reporting. Quality of colonoscopy performance was evaluated by using the cecal intubation rate and adenoma detection rate (ADR).

Results: A total of 4800 colonoscopies were performed by 116 endoscopists: 70% by gastroenterologists, 16% by gastroenterology fellows, 10% by internists, 3% by nurse-endoscopists, and 1% by surgeons. The mean age of the patients was 59 years (standard deviation 16), and 47% were male. Reports contained information on indication, sedation practice, and extent of the procedure in more than 90%. Only 62% of the reports mentioned the quality of bowel preparation (range between departments 7%-100%); photographic documentation of the cecal landmarks was present in 71% (range 22%-97%). The adjusted cecal intubation rate was 92% (range 84%-97%). The ADR was 24% (range 13%-32%).

Limitations: Dependent on reports, no intervention in endoscopic practice. No analysis for performance per endoscopist.

Conclusion: Colonoscopy reporting varied significantly in clinical practice. Colonoscopy performance met the suggested standards; however, considerable variability between endoscopy departments was found. The results of this study underline the importance of the implementation of quality indicators and guidelines. Moreover, by continuous monitoring of quality parameters, the quality of both colonoscopy reporting and colonoscopy performance can easily be improved.

INTRODUCTION

Quality assurance (QA) in endoscopy has become an important topic in the recent decades.[1, 2] Many quality improvements have been studied to optimize the endoscopy procedure from the perspective of both the patient and physician. The implementation of colorectal cancer (CRC) screening has driven a significant portion of these quality initiatives in colonoscopy.[3-5] Suggested quality indicators for colonoscopy include, among others, the cecal intubation rate, adenoma detection rate (ADR), and withdrawal time.[6] These are eventually all surrogate markers because the only marker with true clinical relevance is the occurrence of interval CRC.

Without complete and accurate reporting of colonoscopy parameters, continuous QA is meaningless because deficits in service and quality improvements over time cannot be identified.[7] Moreover, by comprehensive reporting, possible causes of shortfalls can be identified by correction for certain variables and case mix. By determining underlying reasons for quality deficits, specific training and education projects can be implemented to achieve the maximum benefit from colonoscopic procedures. Studies of quality indicators focus to a great extent on single quality indicators and often show the results of QA in nondaily clinical practice, such as screening programs and study settings, where endoscopists were aware of the quality audit or were obliged to complete automated colonoscopy reporting systems.[8-12] Less is known about the compliance with colonoscopy reporting and performance in daily clinical practice. This study aimed to assess the quality of colonoscopy reporting performed in daily clinical practice and to evaluate the quality of colonoscopy performance.

METHODS

This study took place in the daily clinical practice of 12 endoscopy departments in the Netherlands (6 teaching hospitals and 6 general hospitals). At the time of the study, there was no comprehensive QA program either nationwide or at any of the endoscopy departments individually, although over the past 15 years, the Dutch Society of Gastroenterologists has put in place and maintained a quality audit system for endoscopy units. This system requires that endoscopy units and their staff undergo a thorough quality audit every 5 years according to a fixed format by trained external auditors from the Dutch Society.

The audit focuses on, for example, organizational aspects of the units, case mix, number of endoscopy procedures performed, waiting lists, and complication registration, but not on specific performance indicators of individual endoscopists such those as investigated in this study (i.e., cecal intubation rate and ADR). The staff of each participating endoscopy department was informed about the study protocol and parameters of interest, and ethical approval

was obtained from each institutional review board. During the study period, colonoscopies and colonoscopy reporting were performed according to local protocols.

Data collection

A total of 400 consecutive colonoscopy reports from each department were included. Emergency colonoscopies were excluded from the data collection. The first 200 reports were included retrospectively, starting in March 2009; reports from 3 months before the first contact with the department were incorporated. The other 200 reports were collected prospectively, starting in December 2009, after informing all endoscopists about the study. This approach was chosen to control for the Hawthorne effect, i.e., the awareness of being observed may alter the practice of individuals.

Data were collected from the electronic reporting system and patient records. The data extracted from the colonoscopy report consisted of endoscopist name and specialty, patient demographics, referrer, indication, use of conscious sedation, quality of bowel preparation, findings, interventions, follow-up advice, and occurrence of direct complications. If there was more than 1 indication, the most severe or important one was used in the analyses. From all polyps found, the location, size, morphology (pedunculated, sessile, flat), and method and completeness of polypectomy were recorded. The electronic reporting system was used to obtain the total procedure time and the withdrawal time, which were calculated by subtracting the time on the photograph of retroflexion in the rectum from the time on the cecum photograph. The patient record was used to acquire data about the relevant medical history (cardiac or abdominal surgery) and pathology results. Advanced neoplasia was defined as adenomas 10 mm or larger with villous histology, high-grade dysplasia, or CRC. For the cecal intubation rate, both the unadjusted and adjusted rates were calculated. Cecal intubation was adjusted for very poor bowel preparation, severe colitis, and an intervention as indication.[6]

Statistical analyses

Statistical analyses were performed by using SPSS PASW, version 17.0.2 (SPSS Inc, Chicago, Ill). Retrospective and prospective collected reports were analyzed together. Descriptive data were given as total numbers, mean scores (for nonparametric data median), and the data range among the departments.

The main outcomes of the quality of reporting were the percentage of reports containing the following parameters: patient demographics, procedure indication, sedation, quality of bowel preparation, extent of examination, photographic documentation of cecal landmarks, withdrawal time, polyp features (location, size, morphology, method of polypectomy), and

follow-up plan. These parameters were chosen based on the recommendations from the American Society for Gastrointestinal Endoscopy for colonoscopy reporting.[7]

The main outcomes of the quality of performance were the cecal intubation rate, ADR, cancer detection rate, advanced neoplasia detection rate, and complication rate. The ADR was calculated by dividing the number of colonoscopies that revealed an adenoma or CRC by the total number of procedures. Withdrawal time was given for colonoscopies without interventions.

Multivariate logistic regression analysis was performed to assess the relationship between a complete colonoscopy (cecum intubated) and the following variables: sex, age, use of sedative medication, previous abdominal surgery, quality of bowel preparation (missing values regarded as sufficient bowel preparation), and specialty of the endoscopist. The same variables, except for previous abdominal surgery, were used to assess the correlation with the detection of an adenoma, whereas a personal history of adenomas and cecal intubation were added in this model. Variables were regarded as significantly correlated if a 2-sided P value was <0.05.

Finally, the retrospective and prospective data were compared to see whether there were any differences.

RESULTS

Overall

A total of 4800 colonoscopy reports were included, covering colonoscopies performed in 4738 patients. Table 1 shows the characteristics from the included patients and their colonoscopies. Table 2 shows the characteristics of the 12 endoscopy departments that participated in this quality evaluation.

A total of 117 endoscopists performed the colonoscopies, with a median of 29 procedures per endoscopist (interquartile range 13-64). Conscious sedation was used in 88% of the procedures. The quality of bowel preparation was sufficient in 80.7% (range 68.3%-93.1%), moderate in 12.8% (range 1.5%-26.9%), and insufficient in 6.5% (range 3.0%-10.4%).

Colonoscopy reporting

Colonoscopy reporting was done in the departments under study by means of a computerized system with standardized text blocks (n=11) or the use of a Dictaphone (n=1, department 1). Figure 1 and Table 3 show the quality of colonoscopy reporting, including data per endoscopy department. Almost all reports contained the procedure indication (98%), description of sedation performed (94%), and extent of the procedure (99%). The least compliance in

Table 1. Cohort characteristics

	n	(%)	Range between hospitals (%)
Male patients	2264	(47.2)	43.0 - 54.3
Mean age (SD)	59.36	(15.9)	55.8 - 62.2
Prior colonoscopy	1,584	(33.0)	21.9 - 43.8
History of abdominal surgery	922	(19.2)	11.8 - 28.9
Indication[17]			
- Anemia	394	(8.4)	3.5 - 14.4
- Rectal blood loss	753	(16.1)	9.2 - 24.4
- Lower abdominal symptoms	1,343	(28.7)	18.9 - 36.3
- Diarrhea	169	(3.6)	2.0 - 5.3
- IBD	344	(7.3)	2.9 - 17.1
- CRC screening	414	(8.8)	3.8 - 17.6
- CRC surveillance	712	(15.2)	7.1 - 21.6
- Other	553	(11.8)	8.5 - 17.0
Endoscopist			
- Gastroenterologist	3368	(70.2)	17.3 - 100
- Trainee	744	(15.5)	0.0 - 71.5
- Internist	475	(9.9)	0.0 - 31.1
- Surgeon	475	(1.0)	0.0 - 8.5
- Nurse endoscopist	164	(3.4)	0.0 - 18.3

SD: standard deviation; IBD: inflammatory bowel disease; CRC: colorectal cancer

reporting was found for the withdrawal time (9%), polyp features such as size (51%) and morphology (43%), the quality of bowel preparation (62%), and photographic documentation of at least 1 of the cecal landmarks (71%). In addition, there was a great variance in reporting practice found (Figure 1 and Table 3). Missing values in the quality of bowel preparation were replaced by "sufficient bowel preparation" for further analyses. The validity of this assumption was evaluated by using 2 analyses: (1) performing all analyses without the missing values replaced and (2) predicting the missing values by using a logistic regression model. Both analyses showed that the results were robust (results not shown) and did not alter the outcomes much.

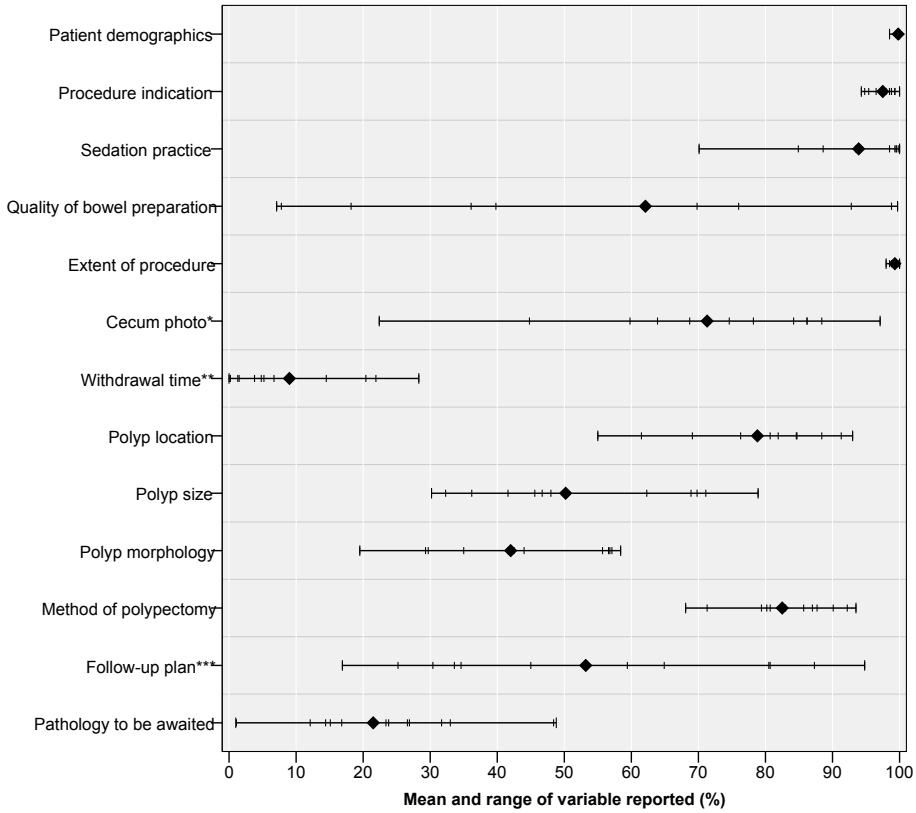
Colonoscopy performance

Table 4 shows the results for quality of colonoscopy performance. The unadjusted cecal intubation rate was 90%, and the adjusted cecal intubation rate was 92%. In 53% of procedures,

Table 2. Endoscopy department characteristics

Department	A	B	C	D	E	F	G	H	I	J	K	L
Specialty makeup												
Gastroenterologists (n)	2	4	4	3	6	10	5	6	6	4	10	6
Fellows (n)	0	0	1	0	1	14	0	2	1	0	8	3
Surgeons (n)	1	0	0	0	0	0	0	0	0	2	0	2
Internists (n)	1	0	0	3	1	0	4	1	0	1	0	1
Nurse endoscopists (n)	0	0	3	0	0	1	0	0	0	0	0	2

Figure 1. Quality of reporting: percentages of completeness of data.



*In colonoscopies that were complete according to report. **In all colonoscopies (including colonoscopies with an intervention). ***In colonoscopies in which no pathology was to be awaited.

samples for histology were taken; histologic findings were normal in 8%, and hyperplastic polyps were found in 7%, tubular adenomas in 13%, (tubulo-)villous adenomas in 6%, CRC in 5%, inflammation in 9%, and other pathology in 5%.

The overall ADR was 24% (range 13%-32%). There was a significant difference in ADR between the endoscopy department with the highest and the one with the lowest (13% vs 32%, P<0.001). A positive correlation was observed between the ADR and cecal intubation (Figure 2, P<0 .04).

Six perforations occurred in the 4800 colonoscopies (0.1%). In 4 of these 6 patients, polypectomy had been performed; 1 patient had extensive diverticulosis, and the last patient was an 80-year-old man with an extensive GI history, but no particular abnormalities found during the colonoscopy. Bleeding was reported to occur in 60 colonoscopies (1.3%). In 97% of these patients, polypectomy was performed; 40 patients (67%) required a clip to coagulate the bleeding, and 3 of the patients with bleeding (5%) were admitted to the hospital.

Table 3. Quality of reporting (percentage complying with reporting)

Department	1	2	3	4	5	6	7	8	9	10	11	12	Overall
Patient demographics	99.8	100.0	100.0	99.8	100.0	99.8	100.0	99.5	100.0	100.0	98.5	99.8	99.8
Procedure indication	99.3	94.3	99.3	98.0	94.8	97.3	98.8	98.5	100.0	96.5	95.4	98.5	97.5
Sedation practice	99.8	93.5	99.3	100.0	98.5	70.1	99.5	99.5	100.0	84.9	88.6	93.5	93.9
Quality of bowel preparation	76.0	36.1	98.8	39.8	7.8	18.2	98.8	99.7	99.7	92.8	7.1	69.8	62.1
Extent of procedure	99.8	98.8	99.3	99.3	98.0	98.8	100.0	100.0	100.0	99.0	99.7	98.5	99.3
Cecum photo*	44.8	86.2	22.4	74.6	59.8	63.9	68.7	97.1	88.4	78.2	84.2	86.2	71.3
Withdrawal time**	28.3	21.9	5.2	0.0	1.3	6.78	1.5	20.4	14.5	0.2	4.8	3.8	9.0
Polyp location	69.1	61.5	78.7	76.3	93.0	84.7	81.9	88.4	55.0	84.6	91.3	80.7	78.8
Polyp size	36.2	48.0	45.6	69.8	78.9	68.9	71.1	30.2	62.3	41.6	46.7	32.3	50.2
Polyp morphology	29.3	41.6	35.0	58.4	56.8	55.7	29.7	44.0	7.1	19.5	56.6	42.5	42.0
Method of polypectomy	71.3	79.4	68.1	80.7	80.2	83.0	92.2	87.0	93.5	85.7	90.1	87.7	82.5
Follow-up plan***	16.9	25.2	80.7	45.0	33.6	34.6	80.5	87.3	94.8	30.4	64.9	59.4	53.2
Pathology to be awaited	14.4	15.1	12.1	48.8	33.0	26.9	16.8	23.8	1.0	31.7	23.4	26.6	21.5

* In colonoscopies that were complete according to report

** In all colonoscopies (including colonoscopies with an intervention)

*** In colonoscopies in which no pathology was to be awaited

Table 4. Quality of performance

n = 4,800 unless stated otherwise	%	Range between hospitals (%)
Cecal intubation rate		
- Unadjusted (n = 4,764)	89.7	80.6 - 95.7
- Adjusted (n = 4,630)	92.3	83.8 - 96.7
Adenoma detection rate	24.4	13 - 31.5
- Males	30.1	14.2 - 39.5
- Females	19.3	11.4 - 27.4
Advanced neoplasia detection rate	14.8	8.7 - 20.8
Cancer detection rate	4.8	1.8 - 7.2
Complications	2.4	0.5 - 4.3
- Perforation	0.1	0 - 0.5
- Bleeding	1.3	0 - 2.5
- Other	1.3	0 - 3.6

* Missing values regarded as sufficient bowel preparation

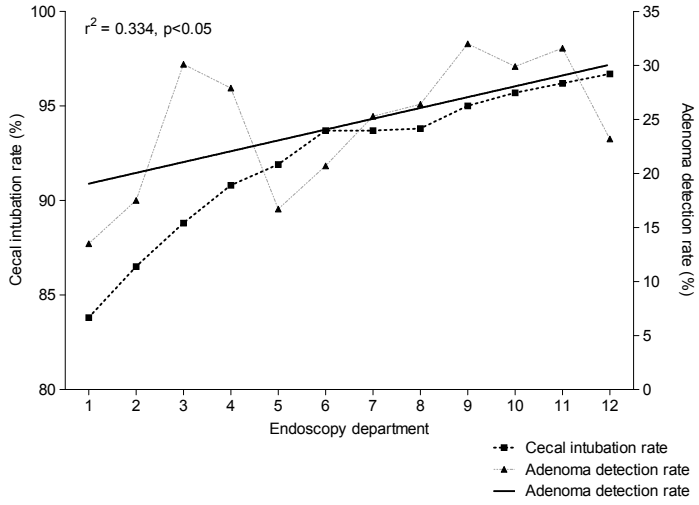
** In colonoscopies without an intervention

Predictors of quality outcomes

Table 5 shows the results of the multivariate ordinal and logistic regression analyses. The cecal intubation rate was higher in male patients (odds ratio [OR] 1.6; 95% CI, 1.2-2.0), but lower in older patients (OR in patients 75 years and older compared with younger patients 0.4; 95% CI, 0.3-0.6) and in colonoscopies performed by surgeons (OR 0.3; 95% CI, 0.1-0.7) and internists (OR 0.4; 95% CI, 0.3-0.5) compared with gastroenterologists.

Age was found to be a predictor of finding an adenoma with OR increasing from 2.8 (95% CI, 2.3-3.5) for the age group 55 to 64 years to 4.3 (95% CI, 3.4-5.4) for those 75 years and older compared with patients younger than 55 years of age. Other adenoma predictors were male

Figure 2. Correlation between adjusted cecal intubation and adenoma detection rate.



sex (OR 1.8; 95% CI, 1.6-2.1), history of adenomas (OR 1.6; 95% CI, 1.3-2.0), the use of sedation (OR 1.5; 95% CI, 1.2-1.9), and poor bowel preparation (OR 0.5; 95% CI, 0.3-0.7). Surgeons (OR 0.2; 95% CI, 0.1-0.6) and internists (OR 0.7l 95% CI, 0.5-1.0) found fewer adenomas compared with gastroenterologists, whereas nurse-endoscopists (OR 1.5; 95% CI, 1.1-2.2) and fellows (OR 1.3; 95% CI, 1.1-1.6) found more adenomas.

Retrospective versus prospective

There was no significant difference in quality of reporting and performance between the retrospective and prospective data collection, although the quality of bowel preparation was more often missing in the retrospective study period (42 vs. 34%, P<0.001).

DISCUSSION

Colonoscopy is one of the most performed procedures in gastroenterology practice. It is the criterion standard for CRC prevention and thus is used for primary and secondary screening. The efficiency of a colonoscopy and the preventive effect are highly dependent on the quality of the procedure.[6] To successfully improve the quality of colonoscopy, regular assessment of colonoscopy performance in daily clinical practice is required.

Table 5. Multivariate regression model

Cecal intubation **	Actual cecal intubation (%)	OR	(95%CI)
- Female patient	90.8	Ref	
Male patient	93.9	1.56	(1.23 - 1.98) *
- Age <55 years	94.5	Ref	
55-64 years	92.3	0.64	(0.47 - 0.88) *
65-74 years	92.1	0.63	(0.45 - 0.86) *
≥75 years	87.6	0.41	(0.30 - 0.57) *
- No abdominal surgery in the past	92.6	Ref	
Abdominal surgery in the past	90.9	1.05	(0.79 - 1.40)
- Good bowel preparation	92.1	Ref	
Moderate bowel preparation	94.7	1.31	(0.90 - 1.92)
Poor bowel preparation	88.0	0.65	(0.42 - 1.03)
- No sedation	92.6	Ref	
Sedation	92.2	0.87	(0.59 - 1.27)
- Gastroenterologist	93.3	Ref	
Fellow	93.2	0.97	(0.69 - 1.35)
Surgeon	80.4	0.30	(0.14 - 0.66) *
Internist	84.1	0.36	(0.26 - 0.49) *
Nurse-endoscopist	93.9	1.11	(0.56 - 2.22)
Adenoma detection * **	**Actual ADR (%)**	**OR**	**(95%CI)**
- Female patient	20.8	Ref	
Male patient	32.2	1.81	(1.55 - 2.10) *
- Age <55 years	11.8	Ref	
55-64 years	28.7	2.83	(2.28 - 3.52) *
65-74 years	37.2	4.43	(3.57 - 5.51) *
≥75 years	35.2	4.26	(3.38 - 5.39) *
- No history of adenomas	24.5	Ref	
History of adenomas	39.7	1.63	(1.32 – 2.02) *
- Good bowel preparation	26.0	Ref	
Moderate bowel preparation	32.3	1.21	(0.98 - 1.49)
Poor bowel preparation	16.6	0.47	(0.33 - 0.67) *
- No sedation	24.1	Ref	
Sedation	26.8	1.48	(1.16 - 1.89) *
- Cecal intubation	26.2	Ref	
No cecal intubation	26.8	1.15	(0.87 - 1.51)
- Gastroenterologist	26.2	Ref	
Fellow	30.3	1.28	(1.05 – 1.57) *
Surgeon	7.9	0.18	(0.05 - 0.60) *
Internist	19.0	0.72	(0.54 - 0.95) *
Nurse-endoscopist	34.5	1.53	(1.05 - 2.24) *

* $p<0.05$

** Severe colitis, very poor bowel preparation, and intervention as indication excluded

*** IBD or intervention as indication excluded

Quality of reporting

To achieve a valid and valuable assessment of the quality of colonoscopy performance in daily clinical practice, compliance with reporting of procedure parameters should be high. Only complete colonoscopy reporting provides endoscopists with a reliable comparison with

standards or with other endoscopists. In 2007, guidelines on reporting practice were published by the Quality Assurance Task Group of the National Colorectal Cancer Roundtable.[7] In the Netherlands, no guidelines are currently available for this purpose, and therefore the assessment of compliance with colonoscopy reporting is based on these guidelines.

The first part of this quality evaluation showed that important aspects of colonoscopy are well reported in daily clinical practice, with more than 90% of the reports mentioning the indication, sedation practice, and extent of the procedure. On the other hand, significant improvement in reporting should be realized for other parameters. For example, reports on the quality of bowel preparation and withdrawal time were missing in 38% and 91%, respectively, as were data on polyp descriptors such as size (49% missing) and morphology (57% missing). One endoscopy department dictated its reports (department 1). This was associated with lower compliance with reporting different variables, especially with respect to description of polyps and the process of their removal.

The quality of colonoscopy reporting among endoscopy departments varied widely. However, none of the endoscopy departments using automated reporting systems showed consistently low compliance with reporting for all variables, indicating that the quality of reporting can easily be improved by including new and mandatory text fields in the reporting system. High compliance was found in reporting on sedation practice (94%, range 70%-100%). The high mean, but left-tailed skewed range indicates that some departments can significantly improve in this aspect. This is in line with some reports in the literature. In the Colorectal Adenoma Prevention Trial, information about sedation was given in only 76% of reports.[13] Sedation plays an important role in QA, both in the occurrence of complications and patient satisfaction.[14, 15] Therefore, reporting on sedation practice is of great value to evaluate possible reasons when any of these outcomes fall below expected values. It is reassuring that almost all reports mention the extent of the procedure (99%). This high compliance is consistently found in the literature, ranging from 91% to 100%.[13, 16] It reflects the fact that it is an easy-to-report and well-accepted quality indicator. Photographic documentation of the cecal landmarks was, however, performed in only 71%. This discrepancy may be related to the opinion of some endoscopists that a landmark photo has no additional clinical benefit. Studies have in addition showed that reviewers may disagree whether a photograph is representing the cecum.[17, 18]

Apart from cecal intubation, the quality of a colonoscopy depends on the quality of bowel preparation. It was found that compliance with reporting about the quality of bowel preparation was low (62%). This is in line with previous research. In the Colorectal Adenoma Prevention Study, the quality of the bowel preparation was mentioned in only 30% of the reports.[13] In the Maryland CRC Screening Program, 27% of the reports did not include quality of bowel preparation.[19] The latter study only assessed a single report per participating endoscopist and may therefore not be representative for clinical practice. However, these findings were similar to a recent cross-sectional analysis of community practices.[20]20 In our study, many

endoscopists argued that they only reported on the quality of bowel preparation when it was insufficient. However, because the quality of bowel preparation is such an easily available parameter, with significant relevance to both cecal intubation and colonoscopic findings, it should be included in any report.[21]

The parameter with the lowest compliance in reporting was the withdrawal time. This low compliance was also found in another study on community practices.[20] It probably reflects the on-going discussion about its value as a quality indicator.[22-24] The correlation between ADR and withdrawal times has been inconsistent in various studies. Moreover, this quality parameter can be easily manipulated, is relatively labour-intensive to measure, and needs to be corrected for the duration of interventions such as polypectomy.

In addition to determining the quality of the colonoscopy, a complete description of the relevant findings is also important. We found that data on polyp size were missing in 51% of reports. It should be mentioned that in our study, qualitative descriptions of lesions such as "small" or "diminutive" were not considered sufficient descriptors; therefore the result might overestimate the real problem. Remarkably, even in an adenoma prevention trial, 26% of the reports did not include data on polyp size.[13] This may in part have been related to the difficulty in objectively measuring the size of a polyp in situ.[25] The post-polypectomy surveillance guidelines in the Netherlands only take the number of adenomas into account to determine surveillance intervals. This may be another reason for the low compliance in reporting size in most departments (range 30%-79%).

Quality of performance

Simultaneously with the quality of colonoscopy reporting, we evaluated the quality of colonoscopy performance. The colonoscopy performance in this observational, cross-sectional study reaches the international suggested quality indicators.[6] An adjusted cecal intubation rate of 92% and an ADR of 24% were found.

The cecal intubation rate is accepted as quality indicator for colonoscopy, although its value has been debated as well.[26, 27] Because a significant proportion of adenomas was found in the proximal colon (40%, data not shown), the importance of a complete colonoscopy up to the cecum is again emphasized and the extent of the procedure should be reported. Significant variance between the endoscopy departments in cecal intubation was found (range 84%-97%). This is in line with the literature, with cecal intubation rates ranging from 77% to 97% in different study settings.[8, 27-29] The multivariate regression analyses showed that specialty of the endoscopist was a significant predictor in reaching the cecum, with surgeons (OR 0.30) and internists (OR 0.36) having lower cecal intubation rates compared with gastroenterologists. In our study, the 3 departments with the lowest cecal intubation rates were also the only departments in which surgeons performed endoscopies. However, the differences in cecal intubation between endoscopy departments remained significant when the colonos-

copies performed by surgeons were excluded from the analyses because the total number of colonoscopies that they contributed to the study was limited (1%, 6%, and 15%, respectively). Although internists were also found to have lower cecal intubation rates, their results seemed not to have an impact on the overall results of the department where they were employed because the cecal intubation rates of the departments with internists were not consistently low. Our results add to the evidence that other specialties have lower ADR and higher CRC miss rates.[26, 30, 31] They further emphasize that the differences in performance among units are not solely attributable to the background of the endoscopists, but also among units with a similar workforce. This emphasizes the need for dedicated training programs and feedback on endoscopist performance to optimize the quality of the colonoscopy.

In the current era of screening, the ADR is one of the best accepted quality indicators.[6] Recently, it was shown that the risk of interval CRC was significantly increased in endoscopists with lower ADR.26 Previous studies showed that in general the accepted ADR is achieved.[8, 29, 32, 33] However, in line with this audit, significant variance is found between studies and endoscopists. This underscores the importance of continuous monitoring of colonoscopy quality to increase the efficiency of colonoscopy. Several hypotheses may explain the variance in quality of colonoscopy performance between endoscopy departments. First, both teaching and nonteaching hospitals were included. This could have led to differences in the patients seen in the endoscopy departments. Second, because some departments were in the same urban area, departments may specialize in certain patient groups. Both hypotheses underscore the importance of complete reporting of indication. Third, differences may exist in patient populations throughout the country because ethnicity, socioeconomic status, and living environment (urban or rural) influence the incidence of CRC.[34] Individual endoscopy departments should take these differences into account when comparing their results with those of others.

Finally, the quality of colonoscopy varies greatly among individual endoscopists.[22, 30, 31, 35] Thus, reasons for variance can lie in individual endoscopist characteristics or techniques. Feedback, education, and training programs should thus be tailored to improve specific factors. Interestingly, as was the case with cecal intubation, the 3 endoscopy departments including surgeons in the quality evaluation had the lowest ADR except for 1 of them (13%, 18%, and 30%, respectively). The results of the internists, who also had lower ADRs, had less impact on the results of the department where they were employed. Although the total number of colonoscopies performed by surgeons included in the study was limited, this again emphasizes the impact of specialty training and dedicated endoscopy training on the quality of colonoscopy performance.

Limitations

Our study has several limitations. First, items that were not reported could not be measured. However, because we found a high level of compliance with the most important quality parameters, we think that our quality audit provides an adequate representation of clinical practice.

Second, we did not intervene in the practice of the endoscopists. Therefore, we were not able to reliably measure all possible factors influencing the colonoscopy outcomes, such as withdrawal time. Last, we focused on quality performance per unit and did not report on endoscopist specific performance quality. As more advanced automated reporting systems become available, future quality audits could make more evidence available on the quality of reporting and quality of performance of endoscopists individually.

Conclusions

Overall, the quality of colonoscopy reporting is high, although significant variance exists. This variance suggests that, with little effort, the quality of reporting can be significantly improved. This may likely be achieved with the widespread introduction of computerized image storage and endoscopy reporting.[36] This will also be eventually cost-saving compared with handwritten or dictated reports.[36, 37]

The overall quality of colonoscopy performance reaches international standards, although remarkable variance between endoscopy departments was found. By continuous quality monitoring and disclosure of results, the overall quality of performance can be further improved. This study emphasizes that national guidelines for both colonoscopy performance and reporting parameters are needed to set common targets for the quality of colonoscopy, thereby improving the uniformity in daily clinical practice of both colonoscopy reporting and colonoscopy performance.

TAKE-HOME MESSAGE

- Regular quality assessment of colonoscopy reporting and performance is required because considerable variance in performance is observed. Guidelines with quality indicators help to set targets for quality improvement projects.
- Collaboration in quality evaluations can help improve quality of colonoscopy.

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Chapter 8

The adenoma detection rate and polyp detection rate as quality indicators in colonoscopy performance

Submitted

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ABSTRACT

Introduction: Adherence to surveillance colonoscopy (SC) guidelines is important to prevent colorectal cancer (CRC) and unnecessary workload. This study evaluated how well Canadian gastroenterologists adhere to colonoscopy surveillance guidelines after adenoma removal or treatment for colorectal cancer (CRC).

Methods: A retrospective study of patients with a history of adenomas or CRC who had surveillance performed between October 2008 and October 2010. Time-intervals between index colonoscopy and surveillance were compared to the 2008 guidelines of the American Gastroenterology Association (AGA) and regarded as appropriate when the surveillance interval occurred within 3 months of the recommended time interval.

Results: 265 patients were included (52% male; mean age 58 years). Among patients with a normal index procedure (n=110), 25% received surveillance on time, 46% too early (median difference=1.8 years too early), and 30% too late (median difference=0.9 years too late). Among patients with non-advanced adenomas at index (n=96), 13% received surveillance on time, 65% too early (median difference=1.84), and 22% too late (median difference=0.72). Among patients with advanced neoplasia at index (n=59), 17% received surveillance on time, 37% too early (median difference=1.79), and 46% later than recommended (median difference=1.12).

No significant difference in adenoma detection rates was observed when comparing too early surveillance vs. appropriate surveillance (36 vs. 35%, p=0.89) and too late surveillance vs. appropriate surveillance (22% vs. 35%, p=0.14).

Conclusions: A minority of surveillance colonoscopies are being performed according to guideline recommendations. Deviation from the guidelines did not alter the adenoma detection rate. This underlines the importance of adherence to surveillance guidelines.

INTRODUCTION

Colorectal cancer (CRC) is a leading cause of cancer-related mortality in the Western world.[1] Screening for CRC decreases CRC-related mortality and CRC incidence.[2] The adenoma-carcinoma sequence is accepted as the pathway of development of CRC and hence one of the main aims of screening colonoscopy is to detect and completely remove all adenomas.[3, 4] After neoplasia removal, patients remain at increased risk for adenoma recurrence. Therefore, surveillance after removal of adenomas or CRC is recommended. Some factors are associated with an increased risk of adenoma recurrence such as number and size of previous polyps and presence of villous features on histology.[5] The surveillance interval is generally based on these findings at the index colonoscopy.[6]

The demand for colonoscopy procedures has risen considerably over the last years which results in increased wait times for gastroenterology care in many regions in the world, including Canada.[7-9] The increase in demand for future colonoscopies as a result of CRC screening is likely to lengthen wait times even further. Deviation from surveillance guidelines may lead to unnecessary workload, and hence decreased cost-effectiveness of CRC screening.[10] Previous studies have shown that a significant proportion of gastroenterologists recommend follow-up intervals that deviate considerably from the published guidelines.[11-14]

The objective of this study was to assess the appropriateness of recommended surveillance colonoscopy intervals in the Canadian endoscopy setting.[6] Furthermore, we aimed to determine whether the appropriateness of surveillance intervals influenced the adenoma detection rate.

METHODS

This retrospective cohort study was conducted at the University of Alberta Hospital, Edmonton, Alberta, Canada. Ethical approval for this study was obtained by the Health Research Ethics Board (Pro000013953). Patients were identified and selected from a pilot study carried out as a first step in the creation of a CRC screening program (NCT00893503). This screening program, called SCOPE (Stop Colorectal Cancer through Prevention and Education), was launched in Edmonton to start a regional CRC screening program. The program was designed to test several steps in the referral process. The average risk patient could be referred only if they had a positive fecal occult blood test. Patients were also eligible to be referred to the program if they had a personal history of CRC or adenomatous polyps, a family history of CRC or polyps. In the pilot study the program only accepted referrals coming from gastroenterologists. For all accepted patients in the program who had a index colonoscopy during which adenomatous polyps were removed, the program did accept the recommendation that was made by the colonoscopist who performed the index colonoscopy. Patients with a history

of inflammatory bowel disease, a known hereditary CRC syndrome or patients with colonoscopies that were performed for the evaluation of gastrointestinal symptoms were excluded. Only patients in whom the index endoscopy report and histology of removed polyps was available, were included in the current study.

Patients with a personal history of adenomas or CRC who had a surveillance colonoscopy performed between October 2008 and October 2010 were included. The colonoscopy performed before this procedure was defined as the index colonoscopy. As all patients had an adenoma history this index colonoscopy might not have been their actual first-time colonoscopy done for adenoma or CRC surveillance. Consequently, even if our defined index colonoscopy was normal, these patients according to the AGA guidelines were supposed to undergo surveillance colonoscopy every 5 years because of their adenoma or CRC history.[6]

Data collection

The following data were collected from endoscopy reports: demographic data (age and gender), family history for CRC, index and surveillance colonoscopy characteristics such as date, cecal intubation rate, quality of bowel preparation (if not mentioned in the report it was assumed to be acceptable), and endoscopic findings including diagnosis, number, histology and site of polyps or cancer. Patients were categorized in different surveillance groups based on their most advanced lesion at index colonoscopy: normal, non-advanced adenoma, or advanced neoplasia. Advanced neoplasia was defined as ≥3 adenomas or adenomas >10mm, with >25% villous histology or high-grade dysplasia, or CRC. For patients who were diagnosed with CRC during index colonoscopy, the date of their surgery was used in order to calculate the optimal surveillance interval.

The actual interval between the index and surveillance colonoscopy was compared to the recommended interval stated in the 2008 guidelines from the American Gastroenterogical Assocation (AGA).[6] This guideline was used as the Canadian guideline, which has not been updated since 2004, does not list explicit recommendations for surveillance. A margin of three months around the recommended date was considered as an appropriate surveillance interval. Outcome measures were defined as the percentage of appropriate, too early, and too late procedures. Secondary outcomes were the adenoma detection rates (ADR) of the three categories, defined as the proportion of patients who had at least one adenoma at surveillance colonoscopy.

Statistical analysis

Descriptive statistics were used. Differences were assessed for significance by means of the Student's t-test for continuous data and the Chi-square test for categorical data. The level of

statistical significance was defined as a two-sided p-value <0.05. All analyses were performed using statistical software package SPSS PASW 17.0, Chicago, IL, USA.

RESULTS

After excluding 11 cases in whom no information was available about the index findings, 265 patients were included for analyses (52% male; mean age on index: 58 yrs, SD=11). Table 1 shows the patients' characteristics stratified for the findings at index colonoscopy. The median number of previous colonoscopies was 1 (range: 0-6). Index colonoscopy was normal in 42% of the patients (n=110/265), non-advanced adenomas were found in 36% (n=96/265), and advanced neoplasia was detected in 22% of the cases (n=59/265). Three patients (1%) had CRC.

Table 1. Patient characteristics at index colonoscopy

	Total (n=265)	Normal index findings (n=110)	Non-advanced adenoma (n=96)	Advanced neoplasia (n=59)
Mean age at index colonoscopy	58 years (SD=10.5)	59 years (SD=10.8)	57 years (SD=10.0)	59 years (SD=11.0)
Male gender	52% (n=138)	56% (n=61)	48% (n=46)	53% (n=31)
Cecal intubation	95% (n=230)	94% (n=98)	97% (n=84)	94% (n=48)
Adequate bowel preparation	90% (n=238)	88% (n=97)	90% (n=89)	93% (n=55)
Positive family history for CRC*	23% (n=61)	19% (n=21)	28% (n=27)	22% (n=13)
Mean interval until SC (years, SD)	3.8 (1.7)	4.3 (1.5)	3.8 (1.5)	2.8 (2.0)

SC= surveillance colonoscopy; SD=standard deviation; * first degree relatives with CRC extracted from endoscopy report if available

Surveillance colonoscopy

Of all 265 surveillance colonoscopies, 19% (n=49/265) were classified as procedures performed on time according to the AGA guidelines. In 51% of the patients (n=134/265) the surveillance interval was shorter than recommended, and the remaining 30% (n=82/265) underwent surveillance later than recommended compared to the surveillance guidelines.

Figure 1 shows the actual observed mean time interval between index and surveillance colonoscopy compared with the recommended time interval stratified for the index finding. The median difference between the recommended time interval and the observed interval was -1.8 years (inter quartile range (IQR)=1.21) for surveillance colonoscopies which were performed too early, and +0.9 years (IQR=1.22) for those which were performed too late.

Table 2 shows the findings at index colonoscopy per appropriateness category. In 16% of the patients who received surveillance colonoscopy too early, an inadequate bowel preparation quality was mentioned at index procedure compared to 2% at surveillance procedures

Figure 1. Mean time interval between index and surveillance compared to time interval recommended by AGA guideline.

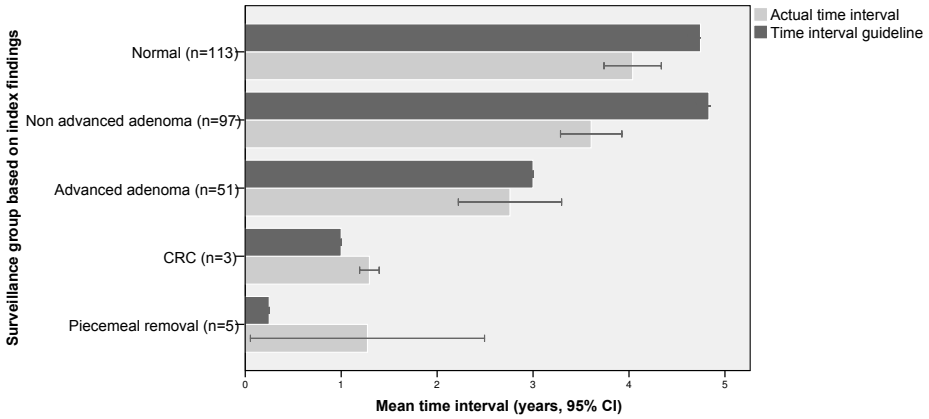

Table 2. Findings at index stratified for appropriateness according to the guidelines

	SC on time (n=49)	SC too early* (n=134)	SC too late* (n=82)
Positive family history CRC	18% (n=9/49)	25% (n=33/134)	23% (n=19/82)
Cecal intubation rate at index #	98% (n=45/47)	95% (n=121/129)	96% (n=64/69)
Adequate bowel prep at index	94% (n=46/49)	84% ** (n=112/134)	98% (n=80/82)
Median difference yrs (IQR)***	0.04 (0.25)	-1.8 (1.21)	0.9 (1.22)
Findings at index			
Normal index	55% (n=27/49)	37% ** (n=50/134)	40% (n=33/82)
Non advanced adenoma at index	25% (n=12/49)	46% ** (n=62/134)	27% (n=22/82)
Advanced adenoma∞ at index	20% (n=10/49)	16% (n=22/134)	33% (n=27/82)

SC= surveillance colonoscopy; IQR=inter quartile range; *= earlier respectively later than recommended in the AGA guideline; **= statistically significant compared to surveillance on time; ***=mean difference between the recommended time interval and the observed interval between index and surveillance; #= total numbers differ by missing values; ∞= ≥3 adenomas or >10mm, with (tubulo-) villous histology or high-grade dysplasia

performed on time (p<0.01). No significant differences for a positive family history and cecal intubation rates were observed between the three appropriateness categories (all p-values > 0.1).

Normal index colonoscopy

Among patients with a normal index colonoscopy (n=110), 25% of patients (n=27/110) received surveillance colonoscopy on time, 46% (n=50/110) too early (median difference= -1.61 years

too early; IQR=1.54), and 30% (n=33/110) too late (median difference=0.76 too early; IQR=0.92). Inadequate bowel preparation on index was reported in 20% (n=10/50) in the too early group.

Non advanced adenoma at index colonoscopy

Among patients with non-advanced adenomas at index colonoscopy (n=96), 13% (n=12/96) received surveillance colonoscopy on time, 65% of cases (n=62/96) too early (median difference= -1.84 years too early; IQR=1.26), and 22% (n=22/96) of patients received their surveillance colonoscopy too late (median difference=0.72 years too late; IQR=0.90). Inadequate bowel preparation on index was reported in 15% (n=9/62) in the too early group. Among patients with normal or non-advanced findings on index (n=206), the percentage of patients undergoing surveillance earlier than recommended was significantly higher (54%; n=112/206) than in patients with advanced neoplasia (37%; n=22/59) (p=0.021).

Advanced neoplasia at index colonoscopy

Among patients with advanced neoplasia, 17% (n=10/59) received surveillance colonoscopy on time, 37% (n=22/59) too early (median difference= -1.79 years too early; IQR=1.01), and 46% (27/59) later than recommended (median difference=1.12 years too late; IQR=1.70). Inadequate bowel preparation on index was reported in 14% (n=3/22) in the too early group. Two of the three patients that had CRC detected at index colonoscopy, did receive surveillance later than recommended. Of the five patients who had a piecemeal removal of their advanced adenoma at index colonoscopy, two returned too late and both of these patients had advanced neoplasia at surveillance colonoscopy. Among patients with advanced neoplasia on index (n=59), the percentage of patients undergoing surveillance later than recommended was significantly higher (46%; n=27/59) than in patients with non-advanced or normal findings (27%; n=55/206) (p=0.005).

Findings at surveillance colonoscopy

Adenomas were found on surveillance in 32% of cases (n=83/265), 8% of patients (n=20/265) had advanced adenomas. No CRC was identified at surveillance colonoscopy. Advanced neoplasia was found in 6% (n=3/49) at surveillance colonoscopies that were performed on time according to the guideline, including two patients with ≥3 tubular adenomas.

Adenoma detection rate at surveillance colonoscopy

The ADR for appropriate versus non-appropriate surveillance colonoscopy (stratified for index findings) are summarized in Table 3. The ADR at surveillance colonoscopy was significantly

Table 3. Adenoma detection rate at SC stratified for appropriateness according to the guidelines

	SC on time (n=49)	SC too early* (n=134)	SC too late* (n=82)
ADR at SC			
Adenoma at SC	35% (n=17/49)	36% (n=48/134)	22% (n=18/82)
Non advanced adenoma at SC	29% (n=14/49)	27% (n=36/134)	16% (n=13/82)
Advanced adenoma∞ at SC	6% (n=3/49)	9% (n=12/134)	6% (n=5/82)
ADR at SC per index			
- Normal index	22% (n=11/49)	8% ** (n=11/134)	7% (n=6/82) ** 6% (n=5/82)
- Non-advanced adenoma index	8% (n=4/49)	15% (n=20/134)	9% (n=7/82)
- Advanced adenoma at index	4% (n=2/49)	13% (n=17/134)	

*= earlier respectively later than recommended in the AGA guideline; **= statistically significant compared to SC on time; ∞= ≥3 adenomas or >10mm, with (tubulo-)villous histology or high-grade dysplasia

higher in patients with advanced neoplasia at index (n=26/59) vs. normal index colonoscopy (n=28/110): 45% vs. 26%, p=0.01). No significant difference in the ADR on surveillance was observed for procedures that were performed on time according to the guidelines compared to too early performed procedures (35% (n=17/49) vs. 36% (n=48/134 respectively), p=0.89). The ADR was also not significantly different between appropriate versus too late procedures (35% (n=17/49) vs. 22% (n=18/82) respectively, p=0.14). The detection of advanced adenomas at surveillance colonoscopy was not significantly different between appropriate vs. too early performed procedures (6% (n=3/49) vs. 9% (n=12/134), p=0.54) nor for appropriate vs. too late performed surveillance according to the guidelines (6% (n=3/49) vs. 6% (n=5/82), p=0.99).

DISCUSSION

Recent reports have shown that there are significant problems with long wait times for colonoscopy procedures in many centers in Canada.[7] It is expected that, in the context of CRC screening and its associated need for surveillance procedures, the demand for and burden of colonoscopies will increase. This study aimed to assess the appropriateness of surveillance colonoscopies in the Canadian endoscopy department, whether improvements are achievable to decrease waiting times.

Our study showed that in a significant proportion of patients, surveillance colonoscopy was not performed at the recommended time interval. Only 19% of the patients underwent a surveillance colonoscopy according to the AGA guidelines. The majority of procedures (51%) were performed earlier than recommended, with the range varying from 0.28 to 4.46

years. Underuse was also reported, as 30% of the patients received their colonoscopy too late. Shortening or lengthening the surveillance intervals did not significantly affect the ADR. Surprisingly there were more delays in surveillance in patients who had advanced adenomas at the index colonoscopy compared to those who had non-advanced adenomas. In 16% of patients earlier surveillance could be explained by poor or suboptimal bowel preparation during the index colonoscopy but even taken this into account, the compliance with the guidelines was poor. This means that there is an important role for education of physicians in this area which should be supported by a quality improvement program to document that adherence to accepted guidelines improves. This may also result in better utilization of endoscopy resources as many repeat procedures were done too early.

The three-month margin around the optimal follow-up date for colonoscopy was arbitrarily chosen. There are no data in the literature to indicate what an optimal choice is for a time interval around appropriateness. However, we believe the three-month interval was a reasonable choice as it gives some indication of the number of colonoscopies that were done either too early or too late according to existing guidelines. Even if a longer interval than three months had been chosen (for example, 6 months) our data still would demonstrate that for a substantial proportion of patients the recommended interval is inappropriate.

Several surveys have documented suboptimal usage of surveillance colonoscopy, with physicians often recommending surveillance intervals that are too short.[12, 15] A Dutch study reported that 52% of the respondents used shorter surveillance intervals than stated by the national recommendations.[11] Suboptimal usage of adherence in daily practice has also been shown in clinical studies.[14, 16-18] A study from the USA observed a considerable disparity between guidelines and endoscopists' recommendations in the colonoscopy report, with more surveillance colonoscopies occurring too soon; in only 37% of the cases were the recommendations consistent with the guidelines .[14] Another study from the Netherlands reported low follow-up rates for surveillance colonoscopy after the removal of adenomas or CRC; the majority of patients tended not to undergo surveillance colonoscopies although overuse was also observed.[17] We recently conducted a questionnaire based study on follow-up recommendations for colonoscopy for different scenarios among members of the Canadian association of Gastroenterology. Adherence by respondents to the guidelines varied from 23% to 96% in different clinical scenarios, reflecting both over- and underuse.[13]

As the risk for adenoma recurrence on surveillance colonoscopy is determined by baseline findings, guideline recommendations for surveillance colonoscopy are stratified based on the index results.[5, 6] There is evidence that surveillance colonoscopy is over-utilized in low-risk subjects and underutilized in high-risk subjects.[16] A US community practice assessment of utilization of surveillance colonoscopy showed under-usage of surveillance practice in terms of longer follow up intervals if high risk lesions at index colonoscopy were present (31%).[14] In our study a similar trend was observed in adherence patterns for surveillance practice between advanced and non-advanced lesions on index procedures.[18] Patients with

non-advanced adenomas (54%) often received surveillance too early while pPatients with advanced neoplasia more often received surveillance colonoscopy too late (46%).

Of all patients with index procedures that revealed advanced adenoma, 44% also had adenomas at surveillance colonoscopy (n=26/59). This underscores that advanced adenoma at index colonoscopy is an important risk factor for adenoma recurrence and thereby supports the guidelines for more vigilant surveillance.[16] In patients who had a normal index colonoscopy (but adenomas on prior colonoscopies), recurrent adenomas were detected in 25% of patients. All patients in this study had a personal history of adenomas or CRC. The fact that 25% still had adenomas at surveillance colonoscopy indicates that these patients remain at high risk for developing metachronous adenomas, despite normal findings at a previous surveillance colonoscopy.

The yield of surveillance colonoscopy did not significantly change between colonoscopies at appropriate or inappropriate times, suggesting that deviating from the guidelines does not necessarily increase the yield of surveillance colonoscopy. In addition, no differences in detection rates in advanced adenomas either between on time vs. too late procedures (6%) were observed, or on time (6%) vs. too early (9%). The reason for the high ADR in the too early group may in part be explained by the fact that in 16% of patients was reported to have a poor bowel preparation during the index procedure. This was significantly higher compared to patients receiving their surveillance procedure on time (2%, $p<0.01$). The detection of adenomas is largely dependent on the quality of bowel preparation.[19] Clinical decisions about the surveillance interval derived from colon cleanliness assessment can vary considerably among endoscopists and there is little agreement on what constitutes an insufficient bowel preparation.[20]

Apart from suboptimal bowel preparation on index procedure, several other explanations have been suggested for non-adherence to surveillance recommendations such as an incomplete examination, possibly incomplete removal of lesions and the presence of a family history of CRC.[15] Although in the too early surveillance cohort relatively more patients had a family history for CRC (25%) compared to the surveillance on time population (18%), it was not significant ($p=0.373$). Additionally, there were no significant differences in cecal intubation rates between the three appropriateness categories.

Additionally, insufficient awareness of guidelines may be an important factor for non-adherence by physicians. Several studies have shown that appropriate use of surveillance after the detection of adenomas or CRC depends to a great extent on the knowledge of surveillance guidelines of physicians.[12, 15] A recent study demonstrated that priming endoscopists by means of distributing guideline pocket pamphlets for use in endoscopy units among endoscopists, may help increase the compliance to guidelines.[21] Alternatively within CRC screening programs follow up recommendations may be centralized and hence more in accordance with guidelines. Centralization of follow up recommendations has been instituted as part of the recently launched provincial Alberta Colorectal Screening Program.

Other explanations for less effective surveillance programs besides nod-adherence by physicians can be found in patient related factors such as non-attendance to surveillance colonoscopy. Most studies in this area focus on clinician adherence to published guidelines, rather than patient adherence to clinician recommendations. Because our study design was limited to only patients who had returned for their surveillance colonoscopy, we do not know how many patients had similar findings during index colonoscopy, did not return for surveillance colonoscopy.

As previously indicated patients who had a prior history of CRC or removal of adenomas could be referred to the SCOPE Program and were eligible for inclusion. This pilot program did not change any of the recommendations that were made by colonoscopists, because this was beyond the scope of the pilot program. In general terms, it is often difficult for physicians changing follow-up recommendations made by other physicians, in particular if this would mean that follow-up colonoscopy is postponed to a later date. It is expected that this is also the general practice in our region, although this was not studied as part of this project. One of the advantages of having an organized CRC screening program is that follow-up recommendations will be standardized, which will lead to more optimal use of resources.

Our study has several limitations. One is the small sample size. Furthermore, the results of our study were collected from one region in Canada and may not be generalizable. Additionally, since the guidelines have been revised in 2008, differences in practice by clinicians in the different time intervals can be attributable to adaptations in guidelines explaining the disparities observed in clinical practice. Our results should be interpreted knowing there is a lack of a explicit guidelines from the Canadian Association of Gastroenterology (CAG) compared to the AGA guideline, as the CAG surveillance recommendation recommends that endoscopists should decide about the appropriate surveillance interval to a greater extent based on clinical judgment.[22]

In conclusion, in our study a minority of the surveillance colonoscopies are being performed according to the revised recommendations for surveillance colonoscopy after polypectomy. A large proportion of patients receive surveillance colonoscopies after the previous detection of adenomas or CRC too soon, while another group of referred patients return after an inappropriately long interval. The results make clear that education is required to raise awareness among endoscopists about proper surveillance intervals and that quality improvement programs likely will result in tangible benefits in terms of outcomes and resource utilization. This may also positively impact wait times for colonoscopy.

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Chapter 9

A prospective audit of patient experiences in colonoscopy using the Global Rating Scale: a cohort of 1187 patients

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ABSTRACT

Background: The Global Rating Scale (GRS) comprehensively evaluates the quality of an endoscopy department, providing a patient-centered framework for service improvement.

Objective: To assess patient experiences during colonoscopy and identify areas which need service improvement using the GRS.

Methods: Consecutive outpatients undergoing colonoscopy were asked to complete a pre- and post-procedure questionnaire. Questions were based on GRS items and a literature review. The pre-procedure questionnaire addressed items such as patient characteristics and information provision. The post-procedure questionnaire contained questions regarding comfort, sedation, the attitude of endoscopy staff and aftercare.

Results: The pre-procedure questionnaire was completed by 1187 patients, whereas the post-procedure part of the questionnaire was completed by 851 patients (71.9%). Fifty-four per cent of patients were first seen in the outpatient clinic. The indication for colonoscopy was explained to 85% of the patients. Sixty-five per cent of the patients stated that information about the risks of colonoscopy was provided. Sedation was used in 94% of the patients; however, 23% judged the colonoscopy to be more uncomfortable than expected. Ten per cent of patients rated the colonoscopy as (very) uncomfortable. Preliminary results of the colonoscopy were discussed with 87% of patients after the procedure. Twenty-one per cent of the patients left the hospital without knowing how to obtain their final results. Being comfortable while waiting for the procedure (OR: 9.93) and a less uncomfortable procedure than expected (OR: 2.99) were important determinants of the willingness to return for colonoscopy.

Conclusions: The present study provided evidence supporting the GRS in identifying service gaps in the quality of patient experiences for colonoscopy in a North American setting. Assessing experiences is useful in identifying areas that need improvement such as the provision of pre- and post-procedure information.

INTRODUCTION

Colonoscopy is the most commonly used and most accurate procedure to image the large bowel.[1] The demand for colonoscopy has increased over the past decade, largely for the purpose of colorectal cancer screening and the surveillance of adenomas.[2, 3]

Simultaneously, interest in quality assurance (QA) has increased.[1, 4] Several studies have addressed factors that influence the technical quality of colonoscopy including female sex, poor bowel preparation, lower endoscopist skills, and a history of abdominal or pelvic surgery.[5, 6]

Patient experiences are also important to the overall quality assessment of the procedure and have been suggested as quality indicators for colonoscopy.[7] Several studies have identified variables that are associated with increased levels of discomfort during a colonoscopy such as higher socioeconomic status, the presence of psychological distress and previous hysterectomy.[8, 9] High tolerance and satisfaction are required for patients to be compliant with medical care.[10] Dissatisfied patients are more likely to change physicians and to engage in litigation.[11-14]

In 2004, the results of an audit conducted in the United Kingdom (UK) demonstrated an urgent need to improve the quality of endoscopy.[15] For that purpose, a comprehensive program was developed to evaluate and improve all aspects of endoscopy and has become known as the Global Rating Scale (GRS).[16] The GRS is a patient-centered QA program that provides objective measures for the overall quality of the endoscopic service. Acceptance of the GRS by endoscopy units in the UK has been high, and improvements in quality have been achieved.[17]

The GRS has four main domains: 'Clinical quality', 'Quality of patient experience', 'Training' and 'Workforce'.[16] Each domain consists of different items, which are presented in Table 1. Items were discussed and created at several national meetings in which input was provided by health care providers, patient groups and others. Recently, efforts have been made to adopt the GRS outside of the UK, including Canada.[18]

The aim of the current study was to evaluate several items within the 'Quality of patient experience' domain of the GRS outside the UK, in a North American setting.

Table 1. Global Rating Scale domains

Clinical Quality	Quality of Patient Experience	Training	Workforce
Informed consent and information	Equality of access and equity of provision	Environment and training opportunity	Skill mix review and recruitment
Complications/safety	Timeliness	Endoscopy trainers	Orientation and training
Comfort	Booking and choice	Assessment/ appraisal	Assessment/ appraisal
Quality procedure	Privacy and dignity	Equipment and educational materials	Staff care
Appropriateness	Aftercare		Involve staff for development service
Reporting	Ability to provide feedback for service		

METHODS

The present prospective cohort study was performed in the endoscopy departments of the following four hospitals in Edmonton, Alberta: The University of Alberta Hospital (UAH), Royal Alexandra Hospital (RAH), Misericordia Community Hospital (MH) and Grey Nuns Community Hospital (GNH). The study protocol was submitted to the Health Research Ethics Board of the UAH and RAH, and the Ethics Board of the Caritas Health Group of the MH and GNH. Both boards deemed that the study fell under the umbrella of QA projects and, subsequently, research ethics approval was granted.

Patients

Consecutive patients undergoing colonoscopy in one of the four hospitals included in the present study were asked to participate. Patients were enrolled between May and August 2008. Verbal consent was obtained from all patients participating in the present study. The main inclusion criterion was that patients were scheduled to undergo an outpatient colonoscopy. Exclusion criteria consisted of the following: patients who did not consent to participate, were not able to speak or read English, or had a medical condition that made it difficult to complete the questionnaire.

Colonoscopies were performed by gastroenterologists and fellows. No information regarding the specifics of sedation (neither drugs nor dosage) used during the procedures was collected.

Questionnaire

A questionnaire that was used in the UK, which contained the relevant items of the GRS, was adopted for the present study (available online).[16] The items in the GRS were developed based on focus group discussions with all stakeholders of endoscopy, including patients. Some questions derived from the previously validated modified Group Health Association of America nine-item survey[14] were incorporated to address all of the established domains that may influence patient experiences. Because the modified Group Health Association of America nine-item survey does not incorporate questions regarding pain tolerance, acceptance and embarrassment, questions based on the 'Health Belief Model'[19] were also included. The following aspects were assessed: accessibility and timeliness, informed consent and information, interpersonal skills of staff, privacy and dignity, comfort and discharge.

First, the questionnaire was pretested at the UAH endoscopy outpatient department. During the pretesting phase, 30 patients were asked to complete the pre- and post-procedure questionnaire. These patients were subsequently interviewed by the investigators to evaluate the clarity of the tool. Input from health care professionals was also obtained during this

period. After feedback, the final questionnaire was designed. Patients completed the first part of the questionnaire before their colonoscopy while waiting in the pre-procedure area. Patients received a postage-paid, pre-addressed envelope and were asked to complete the post-procedure questionnaire at home within three days and return it by mail.

Statistical analysis

Analyses were performed using SPSS version 15.0.1 (SPSS Inc, USA). Categorical data differences between hospitals were analyzed using c2 tests. Numerical data were analyzed using one-way ANOVA. To determine differences in nominal data between hospitals, the Kruskal-Wallis test and Mann-Whitney U test were used. A two-sided $p<0.05$ was considered to be statistically significant.

Multivariate logistic regression analysis was used to identify associations among the willingness to return for colonoscopy, overall comfort, acceptance and the following factors: sex, age, body mass index, specialist consultation before colonoscopy, receipt of an information sheet before colonoscopy, comfort in the waiting area, excessive delay before or after the colonoscopy, adequate time in the endoscopy room, a colonoscopy that was more uncomfortable than expected, discussion of preliminary results and embarrassment during the colonoscopy.

For this purpose, the outcome variables were transformed into binary variables (patients who were either [very] satisfied or willing to return, or somewhat or not [very] satisfied or willing to return), as was previously performed by others.[20]

RESULTS

Pre-procedure questionnaire

Patient characteristics: A total of 1187 patients (43.1% men, mean age 56 years) completed the pre-procedure questionnaire during the study period. Tables 2 and 3 summarize the patient characteristics and results. Overall, 656 patients (59.6%) had undergone a previous colonoscopy. Patient characteristics were similar among the hospitals.

Booking procedure

Before undergoing colonoscopy, 634 patients (54.0%) had seen the specialist in an outpatient setting and 541 (46.0%) were directly referred for the procedure without previous consultation of the specialist. Among 442 patients who underwent first-time colonoscopy, 218 (49.3%) had not consulted with the physician before the procedure in the outpatient clinic. The rate

Table 2. Patient characteristics

	Overall *	Hospital (%)			
	n (%)	UAH	RAH	MH	GNH
Completed pre-procedure questionnaire	1187 (100)	36.3	28.2	16.7	18.8
Gender (male) [d]	509 (43.1)	47.6	41.4	41.8	38.2
Mean age (SD) [a,b,c]	55.7 (15.0)	53.3	56.9	58.1	57.1
History of previous bowel investigation**	853 (73)	73.4	75.2	74.0	67.9
Colonoscopy	656 (59.6)	59.5	61.8	59.6	56.4
Sigmoidoscopy	190 (25.4)	24.8	31.9	20.7	21.0
History of abdominal or pelvic surgery [a,e]	457 (40.7)	37.2	46.4	43.1	36.2
Indication for procedure					
Family history of CRC [a,c,d,f]	263 (22.9)	19.4	29.1	13.5	28.7
Personal history of CRC and/or polyps	152 (13.3)	11.5	14.2	13.0	15.3
Screening colonoscopy [a,b,c]	67 (5.8)	9.1	5.2	3.1	3.2
Rectal bleeding [c]	195 (17.0)	13.3	17.0	19.2	22.2
Abdominal pain [c,d,f]	111 (9.7)	11.3	7.6	15.0	5.1
IBD [a,b,c]	185 (16.1)	22.6	13.3	15.0	9.3
Other [b,d]	173 (15.1)	12.8	13.6	21.2	16.2

CRC: Colorectal cancer; IBD: Inflammatory Bowel Disease; SD: Standard Deviation

*Because of missing values totals differ

**More than one can apply

p<0.05: [a] UAH vs. RAH; [b] UAH vs. MH; [c] UAH vs. GNH; [d] RAH vs. MH; [e] RAH vs. GNH; [f] MH vs. GNH

Table 3. Results pre-procedure questionnaire

	Overall *	Hospital (%)			
	n (%)	UAH	RAH	MH	GNH
Specialist seen as outpatient before colonoscopy [a,b,c,e,f]	634 (54.0)	40.3	54.2	53.3	80.5
Booked in a timely fashion [a,b,e]	246 (77.6)	84.4	67.9	70.6	83.6
Offered a choice of dates or times [e]	427 (37.0)	37.9	32.3	36.3	42.8
Want more choice for dates or times [a]	418 (38.8)	36.1	43.5	37.4	38.5
Information sheet received [a,b,d,e,f]	1046 (89.3)	94.8	79.5	87.8	95.0
Explanation what colonoscopy involved [a,d,e]	906 (77.8)	81.5	70.4	80.4	79.4
Explanation of indication of colonoscopy	982 (84.7)	85.1	84.4	82.8	86.3
Mentioning complications (any) [a,b,c,d,f]	729 (65.1)	75.2	62.0	49.7	63.7
Perforation [a,b,c,f]	660 (59.0)	70.1	53.0	46.4	57.1
Bleeding [a,b,c,d,f]	652 (60.3)	71.6	56.0	44.8	58.4
Missing cancer [a,b,c,f]	478 (44.9)	57.7	37.4	32.0	42.8
Risk of sedation [a,b,c]	555 (53.5)	65.0	49.5	41.0	49.2

*Because of missing values totals differ

p<0.05: [a] UAH vs. RAH; [b] UAH vs. MH; [c] UAH vs. GNH; [d] RAH vs. MH; [e] RAH vs. GNH; [f] MH vs. GNH

of patients who had a pre-procedure visit with their physician differed significantly among hospitals, with rates ranging from 40.3% to 80.5% (p<0.01). A choice of date and time for the procedure was offered to 427 patients (37%).

Information provision

Before colonoscopy, 1048 patients (89.3%) received an information sheet (range among hospitals 79.5% to 95.0%; p<0.01). In addition, before the actual procedure, the endoscopist or nurse explained the details of the procedure to 906 patients (77.8%).

While waiting for colonoscopy, the indication for the procedure was not known or could not be recalled by 177 patients (15.3%).

When the analysis was stratified according to pre-procedural outpatient visits, 61 patients (9.8%) who had previously visited the outpatient clinic did not know the indication for their colonoscopy compared with 116 patients (21.8%) who had not consulted with their specialist before the procedure (p<0.01).

Overall, any of the complications (Table 3) were mentioned to 729 patients (65.1%; range among hospitals 49.7% to 75.2%; p<0.01), and 433 patients (41%) recalled that they were informed about all four complications assessed in this questionnaire (range among hospitals 29.6% to 52.1%; p<0.01). Patients who consulted with their specialist before colonoscopy recalled more often that any of the risks of complications were mentioned to them compared with patients who were directly referred (167 [27.7%] versus 223 [43.4%]; p<0.01). Among 999 patients who received an information sheet, 326 patients (32.6%) were not aware of the potential complications of colonoscopy, compared with 63 (53.8%) of the 117 patients who did not receive an information sheet (p<0.01).

If patients received both an information sheet and a pre-colonoscopy consultation, they retained more information about complications than when information provision was limited to one of these methods or when they received no information whatsoever (394 [73.4%] versus 330 [57.3%]; p<0.01).

Post-procedure questionnaire

A total of 851 patients completed the post-procedure questionnaire (response rate 71.7%). The results of the post-procedure questionnaire are summarized in Tables 4 and 5.

Admission and waiting before procedure

Almost all patients (824 [97.3%]) were comfortable waiting for their procedure in the pre-procedure area. However, 165 of the patients (19.7%) believed there was an excessive delay before entering the endoscopy room. Virtually all patients (842 [99.5%]) signed an informed consent form before undergoing the procedure.

Table 4. Results post-procedure questionnaire

		Overall*	Hospitals (%)			
		n (%)	UAH	RAH	MH	GNH
Response rate		851 (71.7)	71.9	77.0	60.6	73.1
Admission	**Admission Journey well coordinated**	831 (98.6)	98.0	98.8	100.0	98.1
	Excessive delay time admission-procedure c	165 (19.7)	15.8	19.4	22.7	25.2
Procedure	**Discouraged from having sedation** [a,b,d]	46 (5.5)	8.1	2.0	6.8	5.0
	Sedation given [d]	756 (94.0)	93.8	92.1	97.4	94.9
	Choice given for sedation [a,c,d]	195 (24.0)	30.7	16.5	27.8	20.5
	Courteous doctor	831 (99.5)	99.7	99.2	99.2	100.0
	Courteous nurses	833 (99.5)	98.7	100.0	100.0	100.0
	More uncomfortable than first thought	189 (22.7)	23.3	23.5	18.5	23.5
	Treated with respect	788 (99.6)	99.7	99.1	100.0	100.0
Discharge	**Preliminary results discussed after procedure** [a,b,c]	707 (86.9)	93.4	82.3	85.7	83.0
	Know how to get the final results [a,d,e]	641 (78.9)	82.9	70.2	84.0	81.6
	Time to discharge too long	37 (4.5)	5.7	4.0	5.0	2.5
	Aftercare information sheet [a,b,c,d,e,f]	710 (87.3)	90.6	84.2	74.1	96.2
	Know what to do if problems come up [b,d,f]	736 (92.0)	93.4	92.2	82.9	95.5

*Because of missing values totals differ

$p<0.05$: [a] UAH vs. RAH; [b] UAH vs. MH; [c] UAH vs. GNH; [d] RAH vs. MH; [e] RAH vs. GNH; [f] MH vs. GNH

Table 5. Overall patient experiences of colonoscopy

	(Strongly) disagree	Neutral	(Strongly) agree
	n (%)	n (%)	n (%)
Comfortable (n=819)	81 (9.9)	147 (17.9)	591 (72.2)
Acceptable (n=822)	21 (2.6)	53 (6.4)	748 (91.0)
Embarrassing (n=829)	753 (90.8)	61 (7.4)	15 (1.8)
Willing to return (n=826)	43 (5.2)	90 (10.9)	693 (83.9)

Procedure

According to patient reports, sedation was used in 756 procedures (94%). A choice to receive sedation was recalled to be offered by 195 patients (24%). Among the patients who were not offered a choice, 128 (22.3%) would have preferred to have a choice.

Acceptability of the procedure is shown in Table 5. Colonoscopy was rated as (very) comfortable by 591 patients (72.2%), and 748 found the burden (very) acceptable (91.0%). However, 189 patients (22.7%) rated the experience of the colonoscopy as more uncomfortable than expected (Table 4). Patients who were seen in a pre-colonoscopy consultation by the specialist rated the experience of the colonoscopy as more uncomfortable than anticipated more frequently (n=114 [26.1%]) than patients who were directly booked for colonoscopy (n=74 [18.9%]) ($p<0.05$). There was no difference between patients who underwent their first colonoscopy and those who underwent a previous colonoscopy.

If necessary, the majority of patients (693 [83.9%]) were (absolutely) willing to return for a repeat procedure.

Discharge and aftercare

The preliminary results of the colonoscopy were discussed by the endoscopist before discharge with 707 patients (86.9%). A total of 608 patients (74.6%) stated that a written result would be (very) important. Additionally, 470 patients (58.5%) would (very much) prefer to consult with the endoscopist before discharge.

Before being discharged, 710 patients (87.3%) received an aftercare information sheet (range among hospitals 74.1% to 96.2%; p<0.05). Among 93 patients who did not receive an information sheet, 26 (28%) were not aware of what to do if problems arose, as opposed to 35 of 692 patients (5.1%) who did receive an information sheet (p<0.01).

At discharge, 171 patients (21.1%) did not know how they would receive their final results. When patients received an aftercare information sheet, they knew more often how they would receive the final results (556 [80.5%] versus 67 [68.4%]; p<0.01).

Factors influencing patient satisfaction

The results of the multivariate logistic regression models are summarized in Table 6. No embarrassment (OR 5.06; 95% CI 2.82 to 9.08) and a less uncomfortable procedure than expected (OR 2.80; 95% CI 1.85 to 4.24) were positively associated with being comfortable during the procedure, while younger age was negatively associated with comfort during the procedure (OR 0.99; 95% CI 0.97 to 1.00).

Furthermore, acceptance of the colonoscopy was positively associated with comfort (OR 23.44; 95% CI 8.96 to 61.28), no embarrassment (OR 3.91; 95% CI 1.76 to 8.68), an acceptable

Table 6. Factors of influence on patient satisfaction

	OR	95%CI
Comfort		
- No embarrassment	5.06	2.82-9.08
- Less uncomfortable then expected	2.80	1.85-4.24
- Younger age	0.99	0.97-1.00
Acceptance		
- Comfort	23.44	8.96-61.28
- No embarrassment	3.91	1.76-8.68
- Waiting time until discharge	3.31	1.01-10.84
- Less uncomfortable then expected	2.48	1.24-4.98
Willingness to return for colonoscopy if necessary		
- Comfortable while waiting for procedure in waiting area	9.93	2.99-32.99
- No embarrassment	6.65	3.51-12.61
- Less uncomfortable then expected	2.99	1.80-4.97
- Waiting time until discharge	2.66	1.00-7.05
- Preliminary results discussed after procedure	2.31	1.24-4.31

OR > 1 indicates a negative association, OR < 1 indicates a positive association

wait time to discharge (OR 3.31; 95% CI 1.01 to 10.84) and a less burdensome procedure than anticipated (OR 2.48; 95% CI 1.24 to 4.98).

The following variables were positively associated with patients' willingness to return for a colonoscopy: comfort while waiting for the procedure (OR 9.93; 95% CI 2.99 to 32.99), no embarrassment (OR 6.65; 95% CI 3.51 to 12.61), less uncomfortable procedure than anticipated (OR 2.99; 95% CI 1.80 to 4.97), an acceptable waiting time until discharge (OR 2.66; 95% CI 1.00 to 7.05), and discussion of preliminary results after the colonoscopy (OR 2.31; 95% CI 1.24 to 4.31).

DISCUSSION

Patient experience has become an important indicator in colonoscopy QA because it is a measure of patients' acceptance of the procedure and is likely a factor in compliance with follow-up recommendations.[14] Our study evaluated the experiences of patients undergoing colonoscopy in four Canadian hospitals using a questionnaire based on the GRS – a comprehensive QA program developed in the UK.[16] The GRS is now the accepted standard for endoscopy units in the UK that participate in the National Health Service colon cancer screening program. Acceptance of the GRS in the UK has been high; however, to date, full-length peer-reviewed publications pertaining to the GRS are lacking.[17, 18, 21]

Overall, patient satisfaction was high for most aspects of colonoscopy; however, the present study identified areas in which improvements can be made. Patients prefer to be offered a choice for booking their procedure on a convenient date and time. In our study, only 37% of patients were offered a choice for their procedure date. Nevertheless, 77.6% of patients believed that their procedure was booked in a timely fashion. The results are similar to those reported in a French study in which only 13.7% of patients responding in a telephone interview were poorly or fairly satisfied with the time they were required to wait to obtain their colonoscopy appointment.[22]

It is important for patients to understand the indication for their procedure and the risk of rare but serious complications, especially because dissatisfied patients may be more likely to engage in litigation.[1, 13, 23, 24] Several studies have addressed ways to improve information provision such as the distribution of information leaflets, video instruction and pre-colonoscopy consultations.[25-27] As our data show, patients appeared to be better informed about several aspects of the procedure when they had a separate outpatient visit or received an information sheet before the procedure was scheduled. This highlights the importance of ensuring that patients receive and read information pamphlets detailing the procedure, and that sufficient time is given to explain the details of the procedure.

In our study, 34.9% of patients stated that they were not aware of any of the complications when this was asked just before the procedure at the time they were waiting for their

colonoscopy. This number is surprisingly high given that the information sheets of all four hospitals explicitly mention perforation and bleeding as risks, and almost all study participants (99.5%) signed an informed consent form. It is unclear whether these patients did not recall, did not read the information sheet carefully or, were indeed, not informed about the complications. Among the patients who were seen by their specialist,

27.7% stated that the complications were not mentioned, while more than 40% of those who did not have an outpatient visit were not aware of them. This is consistent with the results of a small study of 31 patients that showed the benefit of a pre-colonoscopy outpatient consultation resulting in more information about the procedure being retained.[28] Furthermore, our data support the rationale for a physician visit before the actual procedure combined with distributing information sheets because it results in the highest retention of information.

Our results demonstrate that colonoscopy was well tolerated by patients. This is consistent with the results of a study by Eckardt et al. in which 88% to 92% of patients were willing to return for a repeat procedure.[29] Nevertheless, in our study, 22.7% of patients found the colonoscopy to be more uncomfortable than they expected and, surprisingly, this was higher for patients who were seen by the physician in the outpatient clinic before their procedure. This was reported despite the use of conscious sedation in 94% of the procedures. Perhaps patients should be better informed about the extent of discomfort they may experience or, alternatively, physicians should be more aware of discomfort and ensure that measures are taken to mitigate excessive discomfort during the procedure. Additionally, the importance of a representative presentation of discomfort associated with the procedure that can be expected during the colonoscopy is emphasized by the results that patients were more willing to return for a procedure (OR 2.99), reported less discomfort (OR 2.80) and found the colonoscopy to be more acceptable (OR 2.48) when they experienced the colonoscopy as less uncomfortable than anticipated.

Privacy and dignity are important issues addressed by the GRS, and their importance is reflected by the results of our study demonstrating that the absence of embarrassment is positively associated with a comfortable (OR 3.22) and acceptable (OR 3.91) procedure, and the willingness to undergo a repeat procedure (OR 6.65). Ko et al. found that the personal manner, both from nurses and endoscopists, was of importance in patients' overall satisfaction.[20] In our study, no direct association was found among courteous and considerate physicians or nurses and any of the outcome measures because almost none of the patients had a negative experience with the attitude of the endoscopy staff.

The GRS endorses that patients should be informed about the preliminary results and, if final results depend on further testing, such as pathology results, how these will be reported to them.[16] An important finding in our study was that

21.1% of patients left the hospital without knowing how to obtain their final results. A previous study showed that apart from informing the patient of the results after the procedure, it

is beneficial to also provide a written result.[30] In our study, patients who received a written and verbal report were more likely to recall the recommendations for follow-up and therapy, compared with those who only received a verbal report (72% versus 42%, respectively). Our study confirms these results because patients who received an aftercare information sheet were more aware of what to do when problems arose and were more aware of how they would receive their final results. Furthermore, patients who received the preliminary results of their procedure before they left the endoscopy unit were more often willing to return for colonoscopy (OR 2.31). This aspect of care can be easily incorporated into everyday practice.

We reported the data for the four participating hospitals separately because it highlighted the differences that may exist among hospitals that are in the same geographical region. The baseline measurements obtained in the present study provided data that can be used to improve the patient experience during colonoscopy. Our data also demonstrate that the GRS can be easily applied in a North American setting to help identify service gaps.

The present study has some limitations. First, no formal validation of the questionnaire was performed, although previously validated questions were used and the questionnaire was pre-tested by patients.[14] Second, some findings indicate that the parameters that were deemed to be important to doctors were not necessarily considered to be important to patients. Third, although patient groups contributed to the development of the GRS, some of the investigated items may, therefore, be less important to patient satisfaction than others. Fourth, language barriers could be an issue in patient experiences; however, we did not evaluate this in our study. The outcome of patients whose first language was not English (and were excluded from the study) may be worse. Considering the patient population, however, we suspect that the number of patients not enrolled because of language barriers was low, although we do not have formal supportive data. Fifth, the GRS accounts for the equality of access, and future studies should address the current status of information provision among these patients. Finally, we relied entirely on the information the patient provided and did not verify the data with the endoscopist or the colonoscopy report.

CONCLUSION

The results of our study show that overall patient satisfaction with colonoscopy was high; however, differences existed among the four centers, leaving room for improvement in pre- and post-procedure protocols. The GRS appeared to be an excellent tool for identifying service gaps in patient experiences during colonoscopy, which can serve as a guide for future improvement initiatives.

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Chapter 10

Benchmarking patient experiences in colonoscopy using the Global Rating Scale

Endoscopy [accepted]

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ABSTRACT

Introduction: The Global Rating Scale (GRS) is a quality assurance program that was developed in England to assess patient-centered care in endoscopy. The aim of the current study was to evaluate patient experiences of colonoscopy using the GRS in order to compare different departments and to provide benchmarks. The study also evaluated factors associated with patient satisfaction.

Methods: A GRS questionnaire was used both before and after the procedure in outpatients undergoing colonoscopy. The questionnaire assessed the processes associated with the colonoscopy, from making the appointment up until discharge. Mean values and ranges of 12 endoscopy departments were calculated together with P values in order to assess heterogeneity.

Results: In total, 1904 pre-procedure and 1532 (80%) post-procedure questionnaires were returned from 12 endoscopy departments. The mean time patients had to wait for their procedure was 4.3 weeks (range 3.1–5.8 weeks), and 54% (range 35%–64%; $P < 0.001$) reported being given a choice of appointment dates/times. Discomfort during colonoscopy was reported by 20% (range 8%–40%; $P < 0.001$). Recovery room privacy was satisfactory for 76% of patients (range 66%–90%; $P < 0.05$). The majority of patients reported being sufficiently informed about what to do in case of problems after discharge (79%, range 43%–98%; $P < 0.001$), and 85% of individuals stated that they would be willing to repeat the colonoscopy procedure (range 72%–92%; $P < 0.001$). Factors associated with a decreased willingness to return were the burdensome bowel preparation (odds ratio [OR] = 0.25; $P < 0.001$), "rushing staff" attitude (OR = 0.57; $P < 0.05$), low acceptance of the procedure (OR = 0.42; $P < 0.01$), and more discomfort than expected (OR = 0.54; $P < 0.05$).

Conclusion: Overall patient experiences with colonoscopy were satisfactory, but they also showed considerable variation. This study shows that use of a GRS patient questionnaire is feasible in the Dutch endoscopy setting for the assessment of patient experience. The significant variability between endoscopy units can be used to benchmark services and enable shortcomings to be identified.

INTRODUCTION

Quality in colonoscopy has received considerable attention in recent years. Over the past decade the patient experience has been recognized as an important aspect of quality of colonoscopy.[1] However, it is difficult to set uniform, quantitative targets for patient experience. Reasons for this include the lack of standardized surveys and auditable outcomes, and diversity in protocols for colonoscopy procedures. Benchmarking is a promising principle for the determination of the quality of the provided service in terms of auditable outcomes in patient experiences. Benchmarking can help to achieve continuous quality improvement where the standard is set by the best performers.

A promising quality assurance program in endoscopy that was designed to assess patient-centered care is the Global Rating Scale (GRS). The GRS was developed in the United Kingdom (UK) and combines clinical and patient outcomes in endoscopy.[2, 3] The GRS is currently receiving international attention.[3-6]

The GRS may be suitable to assess patient experiences, and can also be used as a benchmark tool to compare different endoscopy departments.

The primary aim of the current study was to evaluate patients' colonoscopy experiences in daily practice. In order to do this, a GRS survey instrument was developed for the Dutch situation and used to benchmark patient experiences between endoscopy departments. A secondary objective was to report on factors associated with patient satisfaction, which could be used to guide future quality initiatives.

METHODS

This study took place in the context of a quality evaluation project for colonoscopy in 12 endoscopy departments in The Netherlands (six teaching and six non-teaching hospitals). Representatives of all hospitals agreed to participate in the study, knowing that their department-specific results would only be disclosed to their own endoscopy department. Ethical approval for the study was obtained from the Institutional Review Boards of all participating hospitals. Data were collected through pre- and post-colonoscopy questionnaires, which were completed by outpatients undergoing colonoscopy.

Design, pre-test, and pilot phase

A survey instrument, which included both pre- and post-colonoscopy sections, was designed to evaluate the complete patient experience, as established in the GRS. The instrument covered the whole experience, from the scheduling of the procedure to discharge from the endoscopy department. A template survey was derived from the English GRS questionnaire,

which has been used previously in the UK and Canada.[4] After a literature review (MeSH: "Patient preference," "Patient satisfaction," "Endoscopy," Health Services Accessibility")[1, 7-14], the Canadian GRS questionnaire was revised and extended to include items found in the literature.[1, 7, 9, 14]

Following development of the questionnaire, five modules were appointed based on the GRS content that covered patient satisfaction aspects of colonoscopy: 1) overall satisfaction, 2) accessibility and timeliness, 3) interpersonal skills, 4) comfort and privacy, and 5) information and aftercare. The 5-point Likert scale questions from the questionnaire were independently classified by two investigators into these five modules.

The questionnaire was translated into Dutch by means of forward–backward translation. Thereafter, the survey was evaluated in a pre-test phase by two gastroenterologists and one health scientist for the comprehensibility of the survey items. During a pilot phase, the questionnaire was reviewed in the endoscopy department for misinterpretations and misspelling by 20 outpatients undergoing colonoscopy. Oral and written feedback from the patients was obtained by the principal investigators. The final survey format can be found in Appendix I (available online).

Inclusion

Between January 2010 and February 2010, outpatients ≥18 years of age who were scheduled to undergo a colonoscopy were asked on the day of the procedure to participate in the study. The pre-procedure section of the questionnaire had to be completed in the waiting room of the department. The post-procedure form had to be completed at home and returned to the investigators within 3 days in a pre-paid envelope. At least 150 pre-procedure questionnaires were required per endoscopy department in order to complete the audit. Written consent was obtained from all patients.

Colonoscopies were performed according to local protocols by all endoscopists of the 12 departments including gastroenterologists, fellows, nurse-endoscopists, surgeons, and internists. In feedback sessions at the end of the study, all departments received their scores, which were calibrated against mean scores of the overall survey outcomes.

Data collection

Data were stored on a database at the initiating academic center (Erasmus MC University Medical Center, Rotterdam). For every patient who completed the pre-procedure questionnaire, the accompanying colonoscopy report was obtained. The investigators extracted data from the reports on the endoscopist, indication, extent of the procedure, quality of bowel preparation, sedation, findings, interventions, and direct complications. Additional data about the bowel preparation protocol were retrieved. The final study cohort for analyses consisted of patients with a completed pre-procedure part, a completed post-procedure part, and a colonoscopy report.

Statistical analyses

To assess the validity of the instrument, the responsiveness of the primary outcomes was evaluated by calculating the percentage of patients who completed questions on overall satisfaction and willingness to return and repeat the procedure. Additionally, internal consistency of the modules assessing aspects of patient experience was calculated using Cronbach's alphas defined as: >0.8 excellent validity; >0.6 good validity; >0.4 fair validity; >0.2 poor internal validity.[15] The 5-point Likert scales were converted to 3-point scales (Positive: 'very satisfied' and 'satisfied'; Neutral: 'neutral'; and Negative: ('dissatisfied' and 'very dissatisfied').

Categorical data were analyzed using the chi-squared test and nominal data were analyzed by means of the independent student's t test.

Overall patient experience outcome and benchmarking

The descriptive data of the departments are presented as the overall mean percentage of positive ratings of the 3-point scales, with the range in these positive ratings between lowest–highest departments. The primary outcome was defined as the percentage of patients who had an overall satisfying experience and the proportion of patients that would be willing to return for repeat colonoscopy. For benchmarking, the overall heterogeneity was tested for every questionnaire item between the 12 departments in the positive ratings, by comparing a logistic regression model with department as the only predictor to a null model based on the likelihood ratio test, as has been done by others.[16, 17]

Factors associated with patient satisfaction

Multivariate binary logistic regression analyses were performed to identify variables associated with discomfort, overall satisfaction, and willingness to return. For the independent variables, the 5-point Likert scales were converted to binary scales: a positive outcome for the answers "very satisfied" and "satisfied;" a negative outcome for "neutral," "dissatisfied," and "very dissatisfied".[1] For outcome variables for "overall satisfaction" and "willingness to return," the "positive" category of the 3-point scale was used. For "discomfort" the "negative" category was used. Variables in the regression models "discomfort" and "overall satisfaction" were based on previous literature.[1, 18] For "willingness to return," variables were determined a priori based on the aforementioned modules, univariately tested, and included in the final model if $P < 0.1$ using the Enter approach. Correlations were performed between bowel preparation protocol and the patient experience in bowel cleansing per department using the Pearson's correlation coefficient. All analyses were performed using the SPSS PASW statistical package version 17.0.

RESULTS

In total, 1904 pre-procedure questionnaires were collected from the 12 departments. After exclusion of questionnaires where no colonoscopy report from the endoscopy database could be retrieved because of incomplete patient demographic data (n = 23), the pre-procedure cohort for analysis consisted of 1881 patients. From these patients, 1509 post-procedure surveys were returned by mail (response rate 80%; range 73%–94%), which made up the final study cohort (Table 1). Non-responders to the post-procedure questionnaire were more likely to be younger compared with older individuals (mean age 54 vs. 58 years, respectively; P < 0.05) but did not differ in sex (male 50% vs. 49%, respectively; P = 0.70). Patient interpretation of the survey instrument seemed satisfactory, with 99% of patients (n = 1486) completing the questions assessing the primary outcomes of overall satisfaction and willingness to return for repeat colonoscopy. Internal consistency was good to excellent (Cronbach's alphas for the five modules ranged from 0.60 to 0.78). Distribution of the 3-point scale for the five modules can be found in Appendix II (available online).

Table 1. Cohort characteristics of the study population with the range of each characteristic among endoscopy departments

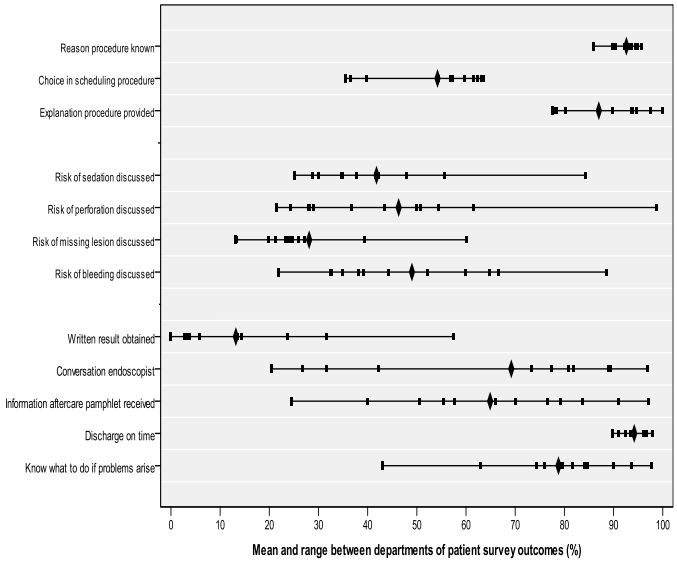
	Overall n (%)	Range	p-value
Total of included patients (n)	n=1,509	92-162	-
Mean age (years)*	58.9	52.2-63.2	<0.001
Male gender	730 (49)	34-54%	<0.001
History of abdominal/pelvic surgery	620 (42)	30-54%	<0.001
Previous colonoscopy**	694 (47)	31-73%	<0.001
Indication			<0.001
Symptomatic	930 (63)	44-80%	
Asymptomatic	302 (20)	7-33%	
IBD	252 (17)	7-40%	
Referrer			<0.001
Gastroenterologist	601 (40)	23-68%	
GP	678 (46)	13-67%	
Other specialist	208 (14)	6-30%	
Cecal intubation (adjusted*)**	1,424 (95)	85-99%	<0.001
Adequate quality bowel preparation#	1,446 (96)	92-99%	<0.010
Sedation used	1,310 (91)	60-99%	<0.001
Endoscopist specialty			<0.001
Gastroenterologist	998 (66)	0-100%	
Fellow	307 (20)	0-86.2%	
Internist	105 (7)	0-34%	
Surgeon	43 (3)	0-18%	
Nurse endoscopist	56 (4)	0-19%	

CRC = colorectal cancer; IBD = inflammatory bowel disease; SD = standard deviation; GP = general physician;
*in years, ** Example: the proportion of patients with a previous colonoscopy, the difference between the department with the lowest proportion of patients with this history (31%, is significantly different compared to the department with the highest proportion of these patients (73%); *** Adjusted for poor bowel preparation, severe colitis, intervention as indication; # Good and fair assumed as sufficient.

Overall patient experience and benchmarking

Figure 1 shows the percentage of patients recalling whether specific care was provided or not and the range for the 12 departments. Significant differences were observed in the majority of items between the departments (Figure 1). Figure 2 shows the questions for evaluation of patient satisfaction grouped into the five modules. For most items significant differences were found between the departments in the proportion of (very) satisfied patients.

Figure 1. Percentages of patients recalling whether specific care was delivered or not with range between departments.



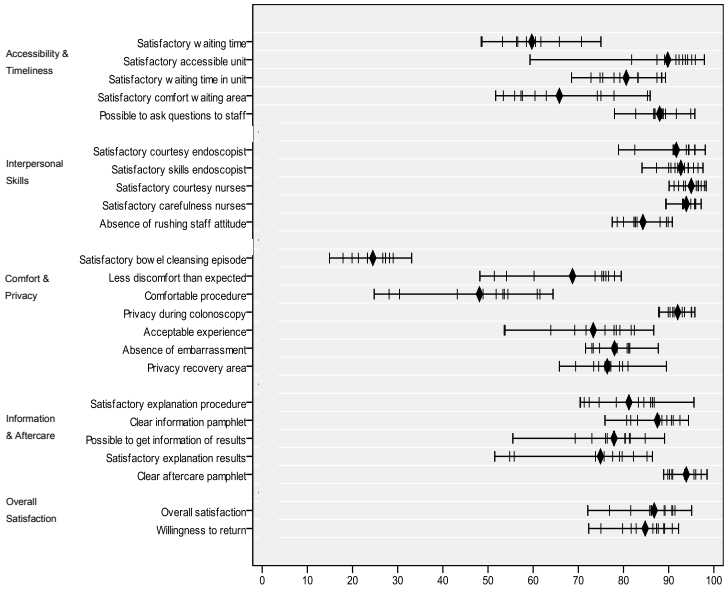
n (%)	Range (%)	p-value
1,373 (93)	86-96	0.353
800 (54)	35-64	<0.001
1,298 (87)	78-100	<0.001
651 (46)	21-99	<0.001
649 (49)	22-89	<0.001
344 (28)	13-60	<0.001
559 (42)	25-84	<0.001
188 (13)	0-57	<0.001
999 (69)	20-97	<0.001
942 (65)	25-97	<0.001
1,292 (94)	90-98	0.093
1,124 (79)	43-98	<0.001

The proportion of patients in number and percentages in recalling whether the specific care was provided. '◆' represents the mean percentage of all 1,509 patients who were informed appropriately. The bar gives the range for departments of the patient reported scores in the corresponding question with the lowest and highest scoring department. 'I'': department specific score.

Module 1 – Overall satisfaction

For the primary outcome of overall patient experience, the majority of patients were (very) satisfied with their endoscopy experience (86%) although considerable variation was observed between departments (72%–95%; P < 0.001) (Figure 2). A total of 85% of patients reported that they would be willing to return for repeat colonoscopy (range 72%–92%, P < 0.001; Figure 2).

Figure 2. Proportion of satisfied patients between departments (%).



n (%)	Range (%)	p-value
864 (60)	49-75	<0.001
1,338 (90)	59-98	<0.001
980 (66)	52-86	<0.001
1,197 (81)	69-89	<0.001
1,310 (88)	78-96	<0.01
1,355 (92)	79-98	<0.001
1,316 (93)	84-98	<0.01
1,412 (95)	90-98	<0.05
1,393 (94)	89-97	0.162
1,254 (84)	78-91	<0.05
356 (25)	15-33	<0.001
923 (69)	48-80	<0.001
583 (48)	25-64	<0.001
1,339 (92)	88-96	0.230
923 (73)	54-87	<0.001
917 (78)	72-88	<0.05
1,053 (76)	66-90	<0.05
1,017 (81)	70-96	<0.001
1,265 (88)	76-94	<0.001
1,118 (78)	56-89	<0.001
996 (75)	52-86	<0.001
872 (94)	89-99	0.111
1,291 (87)	72-95	<0.001
1,262 (85)	72-92	<0.001

The proportion of patients in number and percentage who were satisfied about aspects that involved their colonoscopy procedure for both pre-procedure and post-procedure satisfaction outcomes. '◆' represents the mean percentage of all 1,509 patients who were informed appropriately. The bar gives the range for departments of the patient reported scores in the corresponding question with the lowest and highest scoring department. 'I'': department specific score.

Module 2 – Accessibility and timeliness

Overall, 54% of patients reported that they were given a choice of dates/times for their colonoscopy (range between departments 35%–64%; P < 0.001) (Figure 1). The mean estimated waiting time for the colonoscopy was 4.3 weeks (range 3.1–5.7 weeks). Patients who had to wait >4 weeks were significantly more dissatisfied with their waiting time than patients who had to wait <4 weeks (30% vs. 6%; P < 0.001). The majority of patients had the opportunity to ask endoscopy staff any remaining questions before the procedure (mean 88%, range 78%–96%; P < 0.01) (Figure 2).

Module 3 – Interpersonal skills

A total of 92% of patients (range 79%–98%; P < 0.001) were satisfied with the manner of the endoscopist. Of all patients, 84% (range 78%–91%; P < 0.05) stated that there was no "rushing staff" attitude.

Module 4 – Comfort and privacy

Half of the patients perceived the bowel preparation for colonoscopy as (very) burdensome (mean 51%, range 41%–71%; P < 0.001). Overall, 20% of patients experienced discomfort during the procedure (range 8%–40%; P < 0.001) and 13% of all patients rated the colonoscopy as (more) uncomfortable as expected before the procedure; 69% rated it as less uncomfortable than expected (Figure 2). Patients perceived pain control to be less adequate when the procedure was performed by a gastrointestinal fellow compared with other types of endoscopists (8% vs. 4%, P < 0.01). Privacy in the recovery room was rated as satisfactory by 76% of patients (range 66%–90%; P < 0.05) (Figure 2).

Module 5 – Information and aftercare

The majority of patients received a pre-procedure information pamphlet (98%). With regard to verbal communication of preliminary findings post-procedure, 75% of respondents reported that this was satisfactory (range 52%–86%; P < 0.001). Patients who received the preliminary result from the endoscopist were more satisfied than those who received the result from nursing personnel or those who did not receive any information at all (83% vs. 67%; P < 0.01). A majority of 79% of patients reported to be sufficiently informed about what to do if problems arose after discharge (range 43%–98%; P < 0.001). Patients who received

Table 2. Multivariate model evaluating factors that are associated with discomfort during the colonoscopy

n=1,015*	n	OR	95% CI	p-value
Discomforting experience	199	-	-	-
Comfortable experience	816			
Younger age	-	1.03	1.02-1.04	<0.001
Female gender	514	1.88	1.33-2.65	<0.001
No sedation	82	2.36	1.35-4.11	<0.01
Incomplete examination	50	2.10	1.06-4.17	<0.05
Previous colonoscopy	459	1.58	1.12-2.22	<0.01
Previous abdominal surgery	381	1.04	0.72-1.49	0.85
Endoscopist speciality				
Gastroenterologist	697	Ref		
Fellow	238	2.25	1.31-3.88	<0.01
Internist/surgeon	35	1.88	0.81-4.34	0.14
Nurse endoscopist	45	1.92	0.85-4.34	0.12
Endoscopist experience				
0-2 yrs	163	Ref		
2-5 yrs	222	1.38	0.83-2.30	0.21
5-15 yrs	313	1.24	0.65-2.35	0,52
15-25 yrs	198	1.29	0.64-2.59	0.48
>25 yrs	119	1.85	0.89-3.85	0.10

Nagelkerke R^2= 0.13; OR=odds ratio; OR > 1 indicates more discomfort whereas a OR < 1 indicates less discomfort; *due to missing values in survey items

an aftercare information leaflet recalled significantly more of what to do if problems arose compared with patients who were not given a leaflet (95% vs. 49%; P < 0.001).

Factors associated with patient satisfaction

Results from the multivariate regression models are shown in Tables 2–4. Factors associated with discomfort (Table 2) were younger age, female sex, a gastrointestinal fellow performing the procedure, having undergone previous colonoscopy, an incomplete procedure, and the absence of sedation.

Factors that were associated with increased overall satisfaction (Table 3) were satisfactory scores about waiting time, the personal manner of the endoscopist, less discomfort than expected, higher acceptance of the procedure, the patient's perception of adequacy of pain control, and the possibility to obtain preliminary results from staff.

Table 3. Multivariate model evaluating factors that are associated with a satisfactory experience

n=813*	n	OR	95% CI	p-value
Satisfying experience	715	-	-	-
Dissatisfying experience	98			
Age	813	1.00	0.98-1.02	0.81
Male gender	403	1.33	0.79-2.23	0.29
Satisfied about waiting time to schedule procedure	497	1.72	1.02-2.88	<0.05
Satisfied about explanation pre-procedure	660	1.65	0.91-3.01	0.10
Satisfied about the waiting within the unit	651	1.65	0.91-2.81	0.10
Satisfied about endoscopists' personal manner	764	3.28	1.14-9.46	<0.05
Satisfied about nurses' personal manner	776	1.82	0.50-6.60	0.36
Satisfied about endoscopist's skills	760	0.89	0.35-2.28	0.81
Patients perceived adequate pain control	778	3.34	1.42-7.89	<0.01
Less discomfort than expected	556	2.72	1.54-4.79	<0.001
Higher acceptance of the procedure	596	3.43	1.99-5.90	<0.001
Satisfied about privacy recovery room	619	0.75	0.41-1.39	0.37
Satisfied about possibility to obtain results	626	4.79	2.75-8.35	<0.001

Nagelkerke R^2= 0.39 ; OR=odds ratio; OR > 1 = higher overall satisfaction; OR < 1 = lower overall satisfaction; *due to missing values in survey items

Factors associated with willingness to return for repeat colonoscopy (Table 4) were male sex and absence of symptoms. A burdensome experience with bowel cleansing, a "rushed staff" attitude, more discomfort than expected, and a low acceptance of the procedure were all associated with a decreased willingness to return.

Table 4. Multivariate model evaluating factors that are associated with a high willingness to return for colonoscopy

n=832*	n	OR	95% CI	p-value
Willing to return	712	-	-	-
Not willing to return	120			
Male gender	404	1.89	1.17-3.04	<0.01
Age	832	1.01	1.00-1.03	0.11
History of colonoscopy	353	0.91	0.56-1.47	0.70
Sedation	792	0.50	0.12-2.04	0.34
Complete examination	796	1.82	0.82-2.00	0.14
Indication				
Symptomatic	535	Ref		
Asymptomatic	144	2.20	1.07-4.54	<0.05
IBD	153	1.75	0.94-3.27	0.08
Dissatisfied waiting time to schedule procedure	328	0.91	0.58-1.42	0.67
Dissatisfied bowel preparation cleansing episode	643	0.25	0.12-0.53	<0.001
Dissatisfied waiting time within the unit	172	1.19	0.72-1.96	0.49
Dissatisfied rushed staff attitude	139	0.57	0.34-0.97	<0.05
Dissatisfied endoscopist's skills	69	1.85	0.91-3.74	0.09
Dissatisfied nurses carefulness	47	0.54	0.25-1.16	0.11
More discomfort than expected	272	0.54	0.31-0.92	<0.05
Low acceptance of procedure	229	0.42	0.25-0.71	<0.01
Dissatisfied privacy recovery room	210	0.78	0.48-1.27	0.32
Dissatisfied explanation of the procedure	224	0.81	0.51-1.28	0.37

Nagelkerke R^2= 0.23; OR=odds ratio; OR > 1 = a positive association with willingness to return; OR < 1 = a negative association with willingness to return; *due to missing values in survey items

Bowel preparation

Patients <50 years of age experienced bowel preparation as more burdensome than patients ≥50 years (82% vs. 73%; P < 0.001) as did female patients compared with male patients (79% vs. 72%; P < 0.01). There was a positive correlation between the use of the bowel preparation protocol of 2 L solution of polyethylene glycol (PEG) plus ascorbic acid compared with 4 L of PEG protocols and the satisfaction of patients about the bowel cleansing (R = 0.69; P < 0.05). There was no significant difference in the endoscopic quality of the bowel preparation between the two protocols (R = 0.33; P = 0.291).

DISCUSSION

This patient experience survey study shows that the majority of patients were satisfied with their colonoscopy experience and would be willing to return for a repeat procedure if necessary. Overall, more than half of the patients were allowed to choose the date and time of their

colonoscopy appointment, and the majority of patients were satisfied with the endoscopy personnel.

However, there was significant variability between endoscopy units in most survey items, particularly in patient information provision, comfort and privacy, and aftercare issues. Following the Canadian GRS-related survey study, the current study shows that the GRS content is also applicable in a European country and can be used as a benchmark tool in order to identify service gaps in patient-centered care in colonoscopy.[4] The consequences are that quality improvement initiative should focus on these gaps in service provision, with the GRS being used as a potential tool for both the identification of these gaps, as well as a tool for repeat assessment after interventions.

Accessibility and timeliness

An increased waiting time for a procedure (accessibility) has been reported to be associated with decreased patient satisfaction.[8] In a former GRS-related survey of four Canadian endoscopy units, the majority of patients reported that their procedures were booked in a timely fashion (78%).[4] In the current study, fewer patients were satisfied with the waiting time for the procedure (60% satisfaction). Patients were considerably more dissatisfied if their scheduled colonoscopy required a wait of more than 4 weeks. Satisfaction with respect to procedure accessibility was indeed associated with increased overall satisfaction (OR = 1.72). It underlines the importance of putting maximum effort into optimizing the planning of endoscopy slots. Following the principle of benchmarking, the data show that sharing solutions in optimal use of resources can help to shorten waiting times and thereby increase patient satisfaction.

Interpersonal skills

Satisfaction with the personal manner of the endoscopist was found to be associated with overall satisfaction in a Canadian study.[1] This was also confirmed in the current study (OR = 3.28). However, the perceived skill of the endoscopist was not associated with satisfaction in the current study, which is contrary to previous studies.[1, 14] This may be explained by the fact that a proportion of patients reported that they did not feel qualified to appropriately judge the skill of the endoscopist. Problems concerning reliable patient rating of endoscopist skill have been described before and include the sedation-related amnesia and differences due to cultural backgrounds, thus rendering this variable less reliable.[19]

Comfort and privacy

A considerable proportion (20%) of patients in the present study experienced discomfort, with a wide variation between departments (8%–40%). One of the reasons for this may be

the time of assessment because on-site completion of satisfaction questionnaires tends to yield higher satisfaction rates than mail-back approaches, as was done in the current study. Another explanation for the high proportion of discomfort reported is the fact that discomfort was assessed in a non-screening population (i.e. a population of symptomatic patients). Similar satisfaction rates have been observed in other surveys of symptomatic patients.[1, 20] This suggests that there is a discrepancy between our general impression of patient satisfaction with colonoscopy in daily clinical practice and the results obtained by structured assessment. This observation is a major impetus for departments to adopt a strategy of similar structured assessment, with the adoption of measures to optimize satisfaction and minimize pain scores. In the current study, patient satisfaction was partly explained by factors that can be influenced such as endoscopist profession, and the patient's perception of adequate pain control. Therefore, opportunities for improving patient discomfort scores can be identified, and by comparing the data with other department or units, optimal protocols can be designed.

The expected discomfort was evaluated before the procedure because pre-procedure anxiety has been recognized as a determinant of overall discomfort.[10] Overall, 13% of all patients reported more discomfort than expected, which was lower than that reported in the Canadian GRS-related survey study (22%).[4]

Less discomfort than expected was also an important determinant of the willingness to return for repeat colonoscopy. A determinant for a decreased willingness to return was a burdensome bowel preparation experience (OR = 0.25), in line with previous reports.[20] Half of the patients (51%) reported a low tolerance for the bowel preparation with differences being observed between age and sex comparable with previous findings.[20] Significant variability between departments was also seen, which may be explained by different bowel preparation regimens. Again, the benchmark principle shows that optimizing bowel preparation protocols can be achieved by exchange of knowledge between endoscopy departments and will result in higher satisfaction scores.

Information provision and aftercare

Patient information is an important aspect of the colonoscopy procedure.[21] Previous research has shown that patients want to be well-informed, even about small risks.[22] Half of the patients who completed the questionnaire in the waiting room did not recall a discussion about the risks of possible complications, with wide variation existing between departments. Despite the fact that a pre-procedure information leaflet stating the relevant complications was given (98%), it is the responsibility of the endoscopy department to ensure that the patient is properly informed. Furthermore, in the Canadian GRS-related survey study, 90% were informed about what to do if possible problems arose compared with 79% in the current study.[4] This may also be explained by the differences in proportions of patients who received

an aftercare leaflet between the studies (64% vs. 87%). In the current study, three out of four patients were satisfied with the verbal communication of preliminary findings but again there were large differences between departments. If patients had a conversation about the preliminary results with the endoscopist, they were more often satisfied with this information. This can be achieved easily in order to improve this service deficiency. Alternatively, a written report about the procedure findings with discharge instructions may be desirable. A previous study found that more information was recalled by patients post-procedure when such a written report was provided. By exchanging protocols between departments, such deficiencies are easily identified and remedied, which is the major advantage of using this benchmark approach.

Limitations

This study has some limitations. Due to the study design, the participation rate of patients for the pre-procedure questionnaire remains uncertain, as patients gave their consent in the waiting room of the department. Additionally, recall bias may have played a role in the survey, as patients completed the post-procedure questionnaire at home.[20]

Conclusions

In conclusion, the colonoscopy experience of outpatients undergoing colonoscopy in this study was satisfactory, although important variability was observed between endoscopy departments. The study indicates that the GRS is a useful tool for the identification of service gaps that affect patient experiences in an endoscopy department, and can be used as a benchmark tool to improve the overall quality of the patient experience. The exchange of knowledge and experience between departments will raise the quality of the patient experience. Moreover, the content of the GRS for the evaluation of patient experiences appears to be applicable and appropriate outside the UK in the Dutch endoscopy setting, allowing national and international comparisons in quality of patient experiences in endoscopy.

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Chapter 11

The incidence of 30-day adverse events after colonoscopy among outpatients in the Netherlands

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ABSTRACT

Introduction: Colonoscopy is the gold standard for visualization of the colon. It is generally accepted as a safe procedure and major adverse events occur at a low rate. However, few data are available on structured assessment of (minor) post-procedural adverse events.

Methods: Consecutive outpatients undergoing colonoscopy were asked for permission to be called 30 days after their procedure. A standard telephone interview was developed to assess the occurrence of (1) major adverse events (hospital-visit required), (2) minor adverse events, (3) days missed from work. Adverse events were further categorized in definite-, possible-, and unrelated adverse events. Patients were contacted between January 2010 and September 2010.

Results: Out of a total of 1,528 patients who underwent colonoscopy and gave permission for a telephone call, 1,144 patients were contacted (response: 75%), 49% were male, the mean age was 59 yrs (SD: 14).

Thirty-four (3%) reported major adverse events. These were definite-related in nine (1%) patients, possible-related in 6 (1%), and unrelated in 19 patients (2%). Minor adverse events were reported by 466 patients (41%). These were definite-related in 336 (29%) of patients, possible-related in 36 (3%), and unrelated in the remaining 94 (8%) of patients.

Female gender (OR: 1.5), age <50 years (OR: 1.5), colonoscopy for colorectal cancer screening/surveillance (OR: 1.6), and fellow-endoscopy (OR: 1.7) were risk factors for the occurrence of any definite-related adverse event.

Patients who reported definite-related adverse events were significantly less often willing to return for colonoscopy (81 vs. 88%, $p<0.01$) and were less often positive about the entire colonoscopy experience (84 vs. 89%, $p=0.04$).

Conclusion: Structured assessment of post-colonoscopy adverse events shows that these are more common than generally reported. Close to one-third of patients report definite-related adverse events, which are major in close to one in hundred patients. The occurrence of adverse events does have an impact on the willingness to return for colonoscopy.

INTRODUCTION

Colonoscopies are responsible for more than 50% of all endoscopic procedures performed per year in the US.[1] In 2002 it was estimated that over 14 million colonoscopies were performed in the US.[2] The total volume of colonoscopies has consistently expanded since then and will further increase in the coming years.[3, 4]

In general, colonoscopy is a safe procedure, but a small number of major adverse events do occur. The most serious complication is procedure-related death. A Canadian population-based cohort study showed that colonoscopy-related mortality 30 days after the procedure was 0.007%.[5] Other major adverse events include perforation (0.07%) and bleeding (0.16%) after colonoscopy. [6] The most common adverse events are sedation related, in particular cardiopulmonary events. These adverse events have been reported to occur in >1% of colonoscopies.[7, 8] Furthermore, case reports described sporadic complications such as splenic rupture and colonic explosion.[9, 10]

Most adverse events occur at the endoscopy unit. However, adverse events can also occur in the days after the procedure. The incidence of major adverse events in the days after a colonoscopy is insufficiently clear.[11-13] Furthermore, few data are available on the occurrence of minor adverse events. It has been suggested that up to 30% of patients experience minor adverse events.[11, 14, 15] The occurrence of these minor adverse events may have an impact on the willingness to return for colonoscopy. This loss of adherence and the potential negative advice to others to undergo colonoscopy impair the effectiveness of colorectal cancer (CRC) screening and surveillance.[16]

The aim of this study was to systematically assess the rate of both major and minor adverse events in the 30 days after colonoscopy.

METHODS

This study took place in the context of a quality evaluation of colonoscopy performance in the Netherlands in twelve hospitals. Ethical approval for the study was obtained from the Institutional Review Board in each individual hospital. Consecutive outpatients undergoing a colonoscopy in one of twelve participating centers were asked to complete a patient satisfaction survey about their experiences during the whole endoscopy journey. A total of 150 surveys were required per department to complete the study about the patient satisfaction. The survey consisted of a pre- and post-procedure questionnaire. At the end of the pre-procedure part (completed in the waiting room before the colonoscopy) patients were asked for permission to be called 30 days after the procedure.

Patients were contacted for this adverse event registration study between January 2010 and September 2010. A standard telephone interview was developed based on the most

Figure 1. Standard telephone interview assessing the incidence of adverse events in the 30 days after colonoscopy.

1.	Did you experience any kind of health problem in the last 30 days?
	a. If yes, please describe.
2.	Did you experience any kind of gastrointestinal complaints in the last 30 days specifically?
	a. If yes, please describe.
3.	Did you see any blood in your stool in the days following your colonoscopy?
	a. If yes, how many times?
	b. How much? (3-point scale: mild-moderate-severe)
4.	Did you experience any abdominal discomfort in the days following your colonoscopy?
	a. If yes, for how many days?
	b. How severe was the abdominal discomfort (3-point scale: mild-moderate-severe)
	c. How would you compare the discomfort after the procedure to discomfort you had before the procedure (5-point scale: much milder-milder-the same-more severe-much more severe)
5.	Were you admitted to a hospital in the last 30 days or did you visit an emergency department?
	a. If yes, for how long were you admitted?
	b. For what reason were you admitted or did you visit the emergency department?
6.	Did you visit your general physician or any doctor because of any health problem in the last 30 days?
	a. If yes, please describe.
7.	Did you miss any day from work due to the colonoscopy (excluding the day of the procedure)?
8.	Did you have to cancel any other activities (hobbies, etc.) besides your work due to the colonoscopy?

common adverse events reported in the literature (Figure 1).[11] The standard interview first asked about general health problems in the 30 days after the procedure. Next, the occurrence of gastrointestinal symptoms was assessed, with specific interest in bleeding and abdominal discomfort. We further assessed the severity and duration of bleeding and abdominal discomfort on a 3-point scale. It was also assessed whether patients had visited their family physician, an emergency department or hospital. At last, it was assessed how many days of work (if applicable) were lost as a consequence of the procedure, excluding the day of the procedure.

The target of the adverse event registration study was to include at least 1,000 patients. Three researchers called the individuals 30 days after their procedure. Individuals were called at the end of the day or beginning of the evening of working days. When a subject could not be reached, they were again approached several days later. After two attempts the subject was noticed to be not reached by telephone.

At the end of the study, the related colonoscopy reports were identified in the hospital files and the following data were recorded: date of birth, gender, indication for endoscopy, use of sedation, quality of bowel preparation, therapeutic interventions during the procedure,

extent of the procedure, endoscopic findings, and definite adverse events. Additionally, the telephone interview was linked to the satisfaction survey. Six months after the study end, the hospital records of all patients were checked to see whether patients were deceased during the study period.

For data analyses a distinction was made between major adverse events and minor adverse events. Major adverse events were defined as any health problem that made the patient visit an emergency department or hospital within the 30 days after their colonoscopy. Minor adverse events were defined as any health problem that the patient experienced in the 30 days after the procedure, not requiring a hospital visit. Individual patients could report both major and minor adverse events. When complaints had already existed before the procedure (based on the indication provided in the report, the patient satisfaction survey, or the telephone interview), similar complaints in the 30 days after the procedure were not regarded as an adverse event, unless it was specifically stated that the complaints had deteriorated after the colonoscopy. Both major and minor adverse events were further divided in definite-related, possible-related, and unrelated adverse events. The hospital record was searched to assess the relation between major adverse events and the colonoscopy, time between the colonoscopy and the adverse were also taken into account. For minor adverse events, two investigators discussed and reached consensus whether the event had been definite-, possible- or unrelated.

Statistical analyses were performed using the SPSS statistical package, version 17.0. Descriptive statistics were performed using Chi Square tests (categorical data) and Student's t-test (continuous data). Multivariate binary logistic regression using robust standard errors was performed to find predictors of the occurrence of any (major or minor) definite-related adverse event. The following variables were included in the model: gender, age, screening/surveillance as indication, the use of sedation, polypectomy, and specialism of the endoscopist. A two-sided p-value of <0.05 was considered to be significant.

RESULTS

During the study period 1,528 out of 1,800 patients (84.9%) gave permission in the pre-procedure questionnaire to be called 30 days after the procedure for the adverse event registration. A total of 1,144 persons (response rate: 74.9%) were successfully contacted and included in the study cohort. The number of patients included per endoscopy department ranged from 4.4% to 11.3% (mean: 9.0%). Patients were contacted after a mean of 32 days (SD: 4). Table 1 shows the characteristics of the final study cohort. No differences were found between the responders and non-responders.

Direct complications, extracted from the colonoscopy reports, were (minor) bleeding in nine patients (0.8%), hypoxia in two patients (0.2%) and bradycardia in two patients (0.2%).

Table 1. Patient characteristics of an outpatient cohort (n=1,144) who underwent colonoscopy in the Netherlands

	Responders		Non-responders		p-value
	n	(%)	n	(%)	
Study cohort	1,144	(74.9)	384	(25.1)	
Male gender	564	(49.4)	193	(50.5)	0.71
Mean age (SD)	58.6	(14.3)	57.2	(14.5)	0.10
BMI	26.0	(4.7)	25.8	(4.5)	0.47
Previous colonoscopy	540	(48.8)	180	(48.1)	0.82
Endoscopist					0.46
- Gastroenterologist	754	(67.0)	242	(64.7)	
- Fellow	188	(16.7)	72	(19.3)	
- Internist	114	(10.1)	43	(11.5)	
- Surgeon	36	(3.2)	7	(1.9)	
- Nurse-endoscopist	34	(3.0)	10	(2.7)	
Indication for colonoscopy					0.57
- Rectal blood loss	181	(16.3)	47	(12.7)	
- Anemia	44	(4.0)	13	(3.5)	
- CRC screening/surveillance	313	(28.1)	104	(28.0)	
- Inflammatory bowel disease	84	(7.5)	25	(7.0)	
- Large bowel symptoms	390	(35.0)	151	(40.7)	
- Other	101	(9.1)	30	(8.1)	
Sedation used	973	(90.8)	324	(89.8)	0.57
Biopsy/polypectomy performed	616	(53.9)	213	(55.6)	0.56
Adjusted cecal intubation	978	(95.8)	322	(93.6)	0.10
Polyp detection rate	462	(40.4)	146	(38.1)	0.43
CRC detection rate	34	(3.0)	13	(3.4)	0.68
Adverse event reported during procedure	13	(1.2)	8	(2.1)	0.16

P-value: Pearson's p-value; SD: standard deviation; BMI: Body Mass Index; CRC: colorectal cancer

Major adverse events

Table 2 shows the reported major adverse events in the 30 days after colonoscopy and the range between the participating departments. No mortality was observed in this study cohort. Definite-related major adverse events were reported by nine patients (0.8%), while another six patients had possible-related adverse events (0.5%). All patients with major definite-related events had received conscious sedation and had undergone a complete colonoscopy.

Patients who reported any major adverse event (n=34) were seen at the emergency department or admitted to the hospital for a median of 3.9 days (interquartile range: 1.0-5.5 days). Patients who reported definite-related major adverse events were admitted for a median of 4.0 days (interquartile range: 1.0-2.5)

Table 2. Prevalence of major adverse events in the 30 days after colonoscopy in an outpatient cohort (n=1,144) in the Netherlands

	n (%)	Range between departments (%)
No major adverse event	1,108 (97.0)	94.0 - 99.1
Major adverse events	34 (3.0)	0.9 - 6.0
> Definite-related major adverse event	9 (0.8)	0.0 - 3.4
Rectal blood loss	4	
Abdominal discomfort	2	
Dizziness	1	
Perforation	1	
Angina pectoris	1	
> Possible-related major adverse event	6 (0.5)	0.0 - 4.0
Urinary tract infection	2	
Transient ischemic attack	2	
Pulmonary embolism	1	
Angioedema	1	
> Unrelated major adverse event	19 (1.7)	0.0 - 4.0

Minor adverse events

Table 3 shows the reported minor adverse events in the 30 days after colonoscopy and the range between the participating departments. A total of 336 patients (29.4%) experienced definite-related minor adverse events, 36 patients (3.1%) had possible-related minor adverse events. Most common definite-related minor adverse events were abdominal discomfort (n=195, 17.0%), rectal blood loss (n=64, 5.6%), and change in bowel habits (n=62, 5.4%).

Of the patients who reported abdominal discomfort, 73 patients (37.4%) reported that abdominal discomfort had been absent before the procedure, 100 patients (51.3%) said that their complaints of discomfort was worse than before, and 12 patients (6.2%) said they had less discomfort than before the colonoscopy. Forty-two patients (21.5%) scored their pain as severe, while the other 153 patients (78.5%) reported mild to moderate pain. Patients reported that the abdominal discomfort persisted for a median of 2.0 days (interquartile range: 1.0-4.0 days).

Of the patients who reported rectal blood loss at home, 5 patients (7.8%) reported much blood loss and 59 patients (92.2%) reported little blood loss. Blood loss was reported for a median of 1.0 day (interquartile range: 1.0-3.0).

Of all patients who were not retired (n=749), 64.1% went to work the day after the procedure, 24.8% missed one extra day from work, 4.1% two days, and 6.9% three or more days (mean: 1.4 days). Among patients who were not retired and who reported definite-related minor adverse event (n=226), 59.1% went to work the day after the procedure (p=0.15), 26.1% missed one day from work, 5.9% two days, and 8.8% three or more.

Table 3. Incidence of minor adverse events in the 30 days after colonoscopy in an outpatient cohort (n=1,144) in the Netherlands

	n (%)	Range between hospitals (%)
No minor adverse events	678 (59.3)	40.2 - 72.4
Minor adverse events	466 (40.7)	27.6 - 59.8
> Definite-related minor adverse events	336 (29.4)	19.5 - 49.4
Abdominal discomfort or cramps	195	
Rectal blood loss	64	
Change in bowel habits *	62	
Tiredness	7	
Dizziness	4	
Hematoma	2	
Nausea	2	
> Possible-related minor adverse events	36 (3.1)	1.3 - 5.5
Musculoskeletal symptoms / back pain	10	
Urinary tract infection	6	
Nausea	6	
Cardiac symptoms	6	
Pulmonary symptoms	2	
Stress	2	
Syncope	1	
Epididymitis	1	
Epileptic seizure	1	
Angina pectoris	1	
> Unrelated minor adverse events	94 (8.2)	4.0 - 12.4

* Includes diarrhea (n=20), constipation (11), flatulence (8), fecal incontinence (3), fecal urgency (3), and mucus discharge (2)

Predictors of adverse events

Table 4 shows the predictors of the occurrence of any adverse event. Any definite-related adverse event was significantly more often reported by female patients (OR: 1.5, 95%CI: 1.14-2.01), patients who were <50 years of age (OR: 1.5, 95%CI: 1.09-2.11), when the colonoscopy was performed for CRC screening or surveillance (OR: 1.5, 95%CI: 1.15-2.17) and when the colonoscopy was performed by a fellow (OR: 1.7, 95%CI: 1.20-2.50).

Satisfaction

The colonoscopy was more often perceived as more discomforting than expected by patients who reported definite-related adverse events compared to patients who did not experience definite-related adverse events (59.4 vs. 70.5%, p<0.01). Furthermore, patients with definite-related adverse events found the colonoscopy less often comfortable (40.0 vs. 51.1%, p<0.01), and less often acceptable (60.9 vs. 76.7%, p<0.001), compared to patients who were free of adverse events.

Patients who had experienced any definite-related adverse event were also less willing to return for colonoscopy (80.6 vs. 87.6%, p<0.01) and were less often positive about the

Table 4. Predictors of the occurrence of major or minor adverse events in the 30 days after colonoscopy in an outpatient cohort (n=1,144) in the Netherlands

	Definite-related adverse event		Definite- or possible-related adverse event	
	OR	95%CI	OR	95%CI
Female gender	1.53	1.14-2.01	1.66	1.25-2.21
Age <50 years	1.51	1.09-2.11	1.34	0.98-1.85
Indication CRC screening/surveillance	1.58	1.15-2.17	1.33	0.98-1.81
Sedation used	0.87	0.53-1.44	0.70	0.44-1.13
Polypectomy performed	0.97	0.71-1.32	0.95	0.70-1.28
Specialist				
- Gastroenterologist	Ref	Ref	Ref	Ref
- Fellow	1.74	1.20-2.50	1.75	1.23-2.51
- Internist	1.25	0.76-2.04	1.31	0.82-2.11
- Surgeon	0.51	0.17-1.54	0.57	0.21-1.58
- Nurse-endoscopist	0.84	0.36-1.93	0.74	0.32-1.81

entire colonoscopy experience (83.9 vs. 88.9%, p=0.04). These results were the same when only minor adverse events were taken into account.

DISCUSSION

Major adverse events during colonoscopy occur in a small proportion of patients. Few data are available on the incidence of adverse events in the period after the procedure. Especially little is known about the occurrence of minor adverse events, which might influence the perceived burden of a colonoscopy and thereby the willingness to return.

This study supports that only a small proportion of patients experience major adverse events in the 30 days after their procedure (0.8% definite-related adverse events). However, almost a third of the patients do experience definite-related minor adverse events. These complaints do not result in significant more days lost from work. However, they do affect the willingness to return for colonoscopy (81 vs. 88%).

The credo 'primum non nocere' (first, do no harm) underlies all medical practice. Therefore, adverse events have been a core issue in quality assurance for colonoscopy. Several guidelines have been published to set targets for the occurrence of major adverse events.[17] Large database studies have shown that the occurrence of death (less than 1 in 14,000), perforation (less then 1 in 1,200) and bleeding (less then 1 in 600) are generally low.[5, 6, 13] Limitations of these studies might be the use of administrative databases and failure to follow patients for a longer period.[18] Furthermore, many studies were performed in CRC screening trials, single center settings, academic settings, or focused on single complications. The results of this cross-sectional quality assessment represent the daily clinical practice. The perforation rate (0.1%) and bleeding rate (0.4%) in our study were similar to other series and below the

suggested standards (perforation: 0.2%; bleeding: 1%).[5, 13, 17] Compared to a large prospective cohort study from the US in which patients were called at 7 and 30 days post-procedure, numbers of definite- or possible-related major adverse events were higher in our study: 1.3 vs. 0.33%.[19] This difference might be explained by that in the study from the US the cohort was restricted to patients who underwent colonoscopy for screening or surveillance and thus the included patients might be healthier and have less complicated procedures. Contradictory, we found that patients undergoing colonoscopy for screening or surveillance reported more often adverse events. This result might be explained by the fact that we included all reported adverse events, including minor adverse events. One may hypothesize that patients who do not undergo colonoscopy because of symptoms may sooner notice and report health problems in the period after the colonoscopy. At last, the expected and perceived symptoms after colonoscopy may be different between asymptomatic and symptomatic patients.

As the number of major adverse events was small we were unable to identify significant risk factors for the occurrence of definite-related major adverse events. However, we did show that they were reported more often in older patients and female patients. Age has been proven to be a risk factor before.[5, 6, 19] Results on gender as a risk factor are more inconsistent. A systematic review showed that female gender was a risk factor for colonic perforation (OR: 2.3).[6] On the other hand, a Canadian population-based cohort study found a negative association between female gender and the risk of perforation or bleeding (OR: 0.67).[5] However, for perforation alone, females did have an increased risk (OR: 1.21). In our study, the inclusion of abdominal discomfort might explain why female gender was found to be a risk factor for reporting major adverse events, as they generally experience more discomfort during and after colonoscopy.[11, 20]

Besides the well-known adverse events, in our study other major adverse events that made the patient visit the emergency department were observed as well. Some might be related to sedation or bowel preparation (angina and dizziness), others were probably related to the colonoscopic technique or interventions (discomfort). Furthermore, we observed more uncommon adverse events, such as transient ischemic attack, pulmonary embolism, and syncope. We could not prove a definite relation between the occurrence of these adverse events and the colonoscopy, therefore classified them as possible-related, as has been done before.[19] However, the clinical impact of these adverse events will be the same, as patients will most probably link them to the colonoscopy. Our results thus show that the real incidence of adverse events will be underestimated both in number and in impact when only definitive adverse events are counted. It underlines that conservative quality assessment may underestimate this issue. The results further underline the importance of proper information provision, medication plans, and monitoring of patients after their colonoscopy.

Besides the major adverse events, patients may experience significant burden from minor adverse events. Previous research has found that these minor adverse events occur in 34% of patients undergoing a colonoscopy.[11] Limitations of that study were the smaller sample size

(n=470), the academic single center setting of the study, no assessment of bowel complaints before the colonoscopy, and inclusion of screening and surveillance colonoscopies only.[11] We addressed these items and our results are similar, with definite-related adverse events occurring in 29% of the patients. With respect to the severity of minor adverse events, we provided detail on the duration and experienced severity of the most common minor events, abdominal discomfort and rectal blood loss. Our results show that rectal blood loss mostly was a minor problem, but abdominal discomfort could hold on for several days, and was experienced as more burdensome than before the procedure for the majority of patients that experienced it. Additionally our results show that patients often miss a day from work after the colonoscopy due to the procedure. However, there was only a small difference in absenteeism between all patients and patients who reported direct-related adverse events (36 vs. 41%) indicating that the adverse events in general may not keep patients from their normal work. The number of minor adverse events reported by our and the American study from 2007 are significantly higher compared to a study performed in 1997 in the United States, where 17% of the patients experienced any adverse event.[12] This may be explained by their less comprehensive interview-technique, and the inclusion of colonoscopies performed by experienced colonoscopists only. In our study patients reported significantly more often adverse events when the colonoscopy was performed by a fellow. A retrospective chart audit found that perforation did occur more often when the endoscopist had performed <200 lower GI endoscopies.[13] Moreover has it been established that a longer procedure time increases the risk of minor adverse events.[11, 20] Taken these results together indicate that the risk for any (major and minor) adverse event is higher if procedures are performed by less experienced endoscopists.

Our study does have some limitations. First, as approximately a quarter of the patients were not reached by telephone we could have missed some patients with serious adverse events. However, all patient records were checked for 30-day-mortality. We assured ourselves that these patients were not deceased. However, they might have been admitted for adverse events at the time of the telephone interview. Another limitation might be recall-bias. As we called 30 days after the procedure, patients might have forgotten the exact details of their complaints. However, this would not be the case for serious adverse events, and may lead to an underestimation of the occurrence of minor adverse events.

In conclusion, this study supports that a colonoscopy is a safe procedure in daily clinical practice. Serious adverse events do occur in a small proportion of patients however. Moreover should the burden of the procedure in terms of minor adverse events not be ignored as a significant part of the patients undergoing colonoscopy do experience complaints in the days following their procedure and this decreases their willingness to return for colonoscopy. Patients and physicians should be aware that a colonoscopy is a burdensome procedure. Regular monitoring of the occurrence of both minor and major adverse events can help endoscopy departments improve the patient-centered care.

STUDY HIGHLIGHTS

What is current knowledge?

- Colonoscopy is a commonly performed procedure, generally considered to be safe.
- Patients can experience burden from a colonoscopy in the days after the procedure, the majority being minor adverse events within 7 days.

What is new here?

- Major adverse events occur in approximately 1 in 100 patients.
- A significant proportion of patients (up to one third) experience minor adverse events in the days after their procedure.
- Minor adverse events do hamper the willingness to return for a colonoscopy.

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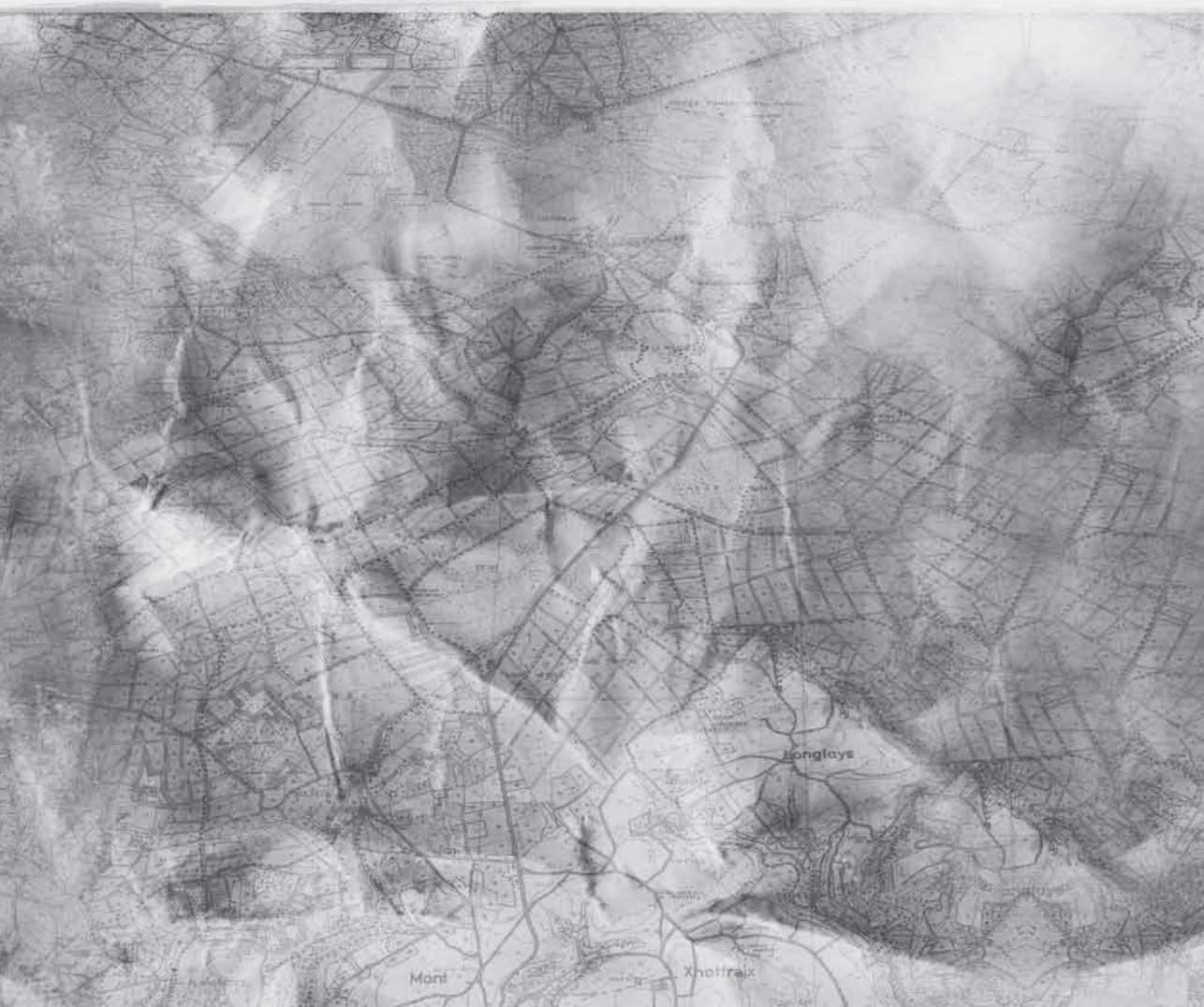
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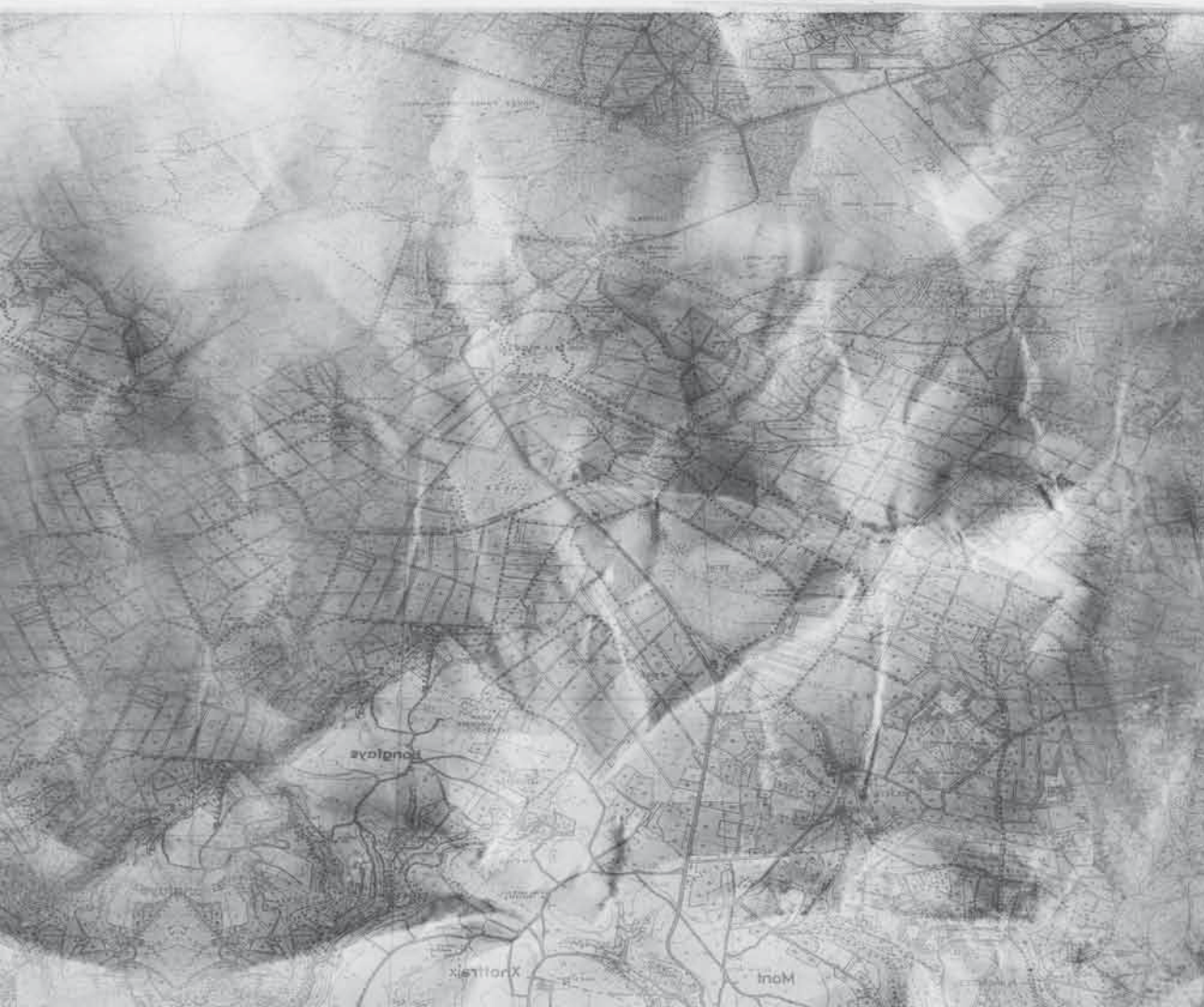
PART III

Quality assurance in colorectal cancer screening and surveillance: how to guide?



Chapter 12

The appropriateness of surveillance colonoscopy intervals after polypectomy

Submitted

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ABSTRACT

Introduction: Adherence to surveillance colonoscopy (SC) guidelines is important to prevent colorectal cancer (CRC) and unnecessary workload. This study evaluated how well Canadian gastroenterologists adhere to colonoscopy surveillance guidelines after adenoma removal or treatment for colorectal cancer (CRC).

Methods: A retrospective study of patients with a history of adenomas or CRC who had surveillance performed between October 2008 and October 2010. Time-intervals between index colonoscopy and surveillance were compared to the 2008 guidelines of the American Gastroenterology Association (AGA) and regarded as appropriate when the surveillance interval occurred within 3 months of the recommended time interval.

Results: 265 patients were included (52% male; mean age 58 years). Among patients with a normal index procedure (n=110), 25% received surveillance on time, 46% too early (median difference=1.8 years too early), and 30% too late (median difference=0.9 years too late). Among patients with non-advanced adenomas at index (n=96), 13% received surveillance on time, 65% too early (median difference=1.84), and 22% too late (median difference=0.72). Among patients with advanced neoplasia at index (n=59), 17% received surveillance on time, 37% too early (median difference=1.79), and 46% later than recommended (median difference=1.12).

No significant difference in adenoma detection rates was observed when comparing too early surveillance vs. appropriate surveillance (36 vs. 35%, p=0.89) and too late surveillance vs. appropriate surveillance (22% vs. 35%, p=0.14).

Conclusions: A minority of surveillance colonoscopies are being performed according to guideline recommendations. Deviation from the guidelines did not alter the adenoma detection rate. This underlines the importance of adherence to surveillance guidelines.

INTRODUCTION

Colorectal cancer (CRC) is a leading cause of cancer-related mortality in the Western world.[1] Screening for CRC decreases CRC-related mortality and CRC incidence.[2] The adenoma-carcinoma sequence is accepted as the pathway of development of CRC and hence one of the main aims of screening colonoscopy is to detect and completely remove all adenomas.[3, 4] After neoplasia removal, patients remain at increased risk for adenoma recurrence. Therefore, surveillance after removal of adenomas or CRC is recommended. Some factors are associated with an increased risk of adenoma recurrence such as number and size of previous polyps and presence of villous features on histology.[5] The surveillance interval is generally based on these findings at the index colonoscopy.[6]

The demand for colonoscopy procedures has risen considerably over the last years which results in increased wait times for gastroenterology care in many regions in the world, including Canada.[7-9] The increase in demand for future colonoscopies as a result of CRC screening is likely to lengthen wait times even further. Deviation from surveillance guidelines may lead to unnecessary workload, and hence decreased cost-effectiveness of CRC screening.[10] Previous studies have shown that a significant proportion of gastroenterologists recommend follow-up intervals that deviate considerably from the published guidelines.[11-14]

The objective of this study was to assess the appropriateness of recommended surveillance colonoscopy intervals in the Canadian endoscopy setting.[6] Furthermore, we aimed to determine whether the appropriateness of surveillance intervals influenced the adenoma detection rate.

METHODS

This retrospective cohort study was conducted at the University of Alberta Hospital, Edmonton, Alberta, Canada. Ethical approval for this study was obtained by the Health Research Ethics Board (Pro000013953). Patients were identified and selected from a pilot study carried out as a first step in the creation of a CRC screening program (NCT00893503). This screening program, called SCOPE (Stop Colorectal Cancer through Prevention and Education), was launched in Edmonton to start a regional CRC screening program. The program was designed to test several steps in the referral process. The average risk patient could be referred only if they had a positive fecal occult blood test. Patients were also eligible to be referred to the program if they had a personal history of CRC or adenomatous polyps, a family history of CRC or polyps. In the pilot study the program only accepted referrals coming from gastroenterologists. For all accepted patients in the program who had a index colonoscopy during which adenomatous polyps were removed, the program did accept the recommendation that was made by the colonoscopist who performed the index colonoscopy. Patients with a history

of inflammatory bowel disease, a known hereditary CRC syndrome or patients with colonoscopies that were performed for the evaluation of gastrointestinal symptoms were excluded. Only patients in whom the index endoscopy report and histology of removed polyps was available, were included in the current study.

Patients with a personal history of adenomas or CRC who had a surveillance colonoscopy performed between October 2008 and October 2010 were included. The colonoscopy performed before this procedure was defined as the index colonoscopy. As all patients had an adenoma history this index colonoscopy might not have been their actual first-time colonoscopy done for adenoma or CRC surveillance. Consequently, even if our defined index colonoscopy was normal, these patients according to the AGA guidelines were supposed to undergo surveillance colonoscopy every 5 years because of their adenoma or CRC history.[6]

Data collection

The following data were collected from endoscopy reports: demographic data (age and gender), family history for CRC, index and surveillance colonoscopy characteristics such as date, cecal intubation rate, quality of bowel preparation (if not mentioned in the report it was assumed to be acceptable), and endoscopic findings including diagnosis, number, histology and site of polyps or cancer. Patients were categorized in different surveillance groups based on their most advanced lesion at index colonoscopy: normal, non-advanced adenoma, or advanced neoplasia. Advanced neoplasia was defined as ≥3 adenomas or adenomas >10mm, with >25% villous histology or high-grade dysplasia, or CRC. For patients who were diagnosed with CRC during index colonoscopy, the date of their surgery was used in order to calculate the optimal surveillance interval.

The actual interval between the index and surveillance colonoscopy was compared to the recommended interval stated in the 2008 guidelines from the American Gastroenterogical Assocation (AGA).[6] This guideline was used as the Canadian guideline, which has not been updated since 2004, does not list explicit recommendations for surveillance. A margin of three months around the recommended date was considered as an appropriate surveillance interval. Outcome measures were defined as the percentage of appropriate, too early, and too late procedures. Secondary outcomes were the adenoma detection rates (ADR) of the three categories, defined as the proportion of patients who had at least one adenoma at surveillance colonoscopy.

Statistical analysis

Descriptive statistics were used. Differences were assessed for significance by means of the Student's t-test for continuous data and the Chi-square test for categorical data. The level of

statistical significance was defined as a two-sided p-value <0.05. All analyses were performed using statistical software package SPSS PASW 17.0, Chicago, IL, USA.

RESULTS

After excluding 11 cases in whom no information was available about the index findings, 265 patients were included for analyses (52% male; mean age on index: 58 yrs, SD=11). Table 1 shows the patients' characteristics stratified for the findings at index colonoscopy. The median number of previous colonoscopies was 1 (range: 0-6). Index colonoscopy was normal in 42% of the patients (n=110/265), non-advanced adenomas were found in 36% (n=96/265), and advanced neoplasia was detected in 22% of the cases (n=59/265). Three patients (1%) had CRC.

Table 1. Patient characteristics at index colonoscopy

	Total (n=265)	Normal index findings (n=110)	Non-advanced adenoma (n=96)	Advanced neoplasia (n=59)
Mean age at index colonoscopy	58 years (SD=10.5)	59 years (SD=10.8)	57 years (SD=10.0)	59 years (SD=11.0)
Male gender	52% (n=138)	56% (n=61)	48% (n=46)	53% (n=31)
Cecal intubation	95% (n=230)	94% (n=98)	97% (n=84)	94% (n=48)
Adequate bowel preparation	90% (n=238)	88% (n=97)	90% (n=89)	93% (n=55)
Positive family history for CRC*	23% (n=61)	19% (n=21)	28% (n=27)	22% (n=13)
Mean interval until SC (years, SD)	3.8 (1.7)	4.3 (1.5)	3.8 (1.5)	2.8 (2.0)

SC= surveillance colonoscopy; SD=standard deviation; * first degree relatives with CRC extracted from endoscopy report if available

Surveillance colonoscopy

Of all 265 surveillance colonoscopies, 19% (n=49/265) were classified as procedures performed on time according to the AGA guidelines. In 51% of the patients (n=134/265) the surveillance interval was shorter than recommended, and the remaining 30% (n=82/265) underwent surveillance later than recommended compared to the surveillance guidelines.

Figure 1 shows the actual observed mean time interval between index and surveillance colonoscopy compared with the recommended time interval stratified for the index finding. The median difference between the recommended time interval and the observed interval was -1.8 years (inter quartile range (IQR)=1.21) for surveillance colonoscopies which were performed too early, and +0.9 years (IQR=1.22) for those which were performed too late.

Table 2 shows the findings at index colonoscopy per appropriateness category. In 16% of the patients who received surveillance colonoscopy too early, an inadequate bowel preparation quality was mentioned at index procedure compared to 2% at surveillance procedures

Figure 1. Mean time interval between index and surveillance compared to time interval recommended by AGA guideline.

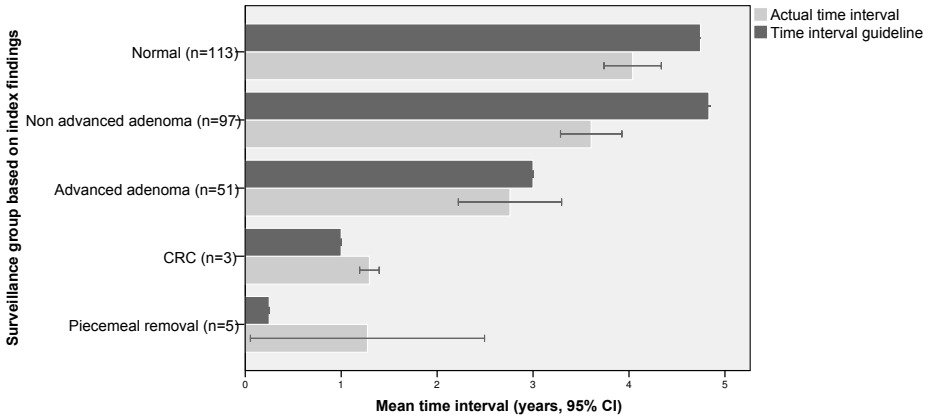

Table 2. Findings at index stratified for appropriateness according to the guidelines

	SC on time (n=49)	SC too early* (n=134)	SC too late* (n=82)
Positive family history CRC	18% (n=9/49)	25% (n=33/134)	23% (n=19/82)
Cecal intubation rate at index #	98% (n=45/47)	95% (n=121/129)	96% (n=64/69)
Adequate bowel prep at index	94% (n=46/49)	84% ** (n=112/134)	98% (n=80/82)
Median difference yrs (IQR)***	0.04 (0.25)	-1.8 (1.21)	0.9 (1.22)
Findings at index			
Normal index	55% (n=27/49)	37% ** (n=50/134)	40% (n=33/82)
Non advanced adenoma at index	25% (n=12/49)	46% ** (n=62/134)	27% (n=22/82)
Advanced adenoma∞ at index	20% (n=10/49)	16% (n=22/134)	33% (n=27/82)

SC= surveillance colonoscopy; IQR=inter quartile range; *= earlier respectively later than recommended in the AGA guideline; **= statistically significant compared to surveillance on time; ***=mean difference between the recommended time interval and the observed interval between index and surveillance; #= total numbers differ by missing values; ∞= ≥3 adenomas or >10mm, with (tubulo-) villous histology or high-grade dysplasia

performed on time (p<0.01). No significant differences for a positive family history and cecal intubation rates were observed between the three appropriateness categories (all p-values > 0.1).

Normal index colonoscopy

Among patients with a normal index colonoscopy (n=110), 25% of patients (n=27/110) received surveillance colonoscopy on time, 46% (n=50/110) too early (median difference= -1.61 years

too early; IQR=1.54), and 30% (n=33/110) too late (median difference=0.76 too early; IQR=0.92). Inadequate bowel preparation on index was reported in 20% (n=10/50) in the too early group.

Non advanced adenoma at index colonoscopy

Among patients with non-advanced adenomas at index colonoscopy (n=96), 13% (n=12/96) received surveillance colonoscopy on time, 65% of cases (n=62/96) too early (median difference= -1.84 years too early; IQR=1.26), and 22% (n=22/96) of patients received their surveillance colonoscopy too late (median difference=0.72 years too late; IQR=0.90). Inadequate bowel preparation on index was reported in 15% (n=9/62) in the too early group. Among patients with normal or non-advanced findings on index (n=206), the percentage of patients undergoing surveillance earlier than recommended was significantly higher (54%; n=112/206) than in patients with advanced neoplasia (37%; n=22/59) (p=0.021).

Advanced neoplasia at index colonoscopy

Among patients with advanced neoplasia, 17% (n=10/59) received surveillance colonoscopy on time, 37% (n=22/59) too early (median difference= -1.79 years too early; IQR=1.01), and 46% (27/59) later than recommended (median difference=1.12 years too late; IQR=1.70). Inadequate bowel preparation on index was reported in 14% (n=3/22) in the too early group. Two of the three patients that had CRC detected at index colonoscopy, did receive surveillance later than recommended. Of the five patients who had a piecemeal removal of their advanced adenoma at index colonoscopy, two returned too late and both of these patients had advanced neoplasia at surveillance colonoscopy. Among patients with advanced neoplasia on index (n=59), the percentage of patients undergoing surveillance later than recommended was significantly higher (46%; n=27/59) than in patients with non-advanced or normal findings (27%; n=55/206) (p=0.005).

Findings at surveillance colonoscopy

Adenomas were found on surveillance in 32% of cases (n=83/265), 8% of patients (n=20/265) had advanced adenomas. No CRC was identified at surveillance colonoscopy. Advanced neoplasia was found in 6% (n=3/49) at surveillance colonoscopies that were performed on time according to the guideline, including two patients with ≥3 tubular adenomas.

Adenoma detection rate at surveillance colonoscopy

The ADR for appropriate versus non-appropriate surveillance colonoscopy (stratified for index findings) are summarized in Table 3. The ADR at surveillance colonoscopy was significantly

Table 3. Adenoma detection rate at SC stratified for appropriateness according to the guidelines

	SC on time (n=49)	SC too early* (n=134)	SC too late* (n=82)
ADR at SC			
Adenoma at SC	35% (n=17/49)	36% (n=48/134)	22% (n=18/82)
Non advanced adenoma at SC	29% (n=14/49)	27% (n=36/134)	16% (n=13/82)
Advanced adenoma∞ at SC	6% (n=3/49)	9% (n=12/134)	6% (n=5/82)
ADR at SC per index			
- Normal index	22% (n=11/49)	8% ** (n=11/134)	7% (n=6/82) ** 6% (n=5/82)
- Non-advanced adenoma index	8% (n=4/49)	15% (n=20/134)	9% (n=7/82)
- Advanced adenoma at index	4% (n=2/49)	13% (n=17/134)	

*= earlier respectively later than recommended in the AGA guideline; **= statistically significant compared to SC on time; ∞= ≥3 adenomas or >10mm, with (tubulo-)villous histology or high-grade dysplasia

higher in patients with advanced neoplasia at index (n=26/59) vs. normal index colonoscopy (n=28/110): 45% vs. 26%, p=0.01). No significant difference in the ADR on surveillance was observed for procedures that were performed on time according to the guidelines compared to too early performed procedures (35% (n=17/49) vs. 36% (n=48/134 respectively), p=0.89). The ADR was also not significantly different between appropriate versus too late procedures (35% (n=17/49) vs. 22% (n=18/82) respectively, p=0.14). The detection of advanced adenomas at surveillance colonoscopy was not significantly different between appropriate vs. too early performed procedures (6% (n=3/49) vs. 9% (n=12/134), p=0.54) nor for appropriate vs. too late performed surveillance according to the guidelines (6% (n=3/49) vs. 6% (n=5/82), p=0.99).

DISCUSSION

Recent reports have shown that there are significant problems with long wait times for colonoscopy procedures in many centers in Canada.[7] It is expected that, in the context of CRC screening and its associated need for surveillance procedures, the demand for and burden of colonoscopies will increase. This study aimed to assess the appropriateness of surveillance colonoscopies in the Canadian endoscopy department, whether improvements are achievable to decrease waiting times.

Our study showed that in a significant proportion of patients, surveillance colonoscopy was not performed at the recommended time interval. Only 19% of the patients underwent a surveillance colonoscopy according to the AGA guidelines. The majority of procedures (51%) were performed earlier than recommended, with the range varying from 0.28 to 4.46

years. Underuse was also reported, as 30% of the patients received their colonoscopy too late. Shortening or lengthening the surveillance intervals did not significantly affect the ADR. Surprisingly there were more delays in surveillance in patients who had advanced adenomas at the index colonoscopy compared to those who had non-advanced adenomas. In 16% of patients earlier surveillance could be explained by poor or suboptimal bowel preparation during the index colonoscopy but even taken this into account, the compliance with the guidelines was poor. This means that there is an important role for education of physicians in this area which should be supported by a quality improvement program to document that adherence to accepted guidelines improves. This may also result in better utilization of endoscopy resources as many repeat procedures were done too early.

The three-month margin around the optimal follow-up date for colonoscopy was arbitrarily chosen. There are no data in the literature to indicate what an optimal choice is for a time interval around appropriateness. However, we believe the three-month interval was a reasonable choice as it gives some indication of the number of colonoscopies that were done either too early or too late according to existing guidelines. Even if a longer interval than three months had been chosen (for example, 6 months) our data still would demonstrate that for a substantial proportion of patients the recommended interval is inappropriate.

Several surveys have documented suboptimal usage of surveillance colonoscopy, with physicians often recommending surveillance intervals that are too short.[12, 15] A Dutch study reported that 52% of the respondents used shorter surveillance intervals than stated by the national recommendations.[11] Suboptimal usage of adherence in daily practice has also been shown in clinical studies.[14, 16-18] A study from the USA observed a considerable disparity between guidelines and endoscopists' recommendations in the colonoscopy report, with more surveillance colonoscopies occurring too soon; in only 37% of the cases were the recommendations consistent with the guidelines .[14] Another study from the Netherlands reported low follow-up rates for surveillance colonoscopy after the removal of adenomas or CRC; the majority of patients tended not to undergo surveillance colonoscopies although overuse was also observed.[17] We recently conducted a questionnaire based study on follow-up recommendations for colonoscopy for different scenarios among members of the Canadian association of Gastroenterology. Adherence by respondents to the guidelines varied from 23% to 96% in different clinical scenarios, reflecting both over- and underuse.[13]

As the risk for adenoma recurrence on surveillance colonoscopy is determined by baseline findings, guideline recommendations for surveillance colonoscopy are stratified based on the index results.[5, 6] There is evidence that surveillance colonoscopy is over-utilized in low-risk subjects and underutilized in high-risk subjects.[16] A US community practice assessment of utilization of surveillance colonoscopy showed under-usage of surveillance practice in terms of longer follow up intervals if high risk lesions at index colonoscopy were present (31%).[14] In our study a similar trend was observed in adherence patterns for surveillance practice between advanced and non-advanced lesions on index procedures.[18] Patients with

non-advanced adenomas (54%) often received surveillance too early while pPatients with advanced neoplasia more often received surveillance colonoscopy too late (46%).

Of all patients with index procedures that revealed advanced adenoma, 44% also had adenomas at surveillance colonoscopy (n=26/59). This underscores that advanced adenoma at index colonoscopy is an important risk factor for adenoma recurrence and thereby supports the guidelines for more vigilant surveillance.[16] In patients who had a normal index colonoscopy (but adenomas on prior colonoscopies), recurrent adenomas were detected in 25% of patients. All patients in this study had a personal history of adenomas or CRC. The fact that 25% still had adenomas at surveillance colonoscopy indicates that these patients remain at high risk for developing metachronous adenomas, despite normal findings at a previous surveillance colonoscopy.

The yield of surveillance colonoscopy did not significantly change between colonoscopies at appropriate or inappropriate times, suggesting that deviating from the guidelines does not necessarily increase the yield of surveillance colonoscopy. In addition, no differences in detection rates in advanced adenomas either between on time vs. too late procedures (6%) were observed, or on time (6%) vs. too early (9%). The reason for the high ADR in the too early group may in part be explained by the fact that in 16% of patients was reported to have a poor bowel preparation during the index procedure. This was significantly higher compared to patients receiving their surveillance procedure on time (2%, $p<0.01$). The detection of adenomas is largely dependent on the quality of bowel preparation.[19] Clinical decisions about the surveillance interval derived from colon cleanliness assessment can vary considerably among endoscopists and there is little agreement on what constitutes an insufficient bowel preparation.[20]

Apart from suboptimal bowel preparation on index procedure, several other explanations have been suggested for non-adherence to surveillance recommendations such as an incomplete examination, possibly incomplete removal of lesions and the presence of a family history of CRC.[15] Although in the too early surveillance cohort relatively more patients had a family history for CRC (25%) compared to the surveillance on time population (18%), it was not significant ($p=0.373$). Additionally, there were no significant differences in cecal intubation rates between the three appropriateness categories.

Additionally, insufficient awareness of guidelines may be an important factor for non-adherence by physicians. Several studies have shown that appropriate use of surveillance after the detection of adenomas or CRC depends to a great extent on the knowledge of surveillance guidelines of physicians.[12, 15] A recent study demonstrated that priming endoscopists by means of distributing guideline pocket pamphlets for use in endoscopy units among endoscopists, may help increase the compliance to guidelines.[21] Alternatively within CRC screening programs follow up recommendations may be centralized and hence more in accordance with guidelines. Centralization of follow up recommendations has been instituted as part of the recently launched provincial Alberta Colorectal Screening Program.

Other explanations for less effective surveillance programs besides nod-adherence by physicians can be found in patient related factors such as non-attendance to surveillance colonoscopy. Most studies in this area focus on clinician adherence to published guidelines, rather than patient adherence to clinician recommendations. Because our study design was limited to only patients who had returned for their surveillance colonoscopy, we do not know how many patients had similar findings during index colonoscopy, did not return for surveillance colonoscopy.

As previously indicated patients who had a prior history of CRC or removal of adenomas could be referred to the SCOPE Program and were eligible for inclusion. This pilot program did not change any of the recommendations that were made by colonoscopists, because this was beyond the scope of the pilot program. In general terms, it is often difficult for physicians changing follow-up recommendations made by other physicians, in particular if this would mean that follow-up colonoscopy is postponed to a later date. It is expected that this is also the general practice in our region, although this was not studied as part of this project. One of the advantages of having an organized CRC screening program is that follow-up recommendations will be standardized, which will lead to more optimal use of resources.

Our study has several limitations. One is the small sample size. Furthermore, the results of our study were collected from one region in Canada and may not be generalizable. Additionally, since the guidelines have been revised in 2008, differences in practice by clinicians in the different time intervals can be attributable to adaptations in guidelines explaining the disparities observed in clinical practice. Our results should be interpreted knowing there is a lack of a explicit guidelines from the Canadian Association of Gastroenterology (CAG) compared to the AGA guideline, as the CAG surveillance recommendation recommends that endoscopists should decide about the appropriate surveillance interval to a greater extent based on clinical judgment.[22]

In conclusion, in our study a minority of the surveillance colonoscopies are being performed according to the revised recommendations for surveillance colonoscopy after polypectomy. A large proportion of patients receive surveillance colonoscopies after the previous detection of adenomas or CRC too soon, while another group of referred patients return after an inappropriately long interval. The results make clear that education is required to raise awareness among endoscopists about proper surveillance intervals and that quality improvement programs likely will result in tangible benefits in terms of outcomes and resource utilization. This may also positively impact wait times for colonoscopy.

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Chapter 13

Utilization of follow-up colonoscopies and the yield of colorectal neoplasia in daily practice

Submitted

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Chapter 14

Systematic literature review and pooled analyses of risk factors for finding adenomas at surveillance colonoscopy

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ABSTRACT

Background and study aim: Colorectal cancer (CRC) screening guidelines recommend surveillance after polypectomy. There is variation in the surveillance intervals that are being advised. This variation also affects adherence. Surveillance intervals need to be based on risk factors at index. We therefore aimed to systematically review risk factors of adenoma findings at surveillance colonoscopy.

Methods: A systematic literature search was performed up to September 2009. Studies that reported on follow-up colonoscopy findings with stratification for index characteristics were included. Pooled relative risks (RR) were calculated using random effects models, and heterogeneity was determined by means of the I^2-statistic.

Results: A total of 27 studies met the inclusion criteria. The most important risk factors for adenoma findings were the presence on index colonoscopy of the following: advanced adenomas (RR: 1.81), ≥3 adenomas (RR: 1.64), size ≥10 mm (RR: 1.66), and age ≥60 years (RR: 1.65). The presence of villous adenomas, high grade dysplasia, proximal adenomas, and male gender were associated with less profound increases in RR. Marked variation in study design and substantial heterogeneity between studies was observed.

Conclusions: Convincing evidence exists that patients with advanced adenomas, ≥3 adenomas, adenomas ≥10 mm, or age ≥60 years have an increased risk of adenoma recurrence. The evidence for other baseline findings for an increased risk of adenoma recurrence is inconclusive. Marked variation and consistently lower RRs in studies of medium or low quality emphasize the necessity for well performed and well reported studies. Given the high impact of surveillance on patients and service providers, there is need for further assessment of the risk(s) of adenoma recurrence.

INTRODUCTION

Colorectal cancer (CRC) is the second most common cause of cancer-related deaths in the Western world.[1, 2] Many studies have addressed the efficacy of CRC screening in the prevention of CRC and its associated morbidity and mortality by removing the precursor lesions-adenomas. Adenomas are found in over 20% of asymptomatic patients aged 50 years and older who undergo a first colonoscopy.[3-5] Incidence rates for CRC in patients who underwent colonoscopy with polypectomy are lower compared with the expected incidence in control populations.[6-10] A Danish cohort study with surveillance among patients with a first-time diagnosis of adenomas, showed a significant decline in the incidence of CRC and CRC-related mortality, compared with the general population.[7] Screening by means of guaiac based fecal occult blood tests has been shown to reduce CRC-related mortality in several randomized controlled trials (RCTs).[11-13] However, to date there is no direct evidence from RCTs that the use of colonoscopy as a screening tool for CRC leads to a reduction in either CRC-related mortality or overall mortality due to adenoma removal. Nevertheless, the expectation is that widespread use of screening programs will decrease CRC-related deaths and therefore many countries have established screening programs for CRC.[14-16] Recently, data became available from an English flexible sigmoidoscopy trial, which showed a significant reduction of CRC incidence and CRC-related mortality by screening using flexible sigmoidoscopy.[17]

Despite their removal, adenomas are still commonly found during follow-up colonoscopies, which is the reason for surveillance. Some polyps may show a more aggressive behavior leading to faster growth and/or earlier recurrence. Studies have suggested that, among others, location, size, histological type, presence of atypia, and number of adenomas detected at index colonoscopy are risk factors for adenoma recurrence.[18-23] Furthermore, adenomas or cancers can be missed during colonoscopy. Miss rates for adenomas range from 2.1% to 26%, depending on for example, size, number, and location of polyps.[24]

Most of the current surveillance guidelines for CRC stratify the surveillance recommendations on findings during the index colonoscopy. However, conclusive evidence for proper surveillance intervals and stratification for index findings are lacking, and therefore recommended follow-up intervals differ between institutions worldwide and are adjusted from time to time.[15, 25, 26] Because colonoscopy is an expensive procedure that also carries a small risk of serious complications, it is important that follow-up recommendations are optimized. Additionally, the colonoscopy resources are finite, and therefore it is important that these recommendations are based on the best available evidence.[27]

Therefore, the aim of the current systematic literature review and pooled analyses was to identify baseline parameters that are risk factors for adenoma findings on surveillance colonoscopy, in order to identify high risk patients who need more vigilant surveillance colonoscopy and to tailor guideline surveillance intervals in colonoscopy surveillance after polypectomy.

MATERIALS AND METHODS

Search strategy

A comprehensive search of the available literature was performed up to October 2009, using MEDLINE and the Cochrane Library. The Medical Subject Heading (MeSH) terms used were "colonoscopy", "colorectal neoplasms", "follow-up studies", "population surveillance", and "neoplasm recurrence, local". In the search query the MeSH terms "Inflammatory Bowel Diseases" and "Neoplastic Syndromes, Hereditary" were used as exclusion criteria. The search query is shown in Appendix 1 (available online).

Study selection criteria

The abstracts of all retrieved citations were evaluated to determine whether they met the inclusion criteria. Studies were only included if they reported on index colonoscopy followed by a surveillance colonoscopy. If a colonoscopy was incomplete and another bowel investigation (e. g. barium enema or computed tomography [CT]-colonography) was performed to visualize the remaining part of the colon, these studies were eligible for inclusion as well.

All eligible studies had to report on adenomas found on surveillance colonoscopy. Moreover, to identify baseline risk factors, stratification for baseline characteristics had to be made.

All study designs were eligible, except case series and case reports. Only articles available in English were included. Only studies published in full text were used. The references of included articles were hand-searched for additional relevant citations. Exclusion criteria were follow-up of patients at increased risk of CRC, such as patients with inflammatory bowel disease (Crohn's disease or ulcerative colitis), hereditary non-polyposis colorectal carcinoma, Peutz-Jegher's Syndrome, familial adenomatous polyposis, or a personal history of CRC. Studies addressing the miss rates of adenomas after colonoscopy were excluded if surveillance colonoscopy was performed within 6 months of baseline.

Studies of surveillance using methods other than colonoscopy or other outcome measures (such as prevalence of CRC after index colonoscopy, risk-benefit analyses, or patient satisfaction) were excluded. Prevention trials were only eligible if there was no statistically significant difference in the recurrence of adenomas between the intervention and the control group, an approach that has been used by others.[28]

Definitions

Definitions were based on recommendations from the World Health Organization and previous literature.[19, 29] Polyps were subdivided into nonadenomatous lesions (hyperplastic

polyps) and adenomas or adenomatous lesions (benign lesions composed of tubular and/or villous structures showing intraepithelial neoplasia).

Adenomas were further divided into non-advanced adenomas (small, tubular adenomas) and advanced adenomas (i. e. adenoma ≥10 mm, containing ≥25% villous component [i. e. (tubulo-) villous adenoma], or high grade dysplasia [HGD], including intramucosal carcinoma or carcinoma in situ). CRC was defined as invasion of malignant cells through the muscularis mucosae. Advanced neoplasia was defined as advanced adenomas, or CRC.

Data extraction

A data quality scoring (DQS) system was designed for quality assessment of included studies in the context of this systematic review. This DQS was partly based on the Newcastle-Ottawa Quality Assessment Scale, which has been previously used in another meta-analysis, and adapted for analysis in the present study based on expert opinion.[30, 31] The final DQS is shown in Table 1.

Table 1. Data quality score

		Points
1.	Characteristics of study cohort are given:	
	Number of included patients	0.5
	Age (mean) and gender (%)	0.5
2.	A clearing colonoscopy was described at baseline	1
3.	The indication for the baseline colonoscopy is mentioned	1
	The number of polyps found at baseline are given and specified to:	
4.	Adenomatous lesions vs. nonadenomatous lesions or no lesions (if applicable)	1
5.	Advanced adenomas vs. non-advanced adenomas	1
6.	Follow-up colonoscopy is at least six months after baseline colonoscopy	1
7.	Follow up cohort consists of patients with and without baseline adenomas	1
8.	A randomized controlled trial is performed	1
9.	The baseline cohort sample size is >100 patients	1
10.	The mean follow up time is given	1
	The number of polyps found at surveillance are given and specified to:	
11.	Adenomatous lesions vs. nonadenomatous lesions or no lesions	1
12.	Advanced adenomas vs. non-advanced adenomas	1
13.	Only completed colonoscopies are included, or a method to obtain a complete bowel investigation is described (such as repeat colonoscopy within 6 months or barium enema)	1
	Exclusion criteria are mentioned	
14.	FAP, HNPCC, personal history of CRC	1
15.	Inflammatory bowel disease, previous colonic resection	1
	Outcome FU colonoscopy was stratified for:	
16.	Polyp characteristics	1
17.	Patient characteristics	1

CRC, colorectal cancer; FAP, familial adenomatous polyposis; HNPCC, hereditary non-polyposis colorectal cancer.

The assessment was performed by two independent raters (VdJ, JSN). In case of disagreement, consensus was achieved through discussion with a third reviewer (SVZ). Arbitrarily it was decided that on the basis of the DQS, studies were deemed to be of high quality if they received ≥12 points, medium quality for 7.5-12 points, and low quality for ≤7 points.

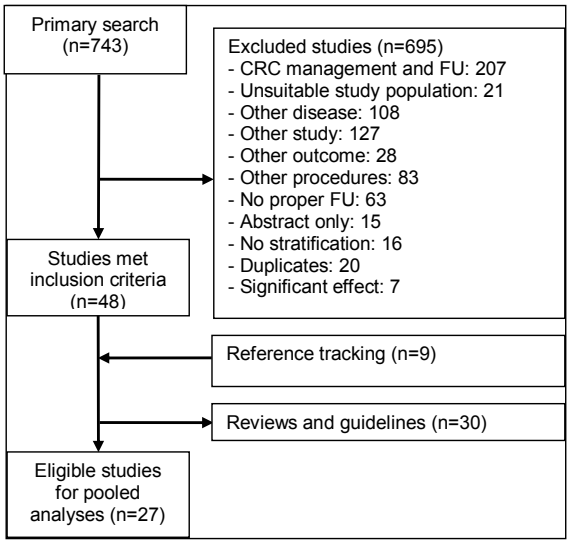
The following data were recorded on a data extraction sheet: year of publication, study design, patient selection (inclusion and exclusion criteria), patient demographics, cohort size, definition of advanced adenoma, time of follow-up, percentage of follow-up, and the findings on index and surveillance colonoscopy.

Statistical analysis

Based on the data, (unadjusted) relative risks (RR) were calculated, accompanied by a 95% confidence interval (95%CI) for the following variables on index colonoscopy: presence of adenomas, size and number of adenomas, histology, dysplasia, location, age, and sex. Pooled RR estimates were calculated using the random effects model.[32] The primary outcome of interest was adenoma recurrence. Studies that specifically reported on the occurrence of advanced adenomas on surveillance colonoscopy were used to determine this clinically relevant outcome.

Heterogeneity in study results was assessed using the I^2-statistic whereas the variability between studies that is likely due to true differences was provided as a percentage.[33] An I^2>50% indicates high heterogeneity, implying that the pooled results should be interpreted with caution. Statistical analyses were performed using STATA version 11.0 (StataCorp, College Station, Texas, USA).

Figure 1. Flow chart of article selection



RESULTS

Study selection

The primary search strategy identified 743 articles. After full assessment, a total of 27 studies were included. The selection process and reasons for exclusion are shown in Figure 1.

The characteristics of the 27 included studies in this systematic review and the pooled analyses are shown in Tables 2 and 3.[18, 20, 23, 34-57]

Table 2. Study characteristics

First author	Year of publication	Study design	Inclusion criteria	Exclusion criteria
Winawer[55]	1993	RCT	Patients with previously removal of adenomas during study period	Family or personal history of FAP, IBD, personal history of polypectomy or CRC, baseline CRC, nonadenomatous polyps, >3 cm sessile polyps
Avidan[34]	2002	Prospective cohort	Asymptomatic patients with surveillance within 5 years	IBD, history of colonic surgery, CRC, previous polypectomy, HNPCC
Leung[46]	2009	Prospective cohort	Asymptomatic, average risk subjects, between 50-70 yrs	Colonic symptoms, family Hx of CRC or colonoscopy, colonic surgery
Lieberman[47]	2007	Prospective cohort RCT	Patients with a screening colonoscopy Age: 50-75 years	Gastrointestinal tract symptoms, prior history of colon disease, evaluation of colon within 10 years
Martinez[20]	2001	RCT	Participants in the wheat bran fiber trial Age: 40-80 years with 1 or more adenomas 3 mm or larger removed 3 months before study entry, normal kidney and liver function	IBD, hereditary colon cancer syndromes, history of colon resection, >3 first degree relatives with CRC, severe metabolic disorder or chronic disease
Laiyemo[45]	2008	RCT	Participants of PPT, >1 adenoma found during screening or diagnostic colonoscopy, 1 clearing colonoscopy within 1 year	Age: <35 years, Hx of surgical resection of adenoma, bowel resection, CRC, FAP, IBD, lipid lowering drugs, >150% of ideal BMI
Jorgensen[43]	1995	RCT	Pts with adenomas	CRC, Hx of colorectal neoplasia, FAP
Ji[42]	2009	Prospective cohort	First time colonoscopy with adenoma or CRC	Advanced cancer, polyposis syndrome, IBD, intestinal tuberculosis, ≥5 polyps
Imperiale[41]	2008	Retrospective cohort	Age: >50 years, asymptomatic, negative colonoscopy and FU 5 years later	Hx of CRC, adenomas or IBD
Yamaji[57]	2004	Prospective cohort	Asymptomatic patients having >3 annual medical health checkups	Other screening tests for CRC (like FOBT, sigmoidoscopy, etc.), history of CRC, history of polyps or IBD, CRC at baseline

Table 2. Study characteristics (continued)

First author	Year of publication	Study design	Inclusion criteria	Exclusion criteria
Rex[52]	1996	Prospective cohort	Asymptomatic patients with negative baseline colonoscopy	Patient refusal for surveillance or not able to contact
Nusko[51]	2008	Retrospective cohort	Patients with colorectal polyps removed by endoscope or surgically	History of adenomas or CRC, FAP, HNPCC
Bertario[35]	2003	Prospective cohort	Positive FOBT or family history of CRC	Hyperplastic polyps, inflammatory polyps, history of CRC or adenomas, FAP, HNPCC.
Fossi[38]	2001	Prospective cohort	Asymptomatic consecutive patients	Symptoms of colorectal neoplasms, personal history of polyps or CRC, IBD, previous colonoscopy, family history, hyperplastic polyps
Fornasarig[37]	1998	Prospective cohort	Consecutive patients with polyps removed Age: <75 years	Incomplete colonoscopy, FAP, VA in the rectum, invasive carcinoma, piecemeal or surgical resection of polyps, synchronous carcinomas, IBD, general diseases and previous intestinal neoplasms.
van Stolk[23]	1998	RCT	Participants in the Polyp Prevention Study with large bowel adenoma removed 3 months before study entry, complete colonoscopy Age: <80 years	CRC, FAP, malabsorption syndromes, any condition potential worsened by vitamins C or E
Triantafyllou[53]	1997	Retrospective cohort	Pts with adenomas and FU 24-48 months later	HNPCC, FAP, IBD, Hx of CRC, colectomy or polypectomy
Keku[44]	2008	Cross-sectional	>30 yrs	IBD, FAP, Hx of colectomy, adenoma or CRC
Neugut[50]	1995	Case-control study	Patients with colonoscopy extended at least to splenic flexure, age: 35-84 years	History of adenomatous polyps, CRC, IBD
Matsuda[48]	2009	Retrospective cohort	Screening pts >40 yrs referred for colonoscopy	FAP, HNPCC, IBD, Hx of polypectomy or CRC and sessile adenoma ≥3 cm.
Noshirwani[18]	2000	Retrospective cohort	Patients with removed adenomas and surveillance colonoscopy within 10-42 months	CRC, UC, FAP
Hixson[39]	1994	Prospective cohort	Patients with tandem colonoscopy for established clinical indications	NA
Blumberg[36]	2000	Retrospective cohort	Patients with positive baseline colonoscopy and 2 follow-up colonoscopies	Personal history of CRC, personal or family history of FAP or HNPCC, >2 family members with CRC, incomplete polypectomy, follow-up within 9 months

Table 2. Study characteristics (continued)

First author	Year of publication	Study design	Inclusion criteria	Exclusion criteria
Waye[54]	1982	Retrospective cohort	Patients with multiple colonoscopies and adenomatous polyps at baseline Age: 18-84 years	Colon resection, history of CRC, incomplete colonoscopy, incomplete polypectomy, FAP, IBD
Woolfson[56]	1990	Retrospective cohort	Patients with polypectomy and follow-up	FAP, juvenile polyps IBD
Nava[49]	1987	Retrospective cohort	Asymptomatic patients with any positive screening test and adenomatous polyps found at baseline colonoscopy	History of removal of previous lesions of the colon or rectum
Holtzman[40]	1987	Retrospective cohort	Outpatients with baseline colonoscopy and 2 surveillance colonoscopies	History of CRC, IBD, FAP, non-adenomatous polyps

CRC = Colorectal cancer; RCT = Randomized controlled trial; FAP = Familial Adenomatous Polyposis; HNPCC = Hereditary Nonpolyposis Colon Cancer; IBD = Inflammatory Bowel Disease; FOBT = Fecal Occult Blood Test; UC = Ulcerative colitis

Data quality score

In Appendix 2 (available online), the results of the DQS are shown per study. Using the DQS, a total of 11 publications were identified as being of high quality[20, 34, 41-43, 45-47, 52, 55, 57], 12 were of medium quality[18, 23, 35-39, 44, 50, 51, 53, 54], and four studies were of low quality[40, 49, 54, 56].

Advanced adenomas at index colonoscopy as risk factor for adenoma recurrence

Eight studies stratified the findings at follow-up colonoscopy on the basis of having advanced adenomas at index colonoscopy.[35, 42, 45-47, 51, 53, 57]

The RRs and pooled estimates for recurrent adenomas based on these baseline findings are shown in Figure 2. The pooled RR for recurrent adenomas was 1.81 (95%CI: 1.13-2.89) if advanced adenomas were found at the index colonoscopy vs. non-advanced adenomas. The overall I^2 was 84.6%, indicating high heterogeneity.

Five high quality studies, which were all prospective cohort studies, reported significantly increased RRs with a pooled estimate of 2.34 (95%CI: 1.88-2.93) and an I^2 of 5.6%.[42, 45-47, 57] The definition of advanced adenoma on baseline was equal between the studies, although the Japanese study[57] did not consider villous histology as an aspect of advanced adenomas, while in the Veterans Affairs Cooperative Study[47] advanced neoplasia (includes CRC) was used instead of advanced adenoma.

Table 3. Study cohort characteristics

First author	Mean age	Male (%)	Definition of advanced adenoma	Follow-up (months)	Patients at baseline (n)	Follow-up (%)	DQS score	Quality*
Winawer[55]	61.2	70	>10mm, HGD, invasive cancer	14-38	1418	68.6	14	HQ
Avidan[34]	68-69	99	>10 mm, TVA/VA	30-31	946	92	13.5	HQ
Leung[46]	60.6	44.4	≥10 mm, TVA/VA, HGD	NA	620	82.4	13	HQ
Lieberman[47]	62.1-67.5	NA	>10 mm, TVA/VA, HGD, CRC	24 - 66	3121	59.5-76.4	13	HQ
Martinez[20]	66.2	67.1	>10 mm, TVA/VA, CRC	36	1429	91	13	HQ
Laiyemo[45]	61.1	64.5	>10 mm, TVA/VA, HGD	48	2079	91.6	12.5	HQ
Jorgensen[43]	NA	56.8	>10 mm, TVA/VA, HGD	NA	673	33.1	12.5	HQ
Ji[42]	55.1	51.7	≥10 mm, TVA/VA, HGD	35.1	232	55.2	12	HQ
Imperiale[41]	56.7	56.7	>10 mm, TVA/VA, HGD	63.6	2436	42.1	12	HQ
Yamaji[57]	48.8	61.3	>10 mm, HGD	35	7620	82	12	HQ
Rex[52]	65.6	68	>10 mm, TVA/VA, HGD	66	496	45***	12	HQ
Nusko[51]	59.3	63	>10 mm, TVA/VA, HGD	36	2783	39.2	11.5	MQ
Bertario[35]	61	55.2	>10 mm, TVA/VA, HGD	NA	1086	100	11.5	MQ
Fossi[38]	58.8-59.9	64	NA	36	436	44	11	MQ
Fornasarig[37]	57.5	64.4	NA	36	164	95	11	MQ
van Stolk[23]	60	77	>10 mm, TVA/VA,HGD, invasive cancer	50	479	87	11	MQ
Triantafyllou[53]	NA	54.5	≥10 mm, TVA/VA, HGD	NA	44	100	11	MQ
Keku[44]	58.4	48	≥10 mm, TVA/VA, HGD	NA	503	51.1%	10.5	MQ
Neugut[50]	58-65	49.3	NA	34	807	34	10	MQ
Matsuda[48]	62.4	63	≥10 mm, intramucosal or invasive CRC	18.3	5309	100	9.5	MQ
Noshirwani[18]	NA	73.3	>10 mm, TVA/VA, HGD, CIS, CRC	18	697	100	9.5	MQ
Hixson[39]	67	98.2	NA	24	90	64	9	MQ
Blumberg[36]	64	NA	>10 mm, >3 adenomas	55	204	100	8.5	MQ
Waye[54]	NA	NA	NA	48	160	19	7	LQ
Woolfson[56]	60-62	67	NA	12	109	100	6.5	LQ
Nava[49]	60	48	NA	12	44	100	6.5	LQ
Holtzman[40]	60.2-61.5	63.8	NA	NA	149	100	6.5	LQ

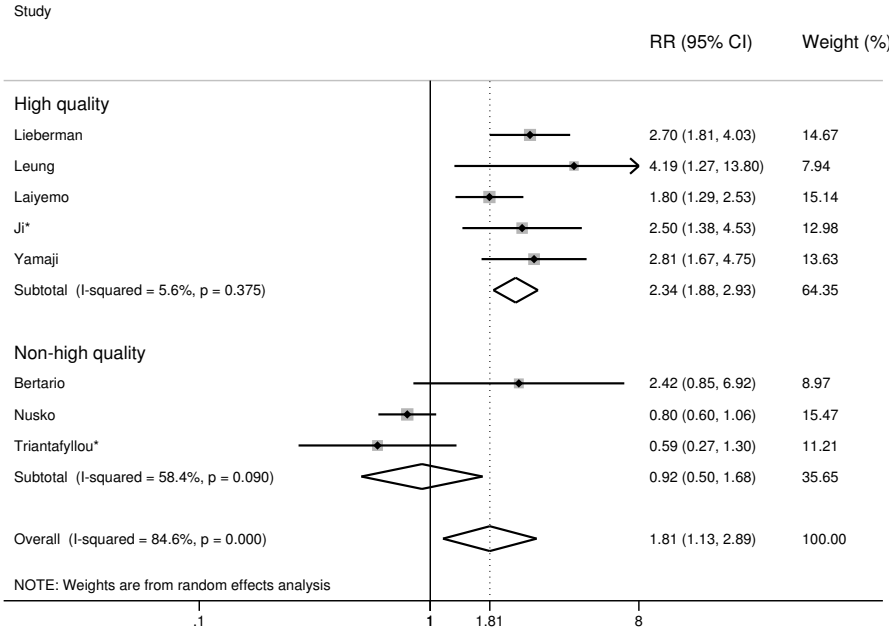
VA = Villous adenoma; HGD = High grade dysplasia; TVA = Tubulovillous adenoma; NA = Not available; CRC = Colorectal cancer; CIS = Carcinoma in situ.

* = High quality (HQ); Moderate quality (MQ); Low quality (LQ)

** = excluding patients with CRC at baseline

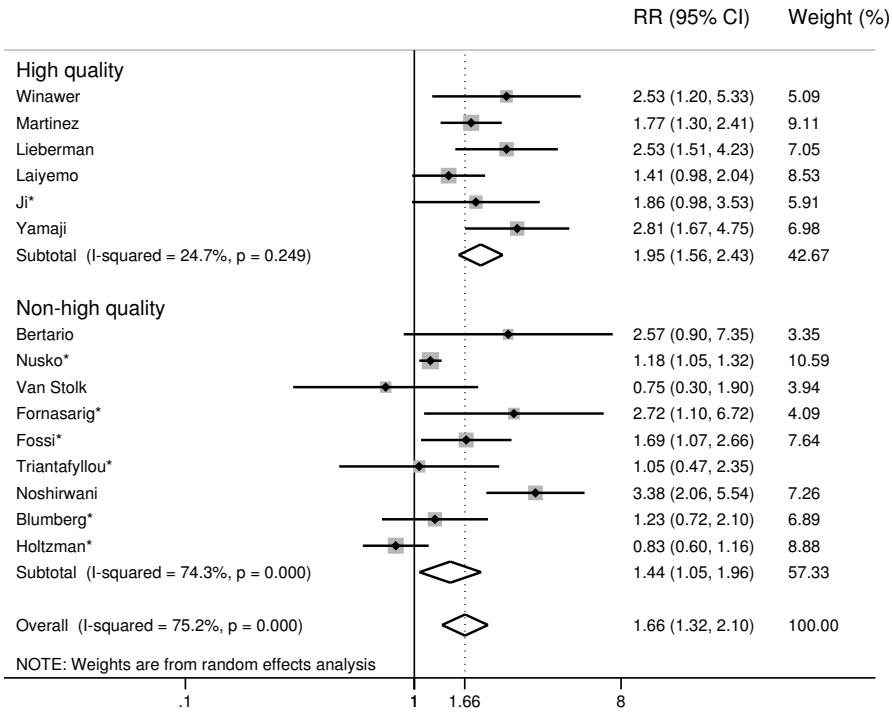
*** = excluding patients with adenoma detected at baseline

Figure 2. Pooled relative risk (RR) of adenoma recurrence for presence of advanced adenomas compared with non-advanced adenomas on index colonoscopy



* Risk for recurrence of all adenomas (nonadvanced included); in the other studies, the recurrence of advanced adenomas was specifically addressed

Figure 3. Pooled relative risk (RR) of adenoma recurrence for presence of adenomas ≥ 10mm compared with < 10mm adenomas on index colonoscopy



* Risk for recurrence of all adenomas (nonadvanced included); in the other studies, the recurrence of advanced adenomas was specifically addressed

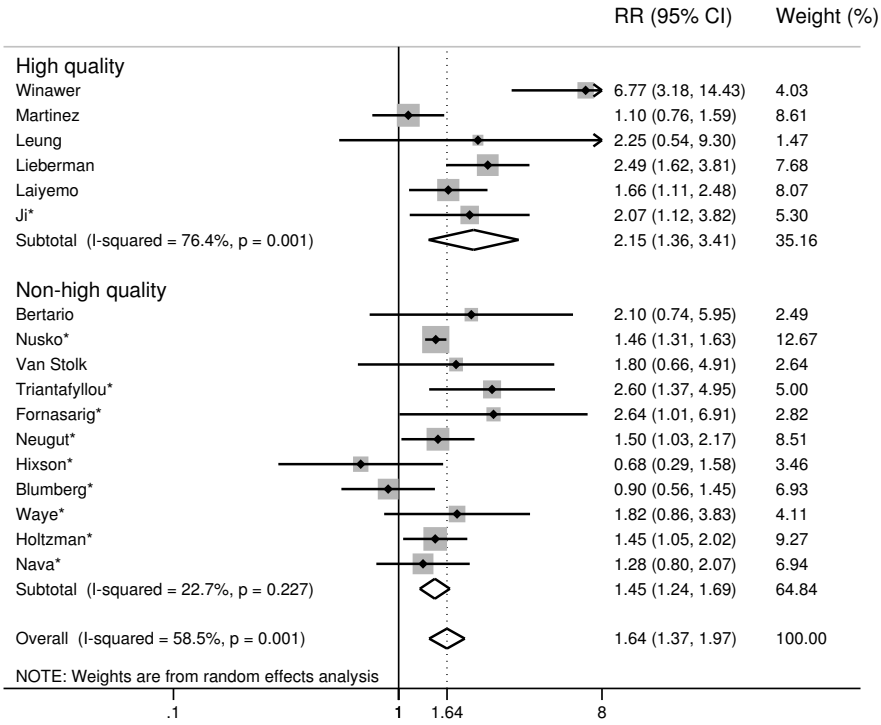
Size of adenomas at index colonoscopy as risk factor for adenoma recurrence

The size of adenomas found at index colonoscopy was assessed as a predictor of recurrence of adenomas in 15 studies (Figure 3).[18, 20, 23, 35-38, 40, 42, 45, 47, 51, 53, 55, 57]

The pooled RR for adenoma recurrence was 1.66 (95%CI: 1.32-2.10) if any index adenoma was ≥10 mm compared with smaller adenomas at index colonoscopy. The I^2 was 75.2%, indicating high heterogeneity. Six studies were of high quality and had a pooled RR of 1.95 (95%CI: 1.56-2.43) and low heterogeneity (I^2: 24.7%).[20, 42, 45, 47, 55, 57]

All high quality studies, except for the Polyp Prevention Trial (PPT)[45] and the Korean study[42], showed a significantly increased RR in our analysis for recurrent adenomas when the baseline endoscopy revealed adenomas ≥10 mm. However, in contrast to our univariate analysis, the multivariate analysis reported by the PPT showed a significantly increased RR (1.57, 95%CI: 1.09-2.27).[45] On the other hand, the multivariate analysis in the National Polyp Study showed no significantly increased RR (OR: 2.2; 95%CI: 0.6-7.8), whereas our univariate analysis found a significantly increased risk.[55]

Figure 4. Pooled relative risk (RR) of adenoma recurrence for presence of ≥ 3 adenomas compared with 1–2 adenomas on index colonoscopy



* Risk for recurrence of all adenomas (non-advanced included); in the other studies, the recurrence of advanced adenomas was specifically addressed

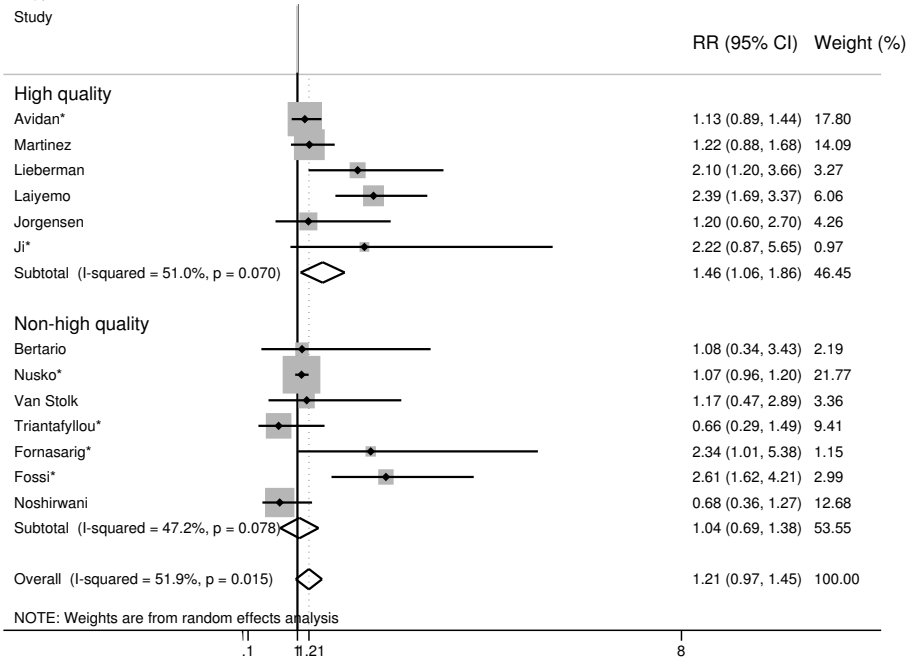
Three or more adenomas at index colonoscopy as risk factor for adenoma recurrence

A total of 17 studies investigated whether presence of ≥3 adenomas at index colonoscopy was a risk factor for adenoma recurrence.[20, 23, 35-37, 39, 40, 42, 45-47, 49-51, 53-55]

The overall pooled RR estimate for adenoma recurrence when ≥3 adenomas were found on index colonoscopy was 1.64 (95%CI: 1.37-1.97) compared with 1 or 2 index adenomas, shown in Figure 4. High heterogeneity was, however, observed (I^2: 58.5%).

The six high quality studies found a pooled RR of 2.15 (95%CI: 1.36-3.41) with high heterogeneity (I^2: 76.4%).[20, 42, 45-47, 55] In all, except the Wheat Bran Fiber Trial[20] and a Chinese prospective screening trial[46], significantly increased RRs were found for the association between three or more adenomas at baseline and recurrent adenomas during surveillance.

Figure 5. Pooled relative risk (RR) of adenoma recurrence for presence of (tubulo-)villous adenomas compared with tubular adenomas on index colonoscopy



* Risk for recurrence of all adenomas (non-advanced included); in the other studies, the recurrence of advanced adenomas was specifically addressed

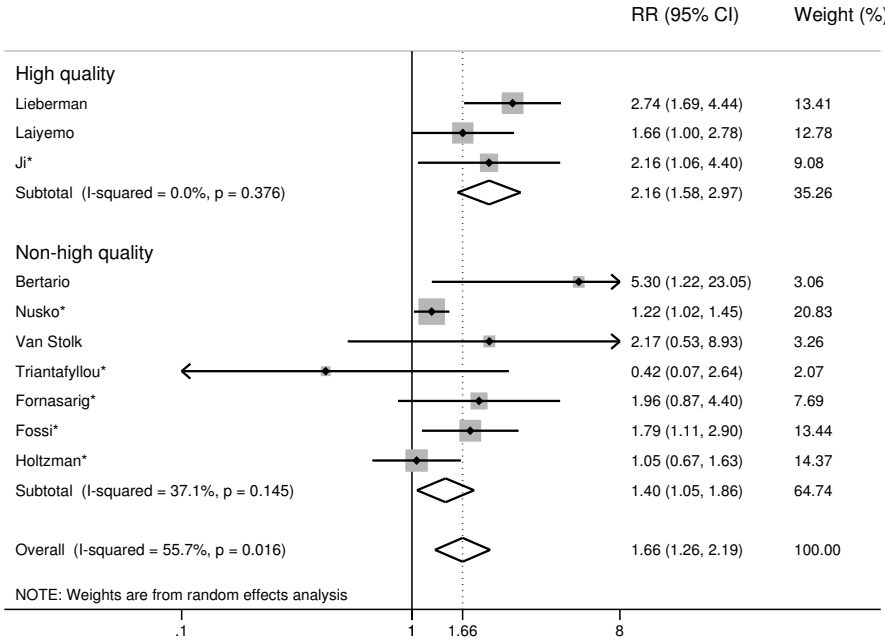
Histology of adenomas at index colonoscopy as risk factor for adenoma recurrence

The presence of ≥ 25% villous component was investigated as a predictor of adenoma recurrence in 13 studies.[18, 20, 23, 34, 35, 37, 38, 42, 43, 45, 47, 51, 53]

The results are shown in Figure 5. The pooled RR was 1.21 (95%CI: 0.97-1.45) with an I^2 of 51.9%.

The pooled RR in the six high quality studies for adenoma recurrence in patients with adenomas with ≥25% villous component at index colonoscopy compared with tubular adenomas was1.46 (95%CI: 1.06-1.86), with high heterogeneity (I^2: 51.0%).[20, 34, 42, 43, 45, 47]

Figure 6. Pooled relative risk (RR) of adenoma recurrence for presence of high grade dysplasia (HGD) compared with non-HGD at index colonoscopy



*Risk for recurrence of all adenomas (non-advanced included); in the other studies, the recurrence of advanced adenomas was specifically addressed

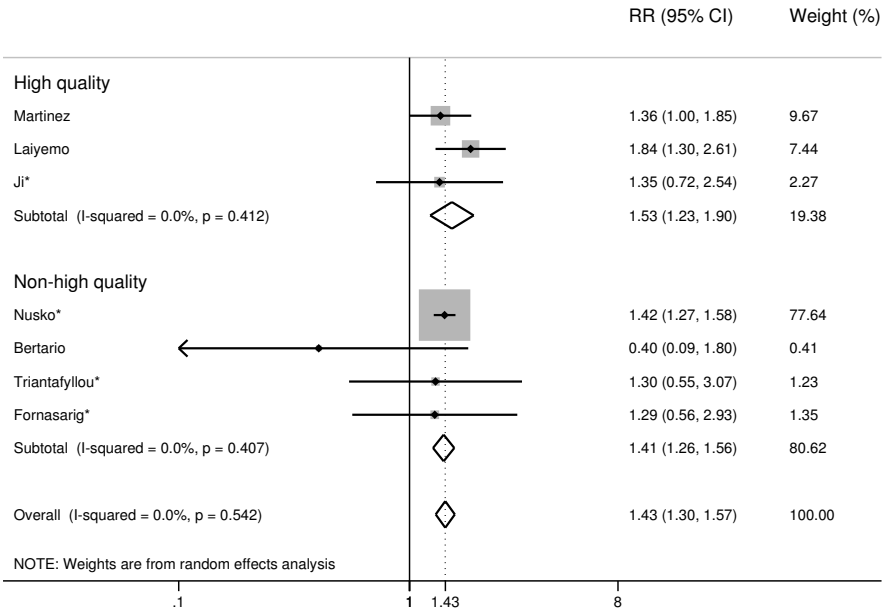
HGD of adenomas at index colonoscopy as risk factor for adenoma recurrence

A total of 10 studies addressed whether the presence of adenoma with HGD at index colonoscopy was a predictor for recurrence of adenomas.[23, 35, 37, 38, 40, 42, 45, 47, 51, 53]

The pooled RR for HGD vs. moderate or low grade dysplastic adenomas was 1.66 (95%CI: 1.26-2.19) with an I^2 of 55.7%, as shown in Figure 6.

Pooling the results of the three high quality studies resulted in a pooled RR of 2.16 (95%CI: 1.58-2.97) with an I^2 of 0.0%.[42, 45, 47]

Figure 7. Pooled relative risk (RR) of adenoma recurrence for presence of any proximal adenomas compared with distal adenomas alone at index colonoscopy



* Risk for recurrence of all adenomas (non-advanced and no lesions included); in the other studies, the recurrence of advanced adenomas was specifically addressed

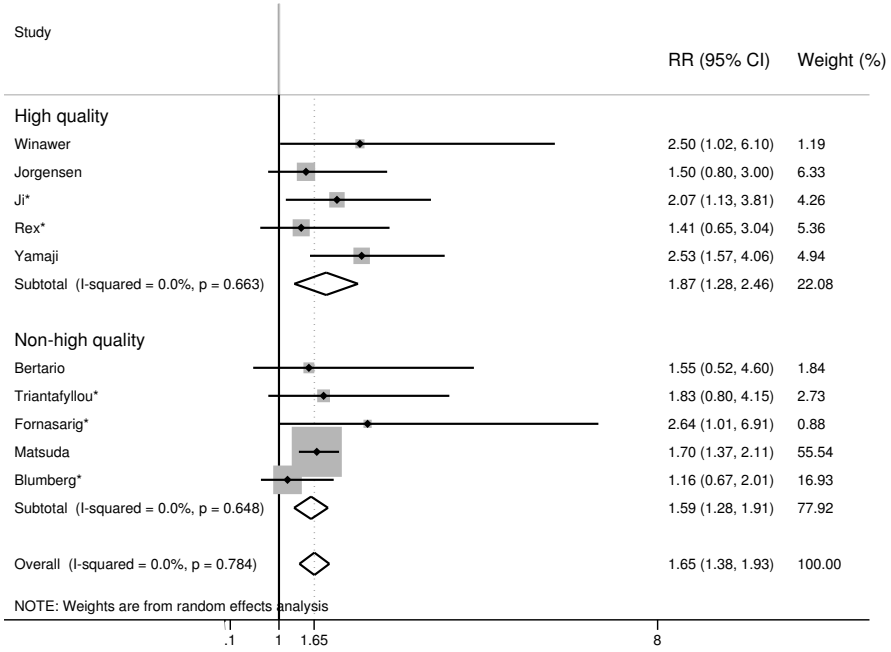
Location of adenomas at index colonoscopy as risk factor for adenoma recurrence

Seven studies evaluated whether the location of index adenomas was a risk factor for adenoma recurrence.[20, 35, 37, 42, 45, 51, 53]

Figure 7 shows the results. The overall pooled RR for adenoma recurrence when any proximal adenoma was present at index colonoscopy was 1.43 compared with distal adenomas alone (95%CI: 1.30-1.57), with no heterogeneity (I^2: 0.0%).

Three high quality studies found a pooled RR of 1.53 (95%CI: 1.23-1.90).[20, 42, 45] No heterogeneity was observed (I^2: 0.0%). The Wheat Bran Fiber Trial showed the strongest association (RR: 4.25; 95%CI: 2.91-6.19), although after adjustment for age, sex, and other adenoma characteristics in the original study, the effect was less profound (OR: 1.65; 95%CI: 1.02-2.67).[20]

Figure 8. Pooled relative risk (RR) of adenoma findings at surveillance colonoscopy for age ≥ 60 years compared with < 60 years at index colonoscopy



*Risk for recurrence of all adenomas (non-advanced and no lesions included); in the other studies, the recurrence of advanced adenomas was specifically addressed

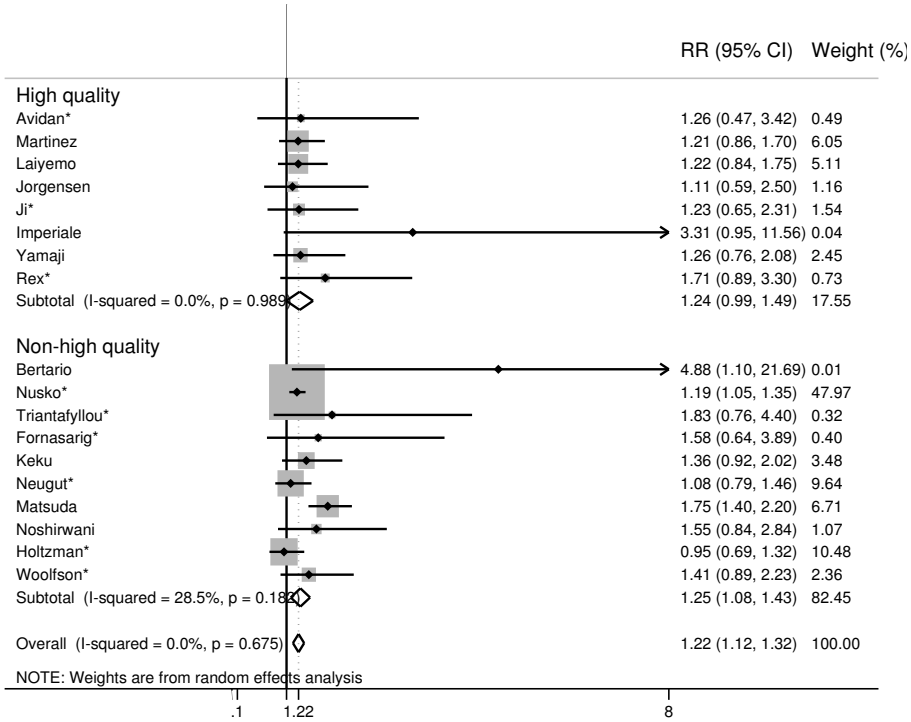
Age at index colonoscopy as risk factor for adenoma findings at surveillance colonoscopy

Age ≥ 60 years was evaluated as a risk factor of adenoma findings on surveillance colonoscopy in 10 studies.[36, 37, 42, 43, 48, 52, 53, 55, 57]

The results are shown in Figure 8. The pooled RR estimate was 1.65 (95%CI: 1.38-1.93) with no heterogeneity (I^2: 0.0%).

The five high quality studies found a pooled RR of 1.87 (95%CI: 1.28-2.46) for adenoma findings on surveillance colonoscopy for patients over 60 years of age at index colonoscopy with an I^2 of 0.0%, indicating no heterogeneity.[42, 43, 52, 55, 57]

Figure 9. Pooled relative risk (RR) of adenoma findings at surveillance colonoscopy for males compared with females



* Risk for recurrence of all adenomas (nonadvanced included); in the other studies, the recurrence of advanced adenomas was specifically addressed

Gender as risk factor for adenoma findings at surveillance colonoscopy

A total of 18 studies addressed the question of whether males had a different risk of adenoma findings on surveillance colonoscopy compared with females.[18, 20, 34, 35, 37, 40-45, 48, 50-53, 56, 57]

The results are summarized in Figure 9. A pooled RR estimate for males of 1.22 (95%CI: 1.12-1.32) was found, with no heterogeneity (I^2: 0.0%).

Eight studies were of high quality.[20, 34, 41-43, 45, 52, 57] None of the individual high quality studies showed a significantly increased RR; a pooled estimate of 1.24 (95%CI: 0.99-1.49) with no heterogeneity (I^2: 0.0%) was found.

DISCUSSION

In this systematic review, pooled analyses were performed to evaluate which risk factors at index colonoscopy best predict the risk of adenoma findings on surveillance colonoscopy. There is variation in the recommendations from different organizations about the recommended colonoscopy surveillance intervals in patients with adenomas detected on index colonoscopy.[15, 25, 26]

Our comprehensive search strategy identified a total of 27 studies reporting on the incidence of adenomas after baseline colonoscopy. In the pooled analyses we found that the presence of advanced adenomas (pooled RR: 1.81), adenomas ≥10 mm in size (pooled RR: 1.66), presence of ≥3 adenomas (pooled RR: 1.64), and age ≥60 years (pooled RR: 1.65) at index colonoscopy are the most important and significant risk factors for adenoma findings on surveillance colonoscopy. The RRs of these predictors were significantly elevated and results were consistent among different studies. The evidence for a higher risk of adenoma recurrence in patients with HGD (pooled RR: 1.66), proximal location of adenomas (pooled RR: 1.43), and in men compared with women (pooled RR: 1.22) was less strong, with high heterogeneity and/or fewer supportive studies, which were of lesser quality. No evidence was found for an increased risk of recurrent adenomas on surveillance colonoscopy when ≥ 25% villous component (tubulovillous or villous adenoma) is observed at index colonoscopy (pooled RR: 1.21, n. s.). The quantitative results should be taken with caution as high heterogeneity (> 50%) was observed in the results.

The results may in part seem contradictory, as ≥ 25% villous histology and HGD are, together with an adenoma size of ≥10 mm, features of advanced adenomas. It may be hypothesized that size is the most important predictor among these three for adenoma recurrence. Another explanation may be that there is significant inter-observer variability in determining the grade of dysplasia and the magnitude of a villous component in a specimen. The inter-observer variability also exists in the assessment of size.[58] However, the assessment of large adenomas, which harbor the greatest risk as they also have a higher change of dysplasia and villous histology, might be less prone to misclassification.[59] Additionally, none of the studies specifically addressed the macroscopic morphology of the polyps (in particular sessile vs. pedunculated), which may influence completeness of polyp removal and thereby the risk on recurrent adenoma findings during surveillance.

With regard to the different risk factors, several points need to be considered. The pooled RR estimate shows that having advanced adenomas at index colonoscopy markedly increases the risk of finding adenomas at follow-up. The results between the studies are consistent, although two studies of moderate quality found decreased RRs. One of these was a very small cohort study, which did not provide inclusion criteria.[53] Therefore this result could be due to selection bias. In the Erlangen Registry of Colorectal Polyps, a significantly increased RR was reported; however, it was not possible to extract the data from the published report

and therefore it was not included in the pooled analysis.[51] Overall, our results support that patients with advanced adenomas should receive more vigilant surveillance, as recommended in current guidelines.[15, 25]

The RR for adenoma recurrence was increased in patients with adenomas ≥10 mm at index colonoscopy. The discrepancy of the pooled result with that of the Polyp Prevention Study may in part be explained by a short duration of follow-up of that study (4 years, ±2 months).[23] In the literature, there is no consensus on the risk of recurrent adenomas in patients with large index adenomas. A meta-analysis by Saini et al. found a non-significantly increased RR of 1.39 (95%CI: 0.86-2.26).[28] Others observed a significantly elevated risk with a pooled OR of 1.56 (95%CI: 1.39-1.74) for advanced neoplasia in 9167 patients during follow-up colonoscopy per 10-mm increment of adenoma.[19] Based on our own and previously reported data the current recommended intensified follow-up interval of 3 years after index colonoscopy appears to be appropriate.[15, 25]

The evidence for ≥3 adenomas at index colonoscopy as a risk factor for adenoma recurrence is convincing. The smallest effect was found by a study of follow-up after a tandem colonoscopy.[39] The tandem colonoscopy at baseline could be the reason for a decreased effect of adenoma recurrence, because the risk of missing lesions would be smaller. Previous meta-analyses also showed an increased risk for advanced adenomas/neoplasia at follow-up when multiple adenomas were found at index colonoscopy. Saini et al.[28] found an RR of 2.52 (95%CI: 1.07-5.97) and Martinez et al.[19] an OR of 1.32 (95%CI: 1.25-1.40) per adenoma. One of the high quality studies that did not find a significant effect did not exclude patients with prior polypectomy.[20] In fact, more than 30% had a history of adenomas before the index colonoscopy. This could be a reason for underestimation of the risk of having multiple adenomas at index colonoscopy. The other high quality study that did not show a significant effect had a very broad confidence interval, because very few recurrent adenomas were observed.[46] The reason for low recurrence could be the voluntary participation in this screening trial, which might attract more healthy individuals. The latter is supported, for instance, by the fact that a low percentage of patients were smokers. The currently recommended follow-up interval of 3 years for ≥3 adenomas after index colonoscopy is supported by the literature and the findings in this pooled analysis.[15, 25]

The evidence for the presence of (tubulo-)villous adenomas at index colonoscopy as a risk factor for adenoma recurrence is less convincing. Nine of the 13 included studies did not find significantly increased RRs. A possible explanation could be the use of different cut-off points for the percentage of villous component in polyps and the fact that there may be considerable inter-observer variability between pathologists.[60] Only six studies mentioned a specific cut-off of villous component to consider an adenoma to be advanced, and all except one used a cut-off of 25%.[20, 36, 41, 47, 55] The other study used a cut-off of 20%, which is also recommended by WHO.[29, 51] A meta-analysis by Martinez et al.[19] did find a significantly increased OR for the presence of villous histology (OR: 1.40; 95%CI: 1.17-1.68), in contrast to Saini et al.[28] (RR:

1.26; 95%CI: 0.95-1.66). Therefore, the stratification of surveillance intervals based on histology is still debatable and better evidence is needed to use this as a determining factor for recommended surveillance.

There is no consensus on whether adenomas with HGD at index colonoscopy are a predictor of adenoma recurrence. Martinez et al. demonstrated in a multivariate analysis a non-significant OR for HGD of 1.08 (95%CI: 0.82-1.41).[19] In contrast, Saini et al. did find an increased RR of 1.84 (95%CI: 1.06-3.19).[28] We did find a significantly increased RR of 1.66, with consistent findings among all studies, with only one Greek study showing a decreased RR with a broad CI overlapping 1.0.[53] The latter may be due to the fact that the sample size of the study was small and only one patient was diagnosed with HGD on follow-up. Future high quality research should focus on the appropriate surveillance interval for patients with HGD and the current guidelines should be taken with some caution because conclusive evidence is lacking.

A slightly increased RR for adenoma recurrence was found for proximal location of index adenomas in this pooled analysis. In the meta-analysis of Martinez et al. an OR of 1.68 (1.39-2.02) among eight large RCTs was found.[19] Within the context of recent findings that colonoscopy might not be able to decrease the incidence of right-sided advanced colorectal neoplasms and mortality from right-sided CRC, it could be argued that a large portion of the proximal adenomas are actually missed adenomas.[61, 62] It has been shown that the quality of a colonoscopy is of paramount importance in detecting lesions. This is determined by a several factors, including the quality of the bowel preparation and the skills of the endoscopist. The type of training the endoscopists received (gastroenterology vs. non-gastroenterology training) and colonoscopy experience have been shown to influence the quality of colonoscopy in terms of adenoma detection rates and missed or interval CRC.[63, 64] As most CRC originates from adenomas, the quality of the procedure will also be important for the rate of adenoma recurrence. As the interest in quality assurance is growing, the risk of adenoma recurrence when proximal adenomas are found might change in the near future, as fewer adenomas will be missed during index colonoscopy. The evidence seems to be insufficient to make changes in follow-up guidelines based on the location of adenomas found on index colonoscopy.

The age of patients has been suggested to be a risk factor for adenoma findings on surveillance colonoscopy. Increasing age is also known to be a risk factor for CRC itself. In our study the risk of recurrence was indeed increased (RR: 1.65), and the results among studies are consistent. Martinez et al. also found a significant trend for an increased risk for recurrence of advanced neoplasia.[19] Taking age into consideration for surveillance intervals seems reasonable. On the other hand, one needs to consider that the benefit of screening for CRC and subsequent surveillance diminishes as age advances, because of competing risk with other causes of death.[65]

The literature suggests that males are at an increased risk for developing adenomas and this has also been reported for adenomas during follow-up colonoscopies.[19] In our pooled analysis a slightly increased RR was found (RR: 1.22). However, none of the high quality studies

in our systematic review showed a significantly increased RR for adenoma findings on surveillance colonoscopy in males. In the meta-analysis of Martinez et al. a significant increased OR was found.[19] Because more than 70% of included patients were male, this study population might not be a representative sample. There is therefore insufficient evidence to stratify surveillance recommendations for gender.

The strength of our study was the comprehensive nature of our search strategy to identify relevant studies and the use of an objective quality assessment score. All 11 high quality studies were prospective and had large sample sizes. All low quality studies were published before 1995 and included relatively small study populations. Our DQS did yield consistently higher pooled RRs in high quality studies compared with moderate and low quality studies. This emphasizes the need for well-designed and well-reported studies, as their results may differ significantly from studies of a lesser quality. Another strength is the inclusion of observational studies and the absence of a limitation to a specific geographic location, in contrast with the study by Martinez et al., which only included six randomized trials and two observational studies from North America.[19] RCTs are considered the most definitive in providing answers to clinical questions but as there are almost none available on this subject, most of the evidence is derived from the results of observational studies. However, if designed and executed appropriately, observational studies often produce effects similar to RCTs.[66, 67]

Our study does have some important limitations. High heterogeneity in some of the pooled estimates was observed. This is likely explained by the differences in study design and variation in included patients and geographic location. Some studies included patients with a history of adenomas, others only screening patients, as shown in Table 2. These differences introduced variance in the background risk between different studies. Furthermore, the raw data were not obtained from the articles or authors and therefore the stratification might not be optimal. The lack of raw data also introduces the problem of no possibility for multivariate analysis. As some of the risk factors are overlapping, stratification for these risk factors in each analysis would have been helpful. For example, it has been shown that villous aspect and size of adenomas are associated with each other.[19] The lack of information also resulted in pooling of studies with different endpoints (either advanced adenomas, advanced neoplasia or adenomas). As the data show that advanced adenomas are the most important risk factors, it should be recommended that future research reports on both advanced and all adenomas separately. Another last important limitation is that, because of the lack of information, it was not possible to take the actual time intervals between colonoscopies into consideration. Moreover, the follow-up in most studies were not that extensive; this makes it harder to draw solid conclusions about the appropriate time intervals. These findings emphasize the need for long term follow-up studies to properly address the appropriate surveillance intervals. As colonoscopy resources are finite, this is an important issue to be addressed, as surveillance colonoscopy presents a huge demand on endoscopy units. Overall costs of the endoscopy department will be influenced by the implementation of CRC screening programs in the

near future. These costs will have to be balanced against the costs and utility of surveillance colonoscopy, as well as the savings on treatment for prevented or early detected CRC.[68] For this, an important question that remains to be answered is which patients benefit most from CRC surveillance and at what interval.

In conclusion, four main risk factors were identified for predicting adenoma findings on surveillance colonoscopy following index colonoscopy: advanced adenoma, size of adenomas ≥10 mm, number of adenomas ≥3, and age. Minor importance of other baseline findings such as HGD, gender, and location and histology of adenomas are in line with previous reviews.[19, 28]

Although the current guidelines published by the different societies and various countries vary, the essence of these guidelines for surveillance concur with our findings.[15, 25, 26] That is, it is reasonable to repeat colonoscopy sooner in patients with the above-mentioned risk factors and after a longer interval in patients without these risk factors. The reliability of the identified predictors of adenoma findings on surveillance colonoscopy has been identified again by this systematic literature review and should therefore be taken into consideration when planning surveillance colonoscopy or developing (new) guidelines. Our study further adds to the body of evidence of quantitative reasoning for more intense surveillance strategies in patients with high risk features, although firm conclusions about appropriate intervals cannot be drawn as data on this subject are insufficient and therefore the reliability of the exact risk remains somewhat uncertain. Additionally, future, prospective, high quality research is needed to determine the optimal interval for patients with adenomas, but without the high risk features at index colonoscopy.

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Chapter 15

Awareness of post-polypectomy surveillance guidelines: a nationwide survey among colonoscopists in Canada

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ABSTRACT

Introduction: As the colonoscopic demand is increasing, adherence to post-polypectomy surveillance guidelines is important. Suboptimal compliance can lead to waste of resources and unnecessary risks. This study aimed to determine the awareness of and adherence to post-polypectomy surveillance guidelines among members of the Canadian Association of Gastroenterology (CAG).

Methods: A survey containing 14 clinical cases was mailed to all physician members (n=411) of the CAG. Respondents had to give a surveillance interval and a reason for this particular interval.

Results: 150 colonoscopists (37%) completed the survey. Adherence to the guidelines varied from 23% to 96% per clinical scenario (median: 64%). Surveillance intervals were too short in 1 to 60% of the different cases (median: 8%). The recommended interval was most often (60%) too short for a patient with one tubular adenoma with high grade dysplasia. Surveillance intervals were too long in 4 to 75% of the cases (median: 9%). The recommended interval was most often too long in a patient with a 15 mm villous adenoma removed piecemeal (75%).

Most often, recommendations were reported to be based on the guidelines (median: 74%, range: 31-94%). However, in 9 out of 14 cases, more than 10% (median: 18%, range: 12-38%) of the respondents said their recommendation was based on the guidelines, but did not state the appropriate surveillance interval.

Conclusions: Compliance to colonoscopy surveillance guidelines is suboptimal and reflects both overuse and underuse. The results show that awareness about the content of guidelines needs to be raised and strategies implemented to increase adherence.

INTRODUCTION

Colorectal cancer (CRC) is the third most commonly diagnosed type of cancer and the second leading cause of cancer-related death in both men and women in Canada.[1] It has been shown that screening of asymptomatic, average-risk individuals and persons at increased risk, such as those with a positive family history of CRC, can reduce CRC-related mortality.[2-4] Therefore many institutions advise to screen for CRC, although different approaches are advised.[5-7]

When a polyp is found at index screening, it is generally removed to establish its histology and to determine the completeness of removal. Despite the removal of adenomas, they are still commonly found during follow-up procedures.[8] Adenomas during surveillance colonoscopies might include both missed adenomas, and recurrent adenomas. The main risk factors for adenoma recurrence are: hereditary CRC syndromes, older age of the patient, detection at index endoscopy of ≥3 adenomas, large adenomas (>10 mm), and adenomas containing villous histology or high-grade dysplasia (HGD).[9] Surveillance recommendations are therefore tailored to baseline findings.

As the endoscopic demand is increasing, adherence to the guidelines for post-polypectomy surveillance intervals is of paramount importance. As endoscopic capacity is limited, performing too many surveillance colonoscopies may hinder access to endoscopic procedures, and decreases the cost-effectiveness of CRC screening programs.[10, 11] Moreover, as rare but serious complications are associated with colonoscopy, surveillance at too short intervals exposes patients to unnecessary risks.[12, 13] Underutilization may also be a problem as patients may be at increased risk of developing CRC. Several studies have shown that many patients do not receive surveillance colonoscopy at the appropriate interval, or do not receive surveillance colonoscopy at all.[14, 15] These studies have been performed before the last publication from the American Gastroenterological Association (AGA) of post-polypectomy guidelines in 2008, and since then the attention to CRC screening and surveillance has greatly increased.[6]

The failure to adhere to post-polypectomy surveillance guidelines may be due to a lack of awareness or familiarity with the guidelines.[16-18] Another possible reason for physicians to deviate from the guidelines might be disagreement with guidelines.[19] Either explanation requires a different approach to improve surveillance and optimalize the use of resources.

This study aimed to determine the awareness of members of the Canadian Association of Gastroenterology (CAG) of post-polypectomy surveillance guidelines. In addition, factors associated with a physician's choice to deviate from the guidelines were assessed.

MATERIAL AND METHODS

A survey was mailed to all 411 registered physician members of the CAG in June 2010. The survey was also sent by email in the CAG Member Newsletter of both June and July. Invitees were given the possibility to complete the survey online or by mail using a self-addressed, pre-paid envelope. Anonymity of the data was guaranteed to the responders as the survey was dispatched by the CAG, while the responses were collected by researchers who had no access to the CAG mailing list.

Questionnaire

The questionnaire focused on the awareness of colonoscopists about current post-polypectomy surveillance guidelines. For that purpose, we used an adapted questionnaire previously used in the Netherlands (Appendix 1).[16] The first part of the questionnaire contained seven questions on demographic characteristics. The second part assessed the recommended surveillance intervals of the colonoscopists in fourteen hypothetical clinical cases of index colonoscopies. To match the different scenarios addressed in the guidelines, each case differed in endoscopic finding, including risk factors such as number, size, histology, or grade of dysplasia of the polyps. In all cases, the patient was assumed to be in good health and to have undergone his/her first colonoscopy, in which cecal intubation had been achieved, bowel preparation was adequate, and adenomas had been completely removed en-block, unless indicated otherwise. In each case the physician was asked if he/she would recommend surveillance colonoscopy at all and if so, at which interval. Second, the respondents were asked why they choose this particular time interval for follow-up.

All data were put in a database. For each case we determined the appropriate surveillance interval. The CAG guidelines on CRC surveillance published in 2004, recommend surveillance colonoscopy in 3 years to patients with ≥3 adenomas, and in 5 years in patients with 1-2 tubular adenomas ≤10 mm.[5] For all other cases, baseline features such as advanced adenoma characteristics (adenomas >10 mm, or containing villous histology or high grade dysplasia) should be taken into consideration, and surveillance intervals should be based on clinical judgment. As more evidence about adenoma recurrence risks has become available since 2004, we decided to use the most recent guidelines from the AGA as is done in daily clinical practice.[6] These guidelines give clear-cut recommendations for surveillance intervals for different index polyp characteristics such as size of the polyp(s), number of polyps, grade of dysplasia and histology.

We divided the recommendations into four categories; no follow-up (FU), appropriate FU, FU at a shorter interval than recommended by the guidelines, and FU at a longer interval than recommended by the guidelines. Recommendations ±3 months around the interval as recommended by the AGA guidelines were considered to be appropriate.

Statistical analyses

Statistical analyses were conducted using the Statistical Package for the Social Sciences (SPSS) version 18.0. Descriptive statistics were used to analyze and report the data. Mean and standard deviation were calculated for normally distributed data, while the median and interquartile range (IQR) were calculated for non-normally distributed data. Analyses on the recommended intervals were performed on each case separately. For further analyses, the cases were divided in categories of low-risk (non-advanced lesions, case 1, 2, and 14), high-risk (advanced lesions, case 3, 4, 5, 6, and 12), and patient with a positive family history (case 8 and 9). Differences in outcome between groups of patients were calculated by means of Student's t-test for continuous data and the Chi Square/Fisher exact test for categorical data, when appropriate.

RESULTS

A total of 150 CAG members returned the survey (response rate: 37%). Responders and non-responders did not differ with respect to gender (81 vs. 76% male, p=0.11), or geographic distribution. Eight respondents (seven pediatric gastroenterologists and one hepatologist) did not fill out the complete questionnaire, as the cases were not applicable to their practice. These were excluded from further analysis, leaving 142 respondents for final analyses.

Demographic data of the respondents

Table 1 shows the characteristics of the respondents. Their mean age was 47.7 years (SD: 10.1) and 81% was male. The majority (97%) was gastroenterologist, the remainder (3%) was internist. Almost half of the respondents (48%) were employed at a university hospital. The mean experience in performing colonoscopy was 16.9 years (range: 1-38 years, SD: 9.9).

Surveillance colonoscopy recommendations

Overall, the mean percentage of appropriate recommendations was 63% (range 23-96%). The proportion of appropriate recommendation was independent from the years of colonoscopy experience, although physicians with more than 12 years of experience had a lower percentage of total appropriate recommendations, compared to physicians with experience between 8 and 12 years (61 vs. 74%, p<0.1). Physicians employed at an academic center did have the same percentage of appropriate recommendations compared to physicians in non-academic settings (66 vs. 62%, p=0.2).The mean percentage of correct recommendations in non-advanced cases was 79% (range 62-93%). The median recommended surveillance inter-

Table 1. Characteristics of respondents

	n	%
Mean age (years, SD)	139	47.7 (10.1)
Specialty		
Gastroenterologist	137	97.2
Internist	4	2.8
Mean experience in performing colonoscopy (years, SD)	136	16.9 (9.9)
Practice setting		
Private individual practice	51	37.0
Private group practice	21	15.2
University practice	138	47.8
Average number of colonoscopies per month		
No	1	0.7
1-10	1	0.7
11-20	5	3.7
21-30	21	15.7
31-40	18	13.4
41-50	24	17.9
> 51	64	47.8

N; number of respondents; SD: standard deviation

val in non-advanced cases was 5 years (IQR: 5-10 years). No differences in overall percentage of appropriate recommendation for non-advanced cases were observed between physicians with different years of colonoscopy experience, or whether physicians were employed at an academic center or not (p>0.1).

When advanced adenomas were present at index colonoscopy correct recommendations were given in a mean of 54% (range 23-96%)The median recommended interval in advanced cases was 3 years (IQR: 1-3 years). No differences in overall percentage of appropriate recommendation for advanced cases were observed between physicians with different years of colonoscopy experience, or whether physicians were employed at an academic center or not (p>0.1).

Per physician, recommendations were correct in a mean of 63% of cases (range: 23%-100%). Only 2 respondents (1.4%) recommended the appropriate interval for surveillance colonoscopy in all cases.

Table 2 shows the appropriateness of the recommendations given by the physicians per case. The highest compliance to the guidelines was found in the case of a 55-year-old female, with 12 tubular adenomas, all <10 mm: 96% of the respondents gave a recommendation for FU within 3 years (median interval: 2 yrs, IQR: 1-3), while 4% offered her a surveillance colonoscopy after a too long interval. The least adherence to the guidelines was found in the case of a 50-year-old female with a sessile villous adenoma of 15 mm, removed piecemeal. Only 25% of the respondents adhered to the guidelines by giving a recommendation for FU in 2-6 months, while the majority (75%) recommended surveillance colonoscopy after a too long interval (median interval: 1.4 yrs, IQR: 1-2).

Table 2. Recommended surveillance interval by respondents per clinical scenario

Clinical scenario	Number of respondents	Interval recommended by guidelines	Correct recommendation (%)	No FU (%)	Too early (%)	Too late (%)	Median recommended interval (yrs, IQR)
55 yrs, 2 hyperplastic polyps	141	10 yrs	61.7	28.4	9.9	-	10.0 (0.0-10.0)
50 yrs, 1 TA of 7 mm	142	5-10 yrs	93.0	-	7.0	-	5.0 (5.0-5.0)
50 yrs, 1 TA of 12 mm	140	3 yrs	64.3	-	2.9	32.9	3.0 (3.0-5.0)
50 yrs, 1 VA of 15 mm	139	3 yrs	62.6	-	25.0	11.5	3.0 (2.5-3.0)
65 yrs, 5 TAs, all <10 mm	140	3 yrs	79.3	-	12.1	8.6	3.0 (3.0-3.0)
50 yrs, 12 TAs, all <10 mm	139	< 3 yrs	96.4	-	-	3.6	1.5 (1.0-3.0)
65 yrs, post curative CRC resection (T2N0M0)	139	1 yr	74.8	-	0.7	24.5	1.0 (1.0-1.0)
45 yrs, one 1st degree relative with CRC < 60 yrs	139	5 yrs	92.1	0.7	2.2	5.0	5.0 (5.0-5.0)
52 yrs, one 1st degree relative with CRC > 60 yrs	140	10 yrs	40.7	3.6	55.7	-	5.0 (5.0-10.0)
50 yrs, 1 sessile VA of 15 mm, removed piecemeal	139	2-6 months	25.2	-	-	74.8	1.0 (0.8-2.0)
55 yrs, 1 VA of 9 mm and inadequate bowel prep	139	NA	NA	NA	NA	NA	1.0 (1.0-2.0)
50 yrs 1 TA of 8 mm, HGD	139	3 yrs	30.2	-	59.7	10.1	1.0 (1.0-3.0)
85 yrs, 1 VA of 6 mm, LGD	139	3 yrs	23.0	58.3	10.8	7.9	0.0 (0.0-3.0)
60 yrs, 4 TA on screening, 1 hyperplastic polyp at 1st surveillance	138	5 yrs	81.9	-	8.0	10.1	5.0 (5.0-5.0)

N: number of respondents; IQR: interquartile range; FU: follow-up; yrs: years; SD: standard deviation; TA: tubular adenoma; VA: villous adenoma; LGD: low grade dysplasia; HGD: high grade dysplasia

The patient with a tubular adenoma of 10 mm (50-year-old male with one tubular adenoma of 12 mm) was recommended to undergo surveillance colonoscopy after 3 years as recommended by the guidelines by 64% of the respondents (median interval: 3 yrs, IQR: 3-5), while 33% recommended surveillance colonoscopy after a longer interval. In the case where a large villous adenoma was found (50-year-old female with one villous adenoma of 15 mm) the recommendation for surveillance colonoscopy was in agreement with the guidelines in 63% (median interval: 3 yrs, IQR: 3-3). In this case, 25% of the respondents recommended surveillance colonoscopy sooner than recommended by the guidelines.

In the case of a 85-year-old male patient, a 50-year-old male with no adenomas at index endoscopy, and a 52-year-old patient with one first-degree relative diagnosed with CRC >60 years, respectively 58%, 28% and 4% of the respondents did not recommend surveillance colonoscopy.

There are no clear-cut guidelines when to perform repeat colonoscopy in case of an inappropriate bowel preparation. The 55-year-old male with inadequate bowel preparation shows that surveillance colonoscopy is recommended by physicians after a short time (median: 1 year, IQR: 1-2).

Reason for surveillance interval recommendation

Table 3 shows the reason from the respondents for recommending a particular surveillance interval. In most cases, the majority of the respondents stated that they followed the guidelines.

In the case of a 50-year-old woman with a villous adenoma of 15 mm, removed piecemeal (case 10), 47% of the respondents said not to follow the guidelines because of their clinical experience. If respondents said they were following the guidelines their recommendation was correct in most cases. However, in nine cases (case 3, 4, 5, 7, 9, 10, 12, 13, and 14), >10% (range: 12-37%) of the respondents stated that their recommendation was based on the guidelines but they did not give the appropriate recommendation for FU, as shown in Table 3.

Despite the absence of guidelines in the case of a 55-year-old male patient with one villous adenoma of 9 mm but poor bowel preparation, 13% stated they followed the guidelines in their recommendation.

Table 3. Reasons for recommending a particular interval for FU colonoscopy

Case	No FU (%)	Guideline adequate interpretated (%)	Guideline but wrong interpretation* (%)	Based on clinical experience (%)	Based on recent evidence (%)	Other reason (%)
1	28.8	48.2	2.2	7.2	4.3	9.4
2	-	83.1	3.5	7.7	5.6	-
3	-	57.2	28.3	10.9	2.2	1.4
4	-	56.5	17.4	20.3	3.6	2.2
5	-	71.3	12.2	11.5	3.6	1.4
6	-	40.6	2.9	40.6	2.9	13.0
7	-	61.3	17.5	19.0	1.5	0.7
8	-	88.6	5.0	4.3	1.4	0.7
9	1.5	36.8	37.5	16.9	2.2	5.1
10	-	11.7	29.2	47.4	2.9	8.0
11	-	12.9	NA	82.0	0.7	4.3
12	-	24.8	24.1	42.3	2.9	5.8
13	38.8	14.4	16.5	24.5	1.4	4.3
14	-	60.2	13.0	22.5	4.3	-

* Colonoscopist stated their recommendation was based on the guidelines, but did not give the appropriate recommendation for FU

DISCUSSION

Because of the risk of adenoma recurrence after polypectomy, optimal prevention of CRC after adenoma removal requires additional surveillance procedures.[9-10] Guidelines aim for maximal prevention with available resources, which are limited when it comes to endoscopy capacity. Surveillance colonoscopy at appropriate intervals is of paramount importance to prevent unnecessary risks, costs, and discomfort for the patient.

Our study showed that a significant proportion of respondents did not follow the guidelines or was not familiar with them. Adherence to the guidelines varied widely for different clinical scenarios: from 23% to 96%. In four cases inappropriate surveillance recommendations were given in ≥50%. Further, in most cases the majority of respondents said they based their recommendations on the guidelines. However, in nine of the fourteen cases 12 to 38% of the colonoscopists said their recommendation was based on the guidelines, but they did not give the appropriate recommendation. These results suggest that an educational intervention which raises awareness and knowledge about the guidelines would be beneficial.

The lack of recent, explicit guidelines in Canada based on the latest evidence is a possible reason for the low adherence to the recommended intervals for surveillance colonoscopy that we observed. The CAG guidelines on adenoma surveillance were last updated in 2004.[5] In 2008 the AGA re-published its guidelines on post-polypectomy surveillance.[6] These are tailored to the presence of risk factors on index colonoscopy. Because there has been no change in the Canadian guidelines based on recent evidence, most physicians use the AGA guidelines in daily practice.

Other reasons that might explain the marked variation in adherence to the guidelines may be that the guidelines are a) not entirely clear, b) subject to variable interpretation, c) not compatible with daily clinical practice, or d) not practicable.[20]

No specific pattern in appropriateness of recommendations for patients with advanced or non-advanced adenomas was found. This is in line with previous research which showed that in both cases colonoscopies are often performed too soon.[16-18, 21] The most important difference between those studies and our findings is that we found both overuse and underuse of endoscopic resources, while the previous reports mainly reported too short surveillance intervals (overuse). The reason for underuse may be related to the increased attention for the endoscopic demand in Canada with rising waiting lists.[22, 23] Recently it was shown that there is a significant longer mean waiting time than recommended for gastroenterology services, including colonoscopy, in Canada. For example, waiting time for a screening colonoscopy was reported as on average 201 days, and for CRC or adenoma surveillance 272 days. These observations underline the importance of appropriate timing of colonoscopy surveillance.

Regarding the specific clinical scenarios several observations merit discussion. This discussion can guide future research, but also guidelines' improvements projects.

First, in the case in which two hyperplastic polyps were found, it should be emphasized that the guidelines state that other screening modalities would be appropriate for surveillance, besides colonoscopy. This patient is regarded as an average risk patient. None of the respondents considered other screening modalities in their answer, and the majority chooses to offer the patient a surveillance colonoscopy. To control the endoscopic demand, the use of other screening modalities should be considered in these non-advanced cases.

In more advanced cases, like villous adenoma, adenomas >10 mm or polyps with high grade dysplasia, the percentage of respondents deviating from the guidelines was larger. The reason might be that there is persistent controversy with respect to optimal management, particularly when dealing with the impact of villous histology and high grade dysplasia on adenoma recurrence. Controversy exists as: a) villous histology or high grade dysplasia is not consistently found to be associated with an increased risk of adenoma recurrence, b) risk of recurrence does not increase as much as for other factors like number and size of polyps, and c) high inter-observer variability is present in determining size and histology.[9, 24, 25]

In the case of a 50-year-old female with one villous adenoma of 15 mm, 25% of the respondents recommended an interval shorter than recommended by the guidelines. The fact that this patient had two risk factors for recurrence (adenoma >10 mm and villous histology) might have been the reason for physicians to shorten the surveillance interval. On the other hand, 12% of the respondents recommended surveillance at a longer interval than recommended, up to an interval of 5 years. Little is known about the additive risk of multiple risk factors, although a recent study found that the risk for adenoma recurrence doubled (hazard ratio: 6.4) when both >3 adenomas and advanced morphology were present.[26] The shortened

surveillance interval might reflect this uncertainty, but should be discouraged as long as definitive evidence for additive risk of multiple risk factors for recurrence is lacking.

Contrasting findings were found for the recommended surveillance intervals for patients with a family history. The large majority (92%) recommended a correct surveillance interval in the case of a 45-year-old female with one 1st degree relative with CRC <60 years. In contrast with this case, the case of a 52 year-old male with one 1st degree relative with CRC >60 years only 41% of the respondents adhered to the guidelines. It should be mentioned that in this case, other screening modalities are also appropriate according to the AGA guidelines. However, no respondents said they would offer other screening tests, and the majority chose to offer surveillance colonoscopy within 5 years instead of the recommended 10 years. Moreover, 38% of the respondents said they followed the guidelines for this scenario, but did not give the correct recommendation. This suggests that colonoscopists are not entirely aware of the differences in guidelines for patients with a positive family history. The differences in surveillance recommendations for a positive family history (1st degree relative <60 years or two 1st degree relatives every 5 years colonoscopy, 1st degree relative >60 years or two 1st degree relatives every 10 years colonoscopy) make the guidelines hard to apply in daily clinical practice. Training and education in this area of trainees and physicians should be considered to improve compliance to the guidelines for surveillance in patients with a positive family history.

In the case of an 85 year-old male with one villous adenoma, only 23% of the respondents followed the guidelines. Fifty-eight percent of the respondents recommended no surveillance at all, which is an option that should be considered when giving recommendations for surveillance colonoscopy to patients of this age. The starting age for screening colonoscopy is well-defined (50 years). However, the age to stop surveillance varies between recommendations. Recently, the CAG stated that persons over 85 years of age should not be screened.[27] No upper age-limit is given in the AGA recommendation.[28] Future guidelines should take this into consideration.

Another interesting finding was that in the case of a 50-year-old female with a piecemeal resection of a 15 mm villous adenoma, only 25% of the respondents adhered to the guidelines. This suggests that colonoscopists are not aware of the fact that complete removal should be verified both pathologically, and endoscopically.[29]

No clear guidelines were available in the case of a 55-year-old male with one villous adenoma of 9 mm but inadequate bowel preparation. The recommendations in this case varied from "as soon as possible" up to an interval of 5 years. The majority (43%) recommended FU after 1 year. It has been shown that a poor bowel preparation is associated with lower adenoma detection rates, but as it is difficult to objectively rate the bowel preparation throughout the entire colon, recommendations in these patients are up to the clinician's judgment.[30, 31]

This study has several limitations. First, the response rate was low (36%). Therefore, the results may not be representative of the actual practice of Canadian endoscopists, and rep-

resent only a fraction of Canadian endoscopy practice. This low response rate is in line with other response rates from similar surveys.[32, 33] However, the non-responders did not differ significantly in gender or province from the responders, which may indicate that we obtained an acceptable sample. Further, no exact information about the specific medical specialty of the responding CAG members was available. The observed response rate might partly be due to the fact that the survey was sent to all members and subspecialties as pediatrics and hepatologists were not excluded. Despite the low response rate, the fact that colonoscopists from all Canadian provinces responded (data not shown) and experience in colonoscopy varied from 1 to 38 years, indicate that the study population is likely to be a good representation of the physicians performing colonoscopies in Canada. It should be noted however that only CAG members were included, and that the results do not represent practice from non-members.

Regarding the study design, the clinical cases were presented in short sentences, while colonoscopists might want to have more background information (such as health status, detailed family history, etc.) to make their recommendation. In particular, colonoscopists were not provided with information about the location of the adenomas. Studies have shown that there might be a difference in risk of adenoma recurrence between right- and left-sided adenomas, although none of the current guidelines incorporates this in their recommendations.[9, 34] Colonoscopy has been shown to significantly reduce CRC related mortality from distal CRC, while the number of deaths from proximal CRC was not significantly reduced.[35, 36] These findings might impact colonoscopists' recommendations for surveillance intervals after polypectomy, and result in less confidence in the guidelines and therefore less adherence to the guidelines.

A last limitation might be that the CAG guidelines for CRC and adenoma surveillance are refer to guidelines from the British Society of Gastroenterology (BSG) and AGA, and do not make specific recommendations by themselves.[37] The AGA guidelines have been discussed extensively above and used in this study as they are commonly used in daily practice. Recently the BSG published an update on its guidelines on screening and surveillance. However, no changes were made in the recommendations for surveillance of adenoma patients compared to 2002. These guidelines include that patient with 3 or 4 small (<10 mm) adenomas at baseline should receive more vigilant surveillance at 3 years, patients with large (>10 mm) adenomas at 1 year, while all others should receive no surveillance or at 5 years. Baseline dysplasia or histology is not taken into account.

As our survey was partly based on a previous survey used in the Netherlands, it should be noted that the Dutch guidelines used in that study are quite different.[16] The Dutch guidelines only take the number of adenomas into account for determining the appropriate surveillance interval: patients with 3 or more adenomas are recommended to undergo surveillance colonoscopy after 3 years, while patients with one or two adenomas are recommended to receive surveillance after 6 years. In the Dutch study, mainly overuse of colonoscopic resources was

observed, as many physicians took other adenoma characteristics such as histology and dysplasia into account.[16] As we found both overuse and underuse, the differences in results might be explained by the fact that physicians are now better aware of the increased risk of adenoma recurrence in certain circumstances.

In conclusion, this study shows that the most recent guidelines on surveillance intervals for colorectal adenomatous polyps and CRC are not well incorporated in the practice patterns of Canadian colonoscopists. Assuming that guidelines are based on the most up-to-date and comprehensive evidence, compliance is expected to be high. However, our data indicate that compliance with the most recent guidelines is low. Awareness of the surveillance guidelines needs to be raised and studies should be performed to determine how adherence to the guidelines can be improved. This will help to ensure that the limited resources available for CRC screening and surveillance are optimally used.

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Chapter 16

Awareness of surveillance recommendations among patients with colorectal adenomas

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ABSTRACT

Background & Aims: The efficacy of colorectal cancer screening programs depends on the rate of attendance at surveillance colonoscopy examinations. Increasing patients' awareness about the importance of surveillance might improve attendance, but it is not clear how much they know about their follow-up recommendations. We assessed the awareness of patients with adenomas about their surveillance recommendations.

Methods: Ten endoscopy departments provided access to their colonoscopy database for quality assurance; 2 datasets were obtained. We analyzed data from 4000 colonoscopies (400 per department) performed on patients with adenomas. All the patients were mailed a survey to determine how much information they had about their colonoscopy results and their follow-up recommendations. Data from 549 patients were included in the analysis.

We also assessed surveillance attendance among 500 patients (50 per department) who had adenomas removed.

Results: Of the patients analyzed, 85% recalled retrieval of polyps during their colonoscopy, and 85% recalled whether they needed surveillance or not. The indication for surveillance was recalled by 69% of patients (range between departments, 55%–83%; p<.01). Factors that were associated with awareness of recommendations were younger age (odds ratio [OR]=1.06; 95% confidence interval [CI], 1.06–1.09), treatment by a gastroenterologist (OR=5.53; 95% CI, 3.28–9.32), and presence of 3 or more adenomas (OR=2.97; 95% CI, 1.29–6.85). Attendance among patients with adenomas varied among departments, from 60% to 89% (p<.01), and was not associated with awareness of patients about their recommendations per department (p=.59).

Conclusions: Not enough patients (only 85%) who receive colonoscopies are aware of their results or surveillance recommendations. Although awareness of findings and recommendations did not correlate with follow-up attendance, patients should be better informed about findings and their need for surveillance.

INTRODUCTION

Screening for colorectal cancer (CRC) with removal of adenomas aims to reduce CRC-related mortality, and depending on the screening method used, also CRC incidence.[1] Individuals with colorectal neoplasia are at high risk to develop metachronous adenomas.[2] Surveillance colonoscopy of patients who have been treated for adenomas or CRC is therefore strongly recommended.[3] Adenoma recurrence is associated with several baseline characteristics including number of adenomas, adenoma with size ≥10 mm, villous histology, or high grade dysplasia. Surveillance guidelines tailor time intervals for repeat procedures based on such characteristics.[3]

In the view of the growing need for colonoscopies due to the implementation of CRC screening programs, suboptimal usage of colonoscopy resources will further increase the burden of the endoscopic capacity, as overutilization in surveillance has been reported.[4,5] Targets for improvement can be found in the adherence to guidelines by physicians but also in the attendance by patients for surveillance procedures.[5-7] Non-compliance rates for attendance in follow-up have been reported to be as high as 30%.[8,9] Some studies mentioned that patients may lack knowledge of the results of their own colonoscopy, the necessity of surveillance colonoscopy, and the required interval as reasons for non-attendance.[9,10]

The aim of this study was to assess the patients' awareness of their colonoscopy findings and surveillance recommendations in order to identify service gaps in surveillance practice. Our secondary aim was to evaluate the attendance for surveillance in the view of the awareness, as attendance is of importance for cost-effectiveness of surveillance programs.

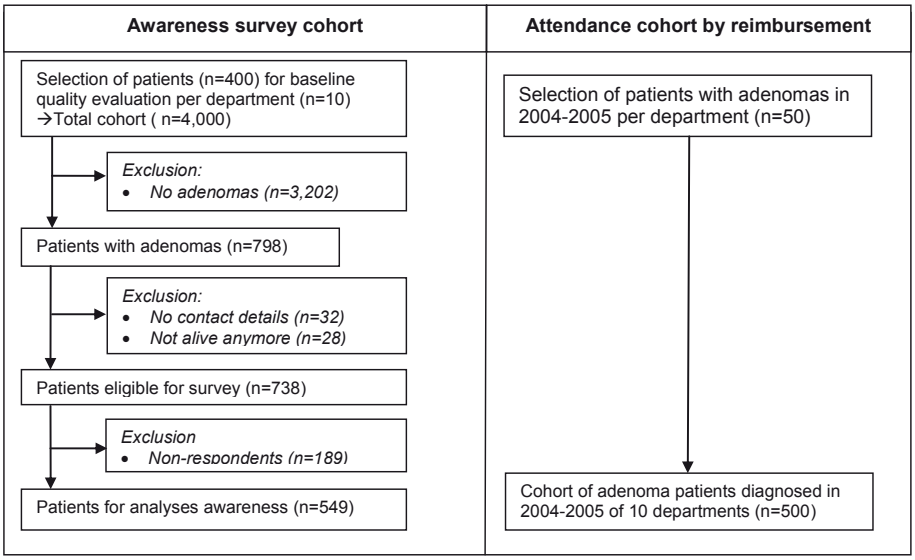
METHODS

A patient survey was used for this study. Items of the survey were selected using discussion with experts in the endoscopy field, after determination of the measurement aim and target population as previously recommended for designing surveys.[11] The survey contained questions evaluating the information and (histological) findings at initial colonoscopy, the knowledge of follow-up recommendations, and knowledge about reasons why follow-up was or was not recommended. Additionally, we assessed patient characteristics and the general health status by means of gender, age, education, ethnicity and the EuroQol-5D score. Recalled surveillance intervals among patients were explored by estimation of the interval in years. In the pre-test phase, two gastroenterologists evaluated the comprehensibility of the survey instrument. The pilot phase included a survey-assessment by twenty patients who had undergone a colonoscopy procedure to test the readability and interpretability of the survey instrument. The investigator obtained oral and written feedback from patients in order to improve the clarity and interpretability of the survey instrument.

Inclusion

The current study about the awareness of surveillance recommendations among patients was part of a baseline quality evaluation in colonoscopy in the Netherlands. For this baseline quality audit, ten endoscopy departments (5 teaching, 5 non-teaching departments) participated in the current study and provided access to their colonoscopy database. From these databases, two datasets were obtained. Firstly, a total of 4000 colonoscopies (400 consecutive colonoscopies per department) were selected and studied for adenoma patients. All patients with adenoma removal, were approached by mail with the survey (Figure 1). Secondly, a total 500 adenoma patients (50 per department) who had in the past undergone adenoma removal were selected and assessed for actual attendance for surveillance (Figure 1). Ethical approval was obtained from the Institutional Review Boards of the participating centers. Advanced adenomas were defined as an adenoma ≥10 mm, with high grade dysplasia or a villous component, or ≥3 adenomas in an individual patient. Patients with known inflammatory bowel disease or a CRC diagnosis on colonoscopy were not included. The patient's contact details were obtained from the electronic patient records. The survey for part one of the study was sent by mail within a range of 6 to 18 months after the index colonoscopy. A reminder was sent six weeks after the initial mailing. Patients who did not respond to both mailing rounds or did not provide consent for the study were labeled as non-respondents.

Figure 1. Selection of patients for the awareness and attendance analyses



Data collection

Awareness of recommendations was defined as the recall of their findings, the awareness whether surveillance was indicated, and the awareness of the follow-up policy. Additionally, we evaluated the agreement between recalled intervals, physician-recommended or guideline-recommended intervals. For each patient, we determined the guideline-recommended intervals using the Dutch surveillance guideline, unless deviation from those guidelines was specified in the endoscopy report by the physician.[12] If no clear follow-up recommendation was stated, we used the guideline-recommended interval. The Dutch guidelines for surveillance after polypectomy base intervals on the number of adenomas at index colonoscopy. For patients with one or two adenomas, the recommended surveillance interval is six years. For patients with three or more adenomas, the recommended interval is three years. For patients with high-grade dysplastic adenomas and piecemeal removed adenomas, the recommended interval is one year. Recalled surveillance intervals of patients were considered appropriate if the recalled interval was ±1 year margins within the recommended interval. Factors associated with (1) the awareness whether surveillance would be required and (2) recall of the explanation with regard to the indication for surveillance, were also evaluated.

The actual attendance for surveillance colonoscopy in all ten departments was simultaneously assessed using the hospital reimbursement systems to randomly select 50 patients per center, who had been diagnosed with adenoma between 2004-2005. The search was based on the diagnostic labels 'colonoscopy' and 'adenoma'. This second set of patients was used to determine the actual attendance for surveillance. This group of patients did not receive a questionnaire and none of them were included in first group of study tested for awareness. This was deliberately done as it was assumed that assessment of awareness of the need for surveillance would likely interfere with actual attendance for surveillance, and thus not reflect the current daily practice.

Chart review was performed whether the patient did undergo a follow-up colonoscopy in the following years up to April 2011. If no follow-up colonoscopy had been done in the subsequent years, the assumption was that patients did not attend their follow-up procedure unless it was stated that follow-up was not required anymore due to co-morbidity, or if the patient had died within the time period. The presence of a polyp follow-up communication system in the department was also taken into account when comparing surveillance attendance rates between the different departments, as attendance has been shown to be affected by automated recall systems.[13] Three out of the ten participating departments had implemented such a system.

Statistical analyses

Descriptive statistics are given as overall findings followed by the range between departments (difference between lowest- and highest scoring department). For categorical data differences were analyzed using Chi-Square tests. To determine differences in nominal data, the Mann-Whitney-U-test was used.

Binary logistic regression analyses with robust standard errors were used in order to identify factors associated with awareness. Factors were a priori chosen and included in the model, such as patient demographics, person who provided follow-up information, education, ethnicity, positive family history of CRC, whether the initial colonoscopy was performed for symptoms or for screening/surveillance, and the presence of ≥ 3 adenomas. To assess whether department specific attendance rates were correlated to the awareness of surveillance recommendations in patients from the same department, we used linear regression analyses. For each department, a correlation was performed between the attendance in the department and the awareness of the surveyed patients per department in (1) if surveillance would be needed and (2) why surveillance colonoscopy would be required in the future. A two-sided p-value <0.05 was considered significant. All analyses were performed using the SPSS PASW statistical software package version 17.0, Chicago, IL, USA.

RESULTS

Among the 4,000 cases in dataset-1, 798 (20%) patients with at least one adenoma were identified for inclusion. Patients were excluded for the survey mailing rounds if they had died (n=28), or if their contact details could not be retrieved (n=32). The remaining 738 patients were approached by mail (Figure 1).

A total of 604/738 patients responded (82%). A total of 55 surveys were withdrawn from the analyses because of incomplete answers, leading to 549 analyzable surveys. The mean time interval between the former colonoscopy and the survey was 13 months (range: 6-23). Demographic characteristics are provided in Table 1. Advanced adenomas had been found in 41% of all respondents with adenoma, 18% of respondents had had ≥3 adenomas removed. Forty-one per cent (n=264) of the respondents had been referred for colonoscopy by a general physician, 37% (n=203) by a gastroenterologist, and 14% (n=77) by another specialist. Significant differences between respondents and non-respondents were observed in the proportion of male gender (62 vs. 53%, p=0.032) and cecal intubation rates (100 vs. 97%, p=0.016).

Table 1. Characteristics of responders and non-responders

	Responders n (%)	Non-responders* n (%)	p-value
Study cohort	549 (74%)	189 (26%)	
Male gender	342 (62%)	101 (53%)	0.030
Mean age (SD)	65.1 (11)	65.0 (13.8)	0.601
Previous colonoscopy	207 (38%)	63 (33%)	0.282
History of CRC	20 (4%)	2 (1%)	0.07
Colonoscopy for screening/surveillance	271 (50%)	88 (50%)	0.422
Sedation received	473 (90%)	160 (90%)	0.908
Adjusted cecal intubation#	545 (100%)	184 (97%)	0.016
Most advanced lesion			0.913
- Tubular adenoma	390 (71%)	132 (70%)	
- Tubulovillous adenoma	140 (26%)	51 (27%)	
- Villous adenoma	19 (4%)	6 (3%)	
Advanced adenomas	223 (41%)	80 (42%)	0.680
High grade dysplasia	40 (7%)	15 (8%)	0.769
≥3 adenomas	96 (18%)	28 (15%)	0.397

SD=standard deviation; * non-responder consist of non-responders and responders that were not willing to participate in the survey; # adjusted for poor bowel preparation, intervention as indication, and severe colitis

Recall of colonoscopy outcome by the patient

Table 2 shows the recalled colonoscopy findings by the patients. Respondents recalled the endoscopy finding as hyperplastic polyps in 46% (n=248) of cases, 24% (n=127) recalled the retrieved polyps as adenomas/polyps with dysplasia and 4% (n=21) recalled to have a malignant tumour. Eight per cent (n=45) said they never got their results, and 17% (n=95) recalled other results such as diverticulosis. The proportion of patients that recalled that colorectal neoplasia had been removed (28%), was significantly higher in patients with advanced adenoma compared to patients with non-advanced adenomas (34% vs. 24%, p=0.007). Males remembered as often that adenomas were found as females (27 vs. 31%, p=0.23).

Follow-up information provision and recommendations

Table 3 shows the results of the follow-up information provided to the patient. The majority of patients had been recommended on follow-up by a gastroenterologist (57%). Seventy-nine per cent of respondents recalled that a surveillance colonoscopy would be necessary in the future (n=422), but 15% (n=83) did not know whether a colonoscopy would be needed or not (range between departments: 4-32%, p<0.001). The recall about the need for surveillance between patients completing their survey between 6 and 12 months was not significantly different compared to patients that completed their survey between 12 to 18 months (81 vs. 76%, p=0.368) or after 18 months (81 vs. 77%, p=0.316).

Table 2. Recalled colonoscopy outcomes by survey respondents

	n (%)	Range between units (%)
Communication preliminary findings by:		
- **Endoscopist**	415 (76%)	60-97%
- **Endoscopy nurse**	62 (11%)	2-25%
- **No communication performed**	13 (2%)	0-7%
- **Other**	56 (10%)	2-21%
Written result obtained at endoscopy unit	52 (10%)	2-18%
Polyps reported as preliminary findings	463 (85%)	81-95%
Final Results		
- **Hyperplastic polyp**	248 (46%)	35-59%
- **Adenomatous polyp**	127 (24%)	12-40%
- **Malignant tumour**	21 (4%)	0-10%
- **Never got final results**	45 (8%)	0-13%
- **Other result**	33 (6%)	2-15%
- **Don't remember**	62 (11%)	6-19%

***Data pertain to the 549 adenoma patients responding to the questionnaire

Table 3. Recalled FU policies and background of survey respondents

	n (%)	Range between units
Person providing final result and FU information		
- **General physician**	36 (7%)	0-19%
- **Gastroenterologist**	302 (57%)	52-63%
- **Surgeon**	68 (13%)	7-27%
- **Internist**	29 (6%)	0-16%
- **Other**	46 (8%)	0-16%
- **Never received follow-up policy**	45 (9%)	5-16%
Recalled FU policy		
- **Surveillance colonoscopy needed in the future**	422 (79%)	67-90%
- **No surveillance colonoscopy needed anymore**	32 (6%)	0-9%
- **Do not remember**	83 (15%)	4-32%
Explanation indication of surveillance	356 (69%)	55-83%
Recalled time interval for surveillance (yrs)	4.3 (0.8-9.6)	3.0-5.0 yrs
Caucasian ethnicity	497 (93%)	86-100%
Highest education completed		
- **Low or Intermediate (elementary or high school)**	399 (76%)	68-82%
- **High (college or university degree)**	126 (24%)	18-32%
Mean EQ-5D score (IQD)	0.86 (0.80-1.0)	0.82-0.90

FU=follow-up, CSPY=colonoscopy, SD=standard deviation, IQD=interquartile range

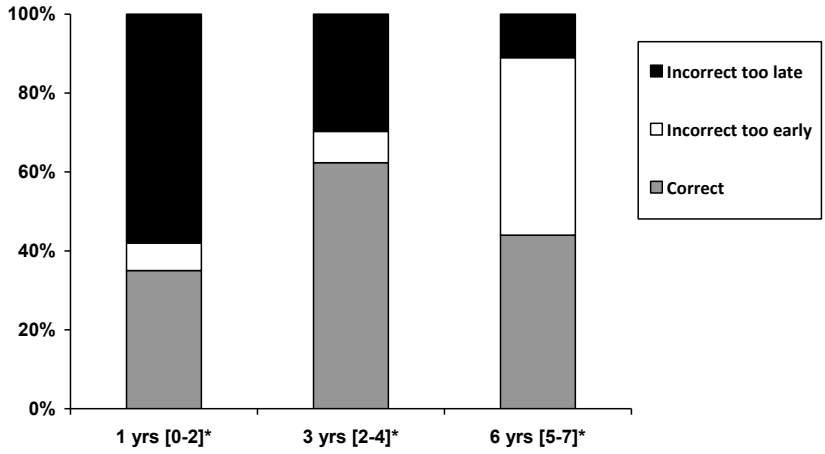
The explanation about the indication for surveillance was recalled by 69% of the respondents (range departments: 55-83%, p=0.014). The recall of the indication between patients that completed their survey between 6 and 12 months was not different compared to completion between 12 to 18 months (73 vs. 70%, p=0.642). The recall between 6 and 12 months vs. after 18 months was significantly different (73 vs. 61%, p=0.012). Provision of information by a gastroenterologist instead of any other specialty was associated with higher indication recall rates: 81% vs. 53%, p<0.001. Patients with higher education recalled significantly more often that surveillance was recommended compared to intermediate and low education groups

(78 vs. 65%, p=0.007). No significant differences were seen between different ethnicity populations (Caucasian vs. non-Caucasian: 69 vs. 62%, p=0.395). If patients had a positive family history for CRC, they recalled significantly more often why surveillance would be required (82 vs. 66%, p=0.004).

Agreement between recalled intervals and physician- and guideline-recommended intervals

Figure 2 shows the proportions of correctly and incorrectly recalled intervals across the specific guideline-recommended intervals. For 47% of respondents (n=189), the recalled interval was in agreement with the physician- or guideline-recommended interval, 28% (n=112) recalled intervals that were earlier than recommended by the physician or guideline, and 25% (n=99) recalled intervals that were later than recommended by the physician or guideline. The overall proportions of correctly recalled intervals ranged in the different endoscopy departments between 30-62%, p=0.06. Patients with a one-year recommendation for surveillance significantly more often than others incorrectly recalled intervals that were too long (58 vs. 17%; p<0.001), whereas the opposite was noted for patients with a recommendation for surveillance at 6-year interval (45 vs. 7%; p<0.001) (Figure 2). Patients who completed their survey within 6 months recalled significantly more often the correct interval compared to patients who completed their survey after 18 months (59 vs. 34%, p<0.001).

Figure 2. Distribution of recalled surveillance intervals across physician-guideline-recommended intervals



*Time periods classified based on physician recommended (endoscopy report) or guideline recommended intervals; Data pertain to the 549 adenoma patients responding to the questionnaire

Factors associated with awareness of surveillance recommendations

Factors associated with the awareness of (1) whether surveillance was needed and (2) the explanation of the indication of surveillance, are provided in Table 4. Significant predictors for whether patients could recall if surveillance would be needed were information provision by a gastroenterologist (OR=5.53, 95%CI: 3.28-9.32) compared to other specialists, younger age (OR= 1.06, 95%CI: 1.03-1.09), and the previous removal of ≥3 adenomas (OR=2.97, 95%CI: 1.29-6.85).

Factors associated with whether patients could recall the explanation for the indication, were younger age (OR=1.04; 95%CI: 1.02-1.08), informed by a gastroenterologist (OR=3.56; 95%CI: 2.33-5.43) and if they had undergone their colonoscopy for CRC screening or surveillance (OR=2.00, 95%CI: 1.30-3.09).

Table 4. Awareness in recall of 'whether' and 'explanation indication' for surveillance colonoscopy

	Recall of whether surveillance would be needed		Recall of the explanation with regard to the indication for surveillance	
	OR	95% CI	OR	95% CI
Gastroenterologist informing about final results and FU	5.53	3.28-9.32	3.56	2.33-5.43
Younger age	1.06	1.03-1.09	1.04	1.01-1.07
Female gender	1.02	0.62-1.69	1.22	0.78-1.89
Higher education (college or university degree)	0.77	0.43-1.38	1.46	0.87-2.45
Non-Caucasian ethnicity	0.73	0.25-2.12	0.57	0.25-1.29
Positive family history of CRC	1.80	0.79-4.14	1.46	0.77-2.75
Colonoscopy performed for CRC screening/ surveillance	1.46	0.89-2.40	2.00	1.30-3.09
≥ 3 adenomas	2.97	1.29-6.85	1.03	0.58-1.84

CRC=colorectal cancer; FU =follow-up; *Data pertain to the 549 adenoma patients responding to the questionnaire

Attendance & awareness rates between departments

In dataset-2, based on a random sample of 50 patients per department, a total of 500 patients (53% male, mean age: 64 ±11 years) were analyzed for attendance (Figure 1). Of these 500 patients, 72% (n=327) had undergone a surveillance colonoscopy in the six years following their index colonoscopy (range of attendances between departments: 60-89%, p=0.001). The proportion of patients seen for surveillance procedures in departments with polyp follow-up communication systems was higher compared to departments without such a system (84% vs. 67%, p<0.001). When comparing data between departments, there was no significant association between the attendance for surveillance and the awareness of the need for surveillance colonoscopy (β= -0.55; p=0.31), nor the explanation about the indication for surveillance colonoscopy (β= -0.23, p=0.59).

DISCUSSION

Patients who underwent endoscopic adenoma removal are at increased risk for adenoma recurrence.[14] Surveillance colonoscopy in adenoma bearing patients, is therefore acknowledged as a key aspect of CRC prevention.[14] Embedded in the effectiveness of CRC screening, the attendance rate for surveillance colonoscopy is of utmost importance.[7, 15, 16] Patient attendance may be influenced by patient awareness of their own colonoscopy findings and knowledge about the necessity for surveillance. Our study showed that only 24% of patients in whom adenomas had been removed indeed recalled that this was the case and one out of twelve patients stated that they had never received their final results. Seventy-nine percent of patients recalled that surveillance was recommended and 69% of all patients recalled the explanation regarding the necessity of surveillance, with a considerable range between departments (55-83%, $p<0.01$). Despite this knowledge, only 47% of patients recalled the surveillance interval in agreement with the physician-or guideline recommended interval.

Improvement of adherence to surveillance colonoscopy can be achieved on both patient-level (information and attendance) and on physician-level (guideline adherence).

Concerning the patients-level aspect information provision, our results suggest that the communication with regard to the colonoscopy result and indication for surveillance to patients was suboptimal. The recall of the type of lesion that had been removed may be considered as less important than recall of the appropriate follow-up. Indeed, a significant proportion of patients stated that they did not know whether further surveillance was indicated. Previous work from our group has already shown that there is room for improvement in information provision to patients who underwent a colonoscopy.[17] Our recent study showed that patients tend to better recall their follow-up policy if they were informed by a gastroenterologist (OR=5.5) compared to other specialists. Similar findings were observed for the explanation with regard to knowledge of the indication for surveillance (OR=3.6). This indicates that other specialists may have less knowledge about surveillance guidelines and / or provide less information. An endoscopy department should feel responsible for communicating the final results and follow-up plan to the patient. Moreover, the department must ascertain that the referrer is also properly informed about the final results and the follow-up recommendations.

The background of the patient may also play a role in information provision, which was underlined in a previous survey among asymptomatic patients evaluating knowledge about CRC in several European countries. These studies showed that awareness in CRC screening among various populations is low.[18, 19] Effective strategies to increase the patient's awareness and their subsequent adherence to primary CRC screening have been proposed such as one-on-one interactions, use of extensive public awareness campaigns, motivation by general physicians, (intensive in-person contact with patients by a health care provider), or providing physician reminder letters but with variable success.[20] Information provision to referrer and

patients should and can be improved, both in whether surveillance would be required and the explanation with regard to the indication.[21-23] It should be noted that participants pointed at single sources of information for immediate post-endoscopy or final information, but that this may have come from additional sources as well.

The question is whether improved awareness of patients on indication and interval of their surveillance increases attendance for surveillance. A previous study suggested that improvement of patient knowledge could be one of the targets to increase the uptake of follow-up appointments for surveillance practice.[8] The lack of information provision to the patient about necessity of surveillance may be associated with non-attendance for follow-up colonoscopy.[9, 10] Our overall attendance rate for surveillance colonoscopy of our random sample of adenoma patients was 72%. This measure of attendance seems in concordance with previous reports.[7-9] Based on our results, the awareness whether patients recalled if and why surveillance was needed, was not associated with department specific attendance rates for surveillance. Our data thus suggest that improving awareness would not necessarily increase patient attendance rates within endoscopy departments and therefore the efficacy of a bowel cancer screening program. However, as attendance was not directly calculated from the awareness survey population, these conclusions should be taken with caution.

Patients who were recommended to undergo surveillance at short interval more often recalled a longer interval than recommended, whereas the opposite was observed among patients who were recommended surveillance with long interval. For improving surveillance adherence on a physician-level, it may be hypothesized that the lack of concordance between recalled surveillance intervals by patients and the physician- and guideline intervals reflect non-appropriate recommendations for surveillance intervals by the endoscopist. In this context previous research showed that the adherence to the surveillance guidelines by endoscopists is not optimal.[4-6, 16] An explanation may be that Dutch endoscopists feel more confident in applying more recent, international surveillance guidelines endorsed by different societies, as the Dutch guidelines are conservative and the evidence about differences in risk of adenoma recurrence has emerged since the publication of the Dutch guidelines.[3, 14] Another target for improvement in surveillance on physician-level has been recently described in terms of improving patient attendance using an automatic alerting system for follow-up appointments in surveillance colonoscopy.[13] In our study the attendance rates were indeed significantly higher in departments with a polyp follow-up reminder system compared to those departments without (84 vs. 67%, $p<0.001$) which seems to support this observation.

Although our multicenter study had strengths such as a high response and a large population, some limitations must also be addressed. Recall bias may have easily occurred as the time interval between the colonoscopy and the administration of the survey was approximately 12 months. Additionally, the intervals recalled by patients were compared to intervals based on the recommendation of the physician or in its absence on the guideline, and may therefore deviate from the actual recommended interval as in endoscopy reports

no pathology information is available yet. Further, the attendance measure may be biased to reflect the actual attendance for surveillance colonoscopy in terms of either overestimation or underestimation. Patients were identified using a reimbursement system that was implemented in the beginning of 2004. However, the identified patients were randomly selected to limit selection bias. Our observed association might be less reliable to draw solid conclusions of the current knowledge about surveillance and attendance rates in retrospect per department. We deliberately addressed awareness and actual attendance in two separate patient groups, as assessing awareness prior to scheduled attendance is likely to interfere with actual attendance

In conclusion, the awareness of surveillance recommendations in a large cohort of patients with adenomas was moderate. Attendance for surveillance per department seemed not associated with the patients' awareness whether surveillance colonoscopy would be required or the explanation with regard to the indication. Endoscopy departments should be responsible for informing the patient about the surveillance interval and standard protocols. This may be accompanied by the inclusion of written to make sure that patients have their follow-up plan available, hereby ensuring the highest quality of care in surveillance.

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Chapter 17

Colorectal cancer in post-liver transplant recipients

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ABSTRACT

Purpose: Several malignancies have been reported to occur more often after liver transplantation (LTx). Whether this is also true for colorectal carcinoma (CRC) is controversial. Our aims were (1) to compare the observed rate of CRC in a post-liver transplant cohort with incidence data from the general Dutch population, and (2) to stratify for patients with and without primary sclerosing cholangitis (PSC), because PSC is well established as a risk factor for CRC.

Methods: Medical records of LTx patients who had an LTx in our center between 1986 and 2007, with a follow-up of at least 3 months were searched. Incidence data from the general population were retrieved from the Dutch Comprehensive Cancer Registry. Outcome measures were defined as Standardized Incidence Ratio (SIR) and incidence rate per 100,000 person-years (pyr).

Results: 394 Patients (58% men, mean age at LTx 46.6 yrs) were included in 1986-2007. Bowel investigation pre-LTx had been performed in 73% of patients. Median follow-up was 5.1 years (0.25-20 years). The mean age at end of follow-up was 52 years (SD 13 years). Four patients (1%) were during follow-up diagnosed with CRC. The overall SIR for CRC in post-LTx recipients was 2.16 (95% CI: 0.81-5.76) compared to the general population and 1.26 (95% CI: 0.31-5.07) for non-PSC post-LTx recipients.

Conclusion: This study suggests that the incidence of CRC is not increased non-PSC post-liver transplants compared to the general population. A more intense CRC surveillance program based on this result remains controversial in non-PSC post-liver transplant recipients.

INTRODUCTION

Liver transplantation (LTx) is being performed in a steadily increasing number of patients for end stage liver disease. Although the intervention is nowadays related with a good long-term prognosis, it is associated with several potentially life-threatening long-term complications. One of these is the development of de novo malignancy associated with prolonged marked immunosuppression. Malignancies have been reported to occur with a cumulative incidence of 5 to 16% in different post-LTx follow-up series.[1] There are contradictory reports on whether colorectal cancer (CRC) is among the neoplasma occurring at higher frequency post-LTx compared to the general population. In a Dutch LTx cohort of 174 recipients a considerably increased risk of CRC was reported compared to the general population (relative risk [RR] of 12.5).[2] However, other studies suggested that the overall incidence of CRC after LTx did not differ from the general population.[3-6]

An indication for LTx is primary sclerosing cholangitis (PSC). It has been acknowledged that PSC patients have a markedly increased CRC risk.[7, 8] PSC is associated with ulcerative colitis (UC) which by itself is also identified as a risk factor for colorectal neoplasia. Therefore, guidelines have been created for colonoscopy surveillance in PSC patients.[9-11] However, quantitative outcome measures in risk assessment for non-PSC post-LTx recipients are lacking in previous published studies. Therefore, it has not been established whether non-PSC LTx recipients belong to a high risk population as well and need more vigilant CRC surveillance. The aims of this study were (1) to compare the observed rate of CRC in a post-LTx cohort with incidence data from the general Dutch population, and (2) to stratify for patients with and without PSC.

METHODS

The LTx database was used to identify all LTx patients treated in the Erasmus MC in the period October 1986 till October 2007. Follow-up time was started from day of transplantation. All medical records of patients with a follow-up of at least 3 months were searched. Patients who developed colorectal cancer within 12 months after LTx were excluded because they were assumed to be unrelated to the LTx. PSC patients with ulcerative colitis (UC) were evaluated separately because of the known increased risk of CRC.

The following data were obtained: date of birth, medical history, date and number of LTx, date and type of malignancies, and date/cause of death. Furthermore, results of the most recent bowel investigation prior to LTx were obtained, if available. Data about the bowel investigations pre-LTx were recorded, including data about the polypectomy, number of adenoma, histology and grade of dysplasia. Patients with more than one lesion were categorized to the most advanced lesion. Advanced adenoma was defined as an adenoma with a

diameter of 10 mm or more; an adenoma with a villous component (i.e. at least 25% villous) or an adenoma with high-grade dysplasia.[12] Furthermore, data about family history of CRC (first and second degree relatives) were obtained from the medical records. Colonoscopies or sigmoidoscopies combined with a barium enema were considered as a pre-transplant screening bowel investigation of the colon. Results of bowel investigations were investigated for patients with acute and subacute or chronic liver failure necessitating LTx. The definition of acute liver failure was described according to O'Grady as hepatic encephalopathy between 8 and 28 days after the onset of jaundice.[13]

Time-dependent age- and sex-specific CRC incidence rates within the general Dutch population were retrieved from the Dutch Comprehensive Cancer Centre.[14] The incidence rate in 2005 was used for the specific age range of our transplant cohort. The total years of follow-up were summed for each age-adjusted incidence category. The expected CRC incidence per person-year for each age category was calculated and multiplied with the follow-up time of each age class in the cohort. Using this method, expected cases of CRC were calculated and compared with the observed numbers of CRC providing a Standardized Incidence Ratio (SIR).[15] This was done for the overall transplant cohort, the non-PSC cohort and the PSC post-LTx cohort. The incidence rate was expressed as cases per 100,000 person-years (pyr).

RESULTS

The LTx database contained 474 patients transplanted between October 1986 and October 2007. Eighty patients were excluded because of a follow-up shorter than 3 months. There were no patients with CRC within 12 months of LTx. A total of 394 patients (227 men [58%]) were included in the cohort. PSC had been diagnosed in 64 cases (16.2%) including 38 patients with both PSC and UC (60%). In the non-PSC population, there were 3 UC patients (0.9%).

Colonoscopy or barium enema combined with sigmoidoscopy pre-LTx was performed in 73% (n=288) of patients. A pre-LTx bowel investigation had been performed in 4.5% (n=3/67) of patients with acute liver failure and in 87% (n=285/327) of patients with 'subacute or chronic indications for LTx'. Table 1 shows the patient characteristics. Pre-LTx bowel investigation using sigmoidoscopy and barium enema was performed in 120 patients and 168 patients underwent a colonoscopy. Data about the presence and characteristics of adenomas prior LTx are given in Table 2. All of them were removed by polypectomy. In 36 of the 288 patients with pre-LTx bowel investigations, one or more adenomas were detected during the pre-LTx bowel investigation. Advanced neoplasia was found in 2.1% patients with pre-LTx bowel investigation (n=6/288). Two patients had a history of adenoma which were not detected in the screening pre-LTx bowel investigation. Concerning family history for CRC, three of the 394 included transplant recipients had at least one relative diagnosed with CRC. None of these 3 patients had adenoma detected during bowel investigation(s) before LTx.

Table 1. Liver transplant recipients characteristics (n=394)

Mean age at LTx in years (SD)	**46.6 (±12.3)**
Male	227 (58%)
Mortality	n = 81/394 (20.1%)
Infection	n = 26
Malignancies	n = 30
Other causes	n = 25
Mean age survivors in years (SD)	52.8 (±12.8)
Median follow up [range] years	5.1 [0.25-20]
PSC population	n = 64
and UC	n = 38/64 (60%)
Type of pre-LTx bowel investigation (n=288)	
Sigmoidoscopy + Barium enema	n = 120/288 (42%)
Colonoscopy	n = 168/288 (58%)
Pre-LTx bowel investigation by LTx indication	
Acute indication LTx	n = 3/67 (4.5%)
Subacute/chronic indication LTx	n = 285/327 (87.5%)
Observed events CRC	n = 4
PSC - non UC	n = 0
PSC and UC	n = 2
Non-PSC - non UC	n = 2

CRC, colorectal carcinoma; PSC, primary sclerosing cholangitis; UC, Ulcerative colitis.

During follow-up, 72 patients (18%) developed one or more malignancies, including 24 patients with skin malignancies (6.1%) and 14 with lymphatic malignancies (3.6%). A total of 4 patients (1%) was diagnosed with CRC. Two PSC (both UC) patients developed CRC at an age 55 and 37 respectively while under colonoscopy surveillance after 1.1 and 1.7 years. One of them had a tubulovillous adenoma with low grade dysplasia found at pre-LTx colonoscopy that was removed. Two non-PSC (both non-UC) patients developed CRC at 65 and 61 years of age, respectively 17 and 1.3 year after LTx. None of these two patients had a bowel investigation prior to LTx.

Table 2. Pre-transplant adenoma characteristics

Pre-transplant adenoma characteristics	**n (%)**
Number of patients with adenoma detected during pre-LTx bowel investigation	n = 36/288 (12.5%)
Histology	
Tubular adenoma	n = 26/36 (72.2%)
Tubulovillous adenoma	n = 4/36 (11.1%)
Villous adenoma	n = 1/36 (2.8%)
Not further specified	n = 5/36 (13.9%)
Grade of dysplasia	
Low	n = 30/36 (83.3%)
High	n = 1/36 (2.8%)
Not further specified	n = 5/36 (13.9%)
Size ≥ 10 mm	n = 2/36 (5.6%)
Number of patients with advanced adenoma during pre-LTx bowel investigation	n = 6/288 (2.1%)

Using the CRC incidence rates in the general population and total follow-up time in years in our cohort, 1.85 CRC cases were expected. A total of 4 CRC cases was observed (incidence rate of 170 cases per 100,000 pyr) giving a SIR of 2.16 (95% CI: 0.81-5.76; p=0.172). When excluding the 2 PSC cases, the expected CRC cases were 1.59 compared to 2 observed non-PSC CRC cases (101 cases per 100,000 pyr). This yielded a SIR of 1.26 (95% CI: 0.31-5.03; p=0.314) for the non-PSC post-LTx recipients (Table 3). For the PSC LTx recipients, 0.25 cases would be expected compared to 2 observed CRC cases in this group. The SIR for the PSC LTx recipients yielded 8.0 (95% CI: 2.0-32.0; p=0.0003) corresponding with an incidence rate of 546 cases per 100,000 pyr.

Table 3. Risk Post-transplant

	Population		
	Overall LTx	Non-PSC LTx	PSC LTx
Person-years (pyr)	2353	1987	366
Observed events	4	2	2
Expected events	1.85	1.60	0.25
SIR	2.16	1.26	8.0
95 % CI	0.81-5.76	0.31-5.03	2.0-32.0

SIR, Standardized Incidence Ratio; pyr, person-years; PSC, primary sclerosing cholangitis; CI, confidence interval.

DISCUSSION

This cohort study shows that the age- and gender-specific incidence rate of CRC in our LTx patients was two-fold increased compared to the age-and gender-adjusted incidence rate of CRC in the general Dutch population, but not significant. Stratified analyses for the PSC group showed a significantly increased SIR compared to the age adjusted general population. The non-PSC liver graft recipients showed no significant difference in SIR for developing CRC compared with the age adjusted general population (SIR: 1.26 [95% CI: 0.31-5.03]; p=0.314). In contrast, a previous Dutch study found a RR for developing CRC of 12.5 (95%CI: 2.5-36.6).[2] None of these CRC cases did occur in PSC liver graft recipients. This result is in line with a study from England presenting a higher SIR for CRC in LTx patients without UC (SIR 3.47 [95% CI: 2.90-7.74]) than in the general population. No stratified analysis was done for non-PSC LTx patients.[16] A Canadian cohort study which used the Canadian Organ Replacement Registry also reported an increased risk of 2.6 [95% CI: 1.4-4.4] for CRC in 2034 LTx recipients compared to the general population.[17] However, no stratified analyses for PSC or UC were performed and therefore no conclusion can be drawn about the CRC risk among non-PSC patients. On the other hand, two studies from the USA did not find an increased CRC risk in LTx recipients which supports our data.[4, 18]

The reason for these differences in reported CRC risk is unclear, but the different sample sizes between these studies might be an explanation. A higher CRC risk in PSC patients with (quiescent) UC is well documented.[19, 20] Also among PSC LTx patients the incidence rate of CRC is higher compared to non-PSC LTx patients.[21] Therefore, guidelines advise that PSC and UC patients should be screened by colonoscopy annually post transplantation to detect CRC in an early stage.[10, 11]

However, to establish the risk for CRC in non-PSC LTx recipients stratified analyses for PSC and non-PSC LTx recipients are important. A possible explanation for the low incidence rate in our study may be the selection of liver graft recipients. Most of our patients had undergone a bowel investigation pre-LTx. If adenoma were detected pre-LTx, polypectomy and follow-up according to the surveillance guidelines was performed.[22] In the study from England a pre-LTx colonoscopy was performed only in patients with an indication for colonoscopy, which could result in a different baseline risk.[16] The pre-LTx findings in terms of advanced adenoma in this cohort (2.1%) seem to be in concordance with advanced adenoma findings in the general Dutch population for asymptomatic individuals (2.0%).[23] In our cohort, only 3 of the 394 patients reported a positive family history. A Dutch study investigated the frequency of family history in the general Dutch population. Within a random cohort among the Dutch population (age range: 45-70 years) a proportion of 11.2% in individuals unaffected for CRC, had at least one first degree relative diagnosed with CRC.[24] We found a positive family history for CRC in only 0.8% of patients, so a positive family history for CRC was not of relevance in our cohort. The low number of positive family history might partly be explained by under-reporting of family history in the medical records.

Furthermore different immunosuppression regimens in different cohorts may have played a role. However, we did not capture and analyze this type of data in our study and a comparison with other reported studies is difficult because of the paucity of data on immunosuppression in most reported series. Long term use of immunosuppressive regimens has been supposed to promote de novo development of malignancies after organ transplantation.[25] Of note, 3 of the 4 CRC cases in our cohort were diagnosed within 2 years post-transplant. This interval appears to be short to confidently relate the appearance of cancer with immunosuppressive therapy. Two of these cancers occurred in patients with PSC and UC. Both patients had undergone a bowel investigation pre-LTx, so there is a chance that early neoplastic lesions were missed. As CRC in UC patients may develop from flat lesions in an inflamed mucosa, false-negative endoscopy is a known problem.[26] Additionally, 1 non-PSC recipient developed CRC 1.3 year post LTx. No pre-LTx bowel investigation was performed which makes it more plausible that a premalignant lesion did already existed pre-LTx.

One of the limitations of our study is the small sample size. Additionally, a colonoscopy was not performed in all post-LTx patients. Asymptomatic CRC might thus have been missed, although this was partially covered by the long-term follow-up.

CONCLUSION

This study shows that the incidence of CRC was not significantly increased in a cohort of non-PSC LTx patients compared to the general population, whereas the CRC incidence was significantly increased in the PSC LTx group. Based on our data, it remains controversial to qualify non-PSC post-LTx recipients as a high risk population for CRC and to adjust the current screening guidelines for these patients. Because our negative findings may have been due to a small sample size, it should be encouraged to obtain stronger evidence for identification of high-risk post-LTx patients for CRC. For that purpose a large prospective study evaluating the yield of a post-LTx colonoscopy needs to be performed.

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Chapter 18

Risk of colorectal carcinoma in post-liver transplant patients: a systematic review and meta-analysis

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ABSTRACT

Liver transplant patients (LTx) have an increased risk for developing de novo malignancies, but for colorectal cancer (CRC) this risk is less clear. We aimed to determine whether the CRC risk post-LTx was increased. A systematic search was performed in MEDLINE and Cochrane databases to identify studies published between 1986 and 2008 reporting on the risk of CRC postLTx. The outcomes were (1) CRC incidence rate (IR per 100 000 person-years (PY)) compared to a weighted age-matched control population using SEER and (2) relative risk (RR) for CRC compared to the general population. If no RR data were available, the RR was estimated using SEER. Twenty-nine studies were included. The overall post-LTx IR was 119 (95% CI 88–161) per 100 000 PY. The overall RR was 2.6 (95% CI 1.7–4.1). The non-primary sclerosing cholangitis (PSC) IR was 129 per 100 000 PY (95% CI 81–207). Compared to SEER (71 per 100 000 PY), the non-PSC RR was 1.8 (95% CI 1.1–2.9). In conclusion, the overall transplants and the subgroup non-PSC transplants have an increased CRC risk compared to the general population. However, in contrast to PSC, non-PSC transplants do not need an intensified screening strategy compared to the general population until a prospective study further defines recommendations.

INTRODUCTION

Liver transplantation (LTx) patients are at an increased risk of developing a variety of cancers, especially skin malignancies and lymphomas.[1] Reports published in the last decade have however shown conflicting results with respect to the colorectal cancer (CRC) risk after LTx.[2,3] Two studies suggested no increased risk for CRC post-LTx.[4,5] However, a Dutch cohort study reported a relative risk (RR) of 12.5 (95% CI 2.5–36.6) for CRC in post-LTx patients compared to an age-matched general population.[6] Furthermore, a study from the University of Cincinnati reported a lower age of onset of CRC after LTx and a decreased 5-year survival compared with the general population.[7]

A markedly increased risk of CRC is well established in patients with primary sclerosing cholangitis (PSC) with associated ulcerative colitis (UC).[8,9] These patients even have an increased CRC risk compared to patients with UC alone, which itself is a known risk factor for the development of CRC.[8,10,11] Given this increased risk, special guidelines exist for surveillance colonoscopy in PSC patients irrespective of LTx.[12-14]

Currently, there are no conclusive recommendations for CRC screening in non-PSC post-LTx patients. This meta-analysis, therefore, aimed to determine whether the relative risk (RR) and incidence rate (IR) of CRC are increased in post-LTx patients in general, and specifically in non-PSC post-LTx patients, compared to the general population.

METHODS

A comprehensive literature search was performed using MEDLINE and the Cochrane Library from 1986 until November 2008. The Medical Subject Heading (MeSH) terms used were 'liver transplantation', 'organ transplantation', 'transplantation', 'colorectal neoplasms', 'neoplasms', 'follow-up studies', 'cohort studies', 'incidence' and 'risk'. Additionally, the 'related articles' feature was used to locate other relevant studies. Finally, a hand search of the references from eligible studies was performed to check for additional potentially relevant studies for inclusion. The full texts of all eligible studies were obtained via the medical library available at one of our institutions if only an abstract was available online.

Inclusion and exclusion criteria

To be eligible, studies could be randomized controlled trials or prospective or retrospective cohort studies. Sufficient data on incidence or risk of CRC had to be provided, such as the 10-year IR, standardized incidence ratio, cases per person-years (PY) of follow-up, RR, or observed cases of CRC in LTx patients and follow-up. Studies that did report the data from transplantation patients in general, but did report separately observed cases of CRC in post-

LTx patients, were also included in the study. Cohort size had to be specified in order to be able to obtain the IR.

The following exclusion criteria were used: case-control studies, case series and case reports (excluded because lacking sufficient data for meta-analysis); studies that did not specify cancers by anatomical site (e.g. mentioned gastrointestinal malignancies but not explicitly CRC); studies investigating CRC incidence in a transplanted PSC and/or UC population; and studies involving only pediatric patients.

Quality assessment

A data quality score (DQS) system was created to assess the quality of the included studies. Two reviewers (JSN and VdJ) rated the quality of the included studies independently. In case of disagreement, consensus was achieved by discussion with a third adjudicator (SvZ). The DQS consisted of fourteen simple yes-or-no questions (see Table 1) and is partially based on the Newcastle-Ottawa Quality Assessment scale for cohort studies.[15] Each study could obtain a maximum of 16 points. For each criterion, studies could receive 0, 0.5 or 1 point depending on absent, partial or complete fulfillment. Additional points were awarded for study design (randomized controlled trials and prospective cohort studies 2 points; retrospective cohort studies 1 point) and for reporting whether screening colonoscopy was performed. Studies were deemed to be of high quality (HQ) if they received ≥10.5 points, medium quality (MQ) if ≥6.5 or ≤10 points were achieved and low quality (LQ) if ≤6 points were given.

Table 1. Data Quality Score (DQS) system with the possible points per yes/no question

1.	Study Design: prospective-(3), Retrospective(2) analysis
2.	Cohort size exceeding 100 patients
3.	Baseline characteristics for sex distribution and age reported (only one of them described: 0.5 point)
4.	Indication for LTx given
5.	Information of immunosuppressant agents
6.	Clear statement of mean FU time of LTx patients
7.	Patients with CRC diagnosed within 1 year after LTx were reported separately
8.	It is made clear how CRC diagnosis was made (by symptoms or by screening)
9.	If screening was done were all patients screened or number of patients screened was reported?
10.	Within cohort total number of PSC cases is described as indication of LTx
11.	PSC cases were analyzed separately
12.	Patients with UC were stratified and separately analyzed
13.	CRC incidence in cohort were compared with incidence in general population
14.	Patients with CRC or other solid organ tumors before LTx (and possible recurrence) were reported separately

Data extraction

All extracted data were organized into a data extraction table. For each study the population size with the proportion of PSC patients, age of LTx, the length of follow-up, the number of CRC cases for the overall LTx cohort and the non-PSC patients were extracted, if available.

If a duplicate study was identified and if uncertainty existed whether study populations did overlap, the study providing the most relevant data was included for analysis. Data from our own institute (Erasmus MC University Medical Center in Rotterdam, the Netherlands) were also included in the analysis.[16] When studies lacked sufficiently detailed data, attempts were made to contact the corresponding authors by formal letter and email to obtain missing information.

Statistical analysis

The main outcome measures for the pooled analyses were (1) CRC IR per 100 000 PY of follow-up and (2) the RR for CRC compared to the general population. The IR was calculated for each study that gave a mean follow-up of the entire cohort or the person-years of follow-up and the number of observed cases of CRC. When the counts of CRC were zero, a correction of 0.5 was added to the number of cases and total follow-up in person-years, as has been previously described.[17, 18] The pooled IR of the included studies was calculated in two ways: (1) the IR for the entire study cohort (all LTx indications included), and (2) the IR stratified for non-PSC post-LTx patients. To obtain a comparison for the pooled IR in post-LTx patients, an age-matched control IR for CRC was created based on data from the NCI SEER database. This is the national electronic database for reporting cancers for the general population in the United States.[19] The age at the end of follow-up was determined in the studies where the age of LTx and mean follow-up could be obtained. Using the age at the end of follow-up of the Rotterdam LTx cohort, we found a normal distribution (mean age 52 years; standard deviation [SD] 12.8 years).[16] The mean age of the other studies was estimated by means of study-specific descriptions of the age distribution (mean and SD, or mean only, with the use of the SD of the Rotterdam data), a technique used in a previous study.[20] For each 5-year age category, the proportion of patients was determined and then multiplied by the corresponding SEER IR for this age category to obtain a study age-weighted IR. The 5-year age categories from the SEER database from 30 to 75 years were used. Finally, the study-specific age-matched control rates were combined to obtain an overall weighted age-matched control population for the pooled IR analyses. A specific weighted age-matched control IR was calculated for the overall IR post-LTx pooled estimate as well as for the non-PSC post-LTx pooled estimate. This was done using only the relevant studies, which were also included in the relevant pooled IR analysis. These two overall weighted age-matched control IRs with corresponding 95% confidence interval were calculated using the Jackknife Bootstrap resampling proce-

dure, where the weight factor was the sample size with the corresponding study-specific age-matched IR.[21] A pooled estimate of the RR for CRC in post-LTx patients compared to the general population was performed in studies that gave the necessary data. When no formal RR meta-analysis could be performed, an extracted RR was calculated using the weighted age-matched control IR based on the SEER and used for comparison to the general population. Because of possible heterogeneity between studies, a random-effects model was used for pooling both the IR and the RR.[22] Confidence intervals were obtained using the Poisson distribution. The I2 statistic was used to provide an estimate of the percentage of variability in results across studies that is likely due to true differences in RR or IR, as opposed to by chance (ranging from 0 to 100%, with 0% indicating no heterogeneity).[23] A sensitivity analysis was performed to test the impact of each study by removing each study from the analysis separately and recalculating the pooled estimates. Publication bias was tested using the Egger's test.[24] If this was significant, a scatter plot was performed. The IRs of studies were plotted against the corresponding person-years mean follow-up time. If publication bias is present, the line has a negative slope. Statistical analyses were performed using STATA, version 9.2.[25]

RESULTS

Study selection

The primary search strategy identified 1490 articles. After scanning all relevant abstracts, 1444 articles were excluded (reasons stated in Figure 1). Nine duplicate reports[26-34] were identified, which reported results from the same transplant center, and only the ones giving the most relevant information were included.[2, 3, 35-39] By hand searching, another 20 articles were identified. When the exclusion criteria were applied, the final 29 studies were included for review (Figure 1). The quality scores according to the DQS results are shown in Tables 2 (HQ), 3 (MQ) and 4 (LQ). Six studies[2, 6, 16, 35, 36, 40] were of high, 15 of medium[3, 39, 41-53] and 8 of low quality according to the DQS.[37, 38, 54-59] A pretransplantation screening protocol for LTx evaluation was mentioned in 2 studies.[16, 35] In the Rotterdam center, pretransplant colon evaluation was part of the standard workup for LTx. Seventy-three percent of all patients were screened pretransplantation in this cohort.[16] A study from Spain performed pretransplant colonoscopy in patients who were 50 years or older. No data were given about the number screened.[35]

Post-LTx screening colonoscopies were offered to a subgroup of patients in only 2 studies.[35, 50] One of them listed a specific reason to screen among their patients. In this study, colonoscopy was offered as part of a posttransplant surveillance program. Details regarding the proportion of individuals receiving screening, the intensity of screening and the findings during follow-up were insufficiently reported by this study.[35] The other study reported about 92 asymptomatic patients who received a colonoscopy ≥5 years post-LTx. Although CRC was

Figure 1. Flowchart of article selection

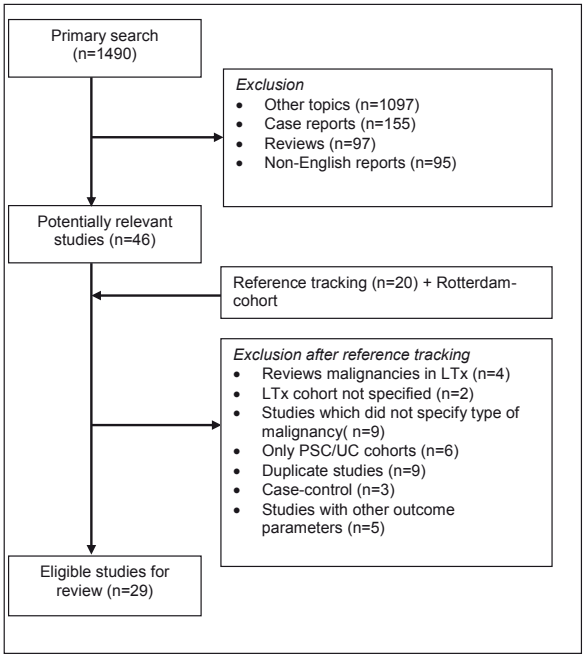


Table 2. High Quality studies

HQ Study	Country	Total cohort BE	PSC cohort BE	Age LTx	Mean/ Median FU	Total observed CRC	Observed CRC in PSC	CI CRC total cohort	CI CRC in non-PSC cohort
Kelly (1998)	USA	N=888	N=72	--	4.4	N=3	N=1	(3/888=) 0.34%	(2/816=) 0.25%
Jain (1998)	USA	N=1000	N=60	42.4	6.5	N=4	N=1	(4/1000=) 0.4%	(3/940=) 0.32%
Haagsma (2001)*	Netherlands	N=174	N=29	43	6.1	N=3	N=0	(3/174=) 1.73%	(3/145=) 2.1%
Aberg (2008)*	Finland	N=540	N=74	43	6.3	N=2	N=1	(2/540=) 0.37%	(1/466=) 0.22%
Herrero (2008)*	Spain	N=280	N=1	56	6.5	N=4	N=0	(4/280=) 1.43%	(4/280=) 1.43%
Sint Nicolaas	Netherlands	N=394	N=64	46.6	5.9	N=4	N=2	(4/394=) 1.0%	(2/330=) 0.6%

All ages and FU in years

CRC = colorectal cancer; PSC=Primary Sclerosing Cholangitis, BE=Baseline; FU=follow up in years; CI=cumulative incidence. * = data provided by authors.

Table 3. Medium Quality studies

MQ Study	Country	Total cohort BE	PSC cohort BE	Age LTx	Mean/ Median FU	Total observed CRC	Observed CRC in PSC	CI CRC total cohort	CI CRC in non-PSC cohort
Jonas (1997)	Germany	N=458	N=28	46	4.2[1]	N=0	N=0	0%	0%
Peyregene (1998)	France	N=330	N=6	45.8	--	N=2	N=0	(2/330=) 0.61%	(2/324=) 0.62%
Xiol (2001)	Spain	N=137	N=3	48.9	5.8[1]	N=2	--	(2/137=) 1.46%	--
Saigal (2002)	UK	N=1140	--	51.5	5.9	N=1	N=1	(1/1140=) 0.1%	0%
Sanchez (2002)	USA	N=1421	--	49.7	5.7	N=8	--	(8/1421=) 0.56%	--
Baccarani (2006)*	Italy	N=202	N=1	50 [1]	6.7	N=0	N=0	0%	0%
Bennloch (2004)*	Spain	N=772	N=0	53	4.5	N=1	N=0	(1/772=) 0.13%	(1/772=) 0.13%
Oo (2005)*	UK	N=1778	N=197	--	5.5[1]	N=18	N=10	(18/1778=) 1.0%	(8/1581=) 0.5%
Aseni (2006)	Italy	N=502	--	46	8.2	N=0	N=0	0%	0%
Aigner (2007)	Austria	N=757	--	--	--	N=4	--	(4/757=) 0.53%	--
Koornstra (2007)	Netherlands	N=92	N=20	--	11.1[1]	N=0	N=0	0%	0%
Johnson (2007)	USA	N=836	N=103	43.4[2]	9.3[2]	N=13	N=2	(13/836=) 1.6%	(11/733=) 1.5%
Dumortier (2007)	France	N=305	N=0	50[1]	5.3[1]	N=0	N=0	0%	0%
Boin (2007)*	Brazil	N=325	N=8	50.2	3.0	N=2	N=2	(2/325=) 0.62%	0%
Jiang (2008)	Canada	N=2034	N±200	--	--	N=14	--	(14/2034=)0.7%	--

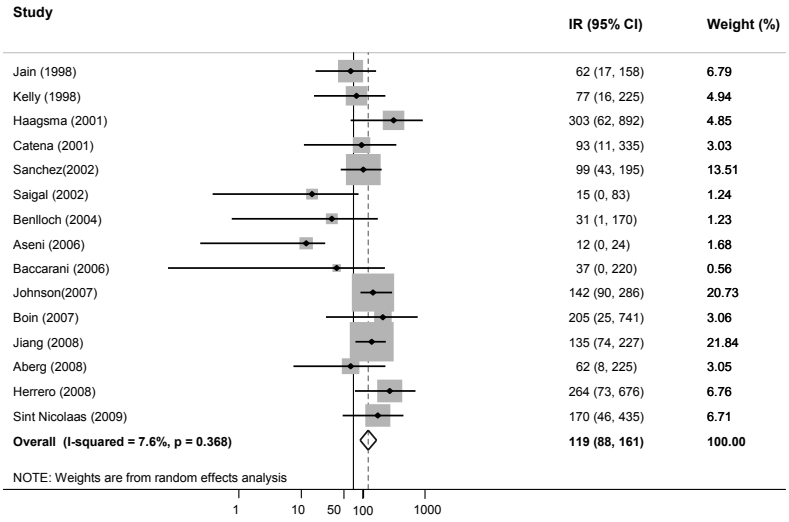
All ages and FU in years; 1= median follow up instead of mean follow up; 2= mean FU with kidney transplants included
CRC = colorectal cancer; PSC=Primary Sclerosing Cholangitis, BE=Baseline; FU=follow up in years; CI=cumulative incidence. * = data provided by authors.

Table 4. Low Quality studies.

LQ Study	Country	Total cohort BE	PSC cohort BE	Age LTx	Mean/ Median FU	Total observed CRC	Observed CRC in PSC	CI CRC total cohort	CI CRC in non-PSC cohort
Sheil (1995)	Australia	N=577	--	--	--	N=0	--	0%	0%
Penn (1996)	USA	N=324	--	--	--	N=18	N=6	(18/324=) 5.6%	--
Galve (1999)	Spain	N=1827	--	--	--	N=4	--	(4/1827=) 0.2%	--
Safadi (1999)	Israel	N=101	--	--	--	N=2	--	(2/101=) 1.98%	--
Catena (2001)	Italy	N=353	--	--	6.1	N=2	--	(2/353=) 0.57%	--
Jimenez (2002)	Spain	N=505	--	--	--	N=0	N=0	0%	0%
Schmilovitz (2003)	Israel	N=98	--	--	--	N=0	N=0	0%	0%
Romero (2006)	Spain	N=490	--	--	--	N=0	N=0	0%	0%

All ages and FU in years; 1= median follow up instead of mean follow up
CRC = colorectal cancer; PSC=Primary Sclerosing Cholangitis, BE=Baseline; FU=follow up in years; CI=cumulative incidence

Figure 2. Incidence rate CRC in overall post-LTx patients



IR=incidence rate in cases per 100 000 PY; bold line: weighted age-matched control IR (SEER)=77.9

not observed, the RR for advanced neoplasia was 8.9 for LTx compared to an asymptomatic cohort.[50] None of the other included studies gave data concerning other screening modalities such as barium enema or fecal occult blood test (FOBT). After attempts to contact all corresponding authors (n = 29) of included studies, 7 of them provided additional data for the overall cohort, non-PSC cohort and observed events, and mean follow-up.[3, 6, 35, 40, 43-45]

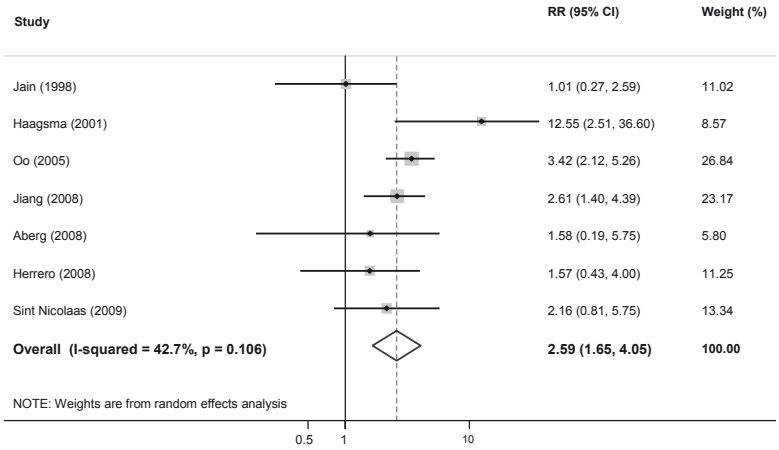
IR in overall post-LTx patients

A total of 15 studies[2, 3, 16, 35, 36, 39, 40, 42-45, 47, 48, 52, 54] (6 HQ, 8 MQ and 1 LQ) allowed the calculation for a pooled IR (Figure 2). The pooled IR estimate for developing CRC in overall post-LTx patients was 119 (95% CI 88–161) cases per 100 000 PY. The I^2 statistic was 7.6% (p = 0.368), indicating low heterogeneity. The Egger's test was statistically significant (p = 0.07), meaning possible publication bias. The scatter plot showed a slight negative slope. Sensitivity analysis indicated no striking differences in the pooled estimate when studies were omitted from the analysis.

Weighted age-matched control IR for the overall IR pooled analysis:

In total, for 13 studies an age at the end of follow-up was extracted.[2, 3, 16, 35, 39, 40, 42-45, 47, 48, 52] In 2 of 13 studies, a standard deviation for age could also be extracted, resulting in a study-specific normal distribution.[35, 39] In one study, the distribution of the age at the end of follow-up was already provided.[47] For the other 10 studies, we used the variance of the Rotterdam LTx cohort (SD 12.8).[16] The study-specific weighted IR for the control population based on the NCI SEER

Figure 3. Relative risk of CRC for the overall post-LTx patients compared to the general population (RR = 1)



ranged between 52[2, 6, 40] and 127[35] cases per 100 000 PY. All the 13 studies were represented in the overall post-LTx IR, and therefore used to calculate the control IR for this analysis. After combining the 13 study-specific control IR values in the bootstrap, the appropriate overall weighted age-matched control IR yielded a CRC IR of 77.9 (95% CI 77.6–78.3) cases per 100 000 PY.

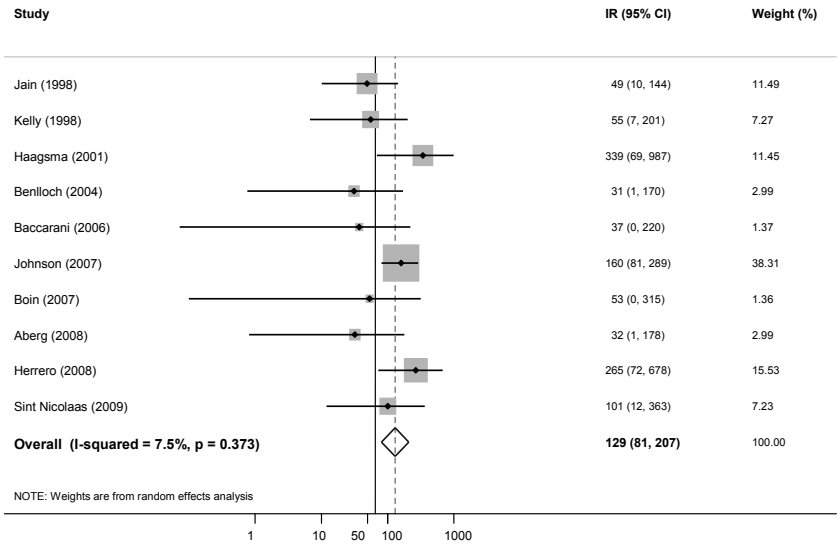
RR in overall post-LTx patients

For the pooled RR analysis (Figure 3), 7 studies[2, 3, 6, 16, 35, 40, 47] (5 HQ and 2 MQ) were included. The outcomes of 7 studies were reported as RR compared to the general population. For one study, the RR for colon cancer and rectal cancer were combined, which gave a CRC RR of 3.43 (95% CI 2.12–5.24).[3] The overall pooled RR for CRC in LTx patients was 2.59 (95% CI 1.65–4.05). I^2 was 42.7%, indicating moderate heterogeneity. The Egger's test was not significant (p = 0.571).

IR in non-PSC post-LTx patients

A pooled analysis (Figure 4) in the subgroup of nonPSC post-LTx patients was performed in the 10 studies that were eligible for this analysis.[2, 6, 16, 35, 36, 40, 43-45, 48] One of the included studies reported the mean follow-up period for the entire transplant cohort (i.e. kidney transplantation and liver transplantation) but did report the data for the LTx population separately (PSC stratification for baseline LTx cohort and observed CRC events).[48] The assumption was made that the mean follow-up of this study was overestimated because renal transplants usually have a longer follow-up period. Thus, person-years of follow-up will be overestimated for the LTx cohort (denominator of the IR) but will also result in an underestimation concerning the CRC IR for the LTx population. Therefore, this study was also included. After pooling the

Figure 4. Incidence rate of CRC for non-PSC LTx patients



IR=incidence rate in cases per 100 000 PY; bold line: weighted age-matched control IR (SEER)=71.2

10 studies (Figure 4), the IR of CRC in non-PSC post-LTx patients was 129 per 100 000 PY (95% CI 81–207). I2 statistic was 7.5% (p = 0.373). Sensitivity analysis indicated that one study (49) (weight in analysis: 38%) was predictive for this high IR (plot not shown). The Egger's test was significant (p = 0.08), meaning possible publication bias. The scatter plot (10 studies) IR against PY showed a negative slope, induced by 2 outliers that reported a higher IR. When the IRs of the 10 studies were plotted against the mean follow-up, a positive slope was observed.

Weighted age-matched control IR for the non-PSC IR pooled analysis

We were not able to extract data for a precise RR in non-PSC post-LTx patients in contrast to the overall post-LTx patients. Therefore, the weighted age-matched control IR for the non-PSC analysis was calculated separately. Nine[2, 6, 16, 35, 40, 43-45, 48] of the 13 studies, which could be used for the weighted age-matched control IR, were also represented in the non-PSC meta-analysis. After combining the nine study-specific weighted IR values in the bootstrap, the appropriate non-PSC weighted age-matched control IR yielded 71.2 cases per 100 000 PY (95% CI 70.6–71.8).

RR non-PSC post-LTx compared to the weighted age-matched control IR

Because it was not possible to extract a precise study specific RR for CRC in non-PSC LTx patients compared to the general population, in this case the non-PSC weighted age-matched control IR was used as the general population (71.2, 95% CI 70.6–71.8, cases per 100 000 PY).

The IR of CRC in non-PSC post-LTx patients was 129 (95% CI 81–207) cases per 100 000 PY. This corresponds with a significant RR estimate of 1.8 (95% CI 1.1–2.9) for the non-PSC post-LTx patients compared to the weighted age-matched control group based on the SEER. No clear relationship was observed in the RR/IR pooled analyses and the DQS of different studies.

DISCUSSION

The main objective of this meta-analysis was to determine whether the risk of CRC in the overall post-LTx population, as well as in the subgroup of non-PSC patients, is increased to the extent that separate surveillance recommendations are warranted. This is to our knowledge the first comprehensive pooled analysis estimating the risk of developing CRC after liver transplantation, stratified for presence or absence of PSC.

In our study we found a pooled IR rate of 119 (95% CI 88–161) cases per 100 000 PY and a pooled RR estimate of 2.59 (95% CI 1.65–4.05) for developing CRC for the overall post-LTx patient. This increased IR and RR may be explained by the well-known increased CRC risk of PSC patients. After excluding PSC patients, the IR was 129 cases per 100 000 PY (95% CI 81–207). This remains higher than expected compared to the pooled age-weighted IR based on the SEER database (71 per 100 000 PY). Compared to this control IR, an RR estimate of 1.8 (95% CI 1.1–2.9) was observed for non-PSC post-LTx patients.

A possible explanation for the increased risk of CRC in post-LTx patients is the long-term use of immunosuppressive therapy for the graft, as has been reported for other malignancies. Several studies reported that the overall incidence of malignancies such as post transplant lymphoproliferative disorder and Kaposi's sarcoma is increased after transplantation.[60-63] A possible mechanism for an increased incidence of colorectal neoplasia post-LTx was recently suggested through immune suppression-induced JC virus reactivation in colorectal mucosa/adenomas in LTx patients.[64]

A different explanation could be the presence of precursor lesions for CRC pretransplantation. Not every study reported whether pre-LTx colonoscopy was performed or reported the time interval between the LTx and diagnosis of CRC.

In contrast with our study, a review of investigators from England stated that the risk of CRC for non-PSC post-LTx patients is similar as the general population matched for age, gender and follow-up. Therefore, they concluded that non-PSC post-LTx patients should be classified as a population that should not require more intensified surveillance than the age-matched population in general.[4] This conclusion was however not based on a systematic review of the pooled available data. Our data are therefore more comprehensive and rigorous. Additionally, we received some missing data to perform the analyses after contacting the authors. Three studies are of particular interest, since they reported about LTx patients with a screening colonoscopy post-LTx. Two of these were case-control studies and therefore not included

in our review.[50, 65, 66] Only a limited number of patients did undergo screening colonoscopy. A study from the United States reported a higher observed prevalence for adenomatous polyps compared to healthy controls undergoing a colonoscopy (OR 4.5, 95% CI 1–21.2), but this case-control study included only 25 LTx cases and 50 controls and no malignancies were observed.[65] The other case-control study, also from the United States, reported 7.3% of advanced neoplasia in the 82 LTx patients compared to 1.2% in 82 controls from the general population.[66] A study from the Netherlands retrospectively identified 92 patients who underwent screening colonoscopy in a cohort of 381 post-LTx patients. No CRC cases were observed in these asymptomatic 92 patients, but the RR for advanced neoplasia (defined as an adenoma of at least 1 cm in size, an/or (tubulo) villous component, and/or high-grade dysplasia, or cancer) was 8.9 for LTx patients compared to a large asymptomatic cohort.[50]

Limitations

There are several potential limitations in the context of this meta-analysis. First, the quality of included studies varied based on reported data. In most studies a comparison with the general population was missing. Therefore, we chose to calculate a weighted age-matched control IR based on the NCI SEER database using the variance from the Rotterdam LTx cohort.[16, 19] It can be questioned whether this variance can be applied to the other studies because sample size varies between studies. Furthermore, the SEER applies to the US population and therefore these data may not be applicable to non-US studies, whereas we included four American studies and six European studies in the non-PSC analysis. We accepted this uncertainty in the knowledge that CRC IRs are similar in the United States and Western Europe.[67] The variance around the estimated IR from the SEER was also taken into account (resulting in a confidence interval for the control IR). This uncertainty was relatively unimportant in the confidence interval of the non-PSC IR, which was primarily affected by the size of the non-PSC studies. Reporting for pre-LTx screening protocols also varied between studies. In the Rotterdam cohort, 73% of LTx patients were screened in the pretransplant setting.[16] In some studies, pre-LTx colonoscopy was performed when an indication existed pretransplantation.[2, 3] In another study, a pre-LTx colonoscopy was standard protocol if patients were 50 years or older.[35] Unfortunately, neither the proportion of patients' pretransplantation screened nor the findings of adenoma/CRC in the pretransplant period were provided in these studies. Pre-LTx screening by colonoscopy could lead to a baseline risk reduction for CRC in LTx patients. Furthermore, some studies only provided the median follow-up of the cohort, which could not be included in the pooled analysis because the mean follow-up is necessary to calculate person-years. Besides this, stratification for non-PSC post-LTx patients was not always performed. To obtain more information about the non-PSC cohort, attempts were made to contact the corresponding authors of included studies. Unfortunately, not all authors provided us with the necessary data.

We found some suggestions for publication bias based on Egger's test (p = 0.07 for the overall CRC IR and p = 0.08 for CRC IR for non-PSC). This test may however be inappropriate with small sample sizes[68], and a regression scatter plot is preferable. For the non-PSC IR analysis, the scatter plot showed a slight negative slope (not shown). Two outliers were observed with a relatively small sample size.[6, 35] One of these two studies reported a mean age of LTx of 56 years.[35] This higher age could be a possible explanation for a higher observed IR of CRC in this cohort. Another explanation for the high IR could be the use of surveillance colonoscopy in this study.[35] Asymptomatic CRC will be missed when no colonoscopy is offered, leading to an underestimation for CRC in those studies. Given the sample sizes of the studies with post-LTx colonoscopy protocol[35, 50], the overall impact of these colonoscopy findings was limited on the outcome of our analyses.

Guidelines

Currently, there are surveillance CRC guidelines for PSC patients with or without transplantation, because of their well-known high risk of CRC. The guidelines are the same for all PSC patients, recommending annual surveillance colonoscopy irrespective of whether they had an LTx.[13, 14] Concerning non-PSC post-LTx patients, the small but increased risk may be an argument for institution of more intensive surveillance protocols than the standard screening for the general population. Several meta-analyses addressing the risk of CRC in individuals with a family history reported a pooled RR estimate of around 2.25 for an individual with at least one first degree relative for CRC at any age.[69, 70] The patients with a first-degree relative for CRC diagnosed at an age <50 years should be considered as a high-risk group (RR = 3) for CRC compared to the general population, and more vigilant screening is advised, resulting in the recommendation of a surveillance colonoscopy every 5 years.[71] The RR for individuals with one first-degree relative diagnosed with CRC above age 50 is 2, and for individuals with at least one second-degree relative this is 1.73.[69] According to the current guidelines, these patients should enter the same screening program as the general population.[71] The point estimate found in the current meta-analysis (RR 1.8) suggests that non-PSC liver transplant patients have a similar risk. However, because of the wide confidence interval and potential biases, no definite answer can be given whether non-PSC LTx patients should receive an intensified CRC surveillance or can participate in the screening programs for the general population. The answer to this question requires a large prospective cohort study evaluating the yield of a post-LTx colonoscopy.

Conclusions

Post-LTx patients have an increased risk for CRC, also in the subgroup of non-PSC post-LTx patients. This pooled increased risk estimate for CRC post-LTx may be too small to justify

the adoption of an intensified surveillance strategy in non-PSC liver transplant patients. The results should be taken with caution, because variations in results between different studies were observed. In conclusion, nonPSC liver transplant recipients do not need an intensified screening strategy compared to the general population until a prospective study further defines recommendations.

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Chapter 19

Colorectal carcinoma in the post-liver-transplant setting - a short overview

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ABSTRACT

Colorectal cancer (CRC) is a major health problem in the Western world. Certain high risk groups are recommended for more vigilant CRC screening and shorter surveillance intervals. There is no consensus whether liver transplant (LT) recipients should be classified as a high risk group for developing colorectal cancer in the post-transplant follow-up. LT recipients do have an increased risk for certain de novo malignancies including skin malignancy and post-transplant lympho-proliferative disorder (PTLD), but it remains controversial whether this also pertains to CRC. Several aspects should be taken into account when evaluating this aspect in post-LT patients. This review aims to provide the most updated evidence concerning CRC in the post-LT period. It focuses on defining high risk groups for CRC after LT, and provides an overview of the incidence of CRC post-LT, the role for pre-LT screening colonoscopy, and the results from post-liver transplant surveillance.

INTRODUCTION

Colorectal cancer (CRC) is the third most commonly diagnosed malignancy in the world.[1] Screening for CRC or its precursor lesions (adenomas) by endoscopy with polypectomy has been shown to reduce CRC incidence and mortality.[2, 3] More vigilant screening and surveillance by colonoscopy is recommended for certain high risk populations, for example patients with a positive family history for CRC and those with long-existing inflammatory bowel disease.[4-6] A group of patients that may potentially be classified to have a CRC risk in the same range as those with a positive family history are liver transplant (LT) recipients. Due to improved patient selection, better short- and mid-term outcomes, and advances in post-transplant management of these patients, long-term complications in terms of de novo malignancy become more apparent and clinically relevant.[7] This increased risk for malignancies (such as skin malignancies and post-transplant lympho-proliferative disorder [PTLD]) in LT recipients has been well documented.[8-10] As a result of these cancer complications in the post-LT follow-up, there is more attention to determine the usefulness of neoplasia surveillance programs in these patients.[11] Whether post-LT patients are also at increased risk for colorectal cancer is still controversial, and the need for more vigilant or different surveillance programs for CRC has not been determined. This short overview aims to provide the most updated evidence on the incidence of CRC in the post-liver transplant setting as well as the usefulness of pre-transplant colorectal cancer screening in a liver transplant candidate.

DEFINING HIGH RISK GROUPS: PSC AS RISK FACTOR FOR CRC POST-LT

Before providing an in-depth review about incidence and risk of CRC in the post-transplant setting, we will discuss certain LT populations that have a higher a priori risk for developing CRC. One indication for LT, primary sclerosing cholangitis (PSC), deserves special interest in this respect. PSC is strongly associated with ulcerative colitis (UC), which by itself is a risk factor for the development of CRC.[12] Approximately 75% of PSC patients suffer from (quiescent) UC.[13] Longer duration and greater extent of UC have been reported to be important predictors for risk of CRC in UC patients.[12, 14] Additionally, it has been reported that the risk for CRC in PSC-UC is excessive compared to UC alone.[15] An overview of studies investigating incidence rates of CRC in PSC LT recipients is given in Table 1.[16-23] The first reports that investigated relationships between PSC, UC and CRC in LT recipients were published in the early 90's.[18-20] Two large transplant studies published by a group in Birmingham (England) and Dallas (USA) reported an increased CRC risk in LT transplant recipients for PSC with associated UC.[16, 22] The Birmingham group determined three important factors for the development of CRC in PSC post-LT recipients in multi-variate analysis: age>45 years, a more than 10-year interval between UC diagnosis and LT, and the presence of polyps at colonoscopy.[16] The cumulative

Table 1. CRC Incidence rate in PSC post-LT recipients

Study (year)	Study cohort PSC (and UC) LT recipients N (N PSC/ N UC)	Mean FU yrs (Range)	Observed CRC N (%)
Higashi (1990)	33 (33/33)	NR	2 (5.6)
Bleday (1993)	27 (27/27)	3.3 (0.5 - 5.8)	3 (11.1)
Knechtle (1995)	41 (29/41)	NR (0.5 - 9)	3 (7.3)
Narumi (1995)	33 (16/33)	3.1 (0.5 - 6.1)	1 (3.0)
Loftus (1998)	57 (57/57)	*4.7* (0 - 10.0)	3 (5.3)
Fabia (1998)	108 (73/108)	NR (0.5-11.0)	5 (8.0)
Vera (2003)	152 (100/152)	NR	8 (5.3)
De Vrie (2003)	31 (18/31)	*5.2* (1.3 - 10.7)	2 (6.5)

PSC=Primary Sclerosing Cholangitis; UC=Ulcerative Colitis; FU=Follow-up; CRC=Colorectal Cancer; NR=Not Reported; *Italic* = median FU; yrs=years

CRC risk was 0% , 20%, and 38% at respectively 1,5, and 10 years in patients with 2 or three of these factors.[16] Interestingly, these two studies did not observe CRC events in patients who had PSC without UC. Another study reported that the annual incidence of CRC in PSC patients (with UC) after LT approximated 1.25%. According to this study, this translated into a fourfold increase in risk for CRC compared to a historical control group of PSC-UC patients with similar follow-up, but not treated with LT.[17] It has been suggested that UC in PSC may be a silent or quiescent disease, where a subclinical time span is present.[24] Therefore, it may be difficult to estimate the exact onset of the disease. For the reasons mentioned above, it is thus recommended to perform annual surveillance colonoscopy in PSC patients, irrespective of having a liver transplant.[6, 25]

INCIDENCE OF CRC POST-LT

It is important to stratify for high risk groups in LT patients for the determination of incidence rates that can be contributed to post-transplant influences. The incidence of CRC in post-LT recipients varies in the literature and most data are derived from retrospective studies. Well-designed prospective studies evaluating the risk of CRC in post-LT cohorts have not been conducted. A recent meta-analysis estimating the risk of CRC furthermore shows the lack of stratification of PSC/UC and non-PSC/UC post-LT recipients in retrospective series.[26] Furthermore, comparisons to the general population (expressed as relative risk [RR] or standardized incidence ratio [SIR]) are lacking in most studies whereas in a large proportion of studies the relevant follow-up data that are necessary to obtain incidence rates, is missing. The studies with a large follow-up from the meta-analysis are listed in Table 2.[8, 10, 11, 27-36] A Canadian study involving 2034 LT recipients found a 2.5 fold increased risk for CRC (95%CI: 1.4 – 4.4) in post-LT recipients compared to the general Canadian population with a considerable follow-up period (10,370 person-years).[33] However, the authors from this study were not able to stratify for PSC and non-PSC LT recipients in the outcome measures for CRC. A study from the University

Table 2. Cohort studies on CRC Incidence in post-LT recipients

Study (year)	Cohort N	FU yrs	Observed CRC N	Non-PSC CRC N
Jonas (1997)	458	*4.2*	0	0
Jain (1998)	1000	6.5	4	3
Kelly (1998)	888	4.4	3	2
Haagsma (2001)	174	6.1	3	3
Xiol (2001)	137	*5.8*	2	NR
Sanchez (2002)	1421	5.7	8	NR
Oo (2005)	1778	*5.5*	18	8
Johnson (2007)	836	9.3[1]	13	11
Jiang (2008)	2034	10,370 PY	14	NR
Aberg (2008)	540	6.3	2	1
Albright (2009)	402	NR	3	3
Herrero (2009)	280	1,515 PY	4	4
Sint Nicolaas (2010)	394	*5.1*	4	2

FU=Follow-up; CRC=colorectal cancer; PY=Person-years; NR=Not Reported; *Italic*=median FU; [1]=overall transplant FU; yrs=years

of Wisconsin (USA) confirmed these results in CRC for overall transplants (mean FU of 9.3 years), where 13 CRC (2 events in PSC patients) were observed in 836 liver transplants.[10] A large cohort in England reported a SIR of 3.47 for LT recipients without ulcerative colitis (UC) compared to the general population, and a study from the Netherlands observed a 12.5-fold (95%CI: 2.5-36.6) increased CRC risk in a cohort of 174 liver transplants with a follow-up > 1 year) compared to the general population.[8, 32] In this study, none of the cancers occurred in PSC patients. These findings contrasted with results from Pittsburgh (USA), where a SIR of 1.06 for CRC was observed compared to the general population.[29] Some other studies also found low CRC incidences but without comparison to the general population.[22, 28, 30] A recent Dutch study substantiated these results with a SIR for non-PSC post-LT recipients of 1.26 compared to the age and gender adjusted general population.[35]

One of the problems with the published data on CRC incidence in post-LT patients is the lack of statistical power in most studies, as a large number of observed events are needed to provide a valid risk estimate. Therefore, the recent meta-analysis aimed to determine the pooled incidence and risk of CRC for non-PSC LT recipients, where the NCI SEER database from the United States was used to derive an age-matched control population. A pooled CRC incidence rate of 129 cases per 100,000 person-years was found with a corresponding SEER weighted age-matched control incidence of 71 cases per 100,000 person-years. Subsequently, an estimated RR of 1.8 (95%CI: 1.1.-2.9) for non-PSC liver transplant recipients compared to the SEER population was provided.[26] The non-PSC liver transplant group is a population that in the absence of post-transplant screening guidelines, is assumed to be eligible for the general population guidelines for CRC screening and surveillance. Based on the pooled estimate, the CRC risk in non-PSC post-LT recipients is too small to adopt a more vigilant CRC surveillance program. Large prospective cohort studies are necessary to determine the CRC risk in the post-LT setting that defines further recommendations. The impact of certain immunosup-

pressive agents may be considered as sub-analysis for dose-response relationships for CRC outcomes in LT recipients.

THE ROLE OF PRE-LT SCREENING

Pre-LT screening may affect the yield of CRC in the post-transplant period and therefore should be taken into account when evaluating CRC incidence in the post-LT follow-up. Reporting of pre-LT colonoscopies and their findings are often not provided in the literature. Subsequently, the type and quality of a screening examination should be taken into account. Sigmoidoscopy for instance is considered as a less effective screening strategy to detect advanced neoplasia compared to colonoscopy.[37] The most relevant studies that evaluated pre-LT colonoscopy screening are provided in Table 3.[38-44] As can be seen, the definition for advanced adenoma could not always be well distinguished between studies and not every study reported histology or pathology data concerning the colonic polyps that were found. Furthermore, except for a study from Japan[44] and the USA[39], all studies were retrospective. In one study, investigating 229 overall transplants recipients and pre-LT colonoscopy findings, 74 patients with polyps at pre-LT were identified. Of them, 45 (61%) had adenomas. The

Table 3. Studies reporting on the yield of pre-LT evaluation in LT candidates

Study (year)	Investigation	Cohort N	Adenoma N (%)	AA N (%)	Age pre-LT (yrs)	Comments
Rabinovitz (1990)	Colonoscopy	412	20 (5)	12 (3)	NR	AA defined as adenoma with villous component
Selingo (1997)	Colonoscopy	86	10 (12)	1 (1)	NR	19.0% colonic polyps; AA defined as CRC; colonoscopy in patients >45 yrs
Weller (1998)	Colonoscopy	56	24 (43)	6 (11)	49	Symptomatic patients were included. colonoscopy in patients >50 yrs; AA defined as size > 1cm;
Zaman (1999)	Sigmoidoscopy	71	15 (21)	4 (6)	52	AA defined as > 1 cm
Parikshak (2002)	Colonoscopy	229	19.6 (45)	13 (6)	49	Cohort, adenoma and AA is mentioned for overall transplants (i.e.; kidney, lung, heart, liver); AA defined as size >1cm;
Gravante (2008)	Colonoscopy	80	7(9)	4 (5)	54	AA defined as TVA and HGD; no difference with control population (defined as non-cirrhotic);
Ishikawa (2009)	Colonoscopy	67	28(42)	8(12)	52	Living Donor LT; 3 CRC were detected during pre-LT evaluation; AA defined as >25% villous component, >1 cm or HGD or CRC
Albright (2009)	Colonoscopy	152	22 (15)	NR	54	Symptomatic and screening patients
Sint Nicolaas (2010)	Colonoscopy/ sigmo-barium enema	288	36 (13)	6 (2)	46	AA defined as >25% villous component, >1 cm or HGD

AA=Advanced Adenomas; CRC= Colorectal Carcinoma; LT=Liver Transplant; HGD= High Grade Dysplasia; NR=Not Reported; yrs=years

Japanese study identified 3 CRC in a total of 67 patients who did undergo colonoscopy as pre-liver transplant work-up. All these patients where living donor liver transplant candidates (LDLT).[44] In a Dutch study, a prevalence of 2.1% for advanced adenomas was observed in the pre-transplant setting; 73% of all patients did undergo a colonoscopy or the combination sigmoidoscopy and barium enema.[35] This prevalence was in concordance with the prevalence in a asymptomatic Dutch general population cohort.[45] It should be mentioned that pre-transplant malignancy or its precursor lesions may have an accelerated progression while patients receive immune suppressive therapy after LT and therefore the diagnosis of pre-existing extra-hepatic malignancy at LT work up is a contraindication for transplantation.[46, 47]

Based on the available literature, no recommendation for a pre-LT screening colonoscopy protocol can be given for liver transplant candidates. Further studies must determine whether colonoscopy as integral part of pre-LT screening work-up would be cost-effective. Screening for CRC in liver transplant candidates should not be more often or earlier performed than in the general population, until survival benefit in post-LT patients or cost-effectiveness can be provided for the pre-LT colonoscopy screening approach.

POST-LT COLONOSCOPY SCREENING/SURVEILLANCE

Evaluating the current evidence, the place for screening and/or surveillance colonoscopy for non-PSC post-LT patients is still questionable. Studies that investigated post-LT surveillance are provided in Table 4.[11, 34, 43, 48-50] As noted before, none of them are prospective and applied a systematic screening strategy in all patients at fixed surveillance intervals. The time interval between LT and post-LT colonoscopy in patients is important. A reasonable interval between LT and post-LT colonoscopy is necessary to observe an increased adenoma prevalence compared to asymptomatic non-LT cohorts (general population) that can be contributed to post-transplant influences. This principle also applies in case of pre-transplant adenoma findings, where the appropriate control values should be derived from surveillance colonoscopy studies stratified for baseline characteristics in the general population. Some of the studies provided in Table 4 suggest that there may be a trend towards increased potential in the post-transplant period for (advanced) adenomas. In a Dutch study, the RR for all adenoma in LT recipients < 50 years old was 3.6 for all adenoma and 8.9 for advanced adenomas compared to an asymptomatic general population cohort.[48] Limitations from this study were the small sample size and the absence for matching in age and gender. A recent study from the same authors suggested a possible mechanism for increased potential in the development of advanced adenoma in post-LT recipients.[51]

Three studies evaluated the utility of surveillance colonoscopy post-LT in a case-control setting. Two of them concluded that an increased risk (odds ratio [OR] 4.5, 95% CI 1–21.1; in-

Table 4. Overview of studies reporting on the yield of post-LT colonoscopy surveillance

Study (year)	Screened cohort N	FU LT-colonoscopy yrs	AA N (%)	CRC by screening N	Design	Comments
Parikshak (2002)	74 vs. 75 controls	2.7	12(13) [cases] vs. 7 (9) [controls]	NR	Case-control setting	Overall transplant (not specified for LT); ;>50 year older and pre-LT colonoscopy as inclusion; AA defined as size >1cm;
Atassi (2003)	25 vs. 25 controls	3.4	NA	0	Case-control setting	Adenoma cases vs. control: 28% vs. 8% ; OR = 4.5 (95%CI: 1-21.1)
Koornstra (2007)	n=92	*11*	8 (8.7)	0	Retrospective cohort	Inclusion >5 yr post-LT FU; exclusion history of adenoma; 21.7% adenomas
Rurdrajaju (2008)	82 vs. 82 controls	6.2	6 (7.3%) [cases] vs. 1 (1.2%) [controls]	1	Case-control setting	>45 yrs old; IBD and family history, history of adenoma excluded, AA defined as villous component, >1 cm or HGD
Albright (2009)	186	*1.2*	NR	3	Retrospective cohort	>1 year post-LT FU; 39 adenomas found in 186 patients (18.3%)
Herrero (2009)	NR	7-10	NR	1	Retrospective cohort	Three symptomatic cancers, 1 by screening detected

NR=Not Reported; NA=Not Applicable; AA=Advanced Adenoma; FU=Follow-up; CRC=Colorectal Carcinoma; LT=Liver Transplant; IBD=Inflammatory Bowel Disease; HGD= High grade dysplasia; VA=Villous component; OR=Odds Ratio; RR=Relative Risk; *Italic*=median FU interval LT-colonoscopy; yrs=years

creased the prevalence 7.3 versus 1.2%) for adenoma was observed in LT recipients compared with their controls from the general population.[49, 50] The third case-control report could not confirm these findings. They reported on 74 overall transplant recipients with polyps at pre-transplant colonoscopy in the setting of the surveillance outcome compared to a surveillance control group (n=75) from the general population. Both groups had polyps at pre-transplant colonoscopy. The pre-transplant adenoma prevalence did not significantly differ between the groups. The outcome was defined as metachronous adenomas found at the first 3-year surveillance procedure. Thirty-eight percent in transplant cases respectively 43% of controls developed metachronous adenoma at surveillance interval in the post transplant setting, although the study reported the effect for the overall transplant population (kidney, liver and heart).[43] Of note, it should be mentioned that the distribution of cancers between liver and for example kidney transplants has been reported to be strikingly different.[52] Therefore, extrapolating assumptions about cancer incidences for overall transplants to LT recipients may not be appropriate.

A study from Spain mentioned surveillance colonoscopy protocol to every patient between 7 and 10 years post-LT. However, data about the findings in terms of advanced adenomas or the proportion screened patients post-LT were not provided. Three out of 4 CRC cases

were diagnosed by symptoms, 1 CRC was detected by screening. Unfortunately, details about the patients with symptomatic CRC were not specifically specified (i.e. lack of adherence of the surveillance protocol or interval carcinoma despite surveillance colonoscopy).[11] In our opinion, based on the available data for surveillance in post-LT patients, the evidence for increased risk for advanced adenomas in the post-LT setting is scant. It does not justify an intensified surveillance strategy post-LT for non-PSC LT recipients.

CONCLUSIONS & FUTURE CHALLENGES

Patients with PSC/ UC patients have an increased risk for the development of CRC. These patients are eligible to enter a surveillance program for colorectal neoplasia. The recommended surveillance interval should be annual colonoscopy, irrespective of having a liver transplant. PSC may also be a confounder for the incidence of CRC in the post-LT period because it is both associated with exposure (indication for LT) and the outcome (CRC). Therefore, stratification is important to obtain precise incidences for CRC in PSC and non-PSC LT recipients. The incidence of CRC in the post-LT period varies in the literature and there are qualitative reporting deficiencies concerning incidence data but also lack of PSC stratification. Furthermore, many studies do not have a formal statistical comparison to the general population. Nevertheless, based on (pooled) available data it seems appropriate to classify non-PSC LT recipients as a higher risk group than the general population. The results should be taken with caution, because differences between studies were observed. The small but increased risk that has been reported (RR=1.8; 95%CI: 1.1-2.9) may be too small to adopt more vigilant surveillance intervals for these patients. Pre-liver transplant evaluation may be a good investment in a liver transplant candidate although studies are insufficiently powered to confirm the benefit. Until that becomes available, no recommendation can be provided if pre-LT colonoscopy should be advocated in these patients or not. Liver transplant candidates may receive the same screening strategy as is recommended for the general population until further evidence becomes available for survival benefit in post-LT patients and cost-effectiveness of pre-LT colonoscopy. Concerning post-LT surveillance, a prospective study with a systematic screening approach would be highly recommended. Such a study is a necessity In order to define the prevalence of advanced neoplasia more precise in liver transplants. In our opinion, no intensified surveillance strategy should be advised for non-PSC LT recipients in the post-liver transplant setting, until the results from such a prospective study are available.

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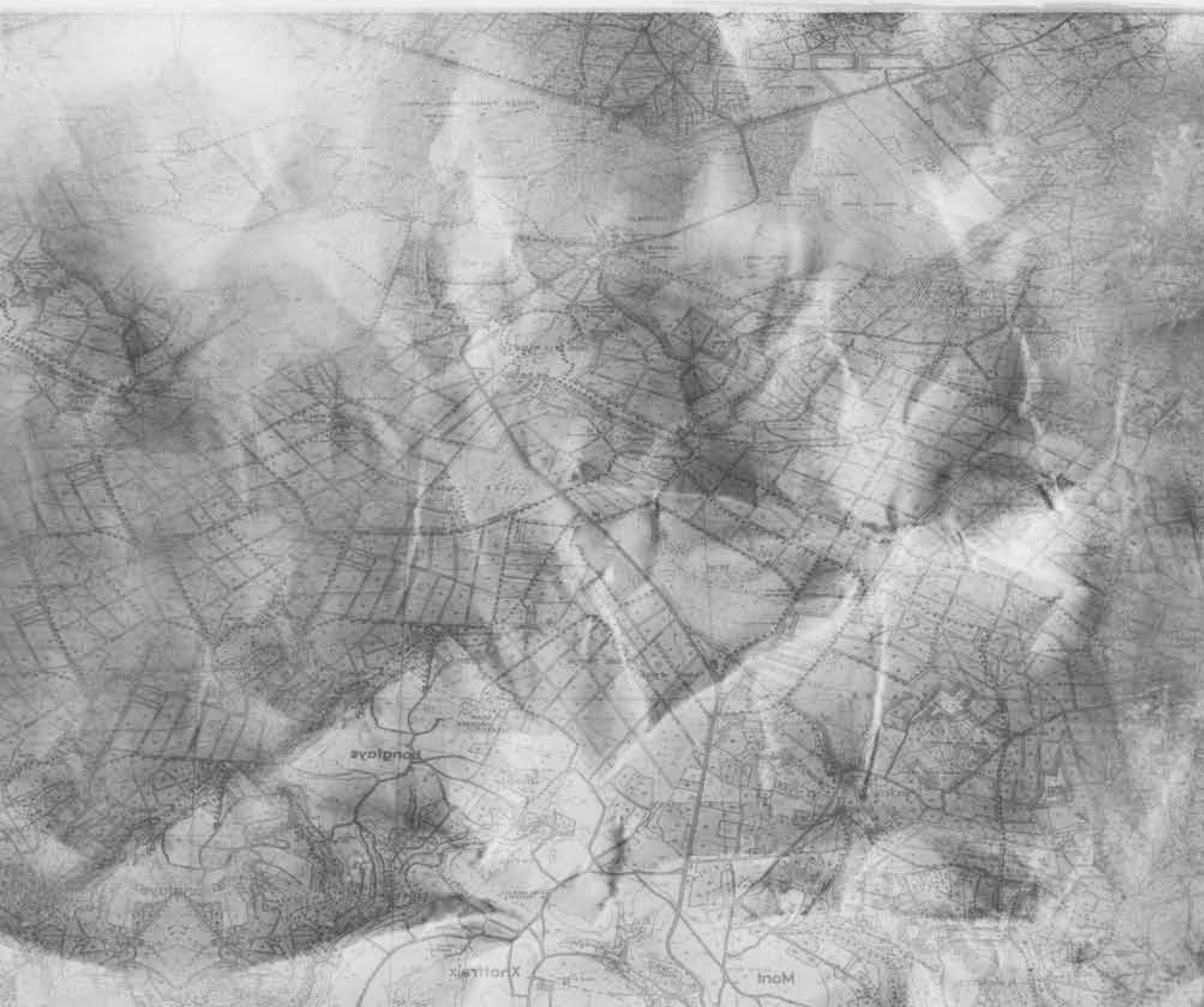
Chapter 20

General discussion and conclusions



The interest in quality assurance (QA) has taken a quantum leap in the health care sector over the last decade. In endoscopy this trend has been observed as well.[1,2] One of the drivers in the growing interest for QA in endoscopy has been the introduction of colorectal cancer (CRC) screening programs.[3]

Quality of care comprises many different factors and can be addressed from various perspectives like societal, patient, physician, endoscopy department, and personnel viewpoints. All different stakeholders in health care have their own perception of and influence on the delivered care. This thesis aimed to assess different aspects that are relevant to improve the quality of the endoscopy service over time, and the quality of colonoscopy specifically, on different levels.

PART I: QUALITY ASSURANCE IN ENDOSCOPY: HOW TO START?

QA on the endoscopy department is regarded as a team task; every member should be involved in this process and quality of care should be part of the team culture.[4] In order to have maximum support for quality projects, it is thus important to take the wishes and expectations of endoscopy personnel into account. We found that significant differences in expectations of QA are present between different key players on the endoscopy department. Some barriers were identified such as the time involved in QA, a decline of capacity, or the fear for disclosure to external parties. These concerns have also been established as barriers in other sectors, such as in family practice.[5] Rating the importance of different quality aspects, we found that patient-related quality parameters (such as accessibility and aftercare) are the main focus of interest for nurses, while endoscopists prioritize clinical outcomes (such as endoscopic performance measures). These results indicate that the endoscopy personnel acknowledge its own opportunities and responsibilities in providing an excellent service. As the nursing staff has longer and more intense contact with the patients, their attitude may have a major impact on patient satisfaction.[6,7] Endoscopists can then pay attention to their primary task: doing the appropriate endoscopy in the right patient in the right way at the right time. In the meantime should all team members respect each other's' priorities and collaborate to achieve common goals.[8] Developing QA projects supported by all team members and reach common targets may be a time-consuming task but will be necessary to get the optimal benefit from the efforts. In the long term, this will get all members on board and lead to a team culture aimed at providing the best service possible.

A successful QA program from England, called the Global Rating Scale (GRS), was investigated to serve as a QA program in the Netherlands. This comprehensive QA program evolved from the desire to provide a patient-centered service and incorporates a wide range of aspects of the endoscopy department. It thereby reflects the fact that QA is multidimensional.[9] The GRS categorizes the quality of the service in four main dimensions: 'Quality of patient

experiences', 'Clinical quality', 'Workforce', and 'Training'. These dimensions are further divided in different items to address relevant aspects of QA within these dimensions. We assessed whether the Dutch endoscopy staff values the same aspects which are part of the GRS checklist, to test the applicability in the Dutch endoscopy setting. As the quality parameters valued by the Dutch staff were similar to the content of the GRS, the GRS maybe well supported by the Dutch endoscopy departments to guide quality improvement projects.

We further investigated how Dutch departments currently score on the GRS. Our study showed that relatively high GRS levels were obtained in the departments in processes of care to diminish waiting times for endoscopic procedures, as well as the communication of results to the referring physician. One may ask whether a department obtaining higher GRS level has indeed higher rates of satisfied patients or better clinical outcomes compared to low level departments. We therefore aimed to provide the rationale for construct validity by using colonoscopy audit data presented later on this thesis. This indeed showed concordance between GRS scores and colonoscopy audit data. Our studies are the first publications that provide a rationale to use the GRS system as QA tool. As different countries are using or have interest in the GRS, the use of this program will also make international comparison and collaboration between endoscopy departments possible. Recently, the results in England did show that the quality of endoscopy service has improved significantly according to the standards set by the GRS.[9] It might be argued that this quality improvement is a self-fulfilling prophecy as it follows its own GRS standards. However, the GRS is continuously being internally validated as it asks for continuous feedback from patients to identify service gaps, followed by incorporation of new items or adaption of the system. Additionally, a recent large audit from the English National Bowel Cancer Screening Program showed a considerable raise in the quality of colonoscopy performance measures (such as the ADR and cecal intubation), since the implementation of standards endorsed by the GRS.[10] The question remains whether an improvement in GRS levels will also lead to improved endoscopic quality outcomes (such as interval cancers). This has to be addressed in future studies, while the current quality audit can serve as baseline audit.

Part I: Conclusions

Dutch endoscopy members support QA and are willing to actively contribute to a continuous QA program. Improvement on employees' own field of expertise is thereby acknowledged, which further supports that endoscopy QA projects can be successfully introduced in the Netherlands. An available QA program from England was tested and found to be applicable for the Dutch situation. Moreover, priorities of the Dutch endoscopy staff appear to be in concordance to the GRS content. Some small adjustments to the GRS may result in a quality improvement tool which satisfactory addresses all different aspects valued by the endoscopy staff. This will help the Dutch endoscopy departments to assess current quality, identify

service deficiencies, to benchmark their results at an international level, and to improve the quality of the endoscopy service.

PART II: QUALITY ASSURANCE IN COLONOSCOPY: WHERE DO WE STAND?

The GRS has received international attention, because of its success in improving the English´ endoscopy status. The work presented in this thesis attributes to the evidence on the applicability of the GRS for patient satisfaction in both the Canadian as well as the Dutch endoscopy setting. With the use of a questionnaire that included aspects of the GRS, we assessed patient experiences in colonoscopy procedures in the Canadian and the Dutch setting, showing in both studies considerable service gaps and differences between endoscopy departments. Most prominently were the deficiencies in information provision pre- and post-procedure. In addition we found great differences in comfort issues. Patient experiences are generally considered to be quality standards for which target outcomes are difficult to define. By means of benchmarking, a technique used in our studies, we showed that without predefined standards endoscopy departments can use outcomes of patient surveys in collaborative studies to determine which areas warrant further attention. As the GRS content is amongst others based on patients' preferences, it is assured that the service is patient-centered.

Besides auditable outcomes with targets that are hard to capture or define, we present data on quality indicators in this thesis. Quality indicators are supposed to have commonly agreed standards. Some of the most renowned quality indicators for colonoscopy are the adenoma detection rate (ADR) and cecal intubation; both were compared between twelve participating departments and individual endoscopists. Recently, it was recognized that the ADR is inversely associated with the occurrence of interval CRC.[11] Benchmark values for the ADR have been proposed by the American Gastroenterological Association where endoscopists must reach an ADR of 25% in males and 15% in female patients during CRC screening colonoscopy.[12] For diagnostic colonoscopy, no data are available on the ADR, while the cecal intubation rate is set on 90%. In our study we showed that the ADR varies markedly between departments and individual endoscopists in daily clinical practice. Reasoning from the 20% target in screening colonoscopies, diagnostic colonoscopies in the Dutch setting were shown to have a similar yield, and this benchmark can be used as minimum target for now. The differences in ADR are partly explained by (fixed) patient-related factors. However, the large variance in the ADR between endoscopists implies that there is room for improvement for individual endoscopists. This is underlined by the fact that training and experience in colonoscopy determine the clinical outcome, as has been illustrated by several studies. A retrospective cross-sectional study showed that surgeons (RR: 0.58, 95%CI: 0.52-0.65) and internists (RR: 0.92, 95%CI: 0.78-1.09) perform fewer diagnostic biopsies.[13] Additionally, a population-based cohort study from Canada showed that a colonoscopy performed by an

internist or general physician was an independent risk factor for the occurrence of subsequent interval CRC (OR: 1.77, 95%CI: 1.14-2.74).[14] This was supported by a study from Poland.[11]

Our results also indicate that using benchmarking principles in quality assessment can guide further investigation for differences in quality outcomes. As shown, sometimes low performance have obvious reasons after in-depth evaluation of the results and by case-mix corrections.

In order to perform adjustment for case-mix differences between departments and individual endoscopists, the importance of adequately reporting of endoscopy procedures is of paramount importance. The ASGE QA Task Force has proposed guidelines what aspects should be included in colonoscopy reports, in the Netherlands such guidelines are still lacking.[15] Based on the American parameters, again great variance exists in the quality of reporting between the different endoscopy centers. The nationwide consortium in the United States previously showed that the quality in reporting can be improved, confirmed by our study using clinical practice data from all type of services.[16] Our results are underlined by the fact that in the GRS census, all departments achieved the lowest scores (Level D) in the item "Quality assessment of the procedure", which assesses whether certain quality indicators are regularly monitored and routinely reported. It is therefore recommended that the Dutch endoscopy society finds agreement on the minimum standards of an endoscopy report, and monitors the quality of endoscopy reporting in the future. Installing automated endoscopy reporting systems contain easy solutions to achieve a standard report, and have the beneficial effect that those abovementioned quality indicators can easily be monitored.

As it is hard to capture the ADR in daily practice due to the absence of a link between pathology and endoscopy reports, we also investigated a more readily available quality indicator: the polyp detection rate (PDR), which appeared to highly correlate with the ADR. Based on our results, a PDR of 40% seems achievable for the male population whereas the benchmark value for the female population yields a PDR of 22%. As long as there is no reliable, readily available link between the pathology and endoscopy report, the PDR can be considered as a quality indicator for continuous monitoring of colonoscopy performance. However, as this indicator can be easily altered by taking biopsies from insignificant, hyperplastic polyps in the rectum, regularly assessment of the ADR should be performed for correlation. This also assures that not only biopsies are taken, but the pathology specimens are being sent for pathologic review as well. In the end, many quality indicators measures are prone to manipulation, which underlines the responsibility of health care workers in QA.

Part II: Conclusions

A patient experience survey based on the Global Rating Scale was able to detect service deficiencies in patient outcomes between endoscopy departments in both Canada and the Netherlands. These results indicate that in an area where targets are hard to define (auditable

outcomes), close collaboration between departments in survey studies with the application of benchmarking is required to guide quality initiatives on endoscopy departments.

Further research on quality indicators found the same variance in colonoscopy performance between the investigated endoscopy departments. Several possible determinants of these quality indicators were also identified, making it possible for endoscopy departments and individual endoscopists to improve the delivered care. Our results can be used to assess and define benchmarks in patient experiences as well as the development in guidelines for quality of endoscopy reporting and colonoscopy performance.

PART III: QUALITY ASSURANCE IN COLORECTAL CANCER SCREENING AND SURVEILLANCE: HOW TO GUIDE?

There are several reasons why quality of colonoscopy may be at stake, including increasing demands and the need to limit expenditures and increasing demand. By keeping the endoscopic resources under control, both the demand and the expenditures can be restricted. As a large proportion of colonoscopies are surveillance procedures, possible solutions in keeping control of endoscopic resources may lie in the utilization of surveillance procedures. Following a screening procedure with polypectomy of adenomas or the detection of CRC, surveillance colonoscopy is recommended by several guidelines of GI societies.[17-20] For adenomas, certain baseline characteristics serve as predictor for the risk of recurrence, and thus influence the timing of surveillance colonoscopy.[21] We assessed these risk factors using the most up-to-date literature in a meta-analysis. We show that the Dutch surveillance guidelines are outdated, as more risk factors can be identified than the number of adenomas alone, currently the only risk factor incorporated in surveillance guidelines in the Netherlands.[20] This explains why Dutch endoscopists often deviate from these guidelines, and supports the recommendation to adjust the guidelines to the latest evidence, to guide the physician's choice of a correct surveillance interval.[22] Based on our results more vigilant surveillance is warranted in patients with advanced adenomas, ≥3 adenomas, adenomas ≥10 mm in size, and higher age. Using these parameters will increase the efficiency of CRC surveillance. A problem is that assessment of some of these risk factors shows considerable inter- and intra-observer variability.[23, 24] Especially assessment of size and histology of adenomas may be unreliable. This problem can probably be partly solved by a learning curve for both endoscopists and pathologists. Further, as villous histology was a less profound risk factor for adenoma recurrence, it can be considered to exclude (tubule-)villous adenomas from the definition of advanced adenomas.

As stated, surveillance colonoscopies produce a high burden on the endoscopy capacity.[25] Recently it was recognized that the indication as well as the interval for a significant proportion of follow-up procedures may be questioned.[26] One of the chapters in this thesis

assessed whether more capacity can be created by optimal resource allocation in follow-up colonoscopy practice. We showed that a considerable proportion of follow-up colonoscopies was being performed in daily practice. In the context of optimal resource allocation, we showed that early-follow-up colonoscopies in symptomatic patients with a complete prior colonoscopy resulted in a low yield of colorectal neoplasia. This questions the need for these procedures. Furthermore, the rationale for decreasing over-utilization in surveillance practice is emphasized, as the yield in terms of the ADR was the lowest for over-utilized FU procedures compared to optimal- and under-utilization according to the American guidelines from the AGA for surveillance of CRC. In a Canadian study we assessed the appropriateness of surveillance intervals and showed that a considerable proportion of surveillance colonoscopies are inappropriate according to this AGA guideline. These findings were also confirmed by the survey study that was being held under Canadian endoscopists.

Efficiency of surveillance programs does not only pertain to appropriateness of intervals, but also to attendance rates for follow-up appointments by patients. Previous work showed that attendance rates can be improved, amongst others by the use of an automated recall system for patients.[27, 28] Additionally, information provision to patients has been mentioned to be of importance in quality of patient experiences and needs some serious attention as shown earlier in this thesis. Besides information provision directly after the colonoscopy, some studies suggested that awareness of patients may also play an important role in affecting attendance to their surveillance appointment.[29] We therefore assessed the awareness of patients diagnosed with colorectal adenomas on the need for surveillance, and found that the overall awareness of patients of the necessity of surveillance was moderate. There was a poor correlation between these awareness levels when grouped per endoscopy unit, and the surveillance endoscopy attendance rates for these departments. Therefore, we conclude that the attendance at surveillance colonoscopy, and thereby the efficiency of surveillance programs, may not be as much altered by raising the awareness of surveillance recommendations. Our study underlines the previous report that the best solution to increase attendance for surveillance colonoscopy is the use of automated recall-systems.

Besides adherence to guidelines, identification of high-risk groups also plays an important role in CRC screening and surveillance. In our thesis, we assessed whether a specific patient population, liver transplant (LTx) recipients, warrants a more vigilant screening or surveillance strategy. The observation that transplant recipients have an increased risk for several malignancies raises the question whether colonoscopy screening should be incorporated in post-transplant malignancy screening programs.[30] Contradictory reports have been published about the risk of CRC post-LTx.[31, 32] Apart from this, patients who are transplanted for primary sclerosing cholangitis (PSC) may confound this risk, as PSC has been associated with ulcerative colitis.[33] Ulcerative colitis is for itself an independent risk factor for the development of CRC, underlining the rationale for stratification of PSC and/or UC LT patients. In the guidelines, PSC patients are recommended to undergo regular screening, i.e. annual

colonoscopy due to this increased risk.[17] We aimed to assess this stratified CRC incidence in the liver transplant cohort from Rotterdam, the Netherlands, and provide a more reliable estimate of CRC risk in the post-LTx period by means of a meta-analysis. The meta-analysis showed a small but significantly increased risk for CRC in the post-LT non-PSC setting (RR: 1.8, 95%CI: 1.1-2.9). The results of our study do at the moment not support a recommendation to intensify screening by means of colonoscopy in the post-LTx patients. However, as the confidence interval is wide and does include a risk which in other patient populations warrants screening, further work is needed in order to determine the additional benefit of intensive post-transplant screening colonoscopy.

Part III: Conclusions

The use of CRC and adenoma surveillance guidelines may be of considerable help in determining the right surveillance interval in daily clinical practice and control colonoscopy resources, when it is assured that physicians are aware of and support the guidelines. For optimal use of surveillance guidelines, they should be based on the most recent evidence. We found that CRC and adenoma surveillance guidelines in the Dutch endoscopy setting are outdated and need to be revised. This will help to reschedule endoscopic resources, as the appropriateness of a significant proportion of repeat-colonoscopies is questionable.

From a patient's perspective, optimal use of the endoscopic resources may be more effectively influenced by the efforts of an endoscopy department to make appointments and recall the patient, than by raising the awareness of the need for surveillance in patients and post-colonoscopy information. This should be plotted against the fact that proper patient information remains an important issue, to prevent uncertainty, stress, and litigation.

GENERAL CONCLUSION

This thesis discussed different aspects of quality of endoscopy. As such, it can first be used by Dutch endoscopy departments and the Dutch Society of Gastroenterology as a guide for priorities in quality improvement projects. We showed that the Global Rating Scale is well applicable in the Dutch setting, in order to assess the quality of current services and as a tool for further improvement in the coming years. As the Dutch government recently decided to implement a population screening program for colorectal cancer, there will be many challenges for the endoscopy departments in the coming years. To keep ahead of these challenges, and prevent them to become problems, a couple of aspects should have high priority in QA, including i) definition of quality indicators for endoscopy, ii) standardization of colonoscopy as well as colonoscopy reporting, iii) identification of differences in quality between endoscopists and endoscopy departments on performance and patient experience

levels, iv) streamlining the endoscopic capacity and v) developing guidelines in the area of CRC and adenoma surveillance.

This thesis attributed to the quality movements started a couple of years ago, and aims to give it a new boost in the next era to strive for an excellent endoscopy service: safe, complete, effective, and respectful.

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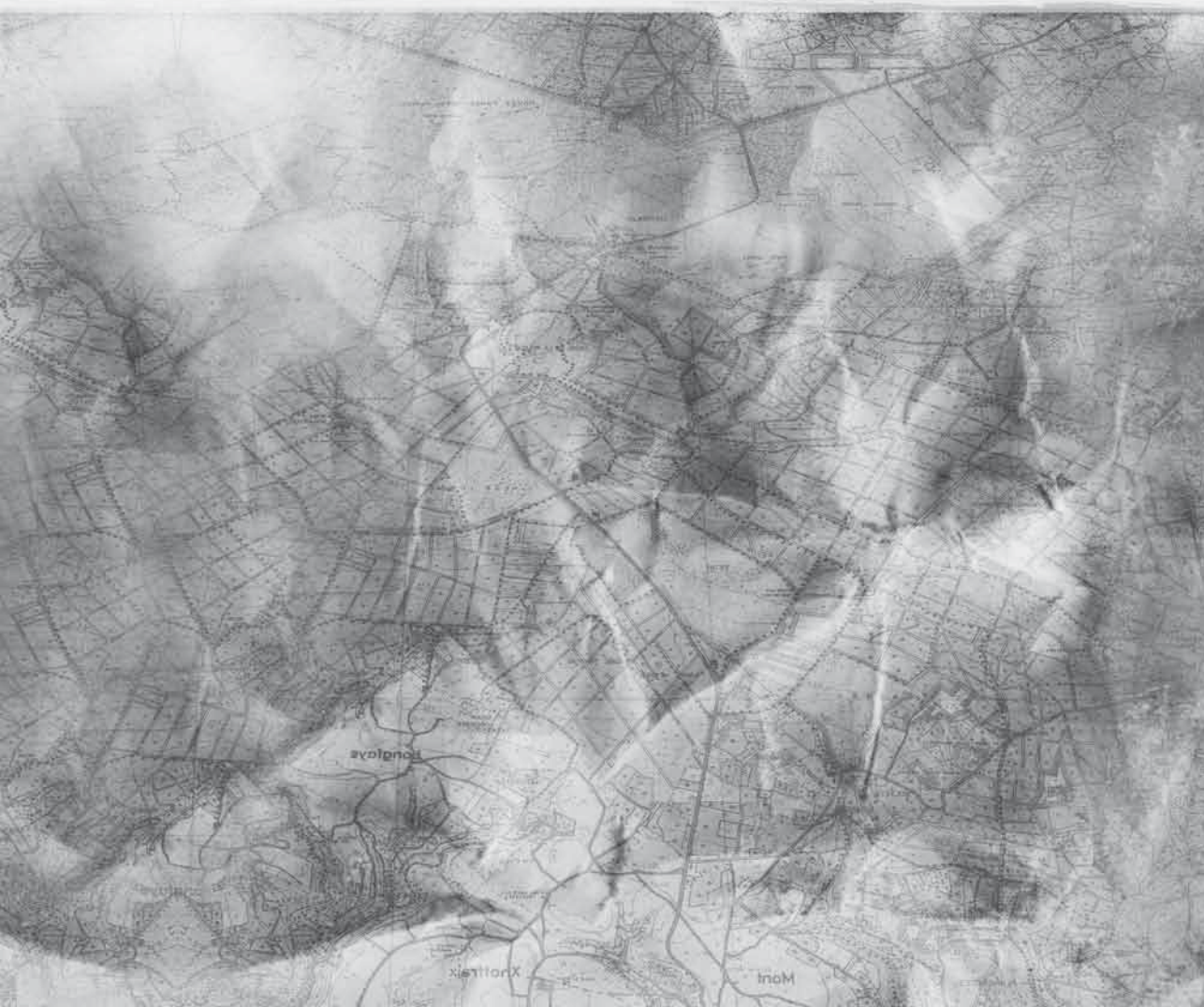
Summary



Summary

Chapter 1 provides the reader with a general introduction to the theme of this thesis. It describes the current status of quality assurance (QA) in health care and how the health care sector got to this point. Furthermore it gives an overview of the current challenges in QA in endoscopy and thereby comes to the aims and outline of the thesis. In **Chapter 2** an overview of important principles of quality assurance (QA) is given. As other industries have been exemplars for the health care sector in service improvement, an overview is given of developments in QA in these industries and its application in the health care sector is described. The importance of the right team culture is emphasized, and principles such as the Plan-Do-Check-Act cycle, benchmarking, and quality indicators are discussed. As many quality initiatives in endoscopy have been driven by the implementation of colorectal cancer (CRC) screening programs, **Chapter 3** discusses a QA program for CRC screening programs. It describes what quality aspects should be incorporated in a QA program for efficient screening, and thereby addresses the complete patient journey. Reviewed items include patient related quality indicators such as patient information and satisfaction, as well as clinical outcomes such as complications and performance indicators.

Following the introduction to QA in endoscopy, at first we performed a survey study under all endoscopy team members in the Netherlands to assess their preferences in QA. **Chapter 4** describes that gastroenterologists are in general positive to the introduction of a QA program in the Netherlands (95% positive attitude). Identified barriers to comprehensive QA in endoscopy were mainly time investment (28% negative) resulting in an expected decrease of endoscopic capacity (38%), and the disclosure of results to insurers and media (23 and 53% negative attitude, respectively). Most important quality measurements were clinical outcomes such as complication registration (97%) and reporting (96%). Besides the opinion of gastroenterologists, we also assessed the opinion of endoscopy nurses and assistants towards QA in **Chapter 5**. Again the majority had a positive attitude towards QA (87%). Patient-related quality indicators such as aftercare and patient experiences were deemed to be the most important in QA (respectively 97 and 96% found this important). As a team culture aimed at providing an excellent service is of utmost important for efficient QA we simultaneously investigated how endoscopy nurses and assistants evaluate their team. Deficits were identified in the team process and the relation with the wider organization, while the respondents were most positive about how their team performed in responsibility and skills necessary to do their job.

A comprehensive QA program that incorporates much of the priorities identified by the endoscopy staff and deals with many of the principles discussed in the first chapters, is the Global Rating Scale. The application of this comprehensive QA program from England is tested in the Netherlands in **Chapter 6**. This chapter shows that the GRS is applicable in the Netherlands as QA program as large variability in performance is shown in results between

eleven endoscopy departments participating in a colonoscopy baseline quality audit. This variability makes it possible to use the GRS as benchmark tool. Favorable scores for Dutch endoscopy departments were found on items such as 'Communicating results to referrer' (46% Level A) and 'Booking and choice' (36% Level A), while service deficiencies were identified for 'Quality assessment of the procedure (100% Level D). Further, for the item 'Equity and equality' all departments achieved the lowest score, indicating the low priority for this item in the Netherlands, such that some adaptations to the system should be performed before implementation.

To determine the effect of quality projects, data about baseline performance are necessary. To assess the current status of colonoscopy performance **Chapter 7** explored the current quality of colonoscopy performance and reporting. In this large cohort study of twelve endoscopy departments' four hundred colonoscopy reports per departments were reviewed. There was large variation in quality of both colonoscopy reporting and performance. Indication, sedation practice, and extent of the procedure were well reported in most departments (>90%), while the quality of bowel preparation and photographic documentation of the cecal landmarks were often absent (reported in respectively 62 (range between departments: 7-100%) and 71% (range: 22-97%)). The adjusted cecal intubation rate was 92% (range 84%-97%). The ADR was 24% (range 13%-32%). **Chapter 8** further explores the obtained baseline data from the colonoscopy audit in the context of one of the best established quality indicators, the adenoma detection rate. It is shown that there is a wide variance in adenoma detection rates between both endoscopy departments (27-47%) and individual endoscopists (10-40%).

Besides quality indicators assessing colonoscopy performance, it is challenging to define standards for patient experiences in colonoscopy. As the GRS is a patient centered program, its content may be used to develop standards for patient satisfaction, which is tested in **Chapter 9** in a Canadian situation. This study, using a pre-and post-procedure questionnaire, showed significant deficits in pre- and post-procedure protocols regarding patient-centeredness. This includes discussion of the risk of complications in 65% of respondents, while overall almost everyone signed informed consent (99%). Further, 23% of patient experienced a more burdensome colonoscopy than expected. Twenty-one percent left the hospital without knowing how to get the final results. **Chapter 10** aimed to assess patient experiences by means of benchmarking using the GRS in the Netherlands to further evaluate the use of the GRS as a tool for QA in patient experiences. This study, similar in design as the Canadian study, showed great heterogeneity between twelve different endoscopy departments, underlining its benchmark utility. Large variance in informing the patient about the results after the procedure (0-57%) and information on complications (43-98%) were identified. Additionally, the experienced comfort (25-64%) and satisfactory discussion of results after the procedure (52-86%) varied strikingly. Using structured assessments by means of the survey based on the GRS identifies service gaps. Additionally, the benchmark approach has the advantage to

share solutions between departments. Last, by performing this study, we showed that the GRS content seems applicable in a European context as well.

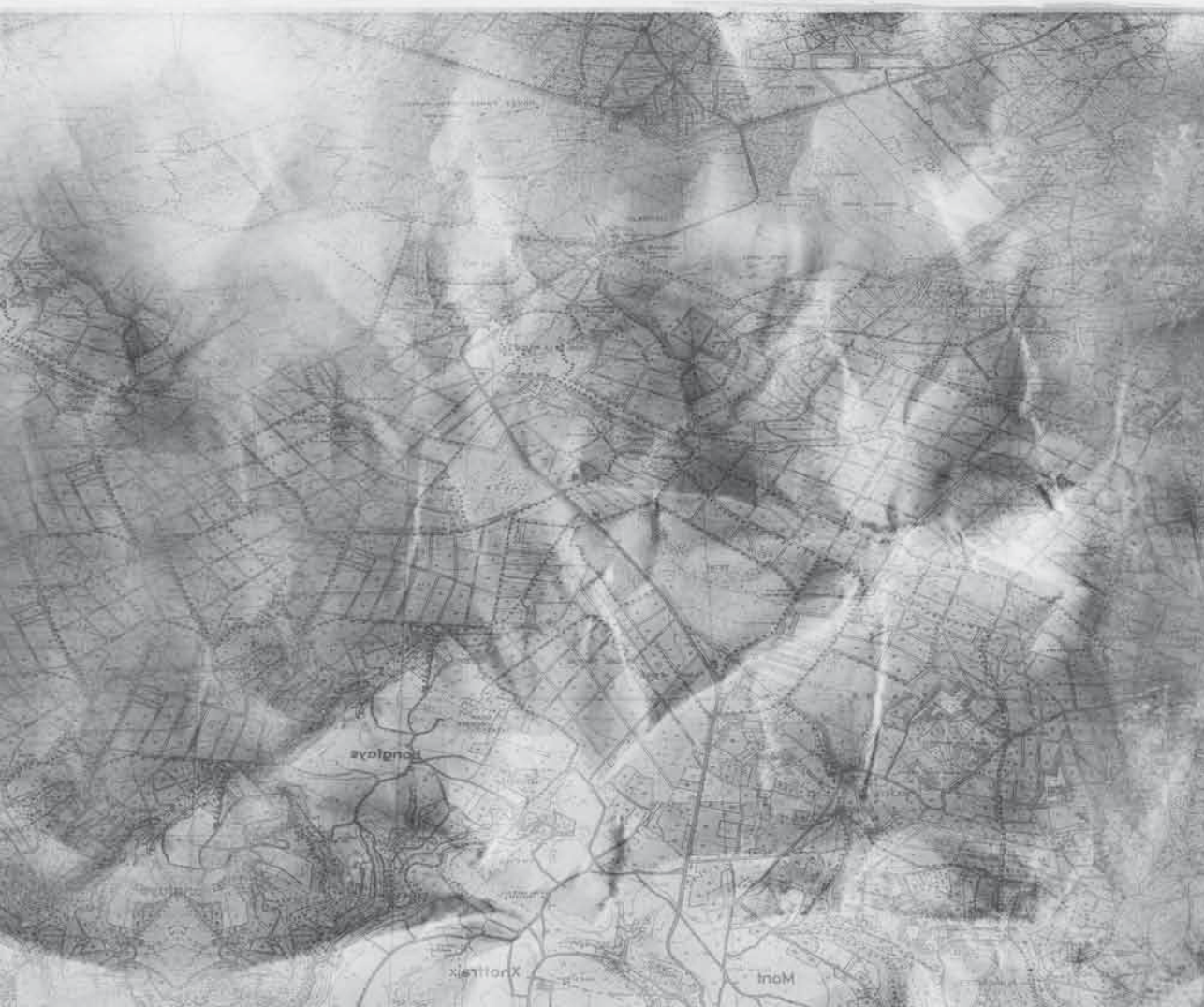
In **Chapter 11** we assessed the incidence of complications after colonoscopy by means of a telephone interview after 30-days. Definite-related major adverse events were reported in 0.8%, while another 0.5% had possible-related major adverse events. Minor adverse events occurred in 29% of all patients within the 30-day period. Additionally, we showed that patients who had experienced any definite-related adverse event were less willing to return for colonoscopy (81 vs. 88%)

Chapter 12 deals with the resource allocation of surveillance colonoscopy practice, important in the context of the increasing demand due to upcoming CRC screening. In this study, the majority of surveillance colonoscopies were not performed according to one of the most recent guidelines for surveillance after polypectomy of CRC or adenomas. As the adenoma detection rates were not significantly different among these too early-, appropriate and too late surveillance procedures, a majority of them were classified as too early (65%) can be regarded as overuse in surveillance procedures. Optimal resource allocation can be found in the surveillance colonoscopy practice, but may also be evaluated for early-follow-up colonoscopies or the diagnostic colonoscopy. **Chapter 13** evaluated how these aspects pertain to the Dutch endoscopy sector, showing that follow-up procedures within 1 year, performed for symptoms, did result in a low yield for colorectal neoplasia (4%), with a complete examination and good bowel preparation on index colonoscopy. Additionally, if applying surveillance guidelines to current follow-up practice, significant higher detection rates were found in optimal utilized follow-up procedures compared to over-utilized follow-up practice (30 vs. 20%). Finding neoplasia on surveillance colonoscopy is associated with certain index characteristics. **Chapter 14** aimed to provide an update of the latest evidence concerning adenoma recurrence by means of a meta-analysis. The most important characteristics on index for recurrence were advanced adenomas (relative risk (RR): 1.81), ≥3 adenomas (RR: 1.64), size ≥10 mm (RR: 1.66), and age ≥60 years (RR: 1.65). As shown in Chapter 12 and 13, physicians deviate often from the surveillance guidelines. Possible reasons may be that physicians are unaware or disagree with them, explored in **Chapter 15** among Canadian endoscopists by means of nation-wide survey study. In nine out of 14 survey cases presented, 12 to 38% of the colonoscopists said their recommendation was based on the guidelines, but they did not give the appropriate recommendation. This suggests possible unfamiliarity where an educational intervention which raises awareness and knowledge about the guidelines would be beneficial. Another reason for suboptimal use of surveillance colonoscopy resources may be the unawareness of patients. **Chapter 16** assesses the awareness of patients in their adenoma findings and their corresponding surveillance policies. We found that the awareness was moderate (60%) in a large cohort of adenoma patients. However, the attendance rates per endoscopy department seemed not to be correlated with current awareness rates.

Chapter 17 assesses the topic of the development of surveillance guidelines for the subpopulation of liver transplant recipients due to their overall increased risk of cancer post-transplantation. The excess risk for CRC in primary sclerosing cholangitis (PSC), an indication for liver transplantation (LT), must be taken into account as confounder as these patients have already an indication for more aggressive surveillance strategies. Our study found a standardized incidence ratio (SIR) for CRC for non-PSC post-LT recipients of 1.26 (95% CI: 0.31-5.03) compared with the general population, implying the need for more vigilant surveillance is not indicated. Following this, **Chapter 18** aimed to determine this CRC risk of liver transplants and a possible more vigilant surveillance strategy by means of a meta-analysis. This study is the first and only thus far that assessed CRC risk in such a comprehensive way, yielding an increased relative risk for CRC in the post-LT non-PSC recipient of 1.8. However, based on comparable risk estimates in the literature that were found, the implication for more aggressive surveillance is not recommended. **Chapter 19** discusses from a broader point of view the risk of CRC in the post-transplant period, what evidence is available concerning the role for pre-transplant screening yield and cost-effectiveness of post-LT surveillance by colonoscopy. As mentioned previously, post-LT surveillance for CRC seems not justified based on the available evidence, where the role of pre-LT screening remains uncertain due the lack of evidence in this area.

Chapter 20 provides the reader with a general discussion of this thesis. It describes how the initiatives fit in the current status of quality assurance (QA) for colonoscopy. It also provides an overview how the results can serve as a platform for endoscopy services in the Netherlands.

Samenvatting



Samenvatting

Hoofdstuk 1 omvat de introductie op het onderwerp van dit proefschrift.Het beschrijft de huidige status van kwaliteitswaarborging in de gezondheidszorg en hoe men tot hier gekomen is. Verder geeft het een overzicht van de uitdagingen die de gezondheidszorg nu te wachten staat en komt hiermee tot de algemene doelstelling van dit proefschrift.

In **hoofdstuk 2** wordt een overzicht gegeven van belangrijke principes in kwaliteitswaarborging. Waar andere industrien vaak als voorbeeld zijn gebruikt voor de gezondheidszorg in kwaliteitsverbetering, is de ontwikkeling van kwaliteitsprogramma's in andere industrien weergegeven en wordt er beschreven hoe deze ontwikkelingen ook de gezondheidszorg verder kunnen helpen. Het belang van een goede team cultuur wordt hierbij benadrukt, en principes zoals de 'Plan-Do-Check-Act cyclus', benchmarking en het gebruik van kwaliteitsindicatoren worden uitgelegd. Aangezien veel van de huidige kwaliteitsinitiatieven in endoscopieen gedreven worden door de invoering van darmkanker screeningsprogramma's, beschrijft **hoofdstuk 3** een kwaliteitsprogramma van darmkanker screening.

Het bespreekt welke kwaliteitsaspecten behandeld zouden moeten worden voor effectieve screening waarbij het van belang is het complete zorgtraject van de deelnemers in kaart te brengen. Behandelde onderwerpen zijn onder andere goede informatievoorziening, hoge tevredenheid, maar ook klinische uitkomsten en complicaties.

Na deze introductie op kwaliteitswaarborging is er eerst een studie gehouden onder alle leden van endoscopieafdelingen in Nederland om hun wensen en prioriteiten voor kwaliteitswaarborging in kaart te brengen. **Hoofdstuk 4** laat zien dat gastroenterologen over het algemeen positief zijn over de introductie van een kwaliteitsprogramma in Nederland (95% positief). Barrieres die zijn voor succesvolle uitvoering van een kwaliteitsprogramma zijn de tijdsinvestering die dit kost (28% negatief) wat zal leiden tot een kleinere capaciteit (38%). Verder maken ze zich zorgen over het openbaar maken van de resultaten aan verzekeraars en media (respectievelijk 23 en 53% negatief). De prioriteit voor kwaliteitswaarborging werd gelegd bij complicatieregistratie (97%) en verslaglegging (96%). Naast de mening van de gastroenterologen is de mening van verpleegkundigen en assistenten onderzocht in **hoofdstuk 5**. Ook bij hen was het meerendeel positief gestemd ten opzichte van een kwaliteitsprogramma (87%). Prioriteit voor hen lag bij patient-gerelateerde kwaliteitsindicatoren zoals patientervaringen en nazorg (respectievelijk 96 en 97% vond dit belangrijk). Als eerder aangegeven is een goede team cultuur van belang voor efficiente kwaliteitswaarborging en dus hebben we in dezelfde studie onderzocht hoe verpleegkundigen en assistenten hun team functioneren beoordelen. Problemen werden aangetroffen in het teamproces en de relatie met de grotere organisatie, terwijl deelnemers positief waren over de kwaliteiten van het team wat betreft verantwoordelijkheidsgevoel voor de afdeling en aanwezige kwaliteiten om een goede afdeling te zijn.

Een compleet kwaliteitsprogramma dat veel van de wensen van de Nederlandse endoscopie medewerkers en principes van de eerste hoofdstukken incoorporeert is de 'Global Rating Scale'. In **hoofdstuk 6** wordt het gebruik van dit Engelse systeem getest in de Nederlandse situatie. Deze studie laat zien dat de GRS bruikbaar is als kwaliteitsprogramma, aangezien het in staat is om een grote verscheidenheid in kwaliteit tussen elf afdelingen die deelnamen aan een nulmeting, aan te tonen. Deze resultaten in variabiliteit maken het mogelijk om de GRS te gebruiken als benchmark systeem. De GRS liet goede scores zien voor items als 'Terugkoppeling van resultaten naar de verwijzende arts' (46% level A) en 'Maken van afspraken en keuzevrijheid' (36% level A), terwijl het aantoonde dat verbetering gehaald kan worden in 'Kwaliteit van de procedure' (100% level D). Verder behaalde alle afdelingen ook een level D voor het item 'Gelijke behandeling bij toegang en dienstverlening', wat waarschijnlijk reflecteert dat dit een minder belangrijk punt is in Nederland en dat er dus kleine veranderingen aan de GRS nodig zijn om het toepasbaar te maken op de Nederlandse situatie.

Om het effect van kwaliteitsinitiatieven te controleren is een nulmeting noodzakelijk. Om de huidige status van de kwaliteit van colonoscopieën te bepalen beschrijft **hoofdstuk 7** de huidige kwaliteit van colonoscopie verslaglegging en uitkomsten. In een grote cohort studie met twaalf endoscopie afdelingen werden 400 colonoscopieverslagen per afdeling onderzocht. Er was een grote variabiliteit in kwaliteit van zowel de verslaglegging als uitkomsten. De meeste afdelingen (>90%) rapporteerden standaard over de indicatie, het gebruik van sedatie en het bereik van de procedure. Echter, de kwaliteit van darmvoorbereiding en het fotografisch vastlegging van het coecum waren vaak afwezig (gerapporteerd in respectievelijk 62 (range tussen afdelingen: 7-100%) en 71% (range: 22-97%)). De gecorrigeerde coecumintubatie ratio was 92% (range: 84-97%). De adenoom detectie ratio was 24% (range: 13-32%). **Hoofdstuk 8** gaat dieper in op de meest geaccepteerde kwaliteitsindicator, de adenoom detection ratio. Het laat zien dat er een groot verschil bestaat tussen zowel endoscopie afdelingen (27-47%) en individuele endoscopisten (10-40%).

Naast de beschikbaarheid van kwaliteitsindicatoren voor klinische uitkomsten, is het moeilijk om standaarden te definiëren voor patiënttevredenheid in colonoscopie. Omdat de GRS een programma is waarin de patiënt centraal staat, zou de inhoud van het programma gebruikt kunnen worden om deze standaarden in patiënt ervaringen te ontwikkelen. Dit concept is getest in **Hoofdstuk 9** in de Canadese endoscopie omgeving. Deze studie, waarbij een pre- en postprocedure vragenlijst werd gebruikt, liet significante tekortkomingen zien tussen afdelingen in pre- en postprocedure protocollen met betrekking tot patiëntgerichtheid. Dit was ondermeer in de bespreking van het risico op complicaties, wat volgens 65% van de respondenten gebeurd was, terwijl de grote meerderheid schriftelijke consent had gegeven (99%). Verder, 23% van de patiënten benoemde de colonoscopie vervelender dan vooraf verwacht. Eenentwintig procent van de patiënten verliet het ziekenhuis zonder te weten hoe men de definitieve uitslag zou krijgen. **Hoofdstuk 10** had als doel om op grotere schaal de

patiëntervaringen bij colonoscopie te benchmarken tussen afdelingen met behulp van de GRS in Nederland, om zodoende een de GRS verder te beoordelen als kwaliteitssysteem in patiënt ervaringen. Deze studie, die een vergelijkbare opzet had met de Canadese variant, liet zien dat er ook in Nederland grote verschillen bestonden tussen twaalf verschillende afdelingen, bevestigend voor het benchmark concept. Grote variaties werden gezien in informatievoorziening naar de patiënt toe over hun resultaten na de procedure (0-57%) alsmede de informatievoorziening met betrekking tot complicatie risico's (43-98%). Daarnaast, de comfort status (25-64%) en de tevredenheid over het bespreken van de resultaten na het onderzoek (52-86%) varieerde enorm tussen afdelingen. Significante afdelingstekortkomingen werden geïdentificeerd door middel van deze gestructureerde beoordeling met behulp van de GRS. Verder heeft een benchmark aanpak zoals deze studie als voordeel dat afdelingen de mogelijkheden hebben om oplossingen voor uniforme problemen te delen. Als laatst, deze studie laat zien dat de GRS inhoud ook toepasbaar lijkt in de Europese context voor het beoordelen van patiënt ervaringen.

In **Hoofdstuk 11** werd de incidentie van complicaties na colonoscopie beoordeeld, door middel van een telefooninterview wat plaatsvond 30 dagen na de procedure. Ernstige complicaties of bijwerkingen, welke definitief toegeschreven konden worden aan de colonoscopie, werden gerapporteerd in 0.8% van alle respondenten. Een additionele 0.5% had een mogelijk gerelateerde ernstige complicatie. Kleinere complicaties of bijwerkingen kwam voor in 29% van alle patiënten binnen de 30-dagen periode. Verder werd duidelijk indien patiënten een definitief gerelateerde complicatie of bijwerking hadden gehad van de colonoscopie, dat ze minder snel terug wilden komen voor een vervolg colonoscopie in de toekomst (81 vs. 88%).

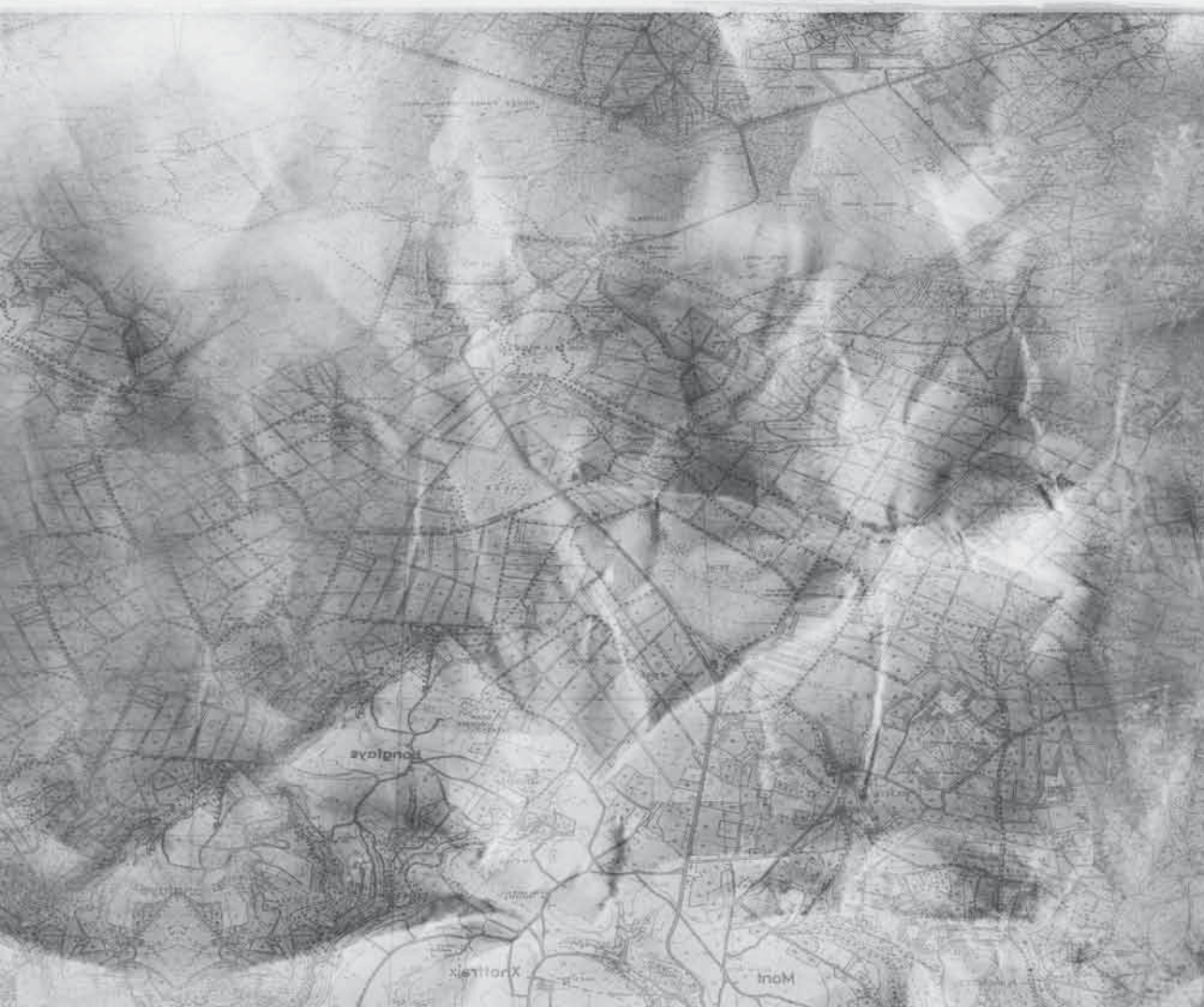
Hoofdstuk 12 heeft betrekking op het optimale gebruik van endoscopie capaciteit op het gebied van surveillance colonoscopie, wat steeds belangrijker word in het kader opkomende CRC screening programma's. In deze studie lieten we zien dat een meerderheid van de surveillance procedures niet werden gedaan volgens de aanbevelingen van de meest recente CRC en adenoom surveillance richtlijnen. Alhoewel detectiecijfers niet significant verschillend waren tussen te vroege-, op tijd- en te late surveillance colonoscopieën, werd het overgrote deel geclassificeerd als te vroeg geplande surveillance colonoscopie (65%). Optimale endoscopie bezetting kan dus worden bewerkstelligd in de surveillance praktijk, maar kan ook worden behaald op het aantal vroege vervolg colonoscopie of de diagnostische colonoscopie. **Hoofdstuk 13** evalueerde deze twee andere aspecten, en hoe dit zich verhoudt in de Nederlandse endoscopie praktijk. Deze studie liet zien dat er een lage opbrengst voor colorectale neoplasie was (4%) voor vroege vervolg colonoscopie die binnen een jaar werden gedaan voor symptomen, en waarbij een compleet en goede darmvoorbereiding op de voorgaande procedure aanwezig was. Daarnaast, lieten we zien als een recente richtlijn werd toegepast op de Nederlandse surveillance praktijk, de hoogste detectiecijfers werden gevonden bij optimale surveillance allocatie ten opzichte van te vroege bezetting van surveil-

lance procedures (30 vs. 20%). De bevindingen voor neoplasie bij surveillance is afhankelijk van bepaalde karakteristieken van de adenomen die gevonden zijn bij het vorige onderzoek. **Hoofdstuk 14** had als doel om een update te geven van de laatst verschenen literatuur door middel van meta-analyse, met betrekking tot het risico van metachrone adenomen bij surveillance colonoscopie. De meest belangrijke determinanten op de index colonoscopie voor dit risico waren advanced adenomen (relatief risico (RR): 1.81), ≥3 adenomen (RR: 1.64), adenoom grootte ≥10 mm (RR: 1.66), en leeftijd ≥60 jaar (RR: 1.65). In Hoofdstuk 12 en 13 was te zien dat endoscopisten vaak afwijken van de surveillance richtlijn. Mogelijke redenen zouden kunnen zijn dat ze niet op de hoogte zijn van deze richtlijnen, of dat men er niet mee eens is. Dit werd onderzocht in **Hoofdstuk 15** onder Canadese endoscopisten door middel van een landelijke vragenlijst studie. Onder negen van de 14 vragenlijst scenario's die werden gepresenteerd aan de artsen, benoemde de colonoscopisten in 12% tot 38% van de gevallen dat hun surveillance aanbeveling gebaseerd was op de richtlijn maar gaven ze niet de juiste aanbeveling die in de richtlijn terug te vinden was. Dit lijkt te suggereren dat onbekendheid een rol speelt, wat mogelijk verbeterd kan worden met een educatie of trainingsprogramma in kennis van de richtlijnen. Een andere reden voor het suboptimale gebruik van surveillance colonoscopie kan ook bij de patiënt gezocht worden, omdat men niet bekend is met het belang van surveillance. **Hoofdstuk 16** had als doel om te bepalen wat patiënten weten over hun bevindingen, en gevolgd door het surveillance beleid. We vonden dat de bekendheid over surveillance matig was (60%) onder een groot cohort van adenoom patiënten. Echter leken de opkomst cijfers voor surveillance colonoscopie per afdeling niet te correleren met de huidige status van informatievoorziening naar patiënten over hun aanbevelingen.

Hoofdstuk 17 is onderdeel van de ontwikkeling van nieuwe richtlijnen voor CRC surveillance voor patiënten die een levertransplantatie ondergaan hebben, door hun verhoogde risico voor het ontwikkelen van maligniteiten na transplantatie. Het excessief verhoogde risico voor CRC in primaire scleroserende cholangitis (PSC), een indicatie voor lever transplantatie (LT), moet hierin meegewogen worden, omdat deze ziekte het risico op CRC beïnvloedt. Daarom hebben deze patiënten al een indicatie voor agressievere surveillance. Onze studie vond een gestandaardiseerde incidentie ratio (SIR) voor CRC in non-PSC post-LT patiënten van 1.26 vergeleken met de algemene bevolking. Dit impliceert dat agressievere surveillance in non-PSC post-LT patiënten niet geïndiceerd lijkt. Hieruit volgend, **Hoofdstuk 18** had als doel om het risico voor CRC in de post-LT periode te bepalen gevolgd door een aanbeveling voor surveillance door middel van een literatuuronderzoek. Deze studie is de eerste in zijn soort tot op heden dat het CRC risico post-LT heeft beoordeeld op deze manier, en vond een significant relatief risico van 1.8 voor CRC in de non-PSC post-LT patiënt. Echter, gebaseerd op vergelijkbare risicomaten in de literatuur, impliceert dit dat intensievere surveillance in de non-PSC post-LT patiënt niet is gerechtvaardigd in de dagelijkse praktijk. **Hoofdstuk 19** bediscussieert dit onderwerp in een breder perspectief, in het kader wat voor bewijs er beschikbaar is voor het risico van CRC post-LT, de rol voor pre-transplantatie CRC screening

opbrengst alsmede post-transplantatie surveillance colonoscopie. Zoals gezegd, post-LT surveillance voor CRC lijkt niet haalbaal en gerechtvaardigd gebaseerd op het beschikbare bewijs, waarbij de rol van pre-LT screening nog onzeker is door het gebrek aan bewijs in dit gebied. **Hoofdstuk 20** geeft de lezer een discussie van deze thesis. Het beschrijft hoe de projecten passen in de huidige stelling van kwaliteitsbewaking van colonoscopie. Het betracht een overzicht te geven hoe dit ligt voor de Nederlandse endoscopie afdeling alsmede hoe deze resultaten als startpunt kunnen dienen voor toekomstige kwaliteitsinitiatieven in de Nederlandse endoscopie sector.

Lists of publications



LIST OF PUBLICATIONS V. DE JONGE

1. V. de Jonge, J. Sint Nicolaas, O. van Baalen, J.T. Brouwer, M.F.J. Stolk, T.J. Tang, A.J.P. van Tilburg, M.E. van Leerdam, E.J. Kuipers. The incidence of 30-day adverse events after colonoscopy among outpatients in the Netherlands. American Journal of Gastroenterology. 2012 [Accepted]
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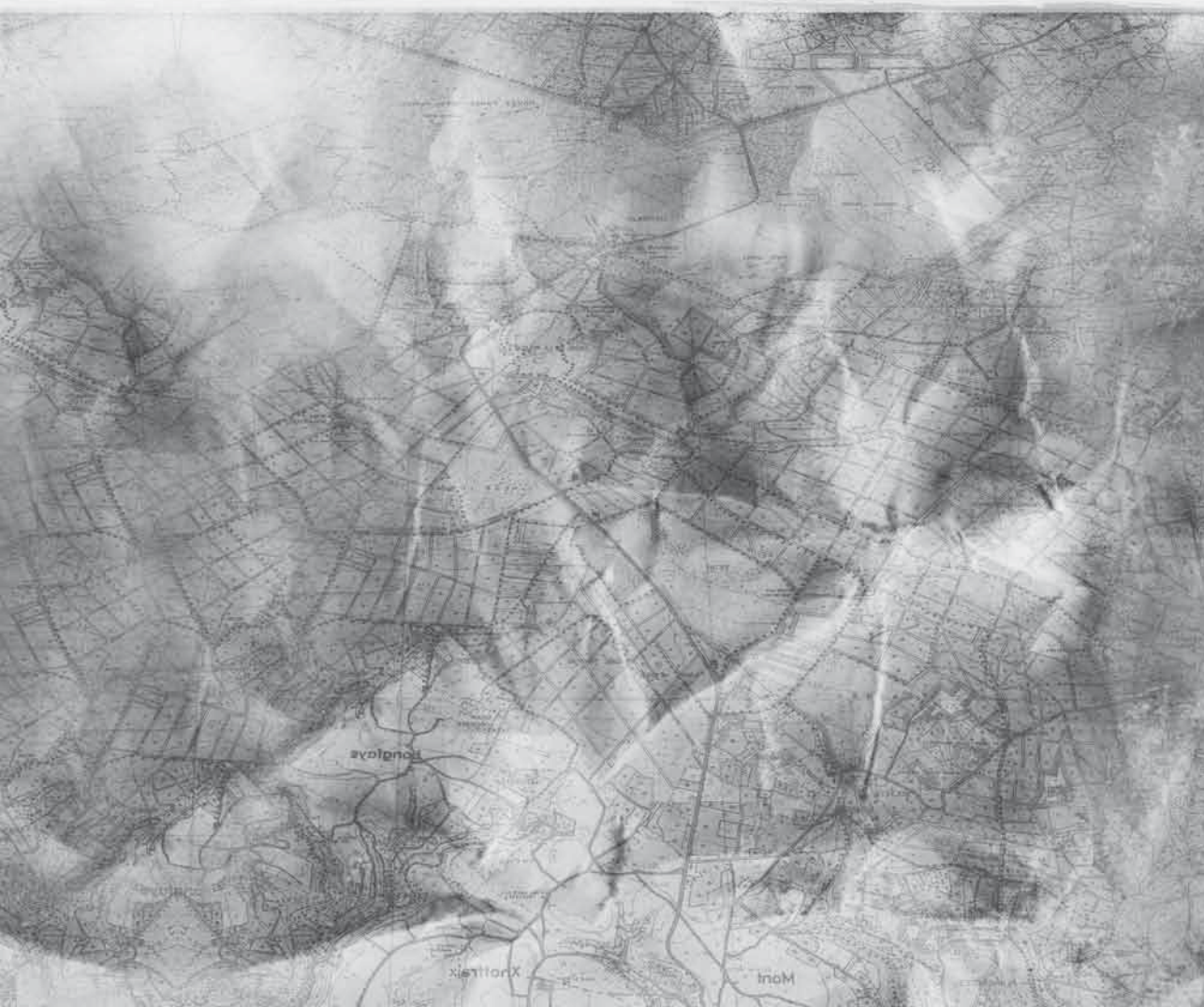
PhD portfolios



PhD portfolio V. de Jonge

ORAL PRESENTATIONS

Quality assurance in colonoscopy – a survey of the patient experience in four hospitals in Edmonton

Gastrointestinal Rounds, University of Alberta Hospital, Edmonton, Alberta, Canada

Global Rating Scale

IKR/Comprehensive Cancer Center Rotterdam, Rotterdam, the Netherlands

Screening for colorectal cancer in The Netherlands; acceptance of faecal occults blood test and sigmoidoscopy

Dutch Society of Gastroenterology 2009, Veldhoven, the Netherlands

The opinion of gastroenterologists towards quality assurance in endoscopy

Dutch Society of Gastroenterology 2010, Veldhoven, the Netherlands

Risk factors of adenoma recurrence at surveillance colonoscopy: a systematic literature review and pooled analysis

Dutch Society of Gastroenterology 2010, Veldhoven, the Netherlands

Quality on the endoscopy departments

Society of Endoscopy Nurses and Assistants 2010, Veldhoven, the Netherlands

Safety in endoscopy: how do we think about it?

National symposium Dutch Society of Gastroenterologists and Hepatologists 2010, Lelystad, the Netherlands

Quality of colonoscopy reporting and performance

Dutch Society of Gastroenterology 2011, Veldhoven, the Netherlands

The occurrence of adverse events in a 30-day period after colonoscopy

Dutch Society of Gastroenterology 2011, Veldhoven, the Netherlands

VIDEO PRESENTATION

Differences in adenoma detection rate between endoscopy departments
Digestive Disease Week 2011, Chicago, Illinois, United States

POSTER PRESENTATIONS

Evaluation of the patient experience in colonoscopy using the GRS: a comparison in 1187 patients in four hospitals in Edmonton, Alberta, Canada.
Canadian Digestive Disease Week 2009, Banff, Alberta, Canada
Digestive Disease Week 2009, Chicago, Illinois, United States

The opinion of gastroenterologists towards quality assurance in endoscopy
Digestive Disease Week 2010, New Orleans, Louisiana, United States

Risk factors for adenoma recurrence at surveillance colonoscopy: a systematic review and pooled analysis
Digestive Disease Week 2010, New Orleans, Louisiana, United States

Quality of colonoscopy reporting and performance
Digestive Disease Week 2011, Chicago, Illinois, United States

The occurrence of adverse events in a 30-day period after colonoscopy
Digestive Disease Week 2011, Chicago, Illinois, United States

Differences in adenoma detection rate between endoscopy departments
Digestive Disease Week 2011, Chicago, Illinois, United States

Attitude of endoscopists and endoscopy personnel towards quality assurance
Digestive Disease Week 2011, Chicago, Illinois, United States

MEMBERSHIPS

2010 Dutch Society for Gastroenterology
2010 Member projectgroup 'Project veilige endoscopie',
Dutch Society for Gastroenterology
2011 Member 'Quality indicators for screening colonoscopy',
Dutch Society of Gastroenterologists and Hepatologists
2011 Member 'Quality indicators for screening colonoscopy',
National Institute for Public Health and the Environment

COURSES

January 2009 Introduction to clinical research, Nihes Rotterdam
April 2009 Liver transplantation for "beginners" part I, Erasmus MC, Rotterdam
July 2009 Methods of health services research, Nihes Rotterdam
January 2010 Regression analysis for clinicians, Nihes Rotterdam
January 2011 Principles of epidemiological data-analysis, Nihes Rotterdam

SUPERVISING GRADUATION PROJECT

Harmke van Kooten, medical student, Erasmus University Rotterdam, the Netherlands.
Awareness of post-polypectomy surveillance guidelines: a nationwide survey among colonoscopists in Canada.

Eline Schreuders, medical student, Erasmus University Rotterdam, the Netherlands.
The appropriateness of surveillance intervals after polypectomy: a retrospective study in Edmonton, Canada

PhD portfolio J. Sint Nicolaas

ORAL PRESENTATIONS

Quality assurance in colonoscopy – a survey of the patient experience in four hospitals in Edmonton

Gastrointestinal Rounds, University of Alberta Hospital, Edmonton, Alberta, Canada

Global Rating Scale

IKR/Comprehensive Cancer Center Rotterdam, Rotterdam, the Netherlands

Is colonoscopy screening mandatory in post-LTx patients?

Dutch Society of Gastroenterology 2009, Veldhoven, the Netherlands

A systematic review of the risk in colorectal cancer (CRC) in post-liver transplant patients

Digestive Disease Week 2009, Chicago, Illinois, United States

Evaluation of colonoscopy performance in daily practice: a multicenter study

Dutch Society of Gastroenterology 2010, Veldhoven, the Netherlands

Quality of colonoscopy: how and where to improve?

Feedback presentations (n=5) to participating endoscopy departments, 2010-2011, the Netherlands

Quality on the endoscopy departments

National Society of Endoscopy Managers 2010, Veldhoven, the Netherlands

Quality of colonoscopy from a patient's perspective using the Global Rating Scale (GRS): a multicenter audit

Dutch Society of Gastroenterology 2011, Veldhoven, the Netherlands

Evaluation of a quality assurance program for endoscopy services in the Netherlands

Dutch Society of Gastroenterology 2011, Veldhoven, the Netherlands

POSTER PRESENTATIONS

Evaluation of the patient experience in colonoscopy using the GRS: a comparison in 1187 patients in four hospitals in Edmonton, Alberta, Canada.
Canadian Digestive Disease Week 2009, Banff, Alberta, Canada

Is colonoscopy screening mandatory in post-LTx patients?
Digestive Disease Week 2009, Chicago, Illinois, United States

Assessment of colonoscopy reporting using the ASGE quality assurance Task Force guidelines: a multicenter study
Digestive Disease Week 2010, New Orleans, Louisiana, United States

Quality of colonoscopy from a patient's perspective using the Global Rating Scale (GRS): a multicenter audit
Digestive Disease Week 2011, Chicago, Illinois, United States

Evaluation of a quality assurance program for endoscopy services in the Netherlands
Digestive Disease Week 2011, Chicago, Illinois, United States

Evaluation of a quality assurance program for endoscopy services in the Netherlands
International Forum on Quality and Safety in Health Care 2011, Amsterdam, the Netherlands

MEMBERSHIPS

2009 Dutch Society of Gastroenterology
2010 Member projectgroup 'Project veilige endoscopie',
Dutch Society for Gastroenterology
2011 Member 'Quality indicators for screening colonoscopy',
Dutch Society of Gastroenterologists and Hepatologists
2011 Member 'Quality indicators for screening colonoscopy',
National Institute for Public Health and the Environment

COURSES

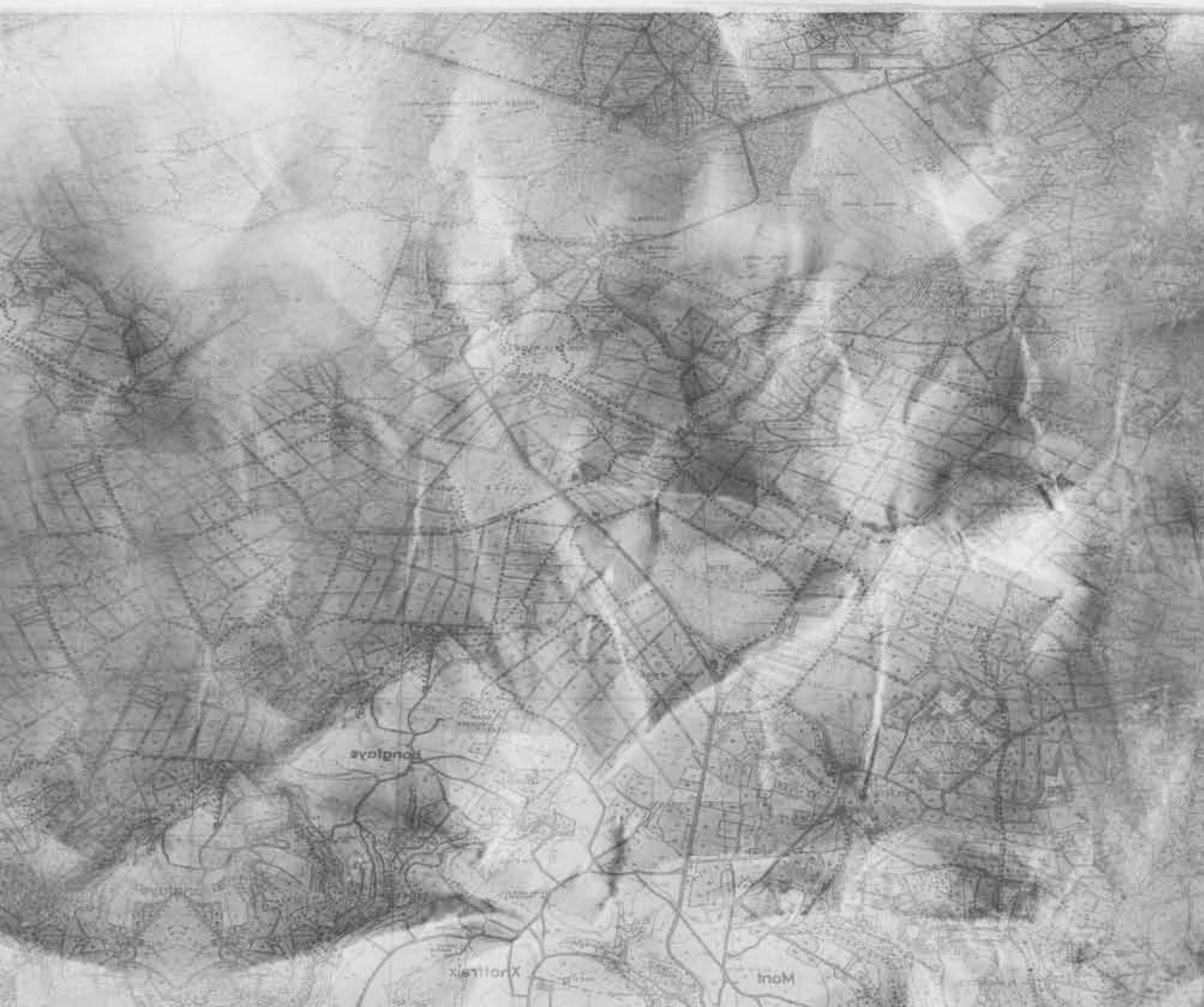
January 2009 Introduction to clinical research, Nihes Rotterdam
April 2009 Liver transplantation for "beginners" part I, Erasmus MC, Rotterdam
July 2009 Methods of health services research, Nihes Rotterdam
August 2009 Topics in meta-analysis, Nihes Rotterdam
October 2009 Liver transplantation for "beginners' part II, Erasmus MC, Rotterdam
January 2010 Regression analysis for clinicians, Nihes Rotterdam
January 2011 Survival analysis for clinicians, Nihes Rotterdam

SUPERVISING GRADUATION PROJECT

Harmke van Kooten, medical student, Erasmus University Rotterdam, the Netherlands.
Awareness of post-polypectomy surveillance guidelines: a nationwide survey among colonoscopists in Canada

Eline Schreuders, medical student, Erasmus University Rotterdam, the Netherlands.
The appropriateness of surveillance intervals after polypectomy: a retrospective study in Edmonton, Canada

Curricula Vitae



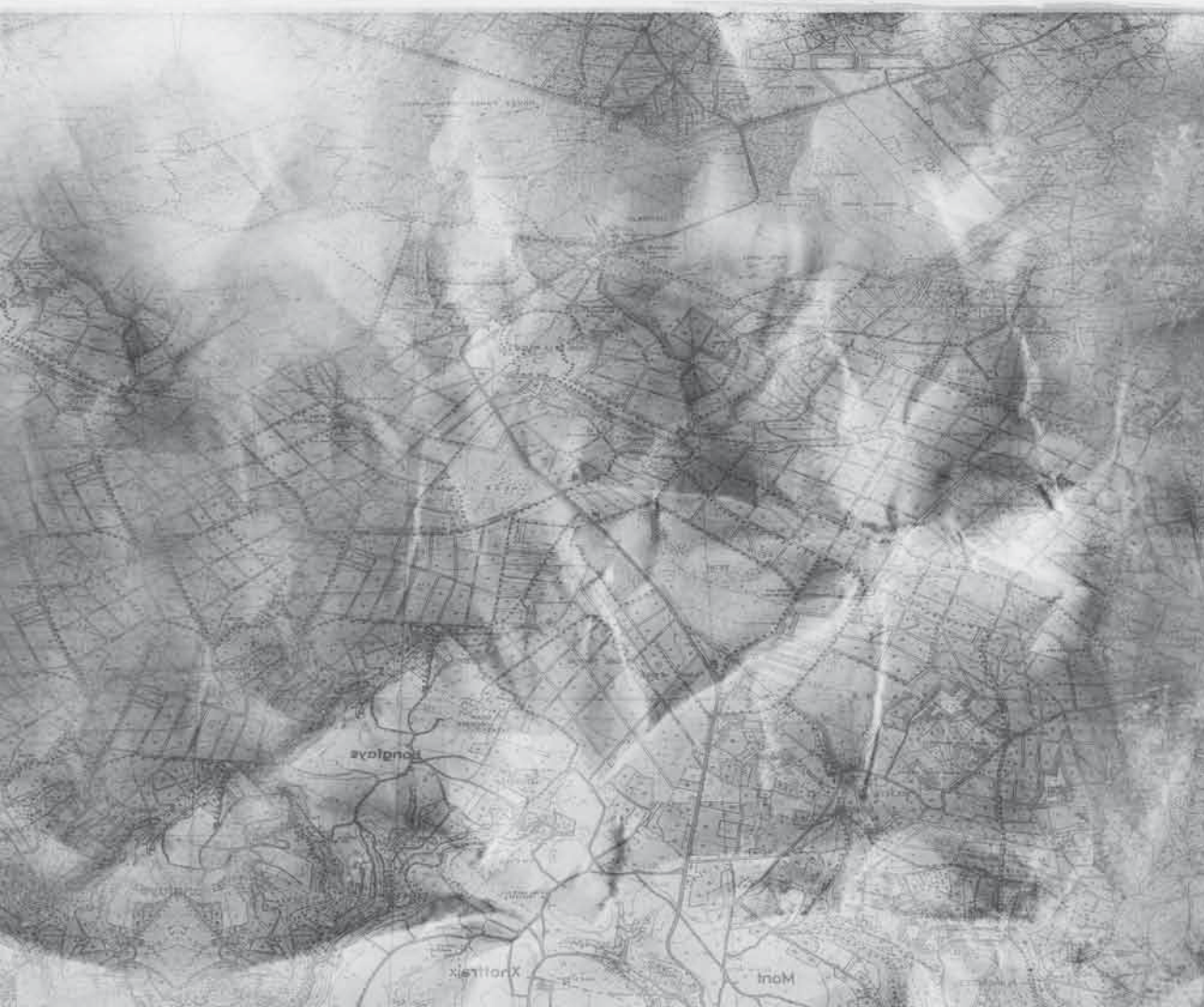
Curriculum Vitae V. de Jonge

Vincent de Jonge werd op 4 september 1985 geboren te Leiden. Na het behalen van zijn gymnasium diploma in het Voortgezet Wetenschappelijk Onderwijs aan het Dr. F.H. de Bruijne Lyceum te Utrecht, ging hij, omdat hij uitgeloot was voor Geneeskunde, eerst een jaar Biomedische Wetenschappen studeren te Utrecht. Na dit jaar werd hij in 2004, via de decentrale selectie, toegelaten tot Geneeskunde aan de Erasmus Universiteit Rotterdam. Gedurende zijn studie heeft hij in het studententeam op de afdeling Maag- Darm- en Leverziekten gewerkt als afdelingsassistent. Via de afdeling kwam hij voor het eerst in contact met wetenschappelijk onderzoek en heeft onder andere een tijd als student-onderzoeker gewerkt voor het proefbevolkingsonderzoek naar dikke darmkanker. In 2008 deed hij, in het kader van zijn wetenschappelijke stage, via deze afdeling 6 maanden onderzoek aan het University of Alberta Hospital in Edmonton, Alberta, Canada. Zijn begeleider bij dit onderzoek waren Prof.dr. S.J.O. Veldhuyzen van Zanten, mw. dr. M.E. van Leerdam en Prof.dr. E.J. Kuipers. Bij terugkomst in Nederland werd hem een promotietraject aangeboden op de afdeling Maag- Darm- en Leverziekten in het Erasmus MC onder begeleiding van zijn promotor Prof.dr. Kuipers, en copromotor mw. dr. M.E. van Leerdam. Tussen januari 2009 en april 2011 was hij werkzaam als onderzoeker in het Erasmus MC. Inmiddels is hij per juli 2011 gestart met zijn coschappen in het kader van zijn studie Geneeskunde. Hij hoopt in de loop van 2013 zijn artsexamen te behalen.

Curriculum Vitae J. Sint Nicolaas

Jerome Sint Nicolaas werd op 7 januari 1986 geboren te Dordrecht. Na het behalen van zijn diploma in het Voortgezet Wetenschappelijk Onderwijs (VWO) aan het Altena College te Sleeuwijk, ging hij per direct Geneeskunde studeren waarbij hij via de decentrale selectie toegelaten werd op de opleiding aan de Erasmus Universiteit Rotterdam. Gedurende zijn studie heeft hij in het studententeam op de afdeling Maag- Darm- en Leverziekten gewerkt als afdelingsassistent en teamleider. In zijn 3e jaar van de studie Geneeskunde kwam hij voor het eerst in aanraking met het doen van onderzoek, waar hij samenwerkte met mw. dr. M.E. van Leerdam aan een studie waarvan de publicatie ook is opgenomen in dit proefschrift. In 2008 deed hij, in het kader van zijn wetenschappelijke stage onderzoek, via dezelfde afdeling 6 maanden onderzoek aan het University of Alberta Hospital in Edmonton, Alberta, Canada. Zijn begeleider bij dit onderzoek waren Prof.dr. S.J.O. Veldhuyzen van Zanten, mw. dr. M.E. van Leerdam en Prof.dr. E.J. Kuipers. Bij terugkomst in Nederland werd hem een promotietraject aangeboden op de afdeling Maag- Darm- en Leverziekten in het Erasmus MC onder begeleiding van zijn promotor Prof.dr. Kuipers, en copromotor mw. dr. M.E. van Leerdam. Tussen januari 2009 en april 2011 was hij werkzaam als onderzoeker in het Erasmus MC. Inmiddels is hij per juli 2011 gestart met zijn coschappen in het kader van zijn studie Geneeskunde. Hij hoopt in de loop van 2013 zijn artsexamen te behalen.

Dankwoorden



Dankwoord V. de Jonge

Aan het einde van een lange beklimming ontvouwt zich, bij de laatste stappen naar de top, langzaam het panorama waar je al die tijd naar toe hebt gewerkt. Tegelijkertijd biedt het bereiken van het einddoel de beste terugblik op het pad dat je daarnaar toe heeft geleid. Zo is het ook nu ik begonnen ben aan het laatste onderdeel van mijn proefschrift, het dankwoord. Hier aangekomen kijk ik terug op een panorama van leerzame ervaringen, geweldige collega's en bijzondere momenten. Zo´n top bereik je alleen met de hulp van vele anderen, die ik dan ook grote dank verschuldigd ben. Nog vier stappen...

Allereerst wil ik mijn promotor, professor Kuipers, bedanken. Dank voor de kans die u mij geboden heeft om dit promotietraject in te gaan en het vertrouwen dat u in mij gesteld heeft. Als grote motivator wist u mij, met uw enthousiasme, iedere keer te overtuigen van het belang van ons onderzoek. Daarnaast wist u met uw input ieder manuscript weer naar een hoger plan te tillen. Ik heb grote bewondering voor uw inzet en enthousiasme als klinicus, wetenschapper en afdelingshoofd.

Ook mijn copromotor, Monique van Leerdam, wil ik bedanken. Als dagelijks begeleider hebben we veel overleg gehad en de drempel om binnen te lopen was altijd laag. Het is bewonderenswaardig om te zien hoe jij de drukke kliniek hebt weten te combineren met zoveel onderzoek en een druk privé-leven. Het AvL heeft er in jou een fantastische arts en collega bij.

Een speciale plek in dit dankwoord is voor prof. Veldhuijzen van Zanten. Beste Sander, de mogelijkheid om onderzoek te komen doen in Edmonton is een onvergetelijke ervaring geweest en een beslissend moment in mijn leven. Jouw enthousiasme leidde ons langs de colonoscopien, cowboys, GRS, Oasis, de Oilers en de Rockies. Volgens mij hebben we samen het maximale uit onze studies en reis gehaald. Ondanks de afstand hebben we altijd goed contact gehouden en ik vind het dan ook heel bijzonder dat je op deze dag in de commissie plaats hebt willen nemen. Ook in de toekomst hoop ik dat onze wegen elkaar nog regelmatig mogen kruisen!

Natuurlijk ben ik ook Prof. Lange en Prof. Metselaar dankbaar dat zij zitting hebben willen nemen in de promotiecommissie en tijd en energie hebben gestoken in de kritische beoordeling van mijn proefschrift. Nog drie stappen...

Zonder collega's die je af en toe overeind helpen, de weg wijzen en aan wie je je kunt optrekken richting het einddoel, was de weg ernaar toe een stuk zwaarder geweest. Met heel veel

plezier denk ik terug aan de gezellige borrels, memorabele congressen en de uitwisseling van zoveel mooie ervaringen. De 'dakpoli' voelde als een warm thuis!

Natuurlijk is dit proefschrift een tandem-prestatie. Waar Bassie is, daar komt Adriaan. Jerome, waar wij begonnen als studiegroepsgenoten in het eerstejaar van geneeskunde (jij weet het nog beter te vertellen dan ik) eindigen we nu met een gezamenlijk proefschrift. De afgelopen jaren hebben we een heel vruchtbare samenwerking gehad. We vulden er elkaar goed aan (ik bijvoorbeeld met mijn 'mappies' en jij met je onfeilbare namenkennis). Het sparren, frustaties afreageren en taaie werk verzetten, het was fantastisch om jou als collega te hebben! Maar buiten het werk hebben we er ook alles uitgehaald. Het kamperen bij -8º, Nahma, Merritt, John D*gweed, zeehonden, de Magic-bus, stappen, de basement, berenjacht, genoeg mooie momenten!

Speciale dank ook voor mijn 'colon-buddies' Aafke en Leonie. Heerlijk om af en toe frustaties te kunnen delen, te kunnen lachen om elkaars uitglijders en elkaar verder te helpen. Aaf, ik heb heel veel bewondering hoe jij je overal doorheen hebt geslagen en je mag ongelofelijk trots op het eindresultaat zijn! Leo, ook jij bent er bijna. De bergen werk die jij verzet hebt zijn werkelijk niet te filmen! Succes met de laatste loodjes.

Ook alle andere collega onderzoekers verdienen een plek in dit proefschrift. Als ik terugdenk aan Veldhoven, de Nihes-cursus, New Orleans, de dakpoli, het buitenterras, Chicago of Houffalize, zie ik één gemene deler: support! Dat is het bijzondere van de grote groep mensen met wie ik het geluk heb gehad samen te mogen werken, altijd stond er ergens wel iemand klaar om steun te verlenen voor welk probleem dan ook! Ook al heb ik altijd de klappen op mogen vangen (Mexicaanse griep, bedwantsen, teken) ik deed het met veel plezier voor jullie, want ik kreeg er heel veel voor terug: gezellige etentjes, mountainbiken, de spirit om snelle tijden te lopen, statistische hulp, onvergetelijke Oranje-wedstrijden, Sinterklaas-borrels, goede stapavonden en sterke verhalen. Bedankt Femme, (grote) Paul, Edmée, Susanne, Vivian, Aria, Robert, (grote) Vincent, Caroline, Roeland, Daphne, Ad, Ludi, Lauran, Celine, Renate, Veerle, Atija, Esther, Florine, Lieke, Pauline, Edith, Else-Mariëtte, Milan, Vera, Judith, Margot, Nicoline, Jurrien, Marjolein, Dew, Marianne, Edith, Lisette, Jildou, Jorie, Lisanne en Desirée. Nog twee stappen…

Evert en Rick, als ik één team naast mij zou wensen op deze dag dan zijn jullie dat! De keus voor jullie als paranimfen was niet zo moeilijk, we hebben elkaar immers al overeind gehouden in sneeuwstormen, bij -20º en in gletsjerspleten. Tien jaar nadat wij ergens in een vaag bos in Delft bijeenkwamen hebben we al zoveel achter de rug. Van Caraz tot aan Bitola en van Bajrum Curri tot aan Imst. We hebben een spoor van TCX over de wereld achter gelaten! Laten we de komende jaren vooral zo doorgaan en al ons grote masterplan verwezenlijken.

Ook de gezelligheid en ontspanning buiten het werk om maken dat ik met veel plezier terugkijk op de afgelopen jaren. Bedankt voor de mooie festivals, het mezelf ongegeneerd kunnen uitnodigen, heerlijke vakanties en sportmomenten Sander, Roy en Nena, Ka-Wing, Sloof, Maerten, Melanie, Han en Lies, Adelina en Patrick en de jongens van NOC Kralingen en PVC.

Mijn broers en zussen wil ik danken voor alle steun de afgelopen jaren. Bedankt dat ik bij jullie zo mezelf kan zijn. We hebben met zijn allen heel veel meegemaakt de laatste jaren en zijn daardoor dicht naar elkaar toe gegroeid. Laten we dat koesteren! Ik vind het heel bijzonder ons geluk met elkaar te delen. Jullie zijn allemaal kranen (en kletsmajoren...)!

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Lieve papa en mama. Ik kan jullie niet genoeg bedanken voor de kansen die jullie me gegeven hebben. Ik voel me bijzonder gezegend met zulke ouders! Ik kan er een heel boek overschrijven (wie weet mijn volgende publicatie), maar het komt er op neer dat jullie echt tonen wat ouderlijke liefde betekent! Dank voor jullie oneindige interesse, liefde en steun.

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Nog één stap... En dan ontvouwt zich een panorama met nieuwe kansen en uitdagingen!

Dankwoord J. Sint Nicolaas

Zoals verondersteld mag worden, is deze dubbelpromotie niet alleen tot stand gekomen door Vincent en mezelf, maar heeft een lange geschiedenis gekend met veel hulp uit binnen- en buitenland.

Allereerst wil ik graag mijn promotor en copromotor bedanken, professor dr. E.J. Kuipers en dr. M.E. van Leerdam.

Beste Ernst, zeer veel dank voor de grote kans die je mij hebt gegeven om dit kwaliteitsproject op poten te mogen zetten in de Nederlandse endoscopie setting. Ik heb altijd met plezier met je overlegd, samengewerkt en suggesties zeer ter harte kunnen nemen voor de artikelen in dit gepresenteerde proefschrift. Het intreden van verscheidene commissies is allemaal dankzij jou bewerkstelligd. Als Sint Nicolaas zeggend: heel erg bedankt voor alles in afgelopen jaren.

Beste Monique, ik herinner me zeer goed in het jaar 2007 dat je op de afdeling MDL in het Erasmus MC naar mij toe kwam, met de vraag of ik interesse had om een statusonderzoek te gaan starten. Ik was toen nog werkzaam als studententeam lid op 3 Noord, als 3e-jaars geneeskunde student. Als 'groene' onderzoeker, heb ik zeer veel van je mogen leren, op het gebied van artikelen schrijven tot statistiek, en heb altijd met veel plezier met je samengewerkt. Ook tijdens mijn promotieonderzoeksperiode was jij altijd bereid om even kort wat dingen door te spreken, zeer toegankelijk met jouw toch al drukke agenda. Heel erg bedankt voor jouw tijd en alle moeite met het vervaardigen van dit proefschrift.

Mijn dank gaat ook uit naar degene met de zowel Canadese als Nederlandse achtergrond, professor dr. S.J.O Veldhuyzen-van Zanten.

Beste Sander, in 2008 kwamen we daar dan aan, in het koude Edmonton in Canada. Vincent en ik hebben het er vaak over gehad hoe uniek de kans was om ons onderzoek in Canada te mogen doen, onder zulke prettige omstandigheden en begeleiding. Na een productief half jaar op wetenschappelijk gebied, heeft ons onderzoek een grote impuls gekregen. We hebben veel aan jou te danken. Er werd ook de basis gelegd voor een goede vriendschap daar we elk jaar proberen op de DDW een korte reünie te houden, iets wat tot dusverre steeds gelukt is. Bedankt voor de mooie ervaringen en je hulp!

Tevens wil ik ook de overige commissieleden bedanken voor het beoordelen van mijn proefschrift, te weten professor dr. H.J. Metselaar, professor dr. J.F. Lange, professor dr. J.D.F. Habbema, dr. I.J. Korfage, dr. W. Moolenaar en professor dr. P.B.M. Robben. Graag ook grote

dank aan alle overige betrokken MDL-artsen van de participerende ziekenhuizen, te weten professor dr. M.J. Bruno, dr. A.J.P van Tilburg, dr. J.T. Brouwer, dr. D.L. Cahen, dr. W. Lesterhuis, dr. T.J. Tang, dr. F.J.G.M. Kubben, dr. R.J.Th. Ouwendijk, dr. O. van Baalen, dr. F. ter Borg en dr. M. Stolk. Mijn dankwensen gaan ook naar alle verpleegkundigen en zorgmanagers die gelieerd zijn aan de twaalf endoscopie afdelingen waarin wij ons onderzoek konden doen. Zonder al deze mensen was het niet mogelijk geweest om de gepresenteerde projecten tot een mooi einde te brengen. Naast de mensen op MDL , wil ik graag mijn dank betuigen aan professor dr. E.W. Steyerberg, van de Maatschappelijke Gezondheidszorg. Dank voor uw (statistische) input en besprekingen, die altijd aangenaam en voor mij zeer waardevol waren. Mijn dank gaat ook uit naar Wendy Holleman, Andrea Lubeek en naar Bernadette Lourens, die ons te allen tijde hebben ondersteund, van opstarten van het promotietraject tot de logistiek en indiening van het proefschrift.

Ook mijn collega's, werkzaam als promotieonderzoekers dan als wel arts-assistenten, dienen niet vergeten te worden.

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