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Minimising risk and improving the management of colonoscopic adverse events

DERBYSHIRE, EDMUND,MICHAEL,HARTLEY

Minimising risk and improving the management of colonoscopic adverse events

Edmund Michael Hartley Derbyshire

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School of Medicine, Pharmacy & Health
Durham University
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Supervisors

Professor APS Hungin

Professor in the School of Medicine, Pharmacy & Health

Durham University

Wolfson Building

Queens Campus

Stockton-On-Tees

TS17 6BH

Professor Matthew D. Rutter

Consultant Gastroenterologist

Honorary Professor of Gastroenterology, Durham University

Director, Tees Bowel Cancer Screening Centre

University Hospital of North Tees

Stockton-On-Tees

TS19 8PE

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Abstract

Introduction

Colonoscopy is the gold standard screening tool for colorectal cancer and is used as such in the English National Health Service Bowel Cancer Screening Programme (NHSBCSP). It does, however, carry a risk of adverse events that may compromise patient safety and the integrity of the screening programme. This thesis examined the colonoscopic adverse events perforation, post polypectomy bleeding (PPB) and post colonoscopy colorectal cancer (PCCRC) in the NHSBSCP.

Aims & Methods

1. Determine the frequency of perforation, PPB and PCCRC in the NHSBCSP.

2. Determine the impact of perforation and PPB on patients and colonoscopists.

3. Identify risk factors for perforation so that its risk can be minimised.

4. Improve the management of perforation and PPB to improve patient outcomes.

To achieve the aims of this thesis I used mixed methodology comprising both quantitative and qualitative health research methods.

Results

The frequency of the colonoscopic adverse events studied was 0.06% for perforation and 0.44% for post polypectomy bleeding.

Perforation led to hospital admission in 98.7% of patients, with 53.9% of admissions having surgery and 26.1% of admissions leaving hospital with a stoma. Only perforations that had surgery developed post perforation morbidity and were admitted to intensive care.

Perforation has a profound psychological impact on the colonoscopist involving four stages of reaction.

Risk factors for perforation include time pressure, colonoscopist fatigue, a longer procedure than the colonoscopist expected and equipment failure.

PPB led to hospital admission in 64.7% of patients studied with 27.9% of patients studied having a repeat endoscopic examination. 1.47% of the patients with PPB studied had surgery and 1.47% of the patients with PPB studied had radiological intervention.

Conclusions

1. The rates of perforation and PPB in the NHSBCSP are in line with other similarly sized studies reported globally. The robust system for capturing details of perforation and PPB in the NHS BCSP suggest the rates reported in these studies accurately reflect their true rate.

2. Perforation leads to hospital admission in nearly all patients. Of those perforations admitted to hospital, surgery occurred in approximately a half, with stoma formation in approximately a quarter and post perforation morbidity in approximately one fifth.

3. PPB leads to hospital admission in approximately two thirds of patients. Over half of the Post Polypectomy Bleeds are of minor severity

4. Colonoscopists should be aware that time pressure, colonoscopist fatigue, a longer procedure than the colonoscopist expected and equipment failure may be associated with perforation.

Authorship Note

I confirm that no part of the material offered has previously been submitted by me for a degree in this or any other university. Material from the work of others has been acknowledged with quotations and paraphrases suitably indicated.

Dissemination

Colonoscopic perforations in the English NHS Bowel Cancer Screening Programme: Beware diagnostic perforations and the sigmoid colon

Top Abstract Prize

United European Gastroenterology Week 2015

Travel Grant (Clinical Science)

United European Gastroenterology Week 2015

Oral Presentation

Opening Plenary Session

United European Gastroenterology Week 2015

Fira de Barcelona – Gran Via Venue

Barcelona

26th October 2015

Poster Presentation

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Post Polypectomy Bleeding (PPB) in the English NHS Bowel Cancer Screening Programme

Oral Presentation

Prevention and management of procedure related GI complications symposium

United European Gastroenterology Week 2015

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27th October 2015

Poster Presentation

Digestive Diseases Federation 2015

The Excel

London

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Asymptomatic radiologically detected perforations in the English NHS Bowel Cancer Screening Programme

Poster Presentation

United European Gastroenterology Week 2015

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Contents

Glossary of Abbreviations

AKI	Acute Kidney Injury
APC	Argon Plasma Coagulation
ASA	American Society of Anaesthesia
ASGE	American Society of Gastrointestinal Endoscopy
AXR	Abdominal X-Ray
BCSC	Bowel Cancer Screening Centre
BCSP	Bowel Cancer Screening Programme
BCSS	Bowel Cancer Screening System
CD	Clinical Director
CI	Confidence Interval
CIR	Caecal Intubation Rate
CT	Computed Tomography
CXR	Chest X-Ray
ESD	Endoscopic Submucosal Dissection
EMR	Endoscopic Mucosal Resection
ESGE	European Society of Gastrointestinal Endoscopy
FOBT	Faecal Occult Blood Test
NHS	National Health Service
ICU	Intensive Care Unit
IPA	Interpretative Phenomenological Analysis
IV	Intravenous
JAG	Joint Advisory Group on Gastrointestinal Endoscopy
LST	Laterally Spreading Tumour

LST-G	Laterally Spreading Tumour of the Granular Type
LST-NG	Laterally Spreading Tumour of the Non Granular Type
MD	Doctor of Medicine
NCDR	National Cancer Data Repository
NBM	Nil By Mouth
PIS	Participant Information Sheet
PPB	Post Polypectomy Bleeding
PPH	Post Polypectomy Haemorrhage
PCCRC	Post Colonoscopy Colorectal Cancer
RR	Relative Risk
SPSS	Statistical Package for the Social Sciences
SSP	Specialist Screening Practicioner
USA	United States of America

Chapter 1

Introduction

Patient safety is one of the primary concerns for all those who are involved in healthcare[1]. This is particularly the case in the setting of a screening programme where people have not initially sought medical attention for the disorder they are being screened for.

Since its introduction into clinical practice, colonoscopy has played an increasing role in the diagnosis, management and screening of colorectal disease[2]. It is now the gold standard screening tool for colorectal cancer and is used as such in the English National Health Service (NHS) Bowel Cancer Screening Programme (BCSP)[3]. As uptake into the BCSP increases and the demand for colonoscopy as a diagnostic and therapeutic tool increases, the need for colonoscopy and colonoscopists is likely to increase further.

Colonoscopy is considered a safe procedure and has been beneficial in the diagnosis, treatment and screening of many people with colorectal disease. However, it will always carry a risk of events that may compromise the safety of patients. Such events, in healthcare, are termed 'adverse events'; in the context of a colonoscopy, these events are called 'colonoscopic adverse events'. A colonoscopic adverse event may be defined as an 'event that prevents completion of a planned procedure, excluding technical failure or bowel preparation, or results in admission to or prolongation of an existing hospital

stay, subsequent medical consultation or another procedure which may be endoscopic, radiological or surgical'[4].

Colonoscopic adverse events may occur at any point from the start of preparation for a colonoscopy to days or even weeks following completion of the procedure. Potential adverse events are numerous and relate to the many facets of having a complete colonoscopy. The potential for a patient to have an adverse event starts with the bowel preparation required. Cardiopulmonary adverse events may occur following the use of analgesia and sedative medication given to patients in the endoscopy room. Therapy performed during a colonoscopy, such as a polypectomy, may be associated with an adverse event, for example, post polypectomy electrocoagulation syndrome[5].

However, it is colonoscopic perforation and post polypectomy bleeding (PPB) that are the most serious adverse events. They have been associated with patient morbidity and mortality[6]. I proposed that post colonoscopy colorectal cancer (PCCRC) can also be included within the definition of an adverse event. A post colonoscopy colorectal cancer, by definition, results in subsequent medical consultation and/or another procedure that may be endoscopic, radiological or surgical. All three of these adverse events potentially pose the greatest threat to the safety of people who take part in colorectal cancer screening as they all have the potential to result in patient death.

This thesis examined these three colonoscopic adverse events in the English NHS BCSP. This examination comprised several distinct themes. Initially, I aimed to

determine how often these events occurred to members of the English public who accept the invitation to have a colonoscopy in the NHS BCSP. It then explored the impact of these adverse events, not only on the patients within the programme, but also on the health care professionals who perform the colonoscopies.

I then intended to identify risk factors for these adverse events with the intention that such risk factors could potentially be removed from subsequent practice. Despite the identification of risk factors these adverse events may continue to occur. It is therefore imperative that those patients who suffer should be assessed and managed to the best possible standard so that they have the best possible outcomes. A further intention of writing this thesis was to provide an evidence base of how to ensure patients have the best possible outcomes.

Work has appropriately focused on patients who have been subject to colonoscopic adverse events. However, it is important to recognise that the association with an adverse event may also affect the colonoscopist. Furthermore, the adverse event may be to the detriment of their subsequent colonoscopic practice.

This thesis also planned to provide a reference point that all colonoscopists could use and relate to should they encounter an adverse event associated with a colonoscopy they perform in the future.

Combining these themes and the research studies in this thesis I aimed to provide an evidence base to minimise risk and improve the management of colonoscopic adverse events. By establishing this evidence base, I intended to improve patient safety surrounding colonoscopy.

Chapter 2

Literature review

2.1 Strategy for literature review

The aims of this literature review were to:

1. Provide an overview of the current use of colonoscopy in screening programmes for colorectal cancer and the benefits that such screening programmes confer.

2. To explain the potential adverse events that are associated with colonoscopy and how they are classified.

3. Provide a detailed overview of the colonoscopic adverse events perforation, post polypectomy bleeding and post colonoscopy colorectal cancer.

4. Critically review the available literature covering the definition, incidence, risk factors, presentation, management and prognosis of perforation, post polypectomy bleeding and post colonoscopy colorectal cancer.

5. Explore the potential reaction of a colonoscopist to an adverse event by reviewing the available literature on the reaction of other health care professionals to adverse events in the health care setting.

The literature review is a comprehensive review of the most up to date, globally published literature on these topics. When I reviewed the incidence of these adverse events, I provided a historical perspective over time.

Online literature searches were performed using PubMed (http://www.ncbi.nlm.nih.gov/pubmed), NHS Evidence (https://www.evidence.nhs.uk/about-evidence-services/journals-and-databases) and the electronic journal resource of the Durham University Library. Personal membership of the British Society of Gastroenterology and the American Society of Gastrointestinal Endoscopy allowed literature searches in Gut online (http://gut.bmj.com) and Gastrointestinal Endoscopy (http://www.giejournal.org).

A review of literature should take place according to guidelines such as those published in the 'Preferred Reporting Items for Systematic Reviews and Meta Analyses' (PRISMA) statement published in 2009. The PRISMA statement was extensively published in order to encourage its widespread use following sub optimal reporting of meta analyses[7].

The PRISMA statement consists of a checklist and flow diagram, which are used in conjunction with an explanation and elaboration document. Checklist items to cover when reviewing literature are: (a) the abstract includes a structured summary (b) the introduction includes the rationale and objectives (c) the methods section includes the protocol, eligibility criteria, information sources, search strategy, process for selecting studies, data collection process, data items, risk of bias, summary measures, synthesis of results, risk of bias across studies and additional analyses (d) the results include the study selection, study characteristics, risk of bias within studies, results of individual studies, synthesis

of results, risk of bias across studies and additional analyses (e) the discussion includes a summary of evidence, limitations, conclusions and (f) that a section relating to describing sources of funding is included[8].

The PRISMA flow diagram records the number of studies that are identified through database searching and other sources then the number of duplicate studies that are removed. This process is termed 'identification'. 'Screening' then follows by documenting the number of records screened and excluded. The number of full text articles assessed for eligibility and number of full text articles excluded with reasons is then documented during the phase of 'eligibility'. Finally, the number of studies then included in the qualitative synthesis is recorded[7].

2.2 The adenoma to carcinoma sequence

The development of screening programmes for colorectal cancer such as the English National Health Service Bowel Cancer Screening Programme is based on the fact that colorectal cancer has a detectable early pre malignant stage. The majority of colorectal cancers develop from pre cancerous polyps called adenomas. The development of pre cancerous polyps to colorectal cancers is commonly referred to as the adenoma to carcinoma sequence. The term describes the stages of progression from normal colonic mucosa to adenoma to cancer. Evidence for the adenoma carcinoma sequence is taken indirectly from epidemiological, histopathological, clinical and genetic data.

The prevalence of both adenomas and carcinomas has been reported to increase with increasing age. Muto et al. reported how those patients who have adenomas were approximately 5 years younger than patients with cancers[9]. Observational studies of polyps left in situ, before polypectomy took place, reported both polyp growth and cancer development at the colorectal location where the polyp was observed[10].

Histopathological studies have shown how both cancer may be present within adenomatous tissue and vice versa. Muto et al. also found that adenomatous tissue was present in 14.2% of colorectal cancers[9]. In addition, the degree of adenomatous tissue has been shown to be related to the stage of the cancer with adenomatous remnants found in 57-60% of cancer limited to the submucosal layer but in only 7-17% of cancers with extramural spread[11] [12]. This suggests as the cancer grows adenomatous tissue is replaced by the cancer.

Clinical studies have shown how the colorectal location of both adenomas and colorectal cancers is similar with most being left sided. Adenomas of the left colon are also more likely to contain invasive adenocarcinoma or severe dysplasia. Eide et al reported how those patients with colorectal cancers will have adenomas elsewhere in the colon at diagnosis[11]. Granqvist et al. showed how the distribution of cancers and adenomas in the colon was similar[13]. More recently the incidence of colorectal cancer has also been shown to fall by breaking the adenoma – carcinoma sequence through colorectal cancer screening using colonoscopy and polypectomy[14].

Vogelstein et al. proposed a genetic model for the adenoma to carcinoma sequence in 1988[15]. The genes involved in genetic alterations include oncogenes, tumour suppressor genes and DNA repair genes. Genes involved in the adenoma to carcinoma sequence include inactivation of the *APC* tumour suppressor gene, K-*ras* oncogene mutation and inactivation of *p53* [16] [17] [18].

2.3 Screening programmes for colorectal cancer

Each year 150,000 European citizens die from colorectal cancer, known colloquially as bowel cancer[19]. The United Kingdom accounts for 16,000 of these cases. Only lung cancer results in a higher annual death rate in the United Kingdom and in Europe[20].

Despite recent advances in the diagnosis and treatment of colorectal cancer, its mortality is not declining. Reducing its mortality rate is dependent on the early detection of the cancer before it has the opportunity to cause symptoms in the individual if affects[19]. Individuals diagnosed with a colorectal cancer earlier in its development have been shown to have a much higher rate of survival than those who are diagnosed when the cancer is more advanced[21]. It is for these reasons, in addition to the fact that colorectal cancer fulfils all of the criteria for a screening programme established by Junger and Wilson in 1968, that many countries across the world have adopted a screening programme for colorectal cancer[22].

The Faecal Occult Blood Test (FOBT) is the most widely used and studied primary screening investigation. It was initially recommended as such following

the research of the American physician, DH Greegor, which was published in 1971[23]. Two different types of FOBT are now used. The guaiac test (gFOBT), proposed by Greegor, is based on the response of guaiac resin to the peroxidase activity of haemoglobin. The immunochemical test detects the globin protein of human haemoglobin[19].

Screening for colorectal cancer with the FOBT has been shown to reduce colorectal cancer mortality. A systematic review of colorectal cancer screening using the FOBT, including four randomised controlled trials, showed that the test resulted in a 16% relative risk reduction in colorectal cancer mortality. When adjusted for screening attendance in the individual studies, there was a 25% relative risk reduction for those attending at least one round of screening using the FOBT[24]. In addition to the reduction in mortality, bowel cancer screening has also been shown to be cost effective. Economic analyses suggested a quality adjusted life year gained of <£3000 for guaiac based FOBT screening[20].

Germany first introduced a FOBT based screening programme for colorectal cancer in 1976[19]. By 2009, screening programmes were planned or fully functional in 19 of 27 European countries. Such programmes vary in their methodology; in data collected from 2007, guaiac based FOBT was used as the primary screening test in 12 European countries including England[25].

By 2007, colonoscopy was the only screening test being used in Poland in an opportunistic nationwide program although roll out of the program was on going. In Austria, Cyprus, Germany, Greece and the Slovak Republic guaiac based

FOBT was used with colonoscopy while Italy used immunochemical FOBT and Flexible Sigmoidoscopy[25]. Colonoscopy is also offered opportunistically in Italy to those aged 45 years or over[19].

The English National Health Service (NHS) Bowel Cancer Screening Programme (BCSP) commenced in 2006, with the programme being fully functional by January 2010. All members of the English public registered with a general practitioner are invited to take part using a gFOBT around the time of their 60th birthday. For those with a negative gFOBT, the invitation to repeat the test is made every two years until the age of 74 years[20]. Those with an abnormal gFOBT are advised of the need for a secondary screening investigation in order to reach a diagnosis. This investigation will usually be a colonoscopy. All colonoscopies are performed at Joint Advisory Group (JAG) on Gastrointestinal Endoscopy approved screening centres by screening accredited colonoscopists who have undertaken both written and practical assessment[20].

Two years into the BCSP in England, 18,135 people had undergone colonoscopy. Of these, 1,772 were diagnosed with a colorectal cancer. 12% of men and 6.2% of women were found to have high risk colorectal adenomatous polyps and invited for a further surveillance colonoscopy one year later. 19.3% of men and 14.6% of women had intermediate risk polyps and were therefore offered a surveillance colonoscopy three years later. Overall, further treatment or investigation was required in 43% of men and 29% of women investigated[20]. In March 2013, the English NHS BCSP piloted flexible sigmoidoscopy as a primary screening tool to all persons around the time of their 55th birthday.

In Germany, a screening colonoscopy is available to all insured persons from the age of 55 onwards. 4.2 million people had undergone colonoscopy by 2010. These screening colonoscopies detected adenomas in 30.1% of men and 19.1% of women. Advanced adenomas were recorded in 9% of men and 5.1% of women, while colorectal cancer was detected in 1.4% of men and 0.8% of women[19].

Of those countries within the European Union, in addition to England, using FOBT as a primary screening investigation, 17,813 screening colonoscopies were carried out in the Czech Republic as a result of positive FOBT between 2006 and 2008. A carcinoma was diagnosed during colonoscopy in 5.9% and adenomas in 30.1% of people examined. In three rounds of screening colonoscopy in Finland between 2004 and 2011 involving 345,283 citizens, colorectal cancer was found in three to four per cent of females and three to five per cent of males with adenomas found in 18-24% of females and 29-35% of males.

The development of such screening programmes in England, across Europe and the rest of the world has, therefore, been to the benefit of many in diagnosing and removing colorectal adenomas, so breaking the adenoma to carcinoma sequence. They have also been to the benefit of many in diagnosing colorectal cancer at an early stage in its development, thus improving the affected individual's chances of survival. However, despite these successes, there is undoubtedly a human cost to pay for them. Colonoscopy and Flexible Sigmoidoscopy are considered safe procedures, but their invasive nature means

they will always carry a risk of events that may harm patients, even in the most experienced operators' hands. The accepted name for such events is 'adverse events'. In the context of a colonoscopy, the event is termed a 'colonoscopic adverse event'. Such events occurring on a regular basis would be disastrous in maintaining the benefits and uptake of screening programmes for colorectal cancer. Minimising the risk of colonoscopic adverse events and ensuring the best possible outcomes, through the development of an evidence base, for when, inevitably, they do occur, is therefore vital to maintaining the integrity of screening programmes for colorectal cancer.

2.4 Colonoscopic adverse events

In 2008, the American Society for Gastrointestinal Endoscopy (ASGE) Quality Task Force convened a workshop specifically to assess the current situation and develop recommendations surrounding endoscopic adverse events. The society termed this a 'lexicon for endoscopic adverse events'[4]. It did so in response to a perceived lack of clarity and standardization regarding adverse event definition, reporting and significance. The phrases 'complications', or 'negative outcomes' may have previously been used synonymously with 'adverse event'; however, the term 'adverse event', it was felt, better encompassed the principles of informed consent which are fundamental to having a colonoscopy[4].

The 'lexicon' had several aims which included: to provide a clear definition of an adverse event, to define levels of adverse event severity grading, to define the minimum level at which an adverse event should be documented and to consider

how to attribute delayed adverse events[4]. The English NHSBCSP incorporated some of the 'lexicon's' report into its quality assurance guidelines for colonoscopy published in 2011 and all of these factors are relevant when examining adverse events in this thesis[26].

The 'lexicon' defined an endoscopic adverse event as 'an event that prevents completion of a planned procedure and/or results in admission to hospital, prolongation of an existing hospital stay or another procedure/consultation'. It recommended their timing may be pre procedure, intra procedure (from entering the preparation area for the endoscopy to leaving the endoscopy room), post procedure (up to 14 days following completion of the procedure) or late (any time after 14 days). Regarding the attribution of an adverse event to the procedure, it recommended these being described as definite, probable, possible or unlikely and when reporting on severity, the recommendation was for adverse events to be graded as fatal, major, intermediate or minor[4].

In a position statement by the European Society of Gastrointestinal Endoscopy (ESGE) of quality in screening colonoscopy published in 2012, the ESGE encouraged national screening boards to use the ASGE's classification of adverse events in addition to their own 'Minimum Standard Terminology Version 3.0' when defining and classifying adverse events[27] [28].

2.4.1 Colonoscopic adverse events occurring before the colonoscopy

Colonoscopic adverse events occurring before the colonoscopy are, for the most part, related to the bowel preparation the patient requires. Colonoscopy requires all faecal matter to be removed from the colon and rectum to enable adequate visualisation of the colorectal mucosa. All bowel-cleansing regimes may be uncomfortable and physically tiring for patients but these factors will only rarely prevent a planned colonoscopy. The agents used may result in fluid and electrolyte shifts. Patients who already have co-morbidity such as renal failure, cardiac failure and hypertension are particularly susceptible to adverse events from the bowel preparation[29].

Polyethylene Glycol solutions are a commonly used group of bowel preparation agents for colonoscopy. Polyethylene Glycol solutions have, however, been associated with Mallory-Weiss tear, toxic colitis, aspiration pneumonia, hypothermia, cardiac arrhythmias, pancreatitis and syndrome of inappropriate anti diuretic hormone secretion[30].

Sodium phosphate solutions are the other major group of bowel preparations currently in use. Due to electrolyte shifts, such solutions may result in Acute Kidney Injury (AKI). The AKI may present symptomatically, within a few hours to days, because of hypocalcaemia with hyperphosphataemia. Some patients with AKI may present much later, from a few days to even weeks, following the ingestion of sodium phosphate solutions. Other reported electrolyte disturbances, with the potential to result in a pre colonoscopic adverse event are hypokalaemia, hypo- or hypernatraemia and hypo- or hypermagnesaemia[31].

2.4.2 Colonoscopic adverse events occurring during the colonoscopy

A patient presenting for colonoscopy will normally be offered analgesia and sedation after entering the endoscopy room but prior to intubation with the colonoscope. Some health care centres will offer colonoscopy under general anaesthesia, using, for example, propofol, although this is rarely used in the English National Health Service. Analgesia and sedation is used in order to aid patients' comfort during the procedure. Additional analgesia and sedation may be required during the examination. The aim should be for the patient to be moderately or consciously sedated. This state can be defined as 'a drug induced depression of consciousness during which patients respond purposefully to verbal commands, either alone or accompanied by light tactile stimulation. No interventions are required to maintain a patient's airway and spontaneous ventilation is adequate'[29]. Analgesia may be inhaled in the form of nitrous oxide or intravenous with opioids. Intravenous sedation is usually administered in the form of a benzodiazepine.

However, such medications can result in over sedation where the patient does not respond to verbal commands, with or without light tactile stimulation, so much so that the over sedation becomes an adverse event. Furthermore, intravenous opioids, while attaching to pain receptors producing an analgesic effect, also attach to receptors in the brain and brainstem controlling respiratory drive. If given in too great a quantity, intravenous opioids may result in respiratory depression and respiratory arrest. Prolonged over sedation or respiratory depression increases the likelihood of aspiration pneumonitis. A

systematic review and meta analysis of randomised control trials of moderate sedation for endoscopic procedures published in 2008 reported a 6% hypoxaemia rate from 706 patients when midazolam was administered in addition to a narcotic. These 706 patients were cumulatively assessed from 12 studies although one of the studies reported sedation for just Oesophagogastroduodenoscopies (OGDs) and not colonoscopies. It is unclear, however, how many of these episodes of hypoxaemia resulted in a failure to complete the procedure or necessitated another consultation[32].

As well as respiratory adverse events, colonoscopy is also associated with cardiovascular adverse events during the procedure. As a possible result of stretching of the viscus and its mesentery, autonomic responses events such as hypertension, arrhythmias, ST segment changes on electrocardiogram, myocardial infarction and stroke may all occur[29]. Hypotension has also been observed during colonoscopy, one study reporting a rate of 480 episodes per 100,000 colonoscopies, however, it is uncertain how many of these episodes would have fallen into the definition of an adverse event I have outlined[5].

Systematic reviews and meta analyses of 20 studies examining the cumulative incidences of both cardiovascular and respiratory complications have reported rates of 19.1% for patients of 65 years and older, increasing to 28.9% for those of 80 years or older. These meta analyses described an approximately even split of severe and non-severe cardiovascular and pulmonary complications in these groups. We could assume, therefore, that half of these cases could be considered to be adverse events, however, the meta analyses do not include a clear

definition of what constitutes a severe complication or the percentage of them occurring during the colonoscopy[33].

A patient experiencing abdominal pain during colonoscopy may also prevent its completion. Pain commonly occurs from over insufflation of air into the colon or from loop formation with stretching of the colon and its mesentery. Pain has been reported in series as occurring in 5-11% of cases[5]. As with the systematic reviews and meta analyses described above, whether the pain described can be considered within the boundaries of an adverse event is unclear.

2.4.3 Colonoscopic adverse events occurring within 14 days following the colonoscopy

Abdominal pain, cardiovascular and respiratory events that require consultation may also occur following completion of the colonoscopy. From a study of 33,086 patients who either had a screening or non screening colonoscopy published by Stock et al. ten non-screening patients presented with a median time to admission of 12 days post completion of colonoscopy due to myocardial infarction. Three screening and eleven non-screening patients presented with a median time to admission of ten and eight days respectively post completion of colonoscopy due to stroke[34]. Although the exact time to admission was not recorded, a similar study by Ko et al. of 21,375 patients having a screening or surveillance colonoscopy recorded adverse events requiring consultation within seven days; angina, myocardial infarction, stroke and transient ischaemic attack were reported as possibly related to the colonoscopy in 13 patients[35].

This study also reported two patients requiring consultation within seven days of colonoscopy with post polypectomy electrocoagulation syndrome[35]. This syndrome occurs as a result of a full thickness burn to the colon with localised peritonitis but no evidence of radiological perforation. Reported incidence varies from 0.003% to 0.1% of colonoscopies[5].

2.4.4 Colonoscopic adverse events occurring after 14 days post colonoscopy

The adverse events reported in chapter 2.3.3 may also require consultation 14 days after completion of the colonoscopy. The previously described study by Ko et al. reported adverse events up to 30 days post colonoscopy. In addition to the patients described from this paper in chapter 2.3.3, a further 12 patients who had a colonoscopy were reported to have angina or myocardial Infarction up to 30 days post colonoscopy. Furthermore, seven patients had a stroke during this time possibly related to the colonoscopy. A further two patients presented with post polypectomy syndrome[35]. These figures were similar in the previously described study by Stock et al. with the incidence of stroke and myocardial infarction being 0.4% per 1000 colonoscopies after 30 days follow up[34].

Other described colonoscopic adverse events include rupture of the spleen, acute appendicitis, diverticulitis, subcutaneous emphysema, intra abdominal haemorrhage, chemical colitis from glutaraldehyde exposure, bacteraemia, and retroperitoneal abscess[36 37 38].

When I considered perforation, post polypectomy bleeding and post colonoscopy colorectal cancer in the context of the adverse events described so far in this chapter I concluded that these three adverse events are among the most serious. It is for these reasons that these adverse events are a major focus of this thesis and are described separately in sections 2.4, 2.5 and 2.6 respectively in this chapter.

2.5 Colonoscopic Perforation

2.5.1 The definition of colonoscopic perforation

A colonoscopic perforation may be defined as evidence of air, luminal contents or instrumentation outside the gastrointestinal tract[39]. The English NHS BCSP uses this definition to identify patients who had a colonoscopic perforation and is, therefore, the definitive definition used in this thesis. However, a small contained perforation into the omental reflection of the colon or a microperforation which is immediately closed by the application of clips may also be regarded, by some, as being a perforation[27].

2.5.2 The incidence of colonoscopic perforation

There is variation in the reported incidence of colonoscopic perforation since the first use of colonoscopy in 1969, both in relation to diagnostic and therapeutic procedures. Some of this variation may be de to the methodology used to capture

details of the perforation. Earlier studies using less robust methodology may be more prone to under reporting whereas as reporting systems have evolved and improved in conjunction with health care systems being more conscious of the need to report adverse events, so more accurate data relating their incidence may be apparent.

By 1974, little research had taken place into 'complications' from colonoscopy. This prompted the committee of endoscopic research of the American Society of Gastroenterology to survey its members regarding 'complication' incidence. A total of 25,298 diagnostic colonoscopies were reported resulting in 53 perforations. Two perforations were reported occurring after biopsy and 6,214 colonoscopic polypectomies were described resulting in 16 perforations. This paper quotes a diagnostic perforation rate of 0.22%, we presume from the 53 perforations from diagnostic colonoscopy plus two from biopsy, i.e. 55/25,298 but this isn't clear. In addition, it is also unclear from the paper whether the colonoscopic polypectomies were included within the figure of 25,298 or are separate colonoscopies. We presume they have been, the methodology states 'diagnostic colonoscopy was considered to be part of every polypectomy' but a therapeutic perforation rate isn't recorded leading to doubts about the above figures. Furthermore, 642 ASGE members were mailed a questionnaire, only 444 returned it and there is no indication of the total number of ASGE members at the time suggesting the perforation rate could have been under reported[40].

A similar large series from the late 1970s, this time a survey from the American Society of Colon and Rectal surgeons, was more concrete. It reported a

perforation rate of 0.358%. This was from a definite total of 20,139 colonoscopies. Again, only 66% of members responded which may suggest under reporting[41]. Lower perforation rates were stated from a survey of West German hospitals in 1978. From 35, 892 colonoscopies, diagnostic and therapeutic perforation rates of 0.14% and 0.34% respectively were reported[42].

The issue of under reporting from surveys was addressed by Macrae et al. in 1983. The detailed records of 5,000 colonoscopies all performed at St. Marks Hospital, London were reviewed. Six perforations producing a rate of 0.12% were recorded in line with the German series[43]. A lower perforation rate of 0.09% was observed, again from the United Kingdom, in a survey of 17,500 colonoscopies in 1991[44]. An even lower diagnostic perforation rate of 0.02% and therapeutic rate of 0.03% was observed in an American series of 26,708 consecutive colonoscopic procedures from 1986 to 1992.

The increasing use of colonoscopy coupled with improved reporting systems and collaboration lead to much larger series being published during the final decade of the twentieth century and the first decade of the twenty first century. The figures from these are similar to the smaller series that preceded them.

A computer based retrospective analysis of 57,028 colonoscopic procedures over a 15-year period from 1980 to 1995 produced a perforation rate of 0.075%[45]. A similar retrospective review of 105,786 colonoscopies performed over a 21 year period from January 1986 to October 2007 resulted in 35 perforations (a rate of

0.033%), 24 of the perforations occurred during diagnostic colonoscopies whereas only 11 occurred were as a result of therapy[46].

A greater number of colonoscopies (116,000) was reviewed by Korman et al. within one network of 45 endoscopic ambulatory surgical centres in the United States of America from before the new millennium reporting an overall perforation rate of 0.03%. Similarly to the series above, nearly two thirds of these perforations occurred as a result of diagnostic procedures[47]. These results are in contrast, however, to a study over twice this size number of colonoscopies by Iqbal et al. published in 2008 that reported a perforation incidence of 0.07%. Diagnostic procedures accounted for 42% of these perforations[48]. Perforation incidence published a year later from a similarly sized study, again from the USA, was marginally higher at 0.08%[2]. An even larger study from France, published in 2013, of a cohort of nearly one million colonoscopies reported 424 colonoscopic perforations, an incidence of 0.04%[49].

Perforation rate in the English NHS BCSP has been reported from the start of the programme in 2006 up to and including January 2012. From 130,831 colonoscopies, the overall perforation rate was 0.06% with a therapeutic perforation rate of 0.09% and diagnostic perforation rate of 0.03%[39].

2.5.3 Risk factors for colonoscopic perforation

Many retrospective observational case control studies have focused specifically on identifying risk factors for colonoscopic perforation. Factors that have been associated with increasing the risk of perforation may relate to the patient

having the colonoscopy, the procedure itself or the colonoscopist who performs the procedure.

Increasing age has consistently been shown to be a patient related risk factor. Gatto et al. showed that patients of 75 years or over had a four times greater risk of perforation than those aged 65-69 years[50]. A Canadian study found age to be a significant risk factor for perforation but only differentiated between those aged 60-75 years and 50-59 years, with a higher odds ratio for perforation in the older group[51]. Age was also significant in larger series than these; the relative risk of perforation increasing over three fold for those over the age of 80 years compared to those 65-80 years in one such study[2]. Similarly, a further study from Thailand reported a six fold rise in the colonoscopic perforation rate in the over 75s when comparing this with those under 75[52]. Blotiere et al. studied age not just between two groups but in 10 year intervals from the age 40 to 80, showing a step wise increase in odds ratios for perforation for each decade. Further series including ones published in 2014 have corroborated these findings[53 54]. A suggested reason for this risk is declining colonic wall mechanical strength, due to changes in its collagen structure[52].

In line with increasing patient age, patient co-morbidity has too been associated with an increased risk of colonic perforation. Those patients with two or more co-morbidities had a higher risk than those with no or one co-morbidity in the study by Gatto et al.[50]. Similar findings were reported by Arora et al. where a Charlson co-morbidity score of two or more was found to increase the risk of

perforation by over 50% and by Warren et al. where those with a history Stroke, COPD, Atrial Fibrillation or Chronic Heart Failure had increased risk[2] [54].

Female sex has been documented as a risk factor for perforation[53] [55]. This may be due to women having longer colons, more mobile transverse colons, smaller body habitus or possibly a hormonal effect on collagen[55] [6]. Indeed, Hamdani et al.'s review of risk factors showed lower Body Mass Index to be a significant predictor of perforation in addition to female sex[53]. These findings are in contrast to those of Rabeneck et al. who found male sex to be significant[51].

The nature of the patient's indication for colonoscopy may too be a factor. Such indications include colonic obstruction or diverticular disease[50] [2] [55]. Crohn's Disease, colitis, strictures and adhesions have all been reported as potential patient related risk factors. Similarly, abdominal pain as the indication for the colonoscopy and an uncooperative patient during the examination have too been reported as risk factors [55] [53].

Factors related directly to the colonoscopy itself are also important. There is consistent evidence that therapeutic colonoscopy, including polypectomy, carries a greater risk of perforation than diagnostic colonoscopy[51] [2] [55] [6]. As the polyp size increases and the number of polypectomies increases, so too perforation risk increases[56]. In a recently published study from France, of 947,061 patients in whom colonoscopy was performed also described in chapter 2.3.2, polypectomy of polyps greater than 1 centimetre and a colonoscopy where more than 4 polypectomies take place was associated with an increased

perforation risk. In addition to increasing polyp size and number of polypectomies, the Munich Polypectomy Study, of 3976 snare polypectomies in 2257 patients, also reported right sided colonic location as a risk factor though reported this using 'complications' overall rather than just for perforation[56]. The polyp morphology and polypectomy method may also be a factor; a study specifically examining endoscopic submucosal dissection of large sized, non-pedunculated colorectal tumours, found that the laterally spreading type of tumour and submucosal injection with hyaluronic acid were independent predictive factors for perforation[57].

When examining the role of the colonoscopist, those colonoscopists who are inexperienced or perform a relatively small number of colonoscopies per year, are a further risk factor for perforation. In one study, the risk was increased below a threshold of 300 colonoscopies per year per endoscopist[51]. Similarly in Lorenzo-Zuniga et al.'s study, the relative risk ratio for complications, including perforation, was highest for those colonoscopists performing less than 591 procedures per year[58]. These findings have been corroborated by other studies, including from Canada where the colonoscopist being a 'family physician' rather than a gastroenterologist or surgeon was significant[49 59 60 61].

Risk factors for perforation studied in the English NHSBCSP, from 130,831 colonoscopies and 167,208 polypectomies, included patient age, gender, physical status, polyp morphology, polyp size, polyp location and polypectomy device. On multivariable analyses of patients undergoing a single polypectomy procedure

who had a perforation, the size of the polyp and a location of a polyp in the caecum were significant[39].

2.5.4 The mechanisms associated with colonoscopic perforation

The mechanism that is most directly associated with a colonic perforation varies depending on what occurs as the colonoscopy progresses. Classifying the direct cause or mechanism depends on whether the colonoscopy is a diagnostic or therapeutic procedure.

Two main mechanisms of perforation have been reported during diagnostic colonoscopy. Mechanical forces against the colorectal mucosa may lead to tearing through the entire wall of the colon. The mechanical force may result from the tip of the colonoscope, for example, following the mistaken intubation of a diverticulum, or from the shaft of the colonoscope, resulting in stretching of the colon, particularly during loop formation or when the colonoscope is advanced by 'sliding by' the mucosa rather under direct visualisation of the lumen[5] [62]. The rectosigmoid colon has been reported as the commonest site for mechanical colonoscopic perforation. This may be due to the sharp angulation of the colon in this segment, the greater mobility of the sigmoid colon, formation of sigmoid loops and the presence of diverticular disease[6]. Diagnostic perforation may also occur from extreme air insufflation or barotrauma[62]. A single centre case series from the Netherlands of the cause of 26 colonic perforations from 19,135 procedures showed that all perforations from mechanical forces occurred in the sigmoid colon whereas those from barotrauma occurred in the

caecum[63]. Air 'trapping' may occur in the caecum, the most proximal segment of colon, where the colonic wall is at its thinnest and most distensible[62].

Therapeutic colonoscopy may be associated with colorectal perforation through a variety of methods and therapies. Instruments such as biopsy forceps and snares inserted blindly, forcibly and without control through the biopsy channel of the colonoscope may directly puncture the colon or rectum[29]. Any therapy involving electrical current may result in perforation, particularly when polypectomy takes place. Polyps larger than six millimetres will usually require some form of current to complete the polypectomy. Electrical current applied close to the colonic wall may burn through the serosa exacerbated by greater current intensity, for longer periods over smaller diameters[29] [62]. There have been reports of perforation from gas explosion in the colon. This can occur when combustible levels of hydrogen or methane gas in the colon and rectum mix with oxygen and electrical current or Argon Plasma Coagulation[5]. Stretching and rupture of the colorectal wall during dilatation of strictures is another therapeutic mechanism of perforation.

2.5.5 How a patient with colonoscopic perforation presents for consultation

Perforations may present during the colonoscopy or after its completion. Those patients presenting following its completion seek consultation because of symptoms that are attributable to the perforation.

The perforation may be visible to the colonoscopist when an extra intestinal structure is seen from the colorectal lumen[6]. It may be apparent as mesenteric fat, mesenteric vessels or the external surface of surrounding bowel[29][55]. Studies up to 2008 suggest this is the mode of presentation in 23% of cases[62]. These figures have been corroborated in more recent studies; one reporting this was the mode of presentation in 37.5% of cases[64]. If the perforation is not visible during colonoscopy, there may be a sudden inability to insufflate the colon to allow adequate mucosal visualisation. A patient complaining of new abdominal or back pain during the procedure with or without changes in vital observations such as tachycardia, tachypnoea, hypotension and pyrexia may also indicate perforation[29]. A recently published 7 year survey from a German university hospital reported the perforation being suspected during colonoscopy in 28% of cases but didn't specify the exact reasons for the suspicion[65].

For those patients who present following completion of the colonoscopy, most complain of abdominal pain, but back pain and abdominal distension may also occur. Abdominal pain occurs as a result of peritoneal irritation. A degree of abdominal pain is expected post procedure, usually because of retained air in the colonic lumen, but this should settle as a patient expels the air. Persistent abdominal pain raises the possibility of peritoneal irritation. Studies up to and including 2008 suggest the majority (74.6%) of patients with perforation will present within 24 hours following completion of the colonoscopy[62]. More recent studies also suggest similar figures, one reporting presentation within 24 hours in 78% of cases, and on the same day as the colonoscopy in 85.1% of cases, although, again the exact nature of the presentation is not described[66][49].

2.5.6 Making the diagnosis of colonoscopic perforation when a patient presents after the colonoscopy

Common clinical signs on examination of such patients who present post procedure include localised or generalised abdominal tenderness, rebound tenderness, rigidity, tachycardia and pyrexia. Routine haematological and biochemical testing may reveal leucocytosis and other raised inflammatory markers.

Radiological investigation may confirm the diagnosis in those patients with symptoms, signs, haematology and biochemistry suggesting perforation. An erect chest x-ray may reveal pneumoperitoneum; abdominal x-ray may reveal intraperitoneal air. Retroperitoneal air can also be seen along the psoas muscle and around the kidneys in certain cases[62].

Cross sectional imaging of the abdomen and pelvis showing intraperitoneal free air may be required if plain x-rays are unhelpful in making the diagnosis. Computed Tomography (CT) of the abdomen and pelvis is better than an erect chest x-ray at detecting intraperitoneal free air[5]. Double or triple contrast scanning may enhance CT findings in relation to the perforation. Magnetic Resonance Imaging of the abdomen also has a role in its detection[6].

2.5.7 The management of colonoscopic perforation

Management options are dependent on many variables, including how the perforation has presented and the timing that the diagnosis is made. Perforations may be managed endoscopically, when the mode of presentation is visualisation or suspicion of the perforation during the colonoscopy, conservatively through medical management only or surgically. These subgroups of management are, of course, not exclusive; patients may require a combination of two of these management strategies, or indeed all three.

2.5.7.1 The endoscopic management of colonoscopic perforation

For the most part, endoscopic management will only occur when the endoscopist visualises or strongly suspects a perforation during the procedure. Yoshikane et al. reported the first successful endoscopic closure of a colonic perforation with clips in 1997. A four millimetre perforation was sealed with five clips using a rotating clip fixing device. The patient was kept nil by mouth, prescribed antibiotics and discharged two weeks later[67]. The feasibility of this technique was enhanced by results from studies in porcine models[68] [69]. Several similar case reports emerged following this initial success with clips placed 'through the scope'[70] [71] [72] [73] [74]. Subsequent series suggested the use of endoscopic clipping was effective in 68-93% of patients who were managed in this way[75] [76] [77] [78].

However, the use of 'through the scope' clips does not allow the trans mural closure of a perforation that would be achieved during surgery. It is also difficult for larger perforations that are beyond the reach of the clip. For this reason, studies of full thickness perforation closure using suturing devices in porcine

models have since taken place with encouraging results[79] [80]. Similarly, 'Over The Scope Clip' devices may be a better method for the endoscopic management of larger perforations[81] [82]. The use of a covered metal stent and endoscopic band ligation has also been described[83] [84].

2.5.7.2 Conservative management of colonoscopic perforation

Many series consider 'conservative' management to involve anything excluding surgery. For the purposes of this review, I considered three distinct management strategies: endoscopic, conservative and surgical, although, of course, there may be overlap between the three.

Standard conservative management of colonoscopic perforation involves the admission to the inpatient ward for observation, keeping the patient nil by mouth in order to rest the colon, the administration of intravenous fluids and prescription of broad-spectrum intravenous antibiotics. This management alone may be successful in a cautiously chosen sub group of patients. Such management has been advocated for a perforation presenting within 24 hours of the colonoscopy, when bowel preparation is good, thus reducing the chances of bacterial and faecal contamination in the peritoneum. The patient being haemodynamically stable, with little or no co-morbidity and without signs of peritonitis are also factors that may favour conservative management[62] [85] [86].

The numbers of patients managed in this way described in recent published series have been small. Tam et al. described four of 26 cases of perforation being

managed non-operatively, however, one of these was also managed endoscopically. None of these patients died or required surgery, though one required a percutaneous drain for an abscess. Their length of in patient stay was not specified. A South Korean study of perforations after endoscopic submucosal dissection successfully managed five microperforations, defined as the presence of free air on radiographic imaging, conservatively. Hagel et al. and Tulchinsky et al. at reported one patient each managed successfully like this, though in the former's case, the patient had refused surgery[65] [87]. One of the largest reported series managed successfully conservatively was by Iqbal et al. including 13 patients, the majority of whom presented within 24 hours, were clinically stable and devoid of peritonitis on physical examination[48]. The Munich Polypectomy Study reported 7 patients managed in this fashion with mortality being zero for all[56].

2.5.7.3 The surgical management of colonoscopic perforation

Those who fail endoscopic management, conservative management, or both will require surgery. Surgery is also recommended for those patients who present after completion of the colonoscopy, who are haemodynamically unstable, who have signs of diffuse peritonitis or who have other pathology that requires surgery. The surgery may be laparoscopic or by open laparotomy. In certain cases a laparoscopy may need to be converted to an open laparotomy. There is a range of surgical options available that depend on many factors[6]. The final decision to operate is also highly subjective and is likely to depend on the clinical judgement of surgeon, their experience and skills.

A primary repair with a suture to close the perforation is an option when the perforation is small and there is little or no faecal matter in the peritoneum. A stoma in the form of a colostomy/ileostomy may be required with such cases. A resection of the perforated segment of colon with anastomosis of the remaining bowel or with colostomy/ileostomy may be required if the perforation is larger. In such cases, colonic resection with anastomosis is more likely if there is little or no faecal peritonitis and there is no concomitant pathology. Iqbal et al. reported that most patients with faecal peritonitis received a stoma compared with those with moderate or minimal contamination[48]. These findings were corroborated by Teoh et al. who identified peritoneal contamination and the presence of malignant colonic neoplasms as significant risk factors for stoma formation[86].

Laparoscopic repair of colonoscopic perforation using the above approaches may also be feasible in certain cases. The laparoscopic approach to surgery has been associated with a lower length of hospital stay and fewer complications than traditional open surgery, however, in one such series was performed on patients who presented sooner with less faecal contamination of the peritoneum[88][89][90]. The quicker time to surgery among perforations repaired laparoscopically was corroborated in a similar series specifically comparing open and laparoscopic techniques [91].

2.5.8 The prognosis following colonoscopic perforation

Any of the management strategies described in chapter 2.3.7 may be associated with in patient admission, patient morbidity and even patient death.

Post perforation morbidity ranges from 31% to 48.7% in recently reported series comprising patients who have been managed endoscopically, conservatively or surgically with morbidity referring to both post operative complications and/or new diagnoses post perforation[66] [86]. In series examining only post surgical morbidity, rates vary from 34.5 – 40%[92] [93]. Post perforation mortality can be as high as 25.6%, with post perforation surgical mortality as high as 10%[86] [92].

Many factors may be associated with increasing the risk of post perforation morbidity and mortality depending on the patient, what happened during the colonoscopy and the time they present. A poorer physical status as defined by higher physical American Society of Anaesthesiology (ASA) grade has consistently been reported as significant[86] [92] [94]. Similarly, patients taking antiplatelet medication or corticosteroids, suggesting other co-morbidity, have also been shown to be significant[86] [48]. Smoking, which can lead to co-morbidity and higher ASA status, was also shown to be significant in one series[95]. As reported earlier, patients who present later with greater faecal contamination of the peritoneum are likely to be more unwell and have poorer outcomes. This chain of events can be linked to post perforation mortality and morbidity; poorer bowel preparation, the size of the perforation and the time to presentation all being significant in 3 separate series[48] [95] [66].

Table 1: Perforation incidence including diagnostic and therapeutic perforation rates

Study	Rogers et al.	Smith et al.	Frumorghen et al.	Macrae et al.	Hall et al.	Lo et al.	Farley et al.
Year	1975	1976	1979	1983	1991	1994	1997
Colonoscopies	25,298	20,139	35,892	5000	17,500	26,708	57,028
Perforations	55			6	15	12	
Perforation Rate	0.23%				0.09%	0.045%	0.075%
Diagnosti Perforations	55					5	
Diagnostic Perforation Rate	0.23%	0.358%	0.14%	0.12%		0.02%	
Therapeutic Perforations						7	
Therapeutic Perforation Rate			0.34%			0.03%	

Averingos et al.	200	105,786	33	0.033%	24	0.022%	11	0.01%
Korman et al.	2003	116,000	37	0.03%	24	0.021%	13	0.011%
Iqbal et al.	2008	258,248	180	0.07%				
Arora et al.	2009	277,434	228	0.08%				
Blotiere et al.	2013	947,061	424	0.04%				
Rutter et al.	2014	130,831		0.06%		0.03%		0.09%

2.6 Post polypectomy bleeding (PPB)

2.6.1 The definition of post polypectomy bleeding

The terms 'bleeding' and 'haemorrhage' are used interchangeably when describing them in association with a colonoscopy and polypectomy. Although haemorrhage may sound more severe, there is no distinction drawn between the two. Blood is commonly visualised in the lumen of the colon or rectum during colonoscopy, for example, the colorectal mucosa may bleed when it comes into contact with the tip or shaft of the colonoscope and blood is nearly always seen after biopsy or polypectomy. When bleeding occurs it may stop spontaneously or require a therapeutic intervention, such as the injection of adrenaline or the application of clips, to stop it, also known as achieving haemostasis. However, bleeding such as this does not usually prevent completion of the colonoscopy, necessitate in patient admission or subsequent consultation and therefore doesn't form part of the definition of an adverse event, as is the case with peri operative bleeding.

For the purposes of this thesis, I defined PPB as blood or melaena in the colorectal lumen following polypectomy that prevents completion of the colonoscopy and/or that results in admission to hospital, prolongation of an existing hospital stay or necessitates subsequent consultation that may be endoscopic, medical, surgical or radiological. This definition of PPB incorporates that of an adverse event proposed by Cotton et al. in 2008 and, therefore, is the definition of a post polypectomy bleeding used in the English NHSBCSP[4] [39]. A

similar definition has been suggested by the European Society of Gastrointestinal Endoscopy[27].

'Post Polypectomy Haemorrhage', 'Delayed Bleeding/Haemorrhage' and 'Secondary Bleeding/Haemorrhage' are all published terms that fall within the boundaries of the definition outlined above.

In this thesis I have considered two types of bleeding; peri procedure bleeding which is controlled during the procedure but results in an admission to hospital and post polypectomy bleeding when the bleeding presents following the completion of the procedure and results in admission to hospital, prolongation of an existing hospital stay or necessitates subsequent consultation that may be endoscopic, medical, surgical or radiological.

2.6.2 Post polypectomy bleeding by grade of severity

Despite the use of the above definition to clearly outline what constitutes PPB, some episodes of PPB may be trivial yet still lead to a patient seeking medical consultation post procedure. As part of the work of the lexicon for adverse events convened by the ASGE in 2008, a severity grading system for adverse events was developed recommending four grades of severity based on the type of medical attention that is required. This severity grading system categorizes an adverse event into minor, intermediate, major or fatal[4]. This severity grading system has been applied to how PPB is reported in the English NHS BCSP and is detailed in quality assurance guidelines published on behalf of the programme[26].

When specifically considering PPB, major PPB is that resulting in surgery, an unplanned admission or prolongation of a hospital stay for more than ten nights or ITU admission for more than one night. PPB would be considered intermediate when leading to any of: a drop in haemoglobin of more than two grams per demi litre, a blood transfusion, an unplanned hospital admission or prolongation of stay for four to ten nights, an ITU admission for one night or an interventional procedure which may endoscopic or radiological. Minor PPB occurs when a colonoscopy is aborted, results in an unplanned medical consultation, admission or prolongation of hospital stay for 3 nights or less.

2.6.3 The incidence of post polypectomy bleeding

Due to the differences in how PPB may be defined, there is wide variation in its reported incidence. Not only do some reports not use the definition outlined in section 2.5.1, PPB incidence has also been reported per number of patients, colonoscopies, colonoscopies where a polypectomy is performed and per polypectomy. Therefore, providing an accurate representation of PPB incidence over time requires clarity in how it is defined and how its incidence has been calculated.

The previously cited 1974 ASGE survey of complications relating to colonoscopy and polypectomy reported a total of 115 cases of haemorrhage. These cases were associated with 6,214 polypectomies. This gave an overall post polypectomy haemorrhage rate of 1.09% when measured per number of polypectomies. As

previously described in chapter 2.4.1, the lack of responses to this survey is likely to have resulted in under reporting. Also, 31 of these haemorrhages were immediate (occurred during the colonoscopy), but it is unclear whether they prevented completion of the colonoscopy and therefore if they would be considered within our definition of PPB. Similarly, in 73 cases the timing of the haemorrhage is not stated, again this may have lead to an inaccurate representation of PPB rate by our definition[40].

Macrae et al.'s report of complications from 5000 diagnostic and therapeutic colonoscopies at St. Marks Hospital, London between January 1971 and November 1980 provided the necessary detail with regard to the classification of PPB. Snare polypectomy of 1,795 polyps over 7mm in size was associated with haemorrhage in 48 patients. Importantly, those with haemorrhage were sub divided into minor, major and secondary haemorrhage. In those with major haemorrhage, measures to control it during the colonoscopy had failed. Those with secondary haemorrhage presented at 5-14 days post procedure. These two groups would therefore be considered within our definition. This gives a rate of 1.06% per number of polypectomies. In this series, however, we are told that late complications, which would include those with secondary haemorrhage however, may not always have been captured which may have lead to under reporting in this group[43].

Studies specifically reporting PPB from single centres may be best placed to reflect its true incidence within the definition I have used in this thesis. Rosen et al. reported on 16,910 patients who had a colonoscopy between 1987-1991.

Polypectomies took place in 4,721 of these patients and 20 (0.4%) of these patients experienced haemorrhage requiring hospital admission[96].

A further study of over 12,000 patients who underwent colonoscopy between 1989 and 1993 resulted in a total of 6,365 procedures where polypectomies or biopsies took place. It described major haemorrhage, which would be considered within our definition of PPB in 13 patients, equating to 0.2% of colonoscopies where a polypectomy or biopsy was performed. Unfortunately, the breakdown of haemorrhage rate is not given for polypectomies and biopsies and therefore the true rate of PPB cannot be determined[97].

We can be confident that more accurate representation of PPB rates, within the definition used in this thesis, are reported by subsequent larger series. This includes Sorbi et al.'s descriptive analysis, which reported on 14,575 colonoscopies where a polypectomy had occurred over a period from 1989 to 1996. 83 cases of post polypectomy bleeding were identified, all of which had been admitted to hospital. This gave a PPB rate of 0.57% per colonoscopy where a polypectomy was performed[98]. A study of 6066 colonoscopies from Sweden published in 2001 describes a total of 2635 hot biopsies and snare polypectomies. The number of post polypectomy bleeds admitted is recorded as 9 of 12 post polypectomy bleeds in total, a rate of 0.34% per polypectomy. An Australian study of 30,463 colonoscopies from 1989 – 1999 breaks down those cases of post colonoscopy bleeding requiring hospital admission to those that occurred specifically after polypectomy; this gave a PPB rate of 0.14% per colonoscopy[99].

Studies published after the turn of the new millennium have specifically reported the incidence of PPB within specific time periods after colonoscopy, thus ensuring it meets the criteria for PPB defined in this thesis. Rathgaber reported complication rates from 12,407 colonoscopies and 5074 polypectomies with 23 Post Polypectomy Bleeds identified. Another such study of 24, 509 lower gastrointestinal endoscopies allowed calculation of PPB rate per number of colonoscopies (0.15%) up to 30 days post colonoscopy but did not offer the total number of polypectomies[60]. The same primary author later reported on 29,990 lower gastrointestinal endoscopies with a PPB rate per number of colonoscopies of 0.07%[100].

A study of severe delayed Post Polypectomy Bleeding among 4,592 patients that underwent colonoscopy and polypectomy published in 2008 helpfully states that all patients presenting 1-14 days after polypectomy with PPB were admitted to hospital or observed for at least 12 hours. This reflects a true PPB rate of 0.89% per number of patients[101]. This figure is similar to the number reported by Kim at al. which was published in 2011, 0.98% per number of patients, all be it with a smaller sample size[102]. A much larger series from Canada reported on hospital admission with bleeding in the 30 days after colonoscopy in 67,632 patients. There were 80 cases of bleeding reported following either hot biopsy polypectomy or snare polypectomy resulting in a PPB rate per patient of 0.12%[103]. The figure of PPB reported by Wu et al. was higher than this at 0.6% per patient but, again, with a smaller sample size[104].

Rutter et al.'s study reporting adverse event rate related to polypectomy, including bleeding, from the English NHSBCSP up to and including January 2012 is one of the few studies to provide the detail allowing PPB rate to be calculated per colonoscopy, per polypectomy and per colonoscopy where a polypectomy was performed. This study used the NHSBCSP definition of bleeding that has also been used in this thesis, reporting a therapeutic bleeding rate of 0.60% per colonoscopy, 0.47% per polypectomy and 1.14% per number of colonoscopies where polypectomy was performed[39].

When considering the studies reported in this chapter over the last 40 years, we are left with a PPB incidence per number of colonoscopies of 0.07-0.60%, per number of polypectomies of 0.34-1.09% and per number of colonoscopies where polypectomy is performed of 0.42-1.14%.

PPB incidence is summarised in table 2. Studies expressing PPB rate with patients in the denominator have been excluded from this table. When expressing PPB incidence it is only using colonoscopies, polypectomies or colonoscopies where polypectomies are performed in the denominator that gives a true representation of PPB incidence.

Table 2: PPB incidence per colonoscopy, polypectomy and colonoscopy where polypectomy performed

Study	Rogers et al.	Macrae et al.	Rosen et al.	Sorbi et al.	Dafnis et al.	Viiala et al.	Rathgaber et al.
Year	1974	1980	1991	2000	2001	2003	2006
Patients			16910		4304	26841	12,407
Colonoscopies		5000			6066	30463	
Polypectomies	6214	1795			2635		5074
Colonoscopies where polypectomies performed			4721	14575			
Post Polypectomy Bleeds	115	48	20	83	9	44	23
PPB incidence per colonoscopy						0.14%	0.19%
PPB incidence per polypectomy	1.09%	1.06%			0.34%	0.19%	0.45%
PPB incidence per colonoscopy where a polypectomy was performed			0.42%	0.57%			

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	Singh et al. 2009	Singh et al. 2010	Inadomi et al. 2012	Saraya et al. 2012	Rutter et al. 2014
	24509	29990	43,456	4719	112024
					130831
			20,571	10,513	167208
					69028
	21		103	66	787
				0.63%	0.60%
	0.15%	0.07%			0.47%
			0.5%		1.14%

2.6.4 Risk factors for post polypectomy bleeding

Risk factors associated with PPB may relate to the patient having the polypectomy, including the specific polyp itself, the colonoscopy and polypectomy or the colonoscopist who performs the colonoscopy and polypectomy. As with the literature reviewed in chapter 2.5.2, it is important to consider the precise definition of PPB used when evaluating PPB risk.

As with colonoscopic perforation, increasing patient age has been shown to be a significant risk factor for PPB[104] [105]. Age was a significant predictor of PPB requiring transfusion in one study which also showed the presence of cardiovascular co-morbidity and renal disease to be significant[98]. Similarly, the presence of cardiovascular co-morbidity in the form of hypertension was found to be predictive of PPB in a further study which specifically examined patient related factors[106]. Although there is clear guidance regarding the use of anticoagulant medication such as Warfarin and antiplatelet medication such as Clopidogrel when attempting polypectomy, such medications have been shown to increase the risk of PPB when restarted within a week of polypectomy taking place[101]. Similarly, a patient taking Aspirin may be at increased risk, which would be consistent with the studies reporting cardiovascular co-morbidity as significant risk factors[105] [107]. Diverticular disease at the site of polypectomy is another reported patient related risk factor for PPB[108].

Studies have reported PPB risk factors specifically relating to the polyp itself. Increasing polyp size has consistently be shown to be important[101] [106] [109] [110].

Location of the polyp in the right colon and particularly in the caecum have also been reported as high risk locations[105] [111] [112] [110]. One of these studies reported the shape of the polyp as being pedunculated as a significant risk factor while another the histology of the polyp as either Juvenile or Peutz-Jegher as being significant[109] [110].

Piecemeal polypectomy, the use of sedation and bleeding visualised during the colonoscopy have all been reported as procedure related factors for PPB[108] [109] [111].

A reported colonoscopist specific risk factor for PPB related to those who are less experienced colonoscopists. One study reported performing less than 591 procedures per year as a significant risk factor, however, a clear definition of PPB is not offered in this study, it being described as that treated endoscopically, leaving the reader to presume this is at the time of the polypectomy and therefore would not be considered PPB by this thesis's definition[58].

Data from the English National Health Service Bowel Cancer Screening Programme is consistent with that reporting polyp size and the right colon as being important; both the size of the polyp and a location of a polyp in the caecum were shown to be significant risk factors for bleeding and bleeding requiring transfusion[39].

2.6.5 How a patient with post polypectomy bleeding presents for consultation

PPB usually presents symptomatically with bleeding or melaena per rectum. If the bleeding is not visually obvious, patients may present symptomatically from haemodynamic instability, orthostatic hypotension, haemorrhagic shock or syncope. In Sorbi et al's descriptive analysis of post polypectomy lower gastrointestinal bleeding, presentation was at a median of five days post colonoscopy, 43% of patients were either tachycardic, hypotensive or had changes of orthostatic hypotension[98].

2.6.6 The management of post polypectomy bleeding

Post polypectomy bleeding may require another colonoscopy in order to provide therapy to achieve haemostasis. However, if this is not successful or possible, radiological intervention or surgery are alternative management strategies.

Fundamental to managing patients who present after the colonoscopy is intravascular volume resuscitation with intravenous fluids and red blood cells. Fresh frozen plasma, platelets, cryoprecipitate and/or vitamin k may be required to reverse the effects of altered blood coagulation. In the series of 20 patients described by Rosen et al. five required blood transfusion[96]. Gibbs et al. described 12 of 13 patients with post polypectomy colonic haemorrhage requiring a mean of 5.5 units of red blood cells, including one who was taking warfarin who was transfused 14 units of packed red blood cells and eight units of fresh frozen plasma[97]. In Sorbi et al.'s larger series of 83 patients, 45 patients required red blood cells, eight patients platelets and ten patients fresh frozen plasma[98].

2.6.6.1 The endoscopic management of post polypectomy bleeding

A repeat colonoscopy or flexible sigmoidoscopy examination may identify the site of PPB. There are a variety of endoscopic methods by which the haemorrhage can then be controlled and stopped.

Mechanical pressure applied to the bleeding mucosa may be sufficient to provide haemostasis. A case report published in 1982 described the use of polypectomy grasping forceps or the "plumber's helper" in order to do this[113]. Using a snare or forceps to provide the pressure required is also feasible[114].

The use of an injection needle through the scope with administration of 1;10,000 dilution of adrenaline alone may be sufficient to stop PPB, though this is commonly used in conjunction with another endoscopic technique. Endoclips left in place to provide pressure to the site of haemorrhage are effective in achieving haemostasis[115]. Of 18 cases of PPB described by Kim et al., one was injected with epinephrine (adrenaline) and 17 were managed with hemoclips, though two suffered rebleeding and required further hemoclips[102]. The use of an endoclip has also been described with a detachable snare and with an endoloop[116 117].

More recent reports have described the use of endoscopic band ligation for post polypectomy haemorrhage of a large pedunculated polyp[118]. Case reports published in 2014 have described the successful use of a polysaccharide

haemostatic system and Ovesco system for control of postpolypectomy haemorrhage[119] [120].

2.6.6.2 The radiological management of post polypectomy bleeding

For those patients who fail endoscopic management, radiological investigation and intervention may be required to identify the source of bleeding and/or stop it.

Technetium tagged red blood cell scintigraphy has been used to identify the bleeding source in cases of PPB. This may be followed by angiography with the administration of selective vasopressin or arterial embolization[97] [98]. In one report of such treatment intra arterial vasopressin infusion of the inferior mesenteric artery was used in the treatment of two patients. These patients had co-morbidity and were a high anaesthetic risk for surgery. Vasopressin infusion controlled the haemorrhage in both patients without compliaction[121]. A further report of a patient who had continued to bleed despite the endoscopic application of clips described the use of angiography and the embolization of the sigmoid branches of the inferior mesenteric artery using microcoils[122]. Similar management was required for a patient with post-polycythaemia myelofibrosis who had been not been taking their usual anti platelet medication seven days either side of a colonoscopy and polypectomy. Haemorrhage at the site of polypectomy was demonstrated by arteriography and selective embolization of the three branches of the ileo colic artery successfully controlled the haemorrhage[123]. Endoclips that are left in place from attempted endoscopic

management may help in locating the source of PPB when angiography is attempted[55].

2.6.6.3 The surgical management of post polypectomy bleeding

Rarely, a patient may require surgery in order to control PPB. Surgery is indicated if the patient is too unstable for, or fails endoscopic or radiological management, or the site of the haemorrhage cannot be identified by these methods.

An over sew of the stump of a polyp to control PPB was reported by Macrae et al. in one of this papers cases of major haemorrhage. Another patient in this series with recurrent haemorrhage eventually required a laparotomy although the exact nature of the operation is not specified[43]. Of 41 patients with post polypectomy bleeding described by Sawhney et al., which would be included in this thesis's definition of PPB, one patient underwent surgery to control bleeding although, again, the exact nature of the case is not specified[101]. Of 11 patients presenting with PPB during the 30 days after colonoscopy in a study comparing PPB in those on Aspirin to those who were not, one patient required emergency surgery though further detail of the surgery is not provided[107]. 12 cases of bleeding associated with 1389 therapeutic colonoscopies from a Swedish database included one with PPB that required an exploratory laparotomy[38].

Colonic resection is the definitive surgical management of PPB if all other attempts at haemorrhage control fail or the source of haemorrhage cannot be

identified. Rosen et al. described one patient requiring subtotal colectomy and Sorbi et al. two patients requiring a hemicolectomy[96 98].

2.6.7 The prognosis following post polypectomy bleeding

There is limited data reported on patient prognosis and outcomes following PPB, including recurrent bleeding, morbidity and mortality from early series. However, Sorbi et al's descriptive analysis of 83 patients published in the year 2000 reported a median in patient hospital stay of three days with one death[98]. Singh et al. reported length of hospital stay in 17 patients with delayed PPB when comparing those on interrupted clopidogrel therapy to those not on clopidogrel. Hospital stay in these patients ranged from 0 to 4 days[124]. Inoue et al. investigated the clinical features of PPB associated with Heparin Bridge therapy. Of 10 patients with PPB, 9 of whom were on Heparin Bridge therapy at the time of polypectomy, hospital stay ranged from 7 to 37 days. Of these 9 patients, 5 (55.6%) had recurrent bleeding[125].

2.7 Post colonoscopy colorectal cancer (PCCRC)

2.7.1 The definition of post colonoscopy colorectal cancer

A colonoscopy has the potential to miss pathology. Patients attending for colonoscopy are made aware of this as part of the consent process. Such pathology may include pre cancerous polyps and indeed colorectal cancers themselves.

When colonoscopy is used during screening programmes for colorectal cancer, cancers that present in between screening colonoscopies are termed interval cancers. Although interval cancers may be included within the definition of an adverse event, interval cancer excludes those cancers that are diagnosed on subsequent screening and surveillance colonoscopies. Such cancers may be regarded as successes when diagnosed as part of a screening programme. However, they could be due to a lesion missed or incompletely resected during a previous colonoscopy, and therefore, can be considered as a colonoscopic adverse event of the initial colonoscopy.

Therefore, the term post colonoscopy colorectal cancer is more encompassing as an adverse event as it includes both interval cancers and cancers diagnosed as part of the screening programme that were potentially missed at a previous colonoscopy.

2.7.2 Post colonoscopy colorectal cancer rate

The rate of post colonoscopy colorectal cancer is dependent on the methodology and formula used to calculate it. There is currently no internationally accepted formula for calculating PCCRC rate; different studies have used differing methodology, which makes the comparison of such figures difficult[126]. Because of this, ensuring methodology is clear when calculating rates is of paramount importance.

The majority of studies have used cancers in the numerator and denominator to calculate PCCRC rate. Such rates, therefore, express PCCRCs within the total number of cancers diagnosed during a period of time. However, different time periods after the initial colonoscopy may used to define when a PCCRC has occurred. In addition, interval cancers may also be defined differently between studies.

Farrar et al defined interval cancer as a colorectal cancer developing five years after a complete colonoscopy. In this study, 830 patients were diagnosed with a colorectal cancer over an approximately 14 year period. Of these patients, 45 were diagnosed within five years of a previous colonoscopy, 5.4% of all these cancers[127]. Huang et al. retrospectively analysed data on patients having a surveillance colonoscopy within five years after a colonoscopic polypectomy. Of 1,794 patients undergoing surveillance colonoscopy within five years of a colonoscopic polypectomy, 14 had cancer[128]. Similarly, Le Clerc et al. also defined PCCRC as colorectal cancer that had been diagnosed within 5 years after an index colonoscopy, 2.9% of all cancers in this study[129].

A time period of a colorectal cancer diagnosed 3 years after an initial colonoscopy has also been used in several studies. Haseman et al. reported a total of 941 cases of colorectal cancer diagnosed by colonoscopy; in 47 a colonoscopy performed within three years of the diagnosis had not detected the cancer[130]. Two retrospective studies from Canada have also used this timescale. Bressler et al. studied a cohort of 12,487 patients with colorectal cancer, 3.4% had a colonoscopy 6-36 months prior to the diagnosis. However, this total study

cohort excluded patients with Inflammatory Bowel Disease and cancers where the colorectal cancer site was not specified in their register. It also assumed that for those patients who had a colonoscopy within six months of the diagnosis, that colonoscopy had made the diagnosis[131]. Similarly, Baxter et al. defined those as having PCCRC when they had undergone complete colonoscopy 7-36 months prior to their diagnosis. The overall rate of PCCRC was 9%[132]. Two more studies from the U.S.A also used this methodology of patients diagnosed 6-36 months after an initial colonoscopy, those cancers being diagnosed within 6 months being attributed to the initial colonoscopy, the rates being 6.9% and 7.2% respectively, the latter being in a larger cohort[133] [134].

Longer follow up periods than five years after an index colonoscopy have been used in studies for calculating PCCRC rate. Brenner et al. studied predictors and characteristics of interval cancers 10 years after a negative index colonoscopy, of 1945 cases of colorectal cancer, 78 were interval cancers[135]. A 15 year follow up period was used by Rabeneck et al. who reported an interval cancer rate of 14.5% among 110,402 individuals who had an initial negative colonoscopy[136].

2.7.3 Risk factors for developing post colonoscopy colorectal cancer

Five possible mechanisms have been suggested to explain the occurrence of PCCRC. PCCRC may develop from lesions that were missed during previous colonoscopy either missed cancers or missed adenomas that progress to cancer. PCCRC may present from an adenoma or cancer that was incompletely resected at the initial colonoscopy[137]. It is for these reasons that PCCRC can be considered

within the definition of a colonoscopic adverse event. A fifth mechanism for the development of PCCRC is rapidly developing colorectal cancers that develop after an initial colonoscopy. These cancers cannot be attributed to the initial colonoscopy.

Considerable recent research has focused on identifying factors that are associated with the development of PCCRC and in identifying differences in characteristics between PCCRC and colorectal cancers that are not PCCRCs. Risk factors for the development of PCCRC may relate to the patient, the colonoscopy itself, the colonoscopist that performs the procedure or the setting in which the colonoscopy is performed.

Increasing patient age has been shown to be a significant predictor of PCCRC. Older age, and an age over 85 years were reported as significant factors in three studies although in one of these this related to only PCCRCs in the distal colon[131] [132] [138]. In one of these studies, male sex is also a reported risk factor, however, this is contrast to Brenner et al. who showed that female sex was strongly and independently associated with development of interval cancer[138] [135]. Baxter et al. also corroborate female sex being a risk factor for PCCRC development although, again this related to distal colonic cancers only. Increasing patient co-morbidity is also reported as a significant predictor of PCCRC development in this study[132]. Likewise Cooper et al. also found increased co-morbidity to be associated with interval cancers[134].

In addition to patient age, sex and co-morbidity the location of the cancer in the patient's colon has consistently been shown to be an important factor relating to the development of PCCRC. A proximal colonic location of the PCCRC has been reported as a significant factor in several studies[127] [129] [131] [132] [133] [135] [134]. The presence of other pathology in the colon, for example, diverticular disease has also been proven significant[131] [134].

As proximal colonic location is such a significant risk factor for PCCRC, factors relating to the colonoscopy itself are also likely to be important. This may relate to a colonoscopy where the proximal colon is not intubated. Brenner et al. showed that the colonoscopy prior to development of the PCCRC was more likely to have been incomplete among patients with interval cancers[135]. Similarly incomplete polypectomy is associated with PCCRC development. Farrar et al. showed that the location of previous polypectomy segments was predictive of the location of interval cancers.

As completeness of colonoscopic examination and polypectomy are important factors in PCCRC development, it follows that factors relating to the expertise of the colonoscopist are also likely to be significant. Colonoscopists performing polypectomies at higher rates was associated with a lower risk of proximal PCCRC in one study and similarly lower polypectomy rate was a risk factor for PCCRC in another[132] [134]. Patients undergoing colonoscopy by a colonoscopist with a Caecal Intubation Rate (CIR) $\geq$ 95% were less likely to have a PCCRC than those with a CIR $\leq$ 80%[132]. The specialty of the colonoscopist also contributes to such factors; a non-gastrointestinal colonoscopist being a significant factor[131] [133]

[136] [138]. Finally, the setting in which the initial colonoscopy has been reported as a risk factor for PCCRC; a non hospital setting being significant in Baxter et al.'s study[132].

2.8 The colonoscopist and adverse events

It is important to recognise that not only the patient, but also the colonoscopist may be affected by an adverse event associated with a colonoscopy they have performed. This is particularly the case in the context of a screening programme for colorectal cancer. Colonoscopists require extensive training and assessment of performance in order to become fully certified to perform colonoscopies independently. Those colonoscopists working within the Bowel Cancer Screening Programme in the England have undertaken further written and practical assessment in order to become screening accredited[20].

Performing a colonoscopy associated with an adverse event may have a negative impact on the colonoscopist, both personally and professionally. The professional impact of such an event may be to the detriment of their future colonoscopic practice. For example, the colonoscopist may be less willing to continue the procedure when it is difficult, perform a large polypectomy or withdraw the colonoscope more quickly than they should meaning they may be more prone to missing pathology.

There is little literature specifically surrounding endoscopists' reaction to

colonoscopic or other endoscopic adverse events. However, many studies have focused on the reaction of different health care professionals to adverse events in a range of other medical and surgical fields. Such studies often refer to the health care professional involved as the second victim of the adverse event, the first victim being the patient and the family of the patient involved[139],[140].

A second victim has been defined as "a health care provider involved in an unanticipated adverse patient event, medical error and/or a patient related injury that became victimised in the sense that the health care provider is traumatised by the event. Frequently, second victims feel personally responsible for the unexpected patient outcomes and feel as though they have failed their patient and feel doubts about their clinical skills and knowledge base".[141]

Scott et al. conducted semi-structured interviews with 31 'second victims' of different professional backgrounds, most of whom were doctors and nurses. Six specific stages in their reaction were identified.

Initially they described a 'chaos and accident response' involving 'chaotic and confusing scenarios of both external and internal turmoil that ultimately led to a realisation of what had occurred'. These often occurred in the immediate aftermath of the adverse event when a patient was unstable and required additional professional input. Secondly, there was a period of 'intrusive reflection' with 'feelings of internal inadequacy and self isolation'. Thirdly, Scott et al. described 'restoring personal integrity' by seeking support from an individual with whom they had a trusting relationship. 'Enduring the inquisition' follows where the second victim starts to wonder about repercussions affecting

job security and future litigation. The second victim then 'obtains emotional first aid' and then, finally 'moves on'. The 'moving on' may involve three potential paths of dropping out, surviving or thriving[141].

The initial reaction of the health care professional to an adverse event is described elsewhere as being similar to that of an acute stress disorder including initial numbness, detachment or even depersonalisation.[142] This mimics the initial stage described by Scott at al.[141].

A range of emotional responses is a recurring theme of other studies examining health care professionals' reactions to adverse events. Common reported reactions among professionals are fear, guilt, shame, self doubt, loss of self confidence, anger and disappointment.[139] The intensity of emotional reaction appears to be related to the extent the patient suffers as a result of the adverse event and the extent to which the professional feels responsible; poorer patient outcomes and greater perceived responsibility increasing the intensity of reaction[143].

Some of these emotions were present in a study reporting specifically on the emotional impact of adverse events on physicians including increased anxiety about future errors, loss of self confidence, difficulty sleeping and reduced job satisfaction.[144]

A qualitative study of second victims of adverse events by Ullstrom et al. using

the same semi structured interview methodology of Scott et al. reported three subcategories to the impact of the adverse event. The first of these was the emotional reaction to the event that included sadness, anxiety, reliving the event, guilt, shame, decreased professional reputation, frustration and sleep disturbance.[144]

Such experiences may result in a significant inability of the professional to continue with their work, some may choose to leave the profession completely and there have been reports of others who commit suicide.[142]

A second and third phase to the impact of the adverse event described by Ullstrom et al. appears to confirm these findings; the impact on professional performance and the duration of the impact. Several of the participants who were interviewed felt insecure in their professional roles following the adverse event. Some doubted their professional judgement and career choice. Over 50% described taking more care over their work so as to reduce the chances of further problems. A majority described the duration of the impact as being long lasting, up to a year or more, with most stating the event will always affect them.[144]

A similar study by Luu et al. using the same semi structured interview framework devised by Scott et al., specifically investigated surgeons' emotional reaction to adverse events[145] [141]. They described 4 distinct phases in the response to an adverse event, 'the kick', 'the fall', 'the recovery' and 'the long term impact'. 'The kick' often involved a physiological response, commonly an

anxiety or stress reaction similar to that seen during Scott et al.'s [141]'chaos and accident' response. 'The fall' follows, a period of spiralling out of control co existent with a need to 'right themselves'. 'The fall' fits with Scott et al.'s 'intrusive reflections', 'restoring personal integrity' and 'enduring the inquisition'. During the third phase, 'The recovery' the surgeon reflected on the event then experienced 'the long term impact' of how the event had impacted on their long term judgement and decision making.[145]

Some authors have described the positive influence that involvement in an adverse event may have[146]. These have included specific changes to their practice. Such positive influences may be pertinent in the case of a colonoscopist who changes a specific part of their colonoscopic technique following an adverse event.

Chapter 3

Research Study Design

3.1 Research Studies

This thesis consists of four interlinked studies relating to colonoscopic adverse events. Two of these studies relate to colonoscopic perforation, with a further two studies of post polypectomy bleeding (PPB) and post colonoscopy colorectal cancer (PCCRC) respectively. These studies can be found in chapters four, five, six and seven of this thesis.

The review of literature described in chapter two of this thesis provided an overview of the current use of colonoscopy in screening programmes for colorectal cancer, including in the English National Health Service (NHS) Bowel Cancer Screening Programme (BCSP). It enabled me to establish the benefits and risks to the public that colonoscopy confers when it is used in such screening programmes. When I explored the risks of colonoscopy in greater detail, it was apparent that adverse events associated with colonoscopy potentially provide the greatest threat to the safety of individuals who accept the invitation to take part in colorectal cancer screening. Evaluating such events still further, it was evident that perforation, post polypectomy bleeding and post colonoscopy colorectal cancer are likely to be major contributors to this potential compromise of patient safety. All have the potential to result in patient death.

My intention in writing this thesis was, therefore, to examine these colonoscopic adverse events in the English NHS BCSP. This examination comprised several distinct themes. Initially, I aimed to determine how frequently perforation, PPB and PCCRC occur in the programme. Furthermore, I intended to stratify PPB by severity; such stratification had not been previously been reported when considering adverse event rate. I then intended to explore the impact of these adverse events, not only on the patients within the programme, but also on the health care professionals who perform colonoscopies. Thirdly, I planned to identify risk factors for these adverse events, so that such factors could potentially be removed from subsequent practice and the risk of such events occurring in the future could be minimised. Fourthly, I wanted to identify best practice surrounding adverse events, which in turn may help improve future management. Finally, I planned to provide a reference point of how a colonoscopist may feel following a perforation so that all colonoscopists could use and relate to this should they encounter such an adverse event associated with one of their colonoscopies in the future.

In order to achieve this examination of these three colonoscopic adverse events, incorporating all of the themes outlined above, I used mixed methodology. The approach I took encompassed both quantitative and qualitative health research methods.

One of the purposes of using quantitative health research methodology was to determine the rates of colonoscopic perforation, PPB and PCCRC in the English NHS BCSP. Quantitative health research methodology was also used to establish

the impact these adverse events had on the patient involved. This involved the capture of data relating to the patient's presentation, assessment, management and outcome following perforation and PPB. I designed three retrospective observational case series in order to collect data relating to perforation, PPB and PCCRC.

Quantitative health research methodology, alone, however, would not achieve all of my stated intentions in writing this thesis. Minimising the risk of these colonoscopic adverse events required identifying factors, some of which could not be measured quantitatively. Similarly, exploring the impact of a colonoscopic adverse event on the professional performing the colonoscopy could also not be achieved quantitatively. Therefore, qualitative research methodology was used to achieve these aims.

I therefore designed a qualitative study surrounding colonoscopic perforation. This study, 'Colonoscopists narratives of a colonoscopy associated with a colorectal perforation' involved colonoscopists, some of whom perform colonoscopy in the English NHS BCSP.

These four studies outlined, when combined, enabled me to achieve the stated aims of writing this thesis. Detailed methodology relating to each study is described within chapters four, five, six and seven.

3.2 Ethics

Ethical approval for the three quantitative studies outlined in this chapter was sought and gained from the Local Regional Ethics Committee: Newcastle & North Tyneside 2. The process of ethical approval for the qualitative study in chapter seven is described in detail in that chapter.

Chapter 4

Colonoscopic Perforation

4.1 Aims

The following aims relate to colonoscopic perforation in the English National Health Service Bowel Cancer Screening Programme only.

1. To determine the rate of colonoscopic perforation.

2. To describe post perforation presentation, assessment, management and outcomes.

3. To determine the post perforation rates of surgery, stoma formation, morbidity and mortality.

4. To identify factors associated with poorer patient outcomes post perforation.

4.2 Methods

4.2.1 The English National Health Service Bowel Cancer Screening Programme Evaluation Group

The English National Health Service Bowel Cancer Screening Programme evaluation group is responsible for reviewing, evaluating and improving the service provided by the BCSP. One of the projects commissioned by the BCSP evaluation group was the 'adverse events' project. An evaluation of the

colonoscopic perforations that have occurred since the start of the programme was a request of the evaluation group with regards to this project. The requirements of the evaluation group, therefore, allowed me to design and conduct this research study of colonoscopic perforation using data drawn from the cases of colonoscopic perforation that had occurred nationally in the BCSP.

4.2.2 Initial Thoughts on Colonoscopic Perforation – 'The patient journey'

I began this study by considering and summarising the 'journey' a patient with colonoscopic perforation in the BCSP would take. Ideas of how such a journey would start, the stages and potential directions the patient would take and how such a journey would finish were conceived from my own personal experience of consulting and managing patients with colonoscopic perforation. Witnessing first hand the assessment and management of these patients by colleagues added to these ideas. Furthermore, discussing the journey with colleagues of an endoscopic, nursing, medical and surgical background enabled me to start to develop definite stages in this journey that would form the basis of the data I would collect. These stages were added to and made more concrete by reviewing the literature that has been described in chapter 2.4 of this thesis.

I proposed the start of the patient journey would begin with the identification and the demographics of a patient accepting the invitation for a colonoscopy following an abnormal Faecal Occult Blood Test (FOBT). The patient would then be assessed as to their suitability for colonoscopy, which would include assessment of their medical history, active medical problems and current

medication. Bowel preparation would be given to the patient prior to their colonoscopy.

The journey would continue when the patient attended for the colonoscopy associated with the perforation. There may be many factors associated with the perforation; for the most part these would probably be related to a polypectomy. The colonoscopist may see the perforation and attempt to manage it there and then, other colonoscopists may not make such an attempt, or may not even realise a perforation has occurred. Following completion of the colonoscopy, the patient may have symptoms requiring immediate assessment and admission to hospital, others may develop symptoms and re-present at a later stage, some may have no symptoms at all.

For those patients that are admitted to hospital, their symptoms may be numerous resulting in multiple investigations in order to reach a diagnosis. These patients may be managed medically or have surgery. Some patients may develop new problems while in hospital, some may die. Others may be discharged home safely without any complication.

Drawing on this overview of the patient journey, I developed the aims of this study, which are outlined in chapter 4.1.

4.2.3 Plan for data capture

Planning how to acquire the data required to answer the aims of this study comprised several distinct stages. Firstly, it was important to establish how many patients in the BCSP had a diagnosis of colonoscopic perforation. Secondly, I needed to ascertain who these patients were and, thirdly, where in England these perforations had occurred. I then needed specific patient details and data relating to the 'journey' the perforation case followed. Determining exactly where I would be able to get this data was the next stage in acquiring it.

Once I had an understanding of where this data would be held, I could finalise a plan for capturing it.

Progressing through these stages required an understanding of how the English NHS BCSP is structured, organised and delivered. Every two years from the age of 60 through to the age of 74, members of the public are invited to take part in screening for bowel cancer by completing a Faecal Occult Blood Test (FOBT). The FOBT kits are posted from and, once completed, returned to, one of five bowel cancer screening testing laboratories, known as 'hubs'. Each of the 'hubs' covers a large geographical region of England: North East, North & West, Eastern, Southern and London[20]. Those people who return an abnormal FOBT are invited for a colonic investigation, usually a colonoscopy, at one of 61 Joint Advisory Group on Gastrointestinal Endoscopy (JAG) approved Bowel Cancer Screening Centres (BCSCs) which are divided among the regions outlined above. When a patient attends for colonoscopy, a Specialist Screening Practitioner (SSP) is also present during the procedure. The SSP enters data relating to the patient and the colonoscopy onto a single national internet based database, the Bowel Cancer

Screening System (BCSS). Patients are informed of this as part of the consent process prior to the colonic investigation.

BCSS enabled me to establish how many patients in the BCSP had a diagnosis of colonoscopic perforation. It also allowed me to ascertain who these patients were and at which BCSC in England these perforations had occurred. The Bowel Cancer Screening System (BCSS) also provided some of the data I required relating to the patient's demographics and the details of the colonoscopy associated with the perforation.

However, not all of the data required for this study was available through BCSS. Following the conclusion of a colonoscopy associated with perforation, the data relating to the patient's subsequent admission to hospital, management and outcome would be entered into the patient's medical notes at the NHS trust where the patient was admitted. In the majority of cases this NHS trust was part of the Bowel Cancer Screening Centre (BCSC), although some patients were admitted to an NHS trust from outside the BCSC where the colonoscopy had taken place. The data needed from the patient's medical notes was therefore delivered to me by a nominated third person from within the NHS trust where the patient had been admitted. This transfer of data took place via a pseudo anonymised online questionnaire from each BCSC.

Data capture therefore comprised two stages; initially from the BCSS database and secondly from an online questionnaire completed at each of the Bowel Cancer Screening Centres which could be delivered to me via an online account.

The process of data capture using these two mediums is outlined in the following sections.

4.2.4 The Bowel Cancer Screening System (BCSS)

BCSS is part of the 'Open Exeter' suite of applications. The 'engine' of BCSS is an oracle database. All of the system logic and processing is performed in oracle, which provides results to the Java front end for display to the user. Data can be exported to a Structured Query Language server to allow specific queries to be written. Data entered into BCSS includes patient demographics and colonoscopy results[20].

Access to data stored within BCSS is restricted. The BCSP evaluation group is permitted access to the database as part of the function that the group performs. As previously described in section 4.2.3, the BCSP evaluation group who subsequently permitted access to BCSS had sanctioned this research. Professor Rutter, as chair of the BCSP evaluation group and a co-supervisor of this MD thesis, facilitated access to BCSS. Access to data within BCSS was provided in conjunction with the NHSBCSP national office, which is part of Public Health England (PHE).

Data entered into BCSS includes if the patient, or subject, as they are recorded in the database, had an endoscopic perforation recorded during their episode of screening. The first stage in me capturing data for this study was to email the project manager at the NHS Bowel Cancer Screening Programme National Office.

I wrote an email from my personal NHS mail account to Miss Claire Nickerson, the project manager at the NHSBCSP's national office, requesting she identify all the subjects recorded as having an endoscopic perforation in the BCSS database. Those subjects recorded as having an endoscopic perforation were identified through their unique subject identifier and their unique NHS number. The NHS number was classified as patient identifiable data whereas the subject identifier was a pseudo anonymised identifier that could only be accessed through BCSS. Miss Claire Nickerson replied to my email confirming that there were 147 cases of endoscopic perforation from the start of the BCSP on 02/08/2006 through until 13/03/2014 recorded on BCSS.

So that I would be able to identify whom these patients were, I then sent an email back to Miss Claire Nickerson requesting the unique subject identifiers and NHS numbers for these patients. I also requested an identifier for the Bowel Cancer Screening Centre (BCSC) where the colonoscopic perforation had occurred so that I knew the geographical location of these perforation cases. The BCSCs in England have a unique screening centre code numbered from BCS001 through to BCS062. (One of the BCSCs is now closed hence 61 BCSCs in total). Miss Claire Nickerson replied with the NHS numbers, subject identifiers and BCSC codes meaning I had completed the first three steps in data capture by confirming how many perforations, who the perforation cases were and where they occurred.

I sent a third email to Miss Claire Nickerson requesting data relating to the demographics of these subjects and the colonoscopy performed that was associated with perforation. The request was split into three sections: subject

demographics, procedure details and polyp details. The subject demographics included the subject age at the time of the colonoscopic perforation, the subject sex and the subject ASA physical status. The procedure details requested were the grade of bowel preparation quality, the date, start time and finish time of the colonoscopy. Procedure details also included whether polyps had been resected during the procedure and if polypectomies did take place, the number of polyps that were resected. The final section related to details of the polyps resected during each of these procedures including the polyp class, the polyp location, the estimated endoscopic size of the polyp, the polyp therapy modality, the polyp therapy device and the polyp therapy success.

Miss Claire Nickerson, replied to me explaining that this data had been extracted from BCSS in three separate Microsoft Excel spread sheets under the workbook titles 'demographics', 'procedure details' and 'polyp details'. Each spreadsheet contained the subject identifier with one of these spreadsheets, 'demographics' also containing the NHS number and BCSC code. These Microsoft Excel spread sheets were then emailed securely to me via NHS mail.

4.2.5 Bowel Cancer Screening Centre (BCSC) contacts

In order to progress to the second stage of data capture that was outlined in chapter 4.2.3, I needed to contact each of the BCSCs where at least one colonoscopic perforation had occurred. I again emailed Miss Claire Nickerson, project manager at the bowel cancer screening national office, requesting a contacts directory for each of the Bowel Cancer Screening Centres (BCSCs). The

directory included the email addresses and telephone numbers of the clinical director, programme manager and lead SSP at each BCSC.

I then designed and wrote a 'contacts' Microsoft Excel spread sheet for each of the cases of colonoscopic perforation, detailing the subject identifier, the BCSC code, the name of the BCSC, the name of the clinical director of the BCSC and an email address of the BCSC clinical director. When this spread sheet had been completed, I could begin the second stage of data capture.

4.2.6 Construction of a questionnaire for data capture

The methodology outlined in chapter 4.2.2 enabled me to decide the key themes and stages of the 'patient journey' surrounding colonoscopic perforation that would need to be examined. I broke the journey down into these stages; all had reasons for being examined, which related directly to the aims of this study.

The sections of the questionnaire and how each section specifically related to the aims of this study described in chapter 4.1 are listed below:

Subject Identifier

Medication:

The use of antithrombotic medication and corticosteroids were potentially risk factors for poorer patient outcomes post perforation.

Colonoscopy Report:

To describe post perforation presentation, assessment, management and outcomes

Representation to hospital:

To describe post perforation presentation, assessment, management and outcomes

Time to presentation was potentially a risk factor for poorer patient outcomes post perforation.

Admission and initial observations:

To describe post perforation presentation, assessment, management and outcomes

Initial Management

To describe post perforation presentation, assessment, management and outcomes

Time to commencing management was potentially a risk factor for poorer patient outcomes post perforation.

Initial Investigations

To describe post perforation presentation, assessment, management and outcomes

Surgery

To determine the post perforation rates of surgery, stoma formation, morbidity and mortality.

To describe post perforation presentation, assessment, management and outcomes

Outcomes

To describe post perforation presentation, assessment, management and outcomes

To determine the post perforation rates of surgery, stoma formation, morbidity and mortality.

The questionnaire listed questions in a structured, formal style. The full questionnaire can be found in the appendix of this thesis.

The full questionnaire was written in a Microsoft word document that was printed on paper for piloting.

A pilot of the questionnaire took place at the Tees Bowel Cancer Screening Centre (BCSC). I used the case notes of a patient who had suffered a colonoscopic perforation during a BCSP colonoscopy at the Tees BCSC. The hospital case notes from North Tees & Hartlepool NHS Foundation Trust were identified using the patient's NHS number. The pilot took place in a written form in the office of the Tees BCSC. Specialist Screening Practitioner (SSP), Miss Emma Fenby, an SSP who was employed at the Tees BCSC, and Miss Jestina Miles, a screening colonoscopist employed at the Tees BCSC performed the pilot. The pilot took approximately 30 minutes to complete. No changes to the questionnaire were made following the pilot.

4.2.7 Questionnaire Medium: Bristol Online Surveys

Following the successful pilot of the questionnaire in paper medium, it was entered into an electronic medium so that it could be easily distributed by email to the BCSCs around England where at least one colonoscopic perforation had

occurred. The electronic medium I used was with the internet based Bristol online surveys. Durham University has an agreement with Bristol online surveys allowing its students and staff access. I created the online survey at the website www.survey.bris.ac.uk. The questionnaire was entered into my personal account under the survey title 'Perforations in the Bowel Cancer Screening Programme'. I typed each question individually into the survey and modified the survey account so that the questionnaire would flow correctly depending on the answers that had been entered. The questionnaire was confidential; only myself and a learning resource manager employed at Durham University, Miss Emma Crawford, were able to view it. Once all the questions had been entered, the survey was launched under the World Wide Web address:

https://www.survey.bris.ac.uk/durham/perforations_in_the_bowel_cancer_screening_programme

The questionnaire in the online survey medium was launched in draft format initially, ready for a further online pilot. The online pilot of the questionnaire took place at Tees Bowel Cancer Screening Centre (BCSC). I used the case notes of a second patient who had suffered a colonoscopic perforation during a BCSP colonoscopy at the Tees BCSC. The hospital case notes from North Tees & Hartlepool NHS Foundation Trust were identified using the patient's NHS number. The pilot took place on a computer in the office of the Tees BCSC. A screening colonoscopist, Miss Jestina Miles, who is employed at the Tees BCSC, performed the online pilot. The pilot took approximately 30 minutes to complete. No changes to the questionnaire were made following the pilot.

Following this pilot, the electronic questionnaire was ready for use in the study. It was launched ready for its online distribution. In order for the electronic questionnaire to be deployed and completed, I then had to make contact with all the BCSCs in England where at least one perforation had occurred.

4.2.8 Questionnaire Location: Bowel Cancer Screening Centres (BCSCs)

The deployment of the online questionnaire to each of the BCSCs took place in three stages. Completion of the online questionnaire required a named person at each BCSC to identify and review the medical case notes of each patient. In order to do this they required the NHS number of each particular patient that had been provided to me so that notes could be requested and reviewed.

In order to provide the NHS number(s) of each of the respective perforation cases, a secure NHS email had to be sent between NHS email accounts. This was because the NHS number is patient identifiable data. The NHS email system is secure and protected the confidentiality of these numbers.

As outlined in chapter 4.2.5, the contacts for each BCSC where at least one perforation had occurred comprised the clinical director of the BCSC and their email addresses. Some of the BCSC clinical director's had an NHS mail account, however, the majority did not. Therefore, an initial email with an accompanying letter outlining the study and its aims was sent to each BCSC CD requesting an

NHS mail account that could be used. The accompanying letter that was emailed can be found in the appendix of this thesis.

The majority of BCSC CDs replied directly to me with the specified NHS mail address. This was an NHS email address either of the BCSC CD themselves or another specified contact at each BCSC, for example, the programme manager or a lead SSP. The NHS email addresses were then collated and added to the Microsoft Excel spread sheet of BCSC contacts.

Two weeks following the first email sent, which is described above, I sent a second NHS only email to the specified NHS email address of the specified contact at each BCSC. This NHS email contained the NHS number and a unique subject identification number of the patient with a colonoscopic perforation. The NHS number in this email allowed each BCSC to request the specified case notes for the patient.

A further two weeks following the second email, I sent a third email to each specified NHS mail address with a link to the web address of the online questionnaire. This email again reminded the specified contact at each of the BCSCs to enter the unique subject identification number into the online questionnaire, it being non-patient identifiable data, and not the NHS number of the patient.

4.2.9 Data Review

The questionnaire within the online account remained open for a period of one month initially, while responses were entered. I reviewed the response rate by opening my account of the Bristol online surveys website. The account also allowed me to review which patient's data had been entered. For those BCSCs who had not responded one week before the end of this initial period of one month, a reminder email to complete the questionnaire was sent to the specified contact at each of the BCSCs.

After the initial period of one month, those BCSCs that had still not responded at that point were again sent an email reminding them to complete the online questionnaire. The email stated the questionnaire would close one month on from the point that the email was sent so that a deadline was set for them to complete this request. This process was repeated again with all those BCSCs who did not respond.

When a response was not forthcoming for a particular subject identifier after multiple attempts, this case was labelled a 'non-responder'. Some BCSCs provided reasons why a response for a particular subject identifier had not been forthcoming. For example, if a patient had been admitted to a trust from outside the BCSC or notes could not be found.

When all possible responses had been received, the data from the questionnaire was exported from the Bristol online survey account into a Microsoft Excel spreadsheet.

4.2.10 Definitions of data collected

A colonoscopic perforation was defined as a patient who had evidence of air, luminal contents or instrumentation outside the gastrointestinal tract during or following a colonoscopy.

Diagnostic perforations were defined as colonoscopies where no tissue was removed from the colorectal location of the perforation, tissue was removed by cold biopsy for diagnostic purposes or a cold biopsy polypectomy occurred at the colorectal location of the perforation.

Therapeutic perforations were defined as those associated any of the following therapeutic devices: cold snare, hot snare, hot biopsy, argon beam, endoscopic knife, injection, heater probe.

4.2.11 Statistical Analysis

The Microsoft Excel spreadsheet was imported into statistical package for the social sciences (SPSS) version 20 for statistical analysis. Normally distributed continuous variables were expressed as mean, non-normally distributed continuous variables were expressed as median. Categorical variables were expressed as a percentage. Pearson chi-square and Fisher's exact test were used to test association between explanatory and outcome variables with a p value < 0.05 considered to be significant.

4.3 Results

The results in this chapter are from colonoscopic data from the start of the English National Health Service Bowel Cancer Screening Programme on the 02/08/2006 up to and including the 13/03/2014.

4.3.1 Overall colonoscopic data from the English NHS BCSP

The total number of colonoscopic procedures performed during this time was 263,129. Of these 263,129 endoscopic procedures, 159,301 (60.5%) were in male patients and 103,828 (39.5%) in female patients. The age of these patients ranged from 60-74 years with a mean age of 65.5. The American Society of Anaesthesia (ASA) grade was 1 (indicating the patient was fit) in 77,536 (29.5%) patients, 2 (indicating the patient had relevant disease) in 141,492 (53.8%) patients, 3 (indicating the patient had restrictive disease) in 19,998 (7.6%) patients, 4 (indicating the patient had life threatening disease) in 903 (0.3%) and 5 (indicating they were moribund) in 9 (0.003%) patients. The ASA grade was unknown in 23,191 (8.8%) patients. The bowel preparation quality of these endoscopic procedures was adequate in 89,032 (33.8%) patients, good in 154,180 (58.5%) patients, poor in 8,257 (3.1%) patients and unknown in 11,660 (4.4%) patients.

4.3.2 Colonoscopic Perforations in the English NHS BCSP

147 patients were recorded as having endoscopic perforation of the colon on the Bowel Cancer Screening System (BCSS). A perforation rate of 0.06% was therefore calculated as follows:

147/263,129 = 0.06%

The online questionnaire was distributed to the relevant Bowel Cancer Screening Centres (BCSCs) for all 147 patients. A response to online questionnaire was received in 117 patients with limited data collected from BCSS on patient presentation, assessment, management and outcome in the remaining 30 patients.

4.3.2.1 The patients with colonoscopic perforation for whom no response to the online questionnaire was received

Of the 30 patients for whom no response to the online questionnaire was received, 24 (80%) of were male and six (20%) were female. Their age ranged from 60 – 74 years with a mean age of 66.07. The American Society of (ASA) Anaesthesia grade was 1 (indicating the patient was fit) in 6 (20%) patients, 2 (indicating the patient had relevant disease) in 21 (70%) patients, 3 (indicating the patient had restrictive disease) in 2 (6.7%) patients and unknown in 1 patient.

During the colonoscopy of these 30 patients the bowel preparation quality was adequate in 12 (40%) patients, good in 15 (50%) patients and poor in 3 (10%)

patients. 25 (83.3%) of these patients had polyps resected. A diagnostic perforation occurred in two patients, these being in the caecum and sigmoid colon. A therapeutic perforation occurred in five patients. One of these therapeutic perforations was in the caecum, three were in the sigmoid colon and in one of these therapeutic perforations the colorectal location of the perforation was unclear. It was unclear in 23 of these 30 patients if a diagnostic or therapeutic perforation had occurred, although two of these were noted to be in the sigmoid colon.

Three of these 30 patients were admitted to hospital immediately following the colonoscopy. Eight were discharged and then re-presented to hospital, of which four were documented to have abdominal pain. Two patients were not admitted to hospital but were reviewed in the out patient department following computed tomography (CT) scans showing radiological evidence of perforation. How the patient presented was unclear in the remaining 17 patients.

Seven of these 30 patients, for whom no response to our online questionnaire was received, had surgery. This included two who had a right hemi colectomy, one with a sigmoid colectomy and one a hartmann's procedure. The operation name was unknown in three patients. Four patients did not have surgery and in 19 it was unclear if the patient had surgery or not. Two of these 30 patients were left with a stoma and two were admitted to the Intensive Care Unit (ICU).

4.3.2.2 The patients with colonoscopic perforation for whom a response to the online questionnaire was received

A response to the online questionnaire was received for 117 patients with colonoscopic perforation. Of these 117 patients, 68 (58.1%) patients were male and 47 (40.2%) patients were female. The patient sex was unknown in 2 patients. Patient age ranged from 60 – 74 years with a mean age of 65.5. The patient age was unknown in 3 patients. The American Society of Anaesthesia (ASA) grade was 1 (indicating the patient was fit) in 42 (35.9%) patients, 2 (indicating the patient had relevant disease) in 63 (53.8%) patients and 3 (indicating the patient had restrictive disease) in 8 (6.8%) patients.

During the colonoscopy of these 117 patients, the bowel preparation quality was good in 67 (57.3%) patients, adequate in 46 (39.3%) patients and poor in 1 (0.9%) patient. The bowel preparation quality was unknown in 3 patients. 97 (82.9%) of the patients had polyps resected.

Of the 117 perforations, there were 82 therapeutic perforations (70.1%) and 22 diagnostic perforations (18.8%). In 13 (11.1%) colonoscopies it was unclear if any therapy had taken place at the colorectal location of the perforation or the colorectal location of the perforation was unknown.

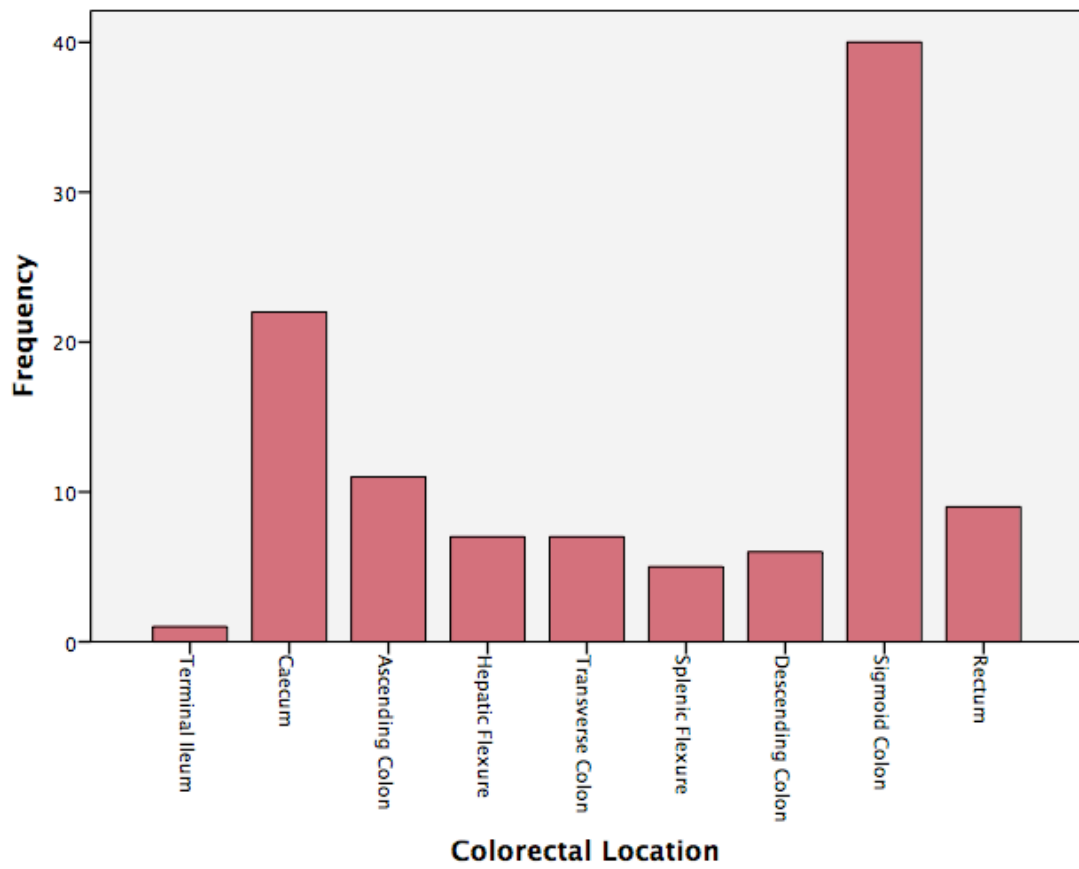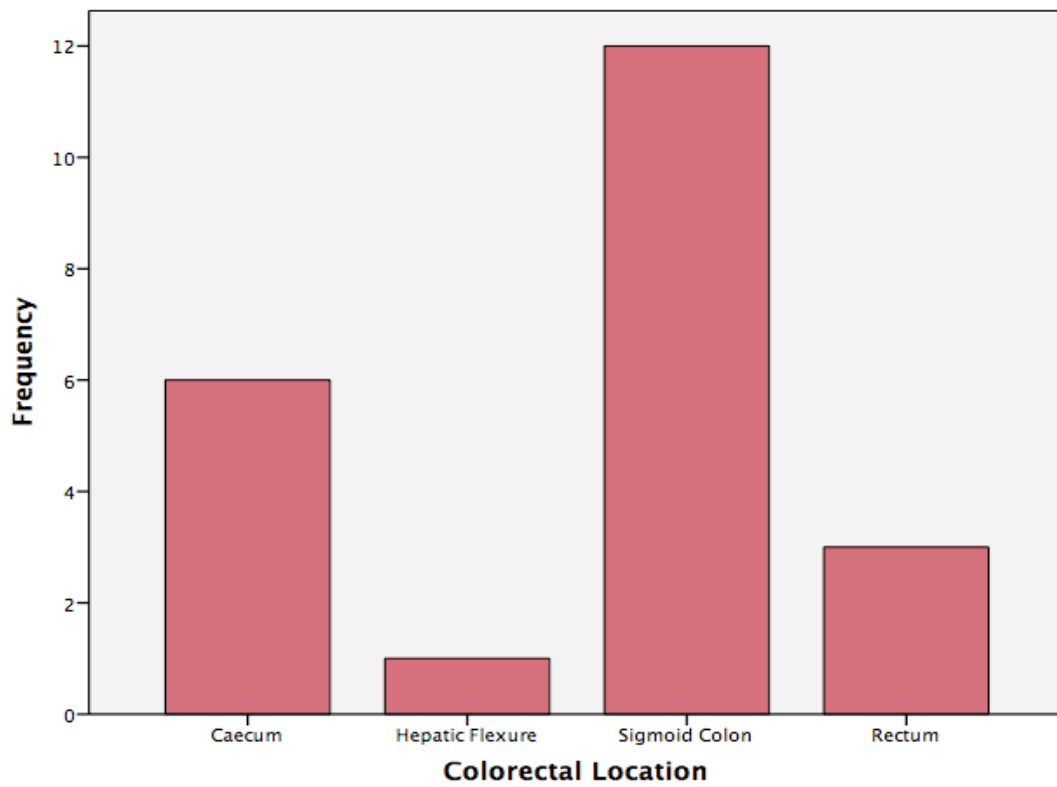**Chart 1: Bar chart of all perforations by colorectal location**

Chart 2: Bar chart of the diagnostic perforations by colorectal location

Of 12 diagnostic perforations in the sigmoid colon, six (50%) also had diverticular disease in the sigmoid colon. Of the 263,129 endoscopic examinations during this study period, in 80,023 a diagnosis of diverticular disease was noted, a rate of 30.4% overall. Of the three diagnostic perforations in the rectum, the endoscopist had retroverted in the rectum in one (33.3%) of these cases. Seven of the diagnostic perforations were at colorectal locations where a biopsy had been performed for diagnostic purposes. Five of these diagnostic biopsies were of a colorectal cancer. Four of these cancers were associated with a sub clinical computed tomography (CT) detected perforation.

There were no significant associations between sex, age, ASA Grade, bowel preparation quality, colorectal Location and a diagnostic or therapeutic perforation occurring ($p < 0.05$).

In 15 (12.8%) of patients the endoscopist had physically visualised the perforation, applying endoclips in 12 (10.2%). Therefore, endoclips were applied in 80% of perforations where the endoscopist had physically visualised the perforation. The endoscopist had physically visualised the perforation by visualising a tear in the serosa (n=6), visualisation of an extra intestinal structure (n=3), visualising a separation of muscle fibres (n=1), visualising a defect (n=3) and seeing the endoscopic knife perforate the colon (n=1). In one of these patients it was unclear how the endoscopist had visualised the perforation. The estimated endoscopic size of these perforations ranged from 2 to 25mm with a median size of 5.5mm.

In the 12 patients in whom the endoscopist had visualised the perforation and endoclips were applied, 10 (83.3%) did not have surgery whereas 2 did, however association between the use of endoclips and not having surgery did not reach significance (p<0.05).

Chart 3: Flow chart representing how the perforation cases presented
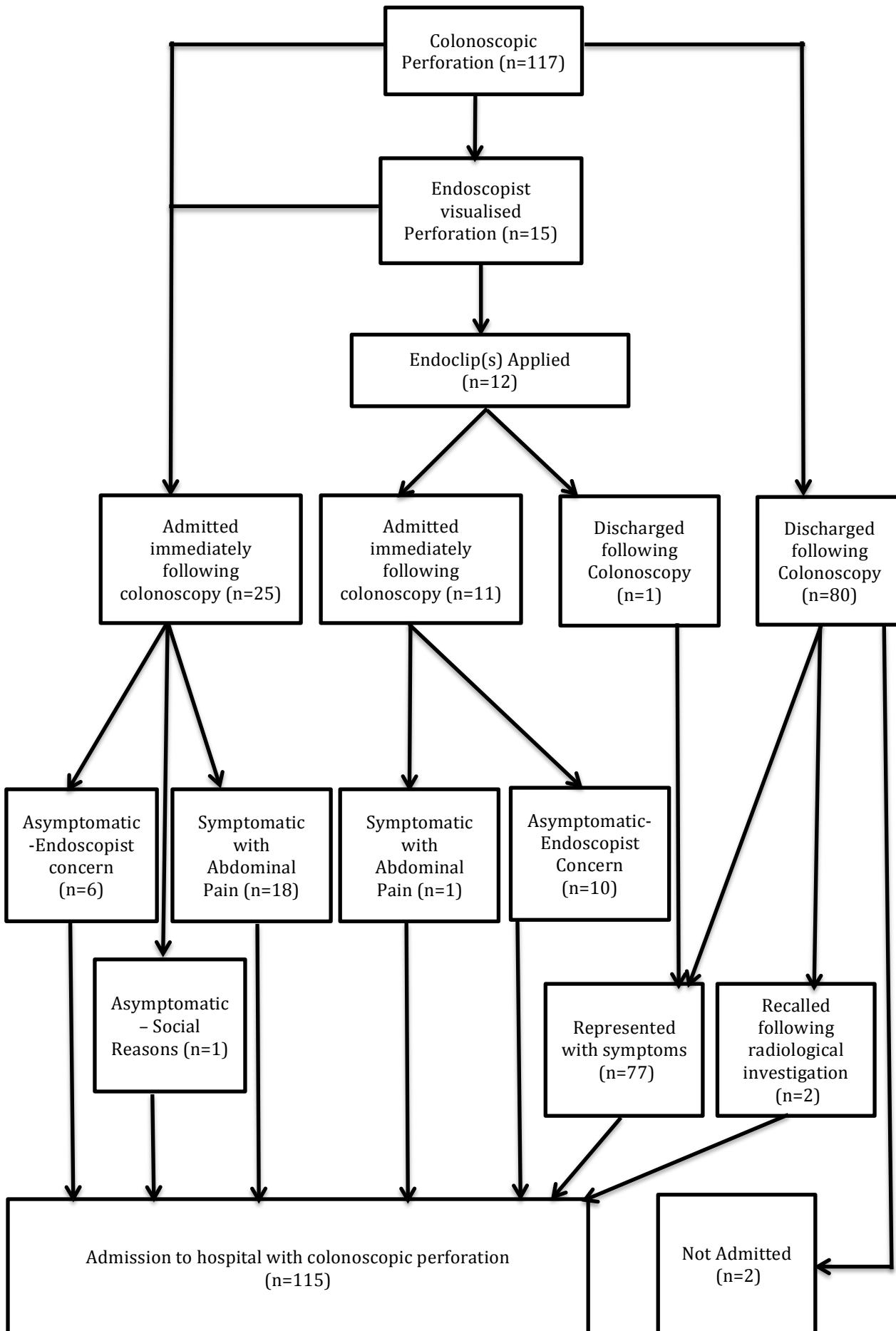
Thirty-six of 117 (30.8%) patients were admitted to hospital immediately following the completion of their colonoscopy. Of the 36 patients admitted to hospital immediately following completion of the colonoscopy, 17 were asymptomatic and 19 complained of symptoms. The asymptomatic patients were admitted due to endoscopist suspicion of perforation (n=15), endoscopist concern regarding bleeding (n=1) and for social reasons (n=1). The 19 symptomatic patients all complained of abdominal pain with five also complaining of abdominal distension. Of these 19 patients one also had evidence of surgical emphysema in their neck and another had a syncopal episode.

Eighty-one of 117 (69.2%) colonoscopic perforations were discharged following the completion of the colonoscopy. Two cases, both subclinical CT detected perforations, found on staging scans for colorectal cancers were not admitted to hospital. A further two cases, both sub clinical CT detected perforations, were recalled to hospital following staging scans for colorectal cancer. 77 patients represented to hospital with symptoms. In the majority of these, 66 of 77 (85.7%), the presenting complaint was abdominal pain. The time to readmission was unclear in 30 patients and in 51 patients the median time to readmission was one day (range 0-8 days).

A total of 115 patients were admitted to hospital with colonoscopic perforation.

When examining the time to presentation of diagnostic and therapeutic perforations, 16 of 32 (50%) patients with a therapeutic perforation, in whom

time to presentation was recorded presented within the first 24 hours. Of the remaining 16 patients with a therapeutic perforation, in whom time to presentation was recorded, six (37.5%) presented at one day, six (37.5%) at two days, two (6.3%) at 4 days, one (3.1%) at six days and one (3.1%) at seven days post perforation. Of 12 diagnostic perforations, in whom time to presentation was recorded, five (41.7%) presented within the first 24 hours, three (25%) at one day, one (8.3%) at four days, two (16.7%) at six days and one (8.3%) at seven days. There was no significant difference in time to presentation between diagnostic and therapeutic perforations (p=0.362).

With regards to presenting complaint, there was no significant difference in whether a diagnostic or therapeutic perforation presented with abdominal pain (p=0.768), the majority of diagnostic perforations in whom presenting complaint was recorded, 15 of 20 (75%) complaining of abdominal pain with 61 of 78 (78.2%) therapeutic perforations also complaining of abdominal pain.

Chart 4: Histogram of time to presentation with symptoms from perforation following colonoscopy:
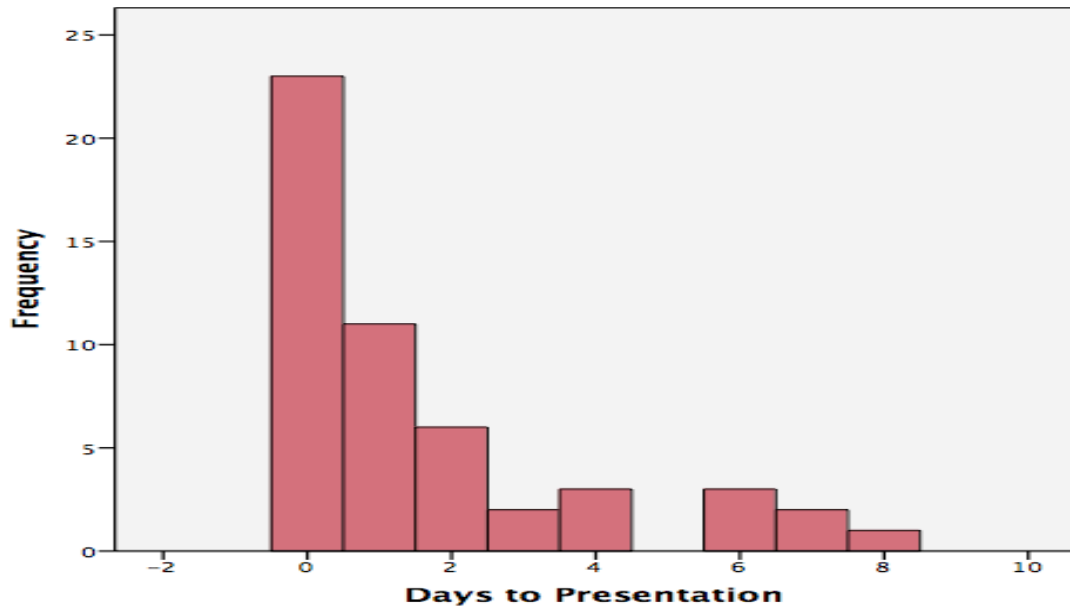
The initial observations recorded following admission to hospital were patient temperature, pulse rate, systolic blood pressure, diastolic blood pressure and respiratory rate. Temperature was unclear in 39 (33.9%) patients with 17 (14.7%) patients' being having pyrexia with a temperature of $\geq$ 38.0°C. 59 (51.3%) patients initial temperature was normal at 35.1-37.9°C. Pulse rate was unclear in 38 (32.5%) patients, with 62 (53%) of patients having a pulse < 100 beats per minute and 17 (14.5%) patients pulse being tachycardic at > 100 beats per minute. Respiratory rate was unclear in 46 (40.0%) patients with 9 (7.8%) patients' respiratory rate being > 20 breaths per minute and 60 (52.2%) patients' respiratory rate being less than or equal to 20 breaths per minute. Systolic blood pressure was unclear in 37 (32.2%) patients with 57 (73.1%) patients systolic blood pressure being > 120mmHg. Diastolic blood pressure was also unclear in 37 (32.2%) patients with 78 (67.8%) patients diastolic blood pressure ranging from 50-102mmHg.

When examining the recorded initial observations of diagnostic and therapeutic perforation, 54 therapeutic perforations and 18 diagnostic perforations had there initial temperature and pulse rate recorded. Five of 18 (27.8%) diagnostic perforations had pyrexia whereas 13 (72.2%) were apyrexial. Of 54 therapeutic perforations, 44 (81.5%) did not have pyrexia whereas 10 (18.5%) did. The presence of pyrexia was not significantly associated with a diagnostic or therapeutic perforation (p=0.504). Similarly, when examining initial pulse rate, three of 18 (16.7%) diagnostic perforations had a tachycardia whereas 15 (83.3%) did not. Thirteen of 54 (24.1%) therapeutic perforations had tachycardia with 41 (75.9%) having a normal pulse rate. The presence of a

tachycardia was not significantly associated with diagnostic or therapeutic perforations (p=0.745). In addition a respiratory rate > 20 breaths per minute was also not significantly associated with a diagnostic or therapeutic perforation (p=0.388).

The initial management recorded was if the patient was kept Nil By Mouth (NBM), given intravenous (IV) fluids or intravenous (IV) antibiotics. It was unclear if 20 (17.3%) patients were kept NBM, 12 (10.4%) patients were not kept NBM whereas 83 (72.2%) patients were. Intravenous fluids were commenced in 90 (78.3%) patients; it was unclear if intravenous fluids were commenced in 19 (16.5%) of patients. Intravenous antibiotics were commenced in 95 (82.6%) patients; it was unclear in 14 (12.2%) patients if intravenous fluids had been commenced.

The initial investigation in these 115 patients admitted to hospital included an erect chest x-ray (CXR), abdominal x-ray (AXR) or computed tomography (CT) scan. An erect chest x-ray (CXR) was performed in 61 (53.1%) patients admitted to hospital. The CXR was reported as normal in 29 (47.5%) of which 21 also had an abdominal x-ray (AXR). The AXR was also reported as normal in 20 with free air in the abdomen in 1 patient. Of the 29 patients with a normal CXR, 21 also had a CT including 2 that were normal but 19 showing evidence of perforation. The erect chest x-ray showed pneumoperitoneum in 28 (45.9%) patients. In these 28, 13 also had an abdominal x-ray; 6 of these abdominal x-ray's showed no evidence of perforation with 7 showing free air in the abdomen. 13 of these patients with an erect chest x-ray showing pneumoperitoneum also had a CT

showing evidence of perforation. 9 patients were taken straight to theatre for surgery on basis of CXR without further cross sectional imaging. 7 patients went onto have a CT before being taken to theatre for surgery. 2 patients managed conservatively on basis of CXR result alone. The CXR result was unknown in 4 patients.

An abdominal x-ray (AXR) was performed in 39 of 115 (35.1%) patients. No evidence of perforation was seen in 28 (71.8%). Of these 28, 19 patients also had a CT. The CT was normal in 1 patient but showed evidence of perforation in 18 patients. The AXR showed free air in the abdomen in 10 (25.6%) patients of which 5 also had a CT, all showing evidence of perforation. The AXR result was unknown in 1 patient. 71 of 115 (61.7%) patients had CT imaging following admission. In 42 of the 71 (59.1%) patients the CT showed a small amount of free air in the abdomen with 29 (40.8%) showing a large amount of free air. Of the 42 patients with a small amount of free air, 13 (30.9%) had surgery. Of 29 patients with a large amount of free on CT, 17 (58.6%) had surgery although the association between the amount of free air and having surgery did not reach statistical significance.

Chart 5: Flow chart representing the management of the perforation cases that were admitted to hospital:
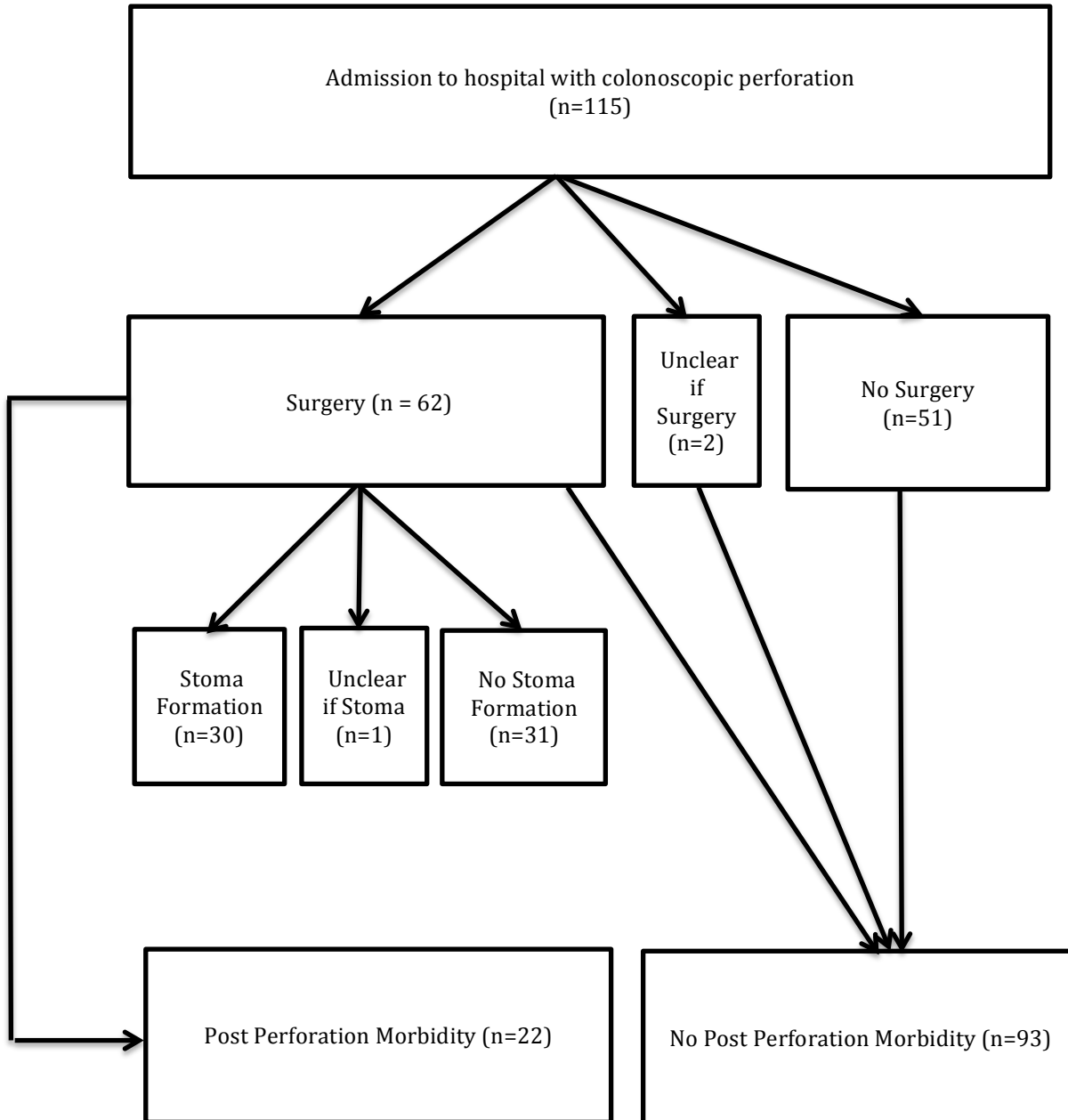
Fifty-one of 115 (44.3%) patients admitted to hospital did not have surgery. None of these patients' admissions were associated with post perforation morbidity or admission to the intensive care unit.

Sixty-two of 115 (53.9%) patients admitted to hospital had surgery. In 16 of 62 patients (25.8%) the surgery was commenced during normal surgical working hours (08:00-17:00). The majority of operations, 43 (69.4%), were performed by consultant surgeons. 35 of 62 (56.5%) operations were performed by colorectal surgeons. Seven laparoscopies occurred including simple closure of the perforation (n=4), sigmoid colectomy (n=2) and an appendicectomy (n=1). Five of the seven laparoscopies were performed by colorectal surgeons and all seven were performed by consultant surgeons. Nine laparoscopies were converted to open laparotomies including a colonic resection and ileostomy (n=1), right hemicolectomy (n=4), hartmann's procedure (n=1), peritoneal lavage (n=1) and simple closure of perforation (n=2). 46 open laparotomies were performed including a simple closure of perforation (n=3), sigmoid colectomy & loop ileostomy (n=1), hartmann's procedure (n=11), over sew with defunctioning loop sigmoid colostomy (n=1), right hemicolectomy (n=15), total colectomy and ileostomy (n=2), hartmann's procedure with extended left hemicolectomy (n=1), defunctioning loop colostomy (n=3), anterior resection with defunctioning loop colostomy (n=1), exploratory laparotomy (n=1), unknown (n=2), exteriorisation of colon (n=1), anterior resection (n=1), simple closure of perforation with sigmoid colectomy and covering ileostomy (n=1), limited left hemicolectomy with loop ileostomy (n=1) and sigmoid loop colostomy (n=1).

Seventeen of 20 (85.0%) diagnostic perforations admitted to hospital had surgery, 38 of 82 (46.3%) of therapeutic perforations had surgery. In 7 of those patients who had surgery following acute admission, it was unclear if a diagnostic or therapeutic perforation had occurred. A diagnostic perforation was significantly associated with the need for surgery compared with a therapeutic perforation (p=0.002). (RR:1.81, 95% CI 1.34-2.43).

Of the 15 patients in whom the endoscopist had physically visualised the perforation at the time of perforation, none of the six perforations that were 5mm or less in size had surgery; all were therapeutic in nature. However of three greater than 5mm in size, again, all therapeutic in nature, two had surgery though this association did not reach statistical significance (p=0.083).

Admission or discharge following colonoscopy (p=0.840) and time to presentation (p=0.996) were not significantly associated with the patient having surgery. When examining the patient's initial presenting complaint, of 25 patients who did not complain of abdominal pain, 17 (68%) did not have surgery but 8 (32%) did. Of 85 patients admitted to hospital complaining of abdominal pain, 52 (61.2%) had surgery and 33 (38.8%) did not. The presence of abdominal pain was therefore significantly associated with the patient having surgery (p=0.012) (RR:0.52, 95% CI 0.29 – 0.95).

On initial observations following admission, there was no association between

a patient being pyrexial with a temperature of $\geq 38.0°C$ and having surgery (p=1.000). Fourteen of 62 (22.6%) patients who had surgery had a tachycardia at initial presentation. In 15 of 62 (24.2%) of those patients who had surgery the initial pulse was unknown and in 33 (53.2%) the pulse rate was normal (60-100 bpm). Of the 51 patients who did not have surgery, in 19 (37.3%) the pulse rate was unknown, in 3 (5.9%) patients the patient was tachycardic (pulse > 100bpm) and in 29 (56.9%) the initial pulse rate was normal (60-100 bpm). The presence of a tachycardia was significantly associated with a patient having surgery (p=0.049) (RR:0.65 95% CI 0.47-0.89). All 9 patients with a respiratory rate of > 20 breaths per minute had surgery. 32 of 62 (51.6%) patients who had surgery had a respiratory rate of less than or equal to 20 breaths per minute and in 21 of 62 (33.9%) of patients who had surgery the respiratory rate was unknown. A respiratory rate of greater than 20 breaths per minute was also significantly associated with the patient having surgery (p=0.009) (RR:0.53, 95% CI 0.42-0.68).

The operations in these 62 patients resulted in stomas being formed in 30 patients. Therefore, 48.3% of patients having surgery left hospital with a stoma, 26.1% of all perforations admitted.

Chart 6: Bar chart of number of stomas by colorectal location:
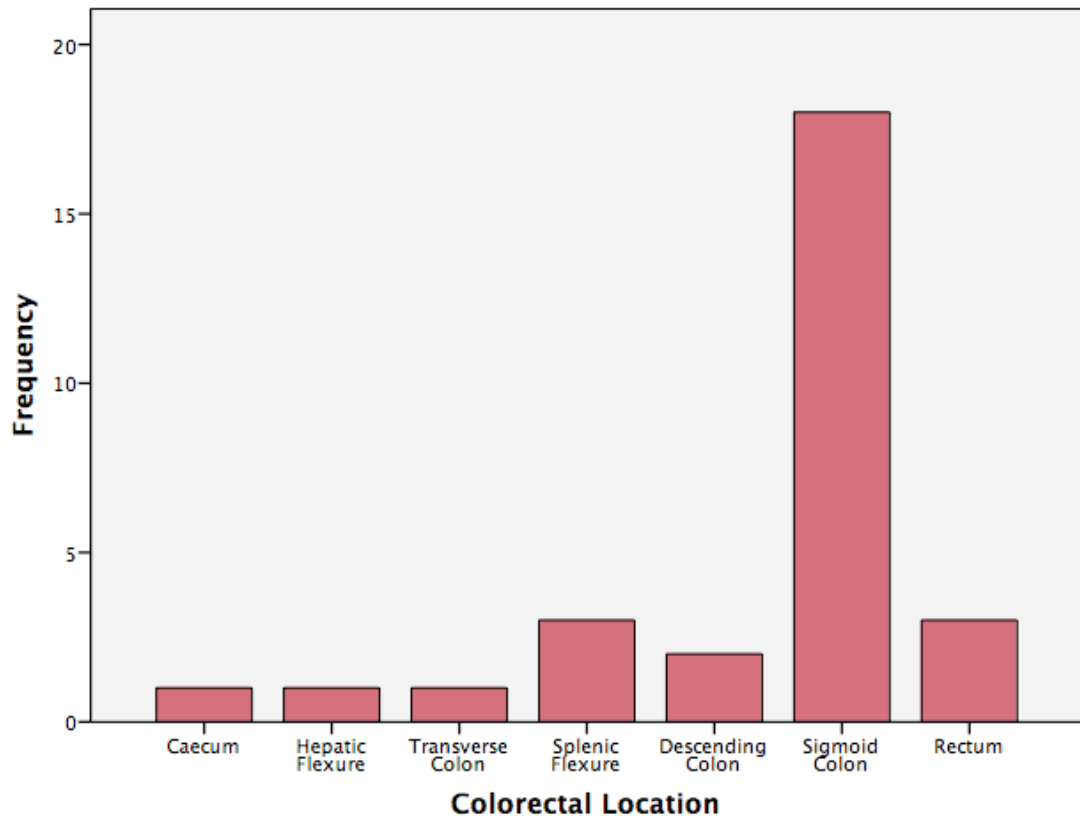
Of 30 patients who left hospital with a stoma, 23 (76.7%) were male patients. The sigmoid colon was the commonest colorectal location for a stoma to be formed (n=18). Male sex (p=0.018) (RR:2.13, 95% CI 1.08 – 4.17) and a colorectal location in the sigmoid colon when compared with all other colorectal locations (p=0.001) (RR:2.49, 95% CI 1.46 – 4.25) were significantly associated with stoma formation.

Post perforation morbidity was defined as any patient who developed a post operative complication or new diagnosis during their in patient admission. Only those who had surgery developed post perforation morbidity. Twenty-two patients developed a complication or new diagnosis post perforation. The post perforation morbidity rate was 19.1% per total number of perforations admitted to hospital and 18.8% per number of perforations overall. The post operative complications that contributed to this figure were renal failure (n=1), respiratory failure (n=3), wound dehiscence (n=2), wound infection (n=6), pelvic collection (n=1), ileus (n=6), mucus plugging (n=1), reduced respiratory rate (n=1), hospital acquired pneumonia (n=2), prolonged multifactorial ITU Stay (n=1), peritoneal collection (n=1), small bowel ischaemia (n=1), pneumothorax (n=1). One patient had both wound dehiscence and renal failure. One patient had both a wound infection and pelvic collection and one patient mucus plugging, a pneumothorax and small bowel ischaemia. Diagnostic Perforations (P=0.012) (RR: 2.84, 95% CI 1.41-5.68) and Surgery (p<0.001) (RR: 37.14, 95% CI 2.31-597.70) were significantly associated with post perforation morbidity. The surgery commencing in normal working hours (08:00-17:00)(p=0.681), the surgeon specialty (p=1.000) and surgeon grade (p=0.734) were not significantly

associated with post perforation morbidity. Of the 40 patients who did not develop post perforation morbidity following surgery, the majority, 23 (57.5%) did not have a tachycardia at initial presentation. Eight (20%) did, with the pulse rate being unknown in 9 (22.5%) of these 40 patients. In the 23 patients who had surgery and developed post perforation morbidity, 11 (47.8%) did not have a tachycardia at presentation and 5 (21.7%) did with the pulse rate being unclear in seven (30.4%). The presence of a tachycardia was not significantly associated with post perforation morbidity in those patients having surgery (p=0.739).

Twenty-eight patients (24.3%) were admitted to the Intensive Care Unit or High Dependency Unit. In all of these cases the patient had just had surgery. Number of nights on ITU/HDU ranged from 1 – 21 nights, with a median of 3 nights stay on ITU. In all 115 patients admitted to hospital, the length of hospital stay ranged from 0 – 40 days in hospital with a median stay of 6 days.

One patient died having presented with abdominal pain following a diagnostic colonoscopy showing diverticular disease in the sigmoid colon. The patient was found to have a sigmoid perforation, had a Hartmann's procedure and was admitted to ITU. This patient subsequently developed complications post operatively including mucus plugging, a pneumothorax and small bowel ischaemia. The patient died 6 days following admission.

4.3.2.3 Comparison of patients with colonoscopic perforation in whom a response to the online questionnaire was and was not received.

To ensure that the 117 colonoscopic perforations, for whom I received a response to the online questionnaire, broadly represented the total number of 147 perforations, five variables were compared between the response (n=117) and the non response group (n=30). There were no significant differences between these groups in whether polyps were resected (p=0.560), the colorectal location of perforation (p=0.626), if a diagnostic or therapeutic perforation occurred (p=0.654), if the patient had surgery (p=0.754) and if the patient was admitted to the Intensive Care Unit (p=0.082). This reassured me that the data received in the response group was not skewed in any way.

4.4 Discussion

The overall perforation rate of 0.06% reported in this study is reassuring when compared with other rates that were described in chapter 2.4.2 of this thesis. This study reports a lower perforation rate than series prior to 1990 reporting rates of 0.12% - 0.48%[42][43]. This study is one of the largest more recent series; three similarly sized series published since 2008 report perforation rates of 0.04 – 0.08% suggesting that the figure in this work is in line with current global data[2][48][49]. The majority of perforations in my study occurred as a direct result of therapy. These results are in contrast to the studies of Avgerinos et al. and Korman et al., both large studies of over 100,000 colonoscopies, that reported diagnostic perforations to occur in greater number[46][47]. Similarly Iqbal et al. reported 56% of perforations being form blunt injuries and not form therapy[48]. Although Arora et al. reported fewer diagnostic perforations (42%), this is still over half the 18.8% diagnostic perforations reported in this chapter[2]. The fewer

number of diagnostic perforations may simply reflect the fact that the majority of procedures in the BCSP are therapeutic in nature but also suggests that the quality of colonoscopy performed in the programme is high. The overall therapeutic perforation rate in this study was 0.03% and diagnostic perforation rate was 0.008%. The lower number of diagnostic perforations is reassuring especially when considering that in this study it is the diagnostic perforations that are significantly associated with the need for surgery and post perforation morbidity.

The sigmoid colon (n=40) and caecum (n=22) were the commonest colorectal locations of perforation. Twelve (30%) of perforations in the sigmoid colon were diagnostic, with 28 (70%) being associated with polypectomy. Similarly, in the caecum 6 (27.3%) of the perforations were diagnostic with 16 (72.7%) being therapeutic in nature. The majority of perforations occurring in these two colorectal locations is consistent with the only other study of those reviewed, reporting outcomes following a larger (165) number of perforations. Iqbal et al. reported 53% of perforations occurring in the sigmoid colon followed by 24% in the caecum[48]. Data in this chapter reinforces our knowledge of the mechanisms associated with perforation. In the BCSP, the majority of therapy occurs in the sigmoid colon, as this is where the majority of polyps are found. Similarly, when considering therapeutic polypectomy, it is the caecum that is significantly associated with therapeutic perforation as reported by Rutter et al.[39]. One hypothesis for this is the thinness of the caecal wall when compared with other colorectal locations. In this study I have been able to break down colorectal location by diagnostic and therapeutic perforation. Again, the majority of

diagnostic perforations occurred in the sigmoid colon (n=12), 30% of all perforations in the sigmoid colon, followed by the caecum (n=6), 27.3% of all perforations in the caecum, which is consistent with our knowledge of the mechanisms of diagnostic perforation described in chapter 2.4.4. Indeed when comparing the number of diagnostic perforations in the sigmoid colon where diverticular disease was also present to the number of endoscopic procedures overall where diverticular disease was found, this data suggests that diverticular disease may contribute to some diagnostic perforations. This may be due to the intubation and perforation of a diverticulum itself or from mechanical forces from the tip or shaft of the scope against a fixed and/or acutely angled sigmoid colon where there is circular muscle hypertrophy secondary to diverticular disease. In one of the diagnostic perforations in the rectum the perforation may have been due to the force of retroverting the colonoscope tearing the rectal wall.

Within the subgroup of diagnostic perforations in this study, four were in asymptomatic patients and were detected radiologically on staging CT scans for colorectal cancer. It is perhaps more likely though that these perforations were due to the invasive nature of the cancer and not any of the biopsies that took place. In two of these patients the TNM staging was at least T4 (T4N1M0 and T4N2M0), which would be consistent with these cancers penetrating the serosa, and causing perforation, however, one was T3N0M0. We should also be aware that it is likely that these perforations will only ever be seen associated with colorectal cancer, as it would only be these patients that have a staging CT scan in an otherwise asymptomatic patient.

The number of perforations physically visualised by the endoscopist (12.8%) in this study is less than that described by other series which range from 23-37.5%[62] [64]. The median size of perforation from my data was 5.5mm. It may be that the fewer number of perforations visualised in this study were due to a smaller perforation size although size isn't specifically mentioned in the above papers. The smaller number of diagnostic perforations in this study may also go some way to explaining this as diagnostic perforations are more likely to be larger as reported by Iqbal et al. and Dafnis et al. [147] [38]. The work in this chapter is in line with other studies that the majority of perforations present within the first 24 hours, and if not in the first 24 hours then at least within 48 hours.

Where the perforation is physically visualised, my data suggests that the use of an endoclip to close the perforation may improve patient outcomes. 83.3% of those perforations in whom the perforation was physically visualised by the endoscopist and had endoclips applied were successfully mananged endoscopically and conservatively without the need for surgery, although this association didn't reach statistical significance. This figure is entirely consistent with the 68-93% of patients reported as being successfully managed in this way by other studies[75] [76] [77] [78].

My work has highlighted how those patients who were managed conservatively, with or without the use of endoclips, didn't develop post perforation morbidity or require intensive care admission. This, of course, reflects the fact that perforations who have surgery are likely to be more unwell at presentation, due

to, for example, a greater degree of faecal peritonitis and haemodynamic instability. These patients, are, therefore, perhaps more likely to have post operative complications. However, it also follows that, where possible, conservative management should be attempted. My data has showed that those patients who have abdominal pain, with a respiratory rate of more than 20 breaths per minute and a pulse rate of greater than 100 beats per minute at initial presentation were more likely to have surgery. This gives a guide as to when medical management may be successful, especially if an endoclip has been used to close the perforation. My data suggests that following perforation a patient without abdominal pain, and/or an initial pulse rate of 60 – 100 beats per minute and/or a respiratory rate of 20 breaths per minute or less may be indicators for medical management. Indeed future prospective data specifically studying the presence of abdominal pain, the respiratory rate and the pulse rate following colonoscopic perforation may add weight to these findings.

Uniquely, I have been able to report the initial radiological investigation used to make the diagnosis of perforation. This confirms how the clinician should not be reassured by a normal plain erect chest x-ray (CXR) or abdominal x-ray (AXR). Of 29 patients with a normal CXR, 21 went on to have a CT abdomen of which most (90.5%) showed evidence of perforation. Similarly, of the 39 patients who had an AXR, 28 showed no perforation but in the majority of these (64.3%) there was evidence of perforation on CT. Where clinical suspicion of perforation is high the clinician will usually proceed to CT even after a normal CXR, however, this data calls into question the relevance of doing an AXR at all.

Over half of the admissions to hospital in this study had surgery, an important fact that can be used when consenting patients prior to future BCSP colonoscopies. In addition, patient information documents can be amended to reflect the potential sequelae of perforation. An important finding of this work is that the diagnostic perforations are significantly associated with having surgery when compared with therapeutic perforations. A possible explanation lies in the larger size of diagnostic perforations, as previously reported, which result in a greater degree of faecal contamination, peritonitis and haemodynamic instability.

Unusually for other studies reporting outcomes following perforation, in this chapter I've been able to report whether surgery was commenced during normal working hours, the grade of surgeon operating and the specialty of surgeon operating (colorectal or non-colorectal surgeon). Operations appear to be performed as the patient presents, 25.8% being performed Monday to Friday from 08:00 to 17:00 hours. When considering this 'normal working hours' period being 45 hours of a total number of hours in the week of 168 hours, the 25.8% figure remains consistent with operations being performed around the clock. Reassuringly consultant surgeons and colorectal surgeons performed the greatest number of operations although none of these factors statistically had any impact on the development of post perforation morbidity. Of note was that the seven laparoscopies were only performed by consultant surgeons, the majority of whom (71.4%) were consultant colorectal surgeons.

Again, when considering the future consent process for patients attending for colonoscopy in the BCSP, data from this study has showed that if surgery occurs post perforation, patients have an approximately 50% chance of leaving hospital with a stoma. This equates to over a quarter of patients admitted to hospital overall. A patient is more likely to be left with a stoma following a diagnostic perforation but it was male sex and the sigmoid colon that were significantly associated with stoma formation. A possible explanation for this is the majority of perforations in the sigmoid colon having a Hartmann's procedure, particularly in the case of the diagnostic perforations where there may be greater faecal contamination. With regard to male sex, 76.7% of the stomas formed were in males. A possible explanation for this may be a subgroup of male patients who have longer sigmoid colons that are more likely to loop during intubation with consequent diagnostic perforation during intubation or loop resolution. In addition eight of the 23 (34.8%) male patients who left hospital with a stoma also had diverticular disease at the colorectal location of perforation of which seven were in the sigmoid colon. In all 30 patients who left hospital with a stoma 10 (33.3%) also had diverticular disease at the colorectal location of the perforation compared with only 1 of 31 (3.2%) who had diverticular disease at the colorectal location of the perforation among those who had surgery without stoma formation.

An important outcome to consider from this study is that only those patients who had surgery developed post perforation morbidity or were admitted to the intensive care unit (ICU). For reasons explained earlier, this may reflect the fact that those patients who had surgery were likely to have been more unstable at

presentation and therefore more likely to develop post perforation morbidity and require intensive care admission. However, it is also reassuring for the BCSP that those patients who were managed without having surgery recovered well. A post perforation morbidity rate of 19.1% in patients admitted acutely compares favourably with other series both when considering morbidity following all perforations and when considering morbidity post surgery only. Distinctively, it is the study in this chapter that has reported both diagnostic perforations and surgery as being significantly associated with developing post perforation morbidity. For the reasons reported above, diagnostic perforations appear to carry the greatest risk of the patient becoming unstable and therefore potentially increasing the chances of them developing complications following surgery. Although any death associated with a screening investigation is disappointing for the screening programme, a post perforation mortality rate of 0.87% does compare favourably with other series that have reported mortality both overall post perforation and post perforation surgery.

4.5 Conclusions

When considering my intentions of writing this thesis, the study in this chapter has reassured us that colonoscopic perforations in the English NHSBCSP occur on an infrequent basis at similar rates to what occurs when colonoscopy is performed on the same scale elsewhere in the world.

I have also been able to explore the impact of the perforation on the patient. As a direct result of this study we now know that 98.2% of patients with perforation

were admitted to hospital and 44.1% of admissions were admitted within 48 hours of the colonoscopy. Data from those admissions shows that 53.9% had surgery, 26.1% left hospital with a stoma, 19.1% developed a complication or new diagnosis while in hospital and 24.3% were admitted to the intensive care unit. Those that developed a complication or new diagnosis while in hospital and/or were admitted to the intensive care unit did so only after having surgery. Unfortunately, one patient died following admission for a perforation. Collectively, all these facts give us a more complete understanding of the impact a colonoscopic perforation has on the patients involved. The data obtained in this study also means this can be presented to patients as part of the consent process for future bowel cancer screening colonoscopies and may directly impact on how patients perceive the benefit and risk of having such a procedure. Ultimately, it is the patient's decision alone as to whether to proceed with colonoscopic examination but they now are able to make this decision on a more informed basis.

We are now also more aware of type of perforation that is likely to result in surgery and therefore may lead stoma formation, post perforation morbidity and intensive care admission. Diagnostic perforations are significantly more likely to lead to this chain of events. Similarly, stoma formation is significantly more likely to occur in the sigmoid colon than any other colorectal location and in male, not female, patients.

A third intention of this thesis specifically relating to this study was how to improve the assessment and management of colonoscopic perforation so that

the patients involved have the best possible outcome. We now know that those patients that did not have surgery did not develop post perforation morbidity and were not admitted to intensive care . This may simply reflect patients not needing surgery being more stable at presentation. However, it is important to emphasize these patients have good outcomes. This chapter has showed potential indicators for where non surgical management may be used in the future. The use of endoclips results, in most cases, in the patient avoiding surgery and these should be considered and used if the endoscopist physically visualises the perforation. This is particularly in the context of a perforation of 5mm or less in size. Similarly, if a patient does not have abdominal pain, has a normal pulse rate of 60 – 100 beats per minute and a respiratory rate of 20 breaths per minute or less following confirmation of a perforation, these are all indicators for managing them non surgically Although the conservative management of perforation is likely to produce a more desirable outcome for patient and clinician, these decisions, as always must be taken by the assessing clinician in the context of the clinical situation that is in front of them.

Chapter 5

Colonoscopists' narratives of a colonoscopy associated with a colorectal perforation

5.1 Aims

1. To identify 'human' and 'environmental' factors that may be associated with a colonoscopic perforation.

2. To explore how colonoscopists react to performing a colonoscopy associated with a colorectal perforation.

5.2 Methods

5.2.1 The qualitative research approach

Two of my intentions in writing this thesis related to the colonoscopist who performs the colonoscopy associated with an adverse event. I planned to explore the impact of the adverse event on the colonoscopist and provide a reference point of such experiences so that other colonoscopists could refer to them should they encounter such an event in the future. As previously stated in chapter 3, I also intended to identify risk factors for colonoscopic adverse events. My examination of these adverse events comprised not only a review of relevant literature, but also my own experience of witnessing the involvement of others with colonoscopic adverse events and conversations with colleagues about such

cases. It was apparent from this examination that not all these risk factors could be determined from quantitative data. Some of these factors would not be documented on endoscopy reports, medical notes or entered into databases. In order to achieve these aims I would need to speak directly to those colonoscopists who had performed colonoscopies associated with adverse events. I therefore designed this qualitative research study surrounding colonoscopists' experience of colonoscopic perforation.

Qualitative research stems from a number of disciplines including philosophy, social psychology, sociology and anthropology. It seeks to determine the perspective of an individual or group. The advantages of qualitative research include that it permits a personal involvement with participants in their natural setting allowing an in depth engagement. This can result in a rich detailed understanding of an issue. Qualitative research can generate new theory, deepen knowledge and illuminate the findings of quantitative research[148].

In determining the impact of a colonoscopic perforation on a colonoscopist and evaluating how the colonoscopist subsequently reacts, I identified an issue that required further exploration. This study provided colonoscopists the opportunity to share their experiences[148].

The study also used qualitative research to identify factors that could not easily be measured. Such factors included the identification of risk factors for perforation other than those that had been established quantitatively. For the purposes of this study these factors were termed 'human' and 'environmental'

factors[148]. 'Human' factors relate to the thoughts, feelings and emotions of the colonoscopist at the time of the colonoscopy associated with the perforation. 'Environmental' factors relate to the setting of the colonoscopy and the situation the colonoscopist was in.

There are six main qualitative research methodologies: case study, phenomenology, grounded theory, ethnography, narrative research and realist evaluation. Case study is 'an empirical enquiry that investigates a contemporary phenomenon within its real life context, especially when the boundaries between phenomenon and context are not clearly evident' and it 'relies on multiple sources of evidence'[149]. Phenomenology describes the lived experience of a phenomenon and can be described as an 'object' of human experience. Grounded theory aims to move beyond description to generate a theory; an analytical schema of a social process or interaction. Ethnography is the study of a culture or subculture and is concerned with the insiders' view of their world. Narrative research is concerned with how a narrative is told, why it is told in a particular way and the forms of telling rather than their content. Realist Evaluation asks 'What works for whom, in what circumstances and in what respects, and how?'[150]

5.2.2 Phenomenology

Of the six qualitative research methodologies outlined above, I used phenomenology in this study. Phenomenology aims to develop a description of shared experiences, which includes both perceptions about what was

experienced as well as how it was experienced. Phenomenology is based on the work of the mathematician, Edmund Husserl (1859-1938) and was later developed by Heidegger and Satre. There are four basic tenets of phenomenology.

1. The pursuit of wisdom; to advance our understanding of the meaning of being human.

2. A philosophy without presuppositions; bracketing or putting aside one's own beliefs and suppositions about the phenomena.

3. The intentionality of consciousness, relates to the individual understanding of reality by virtue of consciousness.

4. Refusal of the subject-object dichotomy; the reality of an object is perceived within the meaning of an individual's experience.

There are broadly three types of phenomenology: hermeneutic phenomenology, transcendental phenomenology and interpretative phenomenological analysis (IPA). Hermeneutic phenomenology usually refers to the interpretation of the texts of life. Transcendental phenomenology is that in which everything is perceived freshly, as if for the first time. IPA combines these two types of phenomenology. Using IPA the researcher begins as a naive observer and moves through a process of sense making towards a more questioning and analytic framework.

I used phenomenology for this study because I aimed to explore a lived experience, the reaction of a colonoscopist, to a phenomenon, a colonoscopic

perforation. I also intended to explore the common meaning of a phenomenon, the colonoscopic perforation, among a group of individuals, the colonoscopists, all of whom had experienced that phenomenon[148].

5.2.1 Study Protocol and Supporting Documents

Following the identification of an appropriate qualitative research methodology and establishing the aims of the study, I drafted and finalised a research study protocol. The protocol had several specific sections. It began with the details of the researchers, which were myself, and the supervisors of this thesis. The background to the study included the literature reviewed in chapter 2.7 of this thesis surrounding adverse events and the colonoscopist. A lay summary was provided along with the study hypothesis, its aims and a description of the methodology. How potential participants would be recruited, including the inclusion and exclusion criteria, was also described. The research study protocol went on to give details of how consent would be obtained, how the confidentiality of participants would be maintained and how data generated from the study would be managed. Ethical considerations and where ethical approval was sought was also described. The protocol finished with details of where a peer review was sought and details of how results from the study would be disseminated.

After completing the study protocol, I devised and wrote an interview guide. The guide comprised a series of questions grouped in specific sections that I felt gave me the basis from which I would be able to achieve the aims of the study. I

devised the questions in the guide based on several distinct processes. Initially, they came from my own thoughts and feelings of what I considered could be potential 'human' and 'environmental' factors surrounding colonoscopic perforation and how I might react to a colonoscopic perforation should it happen in my own practise. Secondly, they came from personal observations and discussions with colleagues surrounding previous perforation cases. Thirdly, the literature reviewed in chapter 2.7 of this thesis provided a basis for exploring how a colonoscopist may react to a perforation. Questions in the interview guide were grouped under the sections: participant demographics, colonoscopy experience, event details, immediate reaction, professional and personal reaction and subsequent practice. The interview guide can be found in chapter 10 of this thesis.

A participant information sheet (PIS) that would be used for distribution to potential participants in the study was also then written. This document was in a question and answer format, the questions being ones that I felt gave potential participants a broad understanding of why I designed this research study and its aims. The design and content of the PIS was based on similar documents used previously by qualitative researchers within Durham University for interview-based studies.

In addition to the PIS, I wrote a consent form for participants to sign confirming and documenting their desire to take part in the study. The consent form was in the format of a series of statements relating to the study, with a yes/no tick box next to each statement and a space for the participant to sign the form.

5.2.2 Peer Review

When the study protocol and the supporting documents described had been completed, I requested a peer review of the study be performed. The comments made by the peer reviewer, focusing mainly on improving the general clarity of study protocol and the rationale for the proposed research were then incorporated into a final version of the study protocol prior to its submission for ethical approval.

5.2.3 Ethics

Ethical approval was sought and granted from the Durham University, School of Medicine, Pharmacy & Health Ethics Sub-Committee. The Ethics Sub-Committee reviewed the study protocol in addition to other supporting documents relating to the study.

5.2.4 Participant Recruitment

Once I had gained ethical approval for the study to start, I wrote an invitation letter that briefly outlined the research study, why I had designed it, and its aims. I attached this letter to an email and emailed it, via NHS mail, to all the Bowel Cancer Screening Programme colonoscopists based at the five Bowel Cancer Screening Centres in the North East of England and North Cumbria. The invitation letter was also then emailed to all consultant gastroenterologists

employed in NHS trusts in the Northern Deanery (now Health Education North East) of England excluding those BCSP colonoscopists already emailed. The letter can be found in the Chapter 10 of this thesis. I received eleven replies to the email from participants indicating their willingness to take part, including one consultant surgeon, three nurse endoscopists and seven consultant gastroenterologists. Those colonoscopists who replied to the email and were willing to be participants in the study were emailed a participant information sheet and a study consent form. A date and time for the interview to take place was arranged via email correspondence directly with the participant or with their secretary. The consent form was signed by the participant and then either emailed or posted back to me prior to commencing the interview.

5.2.5 Interviews

Eleven interviews were performed during October and November of 2014, each at the base hospital of the participant. The interviews took place in rooms with only the participant and myself present. Only one specific perforation case was discussed during each interview. Where the colonoscopist had two or more colonoscopic perforation cases during their practice, the colonoscopist chose which perforation case they wanted to discuss prior to the interview. The interviews were conducted anonymously and were voice recorded.

Each interview was semi structured using the interview guide for reference. The semi-structured nature of the interviews allowed me to explore, in depth, the perforation case and allowed participants to introduce issues that were

important to them. They also gave me the flexibility to pursue issues when they appeared to be important to the participant or merit more exploration.

5.2.6 Data Analysis

When all eleven interviews had been completed, I used the process of 'framework' to analyse the data produced[151]. I personally transcribed the interview recordings on to eleven separate Microsoft word documents. Each transcription was given a code from C1 to C11 representing the interviews in the order in which they took place from colonoscopist number 1 (C1) to colonoscopist number 11 (C11). Transcription of the interviews allowed me to begin the process of 'framework' by 'familiarising' myself with the data. While transcribing and 'familiarising' myself with the data, I began to consciously develop a 'thematic framework'. The 'thematic framework' was developed by the process of 'abstraction and conceptualisation'[151].

When all the interviews were transcribed I identified the 'key issues, concepts and themes'. These were identified by drawing upon 'priori issues, emergent issues and analytical themes arising from the recurrence or patterning of the particular experiences' of the colonoscopists. I used this process to identify different 'key issues, concepts and themes' that arose from the range of colonoscopists that were interviewed[151].

I continued the process of 'framework' by 'indexing'. This was where the 'thematic framework' was applied to data in its textual form. I recorded the index

references on the margins of each transcript by a numerical system that links back to the index. After 'indexing', I 'charted' the data. Data was lifted from its original context and rearranged according to the appropriate thematic reference. This 'chart' was arranged with headings drawn from the thematic framework or the 'priori' issues. The final part of the data analysis involved 'mapping and interpretation'. Once all the data has been charted, the key characteristics of the data were mapped and interpreted as a whole in order to answer the study aims[151].

5.3 Results

Data obtained from the interviews were divided into two main sections in order to answer the aims of this study. Firstly, this related to the reaction of the colonoscopist to the perforation and, secondly, the 'human' and 'environmental' factors associated with perforation. Within the first of these, a difference in the reactions between the three types of professionals that were interviewed emerged and I have therefore described this separately in section 5.3.2 of this chapter.

The interviews among the eleven colonoscopists related to perforation cases from different periods of time prior to the interview. These time periods ranged from four months to approximately 20 years prior to the interview. Despite the differences in time periods, in all eleven cases the participant was clearly able to recall the perforation case and their feelings surrounding it. Evidence of how the

clarity of memory remained with the participant can be found in the following extracts:

'Yes, I can very much remember what happened' (C1)

'I still think about it, I still remember the case quite well, and I would think that almost everyone you speak to, who has damaged somebody that way will remember it quite well' (C9)

'When you've had something like that happen it actually sticks with you for a lot longer than that. Even now, when I'm colonoscoping, I'm always aware; things like that stick with you.' (C10)

The clarity of memory of the case along with the quotes listed above suggests the perforation case had a deep psychological impact on the colonoscopist. The stages of the reaction are described in the following section.

5.3.1 The Colonoscopists' Reaction

The thematic framework produced from the data relating to the colonoscopists reaction to the perforation comprised four distinct themes and stages to their reaction. These are based on the stages of reaction identified by Scott et al., Luu et al. and Ullstrom et al. in their studies[141],[145],[144].

'*The Realisation'* comprises the period in the minutes and hours after the colonoscopist has realised a perforation occurred and involves a range of strong and powerful emotions.

'*Into the Mirror'* then transpired over the following days when the colonoscopist experienced feelings of personal responsibility, self blame and vulnerability.

'*Acceptance and Refocus'* followed in the subsequent days and weeks where the colonoscopist, with support, recommended performing colonoscopy, accepted that the perforation occurred and was able to refocus on their personal and professional life.

Finally, there is a period of *'Reflection and Learning'*; the colonoscopists looks back on the case, learns from it and applies that to the their future practice.

5.3.1.1 *'The Realisation'*

A range of strong and powerful feeling and emotions were evident during the *'The Realisation'* comprising in the participants own words disbelief, shock, sickness, emptiness, horror, terror, fear and annoyance.

'Disbelief initially, Oh My God, that can't be what I think it is' (C3)

'I think complete dismay…I couldn't believe it. Oh…is it really? …I think dismayed'

(C4)

'it was quite shocking….shocked, really shocked' (C8)

'I felt sick inside knowing I had done that' (C1)

'The thought that I had done this was just awful, it really, I wouldn't wish it on

anybody to feel like that' (C1)

'Sinking, gut wrenching feeling' (C8)

'I felt empty, because I knew it had perforated' (C2)

'I think I felt a little bit hollow inside' (C2)

'It was pretty horrific and obviously you feel absolutely awful' (C3)

'Horror, immediate terror, extreme fear' (C11)

'I was just in tears, I took myself away and had a bit of a weep' (C11)

'I was distraught for the rest of the day. I was wiped out with it, with the adrenaline

and everything. I was in tears all day really' (C11)

'Annoyed' (C7)

'Little bit annoyed with myself' (C9)

5.3.1.2 *'Into the Mirror'*

After *'The Realisation'*, in the days following the perforation, the colonoscopist may have started to look *'Into the Mirror'* and take personal ownership of the perforation case, feel personally responsible for it and blame him or herself.

'You feel very responsible for it, as though it's your perforation' (C1)

'I suppose you blame yourself a little bit when you do that, I was asking why did I

do that?' (C4)

'It was almost certainly me that caused his demise' (C8)

'It just sinks in even more that you've caused harm to somebody' (C1)

'It made me feel that I was to blame' (C11)

'I really felt very bad and guilty that I'd inflicted that on the patient' (C1)

Within this period of looking *'Into the Mirror'* the colonoscopist may be embarrassed, question himself or herself and feel vulnerable about their own position. This was highlighted in comments such as those below:

'There is a hesitancy in seeking the support of your colleagues, because you think,

they might think you're not good enough.' (C2)

'But you probably feel a bit embarrassed, I suppose, and probably a bit…you don't

want to share things with people because it doesn't feel good' (C3)

'Especially when you're starting out, particularly when you're a consultant,

consultants tend to have that 'Oh my god, I've got to be able to do this and do it on

my own' (C7)

'I hadn't had that sort of severity of complication, I was only 2 years into my

consultant post so yeah you feel pretty vulnerable' (C8)

'I'm less than a year into a consultant post and I've managed to perforate a colon

inside' (C9)

'I hadn't built up enough base of safely done difficult things to feel….someone might

come down on me like a tonne of bricks' (C9)

Two of the colonoscopists interviewed specifically described emotion in the days following the perforation case relating to decisions that were made regarding the patient's subsequent care and management. In both cases the patient died as a consequence of complications secondary to the perforation. Both colonoscopists were gastroenterologists and the patients' care had subsequently been taken over by surgeons. Neither colonoscopist had been involved in decisions relating to the patients' management and subsequent care.

'Angry. I felt a bit let down. I also felt a little bit disappointed that I wasn't involved in the decision making….I was part of the patient's deterioration, the procedure was part of the patient's deterioration. I felt the least they could have done was involve me in the decision-making. I felt a bit let down by that.' (C4)

'I was upset because I wasn't involved in the decision making' (C8)

5.3.1.3 *'Acceptance and Refocus'*

In the days and weeks after this period of looking *'Into the Mirror'*, the colonoscopist started to re-commence colonoscopy practice, accept that the perforation occurred and was able to refocus on their personal and professional life. I have named this period of their reaction *'Acceptance and Refocus'.* With regards to performing colonoscopy again, colonoscopists described a heightened anxiety, nervousness and even terror when starting their next colonoscopy after the perforation case:

'I was very nervous initially about doing colonoscopy again, I kind of thought to myself, did I really want to be doing colonoscopy, because this is what can happen' (C1)

'I was very very nervous especially the first time I took a polyp off' (C1)

'If there had been another list…to do that afternoon, I don't think I would have been able to do it. Because I don't think I would have picked up another colonoscope as if nothing had happened. So, I don't think I would have been able to do another list straight away' (C2)

'The next time you do anything you're slightly…. you're slightly weary and apprehensive' (C7)

'Terrified. Largely because I couldn't rationalise to myself doing anything significantly different' (C9)

'Certainly for a while afterwards you feel a little apprehensive, certainly a little more attuned to what you're doing' (C10)

However, these feeling were balanced by the determination of some of the colonoscopists to persevere and not stop doing colonoscopy:

'but I don't recall thinking of hanging my scope up and I don't recall thinking of necessarily stopping EMR' (C8)

'but I've never wanted to give up' (C11)

After re-commencing practice, the colonoscopists accepted that the perforation case had occurred and moved on with their personal and professional lives. Part

of this process was aided by the support of other colleagues; the majority of the participants recalled how the support of colleagues played a large part in this:

'I got a lot of support from people who I didn't think I would at the time' (C1)

'I think I got enough support from my fellow endoscopist colleagues' (C1)

'I got a lot of support from other endoscopists…it helped me to get over it and get on' (C1)

'the organisation was extremely supportive, we went through a Root Cause Analysis, and I did feel very supported by that…I'm incredibly grateful to my organisation because it was very open, it wasn't a blame thing' (C8)

'I actually do find it supportive to actually go back over a case and analyse what went wrong' (C6)

The phase of acceptance revolved around the individual's realisation that perforation is inevitable when doing colonoscopy:

'We know perforations happen and it's happened' (C3)

'If you don't have enough complications, you're probably not doing enough work' (C7)

'That's the cost you pay for doing business to a certain extent. You can't make everybody better. You just have to try and organise the net gain in the process' (C9)

'If you do enough colonoscopy, you will perforate somebody' (C9)

'You have to accommodate to it because you're going to kill somebody' (C9)

'Complications happen, one is always careful, but complications happen and will continue to happen' (C2)

After starting to do colonoscopy again and going through the acceptance phase, some of the colonoscopists described how they were able to 'refocus' in both their personal and professional lives:

'In my own mind I just came to terms with it and got on with it'

'That terror has eased off' (C11)

'I did take a little while, but I think once I started to get back into doing colonoscopy again and got my first polypectomy out the way again, I was fine' (C1)

5.3.1.4 *'Reflection and Learning'*

The final stage in the colonoscopists' reaction to a colonoscopic perforation came in the months and even years following the event. The colonoscopist had the opportunity to learn from the case, reflect on what they could have differently or better and then apply that to their future practice going forward. In some cases that reflection and learning may still be being applied to the present day. Most colonoscopists expressed how much they had learnt from the case and how much it had aided their professional development.

'Whenever you have a complication, you try to re-evaluate your practice don't you?' (C6)

'The important thing is to go back, reflect on it, think things through and there's always one little issue, one thing where you think, ah, I could have done that a bit better' (C7)

'It was a tremendous learning thing, and...in retrospect...' (C8)

This reflection and learning was then taken forward into the colonoscopists' subsequent practice. Most colonoscopists expressed how the case had made them more cautious during the procedure:

'I'm a bit more cautious with the diathermy but I think mainly I'm just more cautious in my positioning' (C6)

'definitely now I would have approached it with much more caution' (C8)

'I'm maybe more aware of quality of tissue. I'm maybe more likely to stop' (C9)

'I think I treated colonoscopy far more seriously than I had perhaps before' (C10)

The caecum was identified as a high risk colorectal location for perforations and one case had changed a colonoscopists practice when performing endoscopic mucosal resection polypectomy in the caecum:

'I'm incredibly careful in the caecum these days' (C8)

'Now I'm much more aware of the risk of caecal perforations' (C8)

'now I would have put loads more clips on, and now I, my practice is to pretty much clip everything I take off in the caecum. I leave a long line of clips' (C8)

When specifically referring to patients' symptoms and communication with patients following a colonoscopy, changes to management strategies as a result of the perforation case were also evident:

'I think, now I would be much more careful about those signs' (C8)

'What I do now for all EMRs, I give my telephone number, my mobile telephone number and I give it to them and I say, look, I want you to call me if there's any problem' (C8)

5.3.2 The differences in colonoscopist reaction between specialties and professions

A theme that emerged during the course of the interviews and data analysis was the differences in reaction between the specialties and professions among the colonoscopists. There were three groups of professional interviewed; nurse endoscopist, medical gastroenterologist and surgeon.

All three of the nurse endoscopists interviewed spoke of how they felt the perforation case had a more severe impact on them than they suspected the same event would have on a medical or surgical endoscopist.

'I think, this is going to sound horrible, but I think medical people are more used to things going wrong, whereas, coming from a nursing background, I was the only nurse at the time in the trust doing colonoscopy, that was how I found it difficult. My nursing colleagues could say one thing but it didn't really mean an awful lot because I could tell they couldn't exactly tell how I was feeling' (C1)

'Nurse endoscopists particularly, I think, are prone to crises of confidence, more so than consultants who have to learn to be very confident don't they? But nurses I think are a bit more prone to it so I'd probably be quite supportive of a nurse endoscopist and just check they were ok, you know, and bolster their confidence about the good things they've done.' (C6)

'Because I have a feeling that….I do think, I'm not sure if I'm right or not, but I do think that nurses feel it more because we probably don't have the confidence that medical staff do in actually doing things. We're perhaps more used to 'alleviating discomfort', I'm not saying medical staff don't do that, don't get me wrong' (C11)

The reactions of the nurse endoscopists can be contrasted with the reaction of the surgeon who was interviewed:

'I suppose surgical endoscopists have a slightly different perspective. We're always doing procedures that quite commonly result in serious complications so from a mental point of view I guess it's less of a big deal' (C5)

'You can't be a colorectal surgeon without being able to cope that some of these patients may have bad complications. Some will even die as a result of complications. If you had great difficulty dealing with that without more support than you would get from colleagues and family, I think you would probably be in the wrong job.' (C5)

5.3.3 Human & environmental Factors associated with colonoscopic perforation

5.3.3.1 Human factors

Two distinct 'human' factors associated with perforation emerged from the analysis of data, which were fatigue and expectation.

One colonoscopist described how the perforation case had occurred when he was tired at the end of an all day endoscopy list. He felt that fatigue had contributed somewhat to the perforation:

'It was towards the end of a busy therapeutic list, a therapeutic all day list'
'I suspect it probably does contribute to a certain extent to the decision making'
'probably at the time I thought my brain's tired here' (C7)

Another colonoscopist reported how, although he was aware of the indication for the colonoscopy being an endoscopic mucosal resection of a large polyp, the procedure hadn't been what he was expecting; there was a larger number of polyps in addition requiring polypectomy than he expected which altered the procedure both in terms of timescale and workload:

'probably the significant thing that happened was that there was quite a lot of

polyps to take off. Erm….and, I think, it would be fair to say…… it was a bit of a

struggle, erm, to…….it was slightly more than I was expecting. It was more than I

was expecting.' (C8)

'I didn't want to repeat the procedure so that was a slightly distorting thing' (C8)

5.3.3.2 Environmental factors

Two distinct 'environmental' factors also emerged from the data, which were time and equipment.

One of the colonoscopists described how he felt time was the major contributing factor to the perforation:

'The list had already started late, I forget for what reason…. I was a little bit anxious about the fact that time was ticking on. So, to speed things up I… started snapping off some of these polyps and one or two were a bit bigger and I put the diathermy on and I did some hot snaring, perhaps with a little bit more haste than I would normally. Perhaps because of that not using submucosal injection for cases where I would have probably used it for cases where I would have had more time.'

(C5)

'I'm annoyed with this one because I suspect it was probably an avoidable perforation if we had done the procedure with a bit more time. Without the time pressure we probably wouldn't have had that complication.' (C5)

Another colonoscopist reported an issue with the diathermy equipment during a polypectomy associated with a perforation, which may have been a contributory factor:

'There was a problem with the diathermy equipment, it wasn't really cutting, so half way through the polypectomy we had to switch the diathermy machine over. It did cut through, and at the end I was concerned there might be a bit too much burn there.' (C6)

'At the time I was using endocut, 150 blend 2, but it wasn't cutting at all. If anything it seemed to be more coaging than cutting. We just weren't making any progress, we just weren't cutting through at all and as soon as we changed equipment we cut straight through.' (C6)

5.4 Discussion

Despite differences in timescale between when the perforation had occurred and the interview taking place, all eleven colonoscopists that participated in the study were clearly able to recall, in detail, the perforation case. They were also able to remember, precisely, the events surrounding the case and their subsequent reaction. I found no evidence that the recall of the case was influenced by the amount of time since the perforation. This suggests that such cases are deeply imbedded in the memory of a colonoscopist and the case has a deep psychological impact on them.

The reactions of all the colonoscopists could be grouped in to the four distinct stages described which followed on from each other in time. The exact timings of these stages, the emotions within each stage and the extent of the impact on the colonoscopist varied, however, depending on several factors.

'*The Realisation*' begins when the colonoscopist realises a perforation had occurred and may last minutes or hours. This most closely resembles the 'chaos and accident response' described by Scott et al., 'the kick' described by Luu et al. and the 'emotional reactions' described by Ullstrom et al. [141],[145],[144]. Scott et al. specifically describes 'chaotic and confusing scenarios of internal and external turmoil'. How the colonoscopists came to realise that a perforation had occurred varied depending on how the perforation had presented. This lead to differences in the emotions expressed during 'The *Realisation*'. Two of the colonoscopists who visualised the perforation by visualising an extra intestinal structure during the colonoscopy specifically described 'disbelief' and 'horror' whereas a colonoscopist who heard that the patient had a perforation from a colleague some days after they performed the colonoscopy described 'shock'. Similarly, the experience and profession of the colonoscopist may have influenced the reaction; a senior consultant gastroenterologist specifically described feeling 'annoyed' upon realising a perforation had occurred, another junior nurse endoscopist described being 'upset'.

The feelings expressed by the colonoscopists when looking '*Into the Mirror*' are similar to those described by Scott et al. during 'Intrusive Reflections'. I found that the feelings of vulnerability, however, fitted better with '*Into the Mirror*' as

colonoscopists were thinking about themselves. Scott at al.'s study described similar feelings of vulnerability during the fourth reaction stage of their study 'enduring the inquisition' and similar emotions were present during Ullstrom et al.'s 'professional performance and self confidence'. Where two of the colonoscopists in this study were unique during this stage was the anger and upset they felt at not being involved in decisions relating to the patient's subsequent care.

The majority of the colonoscopists felt well supported by their colleagues and/or organisation in the aftermath of the perforation and spoke of how much this had helped them, particularly during the stage of *'Acceptance and Refocus'.* The support described by colonoscopists is mirrored by the stage of 'restoring personal integrity' described by Scott et al. in their study which involved the victim 'seeking support from an individual from whom they had a trusting relationship such as a colleague, supervisor, personal friend or family member' and the stage of 'obtaining emotional first aid' where the victim sought emotional support[141]. Luu et al. also described such actions during 'the recovery' and Ullstrom et al. reported how peer support had been crucial[145],[144]. Interestingly, one junior nurse colonoscopist didn't feel well supported following the perforation case and made reference to a 'macho' environment among other endoscopists in their department. It was apparent to me that the support of colleagues is vital in helping colonoscopists through the stage of *'Acceptance and Refocus'*, especially in the case of nurse colonoscopists and junior medical colonoscopists. One colonoscopist reported how they wouldn't have been able to carry on doing the endoscopy list after they had realised that a perforation had

occurred during the colonoscopy and may have even struggled to carry on doing them later that week. This evidence leads me to conclude that following a colonoscopic perforation the support of colleagues is vital in helping the colonoscopist through the stages of reaction. I would also recommend that colleagues within an organisation should, at the very least, offer to sit down and discuss the case with the colonoscopist affected by the perforation and be prepared and willing to take over the remaining cases on their list, should *'The Realisation'* start during a colonoscopy, and even take over their lists in the days and week after the perforation case if needs be. The presence of a colleague in the endoscopy room may also help, during, for example, a subsequent polypectomy in alleviating some of the emotions that the colonoscopists described when starting to perform colonoscopy and polypectomy again.

A paradox of the stages of reaction is that even though there are numerous strong emotions felt during *'The Realisation'*, there is always the acceptance that perforation is an inevitable consequence of performing colonoscopy. However, this acceptance doesn't appear to diminish the emotion felt at any point.

The lessons learnt from the perforation case and new practices brought about as a result of the case reported by the colonoscopists during *'Reflection and Learning'* are parallel to those feelings reported during the 'thriving' stage of 'moving on' by Scott et al. and 'the recovery' by Luu et al.[141,145]. The caecum was identified qualitatively from this study as a high risk colorectal location for perforation; one of the colonoscopists described higher caution when performing therapy in the caecum and routinely using endoclips following any

endoscopic mucosal resection of polyps in the caecum as a result of the perforation case discussed. This complements the quantitative studies suggesting caecal location is a risk factor for perforation that have been described in chapter 2.5 of this thesis.

It is not only during the colonoscopy but also in its aftermath where changes in a colonoscopists' practice have resulted as a consequence of the perforation case. One of the colonoscopists, who reported distress at not being involved in subsequent decision making regarding a patients care post perforation, reported how, now, they always give their mobile telephone number to a patient following a high risk procedure and ask the patient to call them first if they develop abdominal pain or feel unwell. This meant they could be fully involved in the patient's care and avoid some of the events and emotions that were described during *'Into the Mirror'*.

The interviews implied that the perforation case may have had less of a psychological impact on those professionals who are used to working with greater clinical risk during their day-to-day practice. The nurse endoscopists interviewed perceived the perforation case had a greater impact on them than it would do on medical or surgical endoscopists. When I explored this further, reasons offered were the relatively small numbers of nurse endoscopists that performed colonoscopy during its infancy, the unfamiliarity with adverse events of this severity during their nursing careers and a general lack of confidence in their abilities. One of the nurse colonoscopists alluded to the fact that because she was a female, the case may have had a greater impact on her than would

have done on a male, potentially indicating colonoscopist sex bears an influence on the psychological impact of the perforation case. Given the increasing need for colonoscopy and colonoscopists coupled with a desire for greater cost saving in the NHS, it is likely that nurse endoscopists will have a greater role in colonoscopy service provision than ever before. It is therefore vital that the medical and surgical colonoscopists are aware of the potential greater psychological impact perforation cases may have on nurse endoscopists, particularly in relation to the support required during 'Acceptance and Refocus', and that they are prepared and willing to offer the necessary support.

One of the prior issues I wanted to explore in this study was that a change in endoscopic environment or performing a colonoscopy in a different environment to which the colonoscopist was used to may be a risk factor for colonoscopic perforation. I am aware that my own personal colonoscopic performance deteriorated following a change in endoscopic environment. Although I asked each participant about this issue neither of these potential 'environmental' factors were relevant to the perforation cases discussed. Time and equipment failure were identified as 'environmental' factors associated with perforation in this study. These associations should be kept in mind by colonoscopists in the future. Similarly, the two 'human' factors identified associated with perforation, fatigue and expectation, should also be kept in mind when performing colonoscopy.

One limitation of this study was the relatively small numbers of colonoscopists that were interviewed, particularly when this is broken down by specialty.

However, because of time and travel constraints this study only took place within Health Education North East. There are seven NHS trusts within this region. When the pool of independent colonoscopists within these trusts, who may have experience of a perforation is considered, along with the fact that not every colonoscopist may wish to discuss their experiences of such an emotive subject with a trainee in the region, eleven interviews provided a reasonable response and an accurate representation of experience.

5.5 Conclusions

Two of my intentions in writing this thesis were to minimise the risk of colonoscopic adverse events, including perforation, and improve its assessment and management.

As a direct result of this study, we have qualitative evidence of the caecum being a high-risk colorectal location for perforation. Colonoscopist caution in the caecum and the routine use of endoclips following endoscopic mucosal resection of large polyps in the caecum may, therefore, minimise perforation risk. My data suggests that not performing a colonoscopy when there is significant time pressure or colonoscopist fatigue may also minimise perforation risk. Similarly, the regular and thorough checking of diathermy equipment prior to commencing colonoscopy may be helpful as would bringing a patient back for a second procedure should the number of polypectomies required and time to do them in during the colonoscopy be far greater than expected.

When considering the assessment and management of colonoscopic perforation we now have qualitative evidence of how this could be improved. A specific named contact point and person for a patient should they develop symptoms following a colonoscopy may help in managing their perforation most appropriately. Similarly, clinician caution with subtle abdominal signs in the aftermath of high risk procedures may improve outcomes.

A further intention of writing this thesis was to explore the impact of an adverse event, including perforation, on a colonoscopist and to provide a reference point that all colonoscopists could use and relate to should they encounter an adverse event associated with a colonoscopy they perform in the future. This qualitative study has revealed what a colonoscopist may experience following such an event, the emotions they may feel and the effect the case may have on their personal and professional lives.

This work has led me to conclude that the support of colleagues is vital in helping a colonoscopist through the stages of response. I believe that colleagues should offer to discuss the perforation case with the colonoscopist and offer to take over/buddy up on the endoscopy list where the perforation occurs or their colleagues' subsequent endoscopy lists if needs be. It may be preferable if such a colleague had been specifically identified prior to the perforation occurring. Indeed this work supports the concept of all colonoscopists having a designated 'mentor'. Mentoring is well established in other healthcare settings; a 'mentor' may be defined as 'a trusted counsellor or guide'. Mentoring may be a formal process, involving a designated named person being allocated to the

colonoscopist or done informally involving, for example, opportunistic discussions with peers and colleagues. The English NHS BCSP has recently introduced a mentoring programme for screening colonoscopists. The BCSP mentor has responsibilities including the support of a colonoscopist through the accreditation process for Bowel Cancer Screening, supporting newly accredited colonoscopists in their new role and, importantly, supporting the colonoscopist after any adverse event[152].

Such a system of mentoring being used in the symptomatic colonoscopy service too, would, based on the evidence in this chapter, be to the benefit of all colonoscopists following a perforation. If the mentor had already been identified, with the chance for a relationship to build, the colonoscopist who is involved with the perforation may be more willing to seek their mentor's support both at the time of the perforation and in its aftermath. That colonoscopist may request the presence of the mentor during their subsequent lists. For this to happen the mentor would need to be available when the mentee colonoscopist was performing colonoscopy, therefore services scheduling mentor and mentee colonoscopy lists separately would be an important requirement of this process.

I hope this work can be used as a reference point so that colonoscopists can be better prepared for and better manage their feelings, emotions and performance in the aftermath of a perforation. The intention of this point of reference is so future perforations will not be to the detriment of a colonoscopist's performance.

Chapter 6

Post Polypectomy Bleeding (PPB)

6.1 Aims

The following aims relate to post polypectomy bleeding within the North East region of the English National Health Service Bowel Cancer Screening Programme only.

1. To determine the rate of post polypectomy bleeding.

2. To determine the rate of post polypectomy bleeding broken down by its grade of severity.

3. To describe post polypectomy bleeding presentation, management and outcomes.

4. To explore the factors that contribute to a post polypectomy bleed's grade of severity.

6.2 Methods

6.2.1 English National Health Service Bowel Cancer Screening Programme Regions

Endoscopic procedures in the English National Health Service Bowel Cancer Screening Programme are performed at 61 Joint Advisory Group on

Gastrointestinal Endoscopy (JAG) approved Bowel Cancer Screening Centres (BCSCs). These are divided by geographical location into five different regions: Midlands & North West, Southern, London, Eastern and North East. Each region has a regional quality assurance lead clinician, part of whose responsibility it is to review any adverse event that occurs at a BCSC within that region. Each BCSC has a clinical director who is responsible for that BCSC.

6.2.2 English National Health Service (NHS) Bowel Cancer Screening Programme (BCSP) 'Adverse Incident Alert to National Office' Forms and 'Clinical Director Reports'

A patient who attends for an endoscopic procedure as part of the English National Health Service Bowel Cancer Screening Programme is contacted by telephone 24 hours after the procedure by a Specialist Screening Practitioner who was present during the procedure. During the telephone conversation the SSP specifically asks the patient about the presence of symptoms, including bleeding per rectum or other symptoms of PPB, following the procedure. Patients also receive a questionnaire through the post from the Bowel Cancer Screening Centre at 30 days post procedure. The patient is asked to complete the questionnaire and return it to the BCSC. Questions specifically relate to whether an adverse event, including bleeding, has occurred with further details of the event and its impact on the patient. If a patient does re present with bleeding per rectum following polypectomy, for the most part this will be to the hospital where the colonoscopy occurred. In addition patients are also specifically asked to contact the BCSP team should they develop symptoms. These methods of

contacting or being contacted by the patient following their procedure form part of the process by which the BCSP is alerted to an adverse event, including PPB.

If an adverse event does occur, data on the adverse event is recorded by the SSP electronically on a specific form, the 'adverse incident alert to national office' form. This form is e-mailed to the BCSP national office. The form is also e-mailed to the regional quality assurance lead clinician for the BCSP region where the adverse event occurred. Each adverse event is subject to a formal report by the clinical director of the BCSC where the adverse event occurred; this report is also e-mailed to the regional quality assurance lead clinician.

6.2.3 The North East Region of the English National Health Service Bowel Cancer Screening Programme

The North East Region of the English National Health Service Bowel Cancer Screening Programme was the setting for this study. Professor Rutter, as regional quality assurance lead clinician for the North East region of the BCSP had reviewed and collected both the 'adverse incident alert to national office' forms and the 'clinical director reports' for all the cases of bleeding that had been reported as an adverse event from four Bowel Cancer Screening Centres in the North East region and a further BCSC, South Yorkshire and Bassetlaw. Professor Rutter as regional quality assurance lead clinician also covered this BCSC. The five BCSCs were North of Tyne BCSC, South of Tyne BCSC, Tees BCSC, County Durham & Darlington BCSC and South Yorkshire & Bassetlaw BCSC. The cases of bleeding reported as being adverse events were from the 06/12/2010 up to and

including the 15/07/2014. Professor Rutter, as co-supervisor of this MD thesis provided me with these documents that contained the data required for this study.

6.2.4 Review of Bowel Cancer Screening Programme 'adverse incident alert to national office' forms and 'clinical director reports'

I reviewed all of the completed 'adverse incident alert to national office' forms and 'clinical director reports' that had been provided to me by Professor Rutter. No patient identifiable data was entered onto these forms.

The 'adverse incident alert to national office' form comprises several sections each containing data relating to the adverse event. The contact details of who has completed the form and the site within the Bowel Cancer Screening Centre where the adverse event occurred are completed first. This is followed by a tick box of the category of the incident; the category being either an incident at the BCSP hub or an incident at the BCSC or screening site. A free text box with a 'description of the incident including date and time' is then completed, followed by a free text box of the 'immediate action taken' and finally a free text of a description of the 'possible impact' on the patient.

The 'clinical director reports' are entered into an electronic form with several sections for free text. These sections include (1) the date of the procedure (2) a description of risk factors/events/therapy with dates (3) interventional procedures/surgery with dates (4) where relevant, kit used and diathermy

settings (5) outcome (6) stratification of severity (as per BCSP QA guidelines for colonoscopy document) (7) attribution of event (as per BCSP QA guidelines for colonoscopy document) (8) learning points and actions taken if any and (9) confirmation the event has been recorded on the BCSS.

6.2.5 Constructing the post polypectomy bleeding database

As I reviewed the forms that are detailed in chapter 6.2.4, I entered data from them into a Microsoft Excel spread sheet. Each pair of 'adverse incident alert to national office' forms and 'clinical director reports' was given a number from 2 - 78 identifying it as a case of bleeding as an adverse event in my database.

Each case of bleeding was entered into a different row in the spread sheet with different columns in the spread sheet relating to the patient, the endoscopy, the polypectomy, how the patient presented, their subsequent management and outcome. The columns were divided into: (1) the date the colonoscopy associated with bleeding took place (2) if the patient was taking any antithrombotic medication (3) the name and dose of the antithrombotic medication (4) how many polyps were resected (5) the polyp location (6) polyp class (7) estimated endoscopic polyp size (8) polyp therapy (9) polyp therapy device (10) endoscopic therapy given during the procedure (11) if the patient was admitted or discharged following the procedure (12) the date of representation with symptoms from bleeding (13) the number of days to representation with bleeding (14) the presenting complaint of the bleeding (15) if intravenous fluids and blood were administrated (16) if a repeat endoscopy

took place (17) the date of the endoscopy (18) the endoscopic therapy performed at repeat endoscopy (19) if surgery occurred (20) the name of the operation if surgery did take place (21) the date the operation was performed (22) the diagnosis (23) the date of discharge (24) the number of days an inpatient and (25) the severity grading of the bleeding.

When all columns and rows and had a value assigned to them the construction of the post polypectomy bleeding database was complete.

6.2.6 Overall endoscopic data for the North East Region of the English National Health Service Bowel Cancer Screening Programme

The final part of the methodology I used for this study was contacting the NHS BCSP national office for the overall endoscopic data relating to the North East Region of the NHS BCSP. I emailed a project manager at the NHS Bowel Cancer Screening Programme national office requesting this data. I wrote an email from my personal NHS mail account to Miss Claire Nickerson, the project manager at the NHS BCSP's national office, requesting she identify the total number of endoscopic procedures and the total number of polypectomies that had been performed in the North East Region of the NHS BCSP from the 06/12/2010 up to and including the 15/07/2014. The project manager, Miss Claire Nickerson, interrogated the Bowel Cancer Screening System to acquire this data and then emailed the figures back to me.

6.2.7 Note on peri procedure bleeding

Peri procedure bleeding was defined as that occurring immediately following polypectomy, controlled during the colonoscopy and not preventing its completion. The vast majority of cases of peri procedure bleeding would not, therefore, be reported as being an adverse event and would not have been included in the dataset used in this study. Peri procedure bleeding was, however, reported as an adverse event and therefore included in the dataset used in this study when a patient was admitted to hospital following completion of the colonoscopy for a period of observation. Where cases of peri procedure bleeding such as this were identified, they were separated from those of post polypectomy bleeding.

6.2.8 Statistical Analysis

The Microsoft Excel spreadsheet that I had produced was uploaded into statistical package for the social sciences version 20 for data analysis. Normally distributed continuous variables were expressed as mean, with non-normally distributed continuous variables expressed as median. Categorical variables were expressed as a percentage. Pearson chi-square and Fisher's exact test were used to test association between explanatory and outcome variables with a p value < 0.05 considered to be significant.

6.3 Results

6.3.1 Overall endoscopic data from the study population

Data was collected from five of eight Bowel Cancer Screening Centres within the North East Region of the Bowel Cancer Screening Programme. The five BCSCs were North of Tyne BCSC, South of Tyne BCSC, Tees BCSC, County Durham & Darlington BCSC and South Yorkshire & Bassetlaw BCSC. The total population recorded by Clinical Commissioning Groups as being registered with a general practitioner within the geographical areas covered by these BCSCs was 4,191,507. All 60-74 year olds within this population were sent an invitation to take part in the Bowel Cancer Screening Programme with a Faecal Occult Blood Test.

During the period of this study period 1,293,672 Faecal Occult Blood Tests were distributed of which 784,359 were returned. 13,869 FOBTs were abnormal leading to 11,564 patients attending for a colonoscopy. 15,285 colonoscopies were subsequently performed, a mean of 1.3 per subject. These 15,285 colonoscopies led to 23,766 polypectomies.

76 cases of bleeding recorded as being an adverse event were identified. Of the 76 cases of bleeding identified, four of these cases sought consultation from bleeding post procedure due to bleeding haemorrhoids following colonoscopies where no polypectomies had taken place. Two of the cases sought consultation post procedure from bleeding thought secondary to the colonoscopy and/or bowel preparation and not from polypectomies. All six of these cases were excluded from the analysis.

Two cases of peri procedure bleeding immediately following polypectomy, controlled during the procedure and not preventing its completion, were subsequently admitted to hospital for observation. Therefore, they can be considered within the BCSP definition of bleeding as an adverse event. However, for the reasons explained in 6.2.7, these cases were separated from those of post polypectomy bleeding.

68 cases of post polypectomy bleeding therefore remained with the rates of PPB calculated below:

PPB rate per colonoscopy = 68/15,285 x 100 = 0.44%

PPB rate per polypectomy = 68/23,766 x 100 = 0.29%

6.3.2 Peri procedure bleeding

A patient who underwent colonoscopy with a hot snare polypectomy of a 15mm sigmoid pedunculated polyp had peri procedure bleeding controlled with adrenaline injection and four endoclips. A second patient with atrial fibrillation had warfarin stopped five days prior to the colonoscopy. Three polypectomies of three sessile polyps took place, two in the caecum of 7mm and 2mm respectively with a 3rd 25mm polyp in the sigmoid. Two endoclips were required to control haemorrhage from the sigmoid polyp. Both patients were admitted to hospital for observation and discharged 24 hours later.

6.3.3 Post polypectomy bleeding (PPB)

12 of 68 (17.6%) patients with PPB were known to have co-morbidity including four with atrial fibrillation. The four patients with atrial fibrillation also had additional co-morbidity including hypertension (n=1), chronic obstructive pulmonary disease (n=1), a permanent pacemaker (n=1) and a previous transient ischaemic attack (n=1). Other patients with co-morbidity included diabetes mellitus & previous stroke (n=1), previous deep vein thrombosis (DVT) and pulmonary embolism (PE) (n=1), hypertension & gout (n=1), hypertension & previous TIA (n=1), COPD & Coagulopathy (n=1), previous TIA (n=1), Idiopathic thrombocytopenic purpura (n=1) and haemophilia (n=1).

13 of 68 (19.1%) patients with PPB were taking antithrombotic medication at the time of colonoscopy and polypectomy including aspirin (n=11) (warfarin stopped five days pre procedure in two of these, one also took dipyridamole), clopidogrel (n=1) (the patient decided to continue clopidogrel with appropriate consent) and warfarin (n=1) (the patient decided to continue warfarin with appropriate consent). Three of 68 (4.4%) patients had stopped antithrombotic medication prior to the colonoscopy including warfarin (n=2) and clopidogrel (n=1). Six of 68 (8.8%) patients stopped warfarin five days prior to colonoscopy and were commenced on low molecular weight heparin (LMWH) two days after stopping warfarin with omission of LMWH on day of the colonoscopy. Although 19.1% of patients with PPB were taking antithrombotic medication it was unclear how this compared with the overall use of antithrombotic medication in the BCSP.

Analysis of single polypectomies enabled accurate attribution of the post polypectomy bleeding to the single polyp. PPB was associated with a single polypectomy in 22 of 68 (31.9%) of patients. Multiple polypectomies took place in 46 (67.6%) of patients.

Chart 1: Bar chart of post polypectomy bleeding polyp location for single polypectomy procedures split by bleed severity
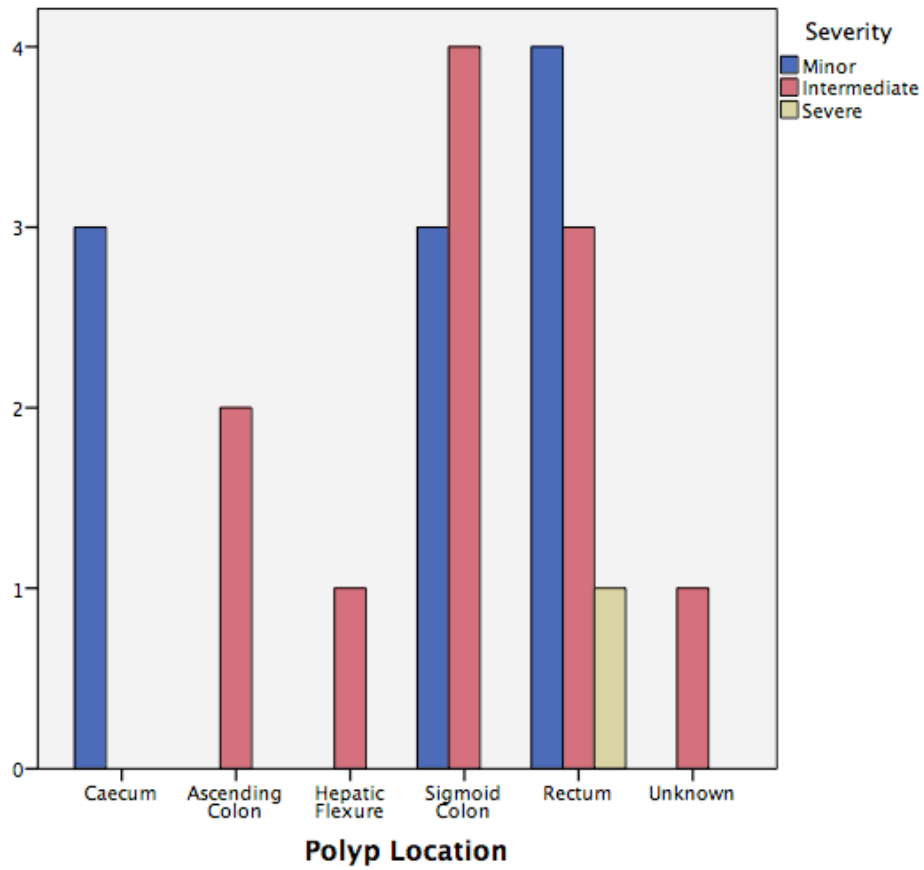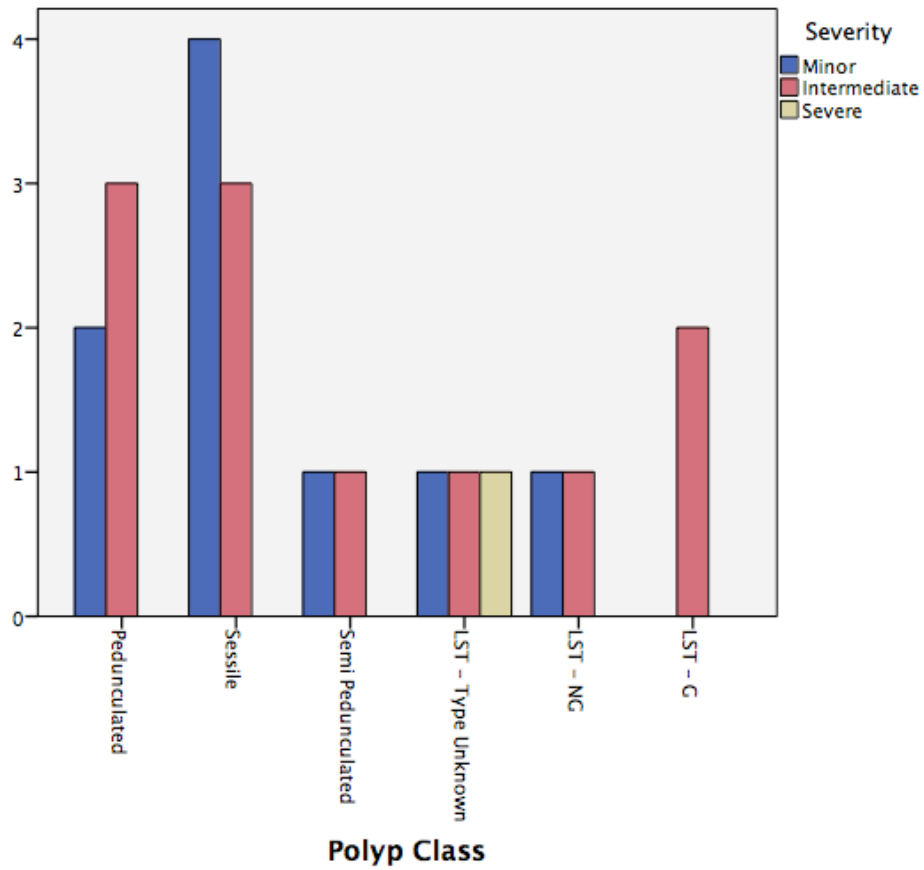
Chart 2: Bar chart of post polypectomy bleeding polyp class for single polypectomy procedures split by bleed severity

Of the single polypectomy procedures associated with PPB, three of the polypectomies were in the caecum: a 30mm laterally spreading tumour of the non granular type resected by endoscopic mucosal resection, hot snare and using argon plasma coagulation, a 10mm pedunculated polyp resected by hot snare, (adrenaline injection was used peri procedure on this polyp) and a 5mm sessile polyp. Two laterally spreading tumours of the granular type were resected from the ascending colon were associated with PPB. These were of 27 and 50mm respectively, resected by EMR and hot snare with APC used on the 27mm polyp. A 25mm LST-NG resected from the hepatic flexure by EMR, hot snare and APC was also associated with PPB. There were seven single polypectomies associated with PPB in the sigmoid colon, four were pedunculated polyps ranging from 11 – 50mm. Two endoclips were applied peri procedure to the largest of these. Two polyps were semi pedunculated of 18 and 27mm respectively. Adrenaline injection was used peri procedure on the 27mm polyp. Of eight single polypectomies in the rectum, three were laterally spreading tumours of 40mm, 50mm and 75mm in size. Five were sessile polyps ranging from 6 – 45mm in size. Two of these sessile polyps in the rectum, both of 10mm, had endoclips applied peri procedure and on one adrenaline injection was used. How this data relating to single polypectomy location, polyp size and polyp morphology compared with procedures on patients who did not have post polypectomy bleeding was unclear as this data wasn't available for use in this study.

In one of 68 patients, the time to presentation was not documented. Time to presentation ranged from the same day of the colonoscopy to 19 days post procedure with a median time to presentation of four days.

Chart 3: Histogram of number of days to presentation with minor severity
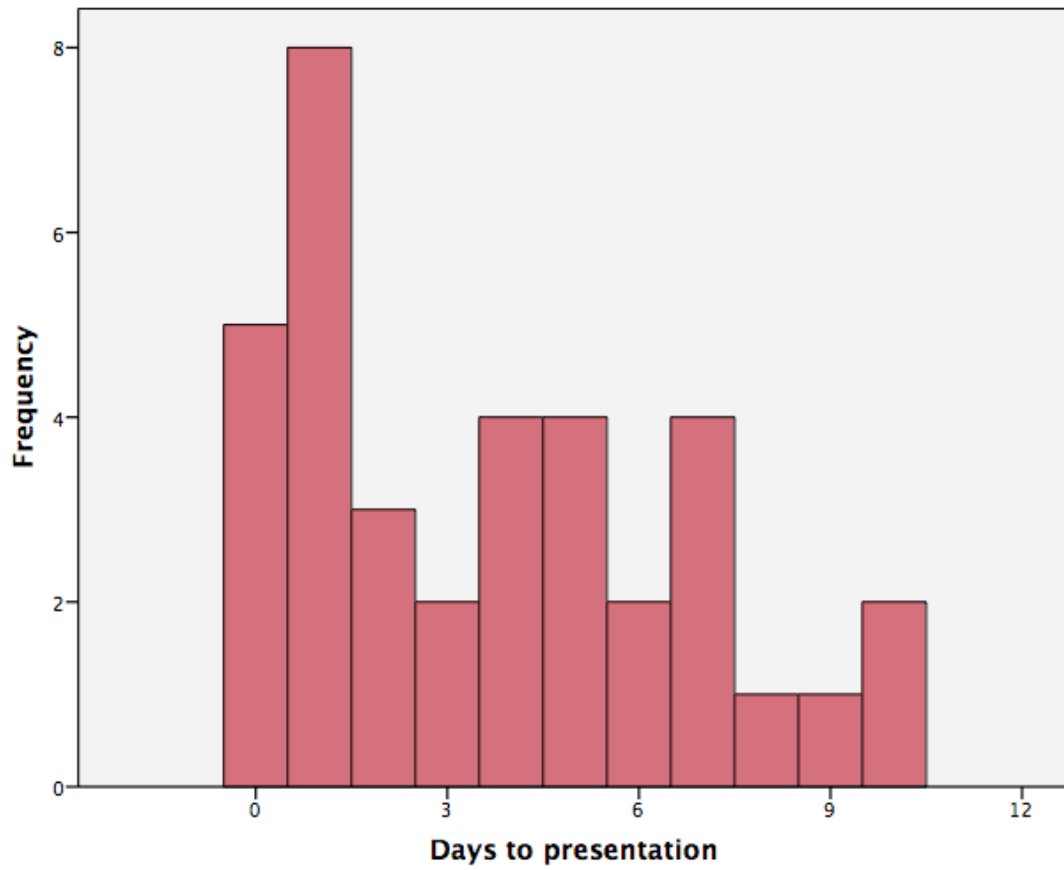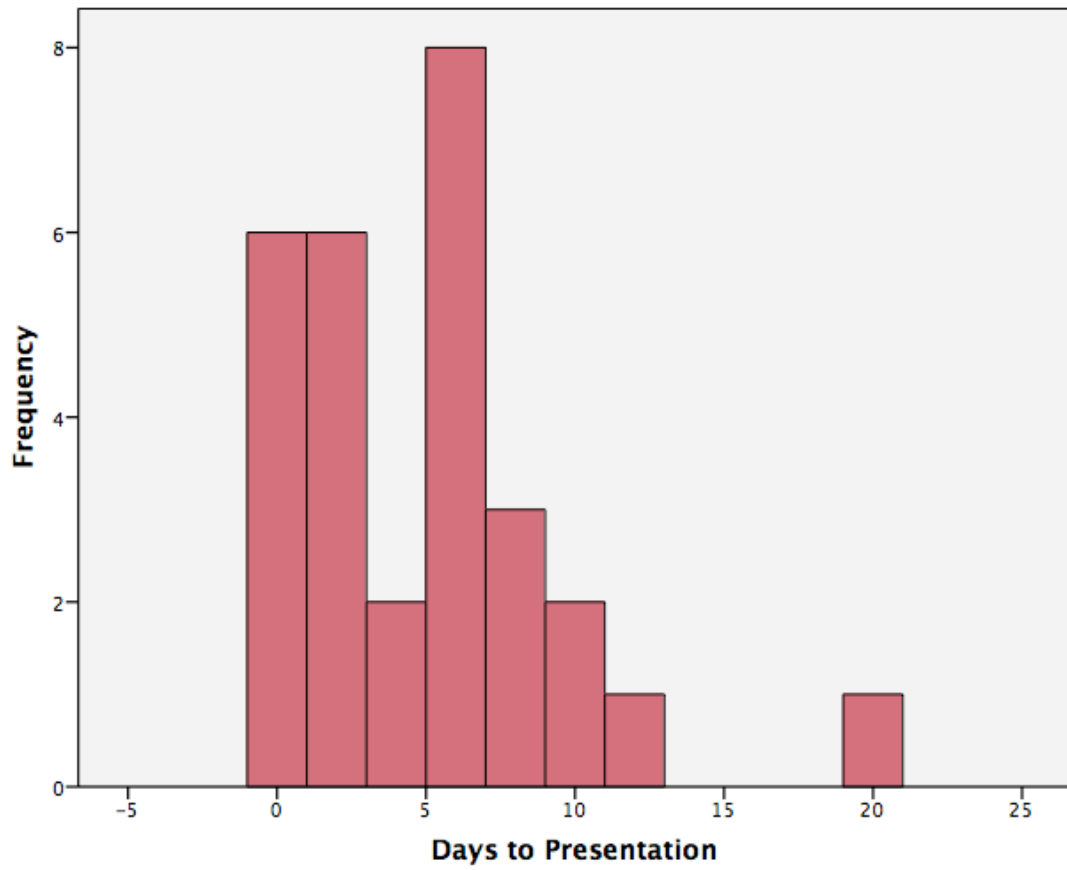
Post Polypectomy Bleeding

Chart 4: Histogram of number of days to presentation with intermediate severity Post Polypectomy Bleeding

67 patients presented with bleeding per rectum. One patient presented with melaena six days following a 5mm polypectomy in the caecum. Of the 67 patients presenting with bleeding per rectum, six of 67 (9.0%) patients had symptoms or signs reflecting haemodynamic changes including: syncope (n=2), dizziness (n=1), lightheadedness (n=1), hypotension (n=1), syncope & hypotension (n=1). Four patients also complained of abdominal pain in addition to bleeding per rectum.

16 of 68 (23.5%) cases of post polypectomy bleeding had medical management comprising a blood transfusion and/or intravenous fluids, fresh frozen plasma, tranexamic acid, factor V111 and oral iron. Nine of 68 (13.2%) patients had a blood transfusion. Repeat endoscopy was performed in 19 of 68 (27.9%) patients and in seven of 68 (10.3%) patients therapy was given at repeat endoscopy. Therapy given to control bleeding included application of endoclips, adrenaline injection or both. In one patient an endoloop was applied to the remaining stalk following a polypectomy of a 20mm pedunculated polyp in the sigmoid. One of the 68 cases of PPB underwent surgery. This was due to rectal bleeding following an EMR with APC to a 50mm LST in the rectum. The patient presented six days following the colonoscopy and had four units of blood transfused. A subsequent Examination Under Anaesthesia and suture of the bleeding point was performed. It was unclear if this surgery had occurred out of normal working hours without access to an endoscopist.

In patient hospital stay ranged from 0 – 6 days with a median hospital stay of

two days. There was no mortality associated with these cases of post polypectomy bleeding. One patient required a second admission having initially presented 6 hours following a colonoscopy during which a total of 8 polypectomies were performed from the caecum, transverse and sigmoid colon. They presented with bleeding per rectum and were transfused a total of nine units blood. At repeat colonoscopy adrenaline was injected at the transverse colon. The patient was discharged after 24 hours but re-presented a further 24 hours later with bleeding per rectum. They had a CT angiography with radiological embolization of an ileocolic vessel and remained an inpatient for a further 3 days.

6.3.4 Post polypectomy bleeding by grade of severity

PPB was graded by severity into major, intermediate or minor bleeding using the NHS BCSP framework based on the American Society for Gastrointestinal Endoscopy (ASGE) grading system[4] [26]. There were two cases of major bleeding (2.9% of post polypectomy bleeds) equating to a rate of 0.01% of major bleeding per colonoscopy. Intermediate bleeding occurred in 29 cases (42.6% of post polypectomy bleeds) a rate of 0.19% per colonoscopy and minor bleeding occurred in 37 cases (54.4% of post polypectomy bleeds), a rate of 0.24% per colonoscopy. This cannot be compared to the current BCSP individual performance standard for PPB of less than 0.01% per colonoscopy where polypectomy occurred as this data equates with all colonoscopies.

Chart 4: Pie chart representing breakdown of cases of post polypectomy bleeding by grade of severity
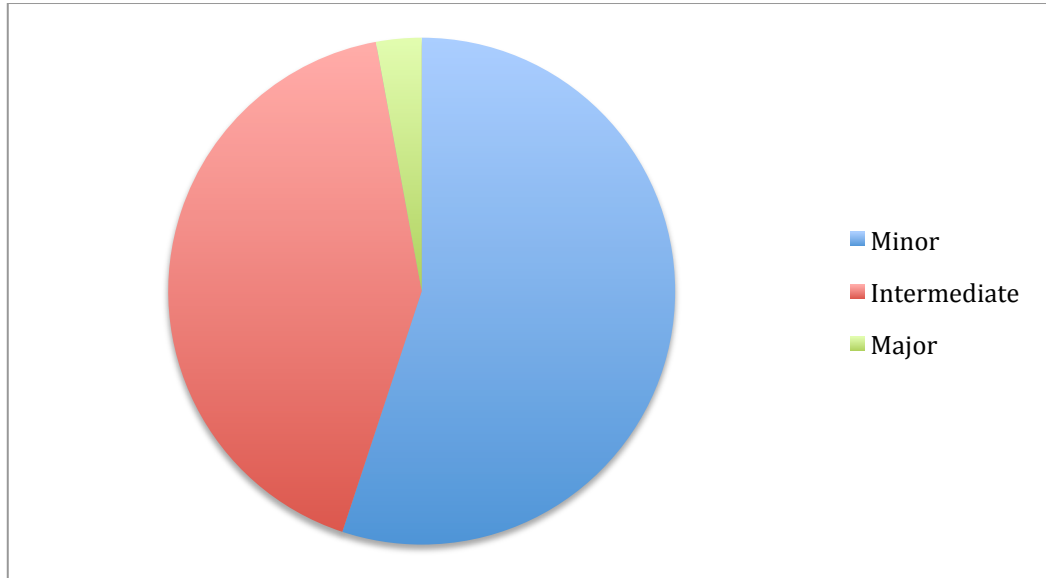
The criteria for how each case of PPB met their specific grading of severity are outlined below:

Table 1: Criteria for meeting major post polypectomy bleeding by case

Cases	Surgery	Unplanned admission or prolongation of hospital stay for > 10 nights	ITU Admission > 1night
1	X		
1			X

Median Time to presentation of major post polypectomy bleeding was 3.5 days (range 1-6 days). Median hospital stay of major post polypectomy bleeding was 3 days (range 2-4 days).

Table 2: Criteria for meeting Intermediate post polypectomy bleeding by case:

Cases	Hgb Drop ≥ 2g	Transfusion	4 - 10 nights	Endoscopy	Therapy at Endoscopy	Radiology Intervention
9				X		
6	X					
4				X	X	
1	X		X			
2	X			X		
2	X	X		X	X	
1	X	X	X	X	X	
1	X	X	X			
2	X	X				
1	X	X		X		X

The median time to presentation of intermediate PPB was 4.5 days (range 0-19 days). Median in patient stay of intermediate PPB was 2 days (range 0-6 days). In 19 cases of intermediate post polypectomy bleeding a repeat endoscopy was performed. In seven of these examinations endoscopic therapy was applied at repeat endoscopy. When examining factors associated with the need for endoscopic therapy in this group of patients in whom a repeat endoscopic examination was performed, 42.8% of those that had repeat endoscopic therapy had a haemoglobin drop greater than or equal to 2g/dL and had a blood transfusion. Only 25% of those that did not have therapy at repeat endoscopy had a haemoglobin drop greater than or equal to 2g/dL and only 8% had a blood transfusion. Neither a haemoglobin drop greater than or equal to 2g/dL (p=0.617) nor having a blood transfusion (p=0.117) were significant predictors of the need for endoscopic therapy.

Table 3: Criteria for meeting minor post polypectomy bleeding by case:

Cases	Unplanned post procedure medical consultation	Unplanned admission or prolongation of hospital stay for ≤ 3 nights
24	X	
13	X	X

The median time to presentation of minor PPB was 3.5 days (range 0 – 10 days). Five patients stayed in hospital for more than one night.

6.3.5 Factors associated with major and intermediate severity post polypectomy bleeding

Factors that were explored as potential predictors of major and intermediate severity PPB were the presence of co-morbidity and the use of antithrombotic medication. Six of 37 (16.2%) minor severity bleeds had co-morbidity and nine of 37 (24.3%) were taking anti thrombotic medication at the time of polypectomy. This compared with six of 31 (19.4%) intermediate and major severity bleeds that had co-morbidity and 13 of 31 (41.9%) intermediate and major severity bleeds that were taking antithrombotic medication. Neither the presence of co-morbidity (p=0.760) nor the use of anti thrombotic medication (p=0.193) were significantly associated with these more severe PPB sub groups of major and intermediate severity PPB.

Explanatory variables among single polypectomy procedures examined were polyp location, polyp size and polyp class. Of 11 minor severity post polypectomy bleeds associated with single polypectomy procedures, three (27.3%) were in the caecum, five (45.5%) were in the rectum and three (27.3%) were in the sigmoid colon. Four were associated with sessile polypectomies, two with pedunculated polypectomies, one with a sub-pedunculated polypectomy and three with Laterally Spreading Tumours (LSTs). One polyp class was not recorded. Size of polyp associated with minor severity PPB ranged from 5mm to 75mm with a median size of polyp of 15mm. Of 11 intermediate and major severity risk post polypectomy bleeds associated with single polypectomy procedures, three (27.3%) were in the rectum, four (36.4%) were in the sigmoid colon, two (18.2%) were in the ascending colon, one (9.1%) was at the hepatic flexure and in one the colorectal location of the polypectomy was not recorded.

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Three of 11 (27.3%) polyps were sessile, three (27.3%) were pedunculated, one (9.1%) was semi pedunculated and four (36.4%) were LSTs. Polyp size ranged from 9mm to 50mm with a median size of polyp of 25mm. Neither polyp location (p=0.177), polyp size (p=0.239) and polyp class (p=0.720) were predictive of intermediate or major severity PPB.

6.4 Discussion

Although the number of colonoscopies (15,285) reported in this study is lower than other similar recent series reporting PPB, we can be reassured that the rate of PPB per colonoscopy (0.44%) in this study is in line with the rates described in chapter 2.5.2 of this thesis. In this study I have reported PPB rate per polypectomy which at 0.23% is lower than the 1.06% reported by Macrae et al.[43]. The majority of studies only give a rate of PPB per colonoscopy and therefore reliably comparing rate per polypectomy is difficult. However, data from this study provides us with the evidence that polypectomy is performed safely in the English NHS BCSP and the rates of PPB are comparable to colonoscopy that is performed worldwide.

Although the lack of data from a control group in this study prevented me exploring whether the presence of co-morbidity and the use of antithrombotic medication are risk factors for PPB, just under one fifth of patients with PPB had co-morbidity and/or were taking anti thrombotic medication at the time of colonoscopy and polypectomy.

The median time to presentation of these post polypectomy bleeds was four days, one less than the five days reported by Sorbi et al. with the range of time to presentation extending to 19 days post polypectomy, 2 more than that described in Sorbi et al.'s study[98]. Unlike some studies, I have presented time to presentation in all patients showing that the majority of post polypectomy bleeds presented within the first 48 hours post polypectomy. This better informs us of when to contact patients in the aftermath of a polypectomy. Specialist Screening Practitioners currently contact patients at 24 hours post procedure, however, using a 48 hour cut off for checking for bleeding per rectum may be more helpful than the current 24 hour period. In Sorbi et al.'s descriptive analysis, 43% of patients had signs of haemodynamic compromise compared with only 9% in my study[98]. This, reassuringly, suggests that the bleeds in my study were less severe, re-affirmed with the data from the grading of PPB severity.

Only 13.2% of the patients with PPB required a blood transfusion compared with the 25% described by Rosen et al., 92.3% described by Gibbs et al. and 54.2% by Sorbi et al.[96 97 98]. Again, these figures add weight to the fact that the bleeds in this study were not as severe as other similar series and reassure us that the extent to which patient safety is compromised by PPB in the English NHS BCSP is minimal.

27.9% of post polypectomy bleeds in my study had a repeat endoscopy, however, endoscopic therapy was given in 10.2% of all bleeds. A repeat diagnostic only endoscopic examination was performed in 17.7% of cases. Although ultimately

the judgement on who has a repeat endoscopic examination is down to the assessing clinician, it would appear from my data that some endoscopic examinations are performed needlessly and could be avoided. How to identify who requires a repeat endoscopic examination is an important question and this remains unclear from my study as neither a drop in haemoglobin greater than or equal to two grams per demi litre or having a blood transfusion were significant predictors of having endoscopic therapy. A larger series may help in answering this question.

Importantly there were no complications or deaths associated with the admissions of PPB which again reflects favourably on how PPB has been managed in this study. One patient had surgery in order to control PPB which is in line with the one patient having surgical intervention described in other series[38][101][107]. This operation was an examination under anaesthesia and suture of the post polypectomy bleeding point rather than a colonic resection as described in other series. One limitation of the methodology I used to collect data was that the exact time of presentation wasn't documented in the majority of cases. It is therefore unclear if the one patient who had surgery had presented out of normal working hours when there wasn't access either to the endoscopist who had performed the polypectomy or an on call endoscopist. It would be suprising if haemostasis in this particular case could not have been achieved endoscopically. It may have been that the initial assessing clinician(s) only had access to a surgical team hence the patient having surgery. This potential chain of events raises questions regarding the advice given to patients about who to contact should they develop bleeding per rectum following polypectomy and

who the assessing clinician(s) should communicate with in these circumstances. For example, a patient is advised to contact a member of the BCSP if they have any bleeding per rectum that concerns them post procedure. This may not be possible out of current normal working hours leading to the patient contacting a general practitioner or presenting to an Accident & Emergency department. In this scenario, if out of hours intervention was felt to be required by the presence of, for example, continuing bleeding, haemodynamic compromise or a drop in haemoglobin of over 2g/dL then a conversation with an on call endoscopist or gastroenterologist would be an appropriate first port of call. If this service wasn't available, only then involving the on call surgical team may be appropriate. As a result of this particular patient having surgery this post polypectomy bleed was graded as severe but potentially this categorization could have been avoided. Unlike the studies by Rosen et al. and Sorbi et al. none of the patients in this study required a colectomy [96] [98].

Only one patient presented for a second time with bleeding per rectum and required radiological management in the form of computed tomography angiography and embolization. The use of this technique to control PPB is limited to isolated case reports so comparison of this management strategy in the context of this retrospective observational case series is difficult. Although data regarding length of hospital stay form other studies is scarce, a median hospital stay of two days in this study again reflects favourably on both the severity of PPB and how it was managed. This figure was a median one day less than that reported by Sorbi et al.[98]. The longest a patient remained in hospital for

was six days, much less than that reported by Inoue et al. but two days more than by Singh et al.[124] [125].

The work in this chapter is distinctive as it has graded post polypectomy bleeding by severity as per the English NHS BCSP's adverse events severity grading framework, based on the American Society of Gastrointestinal Endoscopy's grading system[26] [4]. My data has suggested the post polypectomy bleeds studied were not as severe as those in other series. This was confirmed by the application of the severity grading criteria with over half of these bleeds being of minor severity and therefore clinically insignificant. Only two patients had a severe post polypectomy bleed, one of these because of having surgery, which, as explained above, may have been avoidable. Of those patients with an intermediate severity post polypectomy bleed, the majority were graded as such because of having a repeat endoscopic procedure even though no therapy was required. A limitation of my dataset was that I could only test haemoglobin drop over two grams per demilitre and whether the patient had a transfusion or not as explanatory variables predicting the need for endoscopic therapy, neither of which were significant predictors. A more detailed dataset including, for example, admission pulse and blood pressure or the volume of blood passed may better predict the need for endoscopic therapy and is a specific point for further research. As expected the major severity bleeds were in hospital for a median one day longer and presented a median one day sooner than the intermediate severity bleeds.

Another limitation of this dataset was the small numbers of single polypectomy procedures that took place. When predicting factors associated with the more severe PPB sub groups of major and intermediate severity bleeding using single polypectomy procedures, which enabled accurate attribution of the single polypectomy to the bleed, none of the explanatory variables were significant. Partly, this is due to the small numbers involved and has to be taken in the context of national data from the English NHS BCSP which has showed polyp size and a location of a polyp in the caecum as significant predictors of PPB.

6.5 Conclusions

The data reported in this chapter reassures us that the frequency with which post polypectomy bleeding occurs when measured per colonoscopy is similar to that occurring globally when colonoscopy and polypectomy is performed in similar numbers. In addition, less than half of the bleeds studied would be considered to be clinically significant bleeds; an important statistic in this work.

When considering the impact of PPB on the patients involved there appear to be less serious consequences when compared to perforation. 64.7% of these post polypectomy bleeds were admitted to hospital. There were no complications or deaths following PPB. Surgery was required in only one patient as was the case with intensive care admission.

This work has raised specific points about how the assessment and management of PPB could be improved. We now know that the majority of these post

polypectomy bleeds presented within 48 hours and, therefore, ensuring there is access to either the colonoscopist who performed the initial procedure or an on call endoscopist with whom the case can be discussed during this time period may prevent unnecessary intervention. Alternatively, performing high risk procedures Monday to Wednesday only would be a method of ensuring access to the appropriate personnel in the event of PPB. A post procedure SSP phone call at 48 hours rather than 24 hours to the patient may help in facilitating this. Similarly, this data suggests that the majority of repeat endoscopic procedures are performed needlessly and could be avoided. Predicting those patients whose bleeding does not require any intervention will therefore be an important focus of future research.

Chapter 7

Post Colonoscopy Colorectal Cancer (PCCRC)

7.1 Aims

The following aims relate to Post Colonoscopy Colorectal Cancer (PCCRC) within the English National Health Service Bowel Cancer Screening Programme only.

1. To establish the overall rate of PCCRC.

2. To establish the rate of PCCRC for individual years.

3. To explore if and how the PCCRC rate changes over time.

7.2 Methods

7.2.1 Calculation of Post Colonoscopy Colorectal Cancer (PCCRC) Rate

The first stage in achieving the aims of this study was to establish the methodology for calculating PCCRC rate. As has been described in chapter 2.6 of this thesis there is no standardised definition or formula for calculating PCCRC rate. The English National Health Service Bowel Cancer Screening Programme has adopted a novel method of PCCRC rate calculation, using the number of colonoscopies diagnosing a cancer rather than cancers in its numerator and denominator. The reasoning for this is that using colonoscopies in the rate calculation best enables us to express to patients the chances of a colonoscopy

either missing or not preventing against the development of a cancer. This methodology was proposed and used by Morris et al. to determine PCCRC rate from symptomatic patients in England using data from the National Cancer Data Repository[126].

In order to calculate PCCRC rate using this method we require a numerator and denominator. To provide the numerator and denominator we have to consider two distinct types of colonoscopy; a colonoscopy that detects a colorectal cancer, which I refer to as 'true positive colonoscopy' and a second type of colonoscopy, on a patient that doesn't detect a cancer but when cancer subsequently develops in that patient, termed a 'false negative colonoscopy'. Importantly, there is a finite period of time after the false negative colonoscopy for the PCCRC to develop. I used a period of 3 years after the false negative colonoscopy in this study. To calculate overall PCCRC rate I then used the formula false negative colonoscopies / (false negative colonoscopies + true positive colonoscopies).

7.2.2 Calculation of Post Colonoscopy Colorectal Cancer (PCCRC) rate for an individual year

Aims two and three of this study required a calculation of PCCRC rate for an individual year in the NHS BCSP. In order to do this calculation I again used the two categories of colonoscopy described, true positive colonoscopies and false negative colonoscopies. However, on this occasion we consider them to occur during one and not multiple years. For example if we wish to calculate PCCRC rate for the year x we use the formula: false negative colonoscopies during year

x/(false negative colonoscopies during year x + true positive Colonoscopies during year x). For this calculation I again used a 3 year cut off period after the year x for the colorectal cancer to develop in those subjects who had a false negative colonoscopy.

7.2.3 The Bowel Cancer Screening System (BCSS)

The internet based database of the English NHS BCSP, the Bowel Cancer Screening System, again provided the data required to achieve the aims of this study using the methodology outlined above. Details of BCSS can be found in chapter 4 of this thesis. Access to BCSS was facilitated by Professor Rutter, as chair of the English NHS BCSP evaluation group and co-supervisor of this thesis.

I wrote and sent an email to Miss Claire Nickerson, project manager at the Bowel Cancer Screening Programme national office. The email outlined the study and the data that would be required in order to achieve its aims. I requested data from BCSS on all the subjects' screening episodes that were recorded as having a diagnosis of colorectal cancer from the start of the English NHS BCSP on the 02/08/2006 up to and including the 31/12/2013. Where a subject with a diagnosis of colorectal cancer had been through a previous episode of screening and had a colonoscopy during that episode I also requested data relating to that episode of screening.

For those subjects recorded as having a diagnosis of colorectal cancer I requested data on several variables relating to the subject and that specific

screening episode. These included (1) a unique subject identifier (2) the start date of the screening episode (3) the type of colorectal investigation that made the diagnosis of colorectal cancer (patients in the BCSP may be investigated not only with a colonoscopy, but also with a Virtual CT Colonoscopy, CT Abdomen or Barium Enema) and (4) the date of the colorectal investigation(s) during the episode of screening. For those subjects diagnosed with colorectal cancer who had previously been through one or more episodes of screening prior to the episode where cancer was diagnosed, data was also requested relating to their previous episode(s) of screening. Data from this episode(s) related to the following variables: (5) a unique subject identifier (6) the start date of the screening episode (7) the type of colorectal investigation(s) that took place during the episode(s) and (8) the date of this colorectal investigation(s).

Miss Claire Nickerson, project manager at the BCSP national office, received this email and then wrote a query to extract all of this data from BCSS. The data was then emailed back to me securely via NHS mail. The data was provided in three Microsoft Excel spreadsheets; the first two of these spreadsheets related to the subjects' episodes of screening where cancer was diagnosed. Variables 1-4 as listed above were entered into the columns with data for each subject in rows. The third spreadsheet related to the subjects previous episode(s) of screening with variables 5-8 entered into columns with data for each subject entered into each row.

7.2.4 Analysis of Microsoft Excel spreadsheets

I used the first two of these spreadsheets containing variables 1-4 to calculate the number of true positive colonoscopies. During this process those subjects who had multiple investigations during the episode of screening diagnosing colorectal cancer were identified. A true positive colonoscopy was deemed to have occurred if a colonoscopy was the most recent investigation in that episode of screening. If a colonoscopy and a radiological investigation had taken place on the same day, the colonoscopy 'gave way' to the radiological investigation and wasn't considered a true positive colonoscopy on the basis that the endoscopist would have requested a same day radiological investigation because he or she felt there was an issue with completeness of examination of the colon.

I then calculated the number of false negative colonoscopies by reviewing the third of these spreadsheets. Where a subject had undergone multiple investigations during one or more episodes of screening prior to the episode of screening diagnosing colorectal cancer, a false negative colonoscopy was recorded if it was the most recent full colorectal investigation in the episode of screening immediately prior to the episode of screening diagnosing cancer.

These steps were repeated with respect to each year from 2006-2013. Those cancers that had presented more than 3 years after the false negative colonoscopy were then excluded form the analysis to give the true PCCRC rate for the 4 year time period from 2006 to 2010 and the true annual PCCRC rate each year from 2006 to 2010. PCCRC rate was expressed as a percentage.

7.3 Results

Results are presented in the following tables and graphs:

Table 1: Complete breakdown of true positive colonoscopies and false negative colonoscopies from 2006 - 2013

Year of Investigation	True Positive Colonoscopies	False Negative Colonoscopies
2006	39	1
2007	574	13
2008	1683	43
2009	2314	56
2010	3195	70
2011	3433	35
2012	3311	14
2013	3027	0

Table 2: PCCRC Results by year of colonoscopy (2006-2010) with 3 years follow up

Year of Colonoscopy	True Positive Colonoscopies	False Negative Colonoscopies	To year end	PCCRC Rate
2006	39	1	2009	2.50%
2007	574	7	2010	1.20%
2008	1683	36	2011	2.09%
2009	2314	53	2012	2.24%
2010	3195	70	2013	2.14%
Total	**7805**	**167**		**2.09%**

Graph 1:

PCCRC % 2006-2010 with 3 years follow up

Graph 2:

PCCRC Rate over time in English NHS BCSP with 3 years follow up
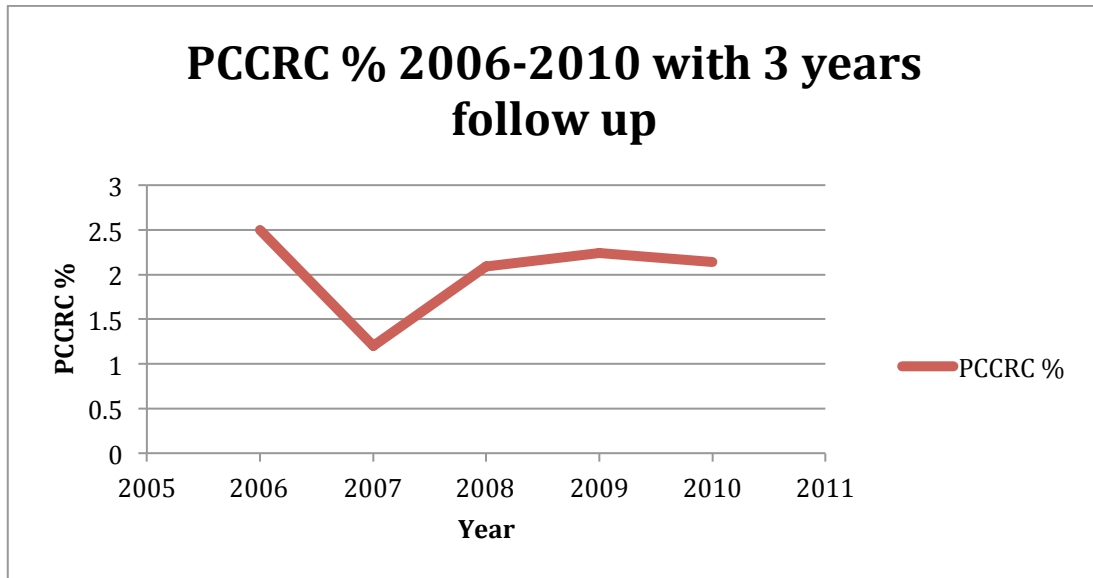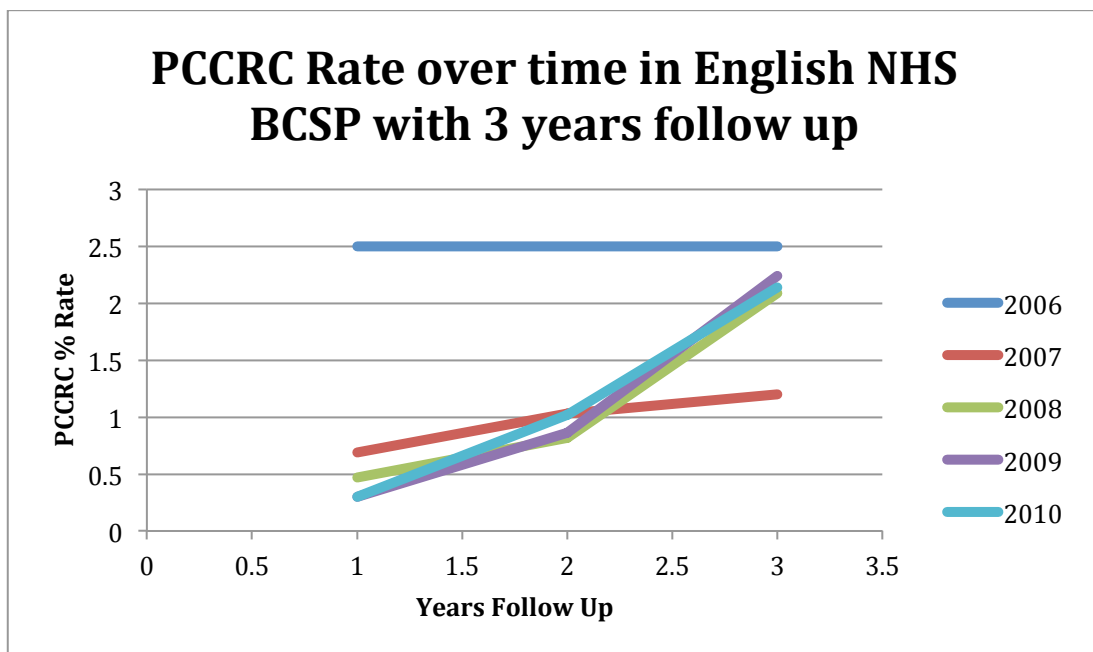
7.4 Discussion

Table 1 shows the complete breakdown of true positive and false negative colonoscopies during this study period. However, this table cannot be used to calculate PCCRC rate as different periods of follow up are in use following the false negative colonoscopy. For example, the period of follow up after the false negative colonoscopy in 2006 would be seven years whereas for 2012 it would be one year. The table shows how the number of false negative colonoscopies starts to decrease after 2011 as there hasn't been sufficient time allowed for the colorectal cancers to present after the false negative colonoscopy takes place.

Table 2 and graph 1 presents this data uniformly, as for each year rate is calculated with a three year period of follow up after the false negative colonoscopy. This gives an overall PCCRC rate of 2.09%. When examining the annual rate calculation, the numbers of false negative colonoscopies in 2006 and 2007 are small and therefore it is difficult to draw any firm conclusions from them. However, having increased from 2007, PCCRC rate plateaus at over 2% from the years 2008 – 2010. This, perhaps, gives a more accurate representation of PCCRC rate.

Graph 2 allows visualisation of when post colonoscopy colorectal cancers are presenting following the false negative colonoscopy. Again, because of the small number of false negative colonoscopies, one in 2006 and seven in 2007, it is difficult to draw any conclusions from the data for these two years. However, from 2008 to 2010 there is a steady increase to 2 years follow up then a much

sharper rise to 3 years follow up, suggesting most PCCRCs present 2 to 3 years

following the false negative colonoscopy.

It is important to point out that the overall figure of 2.09% underestimates

PCCRC rate as it doesn't include data from interval cancers that have presented

symptomatically external to the BCSP. This was a major limitation of the study in

this chapter. However, despite the omission of this data this figure is still lower

than the PCCRC rate of 8.6% reported by Morris et al. from cancers presenting

symptomatically in England from 2001 to 2007. Indeed in Morris et al's study

annual rate fell year on year from 10.2% in 2001 to 6.2% in 2007, perhaps

reflecting an improvement in colonoscopy quality during this time[126]. The figure

of 6.2% is perhaps most relevant to the data in this chapter in terms of the

similar time scale involved. Despite the rates reported in this chapter not seeing

the year on year decrease in PCCRC rate and the annual rate remaining fairly

static at between 2.09 – 2.24%, even with the addition of data from interval

cancers, I would expect PCCRC rate to be below the 6.2% reported by Morris et

al. from 2007. This could be interpreted as showing a higher level of quality and

safety to BCSP colonoscopy when compared with the symptomatic service in

England[126].

It is difficult to compare my results with other studies published globally

reporting PCCRC rate as most have used different formulae to calculate rate

involving using cancers as opposed to colonoscopies in the denominator. Morris

et al. showed how PCCRC rate can vary when applying their dataset to methods

used by Singh et al., Cooper et al., Bressler et al. and Le Clerq et al. hence proving

the point that clarity and consistency of methodology is paramount when researching PCCRC[126 153 134 131 129]. Further population based studies using this methodology for PCCRC rate calculation are required before a fair comparison can be made with the data in this chapter.

7.5 Conclusions

As a result of this study the English NHS BCSP can now report to patients attending for colonoscopy that the chances of the colonoscopy missing or not preventing against the development of cancer is approximately 2%. When considering PCCRC as an adverse event this is an important measure of quality and safety in the programme.

The PCCRC rate of 2.09% reported in this chapter under reports the true rate because of a lack of data on interval cancers. Even with the addition of interval cancer data the true rate is likely to be lower than that seen in the symptomatic service in England.

Chapter 8

Discussion & Conclusions

8.1 Overall Headlines

My first intention in writing this thesis was to determine the frequency with which patients invited for colonoscopy in the English NHS BCSP suffer from colonoscopic adverse events. This thesis has reported that the rate of perforation at 0.06% and of post polypectomy bleeding (PPB) at 0.44% per colonoscopy and 0.23% per polypectomy respectively is similar to other reported rates of these adverse events worldwide and reflects favourably on the safety of the programme. Similarly, a BCSP only post colonoscopy colorectal cancer rate of 2.09% is lower than that reported from colorectal cancers presenting symptomatically in England, using the methodology of PCCRC calculation used in this thesis, and again reflects a reassuringly low compromise of patient safety.

Despite the comparably good rates of adverse events found, it is important to consider the impact of the adverse event on the patient involved. Indeed this was the second theme I intended to examine in this thesis. In the perforation study, one patient died, a post perforation mortality rate of 0.87%. A death, even if it is just one, from a screening investigation is disappointing for any screening programme and this needs to be highlighted. It is also important to recognise that nearly all of the patients who had a perforation were admitted to hospital. Over half of those admitted to hospital had surgery, over a quarter were

admitted to the intensive care unit and over a quarter left hospital with a stoma. One fifth of those with a perforation developed a complication or new diagnosis while in hospital.

The data from this study gives us a complete perspective on the impact a perforation has on a patient and the extent to which patient safety may be compromised in the BCSP. It appears that the poorer sequelae of perforation is much greater than that of PPB. Despite the need for hospital admission and even surgery in one patient with PPB in my study, there were no deaths or complications associated with this adverse event.

Uniquely, I have also been able to explore the impact of the adverse event, in the form of a perforation, on the health care professional who performs the colonoscopy. This thesis reports the substantial physical and psychological impact on the professional and the effect on their personal and professional lives. It highlights the importance of considering and supporting the professional, as well as the patient, in the aftermath of an adverse event.

A third intention of this thesis was to identify risk factors for adverse events so that the risk of them occurring in the future could be minimised. The study of perforations in chapter 4, although not specifically reporting risk factors for a perforation, has nevertheless shown that diagnostic perforations are significantly associated with the need for surgery and therefore post perforation morbidity. It also showed that perforations in the sigmoid colon are significantly associated with stoma formation. The one death that occurred was following a

diagnostic perforation in the sigmoid colon. This work shows, therefore, the type of perforation that is high-risk for poorer patient outcomes. From chapter 5 of this thesis we now have qualitative evidence to add to the quantitative data reviewed in chapter 2.5 that the caecum is a high-risk colorectal location for perforation. Chapter 5 has also shown that human factors such as fatigue and expectation along with environmental factors such as time and equipment problems may contribute to perforation.

A further intention of this thesis was to improve the assessment and management of adverse events so that patients have the best possible outcomes when they do occur. When considering the first of the adverse events studied, perforation, we now have an evidence base that shows which patients have the best outcomes. Those patients that did not have surgery and were managed endoscopically and/or medically avoided both intensive care admission and post perforation morbidity. If the endoscopist visualised a perforation, the application of endoclips resulted in the patient not having surgery in the majority of cases, although the data didn't reach statistical significance when this outcome was measured. Where the visualised perforation was < 5mm in size, this was associated with the patient not having surgery, although, again the association did not reach statistical significance. When considering the presence of abdominal pain, those patients complaining of abdominal pain at presentation were significantly more likely to have surgery. Similarly, when measuring initial pulse rate and respiratory rate, a pulse rate greater than 100 beats per minute and a respiratory rate greater than 20 breaths per minute were both significantly associated with the patient having surgery. This suggests that the

absence of abdominal pain, a normal pulse rate of 60-100 beats per minute and a respiratory rate of less than or equal to 20 breaths per minute may be indicators for successful medical management, especially in the presence of a visualised perforation of less than 5mm where an endoclip had been applied. This work has also shown that the majority of perforations will present within the first 48 hours post procedure. This has implications for our communication with patients in the aftermath of colonoscopy. Likewise, this statement also applies to PPB; the majority of cases of PPB also presenting within 48 hours.

The final intention of writing this thesis has been achieved by providing a reference point that all colonoscopists can use and relate to. This reference point involves not only how to minimise their patients adverse event risk, improve their patients' adverse event assessment and management but is also a reference as to how they, the colonoscopist, may feel in the aftermath of an adverse event. The four stages of reaction of the colonoscopist described in chapter 5, *'The Realisation', 'Into the Mirror', 'Acceptance and Refocus' and 'Reflection and Learning'* is an important headline of this work that I hope all colonoscopists will find useful should they encounter an adverse event in the future

8.2 Implications of findings

The low rates of the adverse events that I have studied in this thesis reassure us that colonoscopy is performed safely in the English National Health Service Bowel Cancer Screening Programme. The benefits of colorectal cancer screening

described in chapter 2.3 of this thesis, therefore continue to outweigh any compromise of patient safety that I have found doing this work.

I hope that the findings of this thesis will influence future patient care surrounding colonoscopy and colonoscopic adverse events. When considering the implications of my findings we must first consider how the risk of the adverse events I have studied can be minimised. With regards to colonoscopic perforation, as a result of quantitative data added to by qualitative data from this thesis, colonoscopist caution when in the caecum and sigmoid colon is urged. The qualitative evidence suggests that colonoscopists are much more cautious when performing therapy in the caecum and one colonoscopist now routinely applies endoclips to the polypectomy site following any endoscopic mucosal resection of polyps in the caecum. Likewise caution is urged during intubation of the sigmoid colon, especially in the presence of diverticular disease and during loop resolution, as these are likely to be the main causes of diagnostic perforations in the sigmoid colon. Colonoscopists may wish to take these recommendations on board in their future practice. The identification from qualitative data of specific human and environmental factors associated with perforation means that colonoscopists may wish to keep such associations in mind when performing colonoscopy.

The second main implication of this work relates to how to improve the assessment and management of adverse events so that patients have the best possible outcome. As a result of this work the focus following a perforation should be trying to ensure that patient is managed endoscopically and/or

medically and doesn't have surgery. Of course, this may not be possible depending on the clinical situation that evolves post perforation. However, my recommendation, as a result of the work in chapter 4, is that all colonoscopists should attempt to close a perforation with endoclips when the perforation is visualised. Attempts should then be made to treat the patient with traditional medical management of intravenous fluids, antibiotics and bowel rest, especially in the context of the absence of abdominal pain, a normal pulse rate of 60-100 beats per minute and a respiratory rate of less than 20 breaths per minute. My qualitative data has, uniquely, showed that a large part of implicating such management plans is not just about informing clinicians about these findings. It is about how we communicate with patients and each other in the aftermath of a colonoscopy and from whom patients seek medical attention should they develop symptoms following a colonoscopy. The qualitative data specifically reported how two medical endoscopists felt

'angry', 'disappointed' (C4) and *'upset'* (C8)

at not being involved in decisions relating to patient's subsequent care. In both cases the patient was under the care of surgeons and not them. This had led one to now always give his mobile telephone number to the patient following a high risk colonoscopy and polypectomy procedure asking them to call him, and him only, if there was a problem or symptom suggestive of perforation. The reason being so the patient is assessed and managed by the appropriate person and doesn't needlessly have surgery where medical management only may have been more appropriate. This provides a useful guide as to how communication with

patients and their understanding of who to seek help from may improve their outcome. While it may be inappropriate to expect all colonoscopists to offer such a service, indeed few may wish to do so, potentially at least the discussion of such a patient's case with an on call endoscopist or the colonoscopist who performed the procedure may prevent unnecessary surgical intervention and hence, as we now know form the quantitative data in this thesis, the poorer post perforation outcomes that are associated with it.

Currently, all patients who have colonoscopy are contacted by telephone at 24 hours post procedure by Specialist Screening Practitioners (SSPs) who attend each procedure. From the quantative data reported in chapter 4 and 6 we are now aware that that the majority of perforations and post polypectomy bleeds present within the first 48 hours post procedure. It may be better, therefore, for contact to be made with patients at 48 hours post procedure. For the reasons described earlier in this chapter, the lines of communication being through the SSP and therefore remaining within the BCSP may result in the patient being reviewed by the appropriate professional and their outcome improved.

A third implication of my work focuses on the colonoscopists themselves. I hope this work will prepare those colonoscopists who have yet to experience a perforation for how they may feel. This work also aims to aid the passage of the colonoscopist through the stages of physical and psychological response reported in chapter 5. All screening colonoscopists in the English NHS BCSP should be assigned a mentor to oversee their colonoscopic performance and provide both endoscopic and psychological support when required. In the light

of the data in chapter 5, the role that the mentor may have in the aftermath of an adverse event takes on added importance. Indeed, I would recommend that all independent colonoscopists be assigned a mentor but particularly junior colonoscopists and nurse colonoscopists. The support of colleagues whether they are a mentor or otherwise is vital in aiding the colonoscopist through the stages of response. Therefore, colleagues or the mentor should be prepared to take over the endoscopy list where the adverse event occurs and even their colleagues subsequent endoscopy lists. They should also offer and be prepared to discuss the case with the colonoscopist involved. It is hoped such actions would help the colonoscopist through the stages of response to the adverse event.

The biggest impact I am hopeful that this work will have, however, is in aiding and developing a culture of openness surrounding adverse events among not only colonoscopists but also other health care professionals more generally. This culture is also in the context of how such experiences are communicated with the public. The qualitative study in chapter 5, more than any other, may go a long way to achieving this. Over the last 9 years of working as a registered medical practitioner in the National Health Service I have been aware of a hesitancy of health care professionals to discuss mistakes, complications and adverse events amongst themselves. Too often, openly discussing such events may be perceived as showing a sign of weakness or inadequacy amongst colleagues both junior and senior. Others may seize upon such events for the purposes of gossip or mockery. From the many local, regional, national and international educational events I have attended, I can rarely remember anyone talking about an adverse

event they had been involved with or a mistake they had made, in the way the colonoscopists did in chapter 5 of this thesis, as a point of learning. I also find this point interesting when considering it in the context of endoscopy, gastroenterology and surgery as specialties and the professionals who work in them. One of the nurse endoscopists interviewed in chapter 5 made reference to

'macho stuff' (C11)

among colonoscopists in her department. I suspect, because of the practical and visual nature of endoscopy, it is a competitive specialty with colonoscopists eager to continually prove and display their skill level to others. Discussion of adverse events is probably difficult for most professionals at the best of times but may be more so amongst colonoscopists in this environment. I also feel this leads onto another important point about communication. My feeling is the same nurse endoscopist who said

'maybe they don't feel comfortable talking about emotions' (C11)

is probably right. I would agree that a lot of professionals, but again particularly in the endoscopic environment, are reluctant to talk about emotions and feelings surrounding events at work; it is, perhaps, something we should do more of. I hope these are points that I can bring out in my own future practice and I now feel well placed to encourage others to do so. Furthermore, I feel well placed to support others if needs be in this context. It is potentially a niche area I would like to develop in my future career.

There are also implications for how the experience of such events is communicated with the public, particularly when they accept the invitation to have a colonoscopy as part of the BCSP. Patients and their relatives will always want to be in the hands of a health care professional who is 'good' at their job; a professional whom they can trust without having to think about it[154]. Clinical and ethical integrity, safety, up-to-date medical knowledge, diagnostic skill, sound judgement and an ability to form a good relationship are all characteristics that may form part of what the public would want from the professional looking after them[155]. The desire for these characteristics may be heightened in the context of a screening programme such as the BCSP. From this, there may come a desire from the public for such professionals to be explicit about adverse events that have occurred in their career so they can make an informed decision about who performs their colonoscopy. Whether this would come in the form of a conversation during the consent process or from freely available data to look at online is open to debate, but patients may want to see this evidence for themselves and expect that this is part of the BCSP service.

8.3 Limitations of research methods

The retrospective observational case series of colonoscopic perforations had several limitations. Initially, this study was dependent on the details of the perforations that had occurred in the BCSP being entered by Bowel Cancer Screening Centres (BCSCs) into the Bowel Cancer Screening System. The BCSP has a robust system for capturing the details of any adverse event, but there may

have been some perforations that were missed by BCSCs in which case they would have been missing from this study. Similarly, I did not receive a response to our online questionnaire for 30 of 147 patients in this study. Reasons for this included no response to emails, notes being unavailable to be reviewed and the patient's admission occurring at a trust outside the BCSC. While I am confident, from the findings reported in chapter 4.3.2.3, that the limited data I obtained for these 30 patients from the BCSS did not skew the findings in the 117 patients in whom a response had been received, it is possible that data from these patients could have added further weight to my findings. Collecting data retrospectively from contemporaneous notes, as was done in this study, will always have limitations in terms of what data is available and how it has been documented. While some of the data in this study will have been collected from endoscopy reports, which for the most part are entered in a standardised form into endoscopy reporting systems, most of it will have come from medical case notes. These notes are made in a free text format. The questionnaire attempted to account for this, however, there are gaps in the data collected when it was unclear from the notes if the specific question could be answered definitively either way.

Different health care professionals within the BCSP completed the questionnaire. Although the questionnaire was designed to so as not to cause any ambiguity, some of the questions may have been misinterpreted by those completing it. Also, when reviewing data in contemporaneous medical notes, such data may be open to misinterpretation by those reviewing it. My own experience of reading medical case notes tells me that notes are kept to varying standards and

occasionally vital information can be omitted or be incorrect. This, again, may have influenced the quality of data received in this study. Human error may too have limited the data received from the questionnaire if those completing it transferred it from case notes incorrectly.

There were also limitations in how data was collected for the retrospective observational case series of PPB. For the reasons specified above, there may have been cases of PPB that were not initially reported to the BCSCs. Therefore no 'adverse event alert to national office' would have been completed and they would have been excluded from both bowel cancer screening records and this study. The data for this study was taken from these forms, which had implications for the study on several levels. The forms were not necessarily completed to a uniform standard and key data may have been omitted. Also, some of the variables for which data would have aided the study or allowed new avenues of exploration were not necessarily asked for on the form and therefore couldn't be analysed. This meant that, unlike the questionnaire used in the perforation study, I could not ask for specific data relating to post polypectomy bleeds but had to use what had already been entered onto the 'adverse event alert to national office' form. The other main limitation of this study was that it was a regional rather than national study, which resulted in fewer numbers of patients being included in the study. The explanatory variables that were explored as predictors of need for endoscopic therapy and of the more severe PPB subgroups may therefore have lacked the statistical power required to produce any significant results.

The one obvious and unfortunate constraint of the retrospective observational case control study of post colonoscopy colorectal cancer was the lack of data from interval cancers. The data used in this study related to those PCCRCs that had been diagnosed within and not external to the BCSP. Therefore, those cancers that had presented symptomatically outside the BCSP were not included in this study. Because of delays in the linkage of two national databases, the Bowel Cancer Screening System and the National Cancer Data Repository, which was needed for this study, I could not access this data in the allotted time in which this thesis was written. The actual rates of PCCRC are, therefore, likely to be higher than those reported in chapter 7, however, it is impossible to predict by how much this would be. I also had no data specifically relating to outcomes following the diagnosis of a PCCRC. Being able to assess the rates of surgery, morbidity and mortality would have given a more complete picture of the impact of PCCRC.

Despite the data produced from the interviews reported in chapter 5, perhaps one limitation that could be labelled at this study is that eleven interviews is a small number of interviews. This point is more pertinent when considering the difference in reaction between the three specialties of colonoscopist that were interviewed; only one surgeon was interviewed. The eleven interviews is a smaller study than others reviewed in chapter 2.8. However, as with all qualitative interview based studies, it is the point at which data saturation is reached when recruitment for participants ceases. After eleven interviews I had reached a point of data saturation. It is also important to consider the context of the study and where it was performed. Invitations to take part were only

extended to those consultant gastroenterologists and bowel cancer screening colonoscopists within Health Education North East. We have to consider that not all of these colonoscopists would have experienced a perforation associated with a colonoscopy they performed, and those that had may not wish to discuss such an emotive experience with a doctor in training from the region with whom they may have worked with or will work in the future. As this study recruited from just one region of England, the experiences and abilities of those colonoscopists may have been similar. Recruiting participants nationally or internationally may have resulted in broader range of experience surrounding perforation though this has to considered within the time, travel and cost constraints this study was performed under.

8.4 Reflections

I feel this work will be of benefit to all colonoscopists in not only their professional life but also potentially in their personal life should they encounter an adverse event. This is especially the case for those colonoscopists who work within the English National Health Service Bowel Cancer Screening Programme whose work the quantitative data directly relates to. I also hope that, in time, at least one adverse event can be avoided as a result of this work. If the adverse event cannot be avoided then I hope that the patient involved will have a better outcome than would have otherwise been the case. The work in this thesis will then have been worthwhile, not only to other colonoscopists, but to the patients themselves.

From a personal point of view I feel this work has aided my knowledge, skills and behaviour in several ways. Writing chapter 2 of this thesis allowed me to develop my ability to review and critically appraise medical literature. I have developed a much greater understanding of both quantitative and qualitative health research methods and of basic statistics.

I now have a much greater knowledge and understanding of screening programmes for colorectal cancer, colonoscopy and colonoscopic adverse events. Furthermore, my knowledge and understanding of colonoscopic perforation, post polypectomy bleeding and post colonoscopy colorectal cancer is now at such a level that I feel well placed to not only reduce my own colonoscopic adverse event risk and manage such patients in my own practice but also advise others of how to do so. Distinctively, this work has led me to have a much deeper understanding of what a colonoscopist my experience following an adverse event. I feel uniquely placed to be able to support colleagues who experience such events and, as reported in chapter 8.2, would like to do so in my future career.

There is a further personal element to this work. I have yet to experience a perforation, post polypectomy bleed or post colonoscopy colorectal cancer in my own colonoscopic practice. I suspect this work will help me for when, inevitably, this does occur; the degree to which it helps me will be interesting to see for those around me. Coupled with this, I hope writing this thesis does not make me too conservative to be an effective colonoscopist. I have already felt a heightened anxiety when, for example, performing polypectomy in the caecum or when

intubating an acutely angled, fixed sigmoid colon with multiple diverticulae. As we now know from the study in chapter 5, part of being a successful colonoscopist is accommodating to the fact that adverse events are inevitable. Conversely, the examination of adverse events in this thesis could have the opposite effect. I am now so aware the adverse events occur and what is required should one that it may, psychologically at least, seamlessly become part of my future practice.

8.5 Conclusions

This thesis has achieved all the intentions I had wanted to achieve in writing it. We can now be confident that colonoscopy is performed safely in the English National Health Service Bowel Cancer Screening Programme and the compromise of patient safety is minimal. The frequency with which adverse events occur is low and in line with other data published globally when colonoscopy is performed on a similar scale. Reassuringly, this means that the benefit the programme confers far outweighs the potential risks.

There is now a more complete picture of the impact that adverse events have both on the patients involved and the colonoscopists. Despite the low rates of adverse events found, we should be mindful of the potential need for in patient hospital admission, surgery, morbidity and mortality all of which may be associated with colonoscopic adverse events. This data gives both us as health care professionals and patients a greater insight into the risks and benefits of screening for colorectal cancer. It allows patients to make a much more informed

decision when they are invited to take part bowel cancer screening. Likewise, the BCSP can now be much more mindful of the effect an adverse event may have on the colonoscopist involved, what they may require and what should be offered to them in its aftermath.

From both quantitative and qualitative data, this work has identified risk factors for adverse events and risk factors associated with poorer outcomes following adverse events. The risk of these adverse events both occurring and the poorer outcomes associated with them may therefore be minimised. We also now have an evidence base for improving the assessment and management of these adverse events so that patients have the best possible outcomes for when they do occur.

The final intention of writing this thesis has been achieved in providing a reference point to all colonoscopists to use in their professional and personal lives should they encounter an adverse event in the future.

It is important to reinforce how to implement the findings of this work. The mixed methodology used in this thesis has showed that presenting quantitative data will only achieve so much. It is how health care professionals communicate with patients, each other and take on board human and environmental factors that will result in us minimising risk and improving the management of colonoscopic adverse events.

8.6 Recommendations for future research

Much of the recent research surrounding colonoscopic perforation has focused on either the endoscopic methods of closing perforations or on minimally invasive surgical techniques for doing so. It is clear from this thesis that avoiding surgery results in better outcomes for patients. Therefore, the development of techniques to close perforations without the patient requiring anything outside the confines of that procedure or that endoscopy room is paramount. I suspect further studies in the near future will continue to develop the use of endoscopic suturing devices and 'over the scope clip' devices as the primary methods of endoscopic repair. The prophylactic use of endoscopic clips following high risk therapeutic procedures, for example EMR of polyps > 2cm in the caecum, may also be an area that warrants further examination when comparing the outcomes of similar procedures that don't use endoclips prophylactically. Prospective data relating to indicators for non surgical management of perforations would add weight to the findings in this thesis, particularly with regards to the presence of abdominal pain, the patient's respiratory rate and pulse rate.

The prophylactic placement of endoclips for minimising risk of Post PPB is also an area for future research, again this would be when comparing their use in high risk therapeutic procedures against procedures where no endoclips are left in situ. An area identified for further research from the study in chapter 7 is how to predict those patients with post polypectomy bleeding that will require therapeutic intervention following representation with bleeding. The two variables that were explored as predictors of this in my study did not show any

statistical association. A larger case series may help reach greater statistical power, but data on other variables such as pulse and blood pressure at presentation or the volume of blood that was lost per rectum may provide the answer.

Post colonoscopy colorectal cancer is currently a topical area of colonoscopy research as an indicator of colonoscopy quality assurance. I hope soon to add data from interval cancers to the data that is presented in chapter 7 so as to give a complete figure for PCCRC rates in the BCSP. While we are aware of five mechanisms that contribute to PCCRC development, it is exploring the differences between PCCRC and non-PCCRC cancer that is likely to be the major force contributing to future research surrounding it. While risk factors for missing cancers and pre malignant adenomas at initial colonoscopy have been identified, it is the factors such as the biology of PCCRCs, that may contribute to the development of rapidly growing or de novo colorectal cancers that will be the focus in the prevention of these cancers in the future.

Chapter 9

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Chapter 10

Appendix

Appendix 1 – Questionnaire for study of perforations

1. What is the patient's unique subject identifier? :   _ _ _ _ _ _ _ _

Medication

2. Was the patient taking an anti coagulant or anti platelet at the time of the colonoscopy that resulted in the perforation?

Yes □
No □
Unknown □

3. If yes, please specify the name(s) and dose(s):_____

4. Was the patient taking steroids at the time of the colonoscopy that resulted in the perforation?

Yes □
No □
Unknown □

5. If yes, please specify the name(s) and dose(s):_____

Colonoscopy Report

6. Where in the colon was the perforation?

Caecum □
Ascending Colon □
Splenic flexure □
Transverse Colon □
Hepatic flexure □
Descending Colon □
Sigmoid Colon □
Rectum □
Unknown □

If unknown, proceed to question 16

7. At the location specified in question 6, did therapy to a polyp cause the perforation?

Yes □

No □
Unknown □

If no or unknown, proceed to question 12
8. What was the polyp class?

Sessile □
Pedunculated □
Semi Pedunculated □
Flat □
Flat - completely flat (IIb) □
Flat – slightly elevated (IIa) □
Flat – Laterally Spreading Type Granualr (LST-G) □
Other (specify):
Unknown □

9. What was the estimated endoscopic size of the polyp?

＿ ＿ millimetres

10. What therapy was applied to the polyp?

Biopsy □
Polypectomy □
Endoscopic Mucosal Resection (EMR) □
Endoscopic Submucosal Dissection (ESD) □
Submucosal Lift □
Tattooing □
Tissue Destruction □
Haemostatic technique □
Other (specify):
Unknown □

11. What was the polyp therapy device?

Cold Biopsy □
Cold Snare □
Hot Biopsy □
Hot Snare □
Injection □
Argon Beam □
Laser □
Endoscopic Knife □
Other (specify):
Unknown □

12. At the colorectal location specified in question 6, was there any pathology other than polyps?

Yes □
No □
Unknown □

13. If yes, please specify the pathology:_____

14. At the colorectal location specified in question 6, did any therapy take place other than that to polyps?

Yes □
No □
Unknown □

15. If yes, please specify the therapy:_____

16. Did the endoscopist recognise there was a perforation during this colonoscopy?

Yes □
No □
Unknown □

If no or unknown, proceed to question 22

17. How did the endoscopist recognise there was a perforation during this colonoscopy?

Visualisation of extra intestinal structure □
Visualisation of tear in serosa □
Unknown □
Other (specify):_____

18. Was the perforation recognised at the site specified in question 6?

Yes □
No □

19. What was the size of the perforation?

_ _ millimetres

Unknown □

20. Was an attempt to close the perforation with an endoclip made during this colonoscopy?

Yes □
No □

21. How many endoclips were used? __ __

22. Was a CT scan performed immediately following the completion of the colonoscopy?
Yes □
No □
Unknown □

If no or unknown, proceed to question 26

23. Why was the CT scan requested?

Patient had abdominal pain □
Patient had back pain □
Patient had abdominal distension □
Patient had abnormal observations □
Endoscopist visualised extra intestinal structure □
Endoscopist visualised tear in the serosa □
Endoscopist clinically suspected a perforation □
Staging CT scan □
Unknown □
Other (specify):

24. Did the CT scan show evidence of a perforation?

Yes □
No □
Unknown □

25. If yes, please specify the result:_____
_____
_____
_____
_____
_____
_____
_____

26. Was the patient discharged or admitted to hospital following completion of the colonoscopy?

Discharged □

If discharged, please proceed to question 27

Admitted □

If admitted, please proceed to question 29

Presentation following readmission to hospital

27. On what date did the patient present with symptoms from the perforation?

Date (dd/mm/yyyy): _ _ / _ _ / _ _ _ _

28. At what time did the patient present with symptoms from the perforation?

Time (hh:mm):   _ _ : _ _

Presenting symptoms and initial observations

29. What was the presenting symptom(s)?

Abdominal Pain □
Back Pain □
Abdominal Distension □
Unknown □
Other (specify):

30. What was the patient's first recorded temperature following admission?

_ _ °C

31. What was the patient's first recorded pulse rate following admission?

_ _ _ beats per minute

32. What was the patient's first recorded blood pressure following admission?

_ _ _ / _ _ _ mmHg

33. What was the patient's first recorded respiratory rate following admission?

_ _ per minute

Initial Management

34. Was the patient kept Nil By Mouth?

Yes □
No □
Unknown □

If no or unknown, proceed to question 37

35. On what date was the Nil By Mouth started?

Date (dd/mm/yyyy):   _ _ / _ _ / _ _ _ _

36. At what time was Nil By Mouth started?

Time (hh:mm):   _ _ : _ _
37. Was the patient given intravenous fluids?

Yes □
No □
Unknown □

If no or unknown, proceed to 40

38. On what date were intravenous fluids started?

Date (dd/mm/yyyy):   _ _ / _ _ / _ _ _ _

39. At what time were intravenous fluids started?

Time (hh:mm):   _ _ : _ _

40. Was the patient given antibiotics?

Yes □
No □
Unknown □

If no or unknown, proceed to question 43

41. On what date were the antibiotics started?

Date (dd/mm/yyyy):   _ _ / _ _ / _ _ _ _

42. At what time were the antibiotics started?

Time (hh:mm):   _ _ : _ _

Initial Investigations

43. Did the patient have an erect chest x-ray?

Yes □
No □
Unknown □

If no or unknown, proceed to question 48

44. On what date was the chest x-ray performed ? (dd/mm/yyyy)

_ _ / _ _ / _ _ _ _

45. What was the Chest X-Ray result?

Normal □
Air under the diaphragm □
Unknown □
Other □

If other, specify the result: _____

46. Was any clinical action taken as a result of the chest x-ray?

Yes □
No □
Unknown □

If no or unknown, proceed to question 48

47. What was the clinical action?

Specify the clinical action: _____
_____

48. Did the patient have an abdominal x-ray?

Yes □
No □
Unknown □

If no or unknown, proceed to 53

49. On what date was the abdominal x-ray performed? (dd/mm/yyyy)

_ _ / _ _ / _ _ _ _

50. What was the abdominal x-ray result?

Normal □
Free air in the abdomen □
Unknown □
Other □

If other, specify the result: _____

51. Was any clinical action taken as a result of the abdominal x-ray?

Yes □
No □
Unknown □

If no or unknown, proceed to question 53

52. What was the clinical action?

Specify the clinical action: _____
_____

53. Did the patient have a CT scan following admission to hospital but not immediately following completion of the colonoscopy?

Yes □
No □
Unknown □

If no or unknown proceed to question 58

54. On what date was the CT scan performed ? (dd/mm/yyyy)

_ _ / _ _ / _ _ _ _

55. What was the CT scan result?

Specify the result: _____
_____
_____
_____
_____
_____
_____
_____

56. Was any clinical action taken as a result of the CT scan?

Yes □
No □
Unknown □

If no or unknown, proceed to question 58

57. What was the clinical action?

Specify the clinical action:_____
_____

58. Did the patient have surgery?

Yes □

If yes, proceed to question 59

No ☐

If no, proceed to question 69

Surgery

59. On what date was the operation performed?

Operation date (dd/mm/yyyy):   _ _ / _ _ / _ _ _ _

60. At what time did the operation start?

Operation time (hh:mm):   _ _ : _ _

61. Was the operation completed in normal working hours? (Monday – Friday, 08:00–17:00)

Yes ☐
No ☐
Unknown ☐

62. What was the primary surgeon grade?

Consultant Surgeon ☐
Surgical Registrar ☐
Surgical Staff Grade ☐
Other Surgical trainee ☐
Unknown ☐

63. What was the primary surgeon specialty?

Colorectal surgeon ☐
Non colorectal surgeon ☐
Unknown ☐

64. Was the operation a laparoscopy or an open laparotomy?

Laparoscopy ☐
Open Laparotomy ☐
Laparoscopy converted to open laparotomy ☐
Unknown ☐

65. What operation was performed?

Simple closure of perforation ☐
Colonic resection with anastomosis ☐

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66. Did the operation result in a stoma?

Yes □
No □
Unknown □

67. What was the name of the operation?

Specify operation name:_____
Unknown □

68. Were there any postoperative complications?

Yes □
No □
Unknown □

If no or unknown, proceed to question 70

69. If yes, what were the postoperative complications and when did they occur?

Complication (1):   _____

Date (dd/mm/yyyy):   _ _ /_ _ /_ _ _ _

Complication (2):   _____

Date (dd/mm/yyyy):   _ _ /_ _ /_ _ _ _

Complication (3):   _____

Date (dd/mm/yyyy):   _ _ /_ _ /_ _ _ _

Complication (4):   _____

Date (dd/mm/yyyy):   _ _ /_ _ /_ _ _ _

Complication (5):   _____

Date (dd/mm/yyyy):   _ _ /_ _ /_ _ _ _

Outcomes

70. Was the patient admitted to the Intensive Care Unit/High Dependency Unit?

Yes □
No □

71. If yes to question 70, how many nights were spent on HDU/ITU? _ _ _ nights

72. On what date was the patient admitted to a general ward? (dd/mm/yyyy):

_ _ / _ _ / _ _ _ _

73. Did the patient develop any new diagnoses during their inpatient stay?

Yes □
No □
Unknown □

If no or unknown, proceed to 75

74. If yes, what were the new diagnoses and when did they occur?

New diagnosis (1):   _____

Date (dd/mm/yyyy):   _ _ / _ _ / _ _ _ _

New diagnosis (2):   _____

Date (dd/mm/yyyy):   _ _ / _ _ / _ _ _ _

New diagnosis (3):   _____

Date (dd/mm/yyyy):   _ _ / _ _ / _ _ _ _

New diagnosis (4):   _____

Date (dd/mm/yyyy):   _ _ / _ _ / _ _ _ _

New diagnosis (5):   _____

Date (dd/mm/yyyy):   _ _ / _ _ / _ _ _ _

75. Did the patient die during this in patient admission?

Yes □
No □

76. If yes to question 75, on what date was the death confirmed? (dd/mm/yyyy):

_ _ / _ _ / _ _ _ _

77. If yes to question 75, what was the cause of death on the patient's death certificate?

1a _____

1b _____

1c _____

11_____

78. If no to question 75 , on what date was the patient discharged from hospital?

(dd/mm/yyyy):

_ _ / _ _ / _ _ _ _

Free Text/Route Cause Analysis

79. Please enter any other details that you feel may be relevant to this case.

80. If a Route Cause Analysis took place for this case, please attach an anoymised copy**.**

Appendix 2 – Letter sent to BCSP screening centres for study of perforations

NHS
Cancer Screening Programmes

June 2014

Colonic perforations in the BCSP

Dear Bowel Cancer Screening Centre Director,

The Bowel Cancer Screening Evaluation Group is reviewing all BCSP-related colonic perforations, capturing details of the potential cause, presentation, management and outcome. This is important so that we can fully understand the implications and outcomes of this complication.

Where possible, we have captured data directly from BCSS. However, additional information is required and we are asking each centre to provide this on a pseudo-anonymised online form. We estimate that it will take approximately 30 minutes to complete the form for each perforation – this will require patient case notes and clinical experience in case note review – you might find it preferable to identify a specialist registrar to do this in conjunction with a member of the BCSP team.

In order to complete the form, please follow the steps described below:

1. We need to send you patient-identifiable information listing each perforation from your centre. We can only do this to & from an <u>nhs.net</u> email address. **If you have not received this email to an nhs.net email address, please reply directly to this email within the next 2 weeks with an nhs.net email address that we can use**.

2. You will then receive an email to your nhs.net email account from the email address <u>edmundderbyshire@nhs.net</u> listing the NHS number(s) of the perforation case(s) from your centre. Next to each NHS number you will see a unique 'subject identifier'. This is required to complete the form.

3. You will then receive an email to your nhs.net email account from the email address <u>edmundderbyshire@nhs.net</u> containing a link to the online form. The form will remain open for 4 weeks after you receive this email. Therefore, we recommend requesting the case notes as soon as you receive the details.

We are particularly interested in those subjects with a sub clinical CT detected colonic perforation. This relates to patients in whom incidental radiological evidence of a colonic perforation was found. Questions 22 -25 in the form specifically relate to these patients.

We do appreciate that this creates additional work for your team. Wherever possible the BCSP Evaluation Group tries to avoid this, but in this case BCSS doesn't capture the level of detail that we require.

Many thanks in anticipation.

Yours Sincerely,

Professor Matt Rutter   Professor Julietta Patnick
BCSP Evaluation Group Chair   Director, NHS Cancer Screening Programme

Appendix 3 – Invitation letter for 'Colonoscopists narratives of a colonoscopy associated with a colorectal perforation'

Dear Northern Deanery Colleague,

Re: Colonoscopists narratives of a colonoscopy associated with a colorectal perforation

This is an open invitation to all fully accredited colonoscopists working in the Northern Deanery.

I am a research and endoscopy fellow in the School of Medicine, Pharmacy & Health, Durham University and at North Tees & Hartlepool NHS Foundation Trust being supervised by Matt Rutter and Pali Hungin.

As part of my work on colonoscopic adverse events, we would like to invite you to take part in a brief interview study surrounding colonoscopic perforaton.

The study aims to explore how colonoscopists react to performing a colonoscopy associated with a colorectal perforation and to identify human & environmental factors that may be associated with colonoscopic perforation.

If you have performed a colonoscopy that resulted in a colorectal perforation and would be willing to discuss your experiences around the case during a brief, anonymised, voice recorded, face-to-face interview with myself, please reply directly to the email address edmundderbyshire@nhs.net so that I can provide you with some more detailed information about the study.

The study has had full ethical approval by the Durham University School of Medicine, Pharmacy & Health Ethics Committee.

Please pass this invitation on to any colleagues you feel may also be interested.

Many Thanks,

Edmund Derbyshire
Research Postgraduate in the School of Medicine, Pharmacy & Health
Durham University
Endoscopy Fellow
North Tees & Hartlepool NHS Foundation Trust

Appendix 4 – Interview Guide for 'Colonoscopists Narratives of a colonoscopy associated with a perforation'

Participant Demographics

1. Age
2. Sex
3. Specialty of Endoscopist: Gastroenterologist
 Physician (specialty other than gastroenterology)
 Surgeon
 Nurse Endoscopist
 GP Endoscopist

Colonoscopy Experience

4. Years of experience in colonoscopy
5. Approximate number of colonoscopies performed to date
6. Approximate number of colonoscopies performed before perforation
7. How confident were you were to perform this procedure/polypectomy?
8. How confident were you in your training to perform this procedure/polypectomy?

Event Details

9. When was the perforation case?
10. Was there anything unusual about the day of the case?
11. Did you feel different to normal on the day of the case?
12. Were there any unusual circumstances surrounding the case on that day?

13. Would you tell me about the case that resulted in the perforation?
14. What specifically caused the perforation?

Immediate Reaction

15. How did you feel after you realised there was a perforation? How did you react to the perforation?
16. Did your feelings change?
17. What happened to the patient?
18. How did you feel about what happened to the patient?

Professional and Personal Reaction

18. How did you react personally?
19. Did you receive personal support?
20. What personal support would you recommend for others in this situation?

21. How did you react professionally?
22. Did you receive professional support?

23. What professional support would you recommend for others in this situation?

Subsequent Practice

24. Has the perforation case changed your subsequent practice?
25. Has your endoscopic technique changed as a result of this perforation?
26. Would you approach the same clinical scenario differently now?