CONTENTS

This Issue in the Journal
4 A summary of the original articles featured in this issue

Editorial
7 Dealing with colorectal cancer in New Zealand
James M Church

Original Articles

11 Continued progress with stage III colorectal cancer—a triple cohort study
Michael Lim, Prashant Sharma, Andrew Ing, Heidi Blackburne, Bridget Robinson, Liane Dixon, Chris Frampton, Frank Frizelle

25 Colonoscopy audit over 10 years—what can be learnt?
Alan G Fraser, Greg D Gamble, Toby R Rose, John P Dunn

36 The diagnostic yield of colonoscopy in patients with isolated abdominal pain
Shaw Hua Kueh, Lifeng Zhou, Russell S Walmsley

45 A novel pathway for investigation of colorectal symptoms with colonoscopy or computed tomography colonography
Andrew D Sanders, Clark Stevenson, John Pearson, Michael Burt, Graham McGech, Ben Hudson, Tim W Eglinton

58 Perceived risks and benefits of surveillance colonoscopy in people undergoing surveillance for family history of colorectal cancer
Gregory P Tarr, Rebecca A Smith, Rhys A John, Andrew P Crowley, Jonathan B C Kok, Ho-Nam Lee, Mohd Hasif B Mustafa, Kia M Sii, Sung-Eun Son, Lauren J Weaver, Claire Cameron, John D Dockerty, Iain A Murray, Michael Schultz

70 Immunochemistry screening for Lynch syndrome in colorectal adenocarcinoma using an initial two antibody panel can replace a four antibody panel
Toni O’Regan, Kai Chau, Michael Tatton, Tania Smith, Susan Parry, Ian Bissett

78 Pathological reporting of malignant colorectal polyps
Chris Gillespie, Arend Merrie, Ian Bissett

87 Carbon dioxide insufflation during colonoscopy: a randomised controlled trial
Anne Cleland, Jenny Carreyer, Steve La Grow
95  Symptom presentations and other characteristics of colorectal cancer patients and the diagnostic performance of the Auckland Regional Grading Criteria for Suspected Colorectal Cancer in the South Auckland population
   John C Hsiang, Wayne Bai, Dinesh Lal

Clinical Correspondence

108  Medical image. An unusual case of granulomatous inflammation of the rectum
   Nicholas J Fischer

111  Medical image. Dementia due to atrophy in the anterior part of the brain
   Sayed Mahdi Marashi, Mohammad Majidi, Mehran Sadeghian, Zeynab Nasri-Nasabadi

Letters

113  A New Zealand doctor visits a Syrian refugee camp in Iraqi Kurdistan
   Karina Cooper

116  Gout—is adequate attention devoted to preventing haemorrhagic risk when benzbromarone is administered with warfarin?
   Lance Gravatt

118  Gout—is Lee’s 2008 risk:benefit conclusion for benzbromarone hepatotoxicity still relevant today?
   Lance Gravatt

120  New urate-lowering therapies in Aotearoa New Zealand: a response to Dr Lance Gravatt's letter on benzbromarone hepatotoxicity
   Nicola Dalbeth, Peter Gow, Lisa Stamp, Tony Merriman, Raoul Stuart, Doone Winnard, Karen Lindsay; for the New Zealand Rheumatology Association and the Māori Gout Action Group

124  Benzbromarone: availability for general prescribing in New Zealand (a response to letters by Dr Lance Gravatt on benzbromarone)
   Richard Day, Hugo Lee, Garry Graham, Kenneth Williams

127  A house call
   Roger M Ridley-Smith

129  Recognition of burns as a marker of child abuse in the paediatric emergency department
   Aisling R Geoghegan

132  Response to NZMJ editorial by Dr Elana Curtis entitled Deserving of more: framing of Māori inequities in cardiovascular care remain a challenge
   Harvey White, Tom Kai Ming Wang, Tharumenthiran Ramanathan, Ralph Stewart
HIV screening in New Zealand: time for a change  
_Nick Gow, Simon Briggs, Judy Gilmour, Rupert Handy, Rebecca Henley, Joan Ingram, Chris Kenedi, Michele Lowe, Susan Mundt, Mitzi Nisbet, Stephen Ritchie, Mark Thomas_

100 Years Ago in the NZMJ
137 The Increase of Cancer in New Zealand (part 2)

Methuselah
138 Selected excerpts from Methuselah

Obituaries
140 Donald Stewart Malcolm
143 Thakshan Lal Udayamitta Fernando
This Issue in the Journal

Continued progress with stage III colorectal cancer—a triple cohort study
Michael Lim, Prashant Sharma, Andrew Ing, Heidi Blackburne, Bridget Robinson, Liane Dixon, Chris Frampton, Frank Frizelle

In this large study of over 1000 patients from Christchurch, New Zealand, survival outcomes from the treatment of colorectal cancer have continued to improve with time. Numerous factors have contributed to this observation—it is thought to be due to greater subspecialisation of surgeons and more involvement of cancer specialists and better use of chemotherapy.

Colonoscopy audit over 10 years—what can be learnt?
Alan G Fraser, Greg D Gamble, Toby R Rose, John P Dunn

Withdrawal time is the time taken to examine the bowel once insertion has been completed. This is the key time for polyp detection as the endoscopist is often more focused on technical issues during insertion. The majority of bowel cancers develop from polyps—therefore identification and removal of polyps can prevent the formation of cancer. Colonoscopy has been proven to prevent bowel cancer but the extent of this effect is dependent on having a quality examination with removal of all polyps. The recognised completion point for colonoscopy is the caecum—the end of the colon. Most endoscopists would consider that continuing on into the end of the small bowel—the terminal ileum—is also important. Completion rates to both landmarks are a useful quality indicator. Completion is important to identify all polyps but is also a marker of technical expertise.

The diagnostic yield of colonoscopy in patients with isolated abdominal pain
Shaw-Hua Kueh, Li Feng Zhou, Russell S Walmsley

Patients with abdominal pain with no other associated symptoms or significant medical history and previously normal investigations prior to referral for colonoscopy accounted for 1.2% of total colonoscopies performed at Waitemata District Health Board. Among these patients, bowel cancer was found in 3.3% which was significantly less than those with iron deficiency anaemia or overt rectal bleeding. When segregated by age, among those younger than 50, no difference in bowel cancer was found between those with abdominal pain, iron deficiency anaemia and overt rectal bleeding. Therefore in patients with isolated abdominal pain, particularly those younger than 50, colonoscopy should not be considered as first line of investigation.
A novel pathway for investigation of colorectal symptoms with colonoscopy or computed tomography colonography
Andrew D Sanders, Clark Stevenson, John Pearson, Michael Burt, Graham McGeoch, Ben Hudson, Tim W Eglinton

The Canterbury District Health Board recently developed the Canterbury Colorectal Symptom Pathway (CCrSP) to attempt to improve prioritisation using a combination of presenting clinical features integrated into a scoring tool. This study describes that pathway and its outcomes over a 6-month period. Some 1369 procedures were performed during the study period. Of the symptomatic patients, 38 colorectal cancers (CRC) were diagnosed from 633 colonoscopies and 253 CT colonographies. Individual factors predictive for CRC were rectal bleeding, iron deficiency anaemia and positive faecal occult blood test. No CRCs were diagnosed in the group scoring below the pre-set threshold for investigation. The CCrSP pathway was accurate for predicting CRC and offers a reliable triage tool.

Perceived risks and benefits of surveillance colonoscopy in people undergoing surveillance for family history of colorectal cancer
Gregory P Tarr, Rebecca A Smith, Rhys A John, Andrew P Crowley, Jonathan B C Kok, Ho-Nam Lee, Mohd Hasif B Mustafa, Kia M Sii, Sung-Eun Son, Lauren J Weaver, Claire Cameron, John D Dockerty, Iain A Murray, Michael Schultz

We conducted a standardised phone interview of 250 randomly selected people who had undergone surveillance colonoscopy at Dunedin Hospital and assessed their ideas of colonoscopy effectiveness, complication rates, and CRC risk. Our results suggest current surveillance education adequately communicates risks and benefits to most patients. A minority have unrealistic views and further education may be indicated.

Immunochemistry screening for Lynch syndrome in colorectal adenocarcinoma using an initial two antibody panel can replace a four antibody panel
Toni O’Regan, Kai Chau, Michael Tatton, Tania Smith, Susan Parry, Ian Bissett

Our study looked at using a two antibody screening test rather than the currently used four antibodies to test for Lynch syndrome (an inherited form of colorectal cancer). The reason this is viable is due to the binding properties of the different mismatch repair or cancer protectant genes that are faulty in Lynch syndrome. Our study confirmed the findings of two previous studies, which suggests that you can screen with two antibodies and still identify 100% of the effected individuals.
Pathological reporting of malignant colorectal polyps
Chris Gillespie, Arend Merrie, Ian Bissett

It has been recognised recently that if a pathologist uses a structured format rather than freetext for their report on cancer resection specimens, the report is more likely to contain all the relevant information required for clinical decision making for the patient. In April 2013 this format for reporting of cancer specimens by pathologists became mandatory in New Zealand. However there is currently no standardised report format for small cancers of the colon arising in polyps (called malignant polyps). This paper shows that if a structured report format is used for malignant polyps, the report is more likely to be complete, and in the case of malignant polyps this is particularly important in dictating whether the patient requires an operation for their malignant polyp or not.

Carbon dioxide insufflation during colonoscopy: a randomised controlled trial
Anne Cleland, Jenny Carryer, Steve La Grow

A randomised, double-blinded, controlled trial with 205 consented patients referred for elective colonoscopy was undertaken at MidCentral Health Gastroenterology Department. Patients were randomised to either air or carbon dioxide. A comparison of pain was undertaken. Those receiving carbon dioxide during colonoscopy experienced less post colonoscopy pain than those who received air insufflation. Carbon dioxide should be considered as the insufflating gas during colonoscopy.

Symptom presentations and other characteristics of colorectal cancer patients and the diagnostic performance of the Auckland Regional Grading Criteria for Suspected Colorectal Cancer in the South Auckland population
John C Hsiang, Wayne Bai, Dinesh Lal

Cancer of the bowel is a common cancer in New Zealand. While bleeding from the rectum and change in bowel habit can be an important symptom of bowel cancer, persistent pain in the abdomen and weight loss should also warrant check up by a doctor as a minority of patients with bowel cancer may have these symptoms only.
Dealing with colorectal cancer in New Zealand

James M Church

This issue of the *New Zealand Medical Journal* features articles about various aspects of colorectal cancer, from screening to diagnosis and treatment. While the disease remains a scourge of the Western World, there is evidence of progress in the way healthcare providers strategize against it.

Colorectal cancer is potentially preventable. Indeed, the adenoma-carcinoma sequence and the average lag phase of 10 years between polyp and cancer offer ample opportunity to remove the premalignant lesion.

Times are changing however. Recently the effectiveness of screening colonoscopy has been questioned, and these questions have provoked an increasing emphasis on colonoscopy quality. In addition, flat adenomas and sessile serrated adenomas/polyps are now recognised as likely causes of interval cancers. Knowledge of the molecular biology of colorectal cancer is impacting clinical care, with tumours now being tested to detect the underlying molecular mechanisms giving rise to the cancer.

All of these issues are touched on in this edition of the *Journal*. However underlying them is the situation that exists in New Zealand, where limited resources must be husbanded and prioritised and where the ideal approach to minimising the impact of a disease is both unaffordable and impractical.

The aim of colorectal cancer screening is the early detection of cancers, assuming that this will lead to more effective treatment. Large studies using guaiac-based occult blood tests have confirmed this assumption, although long-term follow-up shows that the benefits may not last.

Faecal immunochemical testing is considerably more sensitive than guaiac-based tests, and promises to be a practical approach in New Zealand if the barriers of poor patient compliance and lack of access to colonoscopy can be overcome.

Colonoscopy is the only test that provides prevention as well as early detection, but is impractical for population screening. Rather its main use is to diagnose symptoms, and here Kueh et al, in this issue of the *Journal*, confirm that not all abdominal symptoms have the same significance in diagnosing cancer. In fact, abdominal pain is common, and usually due to functional disorders such as constipation or irritable bowel syndrome.

Sanders et al, also in this issue of the *Journal*, report the development of a symptom and family history derived score that predicts likelihood of cancer. Such complex scoring systems are never user friendly however, and a common-sense approach to symptoms based on knowledge of colorectal pathophysiology is likely to be just as effective.

Good clinical acumen is required to triage patients according to the details of their history. The principle of prioritising appointments for diagnostic colonoscopy is appropriate however, when colonoscopy slots are in high demand.
Colonoscopy is also important for screening high-risk patients, where the chances of finding a premalignant polyp are higher than average. The main groups at high risk are those with a family history or a personal history of colorectal neoplasia.

Tarr et al report encouraging data on the level of knowledge of patients with a family history of colorectal cancer and their acceptance of colonoscopy as a screening test. Such a high level of patient “buy in” is unusual and promising.

Identification of the ultimate high-risk families, those with Lynch syndrome, is facilitated by tumour testing for evidence of defective DNA mismatch repair. The most cost-effective way is to perform immunohistochemical stains for mismatch repair proteins on resected cancer specimens.

The paper by O’Regan et al shows that the practice of limiting analysis to the minor partner in each of the two protein pairs involved will detect most mutator tumours. However they do not pursue the test to its conclusion by excluding cancers with loss of MLH1 due to promoter methylation, nor do they provide the results of germline sequencing of the incriminated gene. These are important steps as identifying Lynch syndrome not only helps the management of the proband, but offers the opportunity to screen relatives, with a potentially huge impact on the well-being of the family.

Other papers in this issue focus on details of colonoscopy performance. It is important that colonoscopy quality standards are set and promulgated, and Fraser et al have performed a comprehensive quality audit over a significant length of time. Their study should represent the best in New Zealand endoscopy, involving experienced consultants and patients away from the public system. Their data show improvement over time in quality indicators such as caecal intubation rate, time of withdrawal and polyp detection, although the lack of adenoma detection rate rather weakens the conclusions that can be drawn from the data. However neither adenoma nor polyp detection are really the point of colonoscopy.

The point is to detect or prevent cancer, or perhaps advanced adenomas as a surrogate for cancer. Unfortunately there are no data to show how well this is done. Also missing are data on complication rates, surely a central data point when discussing quality.

Another colonoscopy study in this issue of the Journal concerns the use of carbon dioxide as an insufflation gas for colonoscopy. While this is not an original idea it confirms the value of using a gas that is readily absorbed across the mucosa of the colon, thus avoiding colonic distension. Unfortunately the authors missed an opportunity to look at other endpoints such as adenoma detection rate. If a colonoscopist is not concerned about painful post colonoscopy colonic distension, he/she can blow the colon up and perhaps obtain better views.

Perhaps the most important contribution in this edition is that from Lim et al, who report the outcome of colon and rectal cancer treatment in a retrospective study of 1091 patients from three different time periods. This is important, because in the absence of a national colonoscopic screening programme, colorectal cancer will happen. It may be diagnosed early by faecal occult blood testing but it may also present at a more advanced stage with symptoms.
Hsiang et al show that this is especially likely to occur in Māori and Polynesian communities, a particular cause for concern.\textsuperscript{13} Even in Lim’s study, over half of all patients presented with stage III or IV disease. The primary treatment of colorectal cancer is surgical and many studies have shown that, particularly with rectal cancer, the surgeon influences oncologic outcomes.

Lim’s data show a trend to increasing participation of consultants as the primary surgeon, and to increasing involvement with medical oncologists and radiation therapists, especially for rectal cancers. While there is marked improvement in cancer specific survival in patients with stage III disease when the early cohort is compared to the more recent cohorts, data on local recurrence, perhaps the most sensitive indicator of quality of treatment, are lacking.

The absolute values for cancer-specific survival suggest that there is scope for further improvement, although the entire patient population is elderly (with a mean age of 76 years).

New Zealand faces a difficult problem in colorectal cancer. This is not new. In 1988 I wrote a lead article in the \textit{New Zealand Medical Journal} entitled \textit{Large bowel cancer in New Zealand}.\textsuperscript{14} While the fundamental issues raised in that article have not changed in 25 years, it is encouraging to see recent progress.

The need for a centralised approach to the disease has been answered by the Government in setting up the Bowel Cancer Programme in 2009, and the call for increased public awareness has been answered by the patients themselves who started “Beat Bowel Cancer Aotearoa” in 2010. However, the conclusions of this editorial are still the same as the conclusions of the lead article written 25 years ago:

- Population colonoscopic screening is not possible and so prevention will not occur.
- Early detection is the best that can be hoped for but even this is not currently available on a programmatic level.
- New Zealanders must rely on family practitioner-based faecal occult blood screening, on accurate family histories to determine level of risk, and on prioritisation of what colonoscopy slots are available to screen those at high risk.

Newer thoughts focus on healthcare personnel and the potential of faecal DNA testing.\textsuperscript{15} When colorectal cancer happens, experienced specialists must captain the ship, with a crew that includes oncologists, pathologists and radiation therapists.

Rectal cancer is a special case, where experience and expertise is paramount and treatment by a small cadre of experts in a multidisciplinary clinic is the way to go. For colonoscopy screening, the potential role of nurse endoscopists may be an answer to lack of qualified physician colonoscopists.\textsuperscript{16,17}

Finally, collecting and reporting data, and searching for new solutions to old problems, is key to the future, and is highlighted by this issue of the \textit{Journal}.

**Competing interests:** Dr Church has no conflict of interest related to this work.
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References:

Continued progress with stage III colorectal cancer—a triple cohort study

Michael Lim, Prashant Sharma, Andrew Ing, Heidi Blackburne, Bridget Robinson, Liane Dixon, Chris Frampton, Frank Frizelle

Abstract

**Introduction** Colorectal cancer is a common cause of death in New Zealand and its burden is projected to increase in the future. Oncological outcomes from modern treatment have improved, but evidence from the published literature is conflicting. We studied survival outcomes from a series of patients at our local health board.

**Methods** A retrospective analysis of disease patterns, surgical procedures, adjuvant therapy and oncological outcomes was performed in three patient cohorts; January 1993–December 1994, January 1998–June 1999, and January 2004–December 2005 at Christchurch Hospital. Univariate, multivariate and Kaplan-Meier survival analysis was performed to identify differences between the three cohorts.

**Results** There were 1091 patients [(355, 317, 419 per cohort, 808 colon (281,227,300) and 283 rectal (74,90,119)] with cancer over the 3 cohorts. Median age was 76 (IQR 67-84) years. Median follow-up was 44 (IQR 13-81) months. For both colon and rectal cancer, patients in later cohorts had early disease, were more likely to have the operation performed by a consultant, were more likely to be referred for an oncological opinion and were more likely to receive adjuvant treatment (p<0.05 respectively) Differences in survival were particularly marked in the later cohort of patients with Stage III colonic cancer.

**Discussion** There have been significant improvements in oncological outcome with stage three colon and rectal cancer over the study period. Greater specialisation of surgeons, more operations by consultants and use of chemotherapy are all likely contributing factors.

Colorectal cancer (CRC) is a major health problem in New Zealand as it is the second most common cause of cancer death. The incidence increases with age, with more than 250 cases reported per 100,000 patients in those above the age of 75.1

Recent projections by the Ministry of Health suggest that the burden of patients with new colorectal cancer is likely to increase by 15% in males and 19% in females over the next 5 years.2

The mortality in New Zealand from colorectal cancer has improved steadily between 1998 and 2009. Five year cumulative survival ratios for adults with colorectal cancer were 0.578 in 1998 and 1999; this increased to 0.618 in 2008 and 2009.3

Although initial reports over a 15-year period from New Zealand4 in 1999 and Western Australia5 in 2000 suggested no improvement in survival outcome for patients with colorectal cancer, subsequent reports from Adelaide6 and the rest of...
Europe suggest improvements in survival outcome with later cohorts of patients for both colon and rectal cancer. 7-13

In the last decade, the introduction of colorectal cancer screening, earlier diagnosis, specialisation by colorectal surgeons, and advances in chemotherapy for early and metastatic disease, and radiation for rectal cancer would all be expected to improve survival outcome.

The aim of this study is to review the management and audit the outcome of three cohorts of patients with CRC treated at Christchurch Hospital, New Zealand. We have previously published a comparative audit data for two cohorts of patients with colorectal cancer14 and this study is an update with a third cohort.

The aim of this retrospective analysis was to document differences in disease characteristics and management, and to identify trends in survival between the three cohorts of patients.

Methods

Patients—This retrospective study was performed over a 17-year period with three study cohorts. Cohort 1 consists of patients who received the primary diagnosis of adenocarcinoma of the colon or rectum between January 1993 and December 1994; Cohort 2 between January 1998 and June 1999; and Cohort 3 between January 2004 and December 2005.

The patient population was followed for 5 years. Patients with CRC were located from the database in the Oncology Service and the Christchurch Hospital discharge codes (ICD 9 codes). This was cross-checked with the histology database in the Christchurch Hospital Pathology Department.

All patients with colorectal cancer who had surgery were included in the study, irrespective of method of presentation (i.e. acute/elective), except in the first cohort (1993–94) that was studied. Patients who did not have surgery were not included when this data was first collected for the study published in 2005.14 Christchurch has one public and two private (St. Georges and Southern Cross) hospitals.

Patients were eligible for the study if they had their primary surgery at Christchurch Hospital or if they were referred to Christchurch Hospital by a Christchurch surgeon for consideration of adjuvant or palliative therapy.

Thus, patients having surgery by a private surgeon in Christchurch, but who were not referred to the Oncology Service, were not included. Patients were excluded if the primary site was not confirmed as the colon or rectum.

Diagnosis—It was our standard policy for patients to have preoperative colonoscopy and biopsy for purposes of diagnosis. All patients with colonic and rectal cancer had a chest X-Ray and CT Scan of the abdomen and pelvis for purposes of preoperative staging.

In those patients who presented as emergency, preoperative histology would not have been possible but imaging for purposes of staging would have been performed.

Patients with rectal cancers had lesions with a maximum distance of 15 cm from the anal verge. These patients were not routinely staged with preoperative MRI in our study population. However, all patients with suspected metastatic disease on preoperative imaging underwent further investigations to confirm or refute the presence of distant disease. Multidisciplinary team meetings were introduced in March 2005.

Variables—Patient demographics were collected from hospital notes. Disease variables such as tumour location, tumour type, grade and stage of cancer were obtained from final histopathology reports.

Tumour stage was classified according to the Dukes and AJCC TNM system.14 All operative procedures, grade of surgeon and use of permanent stomas were recorded.

Data on method of presentation was not consistently recorded within the database; hence analysis of outcomes based upon this variable was subsequently not performed.
Follow-up—It was our policy for patients to be monitored closely for complications in the immediate postoperative period. Perioperative complications included any complication within 30 days of the primary surgery.

Patients who were discharged from hospital were routinely reviewed by clinicians within a month. From 2002 onwards, follow-up was done by a nurse-led clinic using a standard protocol. All patients would be seen and examined 3 monthly for the first year, and 6 monthly thereafter for a total of 5 years.

During each consultation, blood test would be performed for a CEA level. A colonoscopy would be performed at 1 and 5 years after surgery to exclude disease recurrence and metachronous lesions. Likewise CT Scans of the abdomen, chest and pelvis would be performed at 1 and 5 years to exclude metastatic disease. All deaths were recorded.

Cause of death was determined by case note review. Those patients who died from cancer related causes (primary, recurrent or metastatic) were coded as cancer-related deaths. Those patients who died from other causes (medical) were coded as non cancer-related deaths. This allowed us to determine the overall survival and cancer-specific survival in our study population.

Statistics—All information was stored, and updated with a Microsoft Access database. Data was exported to an SPSS programme for statistical analysis. The data was found to be parametric using the Kolmogorov-Smirnov test. Categorical data were analysed with the Chi-Square test, continuous data with the Student’s t-test. Significant variables were entered into a logistic regression model for multivariate analysis. Kaplan-Meier survival curves were constructed and the log-rank test was used to determine survival differences. A p-value of less than 0.05 was considered significant.

Results

Patients—There were 1091 patients with colorectal cancer over the three cohorts. There were 355, 317 and 419 patients respectively for each of the cohorts. 808 patients had colonic cancer; the remaining 283 patients had rectal cancer. Median age was 76 (IQR 67–84) years. Median follow-up was 44 (IQR 13–81) months.

Cohort analysis for colonic cancer—Table 1 shows the variables that were studied in the three cohorts of patients. A greater proportion of patients have had their surgery performed by a consultant in the later cohorts.

A smaller proportion of patient in the later cohorts had permanent stomas. Interestingly, a greater proportion of patients in the later cohorts had well differentiated tumours, however lymphovascular invasion was more prevalent.

A greater proportion of patients had early disease (Dukes A and B) in the 2004 cohort; however there were also more patients with metastatic disease (Dukes D) when compared with previous cohort of 1998–99.

Patients in the later cohorts were much more likely to be referred for an oncological opinion and were more likely to receive adjuvant chemotherapy. Twenty-eight percent of patients from the 2004 cohort received adjuvant chemotherapy compared to 8% of patients in the 1993 cohort. The use of adjuvant radiotherapy did not differ between the cohorts.
Table 1. Details of study population for all colonic cancer patients

<table>
<thead>
<tr>
<th>Variables</th>
<th>Group cohort (Number (%))</th>
<th>1993/94 cohort (n=281)</th>
<th>1998/99 cohort (n=227)</th>
<th>2004/05 cohort (n=300)</th>
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</tr>
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<td>6 (2)</td>
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<tr>
<td>transverse colon</td>
<td>25 (9)</td>
<td>30 (13)</td>
<td>28 (10)</td>
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</tr>
<tr>
<td>splenic flexure</td>
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<td>15 (7)</td>
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<tr>
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<td>19 (7)</td>
<td>12 (5)</td>
<td>15 (5)</td>
<td></td>
<td></td>
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<tr>
<td>sigmoid colon</td>
<td>98 (35)</td>
<td>75 (34)</td>
<td>95 (32)</td>
<td></td>
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<td>rectosigmoid junction</td>
<td>35 (12)</td>
<td>16 (7)</td>
<td>19 (6)</td>
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<td><strong>Dukes stage</strong></td>
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<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>A</td>
<td>16 (6)</td>
<td>18 (7)</td>
<td>33 (12)</td>
<td></td>
<td>0.001</td>
</tr>
<tr>
<td>B</td>
<td>106 (43)</td>
<td>92 (41)</td>
<td>101 (36)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>C</td>
<td>117 (47)</td>
<td>74 (33)</td>
<td>78 (27)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>D</td>
<td>8 (4)</td>
<td>42 (19)</td>
<td>72 (25)</td>
<td></td>
<td></td>
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<td><strong>T stage</strong></td>
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</tr>
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<tr>
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<td>25 (10)</td>
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<td>120 (56)</td>
<td>132 (52)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>100 (40)</td>
<td>64 (30)</td>
<td>80 (31)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>N stage</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>170 (68)</td>
<td>111 (53)</td>
<td>143 (56)</td>
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</tr>
<tr>
<td>1</td>
<td>56 (22)</td>
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<td>65 (25)</td>
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</tr>
<tr>
<td>2</td>
<td>23 (10)</td>
<td>45 (21)</td>
<td>48 (19)</td>
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<td></td>
</tr>
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<td><strong>M stage</strong></td>
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<td></td>
<td></td>
<td></td>
<td>0.055</td>
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<tr>
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<td>205 (75)</td>
<td>184 (81)</td>
<td>162 (72)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>69 (25)</td>
<td>42 (19)</td>
<td>63 (28)</td>
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<td></td>
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<td><strong>Differentiation</strong></td>
<td></td>
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</tr>
<tr>
<td>well</td>
<td>1 (1)</td>
<td>5 (3)</td>
<td>31 (14)</td>
<td></td>
<td>0.001</td>
</tr>
<tr>
<td>moderate</td>
<td>104 (89)</td>
<td>189 (84)</td>
<td>133 (60)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>poor</td>
<td>12 (10)</td>
<td>21 (9)</td>
<td>56 (25)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>unknown</td>
<td>0 (0)</td>
<td>10 (4)</td>
<td>3 (1)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Referral to oncology</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>no</td>
<td>190 (68)</td>
<td>140 (62)</td>
<td>134 (45)</td>
<td></td>
<td>0.011</td>
</tr>
<tr>
<td>yes</td>
<td>91 (32)</td>
<td>87 (38)</td>
<td>166 (55)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Adjuvant chemotherapy</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>no</td>
<td>259 (92)</td>
<td>186 (82)</td>
<td>215 (72)</td>
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</tr>
<tr>
<td>yes</td>
<td>22 (8)</td>
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<td>85 (28)</td>
<td></td>
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<td><strong>Adjuvant radiotherapy</strong></td>
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<td></td>
<td></td>
<td></td>
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</tr>
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<td>219 (96)</td>
<td>292 (97)</td>
<td></td>
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<td>4 (1)</td>
<td>8 (4)</td>
<td>8 (3)</td>
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<td></td>
</tr>
</tbody>
</table>

#Data on patients who did not have surgery was not collected for the 1993–1994 cohort.
Cohort analysis for rectal cancer—Table 2 shows the variables that were studied in the three cohorts of patients. A greater proportion of patients with rectal cancer presented with metastatic disease (Dukes D) in the 2004 cohort. The advanced disease at time of presentation precluded one-quarter of all patients with rectal cancer from having curative surgery.

In the later cohorts, a greater proportion of rectal cancer surgery was performed by the consultant grade. The rates of permanent stoma formation were significantly lower in later cohorts although the proportion of anterior resections over abdominoperineal resections did not differ.

The majority of cancers were moderately well differentiated and this did not appear to vary with time. In contrast to patients with colonic cancers, the incidence of lymphovascular invasion was lower in subsequent cohorts of patients.

A greater proportion of patients were referred for an oncological opinion, with up to three quarter of patients from the 2004 cohort. A greater proportion of patients from the later cohorts received adjuvant chemotherapy after surgery for their rectal cancer when compared with earlier cohorts. (49% in 2004 vs. 4% in 1993, p-value=0.001). Similar trends were noted with regards to use of adjuvant radiotherapy in the later cohort of patients.

Table 2. Details of study population for all rectal cancer patients

<table>
<thead>
<tr>
<th>Variables</th>
<th>Group cohort (Number (%))</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1993/94 cohort (n=74)</td>
<td>1998/99 cohort (n=90)</td>
</tr>
<tr>
<td>Procedure</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No surgery</td>
<td>41 (55)</td>
<td>43 (48)</td>
</tr>
<tr>
<td>Anterior resection</td>
<td>8 (11)</td>
<td>10 (11)</td>
</tr>
<tr>
<td>Hartmann's APER</td>
<td>25 (34)</td>
<td>20 (22)</td>
</tr>
<tr>
<td>Permanent stoma</td>
<td></td>
<td></td>
</tr>
<tr>
<td>no</td>
<td>37 (50)</td>
<td>57 (63)</td>
</tr>
<tr>
<td>yes</td>
<td>37 (50)</td>
<td>33 (37)</td>
</tr>
<tr>
<td>Surgeon</td>
<td></td>
<td></td>
</tr>
<tr>
<td>consultant</td>
<td>41 (55)</td>
<td>85 (94)</td>
</tr>
<tr>
<td>registrar supervised</td>
<td>16 (22)</td>
<td>3 (3)</td>
</tr>
<tr>
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</tr>
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<td>12 (16)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Type</td>
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<td></td>
</tr>
<tr>
<td>adenocarcinoma</td>
<td>64 (86)</td>
<td>84 (93)</td>
</tr>
<tr>
<td>mucinous</td>
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<td>5 (6)</td>
</tr>
<tr>
<td>carcinoid</td>
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<td>0 (0)</td>
</tr>
<tr>
<td>unknown</td>
<td>4 (6)</td>
<td>1 (1)</td>
</tr>
<tr>
<td>Lymphovascular invasion</td>
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<td></td>
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<tr>
<td>no</td>
<td>46 (62)</td>
<td>62 (68)</td>
</tr>
<tr>
<td>yes</td>
<td>28 (38)</td>
<td>28 (32)</td>
</tr>
<tr>
<td>Dukes stage</td>
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<td></td>
</tr>
<tr>
<td>A</td>
<td>10 (17)</td>
<td>17 (20)</td>
</tr>
<tr>
<td>B</td>
<td>21 (36)</td>
<td>24 (28)</td>
</tr>
<tr>
<td>C</td>
<td>27 (46)</td>
<td>35 (41)</td>
</tr>
<tr>
<td>D</td>
<td>1 (1)</td>
<td>10 (11)</td>
</tr>
<tr>
<td>T stage</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>6 (10)</td>
<td>8 (10)</td>
</tr>
<tr>
<td>2</td>
<td>10 (17)</td>
<td>23 (29)</td>
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<tr>
<td>3</td>
<td>33 (56)</td>
<td>40 (49)</td>
</tr>
<tr>
<td>4</td>
<td>10 (17)</td>
<td>10 (12)</td>
</tr>
</tbody>
</table>
Variables | Group cohort (Number (%)) | P-value |
--- | --- | --- |
N stage | | | 0.001 |
| 1993/94 | 1998/99 | 2004/05 |
| cohort | cohort | cohort |
| (n=74) | (n=90) | (n=119) |
| 0 | 26 (38) | 41 (52) | 51 (52) |
| 1 | 32 (46) | 20 (25) | 34 (34) |
| 2 | 11 (16) | 18 (23) | 14 (14) |

M stage | | | 0.015 |
| 1993/94 | 1998/99 | 2004/05 |
| | | |
| cohort | cohort | cohort |
| (n=74) | (n=90) | (n=119) |
| 0 | 54 (82) | 80 (89) | 67 (72) |
| 1 | 12 (18) | 10 (11) | 26 (28) |

Differentiation | | | 0.023 |
| | | |
| 1993/94 | 1998/99 | 2004/05 |
| | | |
| cohort | cohort | cohort |
| (n=74) | (n=90) | (n=119) |
| well | 2 (10) | 2 (2) | 8 (12) |
| moderate | 15 (75) | 77 (86) | 51 (76) |
| poor | 3 (15) | 5 (6) | 8 (12) |
| unknown | 0 (0) | 6 (6) | 0 (0) |

Referral to oncology | | | 0.001 |
| | | |
| 1993/94 | 1998/99 | 2004/05 |
| | | |
| cohort | cohort | cohort |
| (n=74) | (n=90) | (n=119) |
| no | 34 (46) | 45 (50) | 31 (26) |
| yes | 40 (54) | 45 (50) | 88 (74) |

Adjuvant chemotherapy | | | 0.001 |
| | | |
| 1993/94 | 1998/99 | 2004/05 |
| | | |
| cohort | cohort | cohort |
| (n=74) | (n=90) | (n=119) |
| no | 71 (96) | 71 (79) | 61 (51) |
| yes | 3 (4) | 19 (21) | 58 (49) |

Adjuvant radiotherapy | | | 0.001 |
| | | |
| 1993/94 | 1998/99 | 2004/05 |
| | | |
| cohort | cohort | cohort |
| (n=74) | (n=90) | (n=119) |
| no | 54 (73) | 69 (77) | 61 (51) |
| yes | 20 (27) | 21 (23) | 58 (49) |

# Data on patients who did not have surgery was not collected for the 1993–1994 cohort.

Survival outcome for colonic and rectal cancer—Table 3 shows the variables that were significant on multivariate analysis for survival outcome. For colonic cancer, three variables were significant. These were lymphovascular invasion, stage of disease (Dukes classification) and presence or absence of metastatic disease. For rectal cancer, none of the variables were found to be significant on multivariate analysis.

Table 3. Multivariate analysis of cancer-specific survival for colonic and rectal cancer patients

<table>
<thead>
<tr>
<th>Variable</th>
<th>Colonic cancer</th>
<th>Rectal cancer</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cohort</td>
<td>0.886</td>
<td>0.462</td>
</tr>
<tr>
<td>Procedure</td>
<td>0.480</td>
<td>0.752</td>
</tr>
<tr>
<td>Permanent stoma</td>
<td>0.755</td>
<td>0.842</td>
</tr>
<tr>
<td>Surgeon</td>
<td>0.973</td>
<td>0.451</td>
</tr>
<tr>
<td>Type</td>
<td>0.611</td>
<td>0.392</td>
</tr>
<tr>
<td>Lymphovascular Invasion</td>
<td>0.002</td>
<td>0.114</td>
</tr>
<tr>
<td>Site</td>
<td>0.323</td>
<td>0.988</td>
</tr>
<tr>
<td>Dukes</td>
<td>0.018</td>
<td>0.504</td>
</tr>
<tr>
<td>T</td>
<td>0.238</td>
<td>0.714</td>
</tr>
<tr>
<td>N</td>
<td>0.431</td>
<td>0.272</td>
</tr>
<tr>
<td>M</td>
<td>0.007</td>
<td>0.991</td>
</tr>
<tr>
<td>Differentiation</td>
<td>0.171</td>
<td>0.594</td>
</tr>
<tr>
<td>Oncology referral</td>
<td>0.124</td>
<td>0.496</td>
</tr>
<tr>
<td>Adjuvant chemotherapy</td>
<td>0.760</td>
<td>0.092</td>
</tr>
<tr>
<td>Adjuvant radiotherapy</td>
<td>0.121</td>
<td>0.775</td>
</tr>
</tbody>
</table>

Cox Proportional Hazards Model, significant variables have a p-value less than 0.05.
Overall survival and cancer specific survival for all patients with colonic cancer stratified by the 3 cohorts are showed in Figure 1 and 2 respectively.

**Figure 1. Overall survival in colonic cancer population. Log-rank test, p=0.001**

**Figure 2. Cancer-specific survival in colonic cancer population. Log-rank test, p=0.023**
Subgroup analysis of patients with Stage III disease was performed to highlight differences in survival between the 3 cohorts of patients. This is detailed in Figure 3.

**Figure 3. Cancer-specific survival in Stage III patients with colonic cancer. Log rank test, p=0.001**

The survival curves are significantly divergent in patients with Stage III colonic cancers with improved survival in patients from later cohorts. (p-value=0.001)

Overall survival and cancer specific survival for all patients with rectal cancer stratified by the three cohorts are showed in Figure 4 and 5 respectively. Subgroup analysis of patients with Stage III rectal cancer was performed. This is detailed in Figure 6.

The survival curves from the 2004 cohort match those from the 1998 cohort and are significantly divergent from those from the 1993 cohort. (p-value=0.001)
Figure 4. Overall survival in rectal cancer population. Log-rank test p=0.53

Figure 5. Cancer-specific survival in rectal cancer population. Log-rank test, p=0.093
Figure 6. Cancer-specific survival in Stage III patients with rectal cancer. Log-rank test, \( p=0.001 \)

Discussion

This study documents the clinicopathological variables, treatment and survival outcome of three large cohorts of patients with colorectal cancer. The patients were unselected, consecutive patients referred to the regional hospital serving Christchurch and its surrounding area. The time periods were chosen to record any impact of greater site specialisation by the surgeons and the general acceptance of adjuvant chemotherapy.

For colon cancer, univariate analysis has revealed that earlier cohorts of patients were less likely to have surgery performed by consultants and were more likely to have permanent stomas compared with later cohorts. There appears to be proximal migration of tumours over a period of time with the proportion of cancers proximal to the splenic flexure increasing from 41% in the first cohort of patients to 52% in the last cohort of patients.

In terms of stage of disease, patients in later cohorts were more likely to either have early disease (Dukes A) or metastatic disease (Dukes D) at presentation compared to earlier cohorts who were either Dukes B or C. There was a stepwise increase in the proportion of patients who were referred to oncologist and this corresponded with an increase in the use of adjuvant chemotherapy.

For rectal cancer, univariate analysis revealed similar trends when compared with colonic surgery. Consultants were more likely to be the primary operator in the later cohorts. Permanent rates of stoma fell from 50 percent in the first cohort to 33 percent in the last cohort.
Interestingly rates of abdominoperineal excision of rectum were fairly consistent, with a third of low rectal cancers not amenable to sphincter preservation. This rate is marginally higher when compared with that from the United Kingdom. In the most recent national audit of bowel cancer, only 25 percent of low rectal cancers were not amenable to sphincter preservation.\textsuperscript{16}

The improvements seen in the outcome of rectal patients' cancers from the first to second cohorts has been maintained in the third cohort though not extended.

When survival analysis was performed, there were several interesting findings. Although, overall survival and cancer specific survival were significantly different between the 3 cohorts of patients with colon cancer, this factor in itself, did not remain significant on subsequent multivariate analysis.

Only the presence of lymphovascular invasion and the stage of disease (Dukes and presence of metastases) were found to be significant predictors of cancer specific survival for all patients with colonic cancer on multivariate analysis.

In patients with rectal cancer, overall survival and cancer specific survival was similar in the three cohorts of patients. On multivariate analysis, there were no useful predictors for cancer specific survival.

The theoretical impact of high quality surgery (with subspecialisation) and adjuvant chemotherapy on survival is best studied in patients with Stage III disease. This is because, patients with early disease (Stage I/II) may not necessarily come to harm from less radical surgery and would under normal circumstances, not be suitable candidates for adjuvant chemotherapy.

Likewise, patients with metastatic disease (Stage IV) are difficult to cure with surgery and chemotherapy. When analysis is confined to those with Stage III disease (the subgroup where treatment variation is most likely to affect outcome), our study shows an improvement in outcome for the later cohort.

Differences in survival were particularly marked for patients with colonic cancer. While similar improvements were noted in patients with rectal cancer, the survival curves of patients with Stage III rectal cancer for the 2004 cohort were not substantially better than those from the 1998 cohort.

The exact reasons for this observation can only be inferred. The presence of vascular and/or lymphatic invasion in the primary tumour has independent prognostic impact, as confirmed in other series.\textsuperscript{17,18}

Likewise a previous publication from this institution has alluded to the importance of lymphovascular invasion as a prognostic factor.\textsuperscript{19} Certainly, patients with colon and rectal cancer in the later cohorts of this study had a lower proportion of lymphovascular invasion.

New well-trained surgeons with subspecialty training in coloproctology, hitherto an unrecognised subspecialty, were employed at Christchurch Hospital in the mid-1990s. Certainly similar improvements in outcome have been attributed to subspecialisation and volume of work in several centres.\textsuperscript{6,8,9} Improvements in lymph node examination on histology and image resolution with modern CT and MRI scanners may also contribute to the phenomenon of stage migration in our later cohort of patients.
Indeed, we have noted a high proportion of patients with advanced Stage 4 disease in our 2004 cohort. Previous studies have confirmed that improvements in the standards and quality of pathology reports along with the introduction of mandatory audits and performance feedback to contributing centres have all help improve survival outcomes in patients with colorectal cancer.12,25

Last but not least, the indications and referral patterns for adjuvant treatment to oncologist may have changed in later cohorts. Adjuvant chemotherapy with 5FU/levamisole and then 5FU/leucovorin was starting to be offered during 1993, and was routinely considered for the 1998–99 cohort as efficacy was confirmed.20–22

Chemotherapy for metastatic disease was sometimes used before 1995, based on reports of survival benefit if used early. By 1998–99 the benefit of chemotherapy for advanced disease was accepted and patients were being entered in clinical trials including the Saltz regimen or received 5FU/leucovorin by Mayo or once weekly regimens followed by irinotecan on failure.23–25

The increased use of adjuvant chemotherapy and radiotherapy for rectal cancer in our later cohorts of patient may explain the observed improvements in survival - our results match those of previous reports following the introduction of such adjuvant treatments.10,11

Our study is limited by not capturing patients treated in the private sector who were not referred for an oncology opinion or treatment and by the omission of patients with did not have surgery in our first cohort. This would include those with early stage disease and those who declined referral.

Patients referred at development of metastases were only included if their primary surgery had occurred during the defined time point. Thus Dukes B and C patients may be relatively over-represented in the studied group. A bias favouring the later cohort could occur if only better prognosis patients were referred.

We also accept that our patient population may have changed over the study periods. This is exemplified by the fact that there were no patients who did not undergo surgery in the first cohort, compared with 19% in the latest cohort.

A further limitation is the resultant inaccuracies in staging that may have occurred with varying extents of CT imaging being used within each cohort. Given the retrospective nature of the study we were unable to have complete data for all the analysed variables and this may account for some of the error in our observations.

In conclusion, we have demonstrated an improvement in outcome for patients with colorectal cancer treated in the Departments of Surgery and Oncology at Christchurch Hospital. Greater specialisation of surgeons, more operations by consultants and use of chemotherapy are all likely contributing factors.

**Competing interests:** None identified.

**Author information:** Michael Lim, Colorectal Fellow, Department of Colorectal Surgery; Prashant Sharma, Surgical Registrar, Department of Colorectal Surgery; Andrew Ing, Surgical Registrar, Department of Colorectal Surgery; Heidi Blackburne, Medical Student, Department of Colorectal Surgery; Bridget Robinson, Medical Oncologist and MacKenzie Chair in Cancer Medicine, Department of Oncology; Liane Dixon, Research Nurse, Department of Colorectal Surgery; Chris Frampton,
References:


Colonoscopy audit over 10 years—what can be learnt?

Alan G Fraser, Greg D Gamble, Toby R Rose, John P Dunn

Abstract

Introduction The goals of colonoscopy are changing over time and it is important to regularly determine if endoscopists are achieving key performance indicators.

Methods Data on key performance indicators were recorded independently by nursing staff for all colonoscopies performed during a 10-year period. The results were discussed at regular meetings and feedback given to endoscopists.

Results Audit data was recorded for 67,570 procedures. The key performance indicators (time to caecum, withdrawal time, adjusted caecal intubation rate and polyp detection rate) all improved over the audit period (p<0.0001 for trend). For each endoscopist the mean withdrawal time was highly variable ranging from 3.1 mins (95%CI 3.0; 3.1) to 11.2 mins (11.0; 11.3). For each endoscopist mean polyp detection rate varied from 29% (CI 26, 31%) to 69% (CI 68, 70%). There was a significant correlation between mean withdrawal time and mean polyp detection rate for each endoscopist (r=0.42; p=0.03). The polyp detection rate improved from 29% in 1999 to 49% in 2010. The proportion of procedures with more than 2 polyps increased from 22% in 2001 to 33% in 2010. There was a significant association of patient discomfort with time to caecum and also to level of consciousness, p<0.0001. There was a significant decrease in the proportion with significant discomfort over the audit period, p<0.0001.

Conclusions Colonoscopy audit as a routine process with data collection by endoscopy nurses over several years may be able to improve key performance indicators by the process of regular feedback to endoscopists. Audit should be encouraged as a routine process rather than simply as a research tool for a limited period.

Endoscopy units need to be sure that they are delivering high quality endoscopy at levels consistent with recognised standards. It is therefore important to regularly determine if endoscopists are achieving these standards by measuring key performance indicators.1-5

Audit is often collected in an ad hoc manner and not consistent over a long period of time. There are limited data on trends for key performance indicators over time and it remains uncertain whether the audit process is enhancing quality.6,7

This study seeks to determine if practice and performance of colonoscopy is influenced by a consistent audit process by looking for improvement in key performance indicators over a 10-year period. Withdrawal times and polyp detection rates have emerged as important performance indicators but have been found to be highly variable between endoscopists.8-13
This study seeks to determine if endoscopists with longer withdrawal times have higher polyp detection rates and if they are more likely to detect polyps more per procedure. A high standard of colonoscopy service implies that patient discomfort is kept to a minimum.

A deeper level of consciousness may be associated with better tolerance but technical expertise may be a more important determinant of patient discomfort.

Methods

Audit data was collected from two large private endoscopy units in Auckland, New Zealand. Audit data was available from 1999-2010 for Endoscopy Auckland and for 2001 and 2004-2010 for MercyAscot Endoscopy. The audit forms used by each unit were very similar which allowed collation of data for most of the important indicators.

Data was routinely collected at both units on caecal intubation (confirmed by nursing staff), terminal ileum intubation, polyp detection, the number of polyps detected, time to caecum, total time for the procedure and patient tolerance. Data on the number of polyps >1cm and level of consciousness was only collated at Mercy Endoscopy. The caecal intubation rate was adjusted (reaching a malignant obstruction and reaching the neo-terminal ileum post ileo-colic resection were determined as a complete colonoscopy).

Withdrawal time has emerged as an important performance indicator for colonoscopy and a withdrawal time of more than 6 minutes has been recommended. Polyp detection increases withdrawal time because of the time taken for polypectomy. A complicated system of stopping timing of withdrawal during polypectomy can be performed but this is not suitable for large scale continuous auditing. Therefore mean withdrawal times for each endoscopist when no polyps were detected were calculated and correlated with mean polyp detection rate for each endoscopist.

Mean withdrawal times for individual endoscopists were only analysed if data was available for more than 100 procedures. Only patients having conscious sedation using the combination of midazolam and fentanyl were included in the audit. Patient discomfort was graded by the nurse immediately after the procedure and by the patient prior to discharge from the endoscopy unit. This was recorded on a 1–5 scale or 0–5 scale (minor difference in scales used in each unit).

A discomfort grade of 3, 4 or 5 was considered to be equivalent for each scoring system (moderate and severe discomfort). Grades of 2 or less were also grouped together (nil or mild discomfort). The deepest level of consciousness during the procedure was recorded by the endoscopy nurse. The level of consciousness was defined as 1=awake; 2=rouses to voice; 3=roused to touch, 4=roused to pain and 5=unrousable (scores of 3, 4 and 5 were grouped together).

Statistical analysis was by stepwise logistic regression and trend by two-sided Cochrane-Armitage statistic (SAS).

Results

Trends—Audit data was recorded for 67,570 consecutive procedures (44,066 at Endoscopy Auckland and 23,504 at MercyAscot Endoscopy). The indications were typical for a busy private practice. Colonoscopies were performed for evaluation of new symptoms or the follow-up of individuals with a family history of bowel cancer or a history of previous polyps.

All procedures were performed by consultants with more than 5 years’ experience after specialist training; 69% were performed by gastroenterologists and 31% by surgeons. The mean time to caecum decreased from 9.0 minutes (CI 8.7; 9.4) in 2001 to 7.3 minutes (7.2; 7.5) in 2010, p<0.001.

For all procedures the withdrawal time increased from 7.5 minutes (7.1; 7.8) in 2001 to 8.9 minutes (8.7; 9.0) in 2010, p<0.001.
For procedures where no polyps were detected, withdrawal time increased over the audit period from 5.6 minutes (95%CI 5.3; 5.9) in 2001 to 6.6 minutes (6.4; 6.7) in 2010, p<0.0001 (Figure 1).

**Figure 1. Trends for mean withdrawal time for all procedures and for procedures where no polyps are detected (p<0.001 for both)**

![Chart showing trends for mean withdrawal time](image)

The mean adjusted caecal intubation rate improved from 96.3% in 1999 to 99.0% in 2010. Terminal ileal intubation rate improved from 63% to 87% from 2001 to 2010 (data for Mercy Endoscopy only). Gastroenterologists had higher caecal and ileal intubation rates than surgeons (98.4% vs. 96.4%; 80% vs. 59% and higher rates of polyp detection (45% vs. 39%) all p<0.001. Increasing age (OR 1.01 (CI 1.01, 1.02), p=0.0005 and female gender OR 1.75 (95%CI 1.36, 2.24) (p<0.0001) were independent predictors of not reaching the caecum.

Stepwise logistic regression showed that the adjusted caecal intubation rate was affected by type of training (gastroenterologists compared with surgeons) and year of the procedure (improving with time).

**Polyp detection**—The polyp detection rate improved from 29% in 1999 to 49% in 2010 and the proportion of procedures with more than 2 polyps increased from 22% in 2001 to 33% in 2010, p<0.0001 for both trends. Polyp detection was lower with lower age OR 0.97 (0.96, 0.97), p<0.0001 and higher for males OR 1.43 (1.35, 1.51), p<0.0001.

**Polyp detection and withdrawal time**—Increasing duration of withdrawal time was significantly associated with higher rates of polyp detection for all polyps and for polyps greater than 1cm in diameter (Table 1). For each endoscopist mean withdrawal time (where no polyps were detected) was highly variable ranging from 3.1 minutes (95%CI 3.0; 3.1) to 11.2 minutes (11.0; 11.3). For each endoscopist mean polyp detection rate varied from 29% (CI 26, 31%) to 69% (CI 68, 70%).
Table 1. Polyp detection rate related to withdrawal time

<table>
<thead>
<tr>
<th>Variables</th>
<th>0–5 min</th>
<th>5–10 min</th>
<th>10–20 min</th>
</tr>
</thead>
<tbody>
<tr>
<td>Polyp detection rate</td>
<td>18%</td>
<td>36%</td>
<td>46%</td>
</tr>
<tr>
<td>Odds ratio (all polyps)</td>
<td>1.0</td>
<td>2.5 (2.4; 2.6)</td>
<td>7.7 (7.4; 8.1)</td>
</tr>
<tr>
<td>Odds ratio of detecting polyp &gt;1cm</td>
<td>1.0</td>
<td>1.9 (1.7; 2.1)</td>
<td>3.9 (3.5; 4.3)</td>
</tr>
</tbody>
</table>

Figure 2. Correlation of mean polyp detection rate with mean withdrawal time for endoscopists with more than 100 procedures

There was a significant correlation between mean withdrawal time and mean polyp detection rate for each endoscopist ($r=0.42$; $p=0.03$) (Figure 2). There was also a correlation between detection of polyps >1cm and mean withdrawal time for each endoscopist ($r=0.51$; $p=0.0025$) and also number of polyps >2 and withdrawal time ($r=0.40$; $p=0.013$) when weighted by annual volume of each endoscopist.

Patient discomfort—Data was available for 33,337 procedures on patient discomfort and level of consciousness. The patient discomfort score was >2 for 9% of procedures (9.8% of procedures if the score was rated by the endoscopy nurse). There was close concordance in scores between the doctor and nurse (kappa=0.63) and between the patient and doctor (kappa=0.63) and but not between patient and nurse (kappa=0.22).
Ratings of patient discomfort were higher for female gender OR 1.30 (1.23, 1.37). There was a significant association of patient discomfort with time to caecum, p<0.0001 (Table 2). The level of consciousness was rated as 1=awake in 34.4% of procedures; 2=rouses to voice for 63%; 3=rouses to touch for 2%, 4=rouses to pain for 0.4% and 5=unrousable for 0.2% of procedures (scores of 3, 4 and 5 were grouped together). By logistic regression a patient discomfort score of 3, 4, or 5 was related to time to caecum and to level of consciousness (Table 3).

Table 2. Patient reported discomfort levels related to time to caecum

<table>
<thead>
<tr>
<th>Discomfort</th>
<th>Time to caecum (minutes)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0–5</td>
</tr>
<tr>
<td>0,1,2 (less)</td>
<td>29%</td>
</tr>
<tr>
<td>3,4,5 (more)</td>
<td>8%</td>
</tr>
</tbody>
</table>

Table 3. Logistic regression of significant factors associated with patient discomfort score of >than 2

<table>
<thead>
<tr>
<th>Variables</th>
<th>Relative risk</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>LOC 3,4,5 versus 1,2</td>
<td>0.73</td>
<td>0.57; 0.94, p=0.02</td>
</tr>
<tr>
<td>Time to caecum (min)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5–10 versus 0–5</td>
<td>2.2</td>
<td>1.8; 2.6 p&lt;0.0001</td>
</tr>
<tr>
<td>10–15 versus 0–5</td>
<td>5.5</td>
<td>4.5; 6.6 p&lt;0.0001</td>
</tr>
<tr>
<td>&gt;15 versus 0–5</td>
<td>12.0</td>
<td>9.8; 14.7 p&lt;0.0001</td>
</tr>
<tr>
<td>Volume &gt;600 versus&lt;600</td>
<td>1.1</td>
<td>0.9; 1.3 n.s.</td>
</tr>
</tbody>
</table>

The mean time to caecum for each endoscopist was significantly correlated with the proportion of procedures that had a patient discomfort score of 3, 4 or 5 for each endoscopist, r=0.90, p<0.0001 (excluding endoscopists with volume less than 500), Figure 3.
There was a significant inverse relationship between mean annual volume of procedures for each endoscopist and patient discomfort ($r = -0.71$, $p < 0.0001$) Figure 4. There was a significant decrease in the proportion with discomfort $> 2$ over the audit period from 20% in 1999 to 7% in 2009/10 ($p < 0.0001$).

Figure 4. Correlation of patient discomfort scores with mean annual volume of endoscopists

Excludes those with fewer than 100 cases
Discussion

There were significant changes in practice and performance over the 10-year time period. Key performance indicators significantly improved over the audit period. In particular, the rate of polyp detection, the rate of terminal ileal intubation and the withdrawal time all increased over the audit period. This may be a result of the audit process but general learning effects, improvement in equipment and the results of attendance at workshops and courses cannot be excluded.

The standards were generally high but continued to improve. This study shows that continuous audit over 10 years can lead to better outcomes even for experienced endoscopists however it is clear that many factors are involved in improving quality. There has been a significant improvement in the performance of colonoscopy in the UK over the last seven years with the caecal intubation rate improving from 76.9% to 95.8% related to a combination of interventions.\(^7\)

There was significant attention given to polyp detection rates at annual audit meetings and this may have led to increased detection rates. The recommendation to increase withdrawal times has been implemented to some degree during the audit period. The data supports this as a key strategy for improving polyp detection rates (both for small and larger polyps) and also for increasing the number of polyps detected per procedure. Therefore the criticism that increased withdrawal times only increases detection of smaller polyps does not seem to be justified.

Better patient tolerance of colonoscopy has been achieved over the audit period consistent with improvement in other areas of technical performance. The patient discomfort score was significantly associated with time to caecum. This may be partly because longer procedures are by definition more difficult, but time to caecum is also likely to be a marker of technical expertise. This is suggested by the significant correlation of patient discomfort with mean time to caecum for individual endoscopists and the inverse relationship with mean annual colonoscopy volume for each endoscopist. This analysis eliminates the potential bias that longer procedures will be more uncomfortable assuming that the case mix of difficulty is similar for all endoscopists.

Ekkelkamp showed a significant negative correlation between caecal intubation rate (also a marker of technical expertise) and a nurse-reported comfort rating \((r=-0.57; \ p<0.005)\).\(^4\) This study shows that only a mild decrease in patient discomfort scores is obtained by giving more sedation and achieving deeper levels of consciousness \((\text{OR } 0.73 \text{ for LOC of } 3, 4 \text{ or } 5 \text{ compared with LOC 1 and 2, Table 3})\). These deeper levels of consciousness were only recorded for 2.6% of procedures and are not part of the desired goals of conscious sedation.

This study also shows that females are more likely to experience discomfort during a colonoscopy similar to other studies.\(^15-17\) Hazeldine found that the degree of sedation had no effect of patient tolerance but females, a high BMI and having a trainee perform the procedure was associated with more discomfort.\(^18\)

There was a high degree of variability amongst endoscopists in polyp detection rate (29 to 69%). A similar variation in polyp detection rate was reported by Williams et al
with a polyp detection rate ranging from 18% to 66% for men and 11% to 43% for women. This audit was considered part of routine practice rather than a research project. The long-term and continuous nature of the audit probably lead to less interest in gaming the system (trying to find diminutive and non-adenomatous polyps) and encouraged steady behavioural change.

Withdrawal time is an easily influenced behaviour but improvement in polyp detection also requires greater vigilance and attention to detail during the procedure. A recent study has shown that a group of endoscopists who participated in a 2-hour training session were able to increase adenoma detection rate from 36% to 47% whereas the adenoma detection rate did not change for a group who did not receive training. The improvement was seen for all polyps types and for larger as well as small polyps.

Regular feedback to the endoscopist was also an important aspect of the improvement. Other studies have shown that monitoring and regular feedback leads to a decrease in incomplete colonoscopies, shortened intubation times and increased withdrawal times although these studies did not clearly show an increase in adenoma detection.

The frequency of feedback may be important. A study using a quarterly report card summarizing colonoscopy quality indicators showed an increased adenoma detection (adjusted for age and sex) from 45% to 54%, p=0.013. This increase was due mostly to increased detection of proximal adenomas.

Overall polyp detection or polypectomy rate is appears to be correlated with adenoma detection rate suggesting that the simpler measure of polyp detection may be adequate. Achieving a polypectomy rate of 40% for men and 30% for women correlated with recommended adenoma detection rates of 25% for men and 15% for women.

The polypectomy rate may prove to be a useful measure as there is growing recognition that some nonadenomatous polyps such as large hyperplastic or sessile serrated polyps are a significant risk of colorectal cancer and therefore need to be carefully identified and removed. The detection of proximal serrated polyps is highly variable and endoscopist dependent.

A significant proportion of proximal serrated polyps may be missed during colonoscopy. A study of 18003 colonoscopies showed a mean serrated detection rate of 20.6% and mean adenoma detection of 31.5%. There was no correlation between adenoma detection rate and serrated polyp detection rate but there was a strong relationship between time of withdrawal and serrated polyp detection rate (r=0.956, p=0.003).

There are some limitations to this study. The data was obtained from an audit process rather than from a research project. The data recorded needed to be achievable within standard working practice i.e. not too time consuming. In particular, withdrawal time was derived from total procedural time minus time to caecum. This has limitations (i.e. does not allow for variation in ileal intubation time or time taken to perform polypectomy) but is easy to use. The large number of observations helps to offset this limitation to some extent.
Routine audit becomes very difficult using a stopwatch recording approach i.e. starting only after ileal intubation and also stopping during polyp removal. The analysis using endoscopists withdrawal time where no polyps were detected is a valid way of using this data. More data on indications for endoscopy, particularly clarifying which patients were follow-up and which patient had new symptoms for initial evaluation would have been helpful.

The audit process was considered a success by all endoscopists and this is now considered as part of the standard of care for both endoscopy units. The goal is to continue to improve key performance indicators, particularly polyp detection rate.

Improving standards of colonoscopy throughout New Zealand is an important issue to consider before introducing bowel cancer screening which will significantly increase the number of individuals having a colonoscopy.

A new quality measure called the Global Rating Scale is being introduced to endoscopy units throughout New Zealand. This should encourage the routine adoption of a similar audit process to that described in this paper. Conscious sedation is acceptable for colonoscopy but continued attention to improving technical expertise is required to continue to decrease patient discomfort levels.

Competing interests: None identified.

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³ Endoscopy Auckland, Auckland

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References:

4. Quality and safety indicators for endoscopy. Formulated by the BSG Endoscopy Committee in conjunction with the National Bowel Cancer Screening Programme, AUGIS and ACP. www.bsg.org.uk/attachments/170_bsg_prs_indic07.pdf

The diagnostic yield of colonoscopy in patients with isolated abdominal pain

Shaw Hua Kueh, Lifeng Zhou, Russell S Walmsley

Abstract

Aim Colonoscopy is an overstretched resource and there is no consensus on whether isolated abdominal pain is an appropriate indication for colonoscopy. We evaluated the proportion of patients referred for colonoscopy with isolated abdominal pain and determined the diagnostic yield for this indication.

Methods All patients registered as having a colonoscopy at Waitemata District Health Board on Endoscribe™ reporting database between March 2005 and February 2010 were included. Patients were recruited based on the indication for colonoscopy of: abdominal pain, iron deficiency anaemia or overt rectal bleeding. All investigations and electronic clinical documents for patients with abdominal pain were retrieved and patients with concurrent anaemia, rectal bleeding, weight loss, altered bowel habit, abdominal mass, previous abnormal investigations and history of inflammatory bowel disease or bowel malignancy were excluded. The diagnostic yield between the 3 study groups were compared using Chi-squared test, Wilcoxon rank sum test and multiple logistic regression models.

Results Total of 10,052 colonoscopies were performed of which only 2,633 fulfilled our inclusion criteria. The abdominal pain group accounted for 1.2% of colonoscopies performed and had the lowest diagnostic yield of 48.8% (P<0.001). Among those with abdominal pain, significant neoplasia was found in 3.3% and was significantly lower than those with iron deficiency anaemia or overt rectal bleeding groups (P<0.001). When segregated by age, the abdominal pain group continued to have significant less neoplasia (3.8%, P=0.001) among those 50 and older but no difference was found among younger patients.

Conclusions A small proportion of colonoscopy resources are being used to investigate isolated abdominal pain, which is appropriate given the low diagnostic yield of significant pathology, particularly amongst those less than 50 years old.

As of 2007 the waiting time for non-urgent outpatient colonoscopy in the public hospital system in New Zealand was at least 6 months.¹ In an attempt to match the growing demand with the scarce resource, patient selection and triaging endoscopy referrals has become critically important.

Several guidelines have been published to assist clinicians in triaging patients for endoscopy. These include documents outlining the role of colonoscopy in various clinical scenario published by the American Society for Gastrointestinal Endoscopy² and the web-based interactive set of more didactic guidelines by the European Panel on the Appropriateness of Gastrointestinal Endoscopy.³,⁴
Use of these guidelines has been shown to significantly improve the diagnostic yield of colonoscopies.\textsuperscript{5-8} At present, no similar guideline exists in New Zealand.

Colonoscopies performed on patients with iron deficiency anaemia and rectal bleeding symptoms give a relatively ‘high’ diagnostic yield\textsuperscript{9-14} which improves further in those older than 50 years of age.\textsuperscript{15} For patients with isolated abdominal pain, however, there is less agreement on whether colonoscopy is indicated. The proportion of patients undergoing colonoscopy who have abdominal pain as their primary indication varies significantly around the world, from 2.9% in New York City\textsuperscript{12} to 53% in a tertiary referral centre in Kuwait.\textsuperscript{13}

The decision to perform colonoscopy is influenced by a number of factors; one of which is the lack of knowledge of the local disease prevalence in patients presenting with isolated abdominal pain. In a report by Neugut from 3 practices in New York City, colon cancer was found in 4.4% and adenomatous polyps of more than 1cm in 2.7% of cases colonoscoped for isolated abdominal pain.\textsuperscript{12} In a larger multi-centred prospective Swedish study with a study population mean age of 54.7, 2.4% had colon cancer and 3.1% had polyps of more than 1cm.\textsuperscript{11} Inflammatory bowel diseases were found in 12.2% and diverticular disease in 18.3%.

To help organise local triage for colonoscopy we set out to evaluate the proportion of the colonoscopies performed in the public health system for patients with isolated abdominal pain and determine the local diagnostic yield in this patient group.

**Method**

The study population was taken from patients attending colonoscopy at North Shore and Waitakere Hospitals, which provide secondary level public healthcare for 513,000 residences in Waitemata District of Auckland, New Zealand. Referral for endoscopy is open-access. There is no standard referral form or guidelines, and so referrals are graded by the Clinical Leader of Gastroenterology, in accordance to Auckland Regional policy used during the study period, as priority 1 (within 1 week), priority 2 (within 3 month) and priority 3 (within 6 months) or return to the referrer if deemed inappropriate.

Registration of all the endoscopies performed at the 2 hospitals was mandatorily and endoscopies were reported on Endoscribe\textsuperscript{TM} database (Mediboss PTY LTD, Bedford Park, South Australia, distributed by Health Communication Network Limited). The following details must be provided before registration was completed and a report of the procedure could be generated: patient’s National Health Index (NHI), name, gender, date of birth, date of the procedure, indication(s), endoscopist(s), procedure(s) performed, findings, biopsy taken and diagnosis.

**Patient selection**—All colonoscopies recorded in the registry between 1 March 2005 and 28 February 2010 were included in the study. Three groups of patients based on indication for colonoscopy as recorded in Endoscribe\textsuperscript{TM} registry were recruited: abdominal pain, iron deficiency anaemia and overt rectal bleeding.

Patients recruited in the abdominal pain group had to have the colonoscopy performed with the sole indication of abdominal pain. Patients were excluded if they had concurrent indications such as anaemia or rectal bleeding. Similarly, patients with colonoscopy performed for iron deficiency anaemia were recruited into the anaemia group and were excluded if they had concurrent symptoms of rectal bleeding. Other exclusion criteria common to all 3 study groups are listed in Table 1.

The abdominal pain group underwent further screening process by searching the full endoscopic reports from Endoscribe\textsuperscript{TM} and interrogating the Concerto\textsuperscript{TM} Medical Application (Orion Health Ltd, Auckland, New Zealand).

Concerto\textsuperscript{TM} allows access to patient details, electronic clinical documentations, hospital admissions and investigations including all blood investigations, tissue histology and radiology reports on all patients in the Greater Auckland area.
Table 1. Inclusion and exclusion criteria

<table>
<thead>
<tr>
<th>Inclusion</th>
<th>Abdominal pain</th>
<th>Iron deficiency anaemia</th>
<th>Overt rectal bleeding</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Group-specific exclusions</strong></td>
<td>Anaemia</td>
<td>Bleeding</td>
<td>–</td>
</tr>
<tr>
<td><strong>Exclusion criteria for all 3 study groups</strong></td>
<td>Altered bowel habit</td>
<td>Weight loss</td>
<td>Abdominal mass</td>
</tr>
</tbody>
</table>

 Patients were excluded if they were found to have a history of weight loss, altered bowel motion, abdominal mass, family history that warranted surveillance for bowel cancer, history of inflammatory bowel disease, diverticulosis, bowel malignancy or had bowel surgery (except appendectomy and cholecystectomy) which had not been recorded in the Endoscribe™ registry.

 Patients with abnormal relevant investigations were also excluded. These include elevated inflammatory markers, anaemia, positive faecal occult blood, raised faecal calprotectin, abnormal barium enema or abdominal Computed Tomography (CT) findings within 6 months prior to colonoscopy.

 All histology reports from all study groups were retrieved and reviewed via Concerto™. Findings inconsistent with inflammatory bowel disease were categorised as non-specific ulcers or non-specific colitis. Mass lesions were categorised by the most significant abnormality found on histology in descending order of adenocarcinoma, advanced adenomas, non-significant adenomatous polyps and non-significant non-adenomatous polyps.

 Advanced adenomas were defined as those with villous or tubulovillous histology, adenoma ≥ 1cm or adenoma with high grade dysplasia. Non-significant non-adenomatous polyps were hyperplastic polyps or metaplastic polyps. Those with polyps reported at colonoscopy but no biopsy taken were presumed to have non-significant non-adenomatous polyps.

 Other diagnoses included for analysis (which may occur concurrently) were diverticulosis and haemorrhoids. Diagnostic yield was defined as any abnormalities found at colonoscopy regardless of whether it explained patient’s presenting symptoms or not.

 Statistical analysis was performed using SAS® v9.1 software (SAS Institute Inc., Cary, North Carolina, USA). Comparisons of categorical variables were undertaken using Chi-squared test, and Wilcoxon rank sum test was employed for continuous variables inappropriate for parametric tests. P-value of < 0.05 was considered to be statistically significant.

 Where sample size is sufficient, multiple logistic regression models were used to analyse the odds ratio (OR) of each diagnosis between patient groups after adjusting for age and gender. The study was registered and approved by Waitemata District Health Board (WDHB) Knowledge Centre (Project Code RM0980711538).

 Results

 From 1 March 2005 to 28 February 2010, a total of 10,052 colonoscopies were performed. Only 2633 complete colonoscopies performed satisfied all our inclusion and exclusion criteria. Abdominal pain accounted for 1.2% of all colonoscopies performed over the 5-year period, 10.3% for iron deficiency anaemia and 14.7% for overt rectal bleeding.
490 subjects were initially eligible for the abdominal pain group from the Endoscribe™ registry search; however after further screening, only 121 satisfied all inclusion and exclusion criteria. Majority of patients were excluded due to other significant concurrent symptoms, abnormal investigations or incomplete colonoscopy.

The patient demographics are shown in Table 2. Patients in the abdominal pain group were generally younger with a median age of 58, while patients in the anaemia group were generally older with a median age of 73. Table 3 gives the diagnostic findings by indication for colonoscopy.

Table 2. Baseline demographics

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Abdominal pain n (%)</th>
<th>Iron deficiency anaemia n (%)</th>
<th>Overt rectal bleeding n (%)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total number</td>
<td>121</td>
<td>1031</td>
<td>1481</td>
<td>–</td>
</tr>
<tr>
<td>Age range</td>
<td>19–82</td>
<td>18–96</td>
<td>14–97</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>Median age</td>
<td>57.7</td>
<td>73.2</td>
<td>62.6</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>&lt;50 years old</td>
<td>41 (33.9)</td>
<td>126 (12.2)</td>
<td>360 (24.3)</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>Female</td>
<td>70 (57.8)</td>
<td>631 (61.2)</td>
<td>683 (46.1)</td>
<td>&lt;0.001*</td>
</tr>
</tbody>
</table>

Table 3. Diagnosis based on indication

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Abdominal pain n (%)</th>
<th>Iron deficiency anaemia n (%)</th>
<th>Overt rectal bleeding n (%)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Malignancy</td>
<td>2 (1.7)</td>
<td>120 (11.6)</td>
<td>122 (8.2)</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td><strong>Polyps</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Advanced adenoma</td>
<td>2 (1.7)</td>
<td>63 (6.1)</td>
<td>119 (8.0)</td>
<td>0.011*</td>
</tr>
<tr>
<td>NS – A</td>
<td>15 (12.4)</td>
<td>110 (10.7)</td>
<td>147 (9.9)</td>
<td>0.623</td>
</tr>
<tr>
<td>NS – NA</td>
<td>17 (14.1)</td>
<td>82 (8.0)</td>
<td>176 (11.9)</td>
<td>0.003*</td>
</tr>
<tr>
<td>IBD</td>
<td>0 (0)</td>
<td>6 (0.6)</td>
<td>23 (1.6)</td>
<td>0.036*</td>
</tr>
<tr>
<td>Crohn’s disease</td>
<td>0 (0)</td>
<td>5 (0.5)</td>
<td>11 (0.7)</td>
<td></td>
</tr>
<tr>
<td>Ulcerative colitis</td>
<td>0 (0)</td>
<td>1 (0.1)</td>
<td>12 (0.8)</td>
<td></td>
</tr>
<tr>
<td>NS colitis</td>
<td>0 (0)</td>
<td>5 (0.5)</td>
<td>37 (2.5)</td>
<td>NA†</td>
</tr>
<tr>
<td>NS ulcer</td>
<td>0 (0)</td>
<td>9 (0.9)</td>
<td>8 (0.5)</td>
<td>NA†</td>
</tr>
<tr>
<td>Diverticulosis</td>
<td>34 (28.1)</td>
<td>392 (38.0)</td>
<td>514 (34.7)</td>
<td>0.047*</td>
</tr>
<tr>
<td>Haemorrhoid</td>
<td>4 (3.3)</td>
<td>64 (6.2)</td>
<td>382 (25.8)</td>
<td>&lt;0.001*</td>
</tr>
</tbody>
</table>

IBD=Inflammatory bowel disease, NS=Non-significant, A=Adenoma, NA=Non-adenoma; NA† Not available due to inadequate sample size for statistical analysis.

The diagnostic yield—The abdominal pain group had the lowest total diagnostic yield at 48.8% (59/121) compared to iron deficiency anaemia group at 65.2% (672/1031) and overt rectal bleeding group at 78.1% (1156/1481), P <0.001. When controlled for age group alone, the abdominal pain group continued to have significantly lower yield: age <50 - abdominal pain 26.8% (11/41), anaemia 27.8% (35/126), overt rectal bleeding 60.6% (218/360), P <0.001; age ≥50—abdominal pain 60% (48/80), anaemia 70.4% (637/905), overt bleeding 83.7% (938/1121), P <0.001.
Amongst those age <50, males with abdominal pain had significantly lower diagnostic yield at 21.1% (4/19) compared to those with anaemia at 36.7% (11/30) or overt rectal bleeding at 65.7% (140/213), P<0.0001. In females, anaemia was associated with lower yield at 25% (24/96) compared to abdominal pain at 31.8% (7/22) and overt rectal bleeding 53.1% (78/147), P<0.001.

In those age ≥50, male with abdominal pain continued to have lower diagnostic yield at 71.9% (23/32) and iron deficiency anaemia was equally low at 72.4% (268/370) compared to those with overt rectal bleeding at 85% (P<0.001). Older females with abdominal pain had significantly lower yield at 52.1% (25/48) compared to anaemia at 69% (369/535) and overt rectal bleeding at 82.3% (441/536), P<0.001.

Using the multiple logistic regression model, patients with abdominal pain were 72% less likely to have an abnormal colonoscopy compared to those with overt rectal bleeding (OR 0.28, 95% CI=0.19–0.42). Similarly, patients with iron deficiency anaemia were 57% less likely to have an abnormal colonoscopy compared to those with overt rectal bleeding (OR 0.43, 95% CI=0.35–0.52).

Patients aged <50 years were 75% less likely to have an abnormal colonoscopy compared to those ≥50 years (OR 0.25, 95% CI=0.2–0.31) and female gender was associated with 25% less likely of having an abnormal colonoscopy compared to male (OR 0.75, 95% CI=0.62–0.90).

**Significant neoplasia**—The rate of significant neoplasia (i.e. malignancy and advanced adenoma) was significantly lower in patients with abdominal pain at 3.3% compared to 17.8% in the iron deficiency anaemia group and 16.3% in the overt rectal bleeding group (P<0.001).

Among younger patients, there was no significant difference in rate of significant neoplasia between the 3 groups (abdominal pain 2.4%, iron deficiency anaemia 0.8%, overt rectal bleeding 4.2%, P=0.175). However in older patients, abdominal pain group had a significantly lower rate at 3.8% compared to iron deficiency anaemia and overt bleeding group, both at 20.1%, P= 0.001.

When controlling for gender alone, both genders of the abdominal pain group had less significant neoplasia compared to the iron deficiency anaemia group which had the highest rate (female, 4.3% vs 16% respectively, P=0.029; male, 2% vs 20.5% respectively, P=0.05).

Among patients age <50, the rates of significant neoplasia were not different between the 3 groups in both gender groups (female - abdominal pain 4.6%, anaemia 1% and overt rectal bleeding 5.4%; male–abdominal pain 0%, anaemia 0%, overt rectal bleeding 3.3%). Chi-squared analysis was unable to be performed due to inadequate number.

In those age ≥50, abdominal pain was associated with the lowest rate of significant neoplasia in both female and male gender groups (female–abdominal pain 4.2%, anaemia 18.7%, overt rectal bleeding 16.6%, P=0.035; male–abdominal pain 3.1%, anaemia 22.2%, overt rectal bleeding 23.4%, P=0.027). Therefore, young females with abdominal pain were less likely to have significant neoplasia (Table 4).
Table 4. Odds Ratio of significant neoplasia according to indication for colonoscopy and patient characteristics using logistic regression model

<table>
<thead>
<tr>
<th>Effect</th>
<th>OR</th>
<th>95% confidence intervals</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abdominal pain versus overt rectal bleeding</td>
<td>0.20</td>
<td>0.07 0.54</td>
</tr>
<tr>
<td>Iron deficiency anaemia versus overt rectal bleeding</td>
<td>1.00</td>
<td>0.80 1.24</td>
</tr>
<tr>
<td>Age (&lt; 50 years versus ≥ 50 years)</td>
<td>0.14</td>
<td>0.09 0.23</td>
</tr>
<tr>
<td>Gender (Female versus male)</td>
<td>0.75</td>
<td>0.61 0.93</td>
</tr>
</tbody>
</table>

**Other diagnosis**—Polyps of any histological type were found to be significantly more amongst those with abdominal pain and overt rectal bleeding (age<50–abdominal pain 19.5%, overt rectal bleeding 19.7%, iron deficiency anaemia 7.9%, P=0.009; age≥50–abdominal pain 32.5%, overt rectal bleeding 33.1%, iron deficiency anaemia 27.1%, P=0.013). Further subanalysis did not demonstrate significant difference between genders within their respective age groups.

Amongst the 120 colonoscopies for abdominal pain, none were found to have inflammatory bowel disease. This was significantly less than those with iron deficiency anaemia and rectal bleeding (Table 3). Further subanalysis for age did not show any significant difference and further analysis for age and gender was not possible due to small numbers.

Haemorrhoid was more frequent amongst those with overt rectal bleeding than those with iron deficiency anaemia or abdominal pain. This continues to be true on subanalysis controlling for gender and age (male, age<50–abdominal pain 0%, iron deficiency anaemia 23.3%, overt rectal bleeding 34.7%, P=0.005; female, age<50–abdominal pain 4.6%, iron deficiency anaemia 4.1%, overt rectal bleeding 28.6%, P=<0.001; male, age≥50–abdominal pain 9.4%, iron deficiency anaemia 4.9%, overt rectal bleeding 25%, P <0.001; female, age≥50—abdominal pain 0%, iron deficiency anaemia 6.5%, overt rectal bleeding 22.4%, P <0.001).

**Discussion**

Isolated abdominal pain accounted for 1.2% of the total number of colonoscopies performed over the 5-year period in our health authority with an open-access referral system. This is lower than the lowest rate previously reported by Neugut et al at 2.9% in New York over a 4-year period. One explanation of this small proportion may be due to triaging of referrals. Abdominal pain was generally not taken as sufficient indication for colonoscopy unless all other reasonable modality of investigations had been exhausted. During the study period, endoscopy service at Waitemata District Health Board continued to be under mounting pressure and waiting time for urgent (Priority 1) would be up to 2 months, while Priority 2 would be up to 6 months.

These long waiting times may have resulted in fewer referrals and may explain the smaller number of colonoscopy performed in this patient group. Although no data was held for the rate of rejection for patients referred with abdominal pain, this was...
estimated to be approximately 10% according to our triaging Clinical Director of Gastroenterology.

Our overall diagnostic yield in patients with isolated abdominal pain was 49%, which was higher than previously reported. However, the definition of diagnostic yield varied significantly between studies.

Our findings are similar to a multi-centred Swedish study where 16% of colonoscopies were performed for abdominal pain, of which inflammatory bowel disease, malignancy, polyps, diverticular disease and benign stricture were found in 48.1% of cases.

Although Al-Shamali et al reported the highest proportion of colonoscopy performed on patients with abdominal pain at 53.6%, the diagnostic yield was only 7%. The study population was different to ours; 53% were Kuwaiti nationals and 47% were from other countries including Egypt, Syria, Jordan and Indian subcontinent, with a much younger average age of 39.2 years.

Accounting for significant pathology of inflammatory bowel diseases and significant neoplasia, the diagnostic yield on our patients with abdominal pain was reassuringly low at 3.3% (4/121). This was 80% less than patients referred with anaemia or overt rectal bleeding (18.3% and 17.8% respectively). On further sub-analysis, the rate of significant pathology was only found in 2.4% (1/41) in those younger than 50 years and 3.8% (3/80) in those 50 and older.

The rate of colorectal malignancy in patients with abdominal pain in our study was comparable to those previously reported from other Western countries of 2.8% in Manchester, UK, 2.3% in Sweden and 0.47% in 2 endoscopy units in San Francisco. In our study, there were two cases of colorectal cancer found in the abdominal pain group (1.7%).

The full paper clinical records were obtained and reviewed for these cases. The first case was a 44-year-old female who was found to have a palpable abdominal mass by the referring general practitioner which was recorded on the paper referral form for colonoscopy but was unfortunately not recorded in the Endoscribe registry and she was therefore included in our study.

The second case was an 81-year-old female found to have a 15mm pedunculated polyp containing adenocarcinoma which was fully excised. The paper referral letter for this patient stated that the faecal occult blood test was positive but since no laboratory result was found on our search she could not be excluded.

Advanced adenomas were found in 2 cases in abdominal pain group and were both older than 50 (1.7%). In a male patient, tubulovillous adenoma with low grade dysplasia was found and in a female, tubulovillous adenoma with high grade dysplasia was found.

Polyps are one of the most common diagnosis reported, however only 2 studies had distinguish those ≤1cm from those ≥1cm. In a prospective study of 68 patients with abdominal pain, 3.05% were found to have polyps ≥1cm.
The histology of these polyps were not reported. In Yee et al.’s report, 0.93% of the 644 patients who had undergone colonoscopy for abdominal pain in San Francisco had polyps of ≥1cm and were all found in patients age >50.17

Among patients with abdominal pain in our study, none were found to have inflammatory bowel disease. The strength of our study therefore lies with our strict criteria under which patients with abdominal pain were recruited. Patients 50 years or older accounted for 97% of diverticulosis found in the abdominal pain group and occurred equally between genders. Similarly, for non-significant non-adenomatous polyps, 82.4% were found in older patients with no difference between genders.

The most significant weakness of our study was that the information available on EndoscribeTM was highly dependent on the endoscopist and was therefore subject to endoscopist variability. The indication for colonoscopy registered was dependent on the endoscopist’s assessment as to the main indication for the colonoscopy.

Similarly the final diagnosis was dependent on the endoscopist to complete and concurrent conditions may not be recorded as the endoscopist may consider these to be irrelevant for patient’s presentation.

**Conclusion**

At our centres, the current triaging system appears to be effective. We have utilised little resources (1.2% of colonoscopy) on patients with isolated abdominal pain in whom we have demonstrated a low rate of significant pathology.

Although the diagnostic yield was 49% in this patient group, significant pathology was only found in 3.3%. This was even lower in patients younger than 50. Therefore in patients with isolated abdominal pain, particularly those younger than 50, colonoscopy should not be considered as first line of investigation.

**Competing interests:** None identified.

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**References:**


A novel pathway for investigation of colorectal symptoms with colonoscopy or computed tomography colonography

Andrew D Sanders, Clark Stevenson, John Pearson, Michael Burt, Graham McGeoch, Ben Hudson, Tim W Eglinton

Abstract

Background Colorectal cancer (CRC) is a common problem in New Zealand and there is significant pressure on colonoscopy resources. Lower gastrointestinal symptoms are common in the community hence the appropriate selection of patients for colonoscopy is problematic. The Canterbury District Health Board recently developed the Canterbury Colorectal Symptom Pathway (CCrSP) to attempt to improve prioritisation using a combination of presenting clinical features integrated into a scoring tool. This study describes that pathway and its outcomes over a 6-month period.

Method Following implementation of the CCrSP, all outpatient referrals receiving colonoscopy or Computerised Tomography Colonography (CTC) over a 6-month period were audited. The clinical features included in the referral, waiting time and outcome of investigation were recorded. Using the scoring tool, a score was calculated for all referrals and compared with outcome.

Results Some 1,369 procedures were performed during the study period. Of the symptomatic patients, 38 CRCs were diagnosed from 633 colonoscopies and 253 CTCs. Individual factors predictive for CRC were rectal bleeding (OR 2.1, 95%CI 1.1–4.2), iron deficiency anaemia (OR 3.2, 95%CI 1.6–6.3) and positive faecal occult blood test (OR 6.1, 95%CI 2.1–16.3). No CRCs were diagnosed in the group scoring below the pre-set threshold for investigation. Multiple logistic regression analysis demonstrated a 1 unit increase in score increased the likelihood of CRC by 7.2% (95%CI 4.4%–10.1%, p<0.001). Of the 11 CRCs suggested by CTC, there was one false positive. The follow up colonoscopy rate after CTC was 11.5% and further radiology was recommended in 7.9%.

Conclusion The CCrSP pathway was accurate for predicting CRC and offers a reliable triage tool. The scoring tool was both sensitive for CRC and predictive of the risk of CRC in patients who received colonoscopy or CTC.

The management of colorectal cancer (CRC) presents a major challenge to the New Zealand health system. New Zealand has one of the highest incidences of CRC in the world and it is the second most common cause of cancer death in New Zealand. CRC is a disease where outcome is clearly related to stage at diagnosis: those diagnosed at an early stage have greater potential for cure. The gold standard for diagnosis of CRC is colonoscopy. Computerised Tomography Colonography (CTC) is becoming more widely used in New Zealand and has similar accuracy to colonoscopy for significant colorectal lesions. The use of colonoscopy
has increased over the last three decades resulting in significant pressure on colonoscopy resources in New Zealand.

A recent survey of capacity in New Zealand’s public hospitals\(^1\) found that 60% of large hospitals were unable to provide symptomatic patients with a colonoscopy within 3 months and 50% could not offer colonoscopy at all to asymptomatic individuals at moderate risk of CRC. Furthermore, there is significant inequity of access to colonoscopy in different regions.

The Ministry of Health is currently considering implementing a national bowel cancer screening programme and a pilot study was commenced in Waitemata DHB in 2011. Implementing screening will further increase the existing gap in colonoscopy demand and availability in NZ and will have implications for equitable access to colonoscopy for symptomatic individuals. While there is extensive evidence for efficacy of population screening of asymptomatic individuals, the assessment and prioritisation of symptomatic individuals for colonoscopy remains problematic and has been poorly researched.

The most predictive symptoms for finding CRC at colonoscopy are rectal bleeding or change in bowel habit to looser stools. Other symptoms that have lower predictive value include constipation and weight loss. Because these symptoms can be non-specific and are common in patients with benign disease, single symptoms have low diagnostic value for cancer.\(^4\)

A recent primary care survey suggested that 7% of primary care visits are for non-specific gastrointestinal symptoms.\(^5\) This high frequency of gastrointestinal symptoms in the community means effective selection and prioritisation of patients is essential to maximise the use of the limited colonoscopy resource. Existing criteria for colonoscopy focus on single symptoms and have been shown to miss a percentage of patients with cancer.\(^6\) Combining clinical features rather than focusing on single symptoms is one strategy that may allow improved prioritisation for colonoscopy.

The CDHB recently introduced a new web-based pathway to prioritise patients for investigation of colorectal symptoms. The pathway was designed to triage patients with the aid of a scoring tool, using a combination of presenting clinical features, rather than just individual symptoms. Thus allowing direct access to colonoscopy or CTC, as appropriate.

This study aimed, firstly, to describe the CCrSP, then to determine its uptake, diagnostic yield and validity for investigation of colorectal symptoms.

**Method**

**Development of the Canterbury Colorectal Symptom Pathway**—In 2008 the CDHB developed a novel pathway for investigating lower GI symptoms to prioritise patients based on symptoms and risk factors. The system aimed to identify those symptomatic individuals at greater risk of CRC, providing them with priority access to investigation directly from primary care.

The pathway was developed collaboratively by a Working Group comprising gastroenterologists, colorectal surgeons, general practitioners, the service manager for general surgery, representatives from the CDHB Planning and Funding Department and the Canterbury Initiative.

The development of the pathway required negotiation amongst many parts of the Canterbury Health system to ensure it was accepted and widely used. The pathway was delivered to general practitioners and specialist referrers on the HealthPathways website. This is one of some hundreds of pathways
developed in Canterbury by the Canterbury Initiative using a standard implementation process backed by multiple methods of communication and education sessions. The working group performed a literature review of published studies and guidelines from which symptoms and risk factors likely to predict significant colorectal pathology were identified. To enable prioritisation with a combination of symptoms, signs, investigations and patient risk factors, a scoring tool was developed.

The aim of the pathway was to triage patients into three categories; urgent, routine and not qualifying for investigation. The pathway also addressed the more effective use of CTC. The intention was that the triaging process be sufficiently transparent that the GP and patient would know the likely outcome at the end of the primary care consultation.

The weighting assigned to each clinical feature and subsequent threshold for investigation were based primarily on the current recognised magnitude of the predictive value of symptoms and risk factors from the literature. The resulting scoring tool is shown in Figure 1 and the rationale for inclusion of the clinical features discussed subsequently.

Figure 1. CCrSP scoring tool

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Yes/No</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rectal Bleeding ( &gt; 6 weeks)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sinister or Outlet</td>
<td></td>
<td>12.5</td>
</tr>
<tr>
<td>Change in Bowel Habit ( &gt; 6 weeks)</td>
<td></td>
<td>10</td>
</tr>
<tr>
<td>Loose or Constipation</td>
<td></td>
<td>5</td>
</tr>
<tr>
<td>Weight Loss (&gt; 5 kg)</td>
<td></td>
<td>5</td>
</tr>
<tr>
<td>Examination Findings</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Abdominal Mass</td>
<td></td>
<td>20</td>
</tr>
<tr>
<td>PR Mass</td>
<td></td>
<td>20</td>
</tr>
<tr>
<td>Bloods</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Unexplained Iron Def Anaemia</td>
<td></td>
<td>20</td>
</tr>
<tr>
<td>Enter the value for these tests (no score applicable)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ferritin</td>
<td></td>
<td>10</td>
</tr>
<tr>
<td>FOB positive (with any symptoms above)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>If Diarrhoea/Loose Motions</td>
<td></td>
<td>10</td>
</tr>
<tr>
<td>CRP &gt;10</td>
<td></td>
<td>10</td>
</tr>
<tr>
<td>Family History CRC</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cat 1</td>
<td></td>
<td>0</td>
</tr>
<tr>
<td>Cat 2</td>
<td></td>
<td>5</td>
</tr>
<tr>
<td>Cat 3</td>
<td></td>
<td>10</td>
</tr>
<tr>
<td>Personal History Adenoma</td>
<td></td>
<td>2.5</td>
</tr>
<tr>
<td>Personal History CRC</td>
<td></td>
<td>5</td>
</tr>
<tr>
<td>Age</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥ 60</td>
<td></td>
<td>10</td>
</tr>
<tr>
<td>40 - 59</td>
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<td>0</td>
</tr>
<tr>
<td>&lt; 40</td>
<td></td>
<td>-5</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

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While overt rectal bleeding has been confirmed as the most consistent predictor of CRC across a number of studies, the significance of the nature and type of rectal bleeding is less clear. Patients with suspicious rectal bleeding (blood which is dark red, clotted, mixed with stool or associated with mucous) appear to be much more likely to have CRC than those with outlet type bleeding, however there is still an important yield of CRC in the latter group. For this reason, the nature of rectal bleeding was differentiated in the scoring system and suspicious bleeding given a greater weighting.

Other gastrointestinal symptoms including change in bowel habit, weight loss and abdominal pain, occurring in the absence of lower gastrointestinal (GI) bleeding have been shown to have a lower predictive value for CRC. Of these, change in bowel habit to looser stools appears to be of greater significance. Hence this was given a greater weighting than constipation and weight loss in the scoring tool. There is evidence the presence of abdominal pain could decrease the diagnostic value of other symptoms, hence it was omitted.

The aforementioned symptoms are more commonly presenting features for left sided cancers, whereas right sided cancers may present with an abdominal mass or iron deficiency anaemia. The finding of an abdominal mass in primary care mandates investigation and was weighted as such in the scoring tool. However, supposed palpable abdominal masses are often extra colonic or not evident on further investigation so these patients were directed to CTC in the management algorithm (see below). The finding of unexplained iron deficiency anaemia (that is following exclusion of menstrual losses, non-gastrointestinal sources of blood loss and dietary factors) also mandates GI investigation and was therefore significantly weighted.

Of patients with rectal cancer, 40% to 80% have a palpable rectal mass and of these, 82% will be detected by GP performed rectal exam. A palpable mass on rectal examination warrants urgent investigation and its inclusion in the scoring system with significant weighting reflects this and acts as a reminder to GPs of the importance of a rectal examination in this setting to aid in prioritisation and rapid diagnosis of CRC.

Irrespective of symptoms, recognised risk factors for colorectal cancer exist. The most significant risk factor has been recognised as age. A personal history of colorectal CRC or adenomas predispose to CRC as does a family history of CRC. The presence of these risk factors in a symptomatic individual will increase the likelihood of a positive colonoscopy, hence their inclusion in the scoring tool.

Lifestyle factors implicated include alcohol, obesity and smoking. As the evidence for these factors and their relative contribution to risk assessment is less clear, they were not included in the scoring tool.

Figure 2 demonstrates the management algorithm according to the scoring tool. The score assigned was categorical and matched to the threshold. Using this approach, the threshold for investigation was set such that patients with high risk symptoms receive urgent investigation as per the latest New Zealand Guidelines Group (NZGG) guideline for suspected cancer in primary care.

In addition, those patients with lower risk symptoms, but with additional risk factors, also receive urgent investigation as suggested by the Association of Coloproctology of Great Britain and Ireland (ACPGBI) guidelines. Patients with low risk symptoms without additional risk factors are directed to either a routine investigation or GP managed care.

All referrals were triaged by a Consultant Gastroenterologist or GP Liaison in the Department of Surgery using the preceding management algorithm as a guide. However, during the study period, referrals continued to be accepted by routes other than the pathway and with criteria falling outside the pathway. Initially the pathway required referrers to print off a paper referral form. An electronic form is now in use.
Figure 2. CCrSP – Algorithm for outcome according to score. (CTC: Computed Tomography Colonography, COL: Colonoscopy, 1: within 4 weeks, 2: within 12 weeks)

Audit of the CCrSP—A retrospective audit of all outpatient referrals for symptomatic patients to Christchurch Hospital who received colonoscopy or CTC was performed approximately one year after the CCrSP was introduced. All referrals from 1 July 2010 to 31 December 2010 were collected prospectively. The demographic information, risk factors, symptoms, signs and investigations contained in the referral were recorded. The scoring tool was used to calculate a score for all referrals, including those that had not been assigned a score at the time of initial prioritisation. The scorers were blinded to the final diagnosis. The results and waiting times of subsequent investigations (colonoscopy and CTC) were then documented. This information was used to determine:

- The percentage of referrals using the pathway
- The predictive value of symptoms and symptom combinations recorded in referred patients
- The correlation of diagnostic yield with score obtained from the pathway
- Waiting times for CTC and colonoscopy
- Follow up colonoscopy and other radiology generated by CTC

Data management and analysis—Data were entered into a custom designed Microsoft access database and statistical analysis was performed using the R environment for statistical computing version 2.14.2.\(^{13}\) Odds ratios (OR), 95% confidence intervals (CI) and p values (mid p exact) were generated with the R package epitools\(^{14}\) with age and sex adjusted OR’s, CI’s and p values produced by logistic regression.
A multiple logistic regression model including all covariates was fitted to cancer outcome. Covariates which did not increase the models fit to the data under the Akaike Information Criterion (AIC) were dropped by forward and backward substitution. All tests were considered significant at a p value less than 0.05; p values less than 0.1 are reported otherwise tables show not significant (NS).

Ethical approval for the study was obtained from the Upper South A Regional Ethics Committee (URA/10/EXP/049).

Results

During the 6-month study period, a total of 1369 procedures were performed. Patients referred for surveillance purposes (n=389) or based on radiology findings (n=71) were excluded. A further 29 patients were excluded due to missing referrals. In 5 patients with multiple referrals, only the initial referral was included. In total, 886 (64.7%) studies were completed for symptomatic patients.

Referral characteristics are presented in Table 1. Two-thirds of referrals came from GPs with the remaining coming from specialists. Over half were female (59.6%) and the average age was 60.8 years.

Table 1. Referral characteristics

<table>
<thead>
<tr>
<th>Variables</th>
<th>n</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Symptomatic referrals</td>
<td>886</td>
<td>100</td>
</tr>
<tr>
<td>Referral source</td>
<td></td>
<td></td>
</tr>
<tr>
<td>GP</td>
<td>567</td>
<td>64.1</td>
</tr>
<tr>
<td>Specialist</td>
<td>319</td>
<td>35.9</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>358</td>
<td>40.4</td>
</tr>
<tr>
<td>Female</td>
<td>528</td>
<td>59.6</td>
</tr>
<tr>
<td>Pathway</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>234</td>
<td>26.4</td>
</tr>
<tr>
<td>No</td>
<td>652</td>
<td>73.6</td>
</tr>
<tr>
<td>Investigation</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CTC</td>
<td>253</td>
<td>28.6</td>
</tr>
<tr>
<td>Colonoscopy</td>
<td>633</td>
<td>71.4</td>
</tr>
</tbody>
</table>

Colonoscopies were performed on 633 symptomatic patients. Of those, CRC was histologically confirmed in 28 patients (4.4%). There were 253 patients triaged to CTC, of these, scans of 11 patients were reported as concerning for cancer. Subsequent colonoscopies confirmed cancer in 10 patients. The remaining patient had a normal colonoscopy to the terminal ileum indicating a false positive CTC. As a result of CTC, colonoscopy was recommended in 29 patients (11.5%) and further radiology for extracolonic findings in 20 patients (7.9%).

Of the 38 patients with confirmed cancer, 21 were female (55.3%). The average age of patients with cancer was 11.8 years older than those without (72.1 years versus 60.3 years, p<0.00001).

Symptoms and signs—The frequency of individual symptoms and their association with cancer are presented in Table 2.
The most common finding, rectal bleeding, was reported in 334 referrals. A history of undifferentiated rectal bleeding was not statistically significantly associated with cancer (OR=1.9, 95%CI 1.0–3.6, p=0.06,) however statistical significance was achieved after adjusting for age and sex (OR=2.1 95%CI 1.1–4.2, p=0.024).

In 239 referrals in which rectal bleeding was reported, the nature of the bleeding was further differentiated as either outlet (153), or sinister (86). A history of sinister bleeding was associated with the presence of CRC (OR=3.1, 95%CI 1.4–6.8, p=0.008), but no association was observed with a history of outlet bleeding.

Positive faecal occult blood test was the most predictive risk factor for carcinoma (OR 8.6, 95%CI 3.2–23.2, p<0.0003) and the presence of iron deficiency anaemia was also significantly associated with cancer (OR 4.2, 95%CI 2.1–8.2, p<0.0001). Although all the remaining signs or symptoms increased the fit of the logistic model for cancer, they did not reach statistical significance when considered as single symptoms.

Rectal bleeding, sinister rectal bleeding, positive FOBT and iron deficiency anaemia all remained statistically significant predictors of cancer after adjustment for age and sex.

Score—The colonoscopic yield for patients grouped according to the symptom score is presented in Table 3. Increased score was associated with an increased likelihood of cancer at subsequent investigation. Three of 427 patients with a score of less than 20 had cancer and no patients with a score less than 10 were diagnosed with cancer. There were 9 cancers found in the patients with a score of 20–29, resulting in an odds ratio of 3.4 (95%CI 0.9–12.6, p=0.08) compared to a score of 10–19.

As scores increased above 30, the risk of cancer increased dramatically, with 26 cancers out of the 221 patients. Patients with scores of 30–39 had an increase in the odds ratio to 11.0 (p<0.001), and if the score was greater than 40, this rose again to 12.4 (p<0.001).

Multiple logistic regression analysis showed that a 1 unit increase in score increased the likelihood of carcinoma by 8.2% (95%CI 5.7%–10.9, p<0.001) and by 7.2% (95%CI 4.4%–10.1%, p<0.001) after adjusting for age and sex. After accounting for age, gender, bleeding, change in bowel habit, weight loss, abdominal mass, rectal mass, iron deficiency anaemia and positive FOBT, there is no effect of score on the likelihood of carcinoma (p=0.14, ANOVA Chi-squared test). This is consistent with an increase in carcinoma risk being a true reflection of the positive clinical variables.
## Table 2. Risk of carcinoma with individual risk factors

<table>
<thead>
<tr>
<th>Variables</th>
<th>Carcinoma</th>
<th>All</th>
<th>Difference/OR (95% CI)</th>
<th>P value</th>
<th>Adjusted for age and sex</th>
<th>OR (95% CI)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients</td>
<td>848</td>
<td>38</td>
<td>886</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sex (female)</td>
<td>507 (59.8%)</td>
<td>21 (55.3%)</td>
<td>528 (59.6%)</td>
<td>0.8 (0.4–1.6)</td>
<td>NS</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>60.3 ± 17.1</td>
<td>72.1 ± 13</td>
<td>60.8 ± 17.1</td>
<td>11.9 (7.5–16.3)</td>
<td>&lt;10⁻⁵</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bleeding (all)</td>
<td>314 (37%)</td>
<td>20 (52.6%)</td>
<td>334 (37.7%)</td>
<td>1.9 (1–3.6)</td>
<td>0.060</td>
<td>2.1 (1.1–4.2)</td>
<td>0.024</td>
</tr>
<tr>
<td>Bleeding Outlet</td>
<td>145 (17.1%)</td>
<td>8 (21.1%)</td>
<td>153 (17.3%)</td>
<td>1.3 (0.6–2.9)</td>
<td>NS</td>
<td>1.4 (0.6–3)</td>
<td>NS</td>
</tr>
<tr>
<td>Bleeding Sinister</td>
<td>77 (9.1%)</td>
<td>9 (23.7%)</td>
<td>86 (9.7%)</td>
<td>3.1 (1.4–6.8)</td>
<td>0.008</td>
<td>3.2 (1.4–7)</td>
<td>0.004</td>
</tr>
<tr>
<td>Change in Bowel Habit</td>
<td>445 (52.5%)</td>
<td>20 (52.6%)</td>
<td>465 (52.5%)</td>
<td>1 (0.5–1.9)</td>
<td>NS</td>
<td>1.1 (0.6–2.2)</td>
<td>NS</td>
</tr>
<tr>
<td>Constipation</td>
<td>131 (15.4%)</td>
<td>3 (7.9%)</td>
<td>134 (15.1%)</td>
<td>0.5 (0.1–1.5)</td>
<td>NS</td>
<td>0.4 (0.1–1.1)</td>
<td>NS</td>
</tr>
<tr>
<td>Loose</td>
<td>329 (38.8%)</td>
<td>18 (47.4%)</td>
<td>347 (39.2%)</td>
<td>1.4 (0.7–2.7)</td>
<td>NS</td>
<td>1.5 (0.8–3)</td>
<td>NS</td>
</tr>
<tr>
<td>Weight Loss</td>
<td>116 (13.7%)</td>
<td>8 (21.1%)</td>
<td>124 (14%)</td>
<td>1.7 (0.8–3.8)</td>
<td>NS</td>
<td>1.4 (0.6–3)</td>
<td>NS</td>
</tr>
<tr>
<td>Abdo Mass</td>
<td>23 (2.7%)</td>
<td>2 (5.3%)</td>
<td>25 (2.8%)</td>
<td>2 (0.5–8.8)</td>
<td>NS</td>
<td>1.5 (0.2–5.6)</td>
<td>NS</td>
</tr>
<tr>
<td>PR Mass</td>
<td>18 (2.1%)</td>
<td>2 (5.3%)</td>
<td>20 (2.3%)</td>
<td>2.6 (0.6–11.5)</td>
<td>NS</td>
<td>2.4 (0.4–9)</td>
<td>NS</td>
</tr>
<tr>
<td>Anaemia</td>
<td>126 (14.9%)</td>
<td>16 (42.1%)</td>
<td>142 (16%)</td>
<td>4.2 (2.1–8.2)</td>
<td>0.00008</td>
<td>3.2 (1.6–6.3)</td>
<td>0.0010</td>
</tr>
<tr>
<td>FOBT-positive</td>
<td>18 (2.1%)</td>
<td>6 (15.8%)</td>
<td>24 (2.7%)</td>
<td>8.6 (3.2–23.2)</td>
<td>0.00032</td>
<td>6.1 (2.1–16.3)</td>
<td>0.00050</td>
</tr>
</tbody>
</table>
Table 3. Risk of cancer by score groups

<table>
<thead>
<tr>
<th>Score</th>
<th>Patients</th>
<th>Carcinoma (%)</th>
<th>OR (95%CI)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>-5 – 9</td>
<td>167</td>
<td>0 (0%)</td>
<td>0 (0–3.8)</td>
<td>NS</td>
</tr>
<tr>
<td>10 – 1 9</td>
<td>260</td>
<td>3 (1.2%)</td>
<td>1 *</td>
<td>NS</td>
</tr>
<tr>
<td>20 – 2 9</td>
<td>239</td>
<td>9 (3.8%)</td>
<td>3.4 (0.9–12.6)</td>
<td>0.078</td>
</tr>
<tr>
<td>30 – 3 9</td>
<td>141</td>
<td>16 (11.3%)</td>
<td>11.0 (3.1–38.3)</td>
<td>&lt;10^{-5}</td>
</tr>
<tr>
<td>40 +</td>
<td>79</td>
<td>10 (12.7%)</td>
<td>12.4 (3.4–46.7)</td>
<td>&lt;10^{-4}</td>
</tr>
</tbody>
</table>

* Odds Ratios (OR) relative to the second lowest score group, no cancers observed in lowest score group produce infinite OR and CI; NS=Not significant.

Table 4. Risk of cancer and advanced neoplasia by score groups

<table>
<thead>
<tr>
<th>Score</th>
<th>Patients</th>
<th>Carcinoma or Advanced Neoplasia (%)</th>
<th>OR (95%CI)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>-5 – 9</td>
<td>167</td>
<td>2 (1.2%)</td>
<td>1</td>
<td>NS</td>
</tr>
<tr>
<td>10 – 1 9</td>
<td>260</td>
<td>10 (3.8%)</td>
<td>3.3 (0.7–15.3)</td>
<td>NS</td>
</tr>
<tr>
<td>20 – 2 9</td>
<td>239</td>
<td>17 (7.1%)</td>
<td>6.3 (1.4–27.7)</td>
<td>0.007</td>
</tr>
<tr>
<td>30 – 3 9</td>
<td>141</td>
<td>19 (13.5%)</td>
<td>12.8 (2.9–56.2)</td>
<td>&lt;10^{-4}</td>
</tr>
<tr>
<td>40 +</td>
<td>79</td>
<td>11 (13.9%)</td>
<td>13.3 (2.9–61.8)</td>
<td>&lt;10^{-4}</td>
</tr>
</tbody>
</table>

Table 5. Risk of colitis by score groups

<table>
<thead>
<tr>
<th>Score</th>
<th>Patients</th>
<th>Colitis (%)</th>
<th>OR (95%CI)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>-5 – 9</td>
<td>167</td>
<td>12 (7.2%)</td>
<td>1</td>
<td>–</td>
</tr>
<tr>
<td>10 – 1 9</td>
<td>260</td>
<td>11 (4.2%)</td>
<td>0.57 (0.2–1.3)</td>
<td>NS</td>
</tr>
<tr>
<td>20 – 2 9</td>
<td>239</td>
<td>13 (5.4%)</td>
<td>0.74 (0.3–1.7)</td>
<td>NS</td>
</tr>
<tr>
<td>30 – 3 9</td>
<td>141</td>
<td>6 (4.3%)</td>
<td>0.57 (0.2–1.6)</td>
<td>NS</td>
</tr>
<tr>
<td>40 +</td>
<td>79</td>
<td>6 (7.6%)</td>
<td>1.06 (0.4–2.9)</td>
<td>NS</td>
</tr>
</tbody>
</table>

Advanced colorectal neoplasia was defined previously as: an adenoma of 10 mm or greater in diameter, or with high grade dysplasia, or with more than 25% villous components, or an invasive cancer. When the finding of advanced colorectal neoplasia, rather than just CRC was considered, the score remained predictive (Table 4). However, higher scores were not associated with a subsequent finding of colitis (Table 5).

Referrals for 234 patients were made using the pathway and the remaining 652 referrals were scored based on the information provided on a traditional referral. The diagnosis of cancer was made in 6.4% of pathway referrals and 3.5% of non-pathway referrals. The odds of cancer were 87% higher in the pathway referrals, however this was not statistically significant (OR = 1.87, 95%CI 0.94–3.65, P = 0.074).

Waiting times—Time from the initial referral to the procedure was evaluated. The median wait time for a colonoscopy was 57 days. The wait time was shorter for CTC (28 days). Wait time was inversely proportional to referral score on a log scale. A 5 point rise in the score decreased wait time by 9.3% on average (95%CI 7%–11%, p<0.0001). This resulted in shorter waiting times for patients who were subsequently diagnosed with cancer for both colonoscopy and CTC (42.5 and 19 days respectively).
Discussion

In this study, the CCrSP demonstrated clinical utility in allowing effective triage of patients for investigation of possible CRC. The scoring system was sensitive for cancer in those receiving an investigation and correlated with the risk of cancer. The only *individual* factors statistically significantly associated with CRC were related to rectal bleeding, however, combining clinical features using the scoring tool increased the predictive value.

Existing international and recently published national guidelines for investigation of lower GI symptoms focus on single symptoms as indications for referral,\(^8,16,17\) However, guidelines such as these have been shown to miss a significant percentage of CRC\(^6\) and combinations of symptoms may have greater predictive value.\(^4\) This contention was supported by a small pilot study from Auckland that demonstrated patients over the age of 67, those with rectal bleeding or with a family history of CRC should be given priority access to colonoscopy.\(^18\)

The present study further supports the notion that combinations of clinical features will increase the yield at subsequent colonoscopy and prioritisation systems should account for this.

With the increasing pressure on colonoscopy resources, CTC is increasingly being used in the investigation of lower GI symptoms. Computed Tomographic Colonography has been shown to be highly sensitive for CRC and local data are consistent with this finding.\(^19\) Despite high sensitivity for CRC, the inappropriate use of CTC can lead to high follow up requirements of both colonoscopy and subsequent radiology for extracolonic findings, decreasing its cost-effectiveness and increasing patients’ exposure to ionising radiation.

The CCrSP was designed to maximise the utility of CTC and minimise duplicate investigations by directing potentially lower yield investigations to CTC, thereby reducing the number of subsequent colonoscopies required. Therefore, patients with lower risk presentations, those more likely to suffer morbidity from colonoscopy, including the elderly and those with comorbidity (for example requiring anticoagulation), were directed to CTC in the first instance.

Patients with high risk presentations, or diarrhoea predominant conditions where mucosal assessment is necessary, were routed direct to colonoscopy. Suspected abdominal masses were also routed direct to CTC as CTC would provide greater accuracy in firstly confirming the existence of a mass and secondly its organ of origin. In the present study, CTC resulted in a low rate of follow up colonoscopy, suggesting this triage approach was effective in minimising duplicate investigation. In addition the low rate of request for subsequent radiology compares favourably with previous studies of extracolonic findings in CTC.\(^20\)

While the CCrSP attempted to account for all colorectal pathologies, it was heavily weighted to predict cancer. As a result, the scoring system performed poorly in predicting the presence of colitis. If the scoring tool was to do this effectively modification would be required. Additional variables could be added, such as faecal calprotectin, or a blanket inclusion for the investigation of “suspected inflammatory bowel disease.”
In addition to difficulty in including non-cancer diagnoses in the algorithm, this pathway and indeed any diagnostic pathway accounts poorly for atypical presentations. Therefore if a pathway is rigidly enforced, patients with unusual presentations of cancer may be denied access to important investigations. This reinforces the importance of clinical override in any diagnostic pathway of this nature.

Experienced specialist staff must still be able to consider referrals and offer investigation, or at least a first specialist assessment (FSA) if patients have atypical, but significant symptoms. Referrers are encouraged on HealthPathways to add text to their referrals to mitigate the risk of missing non-cancer diagnoses and atypical diagnoses. These messages are reinforced in education sessions.

The importance of clinical override is also apparent in any diagnostic pathway with hard cut off points. To use a simple example from the current pathway: a 39 year old with rectal bleeding would be treated differently from a 40 year old with the same presentation. This problem can be avoided if manual triaging with appropriate clinical override continues to occur within the pathway (as has been the case to this point with the CCrSP).

Prior to the introduction of the CCrSP, staff triaging referrals at the CDHB noted a paucity of information in many referrals on which to base triage decisions. The methodology used in the above evaluation did not allow meaningful comparison of the level of information included in pathway and non-pathway referrals. However, the response from triaging staff is that the level of information has improved with the introduction of the CCrSP. The CCrSP provides an educational component to GPs, reinforcing the important clinical information required in diagnosing colorectal disease.

The accuracy of the information in the referrals was not investigated in this evaluation. The introduction of any rationing based on clinical features may produce an element of ‘gaming’ with referrers more likely to exaggerate symptoms in referrals in order to obtain an investigation for their patients. This phenomenon, known as Braess’s paradox, may result in reduced accuracy of referrals and nullify any efficiency gained in introducing such rationing.

While the results suggest the CCrSP has substantial clinical utility, significant limitations in the methodology used in this evaluation must be acknowledged. The major weakness is that only patients who received an investigation were included in the study. Patients with symptoms that did not reach the threshold for investigation may still have remained undiagnosed in the community or been diagnosed with cancer through other routes, such as private sector colonoscopy or radiology. Hence, the high sensitivity for cancer with the threshold for investigation set at a score above 10 demonstrated in this evaluation may not be truly representative.

In addition, knowing the significant pressure and wait times for colonoscopy, GPs may not have referred patients with less severe symptoms, believing it to be futile. These results can’t exclude the possibility of significant unmet need for colonoscopy in the community.

The clinical features included in this analysis were extracted from the referrals retrospectively and are limited by the information contained in the referrals. Many referrals, particularly those not on the pathway, contained very little information.
hence the actual clinical features recorded may not reflect the true situation. This is reflected in the large number of patients in the lowest triage group (score $\leq 10$). Re-interviewing all patients at the time of their investigation could have mitigated against this. Increased uptake of the pathway with the introduction of an electronic referral form with all clinical features as required fields will increase the level of information provided in the future.

The generalisability of these results to other regions of New Zealand is also questionable. In particular, CTC accuracy remains reporter dependent requiring radiologists experienced in the technique. This evaluation has supported previous data from Canterbury in suggesting accurate CTC\textsuperscript{19}. With the algorithm for use of CTC employed, there was a low rate of follow up colonoscopy and further radiology requirement. If quality CTC is not available, both missed cancers and high follow up colonoscopy rates with unnecessary duplication of investigations may occur.

**Conclusion**

The CCrSP was sensitive for predicting CRC at subsequent investigation. As the symptom score correlated with the risk of cancer it provides a tool to triage patients based on a combination of clinical risk factors rather than just individual symptoms. Effective risk stratification aids in the efficient use of CTC in the investigation algorithm.

Uptake at the time of the evaluation had only been moderate; however this can be expected to increase with the introduction of electronic referrals linked to practice management software. The system also has the benefit of increasing the amount of information contained in referrals. The introduction of the scoring tool and clinical pathway has been a successful collaborative exercise which required the cooperation of many parts of the health system. Further evaluation, feedback and monitoring of the pathway is underway.

**Competing interests:** None identified.

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**References:**


Perceived risks and benefits of surveillance colonoscopy in people undergoing surveillance for family history of colorectal cancer

Gregory P Tarr, Rebecca A Smith, Rhys A John, Andrew P Crowley, Jonathan B C Kok, Ho-Nam Lee, Mohd Hasif B Mustafa, Kia M Sii, Sung-Eun Son, Lauren J Weaver, Claire Cameron, John D Dockerty, Iain A Murray, Michael Schultz

Abstract

Aim To determine perceived risks and benefits of colonoscopy surveillance among patients undergoing surveillance colonoscopy due to family history of colorectal cancer (CRC).

Method We conducted a standardised phone interview of 250 randomly selected people who had undergone surveillance colonoscopy at Dunedin Hospital. We assessed perceptions of colonoscopy effectiveness, complication rates, and CRC risk.

Results We included 148 (69%) participants. Most felt well informed about surveillance (66.7%), but many wanted further information (63.2%). Most accurately estimated complication rates (discomfort: Common/Uncommon 70.3%; pain: Rare/Uncommon 58.8%; bleeding: Rare/Uncommon 72.3%; perforation: Very rare 62.8%), and benefits (mean reduction in risk of CRC 72.6% and death 76.2%). Most (55.1%) over-estimated their CRC risk. 13.5% thought perforation never occurred, and 12.8% thought colonoscopy either completely prevented, or had no effect on risk of developing or dying from CRC. Patients giving unrealistic estimates had similar demographics and clinical variables to the wider cohort.

Conclusion Our results suggest current surveillance education adequately communicates risks and benefits to most patients. A minority have unrealistic views and further education may be indicated.

Colorectal cancer (CRC) is a common cause of morbidity and mortality in New Zealand, and this burden may be reduced by the removal of colorectal polyps. New Zealand guidelines currently recommend routine colonoscopy surveillance in high risk groups. Further extension of this service is currently being evaluated through a CRC screening pilot study involving the Waitemata District Health Board.

Before introducing such a programme nationwide it is beneficial to understand the perception of risks and benefits of a group who is currently undergoing surveillance.

Patients need a good understanding of the risks and benefits of colonoscopy to enable them to make informed decisions about whether to undergo the procedure.

The best evidence of the risks and benefits of surveillance colonoscopy come from large prospective cohort studies amongst the general population. The detection of polyps with subsequent polypectomy appears to reduce the risk of development of CRC by between 76% and 90%, and the risk of death from CRC by 53%.
These findings provide a strong incentive to perform surveillance on individuals at high risk of developing polyps, however, neither colonoscopy nor polypectomy are undertaken without risk.

Large cohort studies have shown that bleeding and perforation occur at a rate of 1.6 to 4.5 per 1000\(^5,6\) and 0.85 to 0.9 per 1000\(^5,6\) respectively. Polypectomy is the main cause of both serious bleeding and perforation, which occur around ten times as often as during colonoscopy without polypectomy.\(^5,6\)

While serious complications are relatively rare, minor complications are common, with up to 14.9\% of patients reporting pain and up to 29.0\% reporting discomfort (including bloating and nausea).\(^7\)

Empirical studies suggest patient understanding of the risks of colonoscopy is relatively low,\(^8\) although understanding of the purpose and benefits may be greater.\(^9,10\) In a mixed group of symptomatic and surveillance patients, only half remembered receiving any information about the risks, while rectal bleeding and perforation were each remembered by 30\% of patients.\(^11\)

In controlled studies, groups receiving standard colonoscopy education sessions gave incorrect answers to around one-third of questions after education was completed.\(^8\)

Most patients appear to understand of the benefits of colonoscopy, with most able to explain the purpose of the procedure,\(^9\) and agree that this decreases the likelihood of dying from CRC.\(^10\) There may be an interaction between knowledge and risk, with those at higher risk due to previous polyps or family history being more likely to understand benefits.\(^9,10\)

In a group of patients who had undergone surveillance colonoscopy for a family history of CRC we aimed to assess:

- The perception of the risks and benefits of the colonoscopy surveillance.
- Their perceptions of their own lifetime risk of CRC if they had never undergone colonoscopy.
- The perception of the adequacy of education about colonoscopy surveillance.

**Method**

**Participants**—Eligible participants had undergone colonoscopy surveillance between February 1996 and February 2012 at Dunedin Hospital for a family history of CRC. Exclusion criteria were age over 75 years at recruitment, or a personal history of CRC or inflammatory bowel disease. Patients aged over 75 were excluded as they were not eligible for further colonoscopy surveillance. Participants were randomly selected from the hospital clinical database of approximately 1100 patients. Random numbers were generated from [http://www.random.org/](http://www.random.org/). Because only limited information was available from the hospital database, eligibility was assessed once participant consent had been obtained.

Potential participants were sent an information sheet and a visual aid. This contained some of the questionnaire, and a labelled numerical scale for risk-based questions.\(^12\) We omitted questions about their risk of CRC, the reduction in CRC incidence and death afforded by colonoscopy, and rates of complications to ensure that patients did not research the answers beforehand.

Verbal consent was obtained and the interview was administered by telephone. The interview was standardised across all investigators by provision of a script and a training session. This study was carried out with the approval of the Lower South Regional Ethics Committee.
Questionnaire and information collected—Demographic information recorded included age, gender, ethnicity, marital status and highest level of education. Additional questions and information collected are displayed in Table 1.

Table 1. Information collected from interview and hospital records

<table>
<thead>
<tr>
<th>Family history of cancer</th>
<th>Age at first diagnosis</th>
<th>Type of cancer</th>
<th>Whether each relative was first or second degree</th>
</tr>
</thead>
<tbody>
<tr>
<td>Previous colonoscopies</td>
<td>Number</td>
<td>Results</td>
<td>(Obtained from hospital records; including completeness of procedure, and number of polyps removed).</td>
</tr>
<tr>
<td>Patient perception</td>
<td>Adequacy of information received about need for surveillance</td>
<td>Effect of surveillance on anxiety</td>
<td>Intentions to remain in screening programme</td>
</tr>
</tbody>
</table>

Definitions—The risk of CRC was calculated as per New Zealand Guidelines Group (NZGG) recommendations. NZGG guidelines classify patients depending on presence of family history and features of genetic CRC syndromes. A summary of the features and criteria for each category is displayed in Table 2.

Table 2. New Zealand Guidelines Group categorisation of those at elevated risk of CRC due to family history and guidelines for surveillance

<table>
<thead>
<tr>
<th>NZGG category</th>
<th>Family History</th>
<th>Lifetime risk %</th>
<th>Guidance recommended</th>
</tr>
</thead>
<tbody>
<tr>
<td>General population</td>
<td>None or may have 2° relatives with CRC.</td>
<td>5.9%</td>
<td>No surveillance</td>
</tr>
<tr>
<td>NZGG category 1</td>
<td>One 1° relative CRC &gt;55yrs.</td>
<td>6 to 12%</td>
<td>No specific surveillance (low threshold)</td>
</tr>
<tr>
<td>NZGG category 2</td>
<td>One 1° relative CRC &lt;55yrs. Two 1° relatives on same side of family any age.</td>
<td>18 to 36%</td>
<td>~5 yearly colonoscopy</td>
</tr>
<tr>
<td>NZGG category 3</td>
<td>One 1° + two or more 1° or 2° relatives on same side of family at any age. Other factors: CRC syndromes, multiple polyps, immunohistochemistry.</td>
<td>“up to 50%, or higher if genetic mutations”</td>
<td>Refer to genetic specialist, familial CRC registry, CRC specialist for management &amp; surveillance</td>
</tr>
</tbody>
</table>

Adapted from “Guidance on surveillance for people at increased risk of colorectal cancer” by New Zealand Guidelines Group. CRC = Colorectal cancer. NZGG = New Zealand Guidelines Group.

NZGG category was determined by three investigators, and agreement with clinical documentation was good (Kappa 0.76).

Appropriateness of perceptions of risks and benefits was judged by similarity with true rates of complications, and of relative risk reductions. The following responses were judged to be “Appropriate”: Discomfort and Pain: “Common” or “Uncommon”; Bleeding: “Uncommon” or “Very rare”; Perforation: “Very rare”.

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For the benefits of colonoscopy, appropriateness was judged on the mean estimation of relative risk reduction of CRC incidence and death.

Participants who estimated that colonoscopy surveillance either had no effect on CRC incidence or death, completely prevented CRC incidence or death, or believed that perforation never occurred were considered to have “seriously unrealistic” expectations.

To compare perceived risk to NZGG category, each participant’s estimate was classified as “Appropriate”, “Underestimate” or “Overestimate” as follows: If participants estimated their risk to be within the bounds of their assigned NZGG category or not crossing the bounds of an adjacent category, their estimation was deemed appropriate.

Estimations that fell beyond these bounds were classified as over- or under-estimates. For those not meeting NZGG criteria, the lower bound was set as 1%. For those meeting NZGG category 3, the upper bound was set as 80%, as this is the approximately the lower bound of risk for monogenetic CRC syndromes.

Statistical analysis was performed with Stata v10.0 (StataCorp, Texas) and StatView v5.01 (SAS Institute) software. Non-normally distributed variables were log-transformed.

Results are displayed as mean (95% confidence interval) or number (%) unless otherwise stated. Continuous variables were compared between categories using ANOVA, or Mann Whitney-U and discrete variables were compared using the Chi-square test. A p-value of < 0.05 was considered statistically significant and all tests were two-tailed.

A power calculation determined that a sample size of 150 participants would detect a difference of 10 percentage points between three equal-sized groups with 80% power. Assuming a 60% response rate, we approached 250 patients.

Because this study includes participants undergoing colonoscopy over a long time period, as a sensitivity analysis the participants were split into three eras—1996 to 2003, before New Zealand guidelines were developed, 2004 to 2010, after guidelines were developed, and 2011 to 2012, when Dunedin Public Hospital has been guideline-compliant.

Results

Recruitment and demographics—Of 250 participants initially sampled, 34 were ineligible (previous CRC n=11, inflammatory bowel disease n=4, not in surveillance programme n=1, duplicate n=1, deceased n=4, aged over 75 years n=13).

Of 216 eligible patients, 47 were unable to be contacted, and 21 declined consent. The remaining 148 patients participated, giving a response rate of 69%. Those who were excluded were younger than those included (55.3 [95%CI 53.0 to 57.5] vs. 57.9 [95%CI 56.5 to 59.3]; p=0.045), but similar in terms of composition by gender (42.4% vs. 37.8% male; p=0.63).

The clinical and demographic details of the included population are given in Table 3. Fifteen (10.1%) participants had calculated NZGG category 1, 66 (44.6%) were NZGG category 2, 57 (38.5%) were NZGG category 3. Ten (6.8%) participants did not meet formal NZGG criteria but had undergone colonoscopy surveillance for second-degree family histories.
Table 3. Demographic and clinical characteristics of the study population

<table>
<thead>
<tr>
<th>Variables</th>
<th>N=148</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years</td>
<td>57.9 (56.5 to 59.3)</td>
</tr>
<tr>
<td>Gender, male</td>
<td>56 (37.8%)</td>
</tr>
<tr>
<td>NZ European</td>
<td>142 (96.0%)</td>
</tr>
<tr>
<td>NZ Dep2006*</td>
<td>5.3 (4.9 to 5.7)</td>
</tr>
<tr>
<td>Marital status</td>
<td></td>
</tr>
<tr>
<td>Married/de facto</td>
<td>109 (73.6%)</td>
</tr>
<tr>
<td>Single/widowed</td>
<td>22 (14.9%)</td>
</tr>
<tr>
<td>Divorced/separated</td>
<td>17 (11.5%)</td>
</tr>
<tr>
<td>Education completed</td>
<td></td>
</tr>
<tr>
<td>Primary</td>
<td>6 (4.1%)</td>
</tr>
<tr>
<td>Secondary</td>
<td>75 (50.7%)</td>
</tr>
<tr>
<td>Tertiary</td>
<td>66 (44.6%)</td>
</tr>
<tr>
<td>Personal history of cancer other than CRC</td>
<td>23 (15.5%)</td>
</tr>
<tr>
<td>Colonoscopies, median (IQR)</td>
<td>1 (1–3), range 1–7</td>
</tr>
<tr>
<td>Polyps removed, median (IQR)</td>
<td>1 (0–2), range 0–120</td>
</tr>
<tr>
<td>Number of first-degree relatives, median (IQR)</td>
<td>1 (1–2)</td>
</tr>
<tr>
<td>Age of first degree relative at earliest diagnosis</td>
<td>49.5 (47.5 to 51.6)</td>
</tr>
<tr>
<td>Number of second-degree relatives, median (IQR)</td>
<td>1 (0–2)</td>
</tr>
<tr>
<td>Total number of relatives with cancer, median (IQR)</td>
<td>3 (2–4)</td>
</tr>
</tbody>
</table>

Results are mean (95% confidence interval or number (percentage), unless stated otherwise.
* New Zealand Deprivation Index 2006.
† Number of relatives with CRC.
‡ Number of relatives (first- or second-degree) with any cancer.

Results about the adequacy of information explaining the need for colonoscopy surveillance are displayed in Table 4. Most participants felt the information was sufficient. However, many participants wanted more information about the need for surveillance.

The vast majority of participants wished to remain in the surveillance programme, were undeterred by thoughts of procedural complications, and felt reassured by surveillance.

Perceived rates of complications are displayed in Figure 1. The most accurate response for each question as stated in the literature is marked with a box. The majority of participants accurately estimated risks of complications.

The mean estimate of relative risk reduction conveyed by colonoscopy surveillance was 72.6% (95% CI 68.9 to 76.3%) for developing CRC, and 76.2% (95% CI 73.2 to 79.2%) for dying from CRC.
Table 4. Information received about the need for surveillance and thoughts about surveillance (N=148)

<table>
<thead>
<tr>
<th>How much information have you received about the need for colonoscopy screening?</th>
<th>n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>None</td>
<td>20 (13.5)</td>
</tr>
<tr>
<td>Too little</td>
<td>29 (19.6)</td>
</tr>
<tr>
<td>About right</td>
<td>99 (66.9)</td>
</tr>
<tr>
<td>Too much</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Would appreciate further information</td>
<td>93 (63.2%)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>I intend to remain in the screening programme</th>
<th>n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
<td>142 (96.0)</td>
</tr>
<tr>
<td>Unsure</td>
<td>4 (2.7)</td>
</tr>
<tr>
<td>No</td>
<td>2 (1.4)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Does the possibility of a complication deter you from having the procedure?</th>
<th>n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
<td>2 (1.4)</td>
</tr>
<tr>
<td>Unsure</td>
<td>9 (6.1)</td>
</tr>
<tr>
<td>No</td>
<td>137 (92.6)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Does colonoscopy surveillance reassure you, or increase your anxiety about developing CRC?</th>
<th>n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reassure</td>
<td>128 (86.5)</td>
</tr>
<tr>
<td>No effect</td>
<td>16 (10.8)</td>
</tr>
<tr>
<td>Increase</td>
<td>4 (2.7)</td>
</tr>
</tbody>
</table>

Figure 1. Perceived rates of colonoscopy complications amongst people undergoing colonoscopy surveillance

Participants’ risk estimation by NZGG category is displayed in Figure 2. Most people over-estimated (55.1%) their risk of CRC. Only 34.0% correctly estimated their risk and 10.8% under-estimated it. Risk estimation was not significantly impacted by the level of risk conferred by family history, as quantified by either calculated NZGG category or by the number of affected family members.
A small but significant proportion thought that perforation never occurred. Nineteen (12.8%) thought that colonoscopy surveillance eliminated their risk of dying from CRC whilst 16 (10.8%) thought it completely eliminated their risk of development. Ten participants (6.8%) thought that surveillance completely eliminated both the risk of developing, and of dying from, CRC.

In contrast, five participants (3.4%) responded that colonoscopy surveillance had no effect on their risk of developing CRC. Overall, 42 participants gave at least one answer that we judged to be “seriously unrealistic”. Participants with seriously unrealistic expectations were similar in terms of demographic and clinical variables to that of the wider cohort.

Participant responses were analysed according to the era in which they last underwent surveillance colonoscopy. Those who had undergone surveillance more recently had had more colonoscopies, more polypectomies (both p<0.01) and were more likely to report that perforation happened frequently. However, they were otherwise similar in terms of demographics, NZGG category, and understanding of risks and benefits of surveillance with no other significant differences in any perceptions of risk or benefit.
Discussion

The main findings of our study were that in this high risk group undergoing colonoscopy surveillance the majority have relatively accurate perceptions of the rate of complications and reduction of risk afforded by colonoscopy surveillance.

Most wanted further information about the need for surveillance. The majority felt reassured by surveillance and wanted to remain in the surveillance programme, however most over-estimated their lifetime risk of CRC. A significant minority had “seriously unrealistic” expectations, and these patients were similar in terms of demographic and clinical variables to the wider cohort.

Those undergoing colonoscopy surveillance for high risk of CRC due to family history appear to have a good appreciation of the risks and benefits of colonoscopy. Most people gave estimates similar to the true rates for complications, as well as benefits for both CRC incidence and death.

Our results extend the findings of Liljegren et al and Yim et al who found that nearly all patients were able to describe the purpose of colonoscopy and polypectomy to investigators, and that most patients agreed that colonoscopy decreased their risk of dying.

Bowles et al studied a group of UK patients who had recently undergone colonoscopy, and found that only half remembered being told of possible adverse events of colonoscopy prior to the procedure.

In contrast, most of our study population were able to identify the approximate true rate of multiple complications. Our finding that understanding of risks and benefits of colonoscopy is relatively good is important from an ethical point of view, as an appreciation of both is required for informed consent.

This analysis has not been previously performed in New Zealand, and is encouraging as it suggests that local practice in education is at least as successful as services for high risk patient groups in other countries.

One-third of participants felt they did not receive enough information about the need for colonoscopy surveillance, and no one felt they had received too much information. Indeed, over 60% of participants stated they would have liked further information. In a similar group, patients placed high value on CRC genetic counselling sessions and felt that these allayed anxiety.

Adequate patient knowledge is an important step for adherence to invasive procedures. Anecdotally some participants were concerned with practical issues, such as the frequency with which they should undergo surveillance. Further research could address areas patients perceive to be lacking in information.

Participants appeared to highly value colonoscopy surveillance. These findings are in line with other studies, which suggest high risk patients think medical services to discuss and reduce their risks are important.

Concerns have recently been raised in New Zealand about the implementation of the CRC screening programme increasing patient anxiety. Our results in this high-risk subgroup suggest that patients are reassured although findings from a surveillance high risk group may not be always transferable to an average risk screening
population. Further research could be addressed to look at knowledge or overall risks and benefits in a screening population.

Most participants over-estimated their life time risk of CRC. The profiles of risk estimation were similar across all NZGG categories. While it appears that those in NZGG category 3 were more likely to give accurate risk estimates, this may have occurred by coincidence rather than accurate risk perception (Figure 2). The tendency to over-estimate risk has been confirmed in other studies.9,18,19

This elevated risk perception may be a double-edged sword, both stimulating attendance at preventative services,20 and as a potential harm in high-risk patients, being linked to increased anxiety.21

A randomised controlled trial suggests that provision of cancer risk information based on personal risk factors produces accurate estimation of risk in as much as half of participants, compared to only 10% of controls.18 These findings suggest that addressing patients’ risk estimation during surveillance counselling may reduce psychological morbidity.

While many patients appeared to have a good appreciation of the risks and benefits of surveillance colonoscopy, a significant minority gave incorrect estimates that could have serious clinical consequences.

This small number of “seriously inaccurate” estimates has been found in other studies carried out in cancer prevention populations. In a study of women undergoing mammography screening, 9% believed that 2 yearly mammography prevented practically all breast cancer, when the true figure is nearer 25%.22

There were no defining demographic or clinical indicators of patients with these seriously unrealistic expectations in our study. Domenighetti et al22 found that women with higher educational attainment were more likely to have accurate estimates of benefits of mammography, but this only explained a small amount of variation in the appropriateness of estimates. It may be more clinically useful to question patients directly as part of the informed consent process, to ensure detection of those at risk of clinically important misunderstandings.

Our results may be instructive for the needs of patient education if New Zealand were to adopt a national screening programme. It is likely that our results would be at least partly generalisable to a lower risk population undergoing screening, but there may be important differences.

Speculatively, lower risk populations may see relatively less need for themselves to undergo screening procedures, be less tolerant of invasive procedures, and be less motivated to learn about their risks and preventive measures themselves.

There were a number of limitations to our study. While risk prediction models for colorectal cancer exist, none are validated or widely used in New Zealand. We used the NZGG score which is based only on family history, but is widely used in clinical practice.

A number of our study questions involved numerical estimation. We attempted reduce the influence of participant numeracy by utilising a visual aid with labelled scales, to allow the most consistent responses across those with low and high numeracy.23
We had a satisfactory response rate, indicating that our results are most likely generalisable to those undergoing colonoscopy surveillance for family history. Selection bias may still have occurred, and therefore our findings may not fully represent all patients undergoing surveillance.

We classified participants’ estimates into ‘appropriate’, ‘inappropriate’ or ‘seriously unrealistic’ categories. While we based these classifications on estimates of the true rate of events from cohort studies, there is no gold-standard method for assigning the above classifications to patients’ perceptions. We allowed the ‘appropriate’ classification to have reasonably broad limits around the true value, which may have resulted in over-estimation of true rates of knowledge.

Our study assessed the perceptions of patients who had undergone colonoscopy surveillance in the past. The finding that patients had a relatively accurate perception of risks and benefits, despite some not having undergone a colonoscopy for several years, indicates a good depth of understanding.

We performed a sensitivity analysis which suggested that patient demographics and understanding of risks and benefits were similar regardless of when they last underwent colonoscopy surveillance.

In conclusion, this study has shown that the current informed consent process in New Zealand appears to be working well to educate patients about the risks and benefits of colonoscopy. A small subset of people hold seriously unrealistic expectations, which may be clinically significant. Identification of these patients may be indicated, in order to help them make a truly informed choice in their decision whether to undergo colonoscopy.

We have also reinforced the literature showing that regardless of actual patient risk, estimates of the lifetime risk of CRC are commonly over-estimated.

Competing interests: None.

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References:


Immunochemistry screening for Lynch syndrome in colorectal adenocarcinoma using an initial two antibody panel can replace a four antibody panel

Toni O’Regan, Kai Chau, Michael Tatton, Tania Smith, Susan Parry, Ian Bissett

Abstract

**Aim** The current practice in immunochemistry staining for Lynch syndrome (LS) is to use a four-antibody panel, (MLH1, MSH2, MSH6, PMS2) to screen for the four Mismatch Repair (MMR) gene expressions involved.

We hypothesised that testing two antibodies (MSH6 and PMS2), followed by the other two only when there is loss of expression of the first two antibodies, would be equally effective as a four antibody panel in detecting LS. This hypothesis is based on the biochemical binding properties of the MMR proteins.

**Methods** We tested this hypothesis on a patient cohort consisting of all cases of colorectal cancer that were stained for MMR gene expression at Auckland City Hospital (Auckland, New Zealand) from the years 2000 to 2010 (inclusive), providing a series of 410 cases for this study. Exclusions were made based on heterogeneous staining pattern and unsatisfactory staining results on MSH6 and PMS2, which left n=400 included in the study.

**Results** The MMR gene protein stains were regarded as demonstrating loss of expression (LOE) when there was no uptake in the nucleus of the tumour cells, with a positive internal control. The results from our analysis supported our hypothesis. Seventy-four cases showed LOE of MSH6 or PMS2. One of them showed LOE of all four MMR proteins. For the remaining 326 cases, there was no LOE of all four MMR proteins.

**Conclusion** Our study gives further evidence that an initial two-antibody panel consisting of PMS2 and MSH6 would be as effective as a four-antibody panel in detecting DNA MMR gene protein LOE. This study has implications for significant cost cutting and improved efficiency in detection of DNA MMR gene protein LOE in LS.

Lynch syndrome (LS), also known as hereditary non polyposis colorectal cancer (HNPCC), is an inherited autosomal dominant condition predisposing to early onset colorectal adenocarcinoma.

Whilst environmental factors play a leading role in the aetiology of most colorectal cancers, inherited genetics are significant in between 15% and 30% of all colorectal cancers and approximately 5% of all colorectal cancers are due to an inherited syndrome.¹

LS was first categorised by Professor Henry T Lynch in 1966 and is the most common of the inherited colon cancer susceptibilities, accounting for between 1% and 5% of all colorectal cancers.¹,²
LS is inherited as a dominant disorder and affected individuals are at higher risk of developing colorectal cancer, endometrial cancer and various other types of aggressive cancers with rates quoted in most familial cancer registries of an approximate 80% lifetime risk for colorectal cancer.\textsuperscript{2,3}

LS is caused by germline defects in at least one of a set of mismatch repair (MMR) genes in the mismatch repair system, namely MLH1, MSH2, MSH6 and PMS2.\textsuperscript{1,4-8} Normal mismatch repair requires the function of several different genes products being co-ordinated. Loss of one or more of these MMR gene products leads to micro satellite instability (MSI) and cancer development.\textsuperscript{4-5}

The role of the MMR system is to preserve genomic integrity and prevent replication errors by correcting base substitution mismatches and small insertion-deletion mismatches which are generated by errors in base pairing during DNA replication. Loss of MLH1 can also occur in the absence of germline mutations of the MMR gene, in cases of sporadic CRC. This is due to hyper-methylation of the MLH1 promoter and subsequent silencing of the gene. It is usually associated with BRAF gene mutation and may be seen in up to 15% of all CRC.\textsuperscript{9} It can be identified by use of BRAF V600E mutation testing.

Of the above named MMR genes, germline mutations of MLH1 and/or MSH2 account for 80% - 90% of all cases of LS.\textsuperscript{5,8} As such, the original immunohistochemistry (IH) panel used to screen for LS was a two-antibody panel of MLH1 and MSH2. This panel was later expanded to a four-antibody panel due to shortcomings with IH staining for MLH1.\textsuperscript{10} Namely it was found that whilst loss of MSH2 was very sensitive in detecting MSH2 defect carriers, some mutations of MLH1 still allowed weak positive staining of MLH1 and could lead to false negative results.\textsuperscript{10} This is because up to one-third of MLH1 mutations are missense mutations results in functionally inactive but antigenically intact MLH1 mutant protein.

For such tumours, a false normal staining pattern with MLH will be observed. However, IH expression of its secondary partner PMS2 will be absent. The currently widely used four-antibody panel includes MLH1 and MSH2 as well as MSH6 and PMS2 and these additions have increased the sensitivity of the screening process.\textsuperscript{11}

The biochemical binding properties of MMR proteins in forming functional heterodimer complexes can be extrapolated and used to further refine the current practice of using a four-antibody panel in testing for HNPCC. This is because MLH1 and PMS2 form a heterodimer complex, as do MSH2 and MSH6, in which MLH1 and MSH2 are obligatory partners and stabilise PMS2 and MSH6 (the minor partners).\textsuperscript{11} Loss of either obligatory partner leads to proteolytic degradation of the heterodimer complex and loss of both proteins, whilst the reverse is not true as the obligatory partners can bind with other minor MMR proteins (MLH1 with PMS1 or MLH3 and MSH2 with PMS3) and form stable heterodimer complexes.\textsuperscript{12}

Therefore, mutation of MLH1 or MSH2 would result in loss of either MLH1/PMS2 or MSH2/MSH6 respectively. Conversely, mutation of PMS2 or MSH6 would not result in LOE of MSH1 or MSH2, respectively.
We hypothesise that staining for PMS2 and MSH6 alone will be sufficient to detect all cases of LS, and could replace routine screening with all four antibodies. Two recent papers, Shia et al\textsuperscript{7} and Hall et al\textsuperscript{8} have found the use of a panel consisting of just these two stains reduces costs whilst protecting the accuracy in HNPCC screening.

The aim of this study is to test this hypothesis by retrospectively applying it to the cases previously identified over an eleven year period in the Histopathology Laboratory of Auckland Hospital and if proven accurate to subsequently aid in changing current practice.

**Methods and Materials**

All cases of colorectal cancer diagnosed at or referred to Auckland City Hospital, and underwent IH staining for MMR gene protein expression over the 11 year period (2000-2010) were reviewed. The IH staining was performed in patients who satisfactorily met, at first, either the revised Amsterdam or Bethesda criteria, and later, the revised Bethesda criteria of 2004.\textsuperscript{13,14} The upper age limit was modified to encompass all cases of MMR gene CRC at the Histopathology Laboratory of Auckland Hospital.

Sections of paraffin embedded tissue are cut at 4µm, and incubated for 30 minutes at 60°C. The slides are then stained using extended heat retrieval methods. Slides are incubated at high temperature for 90 minutes in citrate based buffer solution. All four primary antibodies are incubated for between 45 to 60 minutes. In recent years (2009-present) manual immunohistochemical staining has been replaced by automation using Ventana Ultra machines. Novocastra and Cellmarque are the primary antibodies of choice.

Immunohistochemistry staining results were reviewed initially looking for any loss of expression of MSH6 and PMS2. These stains are regarded as demonstrating LOE when there is no uptake in the nucleus of the tumour cells, with positive internal control. If either of these MMR gene proteins were lost then the results of MLH1 and MSH2 were also looked at. These results were then compared with the results found with all four stains interpreted together.

Ten cases show partial or unsatisfactory staining. These cases either involve PMS2/MSH6 (3 and 1 cases respectively), MLH1 with PMS2 LOE (2 cases) or MSH2 with MSH6 LOE (4 cases). Partial staining means weak or negative staining for MMR protein in the tumour cells, which may be either focal or diffuse, with strong staining of the stromal cells.

Unsatisfactory staining refers to negative staining with both tumour and stromal cells and satisfactory external positive control. These slides are repeated at least once, and also repeated on another tumour block. They are only included in this category if all of the slides show unsatisfactory staining. These cases are excluded from the study.

During the study period the four panel MMR staining has also been performed on adenomas, other primary cancers and old cases prior to the study period. These cases were excluded from the study.

Under the permission of the New Zealand Multi-region Ethics Committee, information was gathered on the patients and then all identifying marks removed. The patients were from the greater Auckland region. The patients included in the study ranged from 21 to 108 years old. The sites of cancer were various and included the entire colon.

**Results**

During the 11-year period, MMR staining according to the selection criteria was performed on 410 cases. Ten cases with partial/unsatisfactory staining result were excluded, leaving 400 cases in the study.

Seventy-four cases showed LOE of either MSH6 or PMS2 (18.5%). Among them 25 cases showed LOE of MSH6 (6% of total cases and 34% of cases with LOE) and 50 showed LOE of PMS2 (12% of the total and 67.5% of the cases with LOE). One of them showed LOE of both MSH6 and PMS2.
On subsequent review of the 25 cases with MSH6 LOE, 13 also showed concurrent LOE of MSH2 (52%). Of the 50 cases with PMS2 LOE, 41 showed concurrent LOE of MLH1 (82%). The case with LOE for both MSH6 and PMS has also lost MLH1 and MSH2. After reviewing all 400 cases there was no LOE of either MLH1 or MLH2 in isolation.

Table 1 reflects the pattern in which the expression was lost. In one sample expression of all four genes was lost, whereas the other 73 samples had loss of either the minor constituents (MSH6 and PMS2), or in some cases the major constituents as well. There was no isolated loss of the major constituents.

Table 1. Pattern with which MMR gene loss of expression was demonstrated

<table>
<thead>
<tr>
<th>Loss of expression (LOE)</th>
<th>n</th>
</tr>
</thead>
<tbody>
<tr>
<td>MSH6 only</td>
<td>12</td>
</tr>
<tr>
<td>MSH2 only</td>
<td>0</td>
</tr>
<tr>
<td>MSH6 + MSH2 only</td>
<td>12</td>
</tr>
<tr>
<td>PMS2 only</td>
<td>9</td>
</tr>
<tr>
<td>MLH1 only</td>
<td>0</td>
</tr>
<tr>
<td>PMS2 + MLH1 only</td>
<td>40</td>
</tr>
<tr>
<td>All four stains</td>
<td>1</td>
</tr>
</tbody>
</table>

Discussion

Our study further supports the evidence put forward by two separate recent studies from the USA7 and Australia.8 Shia et al7 tested 232 tumours, and found LOE of at least 1 MMR gene in 70 cases (26%). Hall et al8 tested 344 tumours with LOE in 104 cases (30%). Our study looked at 400 cases, with an 18.5% positive rate of 74 cases. The lower positive rate is probably due to inclusion of a higher age group, as opposed to the revised Bethesda criteria of 50. In these three studies, with a total number of almost 1000 cases, the staining results indicate that the two initial stains (PMS2/MSH6) are equally as specific to diagnose LS when compared to all four stains. There is no LOE of MLH1/MSH6 without concomitant LOE of PMS2/MSH6 respectively. In our study, there is one cases of LOE of all 4 genes. In the series by Hall et al.8 there are two cases of triple LOE for MSH1/PMS2/MSH6.

Shia7 has reviewed four other series of MMR staining studies, which included a total of 1704 cases CRC, with LOE of at least one IH stain shown in 294 cases. There were two cases in one of the series15 that showed loss of MLH1, but not PMS2. In another series from Australia, there are 235 MMR deficient cases from an unknown number of unselected CRC.

Ten cases show either isolated MLH1 loss (8), MSH2 loss (1) or both MLH1/MSH2 loss (1). However, all these 10 cases were confirmed not to be LS by germline mutation analysis.16 It is likely that the two cases from the former series were also non-LS, although there was insufficient information to confirm.

Patients identified as having LOE of either of the two initial stains or partial or unsatisfactory staining patterns should be tested and worked up for the possibility of
LS. Hall et al\textsuperscript{8} has proposed a strategy for germline mutation testing with either or both PMS2/MSH6 deficiency. With PMS2 loss, the suggested next step was to exclude CpG island methylator phenotype by BRAF V600E mutation analysis.

Mutated V600E indicate somatic methylation causing silencing of the MLH1, and excluded LS. Otherwise germline MLH1 mutation testing, and if negative, PMS2 germline mutation testing should be performed. In cases of MSH6 loss, germline MSH2 mutation should be checked for and if negative MSH6 mutation testing should be performed.

Ten cases in our study show partial or unsatisfactory staining in at least one of the four IH stains. The partial staining pattern may indicate mutation that cause partial or weak staining, and have been particularly implicated in MLH1.\textsuperscript{12} It may also be seen in mutation negative and microsatellite-stable cases, and may be related to old paraffin blocks and quality of tissue preservation.\textsuperscript{17}

Unsatisfactory staining pattern has also been well documented. They are best treated and tested as cases with loss of expression of the corresponding gene.\textsuperscript{7,18} However, these cases with partial or unsatisfactory staining do not affect the validity of this study because they do not occur in isolation for the staining of the major constituents of the mismatch repair protein heterodimers. All this cases would have been discovered with the staining for the minor constituents (MSH6/PMS2), and further studies can be performed to determine whether it is a case of LS.

In a study conducted in 2008, Hampel et al\textsuperscript{15} illustrated that when screening CRC patients for LS, IH staining is almost equally sensitive as microsatellite instability testing and is more readily available and helps to direct genetic testing as it identifies which of the MMR genes are abnormal. It also found that limiting tumour analysis to only those that fulfilled the Bethesda criteria would fail to identify 28\% of cases of Lynch syndrome.

Colorectal cancer is the second most common registered malignancy to the New Zealand Cancer Registry.\textsuperscript{19} Screening is an important tool in reducing colorectal cancer incidence and mortality in those most at risk and more frequent screening is required in those with proven LS due to their greatly increased lifetime risk of developing a colorectal cancer.\textsuperscript{20}

Confirmation of LS cases may affect patient management, allow identification of at risk family members, who are in need of raised colonoscopic surveillance, and conversely to allow reassurance and avoid over-screening those at lower risk.\textsuperscript{1}

In the past 10 years, MMR staining was limited to patients satisfying the aforementioned criteria. There has been a trend towards an increasingly liberal staining, which can at times include staining for all CRC cases that are detected. The policy in some hospitals is to do MMR testing on patients less than 50 years old and those with a strong family history.

The study by Hampel et al\textsuperscript{15} illustrated that screening only patients younger than 50, or according to the revised Bethesda criteria, would fail to identify 28\% of cases of LS. Their group also commented that it will become more difficult to identify patients with LS on the basis of family history of CRC in the future because of a) decreases in family size and b) increasing usage of screening via colonoscopy which could prevent
many CRCs through the removal of pre-cancerous polyps. This group suggested comprehensive screening for LS among all CRC patients. This view was echoed in a letter by a group from Austria\(^{21}\) who cited that none of their 700 CRC patients (and only one of the 153 LS patients reported by Hampel et al\(^{15}\)) had been referred by a clinician for genetic testing.

In the series by Hampel et al\(^{15}\) it was found that for each pro-band there was on average three additional family members who carried MMR gene mutations. The potential benefit of increasing the IH screening for CRC in these patients is significant. We propose that a simplified initial MMR staining, utilising the discussed two stain panel, would allow the same resource to be used to screen for almost twice the number of CRC patients without additional cost, thus increasing the diagnostic yield of IH in LS.

In New Zealand, the NZCR recorded 3002 new cases of CRC in 2011.\(^{22}\) If comprehensive screening for LS with IH staining was applied to all cases as an initial procedure, using two stains instead of four stains, this would reduce resource use by almost 6000 IH stains annually, without compromising the yield of LS cases.

The change in the staining strategy would dramatically reduce the number of patients who progress to a four-antibody panel as less than 5% of these CRC patients would require testing with all four antibodies. In turn this would save on laboratory costs, costs of manpower and most importantly save patients undergoing unnecessary tests.

**Conclusion**

Our study further reinforces previous reports from the USA and Australia which suggest that immunohistochemical staining for mismatch repair gene loss of expression can be successfully limited to two of the four stains currently used at the initial stage to detect Lynch syndrome. There are no false negatives by this approach, in which MSH6/PMS2 do not show loss of expression.

This proposed screening panel carries a significant benefit in cost and manpower saving in staining, could allow for greater screening without increased cost and more importantly comes without loss of sensitivity in detecting cases of Lynch syndrome.

**Competing interests:** Nil.

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References:


Pathological reporting of malignant colorectal polyps

Chris Gillespie, Arend Merrie, Ian Bissett

Abstract

Aim The pathological reporting of malignant colorectal polyps plays an important role in determining whether definitive surgical resection is required following endoscopic polypectomy. This study aims to assess the adequacy of reporting on malignant polyp specimens at Auckland Hospital and whether synoptic reporting results in an improvement.

Method The pathology database at Auckland Hospital was accessed using a search strategy to identify all malignant polyps diagnosed between 1999 and 2011. Pathology reports were reviewed retrospectively.

Results In total 121 malignant polyps were found. Of these, 73 were colonoscopic polypectomies, 41 were colectomy specimens, and seven transanal resections.

Of the 41 colectomy specimens, 19 (46%) were reported in synoptic format compared with none of the colonoscopic polypectomies or transanal resections. The status of the margin of excision, differentiation, and presence of lymphovascular invasion were given in 100% of synoptic reports compared with 51% of non-synoptic reports.

Conclusion Synoptic reporting does improve the completeness of pathological reporting in malignant colorectal polyps. Currently none of the colonoscopically excised malignant polyps are reported in this format at Auckland Hospital. The development and routine use of a synoptic system for reporting on malignant polyps would give clinicians more information on which to base decisions.

The malignant colorectal polyp, defined as an adenomatous polyp with infiltration of malignant cells into the submucosa,\(^1\) is the earliest form of bowel cancer. Approximately 5% of all endoscopically removed adenomas are malignant\(^2\) but this number is set to rise.

Population-based screening programmes implemented in Australia and being piloted in New Zealand are causing a shift to earlier diagnosis of bowel cancer, with 32% of screen-detected cancers at stage A compared to 20% diagnosed outside screening.\(^3\)

In colorectal cancer advances in surgical technique, the role of neoadjuvant therapy and the advent of biological agents have placed the pathologist as a key player in multidisciplinary care.

The pathology report is a crucial document for treatment planning and also now stands as a benchmark of surgical quality, a template for audit and a tool for epidemiological study. Identified as an area for improvement over the last 20 years, national guidelines across many countries now have a minimum dataset for the colorectal pathology report.
In Australia and New Zealand, the Royal College of Pathologists of Australasia have introduced the Colorectal Cancer Structured Reporting Protocol,\textsuperscript{4} with mandatory elements for the pathology report for colorectal cancer, although this protocol is designed for tumours removed by surgical resection not polypectomy.

The Cancer Registry Upgrade, overseen by Cancer Control New Zealand and the Ministry of Health, has made structured reporting a requirement for all colorectal cancer reports in New Zealand as of April 2013 although this again does not appear to include malignant polyps.\textsuperscript{5} Structured reporting is considered important to quantify the effect of screening programmes within New Zealand and for comparison of outcomes with other countries.\textsuperscript{5}

There is evidence that the format of the pathology report is important, with synoptic or structured reports more likely to be complete.\textsuperscript{6-7} Freetext reports are prone to recurrent omissions,\textsuperscript{8} time costs\textsuperscript{9} and the potential for misunderstanding.\textsuperscript{6} With this information the recently published New Zealand Guidelines Group (NZGG) clinical practice guidelines\textsuperscript{10} recommend synoptic reporting for all colorectal cancer specimens, and this recommendation is extended to include synoptic reports even for procedures such as colonoscopy and operation reports.

In 1984 a seminal paper from St. Mark’s Hospital showed that endoscopic polypectomy can be an acceptable treatment for malignant polyps.\textsuperscript{11} The following features are associated with a favourable outcome after polypectomy – a clear margin of excision, well or moderately differentiated cancer, the absence of lymphatic or venous invasion, and an endoscopic assessment of total removal.\textsuperscript{12}

The guidelines in New Zealand (NZGG) and Australia (National Health and Medical Research Council (NHMRC)) state no further treatment is required if these ‘favourable’ features are all satisfied, and if not a radical surgical resection should be considered.\textsuperscript{10,12} Three of these four ‘favourable’ features are assessed by the pathologist, making the pathology report a crucial part of clinical decision making following polypectomy for the malignant polyp.

This study aims to assess the completeness of pathology reporting for malignant polyps and whether synoptic reporting improves it.

**Method**

The pathology database at Auckland Hospital was accessed with a keyword text search request for reports containing any of “rectum, rectal, colonic, colon, caecal” and any of “adenocarcinoma, carcinoma” and any of “polyp, polypectomy”. This search strategy was devised after pilot tests to ensure complete collection of all malignant colorectal polyps. The time period for the search was 1 January 1999 to 31 December 2011.

A total of 1622 pathology reports were identified and of these 121 were found to be true malignant polyps, defined as polyps with infiltration of malignant cells into the submucosa. For these 121 patients, the pathology report was reviewed retrospectively to ascertain completeness of reporting.

Reports were checked for margin status, distance from the margin to the tumour, cancer differentiation, and presence of lymphovascular invasion. Reports were also noted to be in either freetext or synoptic format and Haggitt’s level of invasion for pedunculated polyps was recorded if given. Polyp morphology was determined from the endoscopy report.
**Results**

Of the 121 malignant polyps, 73 were from colonoscopic polypectomies, 41 from colectomy specimens and 7 from transanal resections.

Nineteen (46%) of the colectomy specimens were reported as synoptic reports using a template derived from the Royal College of Pathologists of Australasia, however none of the colonoscopic polypectomy specimens or transanal resections were reported synoptically. The results flow chart is presented in Figure 1.

**Figure 1. Results flow chart**

![Flow chart](chart.png)

All 19 synoptic reports from the colectomy specimens were complete with information provided for all necessary pathological features. However of the 102 freetext reports, the status of the margin was given in 97%, cancer differentiation in 70%, and lymphovascular invasion in 63%.

There were 38 colonoscopic polypectomies with clear margins, and in these the distance of the margin was given in 74%, although margin distance is not a specific criterion on the NHMRC guidelines.

Overall only 51% of the non-synoptic reports had complete pathological reporting according to NHMRC guidelines, as shown in Figure 2.

There was a trend to more synoptic reporting over time as shown in Figure 3. Synoptic reporting started at Auckland Hospital for colorectal cancer in 2004 and initially malignant polyps were included although in 2011 only 25% were reported this way.
Thirty-five of the malignant polyps were pedunculated and in only three (8.5%) of these the Haggitt level of invasion was given.

Specimen fragmentation did not appear to significantly alter the confidence in reporting of the margin status. In 27 of the 73 colonoscopic polypectomies the specimen was fragmented due to piecemeal resection and amongst these specimens
the margin status was given in 93%. Of the seven fragmented specimens with clear margins, the distance of margin was given in six (86%).

**Discussion**

The management of malignant colorectal polyps is highly dependent on accurate pathological reporting from the polypectomy specimen. Synoptic reporting has been shown to increase the completeness of reporting for colorectal cancer\(^6,7\) and to possibly reduce misinterpretation.\(^6\)

Many national guidelines are therefore making this a mandatory format for reporting and the Royal College of Pathologists of Australasia have recently published the second edition of their structured reporting protocol,\(^4\) however these recommendations have not specifically included malignant polyps where the pathology report is pivotal in clinical decision making. This study is the first we are aware of looking specifically at the quality of pathology reporting in malignant colorectal polyps.

Our study found that in 49% of non-synoptic reports the information provided was inadequate for future treatment planning, based on current guidelines. However 100% of synoptic reports were complete.

Unfortunately none of the colonoscopic polypectomy specimens were reported in synoptic format, despite the fact that the pathology report is most important in these patients. The trend towards increased synoptic reporting over time probably reflects the push for synoptic reporting for colorectal cancer resection specimens, however the rate of complete reports did not appear to increase over the years of the study. Even in 2011 the rate of complete reports was only 58%.

The main limitation of this paper is that it was retrospective and all of the assessment was made by the formal pathology report on the Auckland Hospital database. Verbal communications made between the pathologist and treating clinicians may not have been included in these reports and therefore treating teams might have been given more information than was recorded. Also different pathologists may have varied in the completeness of their reporting but we did not record the pathologist reporting each specimen.

The group of non-synoptic pathology reports included specimens from colectomies, polypectomies and transanal excisions whereas all the synoptic reports were from colectomy specimens - this may have introduced some confounding bias into our results. However to account for this the 41 colectomy reports were analysed as a subgroup. Of the 22 non-synoptic colectomy reports, 15 (68%) were complete compared with all of the 19 synoptic reports, still a significant result.

The pathologist’s role starts with the technical handling of the specimen, involves collaboration with the surgeon and ends with the pathology report. Srigley et al\(^7\) cited four important features of a cancer pathology report: timeliness, completeness, accuracy and usability. In malignant polyps the completeness and usability of the report are particularly important as this information pertains to future decision making regarding subsequent management.
In terms of collaboration, the importance of communication between the pathologist and treating surgeon cannot be overstated. By working closely with the colonoscopist, the pathologist can improve the quality of interpretation of the colorectal polyp. By the same token, Chapius et al emphasised the importance of adequate information being provided to the pathologist by the surgeon, citing instances where it was evident the pathologist had received insufficient clinical information with bowel resection specimens. They had looked at 2,233 reports from bowel cancer specimens in New South Wales, although endoscopic polypectomy specimens were specifically excluded. There may be improvements to this in the future with the implementation of well-designed histopathology request forms such as those suggested by the Royal College of Pathologists of Australasia where pertinent clinical information of bowel resection specimens is provided by the surgical team.

The results of this study mirror the reporting on colorectal malignant polyps in North America. A recent Q-probe by the College of American Pathologists reviewed surgical pathology reports for a number of cancers across 86 institutions. Seventy-eight malignant colorectal polyps were reported on with complete reporting in only 42.3%. Lymphovascular invasion was the most frequently missed element in the report with 52.6% of reports not having it commented on.

Of all the cancers included in their study, reporting of malignant colorectal polyp specimens performed the worst. The paper notes a continuing need for pathologists’ familiarization with the required elements of a malignant polyp pathology report. The most important features for the pathologist to identify are those ‘favourable features’ outlined in the NZGG and NHMRC guidelines. In terms of margin, most papers cite a margin of 2mm as being safe for a low risk of residual local disease, although margin distance is not formally considered a factor on the NHMRC guidelines.

Where the margin is greater than 1mm, the risk of relapse is 0-2%, but this increases to 21-33% when the margin is less than 1mm. Other potentially significant parameters that have been recently identified are the depth of invasion, tumour budding, lymphatic vessel density, cribriform histology and the presence of certain molecular markers, although these features are yet to be validated in clinical studies.

The site of the tumour may also be important, in particular low rectal lesions which have a high recurrence rate even after full-thickness transanal resection. Lymphovascular invasion is relatively uncommon and often associated with other poor prognostic markers. Its interpretation is marred by difficulty in its interpretation, lack of guidelines for establishing its presence, and significant interobserver variability in its identification. Its usefulness is controversial with some studies finding an association with a poor outcome, but others finding it not to be an independent risk factor. Despite its arguable value, the presence of lymphovascular invasion is considered an important feature to record by the NHMRC.

Specimen fragmentation following piecemeal resection will often render assessment of the margin status impossible. Interestingly in our series 27 patients had a
colonoscopic polypectomy with a fragmented specimen, yet in 93% an assessment of margin status was given and in seven of these the margin was reported as clear.

Guidelines from the National Comprehensive Cancer Network recommend surgical resection for all malignant polyps removed with a piecemeal polypectomy.21 Four of our seven patients underwent resection with no residual disease found and there was no poor outcome for any of the seven patients.

The Haggitt system22 for pedunculated malignant polyps has been widely used by surgeons as a prognostic marker although its utility has been questioned recently. Polyps with level four invasion are considered high risk and therefore candidates for surgical resection, but level four invasion cannot be adequately determined by endoscopic polypectomy.16 Only 8.5% of the pedunculated polyps in our study had the Haggitt level assessed and this reflects the downgrading of its importance by our pathologists.

In 1992 Zarbo et al23 first showed that a standard report form was associated with a more complete colorectal cancer pathology report, and since then similar results for synoptic reporting has been found in other cancers.7 An example of the successful implementation of synoptic reporting is in the Canadian state of Ontario.7

Following a recommendation that all cancer reports are presented in synoptic format, a knowledge transfer strategy was used to increase the rate of synoptic reports for colorectal cancer from 82.3% to 92.1%, and the completeness of synoptic reports from 78% to 93%. Prior to this the completeness of narrative reports was 30.3% compared to 83.6% for synoptic reports.7

Synoptic reports are still not perfect however, with recent studies showing 12-16% of cancer synoptic reports are still inadequate.6,7 Hospital-based6 and web-based systems24 as checks for completeness have been described to optimise synoptic reporting.

In conclusion, a synoptic format does improve the completeness of pathology reporting for malignant polyps. Unfortunately none of the endoscopically excised malignant polyps have been reported using this framework at Auckland Hospital, but these reports are vital for clinical decision making for these patients.

A move to the development and routine use of synoptic reporting for malignant polyps, in line with recommendations for bowel resection specimens, would address this deficiency.

Competing interests: None.

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References:


Carbon dioxide insufflation during colonoscopy: a randomised controlled trial

Anne Cleland, Jenny Carryer, Steve La Grow

Abstract

Aim To determine if carbon dioxide (CO\(_2\)), insufflated during colonoscopy reduces pain experienced by patients post colonoscopy compared to air.

Method A randomised, double-blinded, controlled trial with 205 consecutive consented patients referred for elective colonoscopy was undertaken at MidCentral Health Gastroenterology Department. Patients were randomised to colonic insufflation with either air or CO\(_2\). A comparison of reported pain was undertaken using a 0–10 point numeric rating scale at several time periods; intra procedure, 10, 30, and 60 minutes post procedure. In addition groups were compared on the proportion of participants reporting 0 pain levels at each of the same time periods.

Results CO\(_2\) insufflation was provided to 108 patients and air to 97 patients. No differences in mean pain scores or the proportion of those who report zero pain were found between the groups intra procedure. However, those who received CO\(_2\) insufflation were found to have significantly lower mean pain scores (p<0.001) and to have a significantly greater proportion of persons reporting 0 pain scores (p<0.001) at all three observation times post procedure than those who received air.

Conclusion Those receiving CO\(_2\) during colonoscopy experienced less post colonoscopy pain than those who received air insufflation. Carbon dioxide should be considered as the insufflating gas during colonoscopy.

Many patients experience abdominal discomfort during a colonoscopy and in the hours that follow due to colon distension from the air insufflated during colonoscopy.\(^1\)\(^-\)\(^3\)\(^,\)\(^10\)

Internationally, endoscopy units are slowly beginning to use carbon dioxide (CO\(_2\)) instead of air to insufflate the colon during colonoscopy following the publication of findings which report that CO\(_2\) substantially reduces the pain experienced post colonoscopy.\(^1\)\(^-\)\(^8\)

The advantage of CO\(_2\) is that it is rapidly absorbed by the lumen, enters the venous system and excreted through the lungs. CO\(_2\) absorbs considerably faster than air and thus results in less distension and associated pain.\(^1\)\(^-\)\(^4\)

The aim of this study was to see if studies conducted overseas which demonstrate that CO\(_2\) insufflated during colonoscopy results in less pain post colonoscopy than the air, could be replicated in New Zealand (NZ). At the time of this study, CO\(_2\) insufflation was not being used in this country.
Methods

A randomised, double-blinded, controlled trial with 205 consecutive consented patients referred for elective colonoscopy was undertaken at MidCentral Health Gastroenterology Department, New Zealand.

Trial participants were recruited from the waiting list for elective colonoscopy. They were invited by mail to take part in the trial in conjunction with their planned colonoscopy. Excluded from the trial were participants less than 16 years and over 90, those unable to understand the participant information, people with severe chronic obstructive pulmonary disease and known CO$_2$ retainers.

Sealed envelopes were used to randomly assign participants to colonic insufflation with either air or CO$_2$. The endoscopy assistants were responsible for turning the gas on or off. To ensure blinding, the gas controls were kept covered. The participant, endoscopist and nurse caring for participant were kept blinded to the gas used, until the end of the trial.

An Olympus CO$_2$ delivery system comprised of a gas cylinder, two stage regulator, a flow meter (set at 4 Litres a minute) and a CO$_2$ ‘water bottle’ (MAJ902) was used. An automated delivery system was not available on the New Zealand market at the time of commencing the trial.

Three of the participating endoscopists had extensive experience ranging from 10 to 25 years, while the fourth having had 1 year’s endoscopy experience. Additionally three training registrar endoscopists, under direct supervision, undertook 5.9% of the procedures.

Intravenous (IV) hypnovel and fentanyl was routinely given during the procedure, at the discretion of the endoscopist, with additional occasional use of IV buscopan.

Prior to discharge a comparison of reported pain was undertaken using a 0 -10 point numeric rating scale (NRS) at several time periods; intra procedure (0) and 10, 30, and 60 minutes post procedure. The participants were asked; “Can you tell me if you are in pain? Zero to 10, with 10 being the worst pain you could experience and zero being no pain”. The self-reported score was recorded as interval level data.

240 patients for randomisation was chosen to achieve a 90% power to detect a significant difference in NRS between the air and CO$_2$ group based on published trials. This number allowed a dropout rate of 40.

The statistical analysis was performed using SPSS v17.0 software (SPSS Inc., Chicago, Illinois, USA). Differences in mean NRS scores were analysed using independent samples t-tests. Chi-squared test for independence was used to assess the differences between the proportions of those reporting 0 pain at four time intervals. The P value was set at $\leq 0.05$.

A Bonferroni adjustment was made to account for the increased chance of making a type I error resulting from repeated measures in each case (p=0.05/4). Thus an adjusted p value of $\leq 0.013$ was used to determine significance.

Approval to conduct the study was received from Central Health and Disability Ethics Committee. Informed consent was obtained from all participants before inclusion in trial.

Results

A total of 234 prospective participants presented for colonoscopy. Of these, 29 chose not to participate. A total of 205 patients consented to the trial. No-one was excluded.

The outcome of the randomisation was that 108 patients received the CO$_2$ and 97 had the standard treatment of air (Figure 1).
The mean age of the participants was 61.61 years (SD=14.40). 111 were female (54%) and 94 male (46%). Polyps were removed from 42.2% of participants. The mean duration of the procedure was 26.43 minutes (SD=15.59).

The mean dosages of each of the drugs used during the procedure was 3.8 mg (SD=1.30) for hypnovel (sedation), 82.7 mcg (SD=29.65) for fentanyl (analgesia) and 15.5 mg (SD=5.0) for buscopan (muscle relaxant).

No statistically significant differences were found between the groups on any of these variables (Table 1).
Table 1. Age, sex, duration of procedure, polypectomy rate and dosage of medication for sample and groups

<table>
<thead>
<tr>
<th>Variables</th>
<th>Total</th>
<th>Carbon dioxide</th>
<th>Air</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N</td>
<td>Mean</td>
<td>SD</td>
</tr>
<tr>
<td>Age (years)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>205</td>
<td>61.6</td>
<td>14.40</td>
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<tr>
<td>Duration (min)</td>
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<td>14.59</td>
</tr>
<tr>
<td>Hypnovel (mg)</td>
<td>204</td>
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<td>1.30</td>
</tr>
<tr>
<td>Fentanyl (mcg)</td>
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<td>29.65</td>
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<tr>
<td>Buscopan (mg)</td>
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<table>
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<tr>
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<th>%</th>
<th>N</th>
<th>%</th>
<th>N</th>
<th>%</th>
<th>χ²</th>
<th>P</th>
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<tbody>
<tr>
<td>Male</td>
<td>94</td>
<td>45.9</td>
<td>51</td>
<td>47.2</td>
<td>43</td>
<td>44.3</td>
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<tr>
<td>Female</td>
<td>111</td>
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<td>57</td>
<td>52.8</td>
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<td>55.7</td>
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<td>47</td>
<td>54</td>
<td>40</td>
<td>46</td>
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χ²=Chi-squared.

As can be seen in Table 2 and Figure 2 there were no statistically significant difference found in the mean pain scores recorded between the groups intra procedure. However the patients in the CO₂ group were found to report significantly less pain in comparison with patients in the air group at 10, 30 and 60 minutes post procedure.

The mean amount of pain 10 minutes after colonoscopy expressed using NRS, was 0.43±1.2 in the CO₂ group, compared to 1.61±2.3 (t= -4.41, p<0.001) in the air group. After 30 minutes the mean values were 0.20±0.86 for CO₂ and 1.19±1.97 (t= -4.55, p<0.001), and at 1 hour after the procedure values were 0.17±0.85 for CO₂ and 0.73±1.3 (t= -3.45, p<0.001).

Table 2. Pain scores by group over time

<table>
<thead>
<tr>
<th>Variables</th>
<th>CO₂ (C) / Air (A)</th>
<th>Mean</th>
<th>Standard deviation</th>
<th>N</th>
<th>t</th>
<th>P</th>
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</thead>
<tbody>
<tr>
<td>Pain score @ 0 min</td>
<td>A</td>
<td>4.68</td>
<td>3.342</td>
<td>96</td>
<td>-1.26</td>
<td>0.868</td>
</tr>
<tr>
<td></td>
<td>C</td>
<td>4.05</td>
<td>3.257</td>
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<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Total</td>
<td>4.34</td>
<td>3.304</td>
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</tr>
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<td>Pain score @ 10 min</td>
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<td>1.61</td>
<td>2.359</td>
<td>96</td>
<td>-4.41</td>
<td>&lt;0.001</td>
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<td>C</td>
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<td>1.209</td>
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<td></td>
</tr>
<tr>
<td></td>
<td>Total</td>
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<td>1.931</td>
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<tr>
<td>Pain score @ 30 min</td>
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<td>1.19</td>
<td>1.975</td>
<td>96</td>
<td>-4.55</td>
<td>&lt;0.001</td>
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<td>C</td>
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<td>0.806</td>
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<td></td>
<td>Total</td>
<td>0.67</td>
<td>1.553</td>
<td>204</td>
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</tr>
<tr>
<td>Pain score @ 60 min</td>
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<td>0.73</td>
<td>1.373</td>
<td>96</td>
<td>-3.45</td>
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</tr>
<tr>
<td></td>
<td>Total</td>
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<td>1.162</td>
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</tbody>
</table>
In addition, as can be seen in Table 3, the proportion of participants in both groups reporting zero pain on the NRS was compared at all four time periods. There was no difference in the proportion of groups reporting zero pain during the colonoscopy (Chi-squared=0.836, p=0.361), but there was a significantly greater proportion of those who received CO$_2$ insufflation reporting zero pain compared to those who received air at all post procedure reporting times: 84.3% vs 58.8% at 10 minutes (Chi-squared=15.3, p<0.001), 89.7% vs 61.5% (Chi-squared=20.8, p<0.001) at 30 minutes and 93.5% vs 70.8% at 60 minutes (Chi-squared=16.8, p<0.001).

In conclusion, there was no statistical significant differences in pain scores found between the groups intra procedure (p=0.868). However at 10, 30, and 60 minutes post procedure the pain scores for those who received CO$_2$ were less than that for those who received air insufflation (p<0.001).
An alternative visualisation of the pain score results was undertaken by investigating the proportion of participants reporting no pain on NRS. Again, while there was no difference found between the groups intra procedure (p=0.361), a significant difference was found at all three time periods post procedure (p<0.001).

At 30 minutes post procedure 90% of those who received CO$_2$ had no pain in comparison to 61% of those who received air. Added to this, the pain scores of those insufflated with CO$_2$ dropped faster post procedure than for those insufflated with air.

**Discussion**

The results of this randomised double-blinded trial of patients having colonoscopy showed that those who received CO$_2$ insufflation reported less pain post procedure. The results of the present trial are consistent with findings of all the other published trials.\(^1\)\(^-\)\(^9\)

The present trial was a systematic replication of earlier studies. This study randomised participants to the groups while some used single day whole sessions rather than individual participants.\(^2\)\(^,\)\(^5\)\(^,\)\(^9\)

The use of a visual analogue scale (VAS) requiring participants to mark a scale using a pen or pencil was the most commonly used pain intensity measuring tool in the previous trials,\(^1\)\(^1\) although self-report 5- and 10-point Likert scales have also been used.\(^1\)\(^2\) In the present trial, the use of a self-report NRS to measure pain, appears to be distinctive.

The question of CO$_2$ retention and subsequent acidosis has been investigated and the literature is consistent regarding the safety of CO$_2$ insufflation.\(^2\)\(^,\)\(^5\)\(^,\)\(^7\)\(^,\)\(^8\) Bretthauer et al observed that the level of sedation is the primary cause of CO$_2$ retention, not the use of CO$_2$.\(^3\) Systematic reviews of the use of CO$_2$ during gastrointestinal endoscopy report that CO$_2$ was not retained and there were no adverse pulmonary events related to insufflation of CO$_2$.\(^1\)\(^1\),\(^1\)\(^2\)

It is a common theme from past authors that despite what seemed like convincing research over the last four decades, CO$_2$ insufflation is not in widespread use.\(^1\)\(^2\),\(^1\)\(^4\),\(^1\)\(^9\) It appeared that in 2009 this insufflation method was still not in common practice in the United States of America (USA).\(^1\)\(^2\)

In the same year a survey of 142 endoscopists from European countries revealed that 46.5% were unaware of the option of CO$_2$ use for this purpose and only 4.2% of respondents were actually using this method.\(^1\)\(^4\) A recent meta-analysis reiterates that internationally CO$_2$ use in colonoscopy is still an exception.\(^1\)\(^9\) This method was not in use in New Zealand prior to undertaking the present trial.

Since the completion of the trial, CO$_2$ insufflation is now in standard use for colonoscopy at MidCentral Health and has been proven in practice since. Subsequent to the trial the primary supplier of endoscopy equipment nationally, Olympus New Zealand, released an automated CO$_2$ delivery system (UCR) and to date has sold this system to 25 endoscopy departments within New Zealand (Inmed Medical supply an insufflator called CoEffecient 2). It is not known if all the endoscopists with in these departments are using this method. Despite slow up take of this method
internationally there are some indications of the spread of this insufflation technique in New Zealand.

The implication of reduction in pain for CO$_2$ use in colonoscopy could also be considered for other endoscopy procedures. There are published trials investigating CO$_2$ insufflation in flexible sigmoidoscopy, endoscopic gastric duodenoscopy (OGD), endoscopic retrograde cholangiopancreatography (ERCP) and double balloon enteroscopy.$^{9,15–17}$

The superiority of CO$_2$ use in colonoscopy is obvious, however in light of recent RCTs on these other gastrointestinal procedures the advantages are still uncertain and additional research is suggested.$^{19}$

There are currently a number of New Zealand Ministry of Health initiatives to improve waiting times for colonoscopy and a focus on facilitating a national colorectal cancer screening program.$^{20}$

With the prospect of increasing colonoscopy numbers,$^{18}$ there is a clinical imperative to use CO$_2$ to maximise patient comfort and compliance.

In conclusion the results of this present study confirmed previous work which demonstrates that CO$_2$ significantly reduced pain post colonoscopy. Most of the patients receiving CO$_2$ experienced no pain post procedure. We therefore recommend CO$_2$ insufflation in colonoscopy.

Competing interests: None

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Acknowledgements: The authors thank the staff of the Gastroenterology Department at MidCentral Health for their assistance as well as Olympus New Zealand for providing a CO$_2$ regulator system for the trial.

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References:


Symptom presentations and other characteristics of colorectal cancer patients and the diagnostic performance of the Auckland Regional Grading Criteria for Suspected Colorectal Cancer in the South Auckland population

John C Hsiang, Wayne Bai, Dinesh Lal

Abstract

Aim This study reviews the presenting symptoms of colorectal cancer in the ethnically diverse Middlemore Hospital referral population of South Auckland, New Zealand. The performance of the newly introduced Auckland Regional Grading Criteria as prediction tool for selecting colorectal cancer cases referred from primary care was evaluated in this group.

Method Retrospective review of all colorectal cancer (CRC) cases diagnosed between January 2006 and January 2011. Information extracted from case note review was used to grade patients using the Auckland Regional Grading Criteria.

Results A total of 799 patients were included. The commonest symptoms were: rectal bleeding (25.5–42.3%) and change in bowel habit (20.6–26.8%). Low-risk symptoms including abdominal pain (16.3–46.8%) and weight loss (18.4–26.1%) were not uncommon. 64.4% of Maori and 64.9% of Pacific patients had stage III or IV cancers. Pacific patients had more stage IV disease, 37.7% (p<0.001) and were less likely to undergo tumour resection, 26.0% (p<0.001).

The Auckland Regional Grading Criteria would miss 24.7% of the patients with CRC in the referral population.

Conclusion While rectal bleeding and change in bowel habit are frequent presenting symptoms, low-risk atypical symptoms including constipation, weight loss and abdominal pain were not uncommon. Significant proportion of Pacific patients present with late-stage disease.

The current Auckland Regional grading criteria would miss significant proportion of our study population with colorectal cancer.

Colorectal cancer (CRC) is the most commonly diagnosed non-skin cancer and the second most common cause of cancer death in New Zealand. In 2005 there were more than 2600 new cases and 1200 deaths. In 2008 New Zealand was the fourth ranked OECD country for colorectal cancer incidence with a rate of 40.5 per 100,000 compared to 38.7 in Australia.

Previous data has shown similar rates for colorectal cancer among Māori, Pacific (mostly of Samoan, Tongan, Niuean, or Cook Islands origin), and Asian people for both sexes, with the age-standardised rates ratio of colorectal cancer for the three groups (0.42–0.68) compared to the European group.
CRC presents with a heterogeneous spectrum of symptoms indistinguishable from the majority of lower gastrointestinal (GI) referrals. There are no published data on the presenting symptoms of CRC in New Zealand. Whether there is a difference in presenting symptoms between different ethnic groups is also unknown.

In 2009 hospitals in the Auckland region instituted the **Regional Grading Criteria for Colonoscopy Referral based on the UK National Institute of Clinical Excellence (NICE) Guidelines for Suspected Colorectal Cancer** (see Figure 1). The latter focuses on symptoms with a high probability for colorectal cancer, in particular rectal bleeding and a change in bowel habit to loose or more frequent stools above an age threshold.

The NICE guideline has a weak evidence base, concentrates on typical symptoms and may delay diagnosis in patients with atypical presentations. Commonly patients may present with vague symptoms like weight loss or lower-risk predictors of CRC such as abdominal pain or constipation.

One study has shown abdominal pain and rectal bleeding are significant predictors of CRC 180 days before presentation to secondary care. In another study, the commonest symptoms of CRC were rectal bleeding (58%), abdominal pain (52%), and change in bowel habit (51%).

We performed a retrospective review of the colorectal cancer patient cohort from 2006 to January 2011 at our centre to assess the symptoms at presentation in an ethnically diverse New Zealand population, and to evaluate the performance of the **Auckland Regional Grading Criteria** as a prediction tool for selecting suspected colorectal cancer cases referred from primary care.

**Methods**

**Case identification**

The patient cohort was obtained from two sources. We searched for the syntax term “adenocarcinoma” and “colon” or “rectum” in the Middlemore Hospital Pathology Database that includes all biopsy specimens and resected surgical specimens. We also used the Middlemore Hospital Colonoscopy Database, which is a prospective record of all patients undergoing colonoscopy at our local hospital. All discharge summaries with the coding for ‘Colorectal Cancer’ were also reviewed for collation. Each patient was identified by their unique patient National Health Index Number. CRC cases between January 2006 and January 2011 were collated.

**Data analysis**

**Symptoms presentations and characteristics**—Patient demographics, ethnicity, indication for colonoscopy, body mass index, inpatient or outpatient diagnosis, the site and stage of the cancer were recorded. We retrospectively reviewed the presenting symptoms that led to an acute admission or referral for outpatient colonoscopy, extracting these from medical, general surgical or oncology outpatient clinic letters or discharge summaries. If further clarification of initial symptoms was required patients were contacted by telephone. Only four patients required further clarification of symptoms by phone.

The symptoms for colorectal cancer recorded in our study were both the typical features as described in the **UK NICE Guideline for referrals for suspected colorectal cancer** as well as the atypical features often considered to have low sensitivity. Patients could report multiple symptoms.

**Diagnostic performance of Auckland Regional Grading Criteria**—We excluded all inpatient cases, those with a recent hospital admission for symptoms leading to outpatient colonoscopy referral,
patients with a history of inflammatory bowel disease or colorectal cancer, and all surveillance colonoscopies.

Patients referred for investigation because of abnormal radiological imaging, were excluded from the analysis if they were asymptomatic i.e. the finding was incidental. If symptomatic they were categorised by their presenting GI symptoms. Those with unprovoked thromboembolism were also excluded because these patients are likely to require colonoscopy regardless of the presence of GI symptoms.

We did not assess the duration of the presenting symptoms which is required for some of the criteria in the NICE Guideline. As this study is of retrospective nature, patient’s recall of the symptom duration would be difficult and likely to be unreliable particularly when this is often not stated in the original referral. Regardless, this would unlikely affect study validity as previous studies have shown no association between the duration of symptoms before diagnosis and cancer stage or mortality.6,7,9 Furthermore, we assume symptoms must have been persistent to result in referral to tertiary centre for colonoscopy.

Definitions

- “Change of bowel habit” is defined as recent loose stools and/or increased stool frequency as defined in the NICE Guideline.1
- “Iron deficiency” is a low ferritin below the normal reference range defined by the Auckland regional laboratories (<20mcg/L).
- “Severe iron deficiency anaemia” is defined as haemoglobin <110g/L for males and <100g/L for females with evidence of low ferritin.
- “Mild Anaemia” is defined as any low haemoglobin level for male and females above the threshold for “severe” anaemia.
- “Occult gastrointestinal (GI) bleeding” is the presence of positive faecal occult blood (guaiac or faecal immunochemical) without GI symptoms.
- Ethnicity was obtained from the Hospital database (PIMS). Ethnicity was classified as defined by ethnicity coding used by the New Zealand Ministry of Health;11 Europeans, Māori, Pacific people, Other, and Asians.

Ethics approval

This study was approved by Northern B Ethics Committee.

Statistical analysis

Continuous data was expressed as the mean. A p value<0.05 was considered statistically significant. Statistical analyses was carried out using Graphpad software.12 Proportions were analysed using Mid-P Exact test. Ethnicity specified age-adjusted rate is the weighted average of the age-specific rates, for each of the ethnicity group, using the New Zealand 2006 Census data and its projections for 2007–2010 as the standard population.
Figure 1. Auckland regional grading criteria

<table>
<thead>
<tr>
<th>Auckland Regional Grading Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>Colonoscopy within 2 weeks</td>
</tr>
<tr>
<td>• Known cancer, to be pre-operatively checked for synchronous cancer</td>
</tr>
<tr>
<td>• Abdominal mass</td>
</tr>
<tr>
<td>• Palpable/visible rectal tumour</td>
</tr>
<tr>
<td>• Imaging (CT/colonography/barium enema) suggestive of tumour</td>
</tr>
<tr>
<td>Colonoscopy within 6 weeks</td>
</tr>
<tr>
<td>• Age ≥ 60 yrs, with changed bowel habits (looser, more frequent)</td>
</tr>
<tr>
<td>• Age ≥ 60 yrs, with rectal bleeding without change in bowel habit or perianal symptoms</td>
</tr>
<tr>
<td>• Age ≥ 40 yrs, with rectal bleeding plus change in bowel habit</td>
</tr>
<tr>
<td>• Iron deficiency anaemia (male Hb&lt;110 any age; female Hb&lt;100 (post menopausal/GI symptoms/ positive family history/ positive FOB))</td>
</tr>
<tr>
<td>• Age ≥ 50 yrs, positive faecal occult blood testing (FOB) (appropriately collected in asymptomatic patient)</td>
</tr>
<tr>
<td>Colonoscopy within 12 weeks</td>
</tr>
<tr>
<td>• Age 40-60 yrs, with change in bowel habits</td>
</tr>
</tbody>
</table>

UK NICE Guideline for referrals for suspected colorectal cancer

Urgent referrals should be made if symptom of the following is present:

• Age ≥ 40 yrs, with rectal bleeding plus change in bowel habit, symptoms persisting for 6 weeks or more
• Age ≥ 60 yrs, rectal bleeding persisting for 6 weeks or more without a change in bowel habit and without perianal symptoms
• Age ≥ 60 yrs, with a change in bowel habit to looser stools and/or more frequent stools persisting for 6 weeks or more without rectal bleeding
• Right lower abdominal mass with involvement of the large bowel, irrespective of age
• In patients presenting with a palpable rectal mass (intraluminal and not pelvic) irrespective of age
• In men of any age with unexplained iron deficiency anaemia and a haemoglobin of 110g/L or below
• In non-menstruating women with unexplained iron deficiency anaemia and a haemoglobin of 100g/L or below

Results

799 patients were identified in our cohort. Four “Other” ethnicity patients were excluded from the results given the low numbers. A total of 795 patients with their demographics are shown in Table 1.

The majority was European (77.1%). Height and weight information were only available in 377 patients, however 58.4% of the 377 patients had a BMI ≥25, while 23.3% of the patients were obese (BMI ≥30).

Europeans had a similar distribution of cases across stage I to IV disease (Table 1). The European group had less cases of stage IV disease at presentation compared to other ethnic groups at 18.6% (p=0.005).

Although the number of cases in the other non-European groups is small, the Pacific people group had a significantly higher proportion of stage IV disease at clinical presentation compared to other ethnic groups (37.7%, p<0.001).
Table 1. Demographics

<table>
<thead>
<tr>
<th>Variables</th>
<th>European</th>
<th>Māori</th>
<th>Pacific</th>
<th>Asian</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median age (years)</td>
<td>73.5</td>
<td>62.8</td>
<td>61.9</td>
<td>68.4</td>
<td>71.8</td>
</tr>
<tr>
<td>± IQR (years)</td>
<td>15.8</td>
<td>24.6</td>
<td>11.6</td>
<td>17.5</td>
<td>17.8</td>
</tr>
<tr>
<td>% Male</td>
<td>50.6</td>
<td>42.2</td>
<td>62.3</td>
<td>55</td>
<td>51.6</td>
</tr>
<tr>
<td>TNM stage (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>I</td>
<td>112 (18.3)</td>
<td>6 (13.3)</td>
<td>8 (10.4)</td>
<td>7 (11.7)</td>
<td>133 (16.7)</td>
</tr>
<tr>
<td>II</td>
<td>185 (30.2)</td>
<td>10 (22.2)</td>
<td>18 (23.4)</td>
<td>20 (33.3)</td>
<td>233 (29.3)</td>
</tr>
<tr>
<td>III</td>
<td>186 (30.2)</td>
<td>17 (37.8)</td>
<td>21 (27.3)</td>
<td>21 (35.0)</td>
<td>245 (30.8)</td>
</tr>
<tr>
<td>IV</td>
<td>111 (18.1)</td>
<td>12 (26.7)</td>
<td>29 (37.7)</td>
<td>10 (16.7)</td>
<td>162 (20.4)</td>
</tr>
<tr>
<td>Unknown</td>
<td>19 (3.1)</td>
<td>0 (0)</td>
<td>1 (1.3)</td>
<td>2 (3.3)</td>
<td>22 (2.8)</td>
</tr>
<tr>
<td>No surgery performed (%)</td>
<td>62 (10.1)</td>
<td>6 (13.3)</td>
<td>20 (26.0)</td>
<td>4 (6.7%)</td>
<td>92 (11.6%)</td>
</tr>
<tr>
<td>Inpatient cohort</td>
<td>233</td>
<td>21</td>
<td>37</td>
<td>19</td>
<td>310</td>
</tr>
<tr>
<td>Outpatient cohort</td>
<td>380</td>
<td>24</td>
<td>40</td>
<td>41</td>
<td>485</td>
</tr>
<tr>
<td>Total (%)</td>
<td>613 (77.1)</td>
<td>45 (5.7)</td>
<td>77 (9.7)</td>
<td>60 (7.5)</td>
<td>795</td>
</tr>
</tbody>
</table>

The proportion of Pacific patients who did not undergo primary surgical resection was significantly higher than other ethnicities at 26.0% compared to 10.1% (European), 13.3% (Māori) and 6.7% (Asians) respectively (p<0.001).

Figure 2. Age-standardised colorectal cancer incidence rate per annum (Jan 2006–Jan 2011)

Figure 2 shows the age-standardised incidence of colorectal cancer cases between January 2006 and January 2011. The overall age-adjusted incidence per 100,000 per annum for the European group was 78.9, Māori 17.9, Pacific people 17.7, and Asian 12.4.

310 colorectal cancer cases were diagnosed during an inpatient admission, and 485 cases of cancers diagnosed as outpatient. The presenting symptoms of the inpatient and outpatient groups are summarised in Table 2.
Table 2. Outpatient and inpatient cases characteristics (symptoms can be multiple; CIBH - change in bowel habit/diarrhoea)

<table>
<thead>
<tr>
<th>Outpatient symptoms</th>
<th>European %</th>
<th>Māori %</th>
<th>Pacific %</th>
<th>Asian %</th>
<th>Total %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rectal bleeding</td>
<td>38.4%</td>
<td>50.0%</td>
<td>57.5%</td>
<td>58.5%</td>
<td>42.3%</td>
</tr>
<tr>
<td>CIBH</td>
<td>30.0%</td>
<td>25.0%</td>
<td>5.0%</td>
<td>19.5%</td>
<td>26.8%</td>
</tr>
<tr>
<td>Constipation</td>
<td>8.9%</td>
<td>4.0%</td>
<td>9%</td>
<td>7.3%</td>
<td>10.3%</td>
</tr>
<tr>
<td>Abdominal pain</td>
<td>16.6%</td>
<td>4.0%</td>
<td>16.7%</td>
<td>17.5%</td>
<td>16.3%</td>
</tr>
<tr>
<td>Weight loss</td>
<td>16.1%</td>
<td>7.0%</td>
<td>29.2%</td>
<td>35.0%</td>
<td>18.4%</td>
</tr>
<tr>
<td>Other symptoms</td>
<td>36.8%</td>
<td>16.7%</td>
<td>30.0%</td>
<td>43.9%</td>
<td>35.9%</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>380</td>
<td>24</td>
<td>40</td>
<td>41</td>
<td>485</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Inpatient symptoms</th>
<th>European %</th>
<th>Māori %</th>
<th>Pacific %</th>
<th>Asian %</th>
<th>Total %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rectal bleeding</td>
<td>20.6%</td>
<td>19.0%</td>
<td>18.9%</td>
<td>48.6%</td>
<td>25.5%</td>
</tr>
<tr>
<td>CIBH</td>
<td>20.2%</td>
<td>38.1%</td>
<td>18.9%</td>
<td>10.5%</td>
<td>20.6%</td>
</tr>
<tr>
<td>Constipation</td>
<td>18.9%</td>
<td>23.8%</td>
<td>18.9%</td>
<td>10.5%</td>
<td>18.7%</td>
</tr>
<tr>
<td>Abdominal pain</td>
<td>46.8%</td>
<td>57.1%</td>
<td>45.9%</td>
<td>36.8%</td>
<td>46.8%</td>
</tr>
<tr>
<td>Weight loss</td>
<td>21.0%</td>
<td>28.6%</td>
<td>51.4%</td>
<td>36.8%</td>
<td>26.1%</td>
</tr>
<tr>
<td>Other symptoms</td>
<td>45.1%</td>
<td>33.3%</td>
<td>35.1%</td>
<td>26.3%</td>
<td>41.9%</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>233</td>
<td>21</td>
<td>37</td>
<td>19</td>
<td>310</td>
</tr>
</tbody>
</table>

In the outpatient group, rectal bleeding was the most common symptom for all four ethnic groups (42.3%), followed by change in bowel habit (26.8%). Abdominal pain and weight loss were relatively frequent symptoms (16.3% and 18.4% overall). Constipation was a significant symptom for the Pacific outpatient group (p=0.02) compared to other ethnic groups as 22.5% of all symptoms and diarrhoea was an infrequent presenting symptom in Pacific people compared with other ethnicities (5% compared to 19.5–30%, respectively, p<0.001).

Inpatient symptoms were those leading to an acute hospital presentation and colorectal cancer diagnosis. Abdominal pain was the most frequent presenting symptom for the inpatient cohort, followed by rectal bleeding. European and Pacific patients are likely to present with weight loss as the associated symptom (p=0.001). Constipation is not an uncommon symptom in all four ethnic groups, ranging from 10.5–23.8%.

There were 18 colorectal cancers detected during outpatient surveillance colonoscopy over the 5-year period. All 18 cases were of European ethnicity; six patients had stage I disease, four had stage II disease, six patients had stage III disease, one had stage IV disease and one patient did not have surgery or staging due to severe cirrhosis.

Only 21.3% of the inpatient cohort and 17.9% of the outpatient cohort had severe iron deficiency anaemia. Most of these patients also had GI symptoms. The proportion of patients with iron deficiency anaemia without GI symptoms was 7.4% for inpatients and 4.5% for outpatients. Most of these asymptomatic patients had right-sided cancers (17/23 inpatients and 19/22 outpatients).
The outpatient cohort was more likely to have severe iron deficiency anaemia meeting the guideline cutoff than iron deficiency and/or mild anaemia. A significant proportion of patients with anaemia did not have true iron deficiency (ferritin <20mcg/L) regardless of other symptoms, (42.9% of inpatients and 24.1% of outpatients, data not shown).

### Diagnostic performance of the Auckland Regional Grading Criteria for suspected colorectal cancer

As shown in Table 3, 24.7% of the patients diagnosed with CRC did not fulfill the Auckland Regional Criteria. This proportion was higher in Māori and Pacific patients (34.8% and 30.8%, respectively).

**Table 3. Auckland Regional Grading Criteria for outpatient colonoscopy referral**

<table>
<thead>
<tr>
<th>Grading priority</th>
<th>Criteria</th>
<th>European</th>
<th>Māori</th>
<th>Pacific</th>
<th>Asian</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Within 2 weeks (P1)</td>
<td>1. Abdominal mass</td>
<td>5</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>6</td>
</tr>
<tr>
<td></td>
<td>2. Rectal mass</td>
<td>11</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>12</td>
</tr>
<tr>
<td></td>
<td>3. Abnormal CT</td>
<td>13</td>
<td>2</td>
<td>2</td>
<td>0</td>
<td>17</td>
</tr>
<tr>
<td></td>
<td>4. Age =&gt;60, rectal bleeding (without CIBH/anal symptoms)</td>
<td>64</td>
<td>5</td>
<td>14</td>
<td>9</td>
<td>92</td>
</tr>
<tr>
<td>Within 6 weeks (P2)</td>
<td>5. Age =&gt;60, changed in bowel habit (CIBH)*</td>
<td>47</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>48</td>
</tr>
<tr>
<td></td>
<td>6. Age =&gt;40, rectal bleeding and CIBH</td>
<td>51</td>
<td>2</td>
<td>2</td>
<td>7</td>
<td>62</td>
</tr>
<tr>
<td></td>
<td>7. Men of any age, iron deficiency, Hb &lt;110g/L,</td>
<td>25</td>
<td>0</td>
<td>1</td>
<td>4</td>
<td>30</td>
</tr>
<tr>
<td>Within 12 week (P3)</td>
<td>8. Female, iron deficiency, Hb&lt;100g/L (postmenopausal/ gastrointestinal symptoms/ positive family history/ faecal occult blood positive)</td>
<td>31</td>
<td>1</td>
<td>5</td>
<td>2</td>
<td>39</td>
</tr>
<tr>
<td></td>
<td>9. Faecal occult blood test positive, age &gt;50 yrs, asymptomatic (collected in correct manner)</td>
<td>12</td>
<td>2</td>
<td>1</td>
<td>0</td>
<td>15</td>
</tr>
<tr>
<td></td>
<td>10. Age 40–60, changed in bowel habit (CIBH)</td>
<td>7</td>
<td>3</td>
<td>1</td>
<td>1</td>
<td>12</td>
</tr>
</tbody>
</table>

Number of patients fulfilling criteria 1–9: 266 European, 15 Māori, 27 Pacific, 25 Asian, 333 Total

Number of patients NOT fulfilling criteria 1–9: 79 European, 8 Māori, 12 Pacific, 10 Asian, 109 Total

% NOT fulfilling referral criteria: 22.9 European, 34.8 Māori, 30.8 Pacific, 28.6 Asian, 24.7 Total

CIBH= Changed in bowel habit/diarrhoea, Hb= haemoglobin, iron deficiency is defined by ferritin <20 in NZ; (485 patients from 2006–2011, excluding 43 patients with past history of CRC, history of inflammatory bowel disease and surveillance patients)
Table 4. Clinical features of 109 patients not fulfilling the Auckland Regional Criteria

<table>
<thead>
<tr>
<th>Variables</th>
<th>European</th>
<th>Māori</th>
<th>PI</th>
<th>Asian</th>
<th>Total</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median age (years)</td>
<td>69.4</td>
<td>65.5</td>
<td>56</td>
<td>59.7</td>
<td>66.3</td>
<td></td>
</tr>
<tr>
<td>Rectal bleeding</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>with perianal symptoms</td>
<td>2</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>3</td>
<td>2.8%</td>
</tr>
<tr>
<td>age 45–60</td>
<td>17</td>
<td>3</td>
<td>4</td>
<td>6</td>
<td>30</td>
<td>27.5%</td>
</tr>
<tr>
<td>age&lt;45</td>
<td>2</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>2</td>
<td>1.8%</td>
</tr>
<tr>
<td>Rectal bleeding total</td>
<td>21</td>
<td>4</td>
<td>4</td>
<td>6</td>
<td>35</td>
<td>32.1%</td>
</tr>
<tr>
<td>Abdominal pain</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>with alarm features*</td>
<td>11</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>12</td>
<td>11.0%</td>
</tr>
<tr>
<td>Abdominal pain &amp; CIBH, age &lt;40</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>0.9%</td>
</tr>
<tr>
<td>Abdominal pain only</td>
<td>7</td>
<td>1</td>
<td>0</td>
<td>1</td>
<td>9</td>
<td>8.3%</td>
</tr>
<tr>
<td>Abdominal pain total</td>
<td>19</td>
<td>1</td>
<td>0</td>
<td>2</td>
<td>22</td>
<td>20.2%</td>
</tr>
<tr>
<td>Constipation</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>with alarm features*</td>
<td>8</td>
<td>0</td>
<td>4</td>
<td>1</td>
<td>13</td>
<td>11.9%</td>
</tr>
<tr>
<td>Constipation only</td>
<td>5</td>
<td>1</td>
<td>0</td>
<td>1</td>
<td>7</td>
<td>6.4%</td>
</tr>
<tr>
<td>Constipation total</td>
<td>13</td>
<td>1</td>
<td>4</td>
<td>2</td>
<td>20</td>
<td>18.3%</td>
</tr>
<tr>
<td>Abnormal haematinitics</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Iron deficiency and/or mild anaemia</td>
<td>15</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>16</td>
<td>14.7%</td>
</tr>
<tr>
<td>Mild anaemia only, ferritin &gt;20</td>
<td>5</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>6</td>
<td>5.5%</td>
</tr>
<tr>
<td>Severe anaemia, ferritin &gt;20</td>
<td>4</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>5</td>
<td>4.6%</td>
</tr>
<tr>
<td>Iron deficiency anaemia, age &lt;50</td>
<td>0</td>
<td>0</td>
<td>3</td>
<td>0</td>
<td>3</td>
<td>2.8%</td>
</tr>
<tr>
<td>Abnormal haematinitics total</td>
<td>24</td>
<td>2</td>
<td>4</td>
<td>0</td>
<td>30</td>
<td>27.5%</td>
</tr>
<tr>
<td>Other – Weight loss /faecal incontinence</td>
<td>2</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>2</td>
<td>1.8%</td>
</tr>
<tr>
<td>CUMULATIVE TOTAL</td>
<td>79</td>
<td>8</td>
<td>12</td>
<td>10</td>
<td>109</td>
<td></td>
</tr>
</tbody>
</table>

Note: Primary predominant symptom recorded to best fit into the category.

*Alarm features: weight loss, anaemia, abdominal pain.

In those patients who did not meet the Grading Criteria, presenting with rectal bleeding aged between 45 and 60 years, the average age was 54 years. In the 35 patients with rectal bleeding, 18 patients had cancers localised to the rectum (data not shown).

In the 109 patients who did not fulfill any of the Auckland Regional Criteria, 30 out of 109 patients (27.5%) had abnormal haematinitics in the absence of symptoms such as overt rectal bleeding, or abdominal pain.

Discussion

This retrospective single-centre study shows that there are some ethnic differences in the presenting symptoms and clinical outcomes of CRC. The adherence to the current Auckland Regional Grading Criteria for referral for suspected CRC would miss a significant number of cases of CRC in this diverse population.
In our cohort the median age of CRC diagnosis for the Māori and Pacific group is 63.3 years and 62.2 years respectively, compared to 73.6 years in the European and 68.6 years in the Asian group. Figure 2 shows that the Pacific patients in the age group of 45–59 years have higher age adjusted incidence rate compared to Māori and Asian patients and this rate drops after age of 59 years.

The reason for this observation may be multifactorial. Pacific patients may not live long enough to develop colorectal cancer at an older age, hence explaining the drop in the incidence rate at the later age. The younger age at onset of CRC in these groups may be related to environmental factors such as obesity, and higher intakes of fat compared to the other groups.\(^\text{13,14}\)

We do not know if there is any influence of genetic risk factors in our cohort of early onset colorectal cancers. In a study by Dickson et al,\(^\text{15}\) the prevalence of colorectal adenomas in Māori and New Zealand Europeans parallels the colorectal cancer rates between age 40 and 59 years. We do not know if the prevalence of adenoma rate is higher among Pacific people compared to Māori and other ethnic groups in this age group.

Our current study showed a much lower age adjusted incidence of CRC in Māori and Pacific patients compared to the national data.\(^\text{2}\) The reason for the lower incidence may be multifactorial but beyond the scope of this study.

The other obvious finding is that a third of Pacific patients do not undergo primary resection due to a greater proportion presenting with stage IV disease. Due to the retrospective nature of this analysis, we do not know if this difference is due to a later presentation with a similar duration of symptoms or presentation with atypical and more easily dismissed symptoms such as constipation and weight loss.

Undoubtedly other factors that affect health status will be relevant, such as lack of health knowledge, cultural beliefs, inaccurate reporting of lower GI symptoms to the clinicians and perceived or real barriers to accessing health care. Although Māori patients in our study have a higher proportion of cases in the age <45 years group and a similar median age at diagnosis to the Pacific group, the primary resection rate is similar to that of the European group.

The Auckland Regional Grading Criteria was introduced in 2011 to standardise prioritisation for colonoscopy in the public system. Prior to this, need for colonoscopy was guided by using varying criteria within the Auckland regional hospitals. The Auckland Regional criteria are based on the UK NICE Guideline for referrals for suspected colorectal cancer (Figure 1), with addition of positive faecal occult blood test results and an abnormal CT scan.

It has previously been shown that the NICE guidelines miss a substantial proportion of cancer: 71% satisfied the criteria for urgent referrals in a single district study in the United Kingdom.\(^\text{16}\) Overall one-quarter of our patients did not fulfill the Auckland (24.7% overall) criteria. This trend was seen across all ethnic groups; at least 22.9% of the Europeans, the largest ethnic group in the cohort (n=345) would have their CRC missed in the referral population.

Māori, Pacific and Asian groups have much lower numbers of CRC cases but a higher proportion of patients not meeting the criteria (30.9% combined). Due to the small
numbers of Māori, Pacific and Asian patients, these ethnic groups not meeting the criteria did not reach statistical significance.

Rectal bleeding has a good positive predictive value for CRC.\textsuperscript{7,17} There were 35 patients with rectal bleeding who did not meet the \textit{Regional Criteria} for colonoscopy, and the majority of these (30 out of 35) were between 45 to 60 years of age. This is a significant proportion of patients (30 out of 442 patients; 6.8\%) who did not meet the Criteria.

We did not review the above group of patients to see if they had strong family history of CRC. However it is important to note that this group’s average age was below 55 years. There were 18 out of 35 patients with rectal bleeding (not met the \textit{Regional Criteria}) having cancers localised to the rectum. It is not clear if these patients would have palpable rectal masses, however in our outpatient referral population, only 12 patients (2.7\%) had the criteria of “rectal mass”.

The proportion of palpable rectal mass should be higher given the frequency of CRC found in the rectum. The issue here may be that digital rectal examination has not been routinely performed on every patient with rectal bleeding or lower GI symptoms prior to their referrals for colonoscopy regardless of their age of presentation. Although perianal symptoms had not been clearly defined in the UK NICE Guideline, routine digital rectal examination would detect “rectal mass” in some of these patients with lower GI symptoms.

Atypical symptoms such as constipation and abdominal pain have low positive predictive value as symptoms alone.\textsuperscript{10} In the 109 patients who did not fulfill the Auckland Criteria, 20.2\% had abdominal pain and 18.3\% had constipation, and of these patients 59.5\% (25 of 42 patients) had associated alarm features such as weight loss, abdominal pain or anaemia.

In those patients with constipation, 15 patients had new-onset or progressive constipation symptom in the last one year suggesting a progressive obstructive luminal lesion. Furthermore, 16 out of the 20 patients had distal colorectal cancer located in the sigmoid colon or rectum.

We feel that although constipation as a symptom has low positive predictive value, its association with other alarm features or history of new onset or progressive nature may warrant further investigation particularly in the Pacific people cohort who are more likely to present with constipation as symptom. Perhaps flexible sigmoidoscopy may be an ideal investigative tool in this setting in highly selected patient groups.

Only a minority of the patients without overt gastrointestinal bleeding meet the \textit{Regional Criteria} definition of severe iron deficiency anaemia (data not shown). The threshold for investigation based on haemoglobin values seems high, particularly in comparison to other less objective criteria.\textsuperscript{18} It is not known at what level of haemoglobin investigation should be initiated and there is no reason why mild anaemia should be less indicative of important disease than severe anaemia.\textsuperscript{19} From our study, it seems a proportion of patients in the study may not fulfill the severe iron deficiency anaemia criteria as set by the \textit{Regional Criteria}.

Of the patients who did not fulfill the Auckland Regional Grading Criteria, a considerable number have non-specific symptoms such as constipation and abdominal
pain, traditionally considered low risk. Mortality is highest in patients whose first symptom is abdominal pain and lowest in those with rectal bleeding. However abdominal pain occurs as an isolated symptom in very few patients with colorectal cancer and has low diagnostic value, with sensitivity ranging from 0 to 0.73 and specificity from 0.19 to 0.91 in one study.

Risk assessment tools that score multiple low-risk presenting symptoms such as the Cancer Prediction in Exeter (CAPER) score and the Bristol-Birmingham (BB) equation, have shown to perform significantly better than the UK NICE referral guidelines, with an area under the curve (AUC) of 0.91 to 0.92 for the CAPER score and the BB equation, compared to 0.72 to 0.76 for the NICE guidelines.

This is a retrospective study and is subject to recall bias. Patients may perceive symptoms differently after the cancer diagnosis. Referrals may specify symptoms not reported on specialist review (verification bias). However, more than 95% of the colonoscopy procedures were done by gastroenterologists hence the indications are likely to be reported correctly.

In our study although symptom duration was not reported, we assume the symptoms would have been persistent in the outpatient setting leading to investigations for the diagnosis of cancer. Prospective data collection using a standard clinical pro forma referral form may reduce these biases. With the small numbers of patients in the ethnic minority groups, the finding of symptoms such as constipation did not reach statistical significance.

Future studies with bigger sample size may help evaluate this further. PIMS hospital database is reliant on patient’s self-identified ethnicity which may be subject to error due to mixed ancestry particularly in Māori and European population.

As the NICE guidelines form the basis of prioritization of colonoscopy referrals in Auckland and other New Zealand hospitals (personal communication), prospective studies to examine diagnostic performance of similar scoring systems including CAPER score would be beneficial in improving cost-effective use of resources.

In summary, this study shows rectal bleeding and change in bowel habit are frequent presenting symptoms. Albeit retrospective, this study shows that patients with colorectal cancer can present with a varied number of symptoms and at least in our population a significant proportion of these are atypical symptoms not easily picked up by the current Auckland Regional Grading criteria.

The current grading criteria would miss 24.7% of all the colorectal cancer patients in our study, with a trend to miss an even higher proportion in the Polynesian and Māori groups. Pacific patients presenting with more advanced stage CRC, is an important finding that will need further evaluation and attention as better awareness via different educational programmes may help minimise this problem.
Competing interests: None identified.

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References:


An unusual case of granulomatous inflammation of the rectum

Nicholas J Fischer

Clinical—A 46-year-old male was referred to our surgical service with outlet-type bright red rectal bleeding. He also described perianal lumps on straining with bowel motions then self-reducing. He had had these symptoms for several years. He was otherwise well with no significant medical history, no change in his bowel habit and no weight loss. His haemoglobin was within normal limits. He was booked for flexible sigmoidoscopy with possible banding of haemorrhoids.

On flexible sigmoidoscopy, internal haemorrhoids were identified. Incidentally, in the lower rectum, numerous small white/yellow lesions were seen in or beneath the mucosa.

Biopsies were taken of this affected tissue (Figures 1 & 2).

What is the diagnosis?
Answer—The histological diagnosis was *rectal schistosomiasis granulomata.*

Discussion—Schistosomiasis (also known as bilharzia) is a parasitic disease caused by blood flukes of the *Schistosoma* genus. Four main species are responsible for human infections: *Schistosoma haematobium* (*S. haematobium*), *S. mansoni*, *S. japonicum* and *S. mekongi*—each with their own geographical distribution in tropical regions.

Transmission requires contamination of freshwater with human excreta, with specific freshwater snails as intermediate hosts and human contact with this water.¹ The World Health Organization (WHO) estimates at least 243 million people are infected worldwide.²

The pathophysiology results from the deposition of the *Schistosoma* eggs in various tissues, commonly the colon, rectum and liver (*S. mansoni, S. japonicum*); and the bladder (*S. haematobium*).

Chronic granulomatous inflammation results in the tissues where the eggs are deposited. Bleeding from rectal schistosomiasis inflammation is a well-recognised manifestation of the disease.³

After taking a travel history, our patient had been to several regions where schistosomiasis is endemic, including Southeast Asia, Central and South America, and Southern Africa in the 1990s.

The prevalence of this disease is probably more common in New Zealand than we realise in these increasingly well-travelled times. Indeed, many people are traveling to areas where schistosomiasis is endemic.³

It has been diagnosed in up to 4% of patients presenting to travel clinics for travel related illnesses in New Zealand.⁴ This probably underestimates its true prevalence as many returned travelers would have subclinical infections or would not attend a travel clinic. Furthermore, refugees and migrants from endemic areas would also be at high risk as studies from Australia have demonstrated.⁵,⁶

Endoscopists have an important role to play in the diagnosis and treatment of schistosomiasis due to the ova’s ability to affect almost any organ system, including the gastrointestinal tract.⁷

Our patient’s haemorrhoids may have been responsible for his rectal bleeding, however it remains a possibility that some of his rectal bleeding was in fact from rectal schistosomiasis granulomatous inflammation.

He was treated with banding of his haemorrhoids and with praziquantel and had resolution of his symptoms.

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Acknowledgements: I thank Mr William Pollard, Dr Nicole Smith, and MidCentral Health Laboratory for their assistance.

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References:


Dementia due to atrophy in the anterior part of the brain

Sayed Mahdi Marashi, Mohammad Majidi, Mehran Sadeghian, Zeynab Nasri-Nasabadi

Clinical—A 61-year-old man presented with a 7-year history of decline in mental capacity. Symptoms included gradually onset of changes in personality and behavioural control followed by reduction in verbal skills, seizure, aphasia, apraxia, and faecal and urinary incontinence.

Past medical history was not significant. Family history revealed a similar condition in his cousin, who died about 2 years after the onset of his symptoms.

A computed tomography scanning (Figure 1) and magnetic resonance imaging (Figure 2) were performed.

What is the diagnosis?
Answer and Discussion—Review of the brain CT scanning (Figure 1) showed considerable atrophy in the frontal and anterior temporal regions; coronal MRI scan of the brain showed extremely atrophic (knife like) gyri in both frontal lobes (red arrows), which are compatible with frontotemporal dementia (FTD).

FTD is a group of disorders, consisting of Pick's disease, frontotemporal lobar degeneration, progressive aphasia and semantic dementia. With degenerative changes in the anterior cerebral lobes FTD is responsible for the second most common cause of presenile dementia. FTD is marked by progressive changes in personality, behaviour and also verbal abilities.

There is a positive family history in about 45% of cases with mutation in the tau-gene on chromosome-17. Along with classical presentations, extrapyramidal disorder symptoms frequently occur in familial FTD.

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References:
A New Zealand doctor visits a Syrian refugee camp in Iraqi Kurdistan

My husband and I had not been living in Kurdistan for 2 whole weeks before Kurdistan opened its borders and thousands of Kurdish refugees from Syria began to pour in. With the war in Syria and the violence and trauma the people there have been facing, they were becoming desperate to find safety and so are fleeing into various countries around Syria: Turkey, Lebanon and particularly for the Kurdish refugees, Iraqi Kurdistan.

Kurdistan has had its share of unsettled times, trauma and refugee camps, but now as an autonomously governed region within Iraq it is experiencing relative stability. In fact, Kurdistan is so familiar with refugee camps it is becoming much better at logistics and coordination, all things considered.

Once the refugees cross the Syrian-Iraqi border, government buses pick them up and coordinate their relocation to a few of the various refugee camps in Kurdistan, one of which is in Arbat, about half an hour’s drive east from the city of Sulaimaniyah.

The refugees arrive at their new home, often impressively within a day of their crossing the border. With this latest tsunami of refugees the Arbat refugee camp has sped up its construction, erecting more tents, setting up hygiene facilities and connecting electricity throughout the camp. Of the 200,000 thousand refugees (and rapidly increasing) that have crossed the border, there are now 4,500 thousand Syrian refugees for whom the Arbat refugee camp is now a temporary home.

Across the dusty, treeless flattened dirt there are rows and rows of white tents: each family unit stays in a large one-room tent sleeping around 8–10 people, with an air cooler set up at one end in order to ease the 40ºC heat. Alongside the rows of tents are rows of port-a-loos and shower cubicles, each with electricity and an individual water supply, approximately one toilet and shower per four tents.

Families obtain water from a large water bladder in the centre of the camp, collecting water from a communal tap with large plastic containers and anything else that might carry water. Wheelie bins and rubbish dumpsters and the occasional rubbish truck indicated a functioning rubbish disposal system.

Samaritan's Purse International Relief is one of the various NGOs that has steeled itself for the latest refugee influx and been a part of the first response wave. I was invited to join the team in visiting the camp and taking much-needed commodities with the possibility of needing to help with distribution.

We arrived with several tonnes of rice, sugar, lentils, chickpeas, milk powder, oil, and a whole truck-full of disposable nappies. The relief team had coordinated with the Ministry of Health to provide those items that were most needed, and met with the Arbat officials on our arrival to the camp.

What we were told was encouraging. Our white faces would not be needed to help with the distribution of the commodities as the distribution system at the camp was
already set up and functioning well from the large concrete storage depot in the middle of the camp. In fact, current needs were being met well enough that our supplies were able to be stored rather than immediately distributed.

Our team took a brief wander through the camp, greeting refugees, listening to their stories and hearing their needs. Communication was mainly in Arabic and the Syrian dialect of Kurdish, often supplemented with gestures.

Two elderly women invited us to sit with them in the shade of their tent, they told us how many children they had, who had come out of Syria, and how many sons had stayed. We listened to them speak of family members who had been lost or killed. We smiled together about our language barrier, admired nearby grandchildren and laughed about which of the team were married and which women were still eligible.

Families very readily shared that they were being well cared for, and that all their immediate needs were being met. They felt safe, secure, and felt the blessing of being in a camp that seemed to be so well organised. Their only need now was additional clothing. Local Kurds in our relief team who had had personal experience in refugee camps in years gone by were impressed and amazed at the facilities and provisions, and declared that these refugees were blessed.

I made a beeline for the Red Cross/Red Crescent Health Clinic, the only medical facility in the camp. One long pre-fab unit divided into a pharmacy and the doctor’s office, with two pharmacists, and one doctor. While speaking with the doctor I was astounded: in his 6 square metre office, he saw roughly 100 patients each day, and was on call for 24 hours for 3 days straight.

There were 4 rotating doctors that shared work at the Arbat camp, followed by work at government clinic roughly 35 km further east in Halabja. The doctor I spoke to had had 7 months’ experience as a doctor, worked alone and unsupervised with emergency support from a more experienced doctor in the Arbat town centre or the hospital services in Sulaimaniyah should patients require more treatment than the basic clinic could offer.

The facilities in the clinic were meagre: an examination couch, desk, stethoscope, thermometer, gloves and small slips of paper for each patient. At nights he slept on his examination couch in the corner of the office.

Mostly the patients he saw were children, patients with fevers, sore throats, chest infections and a considerable amount of diarrhoea despite the provision of hygiene facilities. The main problems were the lack of doctors to help share the load, and a lack of certain medications in the pharmacy.

My visit was shortly interrupted by a father bringing his infant for a check, and a mother with her baby shortly after. Privacy and confidentiality was non-existent. The patient sits at the desk and speaks with the doctor, and the waiting patients stand behind the desk, squeezed into the air-conditioned office to wait their turn.

Overall our team was impressed and encouraged by what we had seen. The facilities had been well set up and further accommodation was being constructed for more refugees expected to arrive in the coming weeks. While we have heard a lot about tensions between the coordination of various efforts, what we saw was proof that, for now, immediate needs are being met.
Rather than meet immediate needs as we thought might have been necessary, our team was able to turn our attention to upcoming needs: the local Kurdish women at the community project's sewing centre would be able to provide women's clothing and Samaritan's Purse International Relief 'Operation Christmas Child' boxes are available to give to each child in the camp at our visit next week. Having initially felt like white-faced, camera-flashing tourists, our team began to be more encouraged by the needs that were already being met, and the needs that we will be able to meet in future weeks.

The Samaritan's Purse International Relief team is committed to the Syrian refugee relief effort in Kurdistan for at least the next month, with further extensions should many more refugees cross the border. Coordination with government agencies ensures that we meet relevant needs, fill in gaps and contribute to the combined efforts of various other local and international organisations such as the UNHCR and Unicef.

For more information on Samaritan’s Purse International Relief visit http://www.samaritanspurse.org

For more information on the Syrian refugee crisis and a regional overview, visit http://data.unhcr.org/syrianrefugees/regional.php

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Gout—is adequate attention devoted to preventing haemorrhagic risk when benzbromarone is administered with warfarin?

Benzbromarone, although unapproved by Medsafe, has been reimbursed by New Zealand’s Pharmaceutical Management Agency (PHARMAC) for gout patients in New Zealand from 1 July 2013.

Centre for Adverse Reactions Monitoring (CARM) has already received at least one report of increased bleeding in a gout patient co-prescribed benzbromarone and warfarin.¹ Winnard et al report in this Journal that around 23% of New Zealand patients with gout also have cardiovascular disease (CVD).²

We know that S-warfarin is metabolised by CYP2C9 and that R-warfarin is metabolised by CYP1A2.³ It is also known that benzbromarone is metabolised by both CYP2C9 and CYP1A2.⁴ The enhanced anticoagulation effects of benzbromarone with warfarin have been reported as far back 1996, where the authors (Shimodaira et al) concluded:⁵

> These results verified that the anticoagulant action of warfarin is enhanced by concurrent administration of benzbromarone. Accordingly, adequate consideration must be devoted to the prevention of grave hemorrhagic tendencies when these two drugs are administered concurrently.

It is therefore recommended that patients are not co-prescribed benzbromarone and warfarin because of the increased risk of bleeding and that if co-prescription is necessary there is closer monitoring of INR levels.

Current BPAC guidelines acknowledge that the monthly LFT monitoring necessary with benzbromarone may be difficult due to adherence in these patients. These low adherence problems simply serve to frustrate the necessary closer INR monitoring and thereby increase the risks of bleeds.⁶ However, since benzbromarone is not approved by Medsafe in New Zealand there is no Datasheet available to carry such a warning. Neither do the current Special Authority criteria for benzbromarone carry a warning regarding co-prescription with warfarin.

If benzbromarone is to remain an unapproved yet funded medicine then it is paramount that its prescribing is limited to specialists and that the Special Authority criteria carry a recommendation not to co-prescribe with warfarin. The high level of warfarin co-prescription in gout patients poses a high likelihood of potentially life-threatening bleeds with benzbromarone.

From a medicolegal perspective there is an added onus on the prescriber to alert the patient to such risks when seeking informed consent. Urgent action is needed to better manage the risks associated with benzbromarone (both bleeds with warfarin and intrinsic hepatotoxicity).

In contrast, febuxostat has been shown to minimally inhibit the activity of any CYP and does not affect the plasma binding of warfarin.⁷
Lance Gravatt (PhD)
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Competing interests: Shareholder of the company supplying febuxostat in New Zealand.

References:
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Is Lee’s 2008 risk:benefit conclusion for benzbromarone hepatotoxicity still relevant today?

Benzbromarone was approved for use in Europe and Asia, but was not licensed in the United States because of concerns over hepatotoxicity. Benzbromarone was withdrawn by its sponsor in 2003 because of continuing concerns over hepatotoxicity.\(^1\)\(^-\)\(^5\) The mechanism of benzbromarone hepatotoxicity is believed to be due to its hepatic metabolism by CYP 2C9 and possible effects of the parent compound or its metabolites on mitochondrial function.

While reported cases of hepatotoxicity are sparse,\(^1\)\(^-\)\(^5\) a review by Lee et al ("Lee") reports 11 other cases resulting in 9 deaths.\(^6\) The authors estimated the incidence of hepatotoxicity from benzbromarone to be around 1 in 17,000 and concluded that adverse events are relatively infrequent but potentially severe.

Lee concluded that the “benefit-risk assessment based on total exposure to the drug does not support the decision by the drug company to withdraw benzbromarone from the market given the paucity of alternative options.”\(^6\)

PHARMAC’s Pharmacology and Therapeutics Advisory Committee (PTAC) considered an application for reimbursement of benzbromarone in 2010 and again in 2011 wherein they essentially agreed with the conclusions drawn by Lee. PHARMAC subsequently funded benzbromarone as an unregistered medicine from 1 July 2013. However, since PTAC’s recommendation there have been two important developments that call into question the current applicability of the risk:benefit analysis by Lee.

First, Lee’s conclusion was premised on there being a “paucity of alternative options”. Since Lee’s analysis febuxostat has become generally available around the World including UK, USA and in New Zealand from March 2013. There is now available a very real alternative to benzbromarone.

Second, the Pharmaceuticals and Medical Devices Agency (PMDA) from Japan, where benzbromarone has remained on the market, reported in November 2011 that despite warnings in the package insert, Dear Doctor letter warnings, and an advisory for regular LFTs, around 20 cases a year of “serious hepatic disorder” are reported with benzbromarone.\(^7\)

The contemporary applicability of Lee’s conclusion in 2008 must be seriously called into question and an urgent review of the risk:benefit for benzbromarone undertaken. Although this would ordinarily be the responsibility of Medicines Adverse Reactions Committee (MARC), we are informed by Medsafe that it has no such regulatory powers over benzbromarone due to its unregistered status.

We are left with the haunting question of who is responsible for updating medicine safety when the regulator is powerless?
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Competing interests: New Zealand supplier of febuxostat.

References:
5. Haring B et al., Benzbromarone: A double-edged sword that cuts the liver? Eur J Gastroenterol Hepatol. 2013 Jan;25(1):119-21. (77 year old woman developed jaundice, fatigue and nausea 4 months after switching from allopurinol to benzbromarone due to hypersensitivity with downhill progression despite best efforts and died 53 days later).
New urate-lowering therapies in Aotearoa New Zealand: a response to Dr Lance Gravatt's letter on benzbromarone hepatotoxicity

Gout is now the most common form of inflammatory arthritis in Aotearoa New Zealand, affecting 3.2% of New Zealand European, 6.1% of Māori and 7.6% of Pacific adults. Inadequately treated gout results in joint damage, ulceration and permanent disability. Māori and Pacific people have particularly high rates of severe gout, causing joint pain, accelerated joint damage and work disability.

Given the major impact of this disease in our community, the Māori Gout Action Group and the New Zealand Rheumatology Association welcome both the recent PHARMAC funding of benzbromarone through Special Authority and Medsafe approval of febuxostat.

The key strategy for preventing gout attacks, tophi and joint damage in patients with gout is long-term urate-lowering therapy to reduce the serum urate below 0.36 mmol/L, which leads to dissolution of MSU crystals within the joints. Allopurinol is first-line treatment for urate-lowering therapy, although it is often used at inadequate doses within our community.

Benzbromarone is a potent uricosuric agent that has documented efficacy in patients with gout. It is particularly beneficial for patients with renal impairment who are intolerant to allopurinol or have an insufficient response to recommended doses of allopurinol.

Benzbromarone was widely used in Europe until 2003 when Sanofi-Synthelabo withdrew the drug after reports of fulminant hepatitis leading to death in two patients. Benzbromarone remains available in Japan, Brazil and certain European countries, such as Spain, Germany, and Austria. This complication is extremely rare and is likely to be prevented by regular monitoring of liver function tests in patients receiving this drug.

A number of experts have questioned the rationale for withdrawal of benzbromarone based on a risk-benefit analysis. Randomised controlled trials published in the last 5 years have demonstrated the superior efficacy of benzbromarone over probenecid in patients who have failed allopurinol treatment (due to inadequate serum urate lowering or intolerance), and that benzbromarone has superior efficacy compared with allopurinol 300mg daily.

In these studies, benzbromarone was well tolerated with no reports of hepatotoxicity. Observational studies have also indicated that benzbromarone is effective and well tolerated. The gout treatment guidelines for the European League Against Rheumatism (EULAR) have recommended that benzbromarone can be considered in patients with renal impairment.

Regular monitoring of liver function tests and serum urate is essential to monitor drug safety and efficacy. Benzbromarone may interact with warfarin to increase the
anticoagulant effect and close monitoring of the INR is needed if these drugs are co-
prescribed. Benzbromarone should also be avoided in people with previous
nephrolithiasis. Although now funded on Special Authority for people with gout who
have failed treatment with allopurinol and probenecid, benzbromarone remains
accessed through Section 29 of the Medicines Act.

Recent results from the ‘Genetics of Gout in Aotearoa’ study provide further rationale
for use of benzbromarone for those New Zealanders who are most severely affected
by gout. Genetic variations in a particular renal urate transporter gene SLC2A9 are
extremely common in Māori and Pacific people with gout and strongly increase the
risk of gout in these groups. Unlike other available urate-lowering therapies, benzbromarone specifically inhibits
this transporter. Furthermore, genetic variants in CYP2C9 that might predict poor
metabolism of benzbromarone and higher risk of hepatotoxicity are very rare in Māori
and Pacific people with gout. Our clinical experience in the last 10 years is that
benzbromarone is well tolerated and highly effective in those who managed to access
this drug (through hospital exceptional circumstances or charitable donation
schemes).

Febuxostat is also a potent urate-lowering agent, with greater efficacy than fixed dose
allopurinol (300mg daily for those with normal renal function). This agent has
recently been approved by Medsafe for use in New Zealand but is not currently
funded by PHARMAC.

In the phase 3 studies of febuxostat, abnormal liver function tests were observed in 4–
5% of participants, leading to withdrawal of febuxostat in 1–2% of participants. Liver
function test monitoring is also recommended when prescribing this agent.

Febuxostat is a xanthine oxidase inhibitor, and therefore co-prescription with
azathioprine should be avoided due to the potential for bone marrow suppression.
This drug-drug interaction is of clinical importance, given the severe gout that
frequently occurs in solid organ transplant recipients.

Increased access to these urate-lowering agents offers great promise for improved
management of gout within our community, particularly for those patients who are
intolerant to allopurinol or when adequate dosing of allopurinol does not lead to
serum urate targets.

We hope that the availability of these agents will also promote greater general
awareness of the importance of long-term urate-lowering therapy for gout prevention,
in the first instance allopurinol at doses sufficient to reduce serum urate
concentrations (see http://www.healthpointpathways.co.nz/gout-prevention).

Central to effective management of gout, irrespective of the drug used, is patient
education about medications and potential side effects, consideration of drug
interactions, and monitoring of efficacy and toxicity.

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Competing interests: Nicola Dalbeth has received consulting or speaker fees from Takeda, Menorini, Novartis, Metabolex, Savient, Fonterra, Ardea and AstraZeneca. She is a Principal Investigator on the phase 3 lesionsrulud studies, funded by Ardea. Peter Gow is a Principal Investigator on the phase 3 lesionsrulud studies, funded by Ardea. Lisa Stamp is a member of the PTAC Rheumatology subcommittee. The other authors have no relevant conflicts of interest to declare.

References:


Benzbromarone: availability for general prescribing in New Zealand (a response to letters by Dr Lance Gravatt on benzbromarone)

We read with interest the letters from Dr Lance Gravatt concerning the hazards of prescribing benzbromarone, a potent uricosuric agent indicated for the prevention and treatment of gout.\(^1\,\,^2\)

The drug, although not registered in New Zealand by Medsafe, has been made available via PHARMAC since July 2013. The arrangements for access are clear: failure to tolerate allopurinol or failure to reach a target plasma urate concentration of 0.36 mmol/L despite dose escalation of allopurinol. Further, regular liver function tests are recommended.

Dr Gravatt notes two potential hazards:

1. Bleeding risk in patients taking warfarin because of benzbromarone inhibition of warfarin metabolism by hepatic cytochrome enzymes, and
2. Hepatotoxicity, recently the subject of a warning from the Japanese Medicines Regulatory Agency (PMDA).\(^3\)

Our own analysis published in 2008 concerning the availability of benbromarone\(^4\) noted that the grounds for withdrawal of the drug from the European market by the patent holder Sanofi in 2003, because of hepatotoxicity, was questionable. This opinion was based on the paucity of cases compared to the heavy usage rates, potential for other mechanisms to be involved in the cases available to us for scrutiny and economic considerations.

We went on to recommend access to and use of the drug if alternative therapies, mainly allopurinol, were not tolerated or were unsuccessful in achieving a satisfactory reduction of plasma urate concentrations despite dosage escalation. We also noted that the drug needed to be used carefully in full knowledge of the risks and need for adequate monitoring.

Dr Gravatt notes that, since our analysis, another hypouricaemic drug (that he has a pecuniary interest in) has been registered widely. Febuxostat is a xanthine oxidase inhibitor that is effective and well tolerated although there has been a suggestion of cardiovascular toxicity.\(^5\,\,^6\) It is not retained in renal impairment and, again unlike allopurinol, Stevens Johnson syndrome has not emerged as a significant hazard. Why then has PHARMAC made benzbromarone available but not febuxostat?

New Zealand researchers Dalbeth, Stamp, Gow, Barclay and O'Donnell have lead the World in the ‘treat to target’ plasma urate approach to dosing with allopurinol.\(^5\,\,^7\) It is apparent that we have been under-dosing many patients with allopurinol and are loathe to increase the dose above 300 mg/day for fear of serious hypersensitivity reactions. By increasing the dose slowly and promoting adherence long-term, it is possible to accommodate a much greater proportion of gout sufferers and bring their plasma urate concentrations down to safe levels—e.g. less than 0.36 mmol/L.
Allopurinol, probenecid and benzbromarone all work and in most markets cost a lot less than febuxostat. Once a drug is available under subsidy it tends to get used much more widely than needed and unnecessary costs to the taxpayer follow. Presumably cost-effectiveness has had something to do with PHARMAC’s action.

We second Dr Gravatt’s suggestions that good information about the hazards with benzbromarone be promulgated widely, and that, in the first instance, prescribing be restricted to rheumatologists when alternative drugs, notably allopurinol, cannot be used. We would be surprised if most initial prescribing of benzbromarone was not undertaken by rheumatologists.

Enhanced monitoring of INR in those on warfarin, and dose adjustment if needed, is important. Also, hepatic function review regularly, especially in the first 6 months, as recommended by PHARMAC, with patients warned of relevant symptoms is mandatory. However, it would not be expected that there would be a large proportion of gout patients would ever need to be prescribed benzbromarone.

Finally, until the price of febuxostat renders this option ‘cost-effective’ for a national buyer like PHARMAC or PBS in Australia, the odds of seeing it on subsidised list seem poor.

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A house call

In New Zealand colonial times the doctors went from one patient to another on horseback. A country doctor had to be able to ride a horse, and ride it well, and when a shipment of horses arrived from Australia, the doctor was to be seen down on the waterfront, selecting one of the best of them for his own personal use.

Some years later, an alternative method for getting around was the railway network. In his book “Doctor in the Sticks,” (1972), the late Dr D. A. Bathgate describes a night call done by electric locomotives and railway flat trucks in the early 1920s.

Dr Bathgate, employed on an annual salary of £500, took the job of Medical Officer at Otira, in the Southern Alps. Work on the amazing Otira tunnel, which is over 8.5km long, was still in progress. Construction had begun simultaneously at each end, and years later the workers met somewhere in the middle. The course of the tunnel had been plotted with remarkable accuracy. By the 1920s, one could traverse the tunnel, but it was not fully lined. The mouth of the tunnel at the Arthur’s Pass end is 250 metres higher than at the Otira end, giving a downhill gradient of 1:33 over its entire length.

Patients lived in the settlements at each end of the tunnel, and Dr Bathgate was responsible for all of them. A winding and dangerous road through the steep mountains connected Otira, where a small hospital was situated, and Arthur’s Pass. The tunnel, when completed, would make for a faster and safer journey from one side of the mountain range to the other.

One night Dr Bathgate was asked to attend urgently a female patient at Arthur’s Pass, which is at the eastern and more elevated end of this enormously long tunnel. He phoned the tunnel mouth at Otira, and asked for an electric locomotive to take him to the “top heading,” the point at which the two parts of the tunnel joined up, but which was not yet completed. There was a door to stop the spread of fumes and gases.

He set out on this long journey with a colleague, a Dr Arthur. When the locomotive dropped him off he could expect to walk some distance in very wet conditions, before being picked up by another locomotive, that would start towards the “top heading” from the Arthur’s Pass end of the tunnel.

During the first part of the transit, west to east, in total darkness, the driver of the locomotive sensed that something was coming towards him. He threw the locomotive into reverse, and travelled at speed back down the way he had come. Arriving at a set of points, he ordered Dr Bathgate to throw the switch, and he got the locomotive off the main track into a siding where it was safe.

Hardly had he done so than a rake of trucks, on which were perched two men blowing whistles, flew past, going downhill with a thundering roar, sparks streaming from the brakes on the wheels. It seems that they had no business to be travelling at that hour.

The doctors resumed their journey, and the driver, in the middle of the tunnel, (at the end of the western section of the line), left a flat truck for the two doctors to use when
they returned. Having splashed through a lot of water, they were picked up by another locomotive that had come in from the Arthur’s Pass end.

Arriving at the settlement in the middle of the night with his friend, Dr Bathgate attended the patient, whose husband rewarded him with a couple of hares. He then placed his gift of the two hares, his acetylene lamp, and his medical bag on the “flattie” at the eastern end of the tunnel, and took off again at speed towards the door placed in the middle of the tunnel, regulating his downhill progress by means of a footbrake on the truck.

Going too fast, and, as he himself says, “carelessly missing the landmarks in the tunnel walls,” Dr Bathgate slammed into another rake of loaded trucks that had been left in the blackness for the next shift to clear.

Dr Bathgate was hurled the full length of the truck, and Dr Arthur vanished into the void, holding on to the hares. By the light of his acetylene lamp, Dr Bathgate could see Dr Arthur sitting between the rails. Neither was badly hurt.

Abandoning the blocked truck, the two men walked in a westerly direction along the tunnel until they found, somewhere near the middle of it, the other “flattie” that had been left there for their use. “At a more reasonable pace,” Dr Bathgate writes, “we proceeded down to the Otira portal, [a distance of almost five kilometres] and walked back to the hospital…Dr Arthur had no desire to repeat the experience. Next day we had hare soup for dinner.”

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Recognition of burns as a marker of child abuse in the paediatric emergency department

In 2008, 248 children were admitted to hospital with confirmed cases of abuse in New Zealand.\(^1\) Accurately identifying abuse and knowing when to refer children to social services for suspected abuse can be difficult for junior ED staff with limited experience. The Family Violence Intervention Programme reported 15% of children admitted due to child abuse had sustained burns.\(^2\)

A retrospective audit was performed in the Emergency Department (ED) of Waikato Hospital (Hamilton, New Zealand) leading to the introduction of a scald assessment triage tool and increased education sessions. The Department was re-audited to see if the changes had affected admission practice.

A list of patients under the age of 15 admitted with burns from 1 January 2010 to 31 July 2012 was compiled. 108 children were included in the first audit and 76 in the second. The most common type of burn sustained was a scald (n=51, 67%), followed by contact burn (n=12, 16%).

This compares with the previous audit which reported scalds accounting for 58% of burns, contact accounting for 22%. A higher number of patients were admitted for superficial burns in the second study (81% vs 18%). There were less complications in the second audit (12% vs 28%) and significantly reduced need for surgical treatment (64% vs 82% \(p=0.008\)). The mean length of stay in hospital was 4.9 days (1–21 days) which was reduced from 7.8 days. See Tables 1 and 2.

Documentation of whether or not the child was supervised and who was supervising has improved (78% vs 54%). The Child Protection Service within the hospital received referrals regarding 49% of the cases. This service notified Child Youth and Family Services (CYFS), the national agency in 23% of cases in comparison with only 14% in the initial research.

This audit shows that there is increased awareness of abuse in the ED and more children were admitted possibly for social reasons rather than medical. There was an increase in those referred to CYFS which shows that more cases of actual abuse were detected in the second study. In 2010, Newton et al reviewed six studies of strategies to improve ED documentation and catchment of paediatric patients who were being abused.

The results showed that ‘compared to standard practice, chart checklists paired with an educational program increased physician consideration of non-accidental burns in burn cases, documentation of time of injury, and documentation of consistency and compatibility of reported histories’ by at least 36% in all cases.\(^3\) This paper also demonstrated that ‘decisional flow-charts increased documentation of non-accidental physical injury and had a similar significant effect as checklists on increasing documentation of history consistency and compatibility’ by nearly 70%.\(^3\)
Table 1. Comparison of data between first and second audit

<table>
<thead>
<tr>
<th></th>
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</tr>
</thead>
<tbody>
<tr>
<td>Number of patients</td>
<td>108</td>
<td>76</td>
</tr>
<tr>
<td>Mean age</td>
<td>3.8 (2 month–12 years)</td>
<td>3 (2 month–12 years)</td>
</tr>
<tr>
<td>Aetiology</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Scalds</td>
<td>58% (63)</td>
<td>67% (51)</td>
</tr>
<tr>
<td>Contact</td>
<td>22% (24)</td>
<td>16% (12)</td>
</tr>
<tr>
<td>Friction</td>
<td>2% (2)</td>
<td>7% (5)</td>
</tr>
<tr>
<td>Flame</td>
<td>18% (19)</td>
<td>0%</td>
</tr>
<tr>
<td>Other</td>
<td>0%</td>
<td>10% (8)</td>
</tr>
<tr>
<td>Burn depth</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Superficial</td>
<td>18% (19)</td>
<td>80% (61)</td>
</tr>
<tr>
<td>Mid-dermal</td>
<td>54% (59)</td>
<td>9% (7)</td>
</tr>
<tr>
<td>Full</td>
<td>28% (30)</td>
<td>6% (5)</td>
</tr>
<tr>
<td>No record</td>
<td>0%</td>
<td>5% (4)</td>
</tr>
<tr>
<td>Unwitnessed burns</td>
<td>15% (16)</td>
<td>33% (25)</td>
</tr>
<tr>
<td>Mean length of stay</td>
<td>7.8 days</td>
<td>4.9 days (1–21 days)</td>
</tr>
</tbody>
</table>

Table 2. Further comparison of data between first and second audit

<table>
<thead>
<tr>
<th></th>
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</tr>
</thead>
<tbody>
<tr>
<td>Surgery required</td>
<td>82% (88)</td>
<td>(n=) 64% (49) p value 0.008</td>
</tr>
<tr>
<td>Type of surgery</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Debridement and biobrane</td>
<td>NR</td>
<td>54% (41)</td>
</tr>
<tr>
<td>Skin graft</td>
<td>74% (80)</td>
<td>13% (10)</td>
</tr>
<tr>
<td>Complications from burns</td>
<td>28% (30)</td>
<td>12% (9) p value 0.02</td>
</tr>
<tr>
<td>OPD attendance</td>
<td>65%</td>
<td>72% (55)</td>
</tr>
<tr>
<td>Child protection</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CPASS involvement</td>
<td>NR</td>
<td>49% (37)</td>
</tr>
<tr>
<td>CYFS involvement</td>
<td>14% (15)</td>
<td>23% (17) p value 0.12</td>
</tr>
<tr>
<td>Police involvement</td>
<td>1% (1)</td>
<td>8% (6)</td>
</tr>
</tbody>
</table>

Without an injury and ingestion form there is a chance that subtle cases of abuse will not be identified or conversely, that there could be over-reporting of possible neglect resulting in anxiety for families. Ideally, such a form will be introduced into the ED to appropriately recognise burns which are a result of neglect or abuse. Further auditing in conjunction with continued education can ensure that all children who are at risk of abuse are identified.

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Response to NZMJ editorial by Dr Elana Curtis entitled

*Deserving of more: framing of Māori inequities in cardiovascular care remain a challenge*

We appreciate the comments by Dr Elana Curtis \(^1\) in relation to our recent article \(^2\) about worse morbidity and higher mortality in Māori compared to Europeans undergoing coronary artery bypass surgery (CABG) at Auckland City Hospital. However we are concerned that this could be interpreted to indicate that Māori may get lower quality care and may be contributed to by institutional racism.

We have no information that Māori received reduced quality of care and some findings from our study are reassuring; for example scores to estimate overall need for CABG (access score, Māori: 54.5 (8.5) vs European 53.5 (8.8) \(p=0.39\)) and urgency for surgery (Māori: 38.4 (SD 14.2), European 37.6 (SD 14.1), \(p=0.62\)), were similar for Māori and European patients. Also Māori did not wait longer for in-hospital surgery or elective surgery between evaluation by the cardiology services across the four Auckland hospitals and performing the procedure (in-hospital 8.0 days vs 7.8 days, \(p=0.95\), elective 45.2 days vs 71.4 days, \(p=0.16\)). In addition Māori were prescribed the same high rate of evidence-based medications as Europeans such as aspirin (100% vs 98%) and statins (91% vs 88%) at discharge.

We believe the greater cumulative burden of disease and comorbidity in Māori are the major reason for increased mortality following cardiac surgery, and these factors may not be adequately captured using standard risk scores such as the EuroScore. \(^3-6\) In our study Māori presented later in their disease process as evidenced by lower ejection fractions and more heart failure, and more Māori were on dialysis. Also surgical cross clamp and bypass times were prolonged in Māori suggesting that their operations were more complex.

Previous studies have identified a much higher prevalence of cardiovascular risk factors, and of undiagnosed and untreated cardiovascular disease in Māori, particularly those in rural populations. \(^7\) Risk factors including diabetes, hypertension and smoking, and the quality of medical care over the life course, \(^8\) as well as delays in presentation, investigation and treatment are likely to impact mortality related to CABG, in addition to other adverse health outcomes.

We are very aware of the health inequalities that Māori suffer and are committed to improving outcomes in Māori and made a call in our manuscript to lower the Surgical Priority Score for Māori to improve their access to CABG. Indeed one of us (HW) \(^9\) initiated the screening of Māori in primary prevention to be undertaken 10 years earlier than Europeans (age 35 vs 45 in men and 45 vs 55 years in women) in order to enable Māori to be receive earlier non pharmacologic and pharmacologic therapies as appropriate.

We agree that further research is required to define the basic causes of the inequities in Māori we identified, and importantly open discussion to identify strategies to improve outcomes.
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References:
HIV screening in New Zealand: time for a change

The recommendations for HIV testing and screening in New Zealand need to change. The current Ministry of Health Recommendations for HIV testing of adults in healthcare settings, \(^1\) last updated in 2007, have become outdated in the light of increasing worldwide consensus that HIV testing in adults should be normalised and that HIV screening (detecting disease in asymptomatic individuals) should be performed routinely.

The current policy recommends a risk-based testing approach and states that this approach is “in accord with recently published US guidelines in the Morbidity Mortality Weekly Report”. \(^2\) In fact, the cited 2006 guideline from the US Center for Disease Control and Prevention (CDC) states that HIV screening should be a routine part of medical care for all American adults and adolescents. This approach has subsequently been endorsed by the American College of Physicians \(^3\) and the Infectious Diseases Society of America. \(^4\)

The recommendations from these groups have been further strengthened by new recommendations from the US Preventive Services Task Force (USPSTF), in an updated Recommendation Statement on Screening for HIV published in April 2013. \(^5\) The USPSTF is a panel of internationally recognised health care experts that evaluates the latest scientific evidence on clinical preventive services. The USPSTF advises screening for HIV infection in their setting in adults aged 15 to 65 years where the population prevalence of undiagnosed HIV infection is known to be \(\geq 0.1\%\); in younger adolescents and older adults who are at increased risk of HIV infection; and in all pregnant women.

Current risk-based HIV screening practices in New Zealand are failing to provide an early diagnosis in many people with HIV infection. As a consequence these people remain at risk of AIDS defining illnesses and their sexual partners at risk of acquiring HIV infection. A recent study of men who have sex with men in Auckland found that 21% of the participants who had HIV infection were not aware of this diagnosis. \(^6\)

Late diagnosis, reflecting a failure of timely HIV diagnosis, is common in New Zealand; of the 604 patients diagnosed with HIV infection between 2005 and 2010, 50% met the definition of a late presentation and 32% met the definition of advanced disease at the time of diagnosis. \(^7\)

It should be emphasised that with the use of currently available anti-retroviral treatment, HIV infection has changed from a diagnosis associated with a markedly reduced life expectancy to a very manageable chronic disease with a life expectancy similar to, or better than, many other chronic diseases.

The life expectancy of a person with HIV infection now approaches that of a person without HIV infection, especially if the diagnosis is made early so that anti-retroviral treatment can be initiated at an appropriate time. \(^8\) With this in mind, an HIV test has similarities to other screening tests for chronic diseases such as an HbA1c.
The current New Zealand Ministry of Health recommendations regarding HIV testing are too complex and proscriptive. They recommend oral informed consent be obtained and that this consent be documented in the patient’s medical record.

We believe that HIV screening in New Zealand should be conducted in accordance with the latest CDC recommendations. This will require a revision of the New Zealand Ministry of Health recommendations.

We suggest an approach where adult and adolescent patients aged 15 to 65 in all health-care settings are informed by their medical professional that HIV screening is indicated and should be routinely performed. Of course, patients should have the opportunity to ask questions about HIV infection and the HIV test and decline permission for this test. Consent should be obtained as for other laboratory tests and does not need to be documented. Patients should have access to information about HIV infection and prevention of transmission. Pre- and post-test counselling is not necessary but is useful in certain situations.

Routine HIV screening will result in many patients receiving an earlier diagnosis of HIV infection and earlier access to care. This will allow for more timely initiation of anti-retroviral treatment, which will increase an individual’s life expectancy, and reduce the transmission of HIV infection in New Zealand.

Nick Gow¹; Simon Briggs²; Judy Gilmour³; Rupert Handy²; Rebecca Henley³; Joan Ingram²; Chris Kenedi⁴; Michele Lowe³; Susan Munt⁵; Mitzi Nisbet²; Stephen Ritchie²; Mark Thomas³

¹Registrar, ²Physician, ³HIV Nurse Specialist, ⁴HIV Social Worker, Department of Infectious Diseases, Auckland City Hospital, Auckland, New Zealand

⁴Consultant, General Medicine and Liaison Psychiatry, Auckland City Hospital, Auckland, New Zealand

References:


The Increase of Cancer in New Zealand (part 2)


(Continued from part 1 at http://journal.nzma.org.nz/journal/126-1381/5809)

The age at death is shown in the following table. The greatest incidence is between 55 to 75 years. A suggestion has been recently made that cancer is most frequently encountered at the age when sexual activities are decaying. As it is difficult to fix the age at which this form of degeneration sets in, the following table cannot be used either as an argument for or against this statement. It does, however, support the usual statement that cancer is a disease of approaching old age.

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<th>30 to 35</th>
<th>35 to 40</th>
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<th>45 to 50</th>
<th>50 to 55</th>
<th>55 to 60</th>
<th>60 to 65</th>
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In 1909 Dr. Hislop, of Geraldine, reported in the British Medical Journal a series of thirty-one cases or cancer that had occurred in his practice. He took great pains to investigate each case, with especial reference to the diet, habits, and residence of the patient, and established certain factors which appeared common to the whole series. Each case lived, or had lived, at some period on the banks of or near a small creek.

Sub-acute or chronic rheumatism was common, and each case drank freely of tea. In 11 cases of the 31 immoderate tea drinking was admitted. In support of this Dr. Brittin, who had practised on both coasts of the South Island, stated that during three years' practice on the West Coast he had five deaths from cancer out of a total of 15. The whole country was bush, rheumatism was universal, and the customary diet was "frying pan meat and billy tea."

In ten years' practice on the East Coast, he had one death from cancer out of 70. He ascribed the frequency of cancer on the West Coast to chronic intestinal irritation associated with dampness of climate and chronic rheumatism.
Iron supplementation in pregnancy

Pregnant women are usually given iron supplementation on the grounds that this will be beneficial to the mother and baby. This meta-analysis examines whether there is an association between prenatal anaemia, use of iron, and maternal haematological and pregnancy outcomes, and is a dose-response relation apparent?

Information was obtained from 48 randomised trials and 44 cohort studies. Use of iron significantly increased mean maternal haemoglobin concentration and reduced the risk of anaemia, iron deficiency anaemia and low birth weight.

The effect of iron on pre-term birth was not significant. There was a linear decrease in maternal anaemia with increasing iron doses up to 66 mg/day. An editorial commentator commended the meta-analysis report and noted that a recent Cochrane review has reached the same conclusions.


Treatment decisions in rheumatoid arthritis when methotrexate fails

The use of disease-modifying antirheumatic drugs (DMARDs) has proven to be very successful in the management of rheumatoid arthritis. Methotrexate is the commonest first choice DMARD but it is not always successful. Several biological agents have shown to be useful in this situation.

The option most often preferred by clinicians is to add a tumour necrosis factor (TNF) inhibitor to methotrexate. This is usually effective but very expensive.

This report concerns a trial in which 353 participants with rheumatoid arthritis who had active disease despite methotrexate therapy were randomly assigned to a triple regimen of disease-modifying antirheumatic drugs (methotrexate, sulphasalazine, and hydroxychloroquine) or etanercept plus methotrexate.

Both groups had significant improvement with their treatment and there was no significant difference in adverse events. The conclusions were that “with respect to clinical benefit, triple therapy, with sulphasalazine and hydroxychloroquine added to methotrexate, was noninferior to etanercept plus methotrexate in patients with rheumatoid arthritis who had active disease despite methotrexate therapy.”


Hyperuricaemia and gout in New Zealand

This study set out to determine the prevalence of gout and hyperuricaemia in rural and urban Maori and non-Maori community samples and describe the treatment and comorbidities of participants with gout.
751 participants between 20 and 64 years of age were recruited randomly from the electoral role. There were 252 rural Maori participants, 243 urban Maori and 256 non-Maori.

Seventeen percent of the Maori subjects had hyperuricaemia compared with 7.5% of the non-Maori. There were 57 subjects with a history of gout with Maori having a significantly greater incidence. Eighteen of the 57 gouty subjects were receiving urate-lowering treatment but 38.9% of these had not achieved the target urate levels.

The conclusions reached by the researchers were that “gout and hyperuricaemia were more prevalent in Maori, and participants with gout were more likely to have comorbidities. There was not a higher overall adjusted cardiovascular disease risk in Maori participants with gout. Despite the high prevalence of gout, management remains suboptimal.”

Donald Stewart Malcolm

10 October 1915 – 6 August 2013; Associate Professor Paediatrics, University of Otago; 72388 Major, 26th Battalion 2NZEF

Donald Malcolm brought a strong academic background to his paediatric career pioneering neonatal care in Palmerston North and Dunedin, and community paediatrics in Otago.

He qualified BSc Otago in 1935, with Stage III Physics, Chemistry, Botany, Zoology, MB ChB University of New Zealand, 1941, MD Otago on nerve conduction “A method of measuring reflex times in man”, under Mr Murray Falconer, Neurosurgeon, 1949. He qualified MRACP the same year and FRACP 1961.

His early career was in war service, following a House Surgeon post 1941 in Timaru. He served in the Royal Army Medical Corps (NZ) in Fiji 1942, and at Featherston Prisoner of War Camp 1943, attending wounded Japanese POWs.

From later that year he served in Italy, and was wounded by shrapnel with significant blood loss in 1945.

On returning to NZ, he worked as Lecturer in Physiology, Otago University 1946, House Surgeon Tauranga 1947, and then Registrar Auckland 1948, writing his MD at the same time. He was appointed Chest Physician Palmerston North Public Hospital 1949, with a strong Tuberculosis focus, studying Thoracic Medicine for 6 months in London in 1952.

A far-sighted PN Hospital superintendent, Dr John North, suggested a career change to Paediatrics with the advent of Streptomycin and the promise of Tuberculosis eradication. Donald studied Paediatrics for a year in 1956 at Great Ormond St. Hospital, London.

He returned as Paediatrician in 1957, and developed the second NZ special care neonatal service, encouraged by the support of Dr Gordon Cumming, Obstetrician. He worked in PN Hospital and private practice paediatrics, sharing rooms with his friend Dr Lewis Bieder who described him as “the brother I never had”.

In 1963, Donald moved to Dunedin, as Paediatrician at Dunedin Public Hospital where he founded the third NZ neonatal unit. He was also appointed Senior Lecturer, Paediatrics, University of Otago, becoming an Associate Professor in 1972. He introduced a very successful method of getting fluids into the scalp veins of 28 week premature babies, hand-making “Usher” metal butterfly needles for IV fluids, which were stabilised with plaster of Paris onto the scalp. The needles were sharpened then sterilised for re-use.
Always on the lookout for advances, he and Dr Patricia Buckfield imported the first Loosco neonatal ventilator from the Netherlands in 1968. He assembled the new equipment with his registrars, ventilated babies with it, and then taught the anaesthetists how to use it.

Exchange transfusions for Rhesus babies were frequent and painstakingly slow, often taking 3 hours. He purchased one of the first blood gas analysis machines which took half an hour to calibrate at the beginning of each day. Dunedin babies were some of the first in the world to benefit from this now routine investigation.

His professional collaborations included: with Mr Victor Pearse who patched an infant’s diaphragmatic hernia, with Dr Norma Restieaux, on infants’ difficult cardiac issues, and innovative clinics with Dr Peter Lewis, Child Psychiatrist. He mentored many of the next generation of doctors, including paediatricians with his teaching responsibilities with Otago Medical School. His Paediatric contemporaries included from 1967 Professor Jim Watt the first Chair of Paediatrics, Drs Patricia Buckfield, and David Holdaway who predeceased him.

Donald had a longer term view of the care that neonatal baby graduates needed, and he worked closely with social workers and community agencies to provide this. In 1967 Donald was awarded a Wolfson Fellowship visiting USA and UK Neonatal Units. He shared the findings in a NZ wide speaking tour and applied them at Queen Mary Maternity Hospital Dunedin. He spent sabbatical time in 1970 with his friend and neonatologist contemporary Dr Bill Kitchen, Melbourne. Donald read widely and was dedicated to lifelong learning.

He supported Dr Patricia Buckfield, who had detailed 20,000 Dunedin deliveries and encouraged their registrars to complete data entry, pointing out the potential value of the study if it was done well. Dr Phil Silva followed 1037 of them in great depth from 1972 to found the Dunedin Longitudinal Study, the value of which is now internationally recognised.

Donald had a deep concern for vulnerable children at risk of child abuse and supporting parents. He and his colleague Sheila Monaghan with Dr Roy Muir initiated and participated in the Acorn Club supporting young mothers. Sheila and Roy wrote up their findings in the International Journal of Child Abuse and Neglect. His strong advocacy for families did not always find favour with the hospital administration of the time. He first retired in 1975.

His skills were not to be wasted and in 1977 Dr Peter Hinds, Health Department invited him to work as one of the first NZ Community Paediatricians: a service including paediatric services to schools and social agencies. They collaborated with and supported Grace Thompson’s Home Health book. The role, which he found immensely satisfying, was to have been 3 months but continued for 5 years till his second retirement in 1983. Peter remained a close friend till his death.
Donald is survived by his devoted wife of 67 years, Margaret, son John, daughter Margy-Jean, 5 grandchildren and 2 great-grandchildren. His eldest daughter Anne died in 1996. His legacy in Neonatal and Community Paediatrics was pioneering in NZ, his skills and scope inspiring. Personally and professionally, people experienced him as kind, helpful, insightful and supportive—always seeking the very best for children and their parents.

John Malcolm & Margy-Jean Malcolm wrote this obituary.
Sources: Donald & Margaret Malcolm; Drs Ross Howie, Auckland; Graeme Barnes, Melbourne; John Clarkson, Dunedin; and John Malcolm, Whakatane.
Thakshan Lal Udayamitta Fernando


Thakshan Fernando laid the foundations for major change in New Zealand’s mental health system during his period in the early 1990s as Director of Mental Health at the Ministry of Health.

During the first half of his career, he was a well-loved family doctor in Sri Lanka. Soon after qualifying in medicine from the University of Colombo, Thakshan spent 2 years training in haematology before developing a popular general practice that also served university students.

In 1971 he had an opportunity to take up a French government scholarship in Paris, where he returned to his former study of haematology. Towards the end of his time there he spent an additional 6 months at Cane Hill Psychiatric Hospital, at that time introducing some of the early steps towards supporting long-term residents to return to the community.

Only a year after his return to Sri Lanka, he and his family migrated to New Zealand in 1974, part of a group of doctors recruited to improve the medical workforce in the large psychiatric hospitals. He began his work as a medical officer in Porirua Hospital, under the mentorship of Dr John Hall, the then medical superintendent.

Thakshan rapidly showed himself to be an outstanding doctor, and was persuaded to undertake postgraduate training in psychiatry, which he passed with flying colours. He was appointed a consultant psychiatrist, and established one of the first teams in the Wellington region to specialise in the mental health issues of the elderly.

Before moving to an appointment as a Senior Lecturer in the Wellington School of Medicine he spent a period of study leave at Rochester in the USA, preparing himself to establish and develop a consultation liaison psychiatry service for Wellington Hospital, so that those facing major challenges through physical illness could access psychological and psychiatric support. At the forefront of such new developments in mental health services, the close and respectful inter-professional links he forged served him very well in building and leading multidisciplinary teams that are now central to good clinical practice.

Throughout his work as a psychiatrist he was an inveterate teacher, with a masterly blend of avuncular support and a willingness to share his own reflections on his clinical experience allied to a keen insistence on logic and evidence in support of providing quality care.

He took a personal interest in his students’ careers and became a treasured mentor to many. At a time of significant change in psychiatry he had a critical impact on a cohort of young doctors in training, who were greatly influenced by his holistic
approach, and the wisdom and humanity shown in his relationships with patients. He was universally loved and respected, by both patients and colleagues.

Eager for new challenges, he took up the opportunity of becoming Deputy Director of Mental Health at the Department of Health in 1989, and Director the following year. During this period, he set a new direction for the Mental Health Group, within the Department of Health, then the Ministry of Health, eager to promote a more evidence-based approach to quality assurance within the sector and to give space to consumer and family voices within the services.

He brought the same capacity to inspire others, expecting the same high standards that he required of himself and able to quietly convey his dissatisfaction if that was not forthcoming. During that time, he facilitated the enactment of the 1992 Mental Health Act, which has stood the test of time over 21 years, and demonstrated his passion for quality by establishing the first set of national clinical guidelines to set standards for good, quality practices.

The period that Thakshan was Director of Mental Health set the foundations for the reforms in mental health services of the following 15 years, with the establishment of the Mental Health Commission and the role of the Mental Health Strategy. He was also very active in the Royal Australian and New Zealand College of Psychiatrists, serving as honorary secretary of the New Zealand Branch for many years, acknowledged by the award of a College citation in 1994.

He retired from the Ministry of Health in 1993, having served two Ministers (Helen Clark and Simon Upton) and an Associate Minister (Katherine O’Regan) all of whom had significant respect for him personally and for his advice. He then worked part-time in private practice for a few years, enjoying the extra time this gave him to spend with his family and his wide circle of friends and former students.

He was an active and respected member of the Sri Lankan community and was pleased to remain a conduit to foster professional connections within the Sri Lankan medical community and with the New Zealand mental health system.

Although in recent years he had been increasingly restricted by progressive respiratory problems, he could still pursue his keen interests in sport, literature and poetry. As an enthusiastic cricket fan, Thakshan loved the divided loyalties offered him when Sri Lankan cricket teams began to visit New Zealand.

A clear thinker, he was able to express himself in beautifully articulate English, written or spoken, and in his later years, he used this talent in his writings, especially in his poetry.

As a person, Thakshan radiated calm, peace and personal humility to all around him. This inspired great loyalty from his friends, his patients and from all those who knew him. He was a cherished friend and shining inspiration to many. He was a wise professional who could put patients and their families at ease, a man who generated confidence among policy makers, and a teacher who motivated students in their career development.
Throughout everything he did, he was strongly supported by his family, especially his loving wife Sushila of 56 years, who also worked as the Librarian at Porirua Hospital. He was enormously proud of his four children, Shanthi, Rohitha, Nerupamal and Tushan, and adored his grandchildren, Miles, Sachin and Anouska.

Professor Pete Ellis (Professor of Psychological Medicine, Wellington School of Medicine) and Dr Janice Wilson (Chief Executive, Health Quality and Safety Commission) wrote this obituary.

Sources: A number of close friends and colleagues, and family members.