

Performance and Evaluation in Computed Tomographic Colonography Screening for Colorectal Cancer

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Declaration: I, Anuoluwapo Eytayo Obaro, confirm that the work presented in this thesis is my own. Where information has been derived from other sources, I confirm that this has been indicated in the thesis.

Dedicated to my beloved, Zebedee, and our two wonderful sons,
Zephaniah and Azariah.

ABSTRACT

Performance and Evaluation in Computed Tomographic Colonography Screening for Colorectal Cancer

Each year over 20,000 people die from colorectal cancer (CRC). However, despite causing the second highest number of cancer deaths, CRC is not only curable if detected early but can be prevented by population screening. The detection and removal of pre-malignant polyps in the colon prevents cancer from ever developing. As such, screening of the at-risk population (those over 45-50 years) confers protection against CRC incidence and mortality.

Although the principles and benefit of screening are well established, the adequate provision of screening is a complex process requiring robust healthcare infrastructure, evidence-based quality assurance and resources. The success of any screening programme is dependent on the accuracy of the screening investigations deployed and sufficiently high uptake by the target population. In England, the Bowel Cancer Screening Programme (BCSP) delivers screening via initial stool testing to triage patients for the endoscopic procedure, colonoscopy, or the radiological investigation CT colonography (CTC) in some patients. There has been considerable investment in colonoscopy accreditation processes which contribute to high quality services, suitable access for patients and a competent endoscopy workforce. The performance of colonoscopists in the BCSP is tightly monitored and regulated; however, the same is not true for CTC. Comparatively, there has been little investment in CTC services, and in fact there is no mandatory accreditation or centralised training. Instead, CTC reporting radiologists must learn

ad hoc on the job, or at self-funded commercial workshops. This inevitably leads to variability in quality and expertise, inequity in service provision, and could negatively impact patient outcomes.

To address this disparity and develop evidence-based training, one must determine what factors affect the performance of CTC reporting radiologists, what CTC training is necessary, and what training works. This thesis investigates these topics and is structured as follows:

Section A reviews the background literature, describing the public health burden of CRC and the role of screening. Aspects of CTC screening and its role in the BCSP are explored. The importance of performance monitoring and value of accreditation are examined and the disparity between CTC, colonoscopy and other imaging-based screening programmes is discussed.

Section B expands on radiologist performance by determining the post-imaging CRC (or interval cancer) rate through systematic review and meta-analysis. Factors contributing to the interval cancer rate are evaluated, and an observational study assessing factors affecting CTC accuracy is presented. The impact of CTC training is assessed via a structured review and best principles for training delivery are discussed.

Section C presents a multicentre, cluster-randomised control trial developed from the data and understanding described in Sections A and B.

Section D summarises the thesis and discusses future recommendations and research.

IMPACT STATEMENT

CT colonography (CTC) is an X-ray based investigation used in the diagnosis of colorectal cancer (CRC). Using computer-processed images of the bowel, CTC allows specialist imaging doctors (radiologists) to examine the inside of the colon to detect cancers and pre-malignant growths (polyps). Although CTC is widely used internationally, the real-world performance of CTC reporting radiologists and the factors which can improve their accuracy have not been extensively examined. This, in addition to a lack of centralised training, mandatory accreditation and performance monitoring, underpins variable quality.

The work in this thesis addresses these issues and establishes for the first time a CTC training model with proven long-term impact. After undergoing the novel training intervention reported here (PERFECTS), recruited radiologists saw significant improvements in their diagnostic sensitivity. Although the training was only one day long, this benefit was still apparent 12 months later.

National impact

The successful PERFECTS trial inspired creation of the National CTC Training and Accreditation Programme (NCTCTAP; www.nationalctctrainingprogramme.org), of which the thesis author is Online Training Lead. Recognising the need for evidence-based CTC training, the NCTCTAP was founded on the training principles and results presented herein. Following >£800k funding from Health Education England, national roll-out of training in CTC technique is underway and the prototype for online training in CTC interpretation is under development. The

NCTCTAP has been awarded accreditation from the Society and College of Radiographers and is recognised as the primary offering for CTC training by the British Society of Gastrointestinal and Abdominal Radiology (BSGAR). The creation of NCTCTAP means high-quality, evidence-based CTC training accessible by all practitioners nationally, is now a reality, and future accreditation for radiologists a distinct possibility.

International impact

As well as the significant contribution to CTC education in England, the thesis impact extends internationally. Two studies, including the first detailed narrative review of CTC training, are contributing to new guidelines on CTC quality assurance and training being developed by the European Society of Gastrointestinal and Abdominal Radiology (ESGAR). The thesis author will be coordinating the working groups which will focus on initial CTC training, accreditation, and performance monitoring, addressing the current lack of international consensus.

Peer-reviewed publications arising from this thesis have contributed to the understanding of performance metrics in CTC and are cited in national and international policies and guidelines. These include; Standards of practice for CTC (Joint guidance from the BSGAR and Royal College of Radiologists, 2021), Imaging alternatives to colonoscopy: CT colonography and colon capsule (European Society of Gastrointestinal Endoscopy (ESGE) and ESGAR Guideline, 2020), and the World Endoscopy Organization Consensus Statements on Post-Colonoscopy and Post-Imaging Colorectal Cancer, 2018.

Summary

To date, PERFECTS is the largest published randomised trial of CTC training with the longest follow-up. The benefit of the training intervention developed and tested extends to radiologist participants, but most importantly to the patients being scanned. Improving detection of early cancer improves patient outcomes and reduces morbidity. The work in this thesis has already contributed to national and international policy and will continue to inspire CTC education.

ACADEMIC OUTPUT

Publications arising from directly from this thesis, as of September 2022:

1. **Obaro AE**, McCoubrie P, Burling D, Plumb AA (2022). Effectiveness of training in CT colonography interpretation: Review of current literature. *Seminars in Ultrasound, CT and MR*. DOI: 10.1053/j.sult.2022.06.002
2. **Obaro AE**, McCoubrie P, Burling D, Plumb AA (2022). Training in CT colonography interpretation: Recommendations for best practice. *Seminars in Ultrasound, CT and MR*. DOI: 10.1053/j.sult.2022.06.001
3. **Obaro AE**, Plumb AA, Halligan S, Mallett S, Bassett P, McCoubrie P, Baldwin-Cleland R, Ugarte-Cano C, Lung P, Muckian J, Ilangovan R, Gupta A, Robinson C, Higginson A, Britton I, Greenhalgh R, Patel U, Mainta E, Gangi A, Taylor SA, Burling D (2022). Colorectal Cancer: Performance and Evaluation for CT Colonography Screening- A Multicenter Cluster-randomized Controlled Trial. *Radiology*. DOI: 10.1148/radiol.211456
4. Plumb AA, **Obaro AE**, Bassett P, Baldwin-Cleland R, Halligan S, Burling D (2020). Performance and Evaluation in Computed Tomographic Colonography Screening (PERFECTS): Protocol for a Cluster Randomized Trial. *medRxiv*. DOI: 10.1101/2020.02.25.20027714
5. **Obaro AE**, Plumb AA, North MP, Halligan S, Burling DN (2019). Computed tomographic colonography: how many and how fast should radiologists report? *European Radiology*. DOI: 10.1007/s00330-019-06175-y

6. **Obaro AE**, Plumb AA, Fanshawe T R, Torres US, Baldwin-Cleland R, Taylor SA, Halligan S, Burling DN (2018). Post-imaging colorectal cancer or interval cancer rates after CT colonography: a systematic review and meta-analysis. *The Lancet Gastroenterology & Hepatology*. DOI: 10.1016/S2468-1253(18)30032-3
7. **Obaro AE**, Burling DN, Plumb AA (2018). The role of imaging in screening special feature: Review Article. Colon cancer screening with CT colonography: logistics, cost-effectiveness, efficiency, and progress. *The British Journal of Radiology*. DOI: 10.1259/bjr.20180307
8. Plumb AA, **Obaro AE**, Fanshawe T, Torres US, Baldwin-Cleland R, Halligan S, Burling D (2017). Prevalence and risk factors for post-investigation colorectal cancer ('interval cancer') after computed tomographic colonography: protocol for a systematic review. *Systematic Reviews*. DOI: 10.1186/s13643-017-0432-8

Other publications related to thesis material, but not part of thesis itself:

1. Duxbury O, Burling D, Muckian J, Lung P, **Obaro AE**, Smith K, Plumb AA (2021). Meeting the new joint British Society of Gastrointestinal and Abdominal Radiology and Royal College of Radiologists CT colonography standards: a 6-year experience. *Clinical Radiology*. DOI: 10.1016/j.crad.2021.05.007.
2. Corr A, **Obaro AE**, Burling D (2018). Role of CT colonography for primary colorectal cancer screening. *Trends in Urology & Men's Health*. DOI: 10.1002/tre.625

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PREFACE

This thesis represents original work by the author which has not been submitted to any other university. Any use of work by other people has been appropriately acknowledged in the text.

The research described herein was undertaken at the Centre of Medical Imaging, University College London (UCL) and St Mark's Hospital and Academic Institute, Harrow.

The work reported in this thesis was supervised by Associate Professor Andrew Plumb and Professor Steve Halligan. Additional supervisory support was provided by Dr David Burling (St Mark's Hospital, Harrow) and all three individuals provided oversight of this research.

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LIST OF ABBREVIATIONS

2D: 2-Dimensional

3D: 3-Dimensional

ACGBI: Association of Coloproctology of Great Britain and Ireland

ADR: Adenoma Detection Rate

AER: Adverse Event Rate

AI: Artificial Intelligence

BCSP: English Bowel Cancer Screening Programme

BSGAR: British Society of Gastrointestinal and Abdominal Radiology

BSIS: Breast Screening Information System

BSG: British Society of Gastroenterology

BSP: Breast Screening Programme

C-RADS: CT Colonography Reporting and Data System

CAD: Computer Aided Detection

CI: Confidence Interval

CIR: Caecal Intubation Rate

CPD: Continued Professional Development

CRC: Colorectal Cancer

CRF: Case Report Form

CT: Computed Tomography

CTC: Computed Tomographic Colonography

DID: Diagnostic Imaging Dataset

DVD: Digital Versatile Disc

ESGAR: European Society of Gastrointestinal and Abdominal Radiology

ESGE: European Society of Gastrointestinal Endoscopy

FS: Flexible Sigmoidoscopy

GRADE: Grading of Recommendations Assessment, Development and Evaluation

ID: Identification

IEP: Image Exchange Portal

IT: Information Technology

JAG: Joint Advisory Group on GI Endoscopy

MeSH: Medical Subject Headings
NCDR: National Cancer Data Repository
NHS: National Health Service
NPV: Negative Predictive Value
p: Probability value
PACS: Picture Archiving and Communication System
PCCRC: Post Colonoscopy Colorectal Cancer
PDP: Personal Development Plan
PDR: Polyp Detection Rate
PIR: Polyp Identification Rate
PERFECTS: PERformance and Evaluation in CT colonography Screening
PERFORMS: PERsonal perFORMance in Mammographic Screening
PICRC: Post Imaging Colorectal Cancer
PPV: Positive Predictive Value
PRISMA: Preferred Reporting Items for Systematic Reviews and Meta-Analyses
PROSPERO: Prospective Register of Systematic Reviews
QA: Quality Assurance
RCR: Royal College of Radiologists
RCT: Randomised Controlled Trial
RIS: Radiological Information System
SBoSP: Scottish Bowel Screening Programme
SEER: Surveillance, Epidemiology and End Results staging
SIGGAR: Special Interest Group in Gastrointestinal and Abdominal Radiologists
SSA: Sessile Serrated Adenoma
TC3: Training the CT Colonography Trainers Course
TNM: staging of primary Tumour, locoregional Nodes, distant Metastasis
UCL: University College London
UK: United Kingdom
US: United States of America
USB: Universal Serial Bus
WT: Withdrawal Time

THESIS OVERVIEW

The work presented in this thesis is a collection of linked studies designed to establish why radiologist performance in CT colonography (CTC) for colorectal cancer (CRC) screening is important and how it might be improved through training. The thesis structure is as follows:

Section A provides an overview and background of colorectal cancer, screening, and the use of CTC. Examples of other imaging-based screening programmes and the role of accreditation and performance monitoring are discussed.

Section B is focused on reader performance in CTC and associated factors. Through a systematic review and meta-analysis, a post-imaging CRC rate is established for the first time. Parameters that affect performance are assessed, and current teaching methods are reviewed, concluding with suggestions for best practice in CTC training.

Section C evaluates a training model designed to improve radiologist performance. Through a multi-centre, cluster-randomised controlled trial the hypothesis that radiologists' diagnostic accuracy in CTC interpretation can be improved by an individualised training programme is assessed.

Section D summarises and concludes the thesis and discusses recommendations for future research.

SECTION A: LITERATURE BACKGROUND

The following section sets the scene for the thesis, highlighting the public health burden of colorectal cancer (CRC) and the value of screening in cancer detection. It provides the background and context for subsequent discussions about performance in CT colonography (CTC), the importance of accurate interpretation and how this can be improved with training.

I firstly discuss the pathogenesis and diagnosis of CRC and then highlight the characteristics of CRC screening with CTC. Finally, I review the importance of performance, accreditation and training in the quality assurance of screening programmes.

Chapter 1 Colorectal cancer: development and diagnosis

Summary and contribution statement

The chapter describes colorectal cancer (CRC), its pathogenesis, diagnosis, and the role of screening in prevention. I provide an overview of the two most common whole-colon investigations, colonoscopy, and CT colonography (CTC) and summarise their role in the English Bowel Cancer Screening Programme.

I undertook all the work in this Chapter; sections of which have been published as follows:

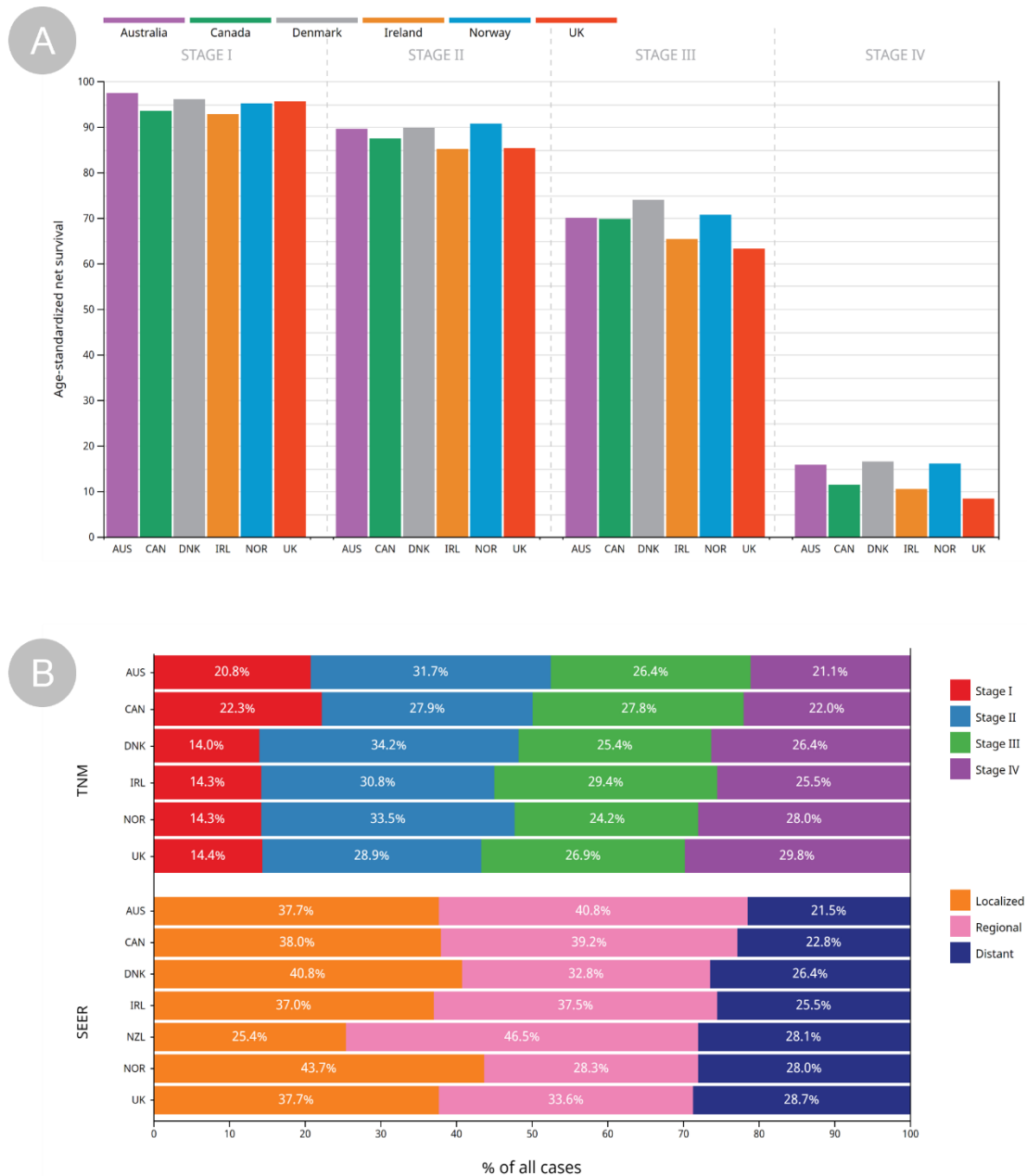
The role of imaging in screening special feature: Review Article. Colon cancer screening with CT colonography: logistics, cost-effectiveness, efficiency and progress. Obaro AE, Burling DN, Plumb AA (2018). The British Journal of Radiology. DOI: 10.1259/bjr.20180307

Introduction

Colorectal cancer (CRC) is the third most common cancer globally, with almost 2 million new cases diagnosed in 2020.¹ The UK has the third highest incidence in Europe, with 52,128 new cases in 2020 and over 21,000 CRC deaths.¹ CRC survival is strongly influenced by disease stage at diagnosis. Early, stage I and II disease, which is localised and confined to the bowel wall, has excellent cure rates (5-year survival >95%), but late presentation at stages III or IV, denoting nodal involvement or distant metastases respectively, has high mortality (5-year survival <15%; Figure 1.1A).^{1,2} The UK has poorer survival compared to other countries, due in part to late stage diagnosis in more than 50% of cases, when treatment is typically palliative rather than curative (Figure 1.1B).^{1,2}

Improving detection of early-stage CRC is therefore crucial, as it facilitates curative treatment, thereby reducing disease-specific mortality.^{3,4} Fortunately, the pathogenesis of CRC allows the opportunity for early intervention which can prevent cancer from ever occurring (i.e. reducing disease incidence).⁵

Figure 1.1: Age-standardised 5-year net survival between 2010 and 2014 according to CRC stage and country (A). Stage of CRC diagnosis (TNM and SEER classifications) between 2010 and 2014 according to country (B)



Survival declines with stage of diagnosis and the UK is the poorest performer with a higher percentage of CRC diagnosed at stages III and IV, when distant spread has already occurred. TNM: staging of primary Tumour, locoregional Nodes, distant Metastasis. SEER: Surveillance, Epidemiology and End Results staging. From Arnold et al 2019¹

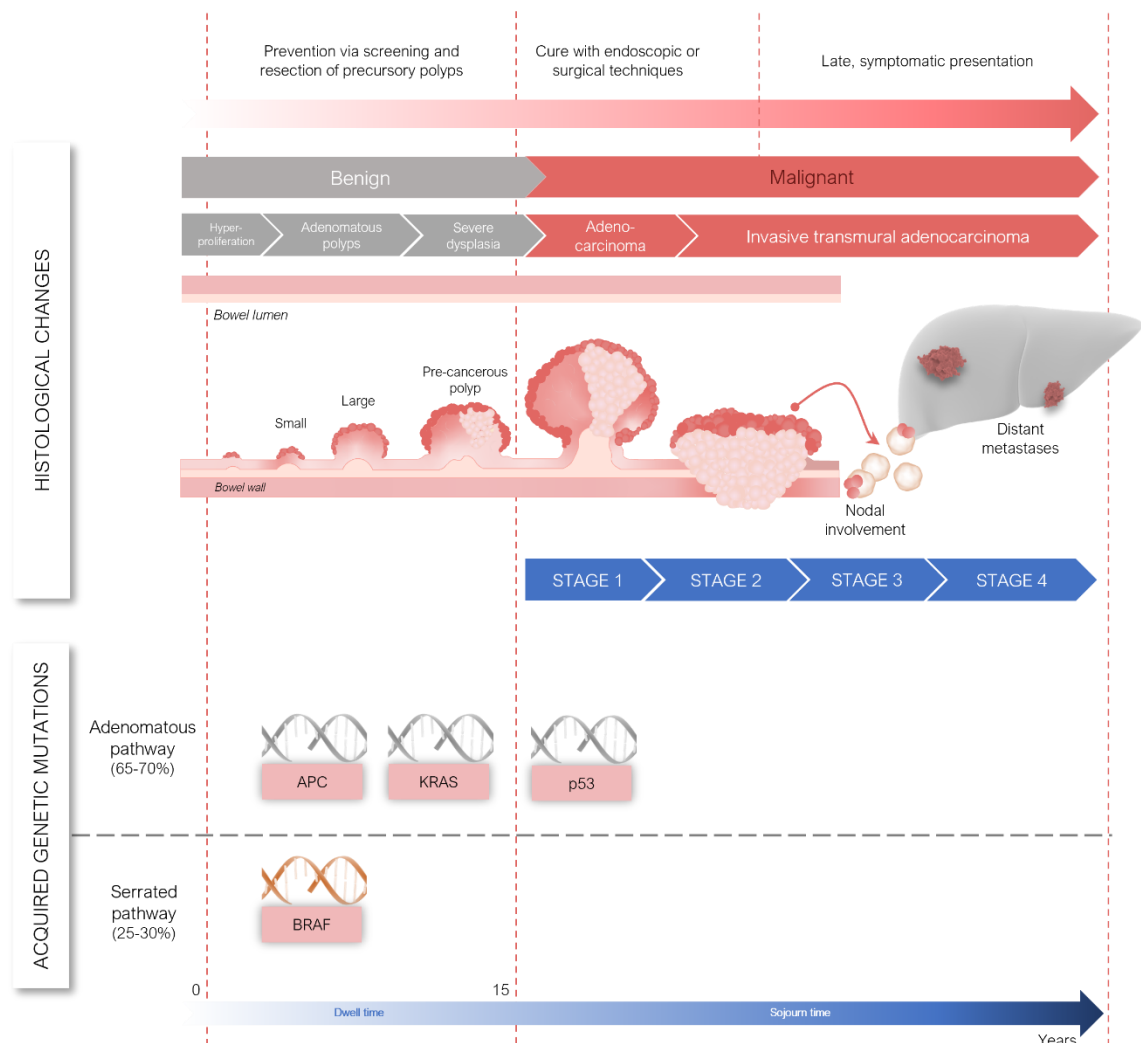
Colorectal carcinogenesis

CRC primarily arises from precursor polyps that undergo malignant transformation.

These polyps are focal areas of abnormal cellular hyperproliferation within the

colonic mucosa, which protrude into the bowel lumen. Over time, the polyps may accumulate sufficient genetic mutations and invade the bowel wall, spreading to locoregional lymph nodes and then on to distant metastatic sites e.g. the liver and lung. There are two main pathways by which these precursor polyps can develop into cancer – the adenoma-carcinoma sequence, and the serrated-neoplasia pathway. The ‘dwell time’, i.e. time taken to develop from adenoma to pre-clinical cancer is in excess of 15 years for both pathways (Figure 1.2).^{6,7}

Figure 1.2: Colorectal carcinogenesis



Two main histologic pathways cause CRC, the majority via the adenomatous pathway. The long ‘dwell time’ provides a timeframe when removal of precursor polyps results in earlier cancer detection and reduced mortality. The ‘sojourn time’ is the time for symptomatic cancer to develop from pre-clinical, asymptomatic cancer. Based on graphics from Simon 2016⁸ and Obaro et al⁹, using elements from www.somersault1824.com

The two main premalignant histological polyp types, adenomas and sessile serrated adenomas (SSAs) have different associated CRC risk. Adenomas are characterised by dysplasia, i.e. a low degree of cellular and structural atypia, and as they grow have increased risk of harbouring malignant cells. Although only ~10% of advanced adenomas will become cancerous, the associated chromosomal abnormalities are observed in 65 to 70% of CRC, and are due to a cascade of mutations in the APC, KRAS and p53 genes.⁸ These polyps often have a stalk of healthy tissue (i.e. are pedunculated), allowing them to be resected by endoscopic snaring. In contrast, SSAs are often flat, carpet-like lesions and are more frequently found in the proximal colon. They begin as mutations in the BRAF gene and account for 25 to 30% of CRC.^{10,11}

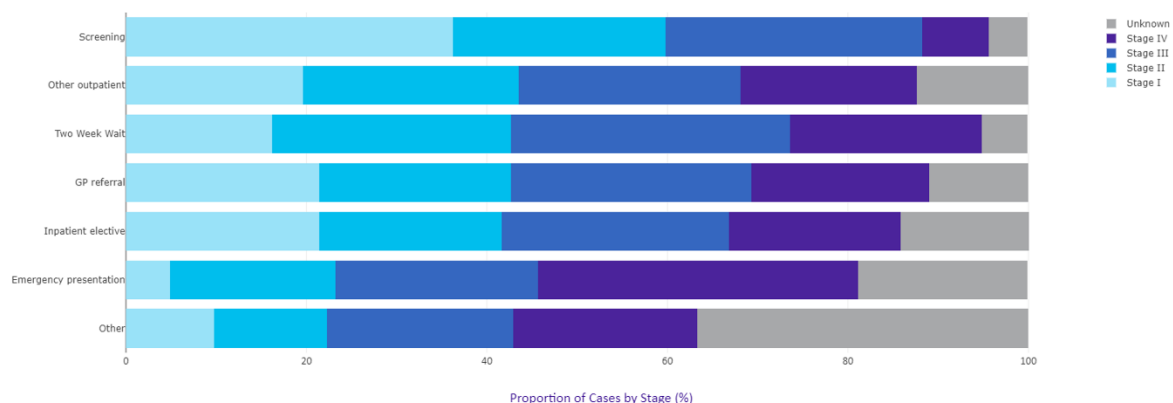
The long time interval between dysplasia of the colonic mucosa and CRC development, creates a window of opportunity in which timely polypectomy can prevent CRC from occurring.¹²

Diagnosis and screening of colorectal cancer

There are several routes to diagnosis for CRC. In the UK, most patients present via the two-week-wait urgent referral pathway for red-flag symptoms such as rectal bleeding and change in bowel habit, (36.4%), followed by emergency presentations (22.1%), GP referrals (18.8%) and screening (9.6%).¹³

The majority of CRC cases identified by screening are early-stage (I or II), while emergency presentations are associated with later stage disease and higher mortality (Figure 1.3).^{13,14}

Figure 1.3: Proportion of CRC cases by presentation route and stage at diagnosis, 2018



From Cancer Research UK¹⁴

A broad definition of screening is the identification of unrecognised disease by the application of tests or examinations which can be rapidly applied.¹⁵ It involves identifying a target population, inviting them to participate in the screening investigation, notifying screenees of results and arranging follow-up investigation/treatment if required or sending reminders for subsequent screening rounds (a ‘call-recall’ programme). All of this requires appropriate governance, reliable infrastructure, and independent systems for evaluation and quality control.¹⁶

The specific term ‘CRC screening’ is generally reserved for population-based programmes (as recommended by the EU Commission)¹⁷ with ‘opportunistic screening’ or ‘asymptomatic assessment’ used for individuals outside organised call-recall programmes, as performed in parts of the United States, Europe and the UK private sector.^{17,18}

As per the principles of early disease detection described by Wilson and Jungner in 1968,¹⁵ colorectal cancer fulfils several key criteria (Table 1.1). The high incidence and burden of CRC, long time interval for carcinogenesis, recognisable and readily

treatable precursor and correlation of mortality with disease stage all support CRC screening.¹⁹

Table 1. 1: Wilson and Jungner principles applied to colorectal cancer

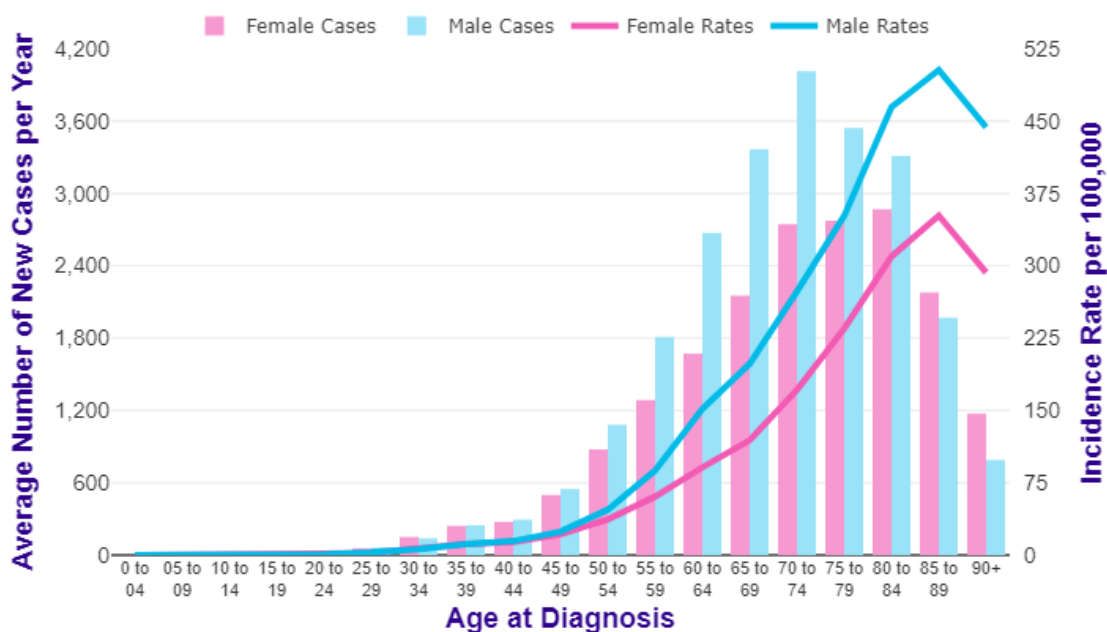
Principle	Colorectal cancer (CRC)
The condition should be an important health problem	CRC has high incidence with poor outcomes at late presentation ²
There is an accepted treatment for patient with recognised disease	Accepted endoscopic, surgical and oncological treatments are available nationally
Facilities available for diagnosis and treatment	Endoscopic and surgical options available for diagnosis/treatment supported by imaging
Recognisable early symptomatic stage and understanding of natural history of the condition	Long dwell time provides timeframe for intervention before progression to malignant lesions and symptomatic presentation ^{6,7}
Agreed policy on who to treat as patients	Typically determined by national guidance and screening programmes ¹⁹
Suitable screening test which is acceptable to target population	Several screening tests available to identify those who may have pre-malignant lesions (see below)
Acceptable cost effectiveness of screening and subsequent diagnosis and treatment	Compared to no screening, all current CRC screening methods (stool tests, flexible sigmoidoscopy, colonoscopy and CTC) are cost effective ^{20,21} (see Chapter 2)

Across Europe, countries with long standing screening programmes (e.g. Austria, Czech Republic, Germany) have observed a substantial decrease in CRC incidence and mortality.²² Conversely, CRC incidence has increased in most countries that lack large-scale screening programmes e.g. Bulgaria, Estonia and Ukraine.²²

Screening options for colorectal cancer

Colorectal cancer incidence is strongly related to age, with a sharp rise in incidence from age 50 onwards, peaking at 85 to 89 years (Figure 1.4).

Figure 1.4: Average number of new CRC cases per year and age-specific incidence rates per 100,000 population in the UK



From Cancer Research UK²³

Consequently, in population-based CRC screening programmes, health authorities systematically target a specific age range of the population, usually between 50 and 74 years. Screening tests may directly visualise polyps or cancers e.g. flexible sigmoidoscopy (FS), colonoscopy or CT colonography (CTC), or are based on the propensity for CRC to bleed resulting in microscopic, but detectable blood products in the stool e.g. non-invasive stool tests: guaiac faecal occult blood test (gFOBT) and faecal immunochemical test (FIT), (Table 1.2).

Stool tests primarily detect early CRC, and have a lower sensitivity (<50%) for large polyps/advanced adenomas as these typically do not bleed.²⁴

Table 1.2: Comparison of colorectal cancer screening tests

Method	Time to perform	Premise	Advantages	Limitations	Sensitivity for CRC	Cost/Tariff ²⁵
Diagnostic colonoscopy	30 mins	Endoscopic visualisation of whole colon	High sensitivity, visualises whole colon, can remove lesions at time of detection	Invasive, requires strong laxatives to prepare bowel, requires sedation, 1 in 1000 perforation risk, high cost	>95% ^{26,27}	£487
Diagnostic flexible sigmoidoscopy	15 mins	Endoscopic visualisation of distal colon	High sensitivity, requires enema only, can remove distal lesions at time of detection	Invasive, only screens distal colon, high cost	>90% ²⁸ (distal colon only)	£340
CTC	20 mins (20-30 mins to report)	Radiological visualisation of whole colon	Only mild laxatives needed to prepare bowel, no sedation required	Minimally invasive, uses ionising radiation (low dose CT scan), 1 in 3500 perforation risk, lesions cannot be removed at time of detection	>95% ²⁶	£306*
FIT	< 10 mins	Immunochemical detection of haemoglobin in the stool	Non-invasive, no bowel prep, accessibility: performed by patient at home, cheap. Higher sensitivity than gFOBT and positivity level can be adjusted. No dietary or medication restrictions. More specific than gFOBT for LGI tract blood	Poor adenoma detection, requires further investigation to confirm abnormality, lesions cannot be removed at time of detection	79% ²⁹	~£5
gFOBT	< 10 mins	Enzymatic detection of haemoglobin in stool	Non-invasive, no bowel prep, accessibility: performed by patient at home, cheap	Poor adenoma detection, requires several stool samples, requires further investigation to confirm abnormality, lesions cannot be removed at time of detection Dietary and medication restrictions for up to 3 days prior to test	33-50% ^{30,31}	~£4

CTC: Computed tomography colonography. FIT: faecal immunochemical test. gFOBT: guaiac faecal occult blood test. LGI tract: lower gastrointestinal tract. CRC: Colorectal cancer. *Including £21 for reporting. Adapted from Simon 2016⁸

gFOBT relies on the oxidation of haem in the faeces and is therefore affected by any dietary peroxidases e.g. in red meat or antioxidant e.g. vitamin C,³² this inherent lack of specificity means the newer FIT is preferred due to greater sensitivity and lack of dietary restrictions.

Internationally, most population-based CRC screening programmes use gFOBT or FIT as they are cheap, readily available, safe and can be delivered via post on a population scale.¹⁹ Moreover, there is level 1 evidence that gFOBT screening reduces CRC mortality; by 16% in one meta-analysis, rising to 25% for those who actually participated in screening.⁴

To date, there are no completed randomised controlled trials (RCTs) for FIT with long-term follow-up using CRC mortality as an endpoint. Baseline results are recently available from a Norwegian RCT comparing the effect of FIT screening and FS on CRC mortality.³³ The study recruited 139,291 individuals aged 50 to 74 years and randomly invited them to either FS or 2-yearly FIT screening.³³ Early results show higher participation and higher detection rates of CRC and advanced adenomas with three rounds of FIT than FS. These initial findings challenge the assumption that because it is both diagnostic and therapeutic, that FS would have a greater effect on CRC mortality than FIT. However, 10-years of follow-up are required before this primary outcome can be fully assessed.³⁴

FIT efficacy has therefore been extrapolated from the strong gFOBT data, and coupled with its increased sensitivity relative to gFOBT,³⁵ is now widely accepted as its replacement as the preferred primary screening test in Europe and the UK.³⁵⁻

³⁷ It is anticipated that FIT will increase the number of cancers detected and

prevented, reduce the number of false positives, and increase uptake (as it is easier to use and requires fewer samples).^{35,37}

FS is also used for population screening, and has been shown to reduce both CRC incidence (by 18%) and mortality (by 26%).³⁸⁻⁴¹ Although colonoscopy is often advocated for CRC screening, like FIT, there are currently no completed long-term RCTs assessing impact on CRC mortality; at the time of writing, the NordICC trial is due to report imminently. To date, Poland is the only country with an organised screening programme using colonoscopy as the primary screening test, with roll-out ongoing.^{42,43} More commonly, as recommended by the European Commission, screening programmes are based on stool tests, gFOBT or FIT, following which positive screenees undergo colonoscopy to confirm neoplasia and resect polyps.⁴³ If colonoscopy is contraindicated then patients undergo alternate colonic assessment with CTC.

Further detailed discussion will focus on colonoscopy and CTC.

Colonoscopy

In colonoscopy, an endoscope (thin, flexible camera) is used to directly visualise the colonic mucosa. Endoscopic evaluation requires strong purgation to cleanse the bowel prior to the procedure and (usually) sedation during the test to minimise patient discomfort. Approximately 700,000 colonoscopies are undertaken each year in England.⁴⁴ Aside from those performed for therapeutic purposes, 60-70% are to diagnose or exclude CRC or pre-cancerous polyps in either screening or symptomatic patients or those undergoing polyp surveillance.^{37,44} If identified, suitable polyps may be resected by polypectomy at the same sitting – therefore

conferring both diagnostic and therapeutic benefit. If unsuitable for resection, polyps or cancers may be biopsied to guide further surgical/oncological management.

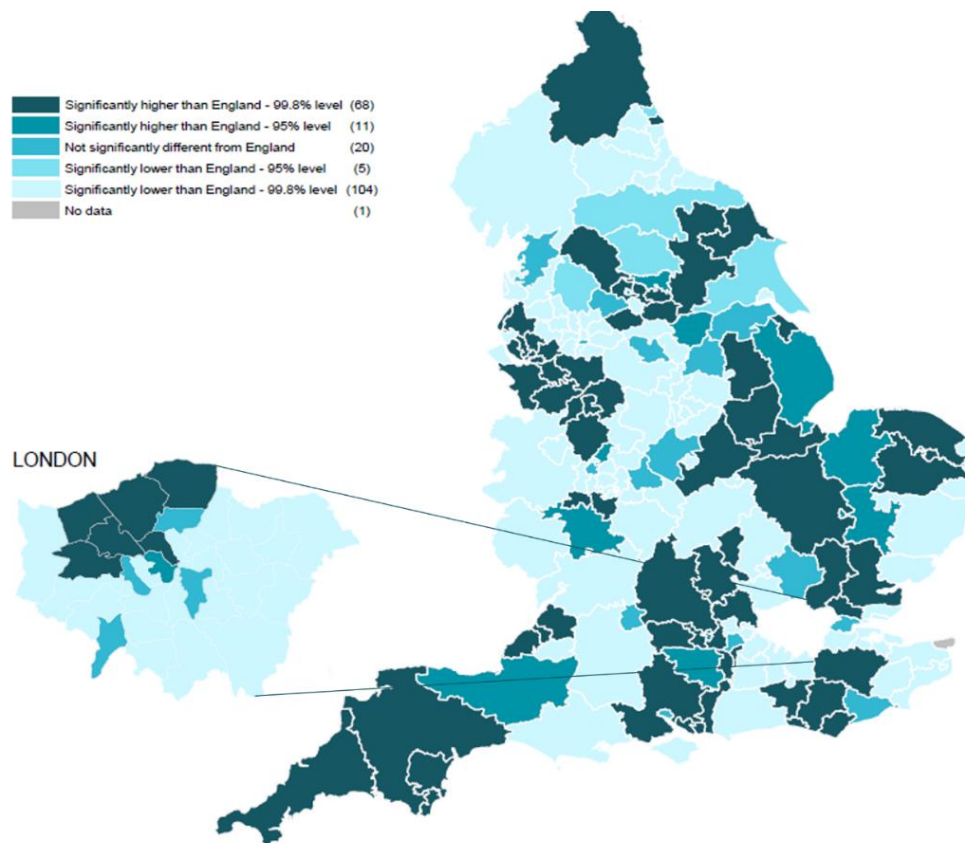
The sensitivity of colonoscopy for detecting CRC is >95% and for advanced adenomas (≥ 10 mm or with high-risk histology), up to 98%.^{26,45} Although reductions in CRC incidence and mortality with colonoscopy have not yet been demonstrated in RCTs (several are underway^{46,47}), case-control studies have shown that patients presenting with CRC are less likely to have had a previous colonoscopy than controls.⁴⁸ In conjunction with data from screening with FS detailed above, there is compelling evidence that undergoing colonoscopy confers protection against CRC.

It is anticipated that the switch from gFOBT to FIT and proposed reduction in screening age from 60 to 50 years, will cause a significant increase in the demand for screening colonoscopies.⁴⁴ Currently, approximately 50,000 are performed each year, which is expected to exceed 100,000 by 2025.^{44,49} The most recent Joint Advisory Group on Gastrointestinal Endoscopy (JAG) census of endoscopy services has already demonstrated a 30% increase in screening colonoscopy activity between 2017 and 2019.⁵⁰ Unfortunately, a recent survey of the screening workforce revealed that a significant proportion (38%) of screening consultants are considering giving up colonoscopy in the next 2 to 5 years, mainly due to retirement and pension issues.⁴⁹ These factors could cause a significant shortfall in colonoscopy availability.

CT colonography

CT colonography (CTC) was first described in 1994 as a diagnostic test for both colorectal cancer and polyps.⁵¹ Its application in diagnostic imaging and screening has disseminated rapidly across the NHS, with now approximately 120,000 performed each year in England.⁵² Unfortunately, despite widespread use, much CTC activity is concentrated in a relatively small number of areas (Figure 1.5).

Figure 1.5: Rate of CTC procedures per weighted population by CCG, adjusted for age, sex and need, 2014/2015



Darker areas perform a higher number of CTCs. From Public Health England, NHS Diagnostic Services³⁷

Magnitude of variation data from the NHS Diagnostic Services reveal that there are between 0.2 and 58.2 CTCs per 10,000 weighted population by Clinical Commissioning Group (CCG); an almost 250-fold difference between CCGs. More than 100 areas are significantly lower than the mean England value of 13.5 per

10,000 weighted population, reflecting geographical inequity in provision. By comparison, the range of colonoscopy and FS procedures per 10,000 population is between 76.5 to 248.8 (a 3-fold difference).³⁷ Possible reasons for the variation in CTC numbers are shown in Table 1.3.

Table 1.3: Reasons for variation in number of CTC procedures in the UK

Differences in:
<ul style="list-style-type: none">• Availability of CT scanners• Availability of radiographers trained in CTC technique• Availability of readers (radiologists/reporting radiographers) skilled in CTC interpretation• Training opportunities in CTC (for radiographers and radiologists) and access to funding• Access to a local CTC service

A successful CTC service requires not only specific resources, but recognition of the complexity of the technique and interpretation. CTC technique involves three main areas: (i) bowel preparation, usually purgation with laxatives; (ii) colonic distension with gas; and (iii) image acquisition in at least two patient positions.⁵³

The use of intravenous contrast during the scan depends on the clinical indication and it is generally administered in symptomatic patients e.g. those with a palpable abdominal mass, significant weight loss or in known colorectal cancer staging.

Patients undergoing bowel cancer screening do not receive intravenous contrast.

There is universal acceptance of the importance of 'faecal tagging' i.e.

administering oral contrast to label or 'tag' any residual stool to distinguish it from polyps when examining the colonic mucosa. While the preferred agent differs

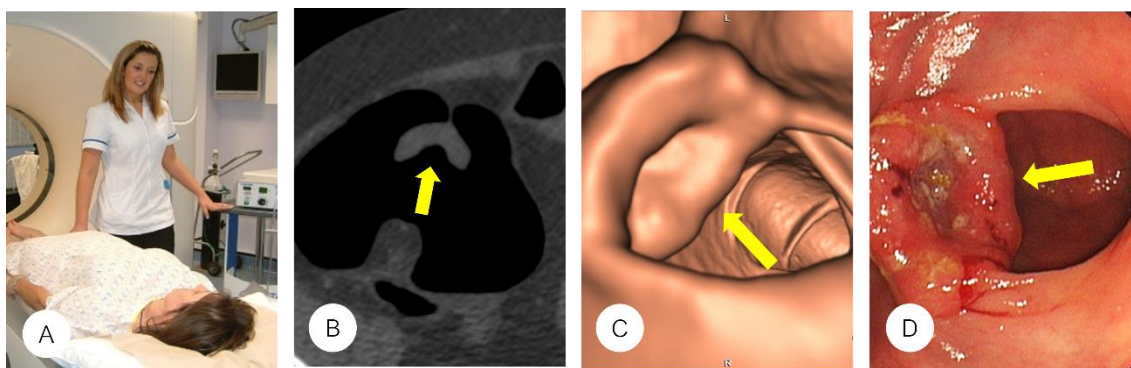
between jurisdictions, in the UK, many centres use Gastrografin (sodium diatrizoate/meglumine diatrizoate, Bayer plc, Newbury, UK). Coincidentally,

Gastrografin has a laxative effect, thereby providing a simple and convenient means to both cleanse the bowel and tag faecal residue.⁵⁴ During the investigation, a thin plastic tube is inserted into the patient's rectum to allow machine-insufflation of gas (usually carbon dioxide), with the aim of sufficiently distending the colon from rectum to caecum. Unless contraindicated, an intravenous antispasmodic, usually hyoscine butylbromide (Buscopan), is administered prior to insufflation to facilitate distension and minimise discomfort.

Scans are performed with the patient in two positions, usually prone and supine, although additional or alternate decubitus positioning may be employed for troubleshooting or dependent on patient mobility. Dual position scanning aims to redistribute any retained fluid or stool to improve visualisation of the colonic mucosa. Despite the requirement for repositioning, CTC is well-tolerated and generally used in older, frail patients unsuitable for endoscopic evaluation.⁵⁵ Complications are rare and the symptomatic perforation risk is far lower than colonoscopy (Table 1.2).⁵⁶

CTC interpretation involves detailed review of the reconstructed 2D and 3D x-ray images to detect cancers, polyps and benign conditions e.g. diverticular disease, as well as any extra-colonic pathology (Figure 1.6).

Figure 1.6: Patient undergoing a CTC (A) and corresponding scan and endoscopy images (B, C, D)



2D axial view of a colonic cancer (B; arrow) opposite the ileocaecal valve. (C) 3D endoluminal view of the colonic cancer (arrow). (D) Corresponding endoscopic view of the tumour (arrow)

Like colonoscopy, CTC has high sensitivity for the diagnosis of CRC²⁶ and large polyps.^{57,58} In a meta-analysis of 49 studies on 11,151 patients, CTC sensitivity for CRC was 96.1% vs 94.7% for colonoscopy (25 studies on 9223 patients).²⁶ The landmark SIGGAR multicentre randomised trial found no significant difference between CTC and colonoscopy for the diagnosis of cancers and large polyps (≥ 10 mm).⁵⁹ Therefore, CTC is probably as accurate as colonoscopy in the diagnosis of CRC, confirming its utility in bowel cancer imaging. The diagnostic accuracy of CTC is further discussed in Chapter 2.

NHS Bowel Cancer Screening Programme

Introduced in 2006, the NHS Bowel Cancer Screening Programme (BCSP) aims to reduce mortality from bowel cancer by delivering evidence-based population screening. Its objects are summarised in Table 1.4:

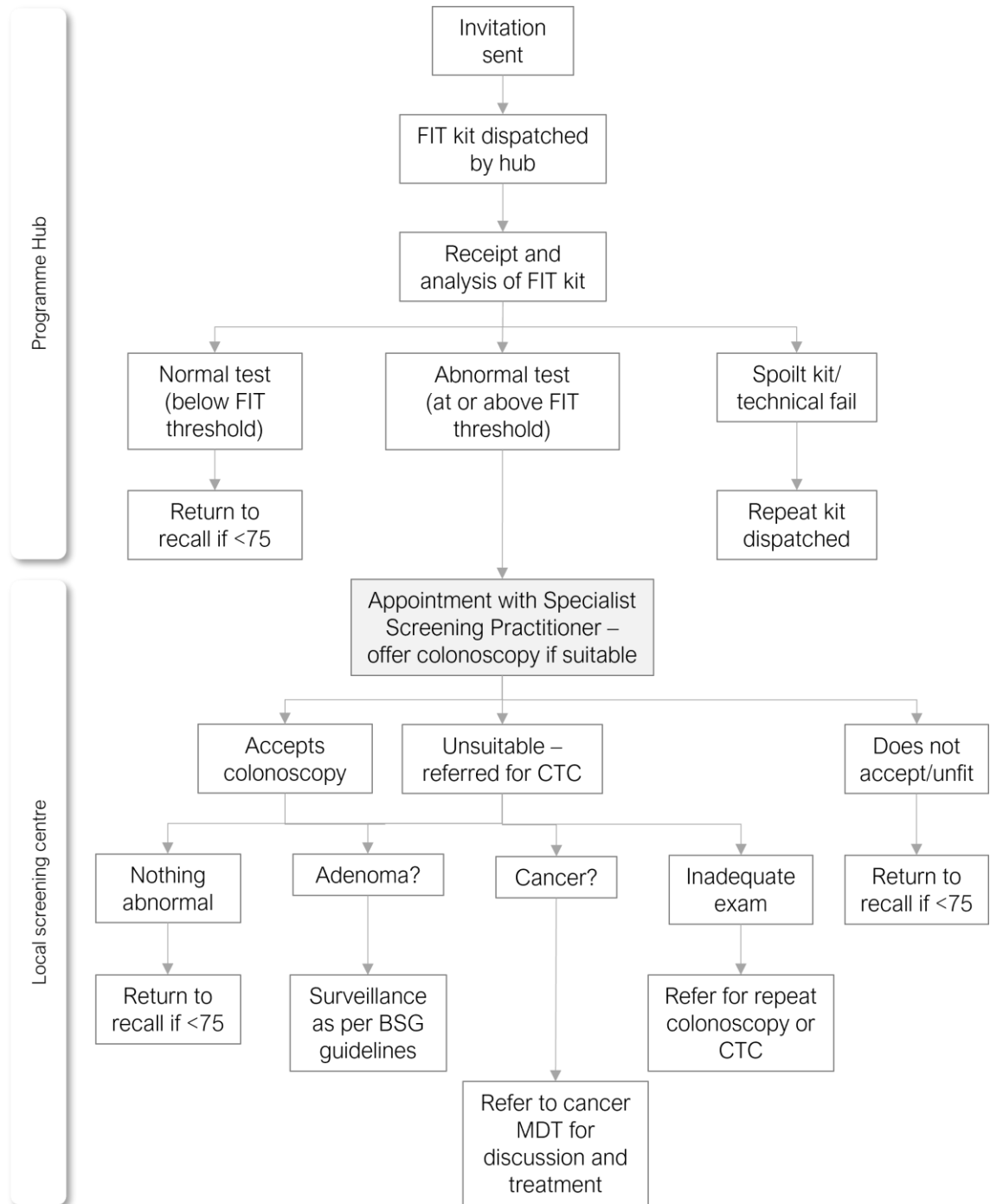
Table 1.4: Objectives of the NHS Bowel Cancer Screening Programme

- To identify and invite adults aged 60 to 74 for screening at 2-year intervals (those 75 years and above can opt into the programme)
- To provide the target population with appropriate information to make an informed choice about participation
- To prevent cancer, lead to early detection, appropriate referral, and improved outcomes
- To deliver an audited service supported by trained, competent and qualified staff
- To ensure that GPs are informed of the screening outcomes of their patients

From NHS Public Health Functions Agreement 2019-2020⁶⁰

The programme is based on a hub and spoke model – with five regional hubs providing the ‘call and recall’ service for England; these are currently London, Southern England, Eastern England, Midlands and North West England, and North East England. Each hub supports up to 18 screening centres and is responsible for testing the returned screening kits. Following a positive gFOBT/FIT result, diagnostic tests are performed at one of 65 screening centres (Figure 1.7).

Figure 1.7: Bowel cancer screening pathway



BSG: British Society of Gastroenterology. MDT: Multidisciplinary Team. CTC: CT colonography

Currently, people aged 60 to 74 years are invited for FIT testing at two-yearly intervals, although the programme aims to gradually reduce the starting age to 50 (so-called 'age extension'). The current threshold for FIT positivity is 120 µg Hb/g faeces and approximately 2% of patients screened will have a positive test. Of

those that go on to screening colonoscopy, approximately 10% will have a cancer and 30% will have adenomas.⁴⁴

Since rollout of the BCSP, over 30 million people have been invited (or re-invited) to participate in screening; however, uptake stands at only 58%, and in some parts of the country is as low as 33%.⁶¹ This may explain why incidence of CRC in the UK has not declined at the same rate as observed in other European countries with established programmes.²² For example, in Austria where 68.8% of the eligible population has undergone FIT within the last two years (or colonoscopy within the last 10 years), there has been an average annual percentage change in CRC incidence of -3.5% for women and -3.2% for men (versus only -1.3% for women and -1.8% for men in England over a similar timeframe).²²

Ethnicity and social deprivation are major determinants of uptake and an area-level uptake analysis of 4.4 million first-time invitees found that there had been a decline in CRC screening uptake between 2011 and 2014 and that participation had a strong socioeconomic gradient.⁶² It is hoped that the use of FIT as opposed to gFOBT will improve uptake, particularly in these hard to reach groups.³⁵

CTC is used in the BCSP as an alternative in patients who cannot tolerate colonoscopy, and with appropriate resourcing and development could offset the colonoscopy shortage. However, despite promising sensitivity in the research literature, the reality of CTC use in the routine clinical setting can be quite different. In fact, when applied in clinical practice across the BCSP, CTC was found to have a 50% lower detection rate for CRC and high-risk polyps than colonoscopy, although whether this was due to genuine poorer sensitivity or selection bias is not

certain.⁶³ In the same study,⁶³ significant variation in detection rate was observed between centres, suggesting that radiologist performance may have contributed to these findings.

Conclusion

Colorectal cancer (CRC) is a significant public health burden, the outcomes of which can be improved by early diagnosis through screening. Population screening is proven to reduce mortality and morbidity with countries deploying various tests in dedicated programmes. Such tests include non-invasive stool-based tests (FOBT, FIT), flexible sigmoidoscopy, CTC and colonoscopy. Typically, stool-based tests are used for population screening, with positive screenees, undergoing subsequent whole-colon investigation with colonoscopy or CTC.

Colonoscopy and CTC have comparable detection rates for advanced neoplasia and are both deployed in the English Bowel Cancer Screening Programme. In this context, CTC is specifically advocated when colonoscopy is contraindicated. The following chapter will review specific aspects of CTC in CRC screening.

Chapter 2 Colorectal cancer screening with CT colonography

Summary and contribution statement

This Chapter discusses the role of CT colonography (CTC) in colorectal cancer screening and three large-scale European trials that have contributed valuable data supporting its use. I provide an overview of the important aspects of screening with CTC, including test acceptability and uptake.

I undertook all the work presented and drafted this chapter which was later modified with the thesis supervisor and Dr David Burling (St Mark's Hospital, Harrow). A version of this chapter has been published as follows:

The role of imaging in screening special feature: Review Article. Colon cancer screening with CT colonography: logistics, cost-effectiveness, efficiency and progress. Obaro AE, Burling DN, Plumb AA (2018). The British Journal of Radiology. DOI: 10.1259/bjr.20180307

Introduction

As discussed in Chapter 1, colorectal cancer (CRC) incidence and mortality can be significantly reduced by population screening. In comparison to other CRC screening techniques, computed tomography colonography (CTC) offers a safe and accurate option that is particularly useful when colonoscopy is contraindicated.

Although CTC is less invasive than colonoscopy and enables review of the appendix and extra-colonic organs in addition to the colonic mucosa, its use for CRC population screening in Europe has, until recently, been hampered by several factors. Lack of long-term randomised control trial (RCT) evidence demonstrating an impact of CTC screening on CRC mortality (or incidence) is perhaps the most important. While similar evidence is also absent from the colonoscopy literature, use of colonoscopy as a screening investigation is extrapolated from robust evidence demonstrating the positive outcome of screening with flexible sigmoidoscopy (FS), with several dedicated colonoscopy RCTs underway.³⁸⁻

40,46,47,64

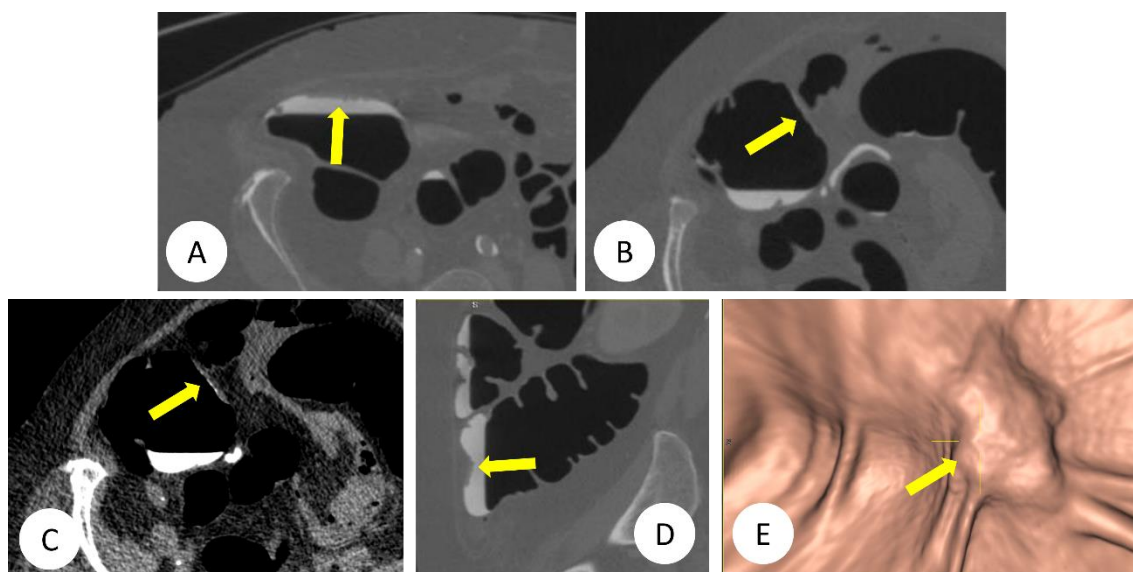
Diagnostic accuracy

There is considerable evidence that CTC is as accurate as colonoscopy for detection of established CRC, including two separate meta-analyses which report sensitivities of 96%.^{26,65} CTC also has excellent sensitivity for large (≥ 10 mm) polyps (93%), confirmed by meta-analyses of screening cohort and RCT studies⁶⁶ and a multicentre pragmatic randomised trial of symptomatic patients.⁶⁷ These results

are achievable in a multicentre setting – for example, in the American College of Radiology Imaging Network (ACRIN) 6664 study of average-risk screenees, diagnostic sensitivity for adenomas measuring ≥ 10 mm was 90%.⁵⁸ Although diagnostic sensitivity is lower for smaller lesions (estimated at 76% for 6-9 mm adenomas in one meta-analysis of studies recruiting asymptomatic screenees),⁶⁶ this must be balanced against their low biological risk.

Specific consideration must also be given to sessile serrated adenomas (SSAs), which account for approximately 15 to 30% of CRC, disproportionately contribute to missed CRCs, and are located more frequently in the right colon.^{7,10} In a Dutch randomised trial, CTC had significantly lower sensitivity than colonoscopy for flat high-risk dysplastic SSAs.⁶⁸ Previous research has also shown right-sided flat colonic polyps are more difficult to detect by both colonoscopy and CTC.^{69,70} However, these studies are largely derived from an era in which techniques to identify SSAs at CTC were largely unknown; more recent data suggests that optimised CTC permits their detection.^{71,72} For example, the recognition that surface coating by oral contrast tagging material increases conspicuity of flat lesions, coupled with greater attention to colonic distension should increase detection (Figure 2.1).^{71,72}

Figure 2.1: Prone (A), supine (B) axial and sagittal (D) 2D images on bone window demonstrating a sessile serrated adenoma.



On the prone images (A) the lesion is submerged under tagged fluid making detection more difficult. Compare with the 2D supine bone (B) and soft tissue window (C) images which show a small degree of oral contrast coating on the surface of the lesion. This characteristic can be used to aid detection of flat polyps. The lesion is more conspicuous on the sagittal reformat (D). Corresponding 3D endoluminal view (E).

Fortunately for radiologists and patients, SSAs are typically indolent, with a mean dwell time of at least 15 years before development of dysplasia which may then progress to carcinoma.⁷ Furthermore, improved radiologist training with superior recognition of subtle, proximally located polyps will likely improve their detection.^{73,74}

Test participation and diagnostic yield

Participation in both population-based and opportunistic CRC screening programmes in Europe, falls well below the 65% recommended by the European Commission.¹⁷ In England, uptake remains stable at only 58% in the target population,⁷⁵ which is similar to participation observed in the United States, estimated at 59%.⁷⁶

Successful population screening requires good uptake (attendance and completion rates), since this affects the population-level diagnostic yield, and therefore the overall effectiveness of the programme. A test with 100% sensitivity that is declined by most patients will be substantially outperformed by a 50% sensitive test with universal uptake.

In randomised clinical trials involving CTC, highest uptake is for FIT (50 to 65%), followed by CTC (25 to 34%), FS (27%) and then colonoscopy (15 to 22%).⁷⁷⁻⁸⁰

The higher participation observed in FIT screening is not unexpected, since this test can be performed at home by the screenee, is quick and non-invasive versus CTC which although, minimally invasive, requires bowel preparation and hospital attendance. Despite differences in participation rate, it is important to note that information garnered from screening with CTC is far more specific than that obtained from FIT. As a result, this leads to a higher colonoscopy referral rate and lower specificity in FIT screening.⁸⁰

In general, screening with CTC is perceived as less onerous than colonoscopy, contributing to increased uptake.⁷⁹ For example, in a multi-centre patient survey of 1417 individuals, 68% chose CTC screening due to the less invasive nature of the investigation and 47% because it avoided colonoscopy risks.⁸¹ There is relatively little data regarding intentions to attend repeated screening rounds after initial CTC, but one Dutch study found 93% of patients stated they were likely to re-attend at their next screening round after initial CTC.⁸²

Reasons for lack of participation in screening by CTC include perceptions and beliefs relating to both CRC screening in general and CTC in particular. For example, in one trial, CTC non-attenders cited lack of symptoms and unpleasantness of the procedure as the underlying reasons.⁸³ Laxative bowel preparation is frequently identified as the most unpleasant factor^{82,84} and reducing discomfort from bowel preparation increases test acceptability.⁸⁴ In support, reduced laxative CTC (stool softener plus tagging agent) significantly increased uptake compared to standard laxative CTC (plus tagging)⁷⁸ in one randomised trial (28.1% vs 25.2%, $p=0.047$), with no reduction in neoplasia detection.⁷⁸

Diagnostic yield

The diagnostic yield of a screening test is essentially a function of its sensitivity and its uptake. Three recent RCTs provide diagnostic yield data of CTC when used for prevalent (first) round population screening, compared to either FIT (up to three rounds) or colonoscopy (SAVE trial, Italy),^{78,80} FS (PROTEUS trial(s), Italy),⁷⁷ or colonoscopy (COCOS trial, the Netherlands)⁷⁹ (Table 2.1).

Table 2.1: Results of three recent European multi-centre trials evaluating CT colonography screening

Study acronym (first author and year)	Number of invitees	Population Age range (years)	Participation rate (%)		Diagnostic yield; advanced neoplasms per 100 participants		Diagnostic yield; advanced neoplasms per 100 invitees	
			CTC	Comparator(s)	CTC	Comparator	CTC	Comparator
COCOS (Stoop et al 2012) ⁷⁹	8,844	Never screened 50-75	34	OC - 22	6.1 ^a	OC - 8.7	2.1	OC - 1.9
(Tutein et al 2016) ⁸⁵	82 ^b				8.6 ^b		2.9 ^b	
SAVE, early results (Sali et al 2016) ⁷⁸	16,087	Never screened 54-65	28 ^c 25 ^d	FIT - 50 ^d OC - 15	5.5 ^c 4.9 ^d	FIT - 1.7 ^e OC - 7.2	1.5 ^c 1.2 ^d	FIT - 0.9 ^e OC - 1.1
SAVE, final results (Sali et al 2022) ⁸⁰	14,981	Never screened 54-65	26	FIT - 65, ^f 49, ^g 33 ^h	5.2	FIT - 3.2 ⁱ	1.4	FIT - 2.0 ⁱ
PROTEUS1 & 2 (Regge et al 2017) ⁷⁷	42,929	Never screened 58-60	30 ^j	FS - 27 ^j	5.1 ^k	FS - 4.7 ^k	-	-

CTC: Computed Tomographic Colonography. OC: Optical Colonoscopy

^aUsing a threshold of 10 mm or greater to precipitate referral for colonoscopy. Patients with 6-9 mm polyps were initially enrolled in CTC follow-up

^bAfter inclusion of the follow-up cohort of patients with 6-9 mm polyps detected at initial CTC

^cReduced preparation CTC group. ^dFull-preparation CTC group

^eFor one round of FIT only

Participated in at least: ^fOne screening round, ^gTwo screening rounds, ^hThree screening rounds

ⁱFor three rounds of FIT

^jData from PROTEUS1. ^kData from PROTEUS2

Taken together, the diagnostic yield for advanced neoplasia ranged from 5 to 6 neoplasms per 100 participants, with CTC superior to flexible sigmoidoscopy (diagnostic yield, 4.7%) and one round of FIT (1.7%; Table 2.1). These results are encouraging since advanced neoplasia is the primary target of CRC screening and there is now RCT evidence to support the inclusion of CTC as a test option.

While CTC significantly outperformed a single round of FIT screening in the early results from the SAVE trial,⁷⁸ FIT is designed to be repeated every one or two years, thereby increasing advanced adenoma yield over time. The final SAVE trial results demonstrate that three biennial rounds of FIT testing improved the cumulative detection rate of advanced neoplasia.⁸⁰ The lower detection rate of FIT observed initially, was offset by increased screenee participation; again highlighting the importance in test uptake for population screening.

When comparing to FS in the PROTEUS study, the detection rate of advanced neoplasia in the distal colon was lower for CTC than FS (2.9 vs 3.9%).⁷⁷ One possible explanation is that this study employed a computer-assisted detection (CAD) program as the primary reader for the CTC scans. Increased reliance on CAD may have compromised detection of distal adenomas. However, detection of proximal advanced neoplasia by CTC (versus FS) is a significant benefit; in the PROTEUS study, approximately 80% of individuals with proximal advanced neoplasia had no distal lesion, and so would have been missed with FS screening.⁷⁷

Data comparing CTC to colonoscopy are more nuanced. When evaluating on a per-attendee basis (i.e. patients attending their randomised procedure), the two most relevant trials showed neoplasia detection rates were lower for CTC than colonoscopy (6.1 vs 8.7% in the COCOS trial and 5.2 vs 7.2% in the SAVE trial).^{78,79} However, consideration must again be given to participation, which was higher for those randomised to CTC, offsetting the lower detection rate. This results in slightly superior per-invitee detection rates for CTC, albeit not statistically significant (2.1% for CTC vs 1.9% for colonoscopy in the COCOS trial, and 1.4% for CTC vs 1.1% for colonoscopy in the SAVE trial).^{78,79}

In the COCOS study (radiologist as first-reader and secondary read with CAD) patients with polyps measuring 6-9 mm detected by CTC were not referred for polypectomy but instead enrolled in a CTC follow-up programme.^{79,85} When polyps were subsequently resected from these individuals, the advanced neoplasia detection rate of CTC mirrored that of colonoscopy per-attendee (8.6% vs 8.7%), and was superior per-invitee (2.9% vs 1.9%).⁸⁵ This radiologist reader approach is how a CTC-based screening programme is likely be deployed in clinical practice. These data replicate existing non-randomised cohorts, in which advanced neoplasia detection rates were equivalent between CTC and colonoscopy.⁸⁶

Overall, the current data strongly suggests CTC is a viable alternative screening strategy to colonoscopy, with potentially superior uptake and similar sensitivity for advanced neoplasia. These data support the role of CTC in screening to investigate patients who have a positive FIT test, but in whom colonoscopy is contraindicated or incomplete. While CTC can be advocated for opportunistic

screening, its use as a first line population screening test (as opposed to FIT) requires further investigation.

Referral thresholds & diminutive polyps

It is currently unclear what number or diameter of polyps found at CTC should trigger referral to colonoscopy for consideration of biopsy or excision. Many radiologists recommend referral of all polyps with maximal diameter 10 mm or greater to colonoscopy, with CTC follow-up or colonoscopy for polyps 6-9 mm, and return to FIT screening for patients with diminutive polyps (≤ 5 mm).⁸⁷ In contrast, endoscopists typically perform routine polypectomy, removing all polyps they identify. However, diminutive polyps have very low risk of high grade dysplasia or malignancy, each less than 0.5%,⁸⁸ supporting Japanese national guidance which permits endoscopists to ignore diminutive polyps unless their morphology is suspicious.⁸⁹ Consequently, referral for colonoscopy without any size threshold appears counterintuitive, since it necessitates considerable use of resources for no gain.^{90,91} A decision analysis model suggested that the 10-year CRC risk for unresected diminutive polyps was 0.08%, equating to over 2000 polypectomies to prevent a single CRC, which in any case would be prevented by detection of a progressing polyp at scheduled 5 year repeat screening CTC.⁹⁰

Small polyps (6-9 mm maximal diameter) can be reassessed by interval CTC (in three years) or referred to colonoscopy for consideration of polypectomy.⁹²⁻⁹⁴

Performing polypectomy for small polyps detected on CTC is dependent on patient comorbidities, the number of polyps present and their morphology.

CTC follow-up for 6-9 mm diameter polyps appears safe; two studies^{95,96} showed no patients (of 259 enrolled) developed invasive cancer during 24-36 months of follow-up. Indeed, small polyps can regress over time; in one series 50% of polyps were unchanged, 28% regressed (decrease in diameter) and only 22% increased in size over a three period.⁹⁵ However, such follow-up requires excellent recall systems; in one series,⁹⁵ a patient with an enlarging polyp was lost to follow-up, and re-presented over 5 years later with established cancer. This management error highlights an important parameter of CTC quality – the rate of missed cancers after an apparently normal CTC scan. This rate is unknown for CTC, although well established for colonoscopy, and is the focus of the subsequent systematic review presented in Chapter 4. This evidence is required to support and affirm current CTC management strategies of not reporting diminutive polyps and the option of CTC follow-up for small polyps.

Safety and radiation dose

CTC is minimally invasive and extremely safe, with no reported deaths and very few severe complications since its inception.⁹⁷ Luminal perforation is very uncommon at CTC (approximately 1 in 3,500 patients overall, and under 1 in 5,000 at screening)⁵⁶ and most perforations are asymptomatic, as CT is exquisitely accurate for detection of extra-luminal gas.⁹⁸ Furthermore, most patients with CTC-associated perforation require no surgical intervention (fewer than 1 in 12,500 require it overall).⁵⁶ It is impossible to know the true number of perforations after colonoscopy, as patients do not undergo routine post-test imaging, even when there is abdominal discomfort. Therefore, known colonoscopy-associated

perforation rates of approximately 1 in 1000 procedures significantly underestimates the total, but is still 20 times more frequent than the 'symptomatic perforation rate' for CTC.⁹⁹ CTC is also associated with fewer serious complications than colonoscopy such as cardiovascular events.^{100,101}

The other commonly-cited concern regarding CTC screening is radiation dose. Many radiation scientists acknowledge there is no conclusive evidence that radiation from medical imaging causes harm to adults.¹⁰² However, given the lack of certainty, radiologists adhere to the principle of minimising radiation dose as much as possible under the linear no threshold (LNT) model of dose-response used to determine risk. This assumes potential harm from all radiation, with a linear relationship between magnitude of dose and risk of inducing cancer (starting at zero for both).¹⁰³ However, these theoretical harms must be balanced against the known benefits of cancer prevention. Under LNT assumptions, one risk projection model estimated that for every radiation-induced cancer, 24 to 35 CRCs are prevented by 5 yearly CTC-screening between the ages of 50 and 80 years.¹⁰⁴ This estimate was based on mean effective doses of 8mSv for women and 7mSv for men, higher than current estimates of 4mSv,¹⁰⁵ implying the benefit-risk ratio is even more favourable. Even assuming a slightly higher CTC dose of 5mSv, the theoretical risk of cancer induction at a screening age of 50 year is 0.04%, reducing to 0.02% by age 70, which is negligible compared to a lifetime risk of developing cancer of 39%.^{106,107}

It is likely that these unproven risks may be even lower, particularly since many centres now use low dose scanning protocols and iterative reconstruction techniques to minimise the effective dose of CTC.^{108,109}

Extra-colonic findings

People who choose CTC for opportunistic screening anecdotally describe extra-colonic organ review as an important factor influencing this choice over competing tests. Indeed, many will recall a close relative or friend who suffered with cancer of an extra-colonic organ and so they seek reassurance from a normal CTC. One study of patient preference supports this anecdote and found 43% of people would prefer CTC to colonoscopy for screening because of its ability to detect abnormalities outside the colon.⁸¹ Importantly, in a primary screening setting (i.e. without a FIT-based triage step), CTC detects extracolonic cancer as frequently as it finds CRC.¹¹⁰ The majority of these extracolonic cancers (54%) were detected at an early stage, implying better prognosis for many.¹¹⁰ CTC also detects important non-malignant conditions such as aortic aneurysm and osteoporosis.

Advances in artificial intelligence (AI) have led to the consideration of opportunistic CT screening, i.e. using the existing imaging data to assess body composition, cardiovascular risk and metabolic profile.¹¹¹ For example, new AI algorithms can automatically measure bone mineral density for osteoporosis screening, quantify aortic calcium for assessment of cardiovascular risk and quantify liver fat for assessment of steatosis.¹¹² The application of such opportunistic screening could add even greater value to CRC screening with CTC.

The potential negative impact from additional tests and related patient anxiety following detection of extra-colonic findings should be balanced against the reassurance patients feel after a normal CTC with no significant abnormality; indeed, most patients would trade many false-positive extra-colonic diagnoses at

CTC for the benefit of finding a single cancer.¹¹³ It is very important that patients are given the opportunity to be counselled about the accuracy, limitations and potential risks of CTC for visualising extra-colonic organs. It is also important that radiologists reporting screening CTC are experienced in detection and management of extra-colonic abnormalities with appropriate pathways in place to manage the follow-up of such.

Overall, the possibility of extracolonic assessment is a unique benefit of CTC in CRC screening and when taken together with the high detection rate, increases the overall diagnostic yield of the examination.

Cost effectiveness

Cost-effectiveness analyses of CTC as a screening test typically use models incorporating assumptions about the natural history of polyps, CTC sensitivity, test uptake, frequency of screening rounds, and use of follow-up colonoscopy (and CTC, where appropriate). These models attempt to estimate the impact on CRC-related mortality using these assumptions, and balance the benefits against the economic costs of the (theoretical) programme. While results have been variable,¹¹⁴ CTC screening is typically more cost-effective than no screening.¹¹⁵⁻¹¹⁷

In comparison to other screening tests, CTC appears less cost-effective than FIT,¹¹⁸ but comparable to gFOBT and FS in an earlier systematic review.¹¹⁴ When compared to colonoscopy, results are variable.¹¹⁴ The reason for such heterogeneous results is multifactorial, but largely related to the sensitivity of economic models to their original inputs and assumptions. For example, applying a

larger polyp diameter threshold for colonoscopy after CTC improves cost-effectiveness, whereas a threshold of ≥ 6 mm is often used for modelling. Moreover, few studies have incorporated a strategy of CTC follow-up for 6-9 mm polyps (versus referral for polypectomy). Complicating matters further is the highly variable unit cost of each test internationally, and different uptake rates for tests by both gender and geographical region; for example, Italian men were more likely to accept CTC than FS, whereas there was no difference for Italian women.⁷⁷ When comparing to colonoscopy, a recent analysis of unit costs and participation rates in the COCOS trial found that CTC was the most cost-effective strategy in participants who underwent more than two lifetime screens.^{117,119}

Fundamentally, all such modelling depends on assumptions regarding the natural history of colorectal polyps (i.e. how many will transition to cancer, and at what rate). Since our knowledge of this biology continues to evolve, existing cost-effectiveness models may be incorrect. For example, most studies ignore the serrated pathway entirely, assuming all cancers arise from adenomas; and predate current knowledge that a significant proportion of adenomas regress over time.⁹⁵ Moreover, we are now aware that both adenomas and serrated polyps have longer pre-malignant phases than previously assumed,^{7,120} meaning existing models may over-estimate the significance of both missed and unresected lesions.

Finally, extracolonic findings are rarely incorporated, despite these having the potential to both increase costs (via additional testing) or reduce them (via prevention of cancer or aneurysm-related morbidity and healthcare costs). The full impact of these findings on cost-effectiveness (up to 11% of which require further work up), remains to be determined.¹¹⁷

Quality assurance

CTC quality assurance (QA) is critical to achieving high standards of examination quality and reporting accuracy. Radiologists reporting CTC in screening settings must be highly experienced and competent to detect and characterise subtle advanced colonic neoplasia and avoid unnecessary referral of healthy asymptomatic people for additional investigation which will in turn increase anxiety, potential for harm and financial cost for no benefit. To help achieve this, screening CTC radiologists must follow their screening colonoscopy colleagues; for example, regularly reporting both symptomatic and screening CTC; demonstrate a subspecialty interest in colorectal cancer imaging; attend multi-disciplinary colorectal cancer and/or polyp meetings; and audit their practice including management recommendations.¹²¹

However, quality of screening CTC has not been subject to the same degree of scrutiny as colonoscopy and pathology. A national survey of CTC in the English Bowel Cancer Screening Programme (BCSP), found 10% of radiographers performing CTC examinations had received no formal training and one-third of radiologists interpreting the images were inexperienced.¹²² Furthermore, in the BCSP, CTC was found to have a 50% lower detection rate for CRC and high-risk polyps compared to colonoscopy.⁶³ There is no mandatory training or accreditation programme for CTC, either in the UK or internationally, and no universally-agreed performance metrics.¹²³ This lack of evidence-based performance indicators hampers the development of the robust QA required for implementation of CTC screening programmes (Table 2.2).

Table 2.2: Logistical factors that would be necessary to implement CTC population screening

Test Characteristics	Patient Management Considerations
Access and availability <ul style="list-style-type: none"> Local and national CTC screening infrastructures Appropriate local colonoscopy services 	Information systems to (a) send out invitations for initial screening with integrated reminders to ensure participation and (b) recall individuals for repeat screening
High diagnostic accuracy and sensitivity	Consensus population age for CTC-screening
Acceptability <ul style="list-style-type: none"> Perceived – optimised to boost initial uptake Absolute– to ensure re-attendance at subsequent screening rounds 	Management and treatment pathways for colonic findings <ul style="list-style-type: none"> Consensus polyp size referral threshold Follow-up pathway for unresected polyps
Consensus quality assurance and training for reporting radiologists, including evidence-based KPIs	Integration with other screening programmes <ul style="list-style-type: none"> E.g. abdominal aortic aneurysm screening / follow-up; thoracic CT for lung cancer
Safety monitoring system to identify and manage adverse events	Management pathways for extracolonic findings
Cost-effective in comparison to alternative screening modalities	

CTC: Computed Tomographic Colonography. KPI: Key Performance Indicators. Adapted from Obaro et al 2016⁹

The use of standardised reporting templates (e.g. CT Colonography Reporting and Data System (C-RADS)), improved recording of CTC data for audit, and follow up of objective endpoints such as post-imaging CRC rates are imperative to the successful implementation of screening CTC. This process will help identify which metrics best permit monitoring and improvement of services and practitioners. The National Co-ordinating Group for Radiology in the BCSP have since updated guidelines for practice and standards for reporting CTC findings.¹²⁴ Radiologists have accompanied BCSP peer review visits, but the evidence base and impact of these initiatives has not been formally evaluated.

Conclusion

Most cases of CRC could be prevented by screening. CTC is accurate for detection of important polyps in both opportunistic and population screening

settings, with advantages in patient safety and experience, while being cost effective.

In their 2020 update, the European Society of Gastrointestinal Endoscopy (ESGE) and European Society of Gastrointestinal and Abdominal Radiology (ESGAR) now recommend that CTC is suitable for CRC screening if there is no FIT-based programme, and recommend it in patients that are FIT positive and unsuitable for colonoscopy in population-screening programmes.¹¹⁷

Further research on the natural history and pathogenesis of CRC will help inform decisions regarding appropriate polyp size thresholds for referral to colonoscopy and length of CTC-screening intervals. Renewed focus on training and accreditation will help assure the quality of CTC screening and reduce variability in practice.

Chapter 3 Performance monitoring, accreditation and training

Summary and contribution statement

The burden of colorectal cancer and importance of early detection are well established. I now discuss the importance of performance monitoring and training in cancer detection, including two case studies focussing on performance and accreditation in colonoscopy for bowel cancer and mammography for breast cancer.

I undertook all the work in this Chapter.

Introduction

Central to the success of any cancer screening programme is the accuracy of the diagnostic investigations involved. Robust quality assurance (QA) of these investigations is essential to achieving high detection rates. The QA processes involved vary between cancer types and their specific screening investigations. Given the benefits of early cancer detection, it is intuitive that the performance of clinicians involved in such programmes is carefully monitored to ensure high standards of competency are achieved and maintained.

Performance monitoring, however, is not a simple process. In the context of screening, one could reasonably assess the performance of individual clinicians as well as the whole service, both of which may have different metrics. Furthermore, key performance indicators (KPIs) which have clinical relevance need to be established, along with appropriate benchmarks for such indicators. Clear performance indicators provide a measure of quality, however, measuring quality alone does not improve performance. For example, monitoring someone's error rate in clinical practice does not in itself prevent them from making said errors. In fact, error rate measurement is an unreliable way to specify what needs to be improved, how to improve it and whether improvement has occurred.¹²⁵ Therefore even if individual KPIs are tracked, performance monitoring and QA should take a holistic view, recognising the system in which the individual operates.

This then leads to the consideration of the role of accreditation and training. Accreditation is typically a rigorous external evaluation that recognises an institution, programme or individual has met a given set of evidence-based

standards for the purpose of promoting quality.¹²⁶ Accrediting organisations may take various forms including universities, government funded health care organisations, professional regulatory bodies, and commercial entities. As well as accrediting services, there is a role for accreditation in training and education; in fact, accreditation is considered an essential component of effective education of healthcare professionals globally.¹²⁷ In this case, accreditation can enhance health outcomes by influencing and standardising training programmes and encouraging continuous curriculum development to align with population needs.¹²⁷

The value of accreditation is well recognised as a method of quality improvement and maintaining minimum standards, with a beneficial effect on patient safety and outcomes. Like performance monitoring, it again seems intuitive that accreditation would be a central component of cancer screening programmes.

Performance and accreditation in colonoscopy

In 2004, Bowles et al¹²⁸ published a landmark study of colonoscopy availability and quality in three NHS regions. They studied 9223 colonoscopies and found that the adjusted caecal intubation rate (CIR; a measure of completeness of the examination) was only 56.9%; only half of patients recalled being informed of possible adverse events; only 17% of colonoscopists had received supervised training for their first 100 colonoscopies; and only 39.3% had attended a training course. They concluded that colonoscopy is often incomplete (not achieving the CIR target of 90%), training was often inadequate and there was wide variation in practice between different units.¹²⁸ This study and subsequent reports, including the NCEPOD Scoping our Practice (2004),¹²⁹ painted a bleak picture of

endoscopy services in the UK, including: inadequate facilities and equipment; long waits and poor patient experience; inadequately trained staff and poor supervision; minimal or no processes to ensure appropriate patient selection and safety; and no monitoring of quality.¹³⁰

As a result, between 2001 and 2010, significant financial investment was made into endoscopy services, to aid modernisation and improve training.¹³⁰ The Joint Advisory Group on Gastrointestinal Endoscopy (JAG), which was established in 1994, played an important role in addressing this challenge. Its original purpose was to support endoscopy training; however, despite clear basic training requirements, services were still operating below JAG standards. With the new investment, JAG created an accreditation scheme for service delivery and endoscopist training which includes certification of endoscopists, a national ePortfolio and accreditation of services. Now, no endoscopist is allowed to perform independently without JAG accreditation.

In 2013, along with the JAG, the British Society of Gastroenterology (BSG) and the Association of Coloproctology of Great Britain and Ireland (ACPGBI) commissioned a working group to define new QA measures and KPIs for colonoscopy.¹³¹ The purpose of these quality standards was to reduce variation, and they now provide the minimum benchmark for colonoscopy performance. They include a minimum CIR of 90% and aspirational target of >95%, adenoma detection rate (ADR) of 15-20%, a withdrawal time of at least 6 minutes (for negative studies), and at least 100 colonoscopies performed per year.¹³¹ These are clinically-relevant quality markers – both low ADR^{132,133} and CIR¹³⁴ are associated with higher rates of ‘missed cancer’ after an apparently normal colonoscopy.

While the impact of the JAG is difficult to quantify, as there are no randomised controlled trials to assess it, the basic training has seen a significant increase in CIR among junior trainees,¹³⁵ and utility of their competency-based training framework is producing trainees that are achieving the national quality standards post-certification.¹³⁶ In addition, JAG accreditation is not used in Scotland, and despite comparable CIR and perforation rates, ADR is 9% lower in the Scottish Bowel Screening Programme (SBoSP) than in the BCSP (37.4% vs 46.5%; $p < 0.001$).¹³⁷ This difference is unlikely due to adenoma prevalence, since Scotland has a higher incidence of CRC, and instead has been attributed to a lack of accreditation and the additional benefit of other JAG processes including peer mentorship and performance feedback.¹³⁷

When considering the role in CRC screening, all BCSP screening centres must have JAG accreditation and new sites should have accreditation in place before starting BCSP colonoscopy lists.¹³⁸ All BCSP colonoscopies are carried out by screening-accredited colonoscopists, which requires a lifetime experience of over 1000 colonoscopies, CIR $> 90\%$ and ADR $> 20\%$ in the preceding 12 months, as well as peer assessment during an observed colonoscopy list.¹³⁹

Performance and accreditation in radiology

While accreditation and performance monitoring are now well established for colonoscopy and its specific role in the BCSP, there are few similar examples in radiology. The most widely recognised analogous programme is seen within NHS breast cancer screening.

Accreditation in mammography (PERFORMS)

The PERFORMS (PERsonal perFORmance in Mammographic Screening) scheme was invented and developed by Professor A.G Gale and E.J Roebuck, and established in 1991.^{140,141} It was created to tackle the challenge of slow feedback on radiologist performance in mammography reporting, particularly regarding studies deemed normal. In breast screening, the patient has two mammography views obtained of each breast, which are then reported as either normal/benign, or if there are suspicious appearances recalled for assessment.

Currently, the NHS Breast Screening Programme (BSP) invites all women age 50 to 70 for screening every 3 years, and more than 2 million women are screened annually.¹⁴² Current recommendations from the Royal College of Radiologists (RCR) are that each breast screening reader reports 5000 cases per year, but the low incidence of breast cancer in screening (approximately 7 per 1000 screened cases) means that each radiologist will see a malignant case less than once a week.^{140,141} When an abnormal case is referred for assessment, the radiologist receives rapid feedback from the multidisciplinary team on whether their decision was appropriate, however, due to the 3-year screening interval, feedback for cases reported as normal or benign is delayed. In these cases, the radiologist will not know if their assessment was accurate until the next screening round, or if the patient presents with an interval cancer before then.¹⁴¹

PERFORMS provides access to additional test cases to expand exposure to difficult screening cases. It is the first national, self-assessment scheme in radiology and has been continuously implemented for the last 30 years. It provides

readers with self-assessment tests on mammography interpretation in comparison to: expert radiological opinion, known case pathology, peer opinions, and also provides additional personalised training.¹⁴¹ Participation in PERFORMS is currently mandated by the NHS BSP, endorsed by the Royal College of Radiologists and Public Health England, and is taken by almost 1000 screening readers each year.^{141,143}

As well as self-assessment via PERFORMS, a new Breast Screening Information System (BSIS) has recently been introduced. This bespoke tool commissioned by PHE and development by NHS Digital collates, analyses and presents national and local breast screening data and performance statistics.¹⁴⁴ Readers can access the system with a unique code and compare their real-life screening performance to others' over a three year period. This has facilitated comparison studies to evaluate how performance in PERFORMS may correlate to real-world screening practice. Two recent studies have observed that the PERFORMS test sets accurately reflect real-life mammography interpretation and can predict poor performers.^{145,146} BSIS real-life cancer detection rate, recall rates, and positive predictive values all positively correlated with the equivalent PERFORMS measures ($p < 0.001$, $p = 0.002$, and $p < 0.001$, respectively).

Participation in PERFORMS allows rapid feedback on performance, facilitating the improvement of underperformers. Mandatory participation is an important quality assurance process within the breast screening programme.

Performance in CT Colonography

Both the JAG accreditation and PERFORMS scheme have contributed to improved quality of bowel and breast cancer screening services respectively. In contrast to the robust, evidence-based KPIs and the formal accreditation process for colonoscopy discussed above, there is no infrastructure to ensure that CTC practitioners and radiologists are performing adequately; neither are there internationally agreed KPIs. Although radiology is included in the general Quality Assurance framework for the BCSP, recommendations are largely based on opinion rather than an appropriate evidence base. Furthermore, outside the BCSP, performance monitoring in routine symptomatic practice (which accounts for >95% of CTC workload)¹²² is non-existent. Essentially, any radiologist can report CTC, with no accreditation or performance monitoring and this is of particular concern since CTC accounts for almost 20% of whole colon testing in the UK.¹⁴⁷ It is therefore critical that radiologists interpreting CTC are adequately trained and monitored, a prerequisite to achieve the diagnostic performance demonstrated in previous RCTs.

Interestingly, radiologists themselves are generally in favour of accreditation for CTC reporting. A national survey of CTC in the BCSP found that 67% of radiologists felt that symptomatic and screening CTC should be accredited together, while another 15% suggested that screening CTC require more rigorous accreditation.¹²² The most favoured strategy was one of periodic testing with cases, similar to the PERFORMS scheme described above. There was a general perception among survey respondents that training and experience are prerequisites for good diagnostic performance.¹²²

For the first time, KPIs for CTC in the UK have been recently published and include the number of CTCs reported per annum, polyp identification rate (PIR; i.e. polyps identified at CTC), positive predictive value (i.e. proportion of patients with polyps identified on CTC who have colonoscopy, surgery or follow-up CTC and have a confirmed polyp of ≥ 4 mm in any segment) and mean interpretation time per scan.¹²¹ These form part of the recommended standards of practice for CTC, with a recommended minimum standard PIR of $>13\%$ for ≥ 6 mm polyps in all patients (symptomatic and screening) and aspirational target of $>16\%$.¹²¹ These standards are set at a pragmatic level to recognise that the prevalence of ≥ 6 mm polyps varies between screening and symptomatic cohorts, increases with age and is generally higher in men.¹²¹

It should be noted that PIR differs from the 'polyp detection rate' (PDR), which refers specifically to the rate of endoscopically confirmed polyps (regardless of histology) and is considered a quality standard, like ADR for colonoscopists. PIR (in conjunction with positive predictive value) is preferred as a performance metric for CTC as not all patients undergoing CTC will have confirmatory colonoscopy, typically due to comorbidities and contraindications.

Adherence to the guidelines and uptake of the performance metrics remains to be seen and will require local resourcing and support.

The need for accreditation and performance monitoring for CTC readers raises the question of whether it is reasonable to mandate accreditation without provision of a formal training scheme. In colonoscopy, the JAG accreditation works within an established infrastructure offering basic training and an ePortfolio to track

competency-based skills assessments. Similarly, in PERFORMS, outliers or underperformers are offered additional training and support. The lack of an analogous scheme for CTC prompted the multi-centre randomised control discussed in Section C and the proposed CTC accreditation model described in Chapter 7.

Conclusion

Performance monitoring and quality assurance are crucial aspects of any screening programme. Significant progress and improvement have been observed in the bowel cancer and breast screening programmes due to the implementation of accreditation and performance monitoring schemes.

We propose CTC training and assessment as a solution for the lack of accreditation for radiologists reporting CTC in the BCSP. If CTC is to achieve its full potential as a diagnostic tool, both in symptomatic practice and in the bowel cancer screening programme, more formal assessment of reader performance will be necessary, to ensure all patients receive an acceptable quality of service.

SECTION B: READER PERFORMANCE IN CT

COLONOGRAPHY AND METHODS TO IMPROVE IT

In the following Section I discuss factors related to performance in CT colonography (CTC). Chapter 4 presents a systematic review and meta-analysis, establishing for the first time the post-imaging colorectal cancer (PICRC) rate. This surrogate marker of examination and interpretation quality is due, in most cases, to perceptual error; raising the possibility that improved training in CTC interpretation could reduce 'missed cancer' rates. Environmental factors can also be optimised to maximise CTC accuracy and Chapter 5 investigates how many scans should be reported in a single session and how long they should each take.

Chapters 6 and 7 go on to review existing approaches to CTC training globally, the impact training has on reader performance and principles for best practice in CTC teaching.

These data inform the rational design of a package of interventions that may improve CTC reader accuracy, a hypothesis that will be tested formally via a cluster randomised control trial in Section C.

Chapter 4 Post-imaging colorectal cancer rate after CT colonography: systematic review and meta-analysis

Summary and contribution statement

Section A provided background context detailing the burden of colorectal cancer (CRC) and the use of screening to aid early detection. The role of CTC in CRC diagnosis and screening has been discussed as well as some key differences between the quality assurance processes for CTC and colonoscopy.

A further measure of the diagnostic quality of an examination is the rate of interval cancer, or 'missed cancer' rate after an apparently normal study. While the interval cancer rate for colonoscopy has been established in various studies, it was hitherto unknown for CT colonography (CTC). This chapter presents a systematic review and meta-analysis of the primary literature to estimate the post-imaging CRC rate after CTC and explores associated factors.

The study protocol was written in conjunction with the thesis supervisors, Dr David Burling (St Mark's Hospital, Harrow) and me. I performed the literature search and primary data extraction in conjunction with Dr Ulysses dos Santos Torres (Grupo Fleury, Brazil). Statistical assistance was provided by Dr Thomas Fanshawe (Oxford University). I conducted the study quality assessment and wrote the draft manuscript which was edited in conjunction with the manuscript co-authors.

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Post-imaging colorectal cancer or interval cancer rates after CT colonography: a systematic review and meta-analysis. Obaro AE, Plumb AA, Fanshawe T R, Torres US, Baldwin-Cleland R, Taylor SA, Halligan S, Burling DN (2018). The Lancet Gastroenterology & Hepatology. DOI: 10.1016/S2468-1253(18)30032-3.

Introduction

As discussed in Chapter 1, Figure 1.2, most cases of CRC arise from potentially premalignant precursor lesions (either adenomatous polyps or serrated lesions),^{6,148} the removal of which reduces incidence of subsequent CRC.⁴¹ Therefore, through polyp detection and removal, colonic investigations in symptomatic or screening populations can both detect and prevent CRC.

Use of CTC has rapidly increased over the last decade, with approximately 120,000 examinations per annum in England alone.⁵² Although both colonoscopy and CTC are highly sensitive for CRC and precursor polyps, neither provides absolute protection against subsequent CRC. These post-test CRCs are termed 'interval cancer' in the context of screening programmes with a defined post-test interval, or 'post-colonoscopy colorectal cancer (PCCRC)' where no such routine interval exists, for example in symptomatic practice.¹⁴⁹⁻¹⁵¹ PCCRC is becoming a widely-reported marker of colonoscopy quality within healthcare systems internationally.¹⁴⁹⁻¹⁵³ The directly analogous term 'post-imaging colorectal cancer (PICRC)' can be applied to CTC.

Although PCCRC has several causes, missed lesions at initial testing likely account for over 50% of cases.¹⁵⁴ Individual colonoscopists with low adenoma detection rates (ADR) have correspondingly higher PCCRC rates.^{132,133} Although meta-analysis shows that CTC and colonoscopy are equally sensitive for detection of established CRC,²⁶ CTC is less sensitive than colonoscopy for small and diminutive (≤ 5 mm) polyps; 74% for 6 to 9 mm polyps in one meta-analysis.⁶⁶ Although such polyps carry negligible immediate clinical risk, the longer-term impact on the

PICRC rate after false-negative CTC is largely unknown. Furthermore, little is known regarding the time to development of PICRCs, nor their stage, anatomical location, prognosis, or predisposing factors when they occur. Consequently, clinicians and policy-makers are unable to provide evidence-based recommendations regarding future testing following apparently negative CTC.

To address this, indexed literature was systematically reviewed to establish the prevalence of PICRC in patients following CTC in both screening and symptomatic settings. The clinical characteristics of PICRCs and factors associated with their occurrence were also explored.

Materials and Methods

This systematic review and meta-analysis adheres to the Preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA) guidelines.¹⁵⁵ The review is registered (PROSPERO number: CRD42016042437) and the protocol is publicly-available.¹⁵⁶

Search strategy and selection criteria

CTC was defined as CT scanning of the prepared, gas-distended colon per international consensus guidelines.⁵³ Component primary studies defined CTC-detected cancers by inspection of radiology reports (retrospective studies) or study case report forms (prospective studies). PICRCs were defined as diagnoses of CRC occurring after a CTC that did not detect cancer. We required that primary studies had identified PICRCs via cancer registries, regional databases or cancer

intelligence networks;¹⁵⁶ or where the true disease status of each individual patient during follow-up was determined by a dedicated whole-colon test.

Inclusion and exclusion criteria. Studies that met the following criteria were included: (i) randomised controlled trials (RCTs), cohort studies, cross-sectional or case-control studies reporting original research data from adult humans; (ii) published between January 1994 (the year CTC was first described in the literature)¹⁵⁷ and February 2017; (iii) reported a PICRC rate or data sufficient for this to be calculated; (iv) minimum follow-up of 12 months; (v) written in English, French, German or Spanish. We excluded studies in which any of the following biases applied: (i) all CTCs were performed due to incomplete colonoscopy (e.g. in the presence of a stenosing cancer); (ii) CTC performed in knowledge of colonoscopy findings; (iii) CTC technique deviating from international consensus guidelines.^{53,158}

Search strategy and article selection. With an experienced information scientist, I used the Ovid SP interface to search MEDLINE and EMBASE databases, and the Wiley interface to search the Cochrane Register of Controlled Trials. A combination of medical subject headings (MeSH) and free-text terms relating to CTC and colorectal cancer were used:

1. ((CT or (comput* and tomogra*)) and colonogra*).af
2. (virtua* and colono*).af
3. 1 or 2
4. colonography, computed tomographic.sh
5. 3 or 4
6. 5 and Journal Article.pt
7. ((colon or colorect*) and (cancer or carcinoma)).af

8. colorectal neoplasms.sh
9. 7 or 8
10. 9 and Journal Article.pt
11. 6 and 10

The reference lists of relevant articles and reviews were examined for possible additional studies.

I retrieved the search results to an Endnote X7 (Thomson Reuters, Toronto, ON, Canada) database and removed duplicates. Dr Ulysses S Torres and I then independently screened all titles and abstracts using the predetermined eligibility criteria, excluding articles where we both rated the study as clearly ineligible. Full text versions of all remaining articles were then reviewed independently by Dr Torres and me, and those that did not meet the inclusion criteria were excluded and reasons recorded. Discrepancies regarding eligibility were resolved by face-to-face consensus, arbitrated by the thesis supervisor, Dr Andrew Plumb.

Data analysis

Data extraction and quality assessment. For each study, Dr Torres and I independently extracted data into a spreadsheet designed specifically for the study (Microsoft Excel 2016, Microsoft, Redmond, Washington, USA). We extracted the following items: (a) study characteristics – author, publication year, recruitment period, geographical location and number of centres, study design and follow-up duration; (b) patient characteristics – number included and lost to follow-up, reason for CTC, gender, age distribution; (c) CTC test characteristics – number of CTC examinations conducted, cathartic vs non-cathartic bowel preparation, use of

faecal tagging, intravenous contrast and spasmolytics, CT scanner type, acquisition parameters and reconstruction interval; (d) radiologist / reader characteristics – number of study radiologists and experience, mode of interpretation (i.e. two-dimensional, three-dimensional or mixed); (e) tumour characteristics – the number of patients with CRC detected by CTC, the number of patients with PICRCs, the colonic location of PICRC, the temporal interval between the index CTC and diagnosis of PICRC, any reported characteristics of PICRC (e.g. morphology and histology), the method of PICRC identification (i.e. national cancer registry, intelligence network or subsequent whole-colon test), and the reason PICRC(s) were not detected initially. This final category was divided into (i) perceptual error, i.e. PICRC visible in retrospect, (ii) technical error, e.g. under-distension of the colon, (iii) management error, e.g. incomplete or non-removal of CTC detected lesion, and (iv) occult lesion i.e. not visible on adequate quality CTC, even in retrospect.¹⁵⁶

Agreement was recorded, and discrepancies were resolved in consensus with arbitration by the thesis supervisor if required. Authors of component studies were contacted for additional data where necessary. The quality of each study was rated independently by Dr Torres and I using an adapted Newcastle Ottawa Scale (NOS) for non-randomised studies.¹⁵⁹ Studies scoring zero for individual components ([i] selection; [ii] comparability; or [iii] outcome assessment) were excluded from the quantitative analysis.^{156,159} The separate components were assigned a star rating by considering separate sub-questions within each component. 'Selection' consisted of sub-questions relating to population representativeness (1 star), ascertainment of CTC result (1 star) and knowledge of

disease status prior to study entry (1 star). 'Comparability' consisted of CTC blinding (1 star) and standardisation of CTC technique (1 star). 'Outcome' consisted of method to identify PICRCs (1 star), length of follow-up (1 star) and rate of loss to follow-up (1 star).

Outcomes. Our *a priori* pre-specified primary outcome was the prevalence of PICRC at 36-month after CTC, expressed as the proportion of PICRC to the total number of cancers detected (i.e. number of CRCs as the denominator). The 36-month time point was chosen since this is the most frequent interval used in the colonoscopic literature.¹⁴⁹⁻¹⁵³ However, since no individual component study reported data for this timepoint, we chose to present a pooled PICRC rate using the maximum follow-up reported by each component study (median = 34 months). We also expressed the PICRC rate as the proportion of PICRC to the total number of CTC examinations conducted (i.e. number of CTC examinations as the denominator). The latter approach is influenced by CRC prevalence (i.e. if no CTC examinations harbour a cancer, then it is impossible to have a PICRC), but nevertheless provides a rate representative of routine clinical practice.¹⁵³

Secondary outcomes included PICRC prevalence at 60 months, since this is the recommended interval between CTC screening examinations,⁹⁴ and PICRC rates per 1000 person-years of follow-up, as recommended by existing colonoscopic literature.¹⁶⁰ Since individual patient data were not available, the total length of follow-up per study (i.e. number of person-years of follow-up) was estimated as the average follow-up per person, multiplied by the number of individuals in the study, discounting those lost to follow-up. The average follow-up per person was taken directly from component study reports by using (in decreasing order of priority) the

mean, median, $0.5 * (\text{maximum} - \text{minimum})$ or $\text{maximum}/2$. These were used on four, two, five and one occasions respectively.

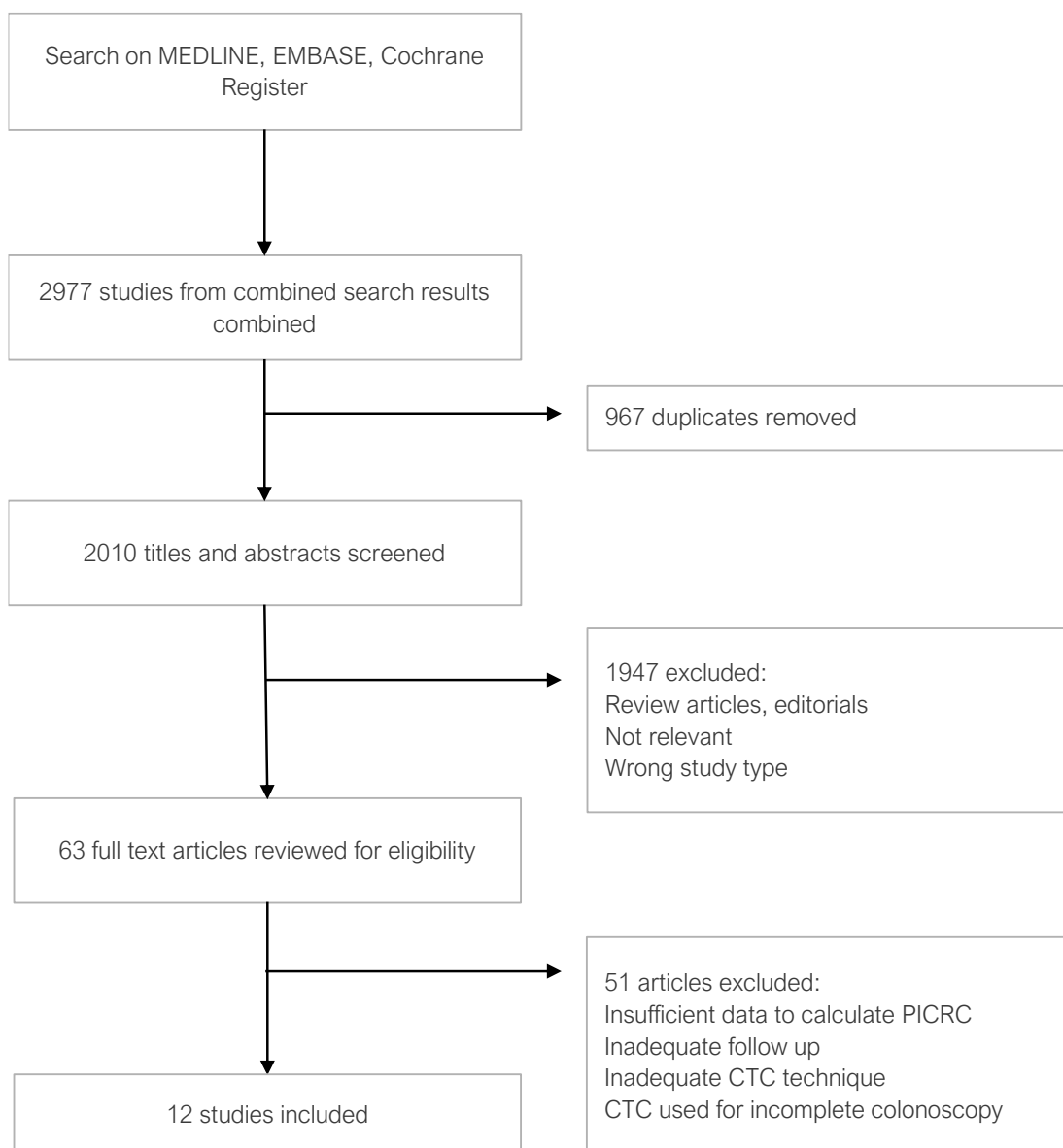
Additional secondary outcomes were the colonic segmental location of detected CRC and PICRC; radiologist, patient and CTC technical scanning characteristics associated with higher PICRC rates; aetiological factors contributing to PICRCs; and literature quality.

Data synthesis. Meta-analysis was conducted using a random-effects model, using the 'meta' package for version 3.2.4 of R (R Foundation for statistical computing, Vienna, Austria).¹⁶¹ The PICRC rate per study was combined to estimate a pooled prevalence with 95% confidence interval (CI). Between-study heterogeneity was assessed using the I^2 statistic and we investigated sources of heterogeneity using meta-regression according to use of faecal tagging, study population type (symptomatic, screening or mixed), patient gender and number of radiologists included in the study. The anatomical distribution of CTC-detected cancers and PICRCs were combined to provide a pooled estimate, presented as the proportion located in the proximal colon (defined as the caecum to the distal transverse colon inclusive). We assessed for publication bias and small study effects using funnel plots.¹⁶² Statistical analysis was conducted by a collaborator, Dr Thomas Fanshawe. The strength of the overall weight of evidence was rated using the GRADE working group methodology.¹⁶³

Results

Initial searching identified 2977 studies; after the removal of 967 duplicates, 2010 studies underwent abstract screening. 1947 studies were excluded following abstract screening, and the full text of 63 studies was reviewed (16 identified by both Dr Torres and myself and 47 identified by just one of us). After full-text assessment, 12 studies were eligible for inclusion (Figure 4.1). Two of these studies^{59,67} were parallel randomised trials, for which some additional data were extracted from a combined, more detailed study monograph published separately.¹⁶⁴ Two further studies^{69,165} that derived from the same research group included partly overlapping patient cohorts; we received additional data from this group, permitting separate analysis of the two patient cohorts to avoid patient duplication.

Figure 4.1: Study flowchart.



Of the 63 full texts reviewed for eligibility, 16 were identified by both abstract screeners and 47 were identified by one screener alone. Of the 51 articles excluded at the full text review stage, 42 were identified by both independent reviewers as clearly ineligible and the other 9 were excluded after consensus discussion with arbitration by the thesis supervisor

Characteristics of included studies^{59,67,69,165-173} are shown in Table 4.1. Most were retrospective (nine studies) and conducted at a single centre (nine studies). Overall, 19,867 patients underwent 19,570 CTCs between March 2002 and May 2015 inclusive, with a mean overall follow-up of 34 months (range 13.5 to 68.3 months). The number of participants may differ from that reported in component articles as here we solely discuss data pertaining to PICRC rates. The number of patients exceeds the number of CTCs because in four studies 147 patients did not have their allocated CTC^{59,67,168,173} and in one study,¹⁷² all 150 patients with post-test CRC were included, rather than just those having CTC. The sex and age range of included patients was only reported in seven of 12 studies (58.3%);^{59,67,166-169,172} 6532 of 11,590 patients with data available (56.4%) were female, ranging from 18 to 99 years of age. Studies frequently included a mixed (i.e. screening and symptomatic) population (41.7%; 5 of 12 studies)^{167-169,171,172} accounting for 10,276 of 19,867 patients (51.7%). Studies including patients with colorectal symptoms alone (41.7%; five of 12 studies),^{59,67,166,170,173} contributed 37.8% (7,519/19,867) of all patients reviewed, and in two of the 12 component studies^{69,165} (16.7%), all patients included were asymptomatic screenees (10.6% [2,111/19,867]).

Table 4.1: Characteristics of studies reporting post-CTC PICRC rates and meeting inclusion criteria

Study	Year	Period (month/year)	Region	No. of sites	Study design	Population	No. of Pts	Age range	No. of radiologists	No. of CTCs	Reconstruction interval	Follow-up* (months)	Purgation	Faecal tagging	IV contrast	Antispasmodic
Atkin et al ¹⁵⁹	2013	03/2004 - 12/2007	UK	21	Prospective	Symptomatic	538	55 to 85	41	503	Variable	36 (0)	Yes	Variable	Variable	Variable
Badiani et al ¹⁶⁶	2011	03/2002 - 12/2007	UK	1	Retrospective	Symptomatic	1177	27 to 96	8	1177	NR	34.5 (18-84)	Yes	No	Yes	Buscopan or glucagon if CI
Halligan et al ⁶⁷	2013	03/2004 - 12/2007	UK	21	Prospective	Symptomatic	1285	55 to 85	39	1206	Variable	36 (0)	Yes	Variable	Variable	Variable
Hock et al ¹⁶⁷	2015	6/2003 - 8/2010	Belgium	1	Retrospective	Mixed	1890	18 to 96	NR	1890	0.625mm	6-60	Yes	Yes	NR	Buscopan
Kim et al ¹⁶⁵	2012	04/2004 - 05/2005	USA	1	Retrospective	Screening	643	NR	NR	643	1mm	54.2 (NR)	Yes	Yes	NR	NR
Lung et al ¹⁶⁸	2014	1/2007 - 12/2011	UK	1	Retrospective	Mixed	4355	23 to 99	4	4349	NR	26.4 (NR)	Yes	Variable	Variable	Buscopan
Moore et al ¹⁶⁹	2013	1/2004 - 7/2009	New Zealand	1	Retrospective	Mixed	2026	19 to 87	6	2026	NR	3-24	Yes	Yes	NR	NR
Pickhardt et al ⁶⁹	2017	01/2004 - 05/2015	USA	1	Prospective	Screening	1429	NR	12	1429	1mm	68.4 (10.8)	Yes	Yes	NR	NR
Sabanli et al ¹⁷⁰	2010	1/2004 - 9/2008	New Zealand	3	Retrospective	Symptomatic	3888	NR	NR	3888	Variable	3-59	Yes	Variable	NR	NR
Simons et al ¹⁷¹	2013	1/2007 - 1/2011	Netherlands	1	Retrospective	Mixed	1855	NR	4	1855	NR	6-24	Yes	Yes	No	Buscopan or glucagon if CI
**Than et al ¹⁷²	2015	8/2010 - 7/2011	UK	1	Retrospective	Mixed	150	32 to 90	NR	NR	NR	NR to 36	NR	NR	NR	NR
Thomas et al ¹⁷³	2009	1/2003 - 12/2005	UK	1	Retrospective	Symptomatic	631	NR	3	604	1.5mm	24-60	Yes	No	Yes	Buscopan or glucagon if CI

The number of included patients may differ from published reports, because we have extracted data solely for the patients in whom we have data regarding their PICRC rate. *Follow-up was reported variably, and is presented, in order of preference, as mean (standard deviation), median (range), or range alone. For studies with standard deviation of zero, all patients were followed up for the same length of time **Than et al included patients with a new CRC diagnosis and identified those with prior CTC NR: Not Recorded. CI: Contra-Indicated. Pts: Patients.

CTC technique was inconsistently reported (Table 4.1). A single study¹⁷² did not report usage of cathartic bowel preparation; all others used cathartics. Faecal tagging was used routinely in five of the 12 studies^{69,165,167,169,171} (41.7%), used variably (either over time or by recruitment site) in four studies^{59,67,168,170} (33.3%), not used at all in two studies^{166,173} (16.7%) and its use was not reported by one study.¹⁷² Seven of 12 studies, (58.3%) did not report radiologist experience, four studies (33.3%) reported variable radiologist experience, and one study reported radiologist experience of less than 100 cases.¹⁷¹ Interpretation method was broadly consistent with 8 of 12 studies (66.7%)^{59,67,69,165-168,171} reporting routine use of two-dimensional (2D) display with three-dimensional display (3D) used additionally for either all cases or problem solving. One study reported using only 2D review for interpretation¹⁷³ and three studies did not report their interpretation method.^{169,170,172} Adjunct use of computer aided detection (CAD) was not stated in seven of 12 studies (58.3%),^{69,165,166,169,170,172,173} while two studies reported routine use,^{167,171} and three studies, optional use only.^{59,67,168} Five of 12 studies used the C-RADS reporting scheme (6 mm polyp reporting threshold),^{69,165,167,169,171} one study used a modified C-RADS scheme (also with a 6 mm threshold),¹⁶⁸ two studies used a 10 mm threshold,^{166,170} two studies^{59,67} allowed radiologists to follow their routine clinical practice and two studies did not detail which reporting threshold was used.^{172,173}

All studies met the pre-specified quality threshold for inclusion in the quantitative synthesis (quality scores for each component study are presented in Table 4.2). We agreed initially on 63.9% of scores (23 of 36), with the greatest variability evident within the comparability category, in which Dr Torres provided lower scores than me. Following discussion, consensus agreement was reached in the remaining 36.1% (13 of 36) of scores.

Table 4.2: Modified Newcastle-Ottawa Scale scoring for included studies, comprised of three components: selection, comparability, and outcome

	Selection (max 3 stars)			Comparability (max 2 stars)			Outcome (max 3 stars)		
	AEO	UST	Consensus	AEO	UST	Consensus	AEO	UST	Consensus
Atkin et al (2013) ⁵⁹	★★★	★★★	★★★	★★	-	★★	★★★	★★★	★★★
Badiani et al (2011) ¹⁶⁶	★★★	★★★	★★★	★★	★	★★	★★★	★★★	★★★
Halligan et al (2013) ⁶⁷	★★★	★★★	★★★	★★	-	★★	★★★	★★★	★★★
Hock et al (2015) ¹⁶⁷	★★★	★★★	★★★	★★	★	★★	★	-	★
Kim et al ¹⁶⁵ (2012)	★★★	★★★	★★★	★★	★ ★	★★	★★	★★	★★
Lung et al ¹⁶⁸ (2014)	★★★	★★★	★★★	★★	-	★★	★★	★★	★★
Moore et al ¹⁶⁹ (2013)	★★★	★★★	★★★	★	★	★	★★	★★	★★
Pickhardt et al ⁶⁹ (2017)	★★★	★★★	★★★	★★	★	★★	★★	★	★★
Sabanli et al ¹⁷⁰ (2010)	★★★	★★★	★★★	★★	★	★★	★★	★★	★★
Simons et al ¹⁷¹ (2013)	★★★	★★★	★★★	★★	★	★★	★★	★★	★★
Than et al ¹⁷² (2015)	★★★	★★★	★★★	★	-	★	★★	★★	★★
Thomas et al ¹⁷³ (2009)	★★★	★★★	★★★	★★	★	★★	★★★	★★	★★★

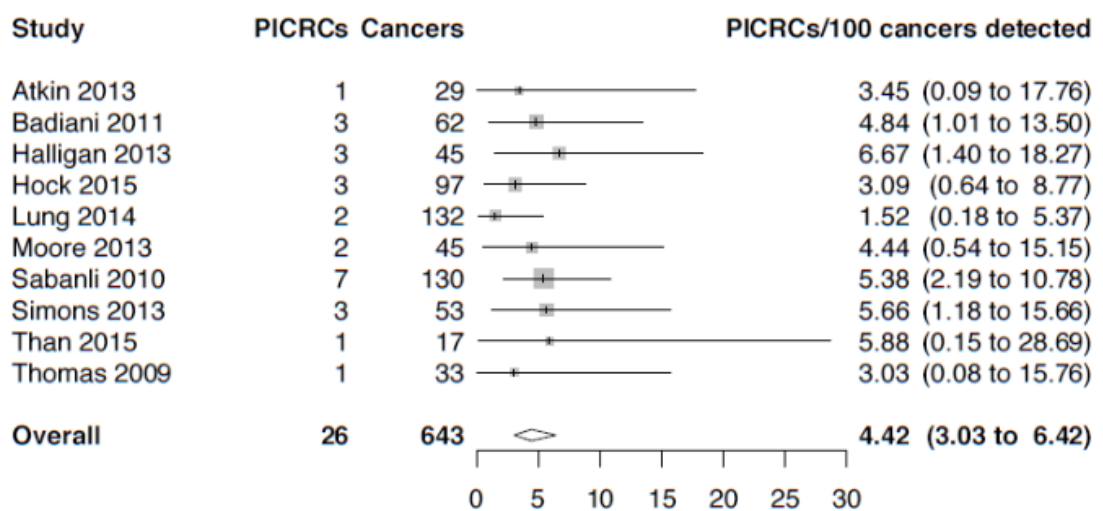
AEO: Dr Anuoluwapo E Obaro, thesis author and Rater 1. UST: Dr Ulysses S Torres, Rater 2

Two studies,^{69,165} reporting a total of three PICRCs, used negative initial CTC as an inclusion criterion, and were therefore excluded from the analysis of PICRC rate per 100 cancers detected, as, by definition, these studies had a zero denominator. A further article,¹⁷² reported only the number of detected cancers and PICRCs, and

not the number of negative CTC examinations, and was therefore excluded from calculations of PICRC rates per 1000 CTCs.

Across all 12 studies, 643 cancers were detected by CTC, with 29 PICRCs diagnosed subsequently. After exclusion of the two studies with negative CTC as an inclusion criterion, the pooled PICRC rate per 100 cancers detected was 4.42 (95% CI: 3.03 to 6.42), with no significant heterogeneity between studies ($I^2=0$; Figure 4.2).

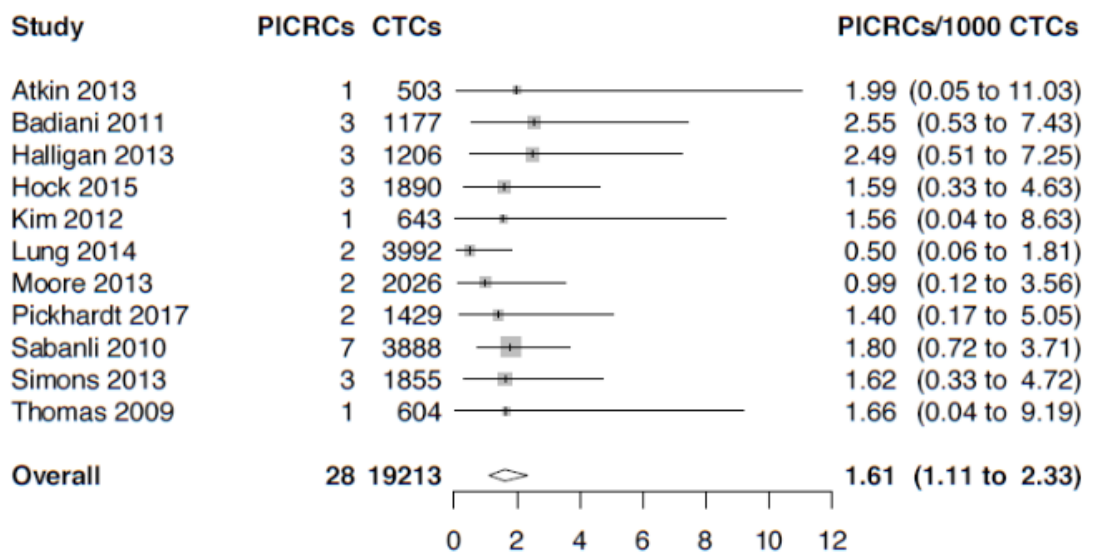
Figure 4.2: Pooled estimate of PICRC rate, presented as the number of PICRCs per 100 cancers detected



Two studies (Pickhardt et al⁶⁹ and Kim et al¹⁶⁵) that used negative initial CTCs as inclusion criteria were excluded from this analysis as the number of detected cancers in these cases was zero

When considering PICRCs as a proportion of the total number of CTC examinations performed, the pooled estimate was 1.61 PICRCs per 1000 CTCs (95% CI: 1.11 to 2.33; Figure 4.3).

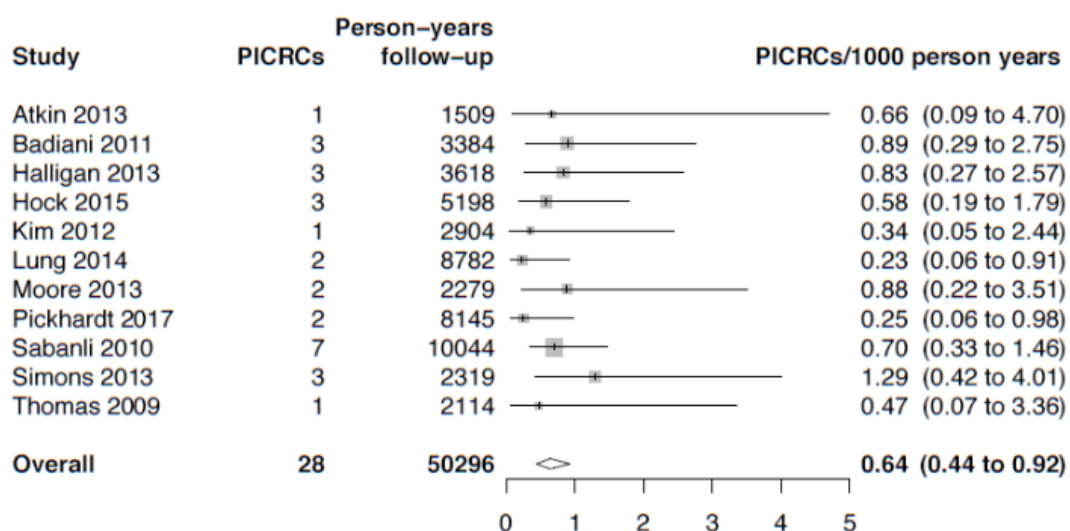
Figure 4.3: Pooled estimate of PICRC rate, presented as the number of PICRCs per 1000 CTCs.



One study, Than et al¹⁷², that reported only the number of cancers and not the number of negative CTCs was excluded

Again, heterogeneity was low ($I^2=0$). The pooled estimate was unaffected by exclusion of the two studies that used negative initial CTC as an inclusion criterion (1.64 PICRCs per 1000 CTCs, 95% CI: 1.11 to 2.42). When presented as incidence per 1000 person-years of follow-up, the pooled estimate was 0.64 PICRCs per 1000 person-years (95% CI: 0.44 to 0.92; Figure 4.4), with low heterogeneity ($I^2=0$).

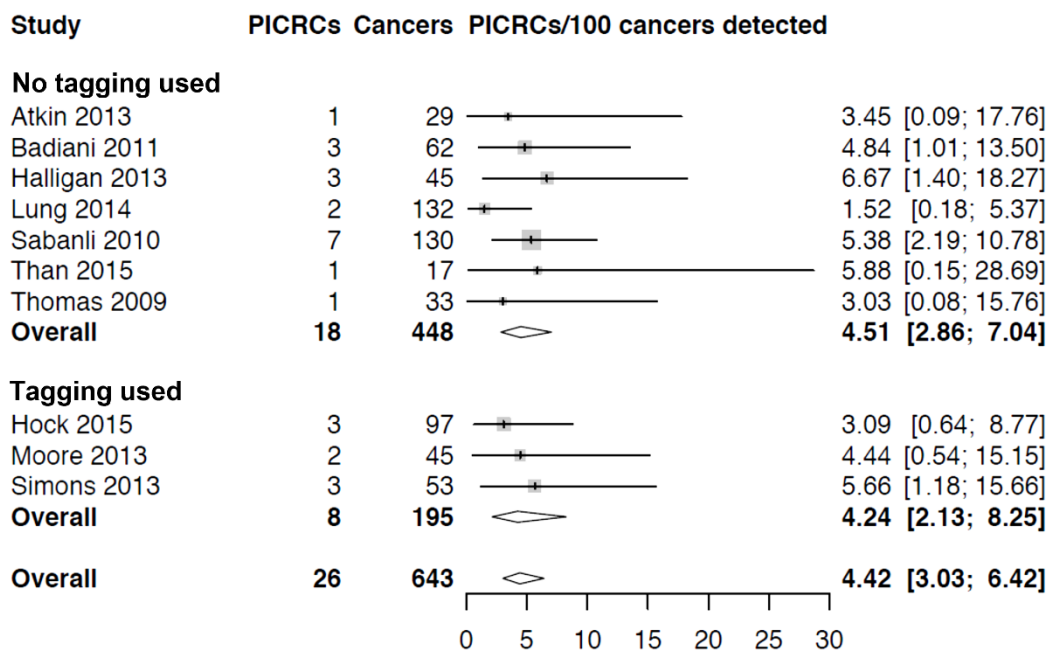
Figure 4.4: Incidence of PICRC per 1000 person-years follow-up



The study, Than et al¹⁷², reporting only the number of cancers detected, rather than the number of negative CTCs was excluded

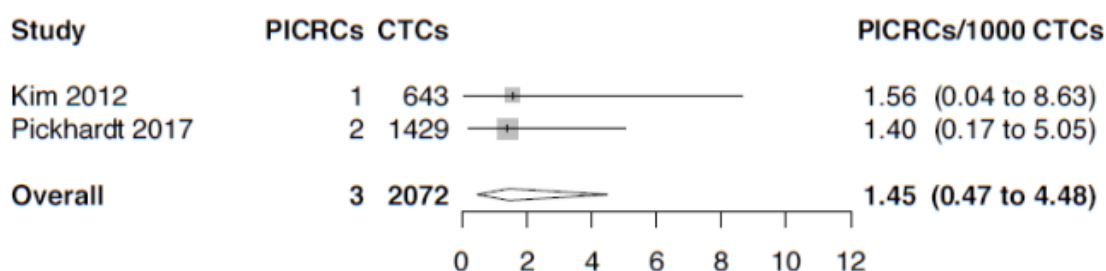
Meta-regression found no statistically-significant variation in the primary outcome according to use of faecal tagging ($p=0.88$; Figure 4.5), screening vs. symptomatic patient population ($p=0.65$), proportion of females ($p=0.74$) or the number of radiologists used ($p=0.48$). There was no significant difference when comparing the number of PICRCs divided by the number of CTCs conducted; or when considering use of faecal tagging as three categories (i.e. used for all patients, used variably, not used at all).

Figure 4.5: Effect of faecal tagging on PICRC



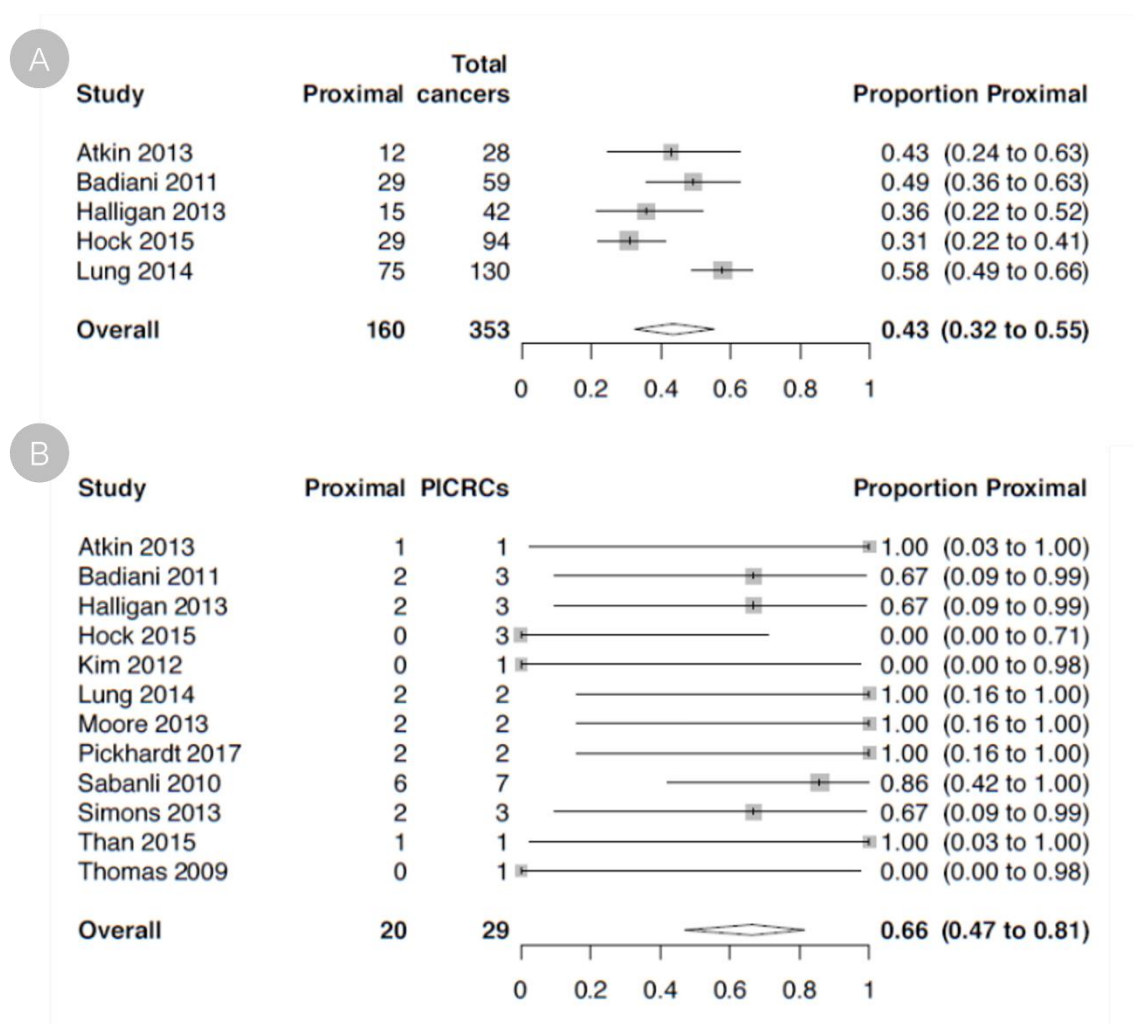
Only two studies (16.7%) had follow-up sufficient to permit estimation of 5-year PICRC rates.^{69,165} These two studies reported 2072 patients (1094 female, 52.8%), all with complete follow-up (pooled estimate: 61 months' average follow-up); and PICRCs were detected at either repeat CTC screening⁶⁹ or interval investigation for colonic symptoms.¹⁶⁵ A total of three PICRCs were diagnosed during this period, corresponding to a pooled PICRC rate of 1.45 PICRCs per 1000 CTCs (95% CI: 0.47 to 4.48, Figure 4.6), similar to the unrestricted analysis.

Figure 4.6: Pooled estimate of PICRC rate, restricted to the studies with an average of 5 years follow-up. Numbers presented as the pooled PICRC estimate per 1000 CTCs



The colonic segmental location of detected CRC was only reported in five studies;^{59,67,166-168} and 160 of 353 (45%) detected CRCs were proximal (i.e. caecum to transverse colon inclusive), corresponding to a pooled estimate of 0.43 (95% CI: 0.32 to 0.55; Figure 4.7A) being proximal by random-effects meta-analysis. Between-study heterogeneity was high ($I^2=77%$, $p=0.002$). In contrast, 20 of 29 (69%) PICRCs were located proximally, with the pooled estimate of this proportion being 0.66 (95% CI: 0.47 to 0.81, $I^2=0$; Figure 4.7B). PICRCs were significantly more likely than detected CRCs to be located proximally (95% CI: 1.19 to 6.05, $p=0.018$).

Figure 4.7: Anatomical distribution of detected CRC (distal vs proximal; A) and of PICRCs (distal vs proximal; B)



Clinical and imaging characteristics of PICRCs were reported incompletely (Table 4.3). In particular, the tumour stage of PICRCs at diagnosis and the time between index CTC and PICRC diagnosis were recorded inconsistently. However, additional data was obtained directly from component study authors in four cases.^{67,167,168,170}

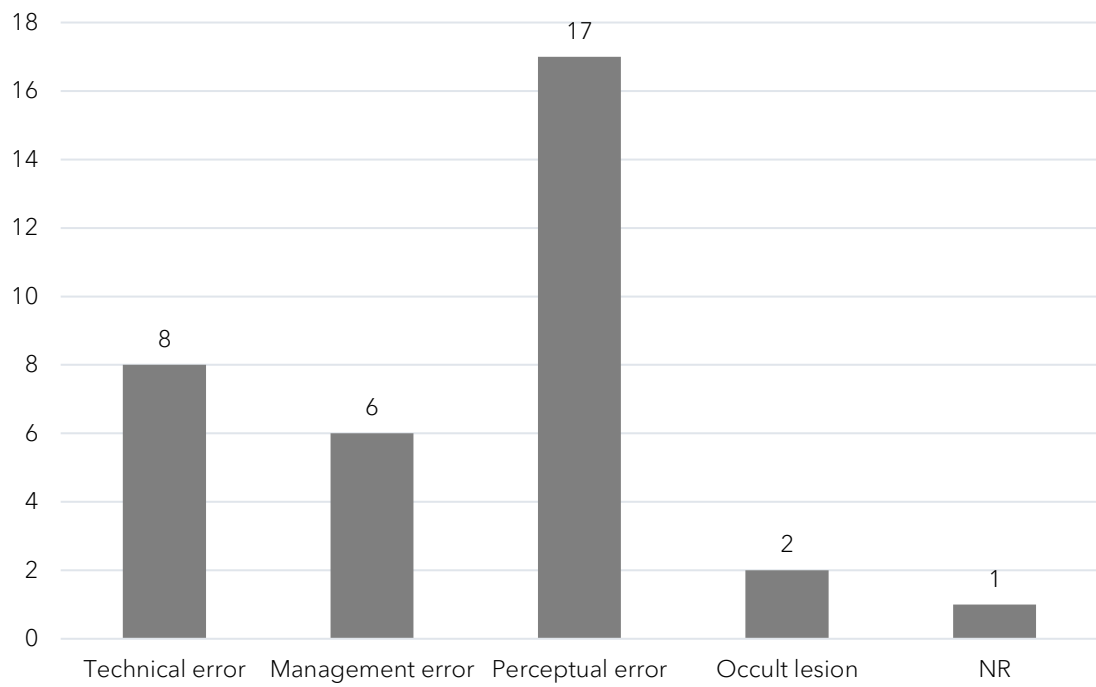
Table 4.3: Occurrences of post-imaging colorectal cancers reported in component primary studies

Study	No. of PICRCs	Details of PICRC occurrence	Aetiological factors contributing to PICRC	Histology/Characteristics of PICRC at detection	Timepoint of detection (months)
Atkin et al (2013) ⁵⁹	1	1. Initial CTC negative (poor distension, no follow-up imaging)	1. Technical error + Management error	1. Rectosigmoid tumour	1. 15
Badiani et al (2011) ¹⁶⁶	3	1. Initial CTC negative (lesion visible in retrospect) 2. Initial CTC negative (lesion visible in retrospect) 3. Initial CTC negative (lesion visible in retrospect)	1. Perceptual error 2. Perceptual error 3. Perceptual error	1. Polypoid sigmoid lesion 2. Sessile ascending colon lesion 3. Flat caecal lesion	1. 5 2. 11 3. 10
Halligan et al (2013) ⁶⁷	3	1. 6 mm caecal polyp not removed 2. Initial CTC negative 3. CTC interpreted as diverticulitis	1. Management error 2. Perceptual error 3. Perceptual error	1. 12 mm caecal adenocarcinoma 2. Ascending colon cancer, Dukes D 3. T4 N0 M0, Dukes B	1. 28 2. 7 3. 10
Hock et al (2015) ¹⁶⁷	3	1. Initial CTC negative (flat lesion visible in retrospect) 2. Non-diagnostic initial CTC (patient declined second view) 3. Initial CTC negative (lesion visible in retrospect)	1. Perceptual error 2. Technical error 3. Perceptual error	1. Adenocarcinoma 2. Adenocarcinoma 3. Adenocarcinoma	1. NR 2. NR 3. NR
Kim et al (2012) ¹⁶⁵	1	1. Initial CTC negative (lesion just visible in retrospect)	1. Perceptual error	1. T3 N0 M0	1. 35
Lung et al (2014) ¹⁶⁸	2	1. Only one of two lesions present identified 2. Initial CTC negative (lesion visible in retrospect)	1. Perceptual error 2. Perceptual error	1. T3 N0 M0, Dukes B 2. T3 N1 M0, Dukes C1	1. 4 2. 42
Moore et al (2013) ¹⁶⁹	2	1. Local recurrence at ileocolic anastomosis (poor distension, very minor smooth wall thickening) 2. Only one of two lesions present identified	1. Technical error + Perceptual error 2. Perceptual error	1. 35 mm 'plaque-like' anastomotic recurrence 2. 10 mm caecal polyp cancer	1. 4
Pickhardt et al (2017) ⁶⁹	2	1. Initial CTC negative (flat lesion visible in retrospect) 2. Initial CTC negative (lesion not visible in retrospect - occult lesion)	1. Perceptual error 2. Occult lesion	1. T3 N1b M0 2. T2 N0 M0	1. 60 2. 120
Sabanli et al (2010) ¹⁷⁰	7	1. Non-diagnostic initial CTC (poor faecal tagging, no follow-up imaging) 2. Non-diagnostic initial CTC (poor distension, no follow-up imaging) 3. Non-diagnostic initial CTC (poor quality scan on single detector CT) 4. Non-diagnostic CTC (motion artefact, poor distension, no follow-up imaging) 5. Initial CTC negative (lesion not visible in retrospect - occult lesion) 6. Lesion misinterpreted as thickened fold (lesion visible in retrospect) 7. Initial CTC negative (lesion visible in retrospect)	1. Technical error + Management error 2. Technical error + Management error 3. Technical error 4. Technical error + Management error 5. Occult lesion 6. Perceptual error 7. Perceptual error	1. Caecal carcinoma 2. Caecal carcinoma 3. Caecal carcinoma 4. Rectosigmoid carcinoma 5. NR 6. Caecal carcinoma 7. NR	1. NR 2. NR 3. NR 4. NR 5. NR 6. NR 7. NR
Simons et al (2013) ¹⁷¹	3	1. Non-diagnostic initial CTC (poor distension) 2. Initial CTC negative (flat lesion visible in retrospect) 3. Initial CTC negative (lesion visible in retrospect, obscured by rectal balloon)	1. Technical error 2. Perceptual error 3. Perceptual error	1. Caecal carcinoma 2. Flat advanced adenoma in ascending colon 3. Distal rectal malignancy	1. 9 2. 14 3. 5
Than et al (2015) ¹⁷²	1	1. NR	1. NR	1. TNM stage II Dukes B	1. 4
Thomas et al (2009) ¹⁷³	1	1. 9 mm sigmoid colon polyp not removed	1. Management error	1. Invasive adenocarcinoma	1. 31

Some post-imaging colorectal cancers were associated with more than one aetiological factor. NR: Not Reported.

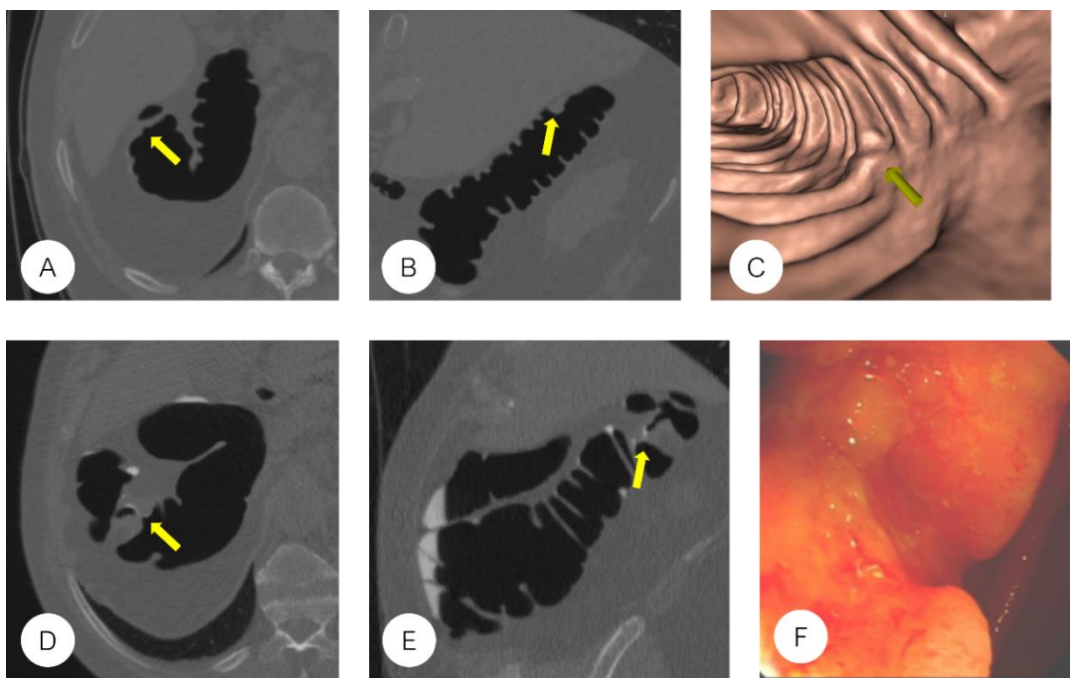
Of the 29 PICRCs, information regarding aetiological factors was available for 28. In 5 cases, more than one aetiological factor was deemed contributory. The majority of PICRCs were missed because of perceptual errors (60.7% [17/28]; Figure 4.8 and Figure 4.9).

Figure 4.8: Aetiological factors contributing to interval cancers



Some post-imaging colorectal cancers were associated with more than one aetiological factor

Figure 4.9: Example of a perceptual error

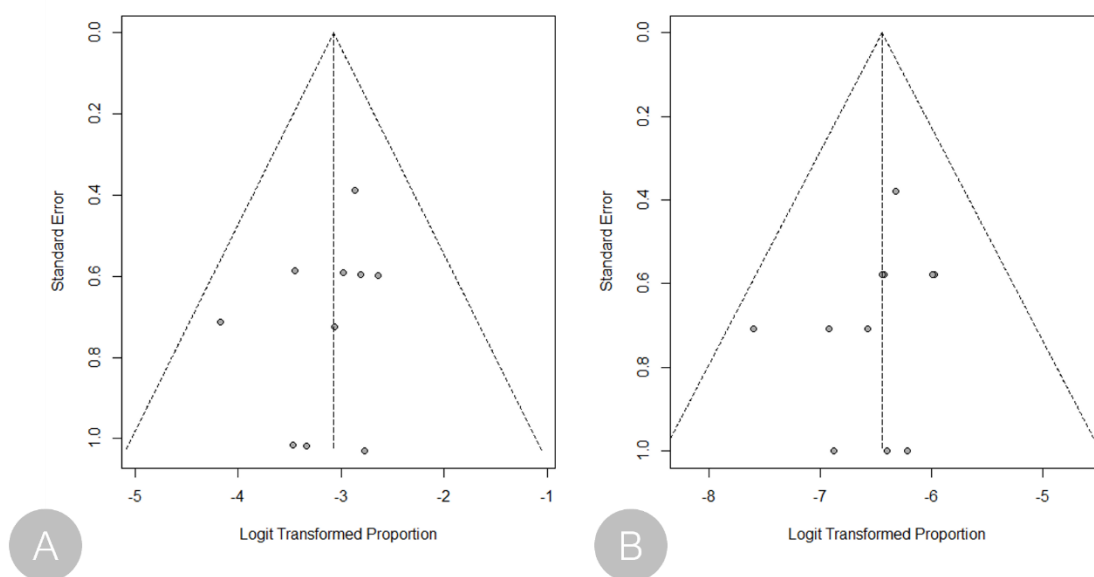


2D axial (A), sagittal (B) and endoluminal 3D (C) images from initial CTC show a 1.4 cm centrally depressed non-polypoid colorectal neoplasm at the hepatic flexure that was not identified (yellow arrows). 2D axial (D) and sagittal (E) images from repeat CTC 4 years later show a near-circumferential mass in the hepatic flexure. Subsequent endoscopy (F) confirms an ulcerated tumour. The patient underwent right hemi-colectomy, with final histology of a pT3 N1 M0, Dukes C1 colorectal adenocarcinoma. Used with permission from Janice Muckian (St Mark's Hospital)

Technical error accounted for 8 PICRCs (28.6%) and management errors were associated with 6 PICRCs (21.4%). Two of the 28 PICRCs were not visible even in retrospect (7.1%).

Funnel plots for the primary outcome showed no clear indication of small study effects, including publication bias, whether presented as a percentage of CRC detected, or as a proportion of CTC examinations conducted (Figure 4.10).

Figure 4.10: Small study effects and publication bias. Funnel plots for the primary outcomes of (A) Number of PICRCs / Total cancers detected; and (B) Number of PICRCs / Number of CTCs



According to the GRADE working group methodology,¹⁶³ the confidence in the result of the quantitative synthesis is summarised as high (i.e. we are confident that the true value lies close to the presented estimates).

Discussion

CRC is preventable because most cancers arise from precursors that can be detected and removed. Both colonoscopy and CTC are highly sensitive for large (≥ 10 mm) polyps and CRC, but colonoscopy better detects small (6-9 mm) and diminutive (≤ 5 mm) adenomas; and serrated lesions. Since lower adenoma detection rates at colonoscopy are known to be associated with higher subsequent PCCRC rates,^{132,133} this might lead to the *a priori* expectation that PICRC rates will be higher for CTC than colonoscopy. This systematic review of 19,867 patients

demonstrates that this is not the case, at least within a 3-year time horizon: We calculated a PICRC rate of 4.4%, at the lower end of the range estimated for colonoscopy (2.9 to 8.6%) at similar follow-up (34 vs. 36 months).¹⁵³ Similarly, the incidence of 0.64 PICRCs per 1000 person-years of follow-up is at the lower end of the range reported for colonoscopy (range from 0.78 to 2.9 cases per 1000 person-years in one review).¹⁶⁰ Importantly, although data were derived from various settings (from multicentre randomised trials to single-centre audits), heterogeneity was low ($I^2=0\%$), meaning that our estimates are consistent across the published literature. The low PICRC rate we found here is consistent with prior observational series showing similar detection rates of advanced neoplasia between CTC and colonoscopy.^{57,86} CTC also detected as many advanced neoplasms as colonoscopy in a Dutch randomised screening trial once all 6-9 mm polyps scheduled for CTC follow-up had been resected and undergone histological analysis.^{79,85} This high diagnostic performance clearly translates to excellent longer-term patient outcomes.

The optimum interval between CTC screening examinations is unknown currently but 60 months is recommended in the USA.⁹⁴ Although fewer data were available for this time threshold (only two studies, both from the same research group), we found PICRC rates remained low and were similar to rates at three years, meaning that the current approach is likely safe. Given that we found PICRC rates after CTC to be similar to those for colonoscopy, the 60-month interval may even be over-conservative. Therefore, the original C-RADS recommendation of a 5 to 10 year interval remains a viable strategy.⁹⁴ A frequently recommended screening interval for colonoscopy is 10 years and so it may be possible to extend the CTC screening

interval safely, thereby reducing programme cost and increasing acceptability. However, that there are no data to support such an approach presently, as there are no published series with sufficiently extended follow-up. Indeed, the impact of lower detection rates for small polyps may have a greater impact between 5- and 10-years post-CTC, since it takes many years for most adenomas to transition to CRC.¹²⁰

PICRCs were nearly three times more likely to be proximal than initially-detected cancers. The reason for this right-sided preponderance (which has also been reported for colonoscopy)¹⁵³ is likely multifactorial. Firstly, in several instances CTC did not employ faecal tagging, which is now universally recognised as a pre-requisite for good practice. We were unable to confirm that failure to use faecal tagging was associated with a higher PICRC rate, but this may be due to underpowering for this subgroup comparison. Secondly, right-sided tumours are more commonly associated with microsatellite instability and the serrated carcinogenesis pathway. Although sessile serrated lesions can be diagnosed by optimised CTC,⁷² historically they are considered harder to detect. In one randomised trial, CTC detected significantly fewer high-risk (large or dysplastic) serrated neoplasms than colonoscopy,⁶⁸ the specific subset that can progress rapidly to carcinoma.¹⁰ As radiologists learn how best to detect these lesions at CTC (e.g. surface coating by oral contrast tagging),¹⁷⁴ it is plausible that this excess of right-sided PICRCs will reduce.

The aetiology of PICRCs is also multifactorial; but, in most cases (61%), the culprit lesion was visible in retrospect and therefore potentially detectable. This is similar to colonoscopy, where many PCCRCs are due to perceptual error and thus

deemed preventable. For example, a pooled multi-cohort analysis of 9,167 patients identified 30 of 58 (52%) post-colonoscopy CRCs as potentially avoidable,¹⁵⁴ similar to our data for CTC. Just as JAG accreditation has improved colonoscopy quality and ADR (thereby lowering PCCRC), it is possible that targeted CTC accreditation and training for CTC radiologists could achieve similar.

We found that technical errors and failures of clinical management were less common, and genuinely CTC-occult lesions were very rare; just two of 28 cases. These findings highlight the need for radiologist training, robust patient management pathways and quality assurance processes to avoid these preventable cancers from accumulating. With optimised CTC, our data suggest that a 36-month PICRC rate of 1% is an achievable target.

Strengths of this study include adherence to published methodological and reporting recommendations, robust data extraction and quality assessment, and comprehensive review of the aetiology of PICRCs, including obtaining additional unpublished data from component study authors. This study also has limitations. Component studies rarely reported PICRC morphology, location and time to diagnosis. Follow-up duration varied between different studies and few included data beyond 36 months, with none exceeding 72 months. Studies rarely reported more than one of mean, median or maximum and minimum follow-up, meaning we were unable to conduct a sensitivity analysis to explore whether such inconsistent reporting has affected our summary estimates of PICRC incidence.

Individual patient data were not available for either detected CRC or PICRCs, meaning it was not possible to link patient-level or radiologist-level factors (such as

radiologist experience, or use of CAD to report) to PICRC rates. Although we aimed to explore the influence of patient, CTC technique, radiologist and institutional factors associated with higher PICRC rates, this was frequently impossible due to incomplete reporting and relative underpowering for such comparisons, meaning it is possible that important drivers of PICRCs have been undetected. Such missing data may also bias these comparisons, although since none of our factors chosen for meta-regression were statistically significant, this will have limited clinical impact. Nonetheless, evaluation of radiologist performance, and impact on PICRC rates is a potential avenue for future research.

Finally, this meta-analysis represents a synthesis of data from clinical trials and observational studies, which are likely derived from experienced, high-volume centres; whether similarly low rates would be replicated in large-scale epidemiological series is unknown. It is surprising (and concerning) that, to date, there are no published data linking national imaging databases to cancer registries; this is another important avenue for future research (discussed further in Chapter 12).

In summary, the estimated rate of post-imaging colorectal cancer (PICRC) 34 months after negative CT colonography is approximately 4.4%, or 0.64 per 1000 person-years of follow-up, at the lower end of the range reported for colonoscopy. PICRCs following CTC are more common in the right colon and most are due to perceptual errors. Improved radiologist training and quality assurance of imaging will likely reduce PICRC rates, as most are potentially avoidable.

Chapter 5 How many and how fast should we report CT colonography?

Summary and contribution statement

In the previous Chapter, I highlighted the contribution of perceptual errors to interval cancer rates after CT colonography (CTC). This data suggests there is a performance gap that could be addressed to improve CTC reader accuracy. A possible contributing factor to CTC accuracy is the time spent reviewing each scan. In this Chapter I present an observational study conducted to determine whether polyp detection at CTC is related to the number of scans reported per day and the time spent on each scan.

Associate Professor Andrew Plumb (UCL), Professor Steve Halligan (UCL), Dr David Burling (St Mark's Hospital, Harrow) and I conceived this study. I coordinated the data collection and analysis which was performed by Mr Michael North and I, with statistical assistance provided by Dr Plumb. The manuscript draft was initiated by me and completed by Dr Plumb during my maternity leave, with contributions from Dr Burling and Professor Halligan. A version of this chapter has been published as follows:

Computed tomographic colonography: how many and how fast should radiologists report? Obaro AE, Plumb AA, North MP, Halligan S, Burling DN (2019) European Radiology. DOI: 10.1007/s00330-019-06175-y

Introduction

CT colonography (CTC) is both complex and time-consuming to interpret. Moreover, it is fatiguing, as the interpretive task (of 'flying' or scrolling through the colon) is repetitive, and the majority of examinations are negative for the primary target condition (colorectal cancer or large polyps),^{57,58,67} a phenomenon that is known to reduce vigilance.¹⁷⁵ Anecdotally, radiologists often admit that they find it tiresome to report more than a handful of CTC examinations in a given reporting session, and that their concentration often wavers if they attempt to do so. It is therefore tempting to interpret CTC rapidly, particularly for the final few examinations in a given reporting session. However, this may well reduce detection rates; in a laboratory environment, more rapid fly-through at endoluminal CTC reduces both the proportion of colonic mucosa viewed by the radiologist and the polyp detection rate.¹⁷⁶ For colonoscopy, endoscopists with shorter withdrawal times (i.e. providing less time to inspect the colon) have lower adenoma detection rates (ADR)¹⁷⁷⁻¹⁷⁹ and higher interval cancer rates.¹⁷⁹ Moreover, ADR tends to drop towards the end of the day and even towards the end of an individual colonoscopy list,^{180,181} implying a 'fatigue effect' when performing multiple examinations consecutively. Whether the same is true for CTC is unknown.

Therefore, this study aimed to determine if polyp detection rates (PDR) and positive predictive value (PPV) at CTC are associated with, (a): the number of CTC examinations interpreted by a radiologist on any given day (i.e. a fatigue effect) and, (b); the length of time radiologists spend on interpretation (as a proxy for completeness of image scrutiny).

Materials and Methods

Data collected

This retrospective study used routinely-collected data and was approved as a service evaluation by the relevant departments. We collected data from the Radiology Information Systems (RIS) for all CTC examinations reported by seven gastrointestinal radiologists at two centres, between January 2013 and December 2015 (Centre 1), and January 2012 and December 2015 (Centre 2). We only included radiologists who had interpreted more than 200 CTC examinations during this period, to ensure percentages could be calculated with sufficiently narrow 95% confidence intervals to be meaningful. All radiologists had pre-existing CTC expertise; each was a gastrointestinal radiologist, had undergone specific training and had interpreted >500 examinations.

In accordance with international guidelines,⁵³ both centres employed a similar CTC protocol during this period, (normal-dose post-contrast supine and low-dose prone scans after combined purgation and faecal tagging, intravenous spasmolytics (hyoscine butylbromide) and automated carbon dioxide insufflation). For each radiologist and the corresponding timeframe, we extracted, (a); the date and time of report verification for all examinations they had reported and, (b); the full text of any CTC examinations reported. Subsequently, we inspected the CTC reports to determine if the radiologist had, or had not reported a ≥ 6 mm polyp or colorectal cancer. We used each hospital's patient record system to ascertain whether or not patients with a positive CTC underwent confirmatory testing (i.e. endoscopy or surgery), and, if so, whether the CTC finding was a true-positive or false-positive.

We regarded the presence of any endoscopically- or surgically-proven polyp or cancer as a true-positive CTC finding, regardless of location or final histology (i.e. a per-patient match as per existing convention for correlation between CTC and colonoscopy findings). For each radiologist, we estimated their potential 'referral rate' (defined as the proportion of CTC examinations in which they reported a ≥ 6 mm polyp or cancer, i.e. that might be expected to precipitate a referral for colonoscopy), their positive predictive value (PPV; defined as the percentage of cases in which a polyp or cancer was ultimately found if confirmatory testing was done), and their polyp detection rate (PDR; defined as the proportion of cases in which a polyp or cancer was ultimately confirmed, relative to the total number of cases reported). For all these proportions (expressed as percentages), 95% confidence intervals were estimated using the Wilson method.¹⁸²

Estimation of time taken for CTC interpretation

Using the extracted dates and times of each radiologist's complete reporting record for this period, for any given CTC examination, we recorded whether it was the first, second, third (and so on) CTC study reported by the radiologist on that particular day. We also estimated the length of time taken to interpret each CTC examination by deducting the time of report verification for a given CTC study from the time at which the immediately preceding report was verified. For example, if a radiologist verified a chest radiograph at 9:00am, and their next report verification was a CTC examination at 9:30am, we assumed that the radiologist had spent 30 minutes interpreting the CTC. If a CTC examination was the first report verified on a particular day, it was retained for the purposes of estimating each radiologist's referral rate, PPV and PDR, but not included when estimating reporting time (since

there was no immediately preceding examination to calculate interpretation time). Since CTC examinations that are positive for polyps or cancers take longer to interpret than those that are negative, for each radiologist we calculated their negative interpretation time (by analogy with the colonoscopic negative withdrawal time), by taking the mean of estimated CTC interpretation time for cases in which no polyp was reported. This better reflects image scrutiny alone (i.e. a normal case) rather than combine both scrutiny and interpretation (e.g. detection followed by characterisation and measurement). To allow for interruptions and batch verification of multiple reports dictated at an earlier time, we set plausible limits on CTC interpretation times; any CTC that appeared to take less than 5 or more than 60 minutes were assumed to have been pre-reported (and therefore re-checked or verified), or reported after an interruption respectively, and were excluded. Both sites had both 2D and 3D interpretation software available, although at one site this was a thin client launched from the PACS, whereas at the other it was a standalone workstation. Computer-aided detection (CAD) was not used routinely at either site. Since the two institutions investigated had different CTC interpretation workflow (e.g. availability of CTC workstations), voice recognition systems and RIS software, we presented negative interpretation time as a proportion relative to their colleagues at the same centre, by dividing by the centre mean.

Analysis

To assess the effect of interpreting multiple CTC examinations on a given day, we calculated referral rate and PDR grouped by the sequence in which the CTC was reported (i.e. first CTC reported that day, second, etc). To estimate effect size and

statistical significance, we used multilevel logistic regression (three levels: CTC, radiologist, centre), with the presence of a polyp as the binary outcome variable and sequence in which the CTC had been performed as the main explanatory variable. To assess the effect of interpretation time on polyp detection, we compared the negative interpretation time for each radiologist with their referral rate, PDR and PPV. We assessed statistical significance using linear regression, with referral rate, PDR and PPV as the outcome variables and negative interpretation time as the explanatory variable. All analysis was performed using R version 3.5.1 for Mac.¹⁶¹

Results

Radiologist referral rate, PDR and PPV

Overall, 5191 CTCs were reported by seven radiologists. Individual radiologist referral rate, PDR and PPV is shown in Table 5.1. There was a moderate spread in referral rate and PDR, ranging from 13.1% to 27.5% for referral rate and 7.8% to 16.3% for PDR. PPV was grouped more tightly, ranging from 83.3% to 96.1%. The radiologist with the highest PDR had the lowest PPV, and the radiologist with the highest PPV had the fourth lowest PDR, but overall, there was no consistent relationship between radiologist-level PPV and PDR (weak negative correlation, Pearson $r=-0.51$, $p=0.25$). Overall, both referral rate and PDR was higher at centre 1 than centre 2 (referral rate: 19.7% vs 16.1%, $p=0.0019$; PDR: 12.2% vs 9.5%, $p=0.0039$), but with lower PPV (85.3% vs 93.5%, $p=0.0018$).

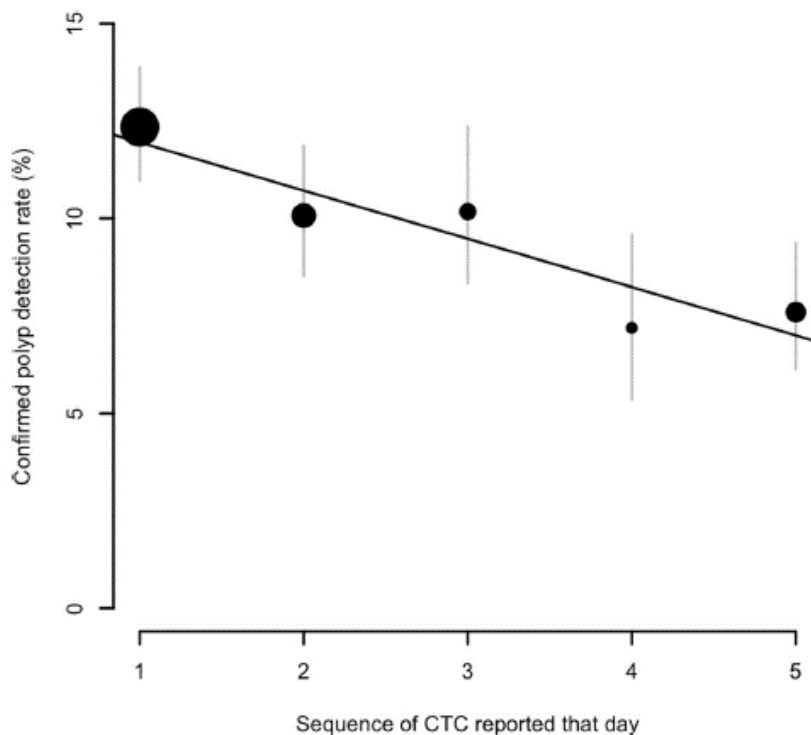
Table 5.1: Number of CTC studies, referral rate, confirmatory testing, positive predictive value (PPV) and polyp detection rate (PDR), split by radiologist and study centre

Radiologist	Number of CTC studies interpreted	Number interpreted as positive	Referral rate % (95% CI)	Number undergoing confirmatory testing	Number with polyp or cancer confirmed	PPV % (95% CI)	PDR % (95% CI)
1	338	93	27.5 (23.0 to 32.4)	66	55	83.3 (72.6 to 90.4)	16.3 (12.7 to 20.6)
2	268	51	19.0 (14.8 to 24.2)	43	37	86.0 (72.7 to 93.4)	13.8 (10.2 to 18.4)
3	964	165	17.1 (14.9 to 19.6)	115	99	86.0 (78.6 to 91.2)	10.3 (8.5 to 12.4)
Centre 1 totals	1570	309	19.7 (17.8 to 21.7)	224	191	85.3 (80.0 to 89.3)	12.2 (10.6 to 13.9)
4	461	106	23.0 (19.4 to 27.0)	74	67	90.5 (81.7 to 95.3)	14.5 (11.6 to 18.0)
5	694	91	13.1 (10.8 to 15.9)	60	54	90.0 (79.9 to 95.3)	7.8 (6.0 to 10.0)
6	410	81	19.8 (16.2 to 23.9)	51	49	96.1 (86.8 to 98.9)	12.0 (9.2 to 15.5)
7	2056	305	14.8 (13.5 to 16.6)	182	173	95.1 (90.9 to 97.4)	8.4 (7.4 to 9.8)
Centre 2 totals	3621	583	16.1 (14.9 to 17.3)	367	343	93.4 (90.5 to 95.6)	9.5 (8.6 to 10.5)
Grand total	5191	892	17.2 (16.2 to 18.2)	591	534	90.4 (87.7 to 92.5)	10.3 (9.5 to 11.1)

Diagnostic yield

The rate of positive CTC examinations declined with increasing numbers interpreted on a particular day (Figure 5.1).

Figure 5.1: Confirmed polyp detection rate for each CTC reported in a given day



The area of the marker is proportional to the number of scans in each category; grey bars indicate 95% confidence intervals. The line corresponds to a fitted linear trend

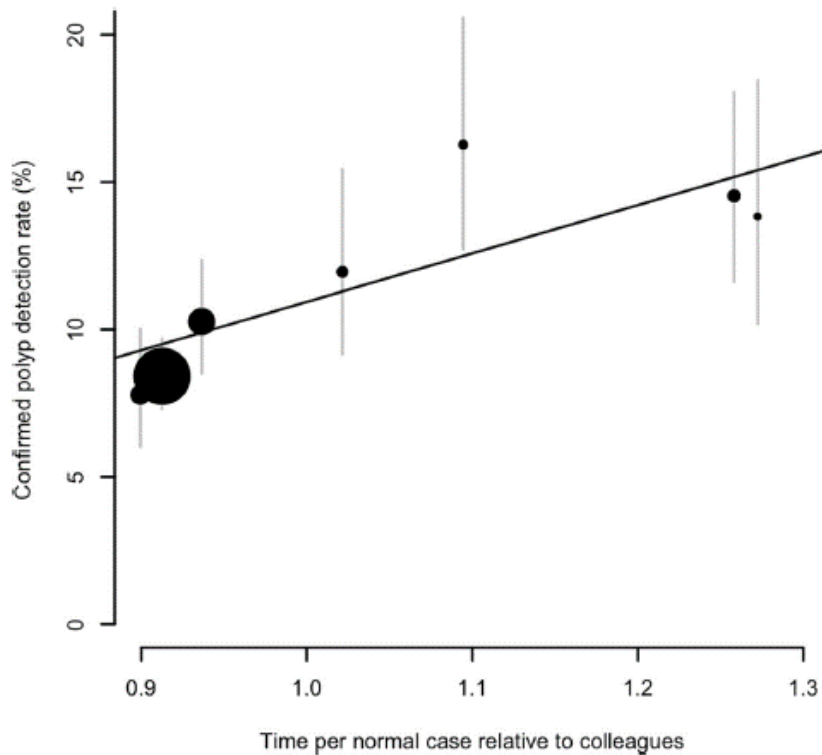
For the first CTC study reported, 21.7% (95% CI: 19.9 to 23.6%) were believed positive for ≥ 6 mm polyps or cancer by the radiologists, with 12.3% (95% CI: 11.0 to 13.9) ultimately having polyps or cancer confirmed. By the time of the fifth (or greater) CTC interpretation, only 13.7% (95% CI: 11.7 to 15.9) were interpreted as abnormal, with a mean PDR of 7.6% (95% CI: 6.1 to 9.4). Therefore, an approximately 40% decline in polyp detection occurred during the day when multiple CTC studies were reported. This was highly statistically significant, with an

odds ratio of 0.93 (95% CI 0.88 to 0.97, $p < 0.001$) for referral rate (i.e. abnormality identified at CTC) and an odds ratio of 0.93 (95% CI: 0.90 to 0.97, $p < 0.001$) for polyp detection (i.e. confirmed at endoscopy or surgery). Therefore, for each successive CTC study reported on a given day, the odds of both identifying and confirming a polyp at CTC dropped by 7%. There was no consistent effect of reporting multiple CTC examinations on PPV, which remained consistent at around 90% regardless of examination sequence ($p = 0.11$).

Negative interpretation time and detection rates

329 CTCs were reported as the first examination on a given day, and so the interpretation time for these could not be estimated. For the remaining 4862 studies, the mean time taken to interpret a negative CTC examination was 30.5 minutes (Centre 1: 17.4 minutes; Centre 2: 34.6 minutes). Overall, there was a weak positive association between negative reporting time and PDR; radiologists who spent longer interpreting cases that they ultimately called normal detected more polyps than those who reported more quickly (Figure 5.2).

Figure 5.2: Confirmed polyp detection rate against the average length of time spent by a radiologist on interpreting a negative case (i.e. negative interpretation time)



Each marker corresponds to a single radiologist; the area of the marker is proportional to the number of scans reported by that radiologist, with grey bars indicating 95% confidence intervals. The line corresponds to a fitted linear trend

This effect was small but statistically significant ($p=0.028$), with the regression model suggesting that each 16% increase in interpretation time was associated with a 1% increase in detection rate. There was no clear relationship between negative interpretation time and PPV ($p=0.478$).

Number of CTCs interpreted, and time spent reporting

As the number of CTC studies reported on a given day increased, the mean time spent interpreting each study reduced at Centre 1 (reducing from a mean of 19.9 minutes for scan 1 to a mean of 16.4 minutes by the time 5 or more scans had been interpreted), a statistically significant reduction ($p=0.0012$). Conversely, the negative interpretation time remained constant at Centre 2, irrespective of how many scans had been reported that day ($p=0.59$).

Discussion

CTC interpretation is time-consuming and fatiguing. We found that as radiologists interpreted more CTC examinations on a given day, their detection rate dropped; by roughly 40% after 5 or more studies had been reported. Moreover, radiologists who spent longer interpreting cases that they ultimately called negative had higher detection rates than their colleagues who interpreted more quickly, with no corresponding detriment to their positive predictive value. These data strongly suggest that radiologists reporting CTC must be protected from pressures to report too quickly, or for too long – or missed pathology will be the consequence.

Although, in most cases, the primary goal of CTC is to confirm or refute colorectal cancer (CRC), it also represents an opportunity to reduce future CRC incidence by detection and subsequent removal of precursor adenomas or serrated lesions. Accordingly, radiologists interpreting CTC must be vigilant not only for large masses that may underpin symptoms, but also for smaller polyps; otherwise, patients may return in the future (usually many years later) with a post-investigation colorectal cancer (PICRC).¹⁸³ Indeed, as determined in Chapter 4, the majority of PICRCs occurring after CTC are visible in retrospect, i.e. are due to perceptual errors due to an overlooked or mis-categorised lesion.¹⁸⁴ Such errors will be impossible to prevent entirely, but systems and methods that diminish this clinical and medicolegal risk would improve patient care substantially. Our findings suggest that relatively simple changes to radiologist workflow might be valuable; avoiding fatigue by reducing the number of CTC studies reported consecutively and introducing a minimum 'negative interpretation time' before a scan is deemed normal. This is entirely reasonable because eye-tracking experiments show that

over-rapid endoluminal fly-through reduces the amount of colonic surface that a radiologist can bring into their central vision, thereby reducing the thoroughness of their interpretation.¹⁷⁶ Slowing down would mitigate this risk. A minimum interpretation time of 20 minutes per case would seem reasonable, since this was the average time taken for the first scan interpreted each day at the quicker of the two centres, with 30 minutes per negative case being a desirable (and achievable) standard.

Of note, in colonoscopy, the importance of prolonging inspection of the colonic mucosa to maximise detection has been recognised for many years.¹⁷⁸ Gastroenterologists who spent less than 6 minutes withdrawing the colonoscope had detection rates that were less than half that of their colleagues spending longer.¹⁷⁸ More recently, data from the BCSP show that extending the examination towards 10 minutes yields further benefits in detection rate,¹⁷⁷ and consequent lower post-colonoscopy colorectal cancer (PCCRC) rates than those who withdraw the scope (too) rapidly.¹⁷⁹ Negative withdrawal time (i.e. calculated only for cases where no polyps are found) is now recognised as a key performance indicator (KPI) for the quality of many colonoscopy services, including in the UK,¹³¹ Europe,¹⁸⁵ and the USA.¹⁸⁶

The concept of slowing down to improve accuracy is not new, nor is it specific to CTC. Requirements to report large numbers of examinations rapidly (to reduce wait times and reporting backlogs) must be balanced against the risks of making errors. If scans are acquired but languish on the PACS remaining unreported, this is a worse situation than them being reported, even suboptimally. This clinical risk has been highlighted in England by the Care Quality Commission (CQC).¹⁸⁷ On the

other hand, patients will rightly not accept that their cancer or polyp was missed due to time pressures and underfunding. It is highly iniquitous and counter-intuitive that a patient may have colonoscopy, where they receive the undivided attention of an accredited endoscopist who will examine their colon for a minimum length of time (i.e., the negative withdrawal time), or – based on local pathways or the whim of a referring doctor – instead undergo CTC where the radiologist may be interrupted repeatedly and without any minimum standard for the duration of interpretation. Such infrastructural and process shortcomings highlight the need for robust minimum standards that protect both patients and radiologists in the face of increasing demand.

We also found that reporting multiple CTC examinations in sequence was associated with progressive deterioration in detection, suggesting a ‘fatigue effect’. This phenomenon has been described in many other areas, including colonoscopy. The adenoma detection rate (ADR) falls as colonoscopy lists progress,^{180,181} and is typically higher in the morning than evening. However, this finding is not universal, and some studies have found the effect either weak¹⁸⁸ or absent entirely.¹⁸⁹ Nonetheless, anecdotally, many radiologists become fatigued after reporting several CTC examinations consecutively, and avoid doing so where possible. Given our findings, it may be prudent to avoid reporting large numbers (4 or more) of CTC without a break. A four-hour session of approximately 8 CTC studies reported in two blocks with a half-hour break would seem an appropriate guideline, since it permits both the minimum negative interpretation time and no more than four cases criteria to be met.

This study has several limitations. Firstly, we investigated just two tertiary care centres, and only 7 radiologists, which may not represent wider practice. Secondly, the data are retrospective and observational, and therefore it is not possible to exclude bias. For example, scans interpreted earlier in a sequence may have been highlighted to the radiologist for prioritisation (for example, marked as 'urgent' on the RIS), although it was the practice at both institutions to report in date order. Even so, if we ignore fatigue, it is difficult to explain why the effect of scan sequence was consistent across two centres with different workflows and for as many as five successive scans. Thirdly, we were forced to make some assumptions when estimating radiologist negative interpretation time; specifically, calculating the time spent interpreting a CTC study by using the time at which the report was verified and relating this to the immediate prior report; and excluding some reports with implausibly long or short interpretation times. The reporting time also includes time spent scrutinising the image for extracolonic findings, which may partly explain the relatively large difference in average interpretation time between the two centres. We mitigated against this by using each radiologist's negative interpretation time normalised to the centre average, but this may have altered the size of the effect that we observed.

In summary, in a retrospective observational study from two NHS hospitals we found that the proportion of positive CTC examinations and polyp detection rates reduced as radiologists reported multiple examinations, suggesting a 'fatigue effect'; and radiologists with longer interpretation times had higher polyp detection rates with no corresponding reduction in positive predictive value. Recommended reporting times now form part of the British Society of Gastrointestinal and

Abdominal Radiology (BSGAR) and Royal College of Radiologists (RCR) standards of practice for CTC, with an advised minimum standard of ≥ 20 minutes average interpretation time and an aspirational target of ≥ 25 minutes.¹²¹ Ensuring that new readers are advised of these targets during their CTC interpretation training, as discussed in Chapter 7, will help to ensure that they are optimising their chance of an accurate read. CTC services also have a responsibility to protect their radiologists and patients by removing the need to report too fast or for too long, thereby optimising the work environment and minimising the chances of perceptual error.

Chapter 6 Effectiveness of CT colonography interpretation training methods

Summary and contribution statement

In next two chapters I review the impact of CTC interpretation training and discuss best practise principles for delivering such training. This work was initially conducted at the design phase of the subsequent randomised trial evaluating training methods (Section C) but has been updated and formalised for the purposes of this thesis report.

I performed all of the work in this chapter. The draft manuscript was edited with advice from the thesis supervisor, Dr David Burling (St Mark's Hospital, Harrow) and Dr Paul McCoubrie (Southmead Hospital), and has been published as follows:

Effectiveness of training in CT colonography interpretation: Review of current literature. Obaro AE, McCoubrie P, Burling D, Plumb AA (2022). Seminars in Ultrasound, CT and MR. DOI: 10.1053/j.sult.2022.06.002

Introduction

Interpretation of CTC images is time-consuming and differs in technique and duration from routine abdominopelvic CT. Readers therefore require additional skills and training to achieve adequate diagnostic accuracy. Consequently, it is recognised that specific training in CTC interpretation is necessary for accurate independent reporting.

Lack of training in CTC interpretation will lead to perceptual errors and missed colorectal polyps and cancers, which in turn contributes to poorer patient outcomes. There is currently no consensus on the most effective method to train readers in CTC interpretation. Many current guidelines and standards for the practice of CTC advocate a minimum case number as the main training requirement.^{121,190,191} However, they do not provide details regarding the distribution of abnormalities that should be reviewed. Moreover, there is wide variation in the number of training cases that is regarded as a suitable basic training requirement, with no clear logic as to why these numbers were selected. Although many studies have been conducted to assess the impact of interpretation training on CTC readers, these have not been comprehensively reviewed or incorporated into societal guidelines for CTC training. In this chapter, I review: (a) the current international consensus guidance for CTC training prior to independent practice and (b) the published literature regarding training methods for CTC interpretation. In Chapter 7, I draw on these data and the educational literature to make recommendations for best practice in CTC interpretation training. The effectiveness of these training methods for UK radiologists will then be tested via the cluster randomised controlled trial, described in Section C.

Methods

Ethical permission is not required by University College London for literature review or subsequent data synthesis.

Current International CTC Training Guidelines

I performed an internet search for CTC training guidelines from the 10 most populous countries according to the World Bank.¹⁹² Search terms included the country name and variations of 'CT colonography', 'CTC', 'CTC training', 'CTC accreditation', 'CTC guidelines', and 'radiology society' or 'college'. In addition, where they could be identified, I searched individual country or region websites, as well as regional or international radiology organisations which were known to have previously published guidance regarding CTC. Where references were identified regarding CTC training guidelines or minimum standard stipulations for readers, these were retrieved, and the source information interrogated.

Literature review of training methods for CTC interpretation

Searching PubMed, I used the following Medical Subject Headings (MeSH) and free-text terms relating to CTC training and performance: (1) (CT OR comput* AND tomogra*) AND (colonograp* OR virtua* AND colono*); (2) train* OR test* OR perform* OR experien* OR error*; (3) 1 AND 2. Inclusion criteria were any type of reader performance or diagnostic accuracy study assessing radiologist diagnostic accuracy or yield either before and after an interpretation training intervention, or simply after interpretation training. The updated search was restricted to dates Jan 1, 2000 to Dec 31, 2020, and only articles published in English were eligible. Excluded studies were those that assessed reader sensitivity

without a training intervention of any kind, those that only assessed the performance of computer-aided detection (CAD) and those that did not involve CTC interpretation or report sensitivity. I screened the abstracts, and the full text of potentially eligible studies was retrieved for further assessment. In addition to the retrieved articles, I examined reference lists from relevant studies.

After confirming eligibility, the following characteristics were extracted for each article: (a) author and publication year; (b) number of sites, readers and faculty participating in the training intervention; (c) training components of the intervention; (d) background of readers undergoing training (e.g. radiologist or radiographer/technician); (e) reader and trainer career CTC experience; (f) number of test cases completed per reader; (g) number of lesions (polyps and/or colorectal cancers) assessed in test(s) both pre- and post-training intervention; (h) characteristics of such lesions; and (i) summary measures of the effect of training on reader diagnostic accuracy, including sensitivity and specificity where available. If data were not available in the original research article report, supplementary materials were examined, but no additional data was sought from primary research authors.

Relevant data were extracted to a Microsoft Excel spreadsheet and summarised with descriptive statistics. Due to considerable heterogeneity of initial reader experience, pre-training diagnostic accuracy and training methodology, quantitative synthesis (meta-analysis) was not attempted.

Results

International CTC training guidelines

I identified several national and international regulatory bodies that have established training recommendations and guidelines for CTC readers (Table 6.1). These include standards which refer to both the CTC service ('service level guidance'), and the competency and performance of CTC readers ('reader level guidance').

Although the importance of training in CTC interpretation prior to independent practice is recognised, none of these bodies mandate the completion of a specific programme or training package prior to independently reporting CTC. The Royal Australian and New Zealand College of Radiologists (RANZCAR) is the only body to accredit (or certify) 'CTC specialists', a status achieved by (a) fulfilling minimum CTC training requirements stipulated by the College, and (b) maintaining an audited CTC logbook. The new Joint Guidance from the British Society of Gastrointestinal and Abdominal Radiology (BSGAR) and the Royal College of Radiologists (RCR) is the only guidance to stipulate objective, quantitative performance indicators for CTC readers, including targets for polyp identification rates and positive predictive values.¹²¹ However, this primarily applies to readers who have already been trained and are reporting in routine practice, rather than those undergoing initial basic training.

Table 6.1: Comparison of international CTC interpretation training guidelines for gastrointestinal radiologists

Metric		International Guideline				
		BSGAR-RCR (2021) ¹²¹	ESGAR (2013) ⁵³	ACR (2019) ¹⁹⁰	CAR (2010) ¹⁹³	RANZCR (2013) ¹⁹¹
Performance indicator	Interpretation time	Min: >20 minutes Asp: >25 minutes	NS	NS	NS	NS
	Polyp identification rate (PIR)	Min: ≥6 mm polyps identified in >13% patients Asp: PIR >16%	NS	NS	NS	NS
	Positive Predictive value	Min: >80% Asp: >90%	NS	NS	NS	NS
Training	Training prior to independent reporting	Min: >175 validated cases. Asp: >300 validated cases	No consensus but recognise that 175 validated cases may be insufficient	Min >50 validated cases. Training on examination technique, pitfalls	Min >50 validated cases. Training on technique, anatomy, pitfalls, complications, pathogenesis, epidemiology	Min >50 validated cases and 10 live cases Training on technique, anatomy, limitations, pathogenesis
	Interpretation method	Competence in 2D and 3D techniques. Double reading as needed*	Competence in 2D and 3D techniques	Competence in 2D and 3D techniques. Double reading*	Competence in 2D and 3D techniques. Consider double reading*	Competence in 2D and 3D techniques
	Maintenance of competence	Min >100/year Asp >175/year	NS	Supervision and double reading by expert. Testing with feedback 25 cases/year	100 cases/year	30/year (recorded in RANZCR CTC logbook)
	Audit requirement	Every 2 years	NS	NS	'Regular'	Every 3 years
	CTC accreditation	No	No	Contributes to National Radiology Data Registry (NRDR)	No	Yes: CTC Specialist Register

BSGAR-RCR: Joint Guidance from the British Society of Gastrointestinal and Abdominal Radiology and The Royal College of Radiologists. Standards of practice for computed tomography colonography

ESGAR: European Society of Gastrointestinal and Abdominal Radiology. ACR: American College of Radiology

CAR: Canadian Association of Radiologists. RANZCR: The Royal Australian and New Zealand College of Radiologists

Min: minimum target. Asp: aspirational target. NS: not specified

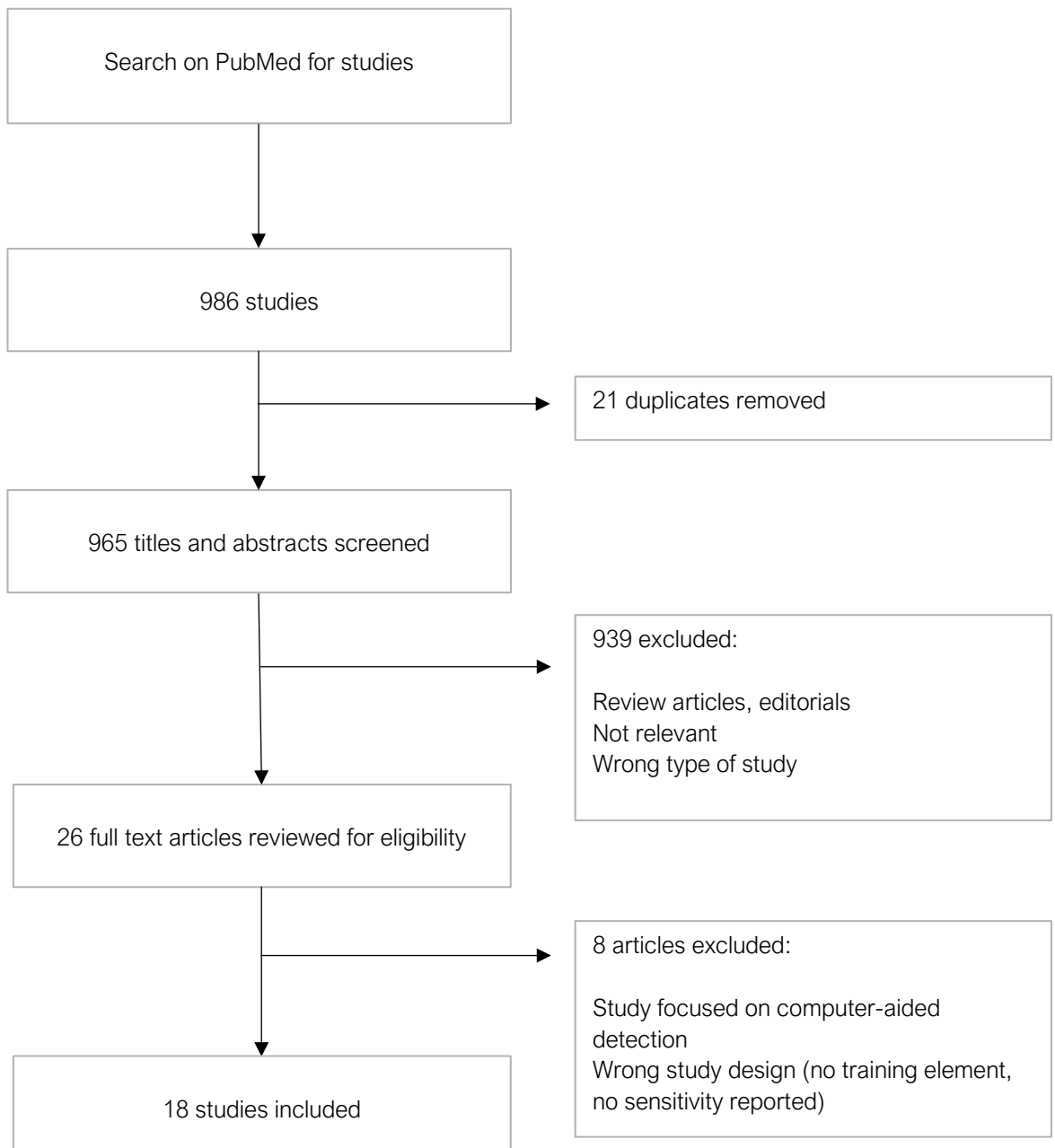
*Double reading suggested for inexperienced readers. Min: minimum target. Asp: aspirational target

There is no consensus on the minimum number of validated scans to be interpreted before achieving reporting competency, and recommendations vary widely between published guidelines. For example, the ACR, CAR and RANZCR all suggest a minimum of 50 training cases, whereas the ESGAR were unable to form a consensus recommendation, and the BSGAR-RCR recommends a minimum of 175 validated cases (by endoscopy or surgery), with over 300 training cases as an aspirational standard.

Study and reader characteristics

The initial search identified 986 abstracts, which was subsequently refined to 26 full text studies for further analysis (Figure 6.1).

Figure 6.1: Study selection



Of these, eight did not include a training intervention or were focused on CAD performance and were excluded, leaving 18 articles for data extraction and analysis. Table 6.2 provides a summary of the included articles, involving 233 readers at 74 centres identifying 1118 lesions.

Where specified, most (85% [11/13]) of these studies were focused on training novice or inexperienced readers (0 to 500 CTC cases),¹⁹⁴⁻²¹⁰ apart from one multi-centre study, which trained experienced readers who had reported more than 500.²¹¹ Most (55% [10/18]) of these studies only assessed diagnostic accuracy after the training intervention (rather than pre- and post-training). Three studies assessed the effect of training with and without CAD used concurrently during interpretation, and all observed some benefit of CAD use.^{201,208,209} Five studies measured interpretation times before and after training, and all except one,²⁰¹ observed a decrease in interpretation time.^{194,196,198,202}

Table 6.2: Summary of CT colonography interpretation training and testing studies between Jan 2000 and Dec 2020

Author	No. Sites	No. Readers	Training components	No. faculty (experience)	Type of readers (experience)	No. test cases per reader	No. lesions in test (characteristics)	Sensitivity (Sn) and specificity (Sp) after training*
Arnesen et al 2005 ²⁰⁴	NS	1	Analysis of 12 CTCs and 12 colonoscopies and supervised visit to a CTC centre	-	1 radiologist (NS)	105 cases with sequential colonoscopy. Normal and 41 abnormal cases.	90 lesions (1 cancer)	Sn: 67% for ≥ 5 mm; 75% for ≥ 10 mm Sp: 84% for ≥ 5 mm; 95% for ≥ 10 mm 55% of false positives due to perceptual error.
Bodily et al 2005 ²⁰⁵	NS	7	Independent review of teaching file of 61 partial CTC datasets focused on on lesion appearance/pitfalls. Didactic tutorials.	-	5 medical students (0 cases) 2 technologists (0 cases) Compared to 15 radiologist controls in Fidler et al 2004. ¹⁹⁵	50 cases with sequential feedback. Technologists repeated test at 6 weeks. Normal and abnormal cases.	35 lesions (8 cancers 20-50 mm; 25 adenomas, 2 hyperplastic polyps 5-50mm)	Sn: 45% (non-radiologists) vs 63% (radiologists) for 5-9 mm polyps. Sp: 79% (non-radiologists) vs 74% (radiologists). Similar Sn and Sp between radiologists and non-radiologists 5-9 mm lesions.
Dachman et al 2008 ¹⁹⁴	1	7	1-day course - lectures on technique, hands-on teaching on 10 cases. 5-10 hrs self-directed reading. Self-study 61 partial cases Observe 3 cases 10 cases with sequential unblinding	1 expert (≥ 500 cases)	1 GI resident (0 cases) 6 medical students (0 cases)	3 sets of 20 cases with sequential unblinding and post-case feedback over 5-8 weeks. Normal and abnormal cases.	93 polyps (61 polyps 6-9 mm; 32 polyps ≥ 10 mm)	Sn: 77% for 6-9 mm polyps ($p > 0.05$); 93% for ≥ 10 mm polyps Sp: 92%. FPs decreased with each 20-case set ($p = 0.04$). Read time decreased ($p = 0.001$).
Fidler et al 2004 ¹⁹⁵	12	15	Independent review of 61 partial CTC datasets focused on on lesion appearance/pitfalls	-	15 GI radiologists (0 to 'limited' cases)	50 cases with sequential review of colonoscopy/histology report. Normal and abnormal cases.	35 lesions (8 cancers 20-50 mm; 25 adenomas; 2 hyperplastic polyps 5-50mm)	Sn: 76% for sessile polyps; 63% for pedunculated; 32% for flat. Sp: 80%. More errors of detection (55%) than characterisation (45%).
Fletcher et al 2010 ²¹¹	15	15	1-day course - hands-on teaching on 15 cases and 27 partial cases then Test 1. Optional second day if Test 1 failed, with retraining on 30 cases	2 experts (NS) 1 app specialist (NS)	4 readers (≥ 500 cases) 11 readers (< 500 cases)	Test 1: 20 cases after 1-day training. Test 2: 8 individualised cases including up to 6 missed cases from Test 1. Normal and abnormal cases in both tests.	Test 1: 25 polyps ≥ 5 mm (5 cancers; 19 adenomas; 1 NS) Test 2: individualised	Sn: 16% difference between Test 1 vs Test 2 ($p < 0.001$). Sp: 1.5x increase in odds of detecting an abnormal case for every 50-case increase in experience and formal training ($p = 0.025$).

Author	No. Sites	No. Readers	Training components	No. faculty (experience)	Type of readers (experience)	No. test cases per reader	No. lesions in test (characteristics)	Sensitivity (Sn) and specificity (Sp) after training*
Gluecker et al 2002 ¹⁹⁶	1	4	24 cases read followed by review of endoscopy results	-	2 radiologists (NS) 2 gastroenterologists (NS)	26 cases. Normal and abnormal cases.	29 lesions (18 polyps \leq 5mm; 5 polyps 6-9 mm; 6 polyps > 9 mm)	Sn: 63% to 45-64% for >5mm polyps, post-training. Sp: improved from 42-58% to 79%; improved with increasing experience (p=0.02). Read time decreased (p=0.002).
Halligan (ESGAR) et al 2007 ²⁰³	9	28	Local training of 19 novices with interpretation of 50 cases and feedback	9 experts (median 750 cases)	9 GI radiologists (\leq 10 cases) 10 technologists (\leq 10 cases)	40 cases over 2 days individualised per centre. Normal and abnormal cases.	24 lesions (8 cancers; 12 polyps \geq 10 mm; 4 polyps 6-9 mm)	Sn: 51% (trained radiologists) vs 66% (experts), p=0.007, all lesion sizes. Sp: Accuracy- 67% (trained radiologists) vs 74% (experts), p=0.17.
Haycock et al 2010 ²⁰⁶	NS	49	4-day course with small group lectures, hands-on training on technique and interpretation	2 experts (>1500 cases)	49 radiographers (NS)	5 baseline and 5 post-training cases. All abnormal cases.	24 lesions (6 cancers; 2 polyps \leq 5mm; 7 polyps 6-9 mm; 9 polyps \geq 10 mm)	Sn: 49 to 60% improvement for \geq 10 mm polyps/cancers (p=0.002) post-training. Sp: 55% to 71% improvement (p<0.001)
Heresbach et al 2011 ¹⁹⁷	26	28	2-day course - lectures/hands-on teaching on 52 cases with 'hard-to-detect' lesions and sequential feedback	3 experts (\geq 300 cases)	28 GI radiologists (NS)	Median case volume: 18 Normal and abnormal cases.	Median # polyps for detection: 19	Sn: 62% for \geq 6 mm lesions. Baseline Sn of \geq 6 mm polyps in training set was only predictor of subsequent per-patient accuracy. Sp: 94% for average risk patients
Jensch et al 2007 ²⁰⁷	NS	4	20 cases reviewed with feedback, for radiographers	1 expert (NS)	1 radiologist (>50 cases) 1 radiology trainee (>50 cases) 2 radiographers (0 cases)	145 cases with sequential colonoscopy. Normal and abnormal cases.	317 lesions (31 polyps \geq 10 mm (including 2 cancers); 29 polyps 6-9 mm; 257 polyps \leq 5 mm)	Sn: 81% (radiologists) vs 87% (radiographers) for \geq 6 mm. Sp: 71% (radiologists) vs 67% (radiographers) for \geq 6 mm. Comparable Sn and Sp between radiologists and radiographers.
Liedenbaum et al 2011 ¹⁹⁸	1	9	Self-directed reading and lectures. Independent hands-on training on 4 cases with tutor for troubleshooting. Additional training on pitfalls with 40 images and MCQs for 5 readers.	1 expert (\geq 400 cases)	1 GI radiologists (0 cases) 3 radiology residents (0 cases) 2 non-radiology researchers (0 cases) 3 technicians (0 cases)	4 sets of 50 cases over 4-6m. Sequential computer feedback after each of the first 25 cases. Normal and abnormal cases.	160 lesions \geq 6 mm (10 cancers; 62 pedunculated polyps; 74 sessile; 14 flat)	Sn: 91% for \geq 6 mm lesions at 4th set post-training (p=0.018). Sn of novice readers equalled experienced readers after 164 cases. Sp: 86% at 4th set post training. Read time decreased between 1st and 2nd sets (p<0.001).

Author	No. Sites	No. Readers	Training components	No. faculty (experience)	Type of readers (experience)	No. test cases per reader	No. lesions in test (characteristics)	Sensitivity (Sn) and specificity (Sp) after training*
McFarland et al 2001 ¹⁹⁹	1	3	Observed testing on 5 datasets (30 colonic segments) with coaching	1 expert (NS)	3 GI radiologists (NS)	Retesting on same 5 datasets 6 weeks later, using different 2D or 3D technique. Normal and abnormal cases.	22 lesions (11 polyps 5-9 mm (4 hyperplastic lesions, 5 adenomas, 2 unknown); 11 polyps \geq 10 mm (3 cancers, 2 hyperplastic lesions, 2 adenomas))	Sn: 89-92%. No significant improvement at retesting. Sp: 72-83%.
Neri et al 2011 ²⁰⁸	1	27	9 hours hands-on training over 3 days, including lectures, practise on 3 normal and 3 abnormal scans	1 radiologist (NS)	11 radiologists (0 cases) 16 radiologists (<10 cases)	26 cases +/- CAD assistance with sequential feedback. All abnormal cases.	38 lesions (12 polyps \leq 5mm, 9 polyps 6-9 mm; 12 polyps 10-30 mm; 5 polyps >3 cm)	Sn: 29% (without CAD); 31% (with CAD) (without CAD), for 6-9 mm polyps (p=0.0027). Sp: unchanged (>96% for all sizes). Increased Sn for all polyp sizes with CAD except \geq 30mm.
Rosenfeld et al 2014 ²⁰⁰	1	4	30 self-directed cases for the 3 novices	-	1 experienced GI radiologist (NS) 1 radiology resident, 2 gastroenterology fellows (0 cases)	90 cases with sequential review of colonoscopy report. Normal and abnormal cases.	52 lesions \geq 6 mm (NS)	Sn: 90% for 6-9 mm polyps (radiology resident) Sp: Accuracy - 98.9% (radiology resident) No learning curve identified (p=0.09-1.0).
Sali et al 2018 ²⁰⁹	3	20	Half-day course (lectures, 5 case demo, individual training on 4 cases). Read 2 articles on pitfalls and lesions. 1:1 computer-based self training on 150 cases +/- CAD over 3-6m.	-	17 radiology residents (0 cases) 3 radiologists (0 cases)	37 cases at baseline (no feedback), repeated same test post-training. Normal and abnormal cases.	24 lesions (2 cancers; 11 polyps 6-9 mm; 11 polyps \geq 10 mm)	Sn: 83% to 87% improvement with CAD (p=0.021) and 74 to 83% without CAD (p<0.001, for \geq 6 mm polyps. Sp: 81 to 86% improvement (p=0.15). CAD alone had no impact on training.
Taylor et al 2004 ²⁰²	1	3	50 cases read over 3-4 weeks, followed by individualised feedback and training	1 expert (\geq 150 cases)	1 GI radiologist (0 cases) 1 radiology fellow (0 cases) 1 radiology trainee (0 cases)	50 test cases over 3-4 weeks. Normal and abnormal cases.	56 lesions (2 cancers; 42 polyps \leq 5 mm; 5 polyps 6-9 mm; 7 polyps \geq 10 mm)	Sn: 25-58% for \geq 10 mm polyps. Trainee significantly improved (p=0.007). Sp: No significant difference in number of FPs after training. Read time reduced for GI radiologist (p<0.001) and fellow (p=0.03).

Author	No. Sites	No. Readers	Training components	No. faculty (experience)	Type of readers (experience)	No. test cases per reader	No. lesions in test (characteristics)	Sensitivity (Sn) and specificity (Sp) after training*
Taylor et al 2008 ²⁰¹	1	6	1-day course - lectures/hands-on teaching	2 experts (≥ 300 cases)	6 GI radiologist (107 cases read twice with no feedback)	20 cases read concurrently with CAD All abnormal cases.	55 polyps (22 polyps 1-5 mm; 33 polyps ≥6 mm)	Sn: 51% for 6-9 mm polyps; improvement of 26% (p<0.001) post-training with CAD. Sp: worsened after training (p=0.03). Read time increased (p=0.03).
Thomsen et al 2016 ²¹⁰	1	3	Diagnostic training programme of 30 lessons (anatomy/pathology) Supervised interpretation of 50 cases E-learning cases	1 radiologist (2 years)	2 radiographers (NS)	44 or 56 cases. Normal and abnormal cases.	9 lesions (cancers; ≥6 mm polyps)	Sn: 100% for cancer, ≥6 mm polyps. Sp: 97% for cancer, ≥6 mm polyps.

*p-values included where specified in original text

2D: two-dimensional. 3D: three-dimensional

FP: false-positive

GI: gastrointestinal

m: month

wks: weeks

No.: number

NS: not specified

Sn: per-lesion sensitivity. Sp: per-case specificity

Training and testing methods employed

Several different training components were described, which can be broadly categorised into (a) hands-on training workshops; (b) trainee-directed independent reading of relevant CTC literature; (c) didactic lectures on CTC-related topics (technique, software applications, interpretation, and pitfalls); and (d) reading of practice cases (independently or supervised; whole data sets or partial studies).

Most studies (83% [15/18]) contained passive, generalised (i.e., non-tailored) teaching components e.g., lectures, self-directed reading, or case review, and were heavily trainer focused. Where specified, seven studies used only a single expert trainer,^{194,198,199,202,207,208,210} and only two studies specified some sort of individualised training.^{202,209}

Where used, the format of the training workshops varied according to study design, but was typically one or two days (ranging from half a day to four days), with teaching delivered by several expert faculty in 1:1, 2:1 or small group tutorial setting.^{194,197,201,206,209,211} If specified, definitions of a faculty expert again varied, but were usually a board-certified abdominal or gastrointestinal radiologist with a career experience of ≥ 300 CTC cases. No studies described relevant training given to experts in how to specifically train readers in CTC.

All studies incorporated an element of CTC interpretation testing in either a formative (throughout the training) or summative (at the end of the course) format.

One study tested only on partial datasets i.e. isolated colonic segments;¹⁹⁹ while most studies (84% [16/18]) used a combination of normal and abnormal cases.

Effect on reader diagnostic accuracy

Post-training per-lesion sensitivity for ≥ 6 mm lesions varied widely between studies, from 51%, up to 100%,^{202,203,210} and can be attributed to differing sample sizes (number of readers, test cases and lesions), reader experience and difficulty of the lesions selected for testing. Generally, studies which included 'hard-to-detect' lesions (for example, those assessing the impact of CAD on radiologist interpretation, or testing on subtle cases with flat/small lesions) observed lower sensitivities compared to those that did not.^{195,197,203,208} All studies where pre- and post-training assessments were administered observed a significant improvement in reader sensitivity,^{198,201,202,206,209,211} except two.^{196,199}

The impact of training on specificity was varied, with several studies reporting reduced specificity after training.^{201,212} While skills of lesion characterisation are being developed and refined, readers often over-call abnormalities immediately after training. Other studies found an improvement in specificity as reader experience increased.^{194,196}

Discussion

CTC is highly sensitive for large (≥ 10 mm) polyps and colorectal cancers and has good sensitivity for 6 to 9 mm polyps.⁵⁷ Accurate interpretation of these studies in routine clinical practice is essential if the outstanding diagnostic accuracy demonstrated in research studies is to be translated to the real world. Earlier CTC

training studies advocated focusing on a minimum number of CTC cases read prior to independent reporting, however, simple case review, even with endoscopic correlation, does not necessarily lead to improved sensitivity, as without appropriate feedback the same errors may just be perpetuated.¹⁹⁶ Accumulation of CTC caseload has a varying effect on reader sensitivity, with a third of readers not reaching competency even after reviewing 175 CTC cases.¹⁹⁸ Studies which have focused on delivering feedback to readers, with or without specific individualised training, have observed significant improvements in reader sensitivity.^{194,195,211} Therefore, developing expertise requires training and feedback in addition to clinical experience.²¹³

Various institutions globally have provided recommendations for radiologist training prior to independent practice, but these recommendations are highly variable. The minimum number of cases varies from >50 to (under ideal circumstances) >300, with limited detail regarding what pathology these cases should be composed of, other than that they should be validated endoscopically (or via surgery). This heterogeneity in recommendations is perhaps due to the relatively small number of published articles investigating the topic of CTC reader training. I identified only 18 such articles published over 20 years, with variable study designs and training interventions.

Although, in general, reader training was associated with higher polyp detection rates, several early studies found no effect on reader sensitivity.^{196,199} Other studies which focused on a broad selection of cases and targeted feedback to those undergoing training have shown greater benefits.^{198,211} Several studies have shown a considerable difference in 'innate' ability to interpret CTC; Heresbach et

al¹⁹⁷ found that the best predictor of final accuracy was initial reader sensitivity at the start of training, and Liedenbaum et al¹⁹⁸ found that some readers were unable to achieve adequate diagnostic accuracy despite prolonged training. Clearly, the number of cases to which a reader is exposed is only one facet of training, and a combination of an individual's aptitude, CTC case mix, training and feedback methods are all important to maximise performance.

In summary, there is considerable variability in national and international guidance recommendations for CTC training prior to independent practice. The published literature shows there is a clear benefit of training, but this is dependent on characteristics of the trainee readers as well as the materials and methods used for training. There is a general lack of data and consensus regarding the impact of training in a randomised setting, the specific impact training may have on experienced CTC readers, the durability of CTC training and the type of training and testing that best improves performance.

Optimising reader training in CTC will require a more sophisticated programme that should ideally be standardised to ensure all those learning how to interpret CTC can achieve the high accuracy that the technique has obtained in research trials.

Chapter 7 Best practice in CT colonography training

Summary and contribution statement

Following the Chapter 6 review of current CT colonography (CTC) interpretation training, I now summarise different methods of CTC training and accreditation, and make recommendations for best practice training, with clinical case examples. These principles underpin the design of the training intervention evaluated in Section C.

I performed all the work in this chapter. The draft manuscript which was edited in conjunction with Associate Professor Andrew Plumb (UCL), Dr Paul McCoubrie (Southmead Hospital) and Dr David Burling (St Mark's Hospital, Harrow). Sections of which have been published as follows:

Training in CT colonography interpretation: Recommendations for best practice.

Obaro AE, McCoubrie P, Burling D, Plumb AA (2022). Seminars in Ultrasound, CT and MR. DOI: 10.1053/j.sult.2022.06.001

Introduction

The importance of training in CT colonography (CTC) interpretation is highlighted by our systematic review which observed that more than half of post-investigation cancers are visible in retrospect and due to perceptual errors at the time of reporting (Chapter 4).¹⁸⁴ It is therefore critical that readers interpreting CTC in clinical practice are adequately trained to minimise such errors and achieve high diagnostic accuracy and low cancer miss rates.

Unfortunately, as discussed previously there is some evidence that CTC performance in a real-world setting may be worse than expected from the research literature. For example, in the BCSP, CTC achieved only 50% of the detection rates of colorectal cancer and advanced neoplasia achieved by colonoscopy,⁶³ and missed cancer rates were twice as common at three years.²¹⁴

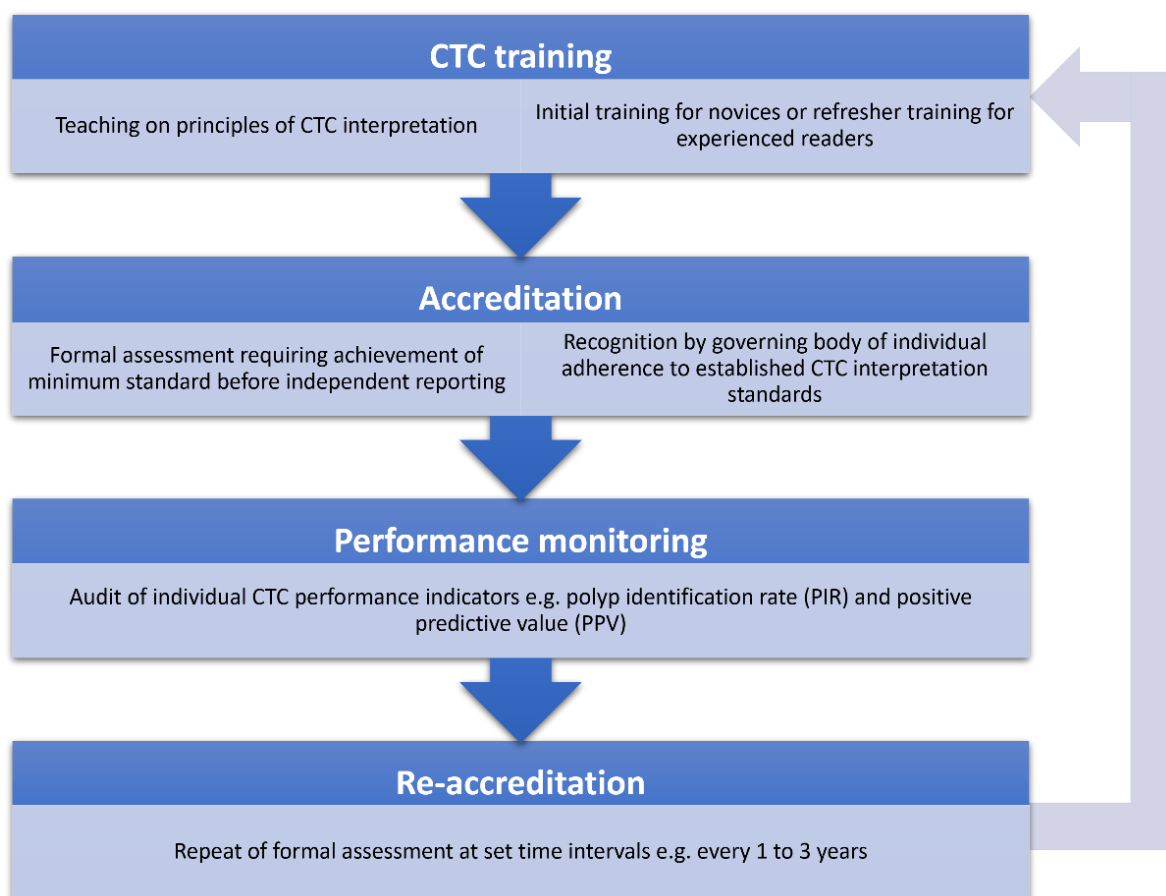
Given the impact of perceptual error on neoplasia detection rates, training for CTC interpretation must be improved. In Chapter 6, I discussed the considerable variation in the training recommendations made by international bodies. The research literature regarding the optimal methods for training in CTC interpretation is scant, and although in general it is consistently shown to improve performance,⁶³ the precise methods used for training and feedback are variable. Similarly, as discussed in Chapter 3, there is little data recognising the role or importance of accreditation and regular performance monitoring – which is at odds with processes for colonoscopy. This impedes the rational design of methods to improve radiologist interpretation performance.

Training in CTC reporting involves teaching on how to interpret cases and may be delivered locally, 'on-the-job', or at a structured workshop or course. Such training does not lead to a recognised qualification and is frequently performed ad hoc.

This contrasts with accreditation, which is a formal process leading to the achievement of a recognised set of objectives or standards. It usually includes some form of training prior to the accreditation being awarded. The accredited individual has been assessed and deemed to fulfil the requirements of the accrediting body. As a condition of maintaining accreditation, there may be a requirement for repeat 'refresher' or 'update' training, and/or periodic or continuous monitoring of performance to ensure that after fulfilling the initial requirements the individual continues to maintain an appropriate skill level.

In most jurisdictions, there is no mandatory training, accreditation process or standardised performance monitoring for CTC readers (Chapter 3). This could contribute to poor performance and variability in polyp detection rates. In addition, the absence of centralised, evidenced-based CTC interpretation training is likely to contribute to lower interpretation accuracy in clinical practice. These issues could be addressed by a formalised process summarised in Figure 7.1.

Figure 7.1: Suggested model of CTC training, accreditation, and performance monitoring. Periods of refresher training can be performed after re-accreditation



Recommendations for best practice

Training in CTC can be broadly categorised into two areas: (i) training in CTC technique (primarily for radiographers) and (ii) training in CTC interpretation (primarily for radiologists). As well as how to perform CTC, radiographers learn how to conduct an 'on-table' review of the acquired images before the patient leaves the scanner. This allows prompt identification of large cancers, facilitating staging scans to be completed at the same time. For radiologists, the most accurate CTC readers will also have a good understanding of how the investigation is performed, allowing them to troubleshoot image acquisition and ensure high quality data are captured for interpretation. Adequate training in technique and

interpretation should be performed according to a dedicated syllabus with clear learning objectives. Further discussion will focus on CTC training related to interpretation.

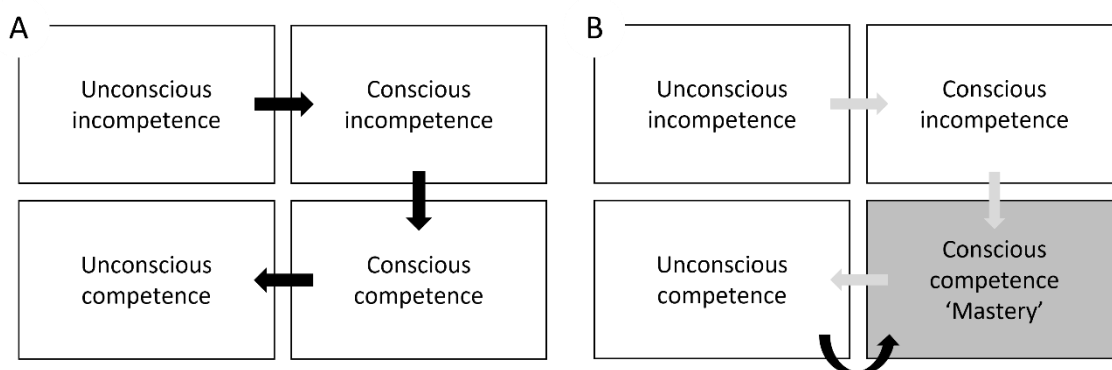
Expert training faculty

There is a clear difference between being an expert in CTC interpretation and being an expert CTC trainer. Most radiologists acting as trainers in CTC will not have received any guidance or teaching on how to deliver CTC training. Indeed, training of the CTC experts was not specified in any of the 18 studies reviewed in Chapter 7. This inevitably leads to variation in teaching quality and skills acquisition between centres. Beyond commercially available short courses, often designed and delivered by CTC software companies, much CTC training has traditionally been accomplished by informal 'on-the-job' teaching in local radiology units. Such an approach lacks standardisation and is dependent on local caseload and radiologist availability.

Similar observations in colonoscopy led to the development of the 'Training the Colonoscopy Trainer' (TCT) course.²¹⁵ Recognition that being able to perform a skill does not explicitly result in an individual also being an effective trainer is based on the concept of Peyton's model of procedural skills acquisition.²¹⁶ According to this model, individuals progress through stages of unconscious incompetence to unconscious competence (Figure 7.2A). Beginners are initially in the unconscious incompetence phase (unaware of what they do not know) and over time their ability develops into conscious incompetence (aware of limitations). If a task is simply learned from experience, without the component elements explained then

the learner may bypass conscious competence directly to unconsciously competent, where the task is automated and habit-like. The unconsciously competent have mastered a technique, allowing it to be performed quickly and efficiently. However, effective teaching requires the ability to deconstruct actions and techniques, thus requiring trainers to move from unconscious competence to 'enlightened' conscious competence or mastery (Figure 7.2B).

Figure 7.2: Peyton's model of procedural skills acquisition (A). Effective teaching of procedural skills requires moving from unconscious to conscious competence (B)



Effective CTC interpretation training therefore requires the trainer to possess explicit knowledge of 'how to interpret' CTC but also 'how to teach' CTC reporting. When a CTC trainer has conscious competence, they are able to verbalize specific steps e.g. how to distinguish a polyp from faecal residue, which facilitates the skills acquisition of the learner.

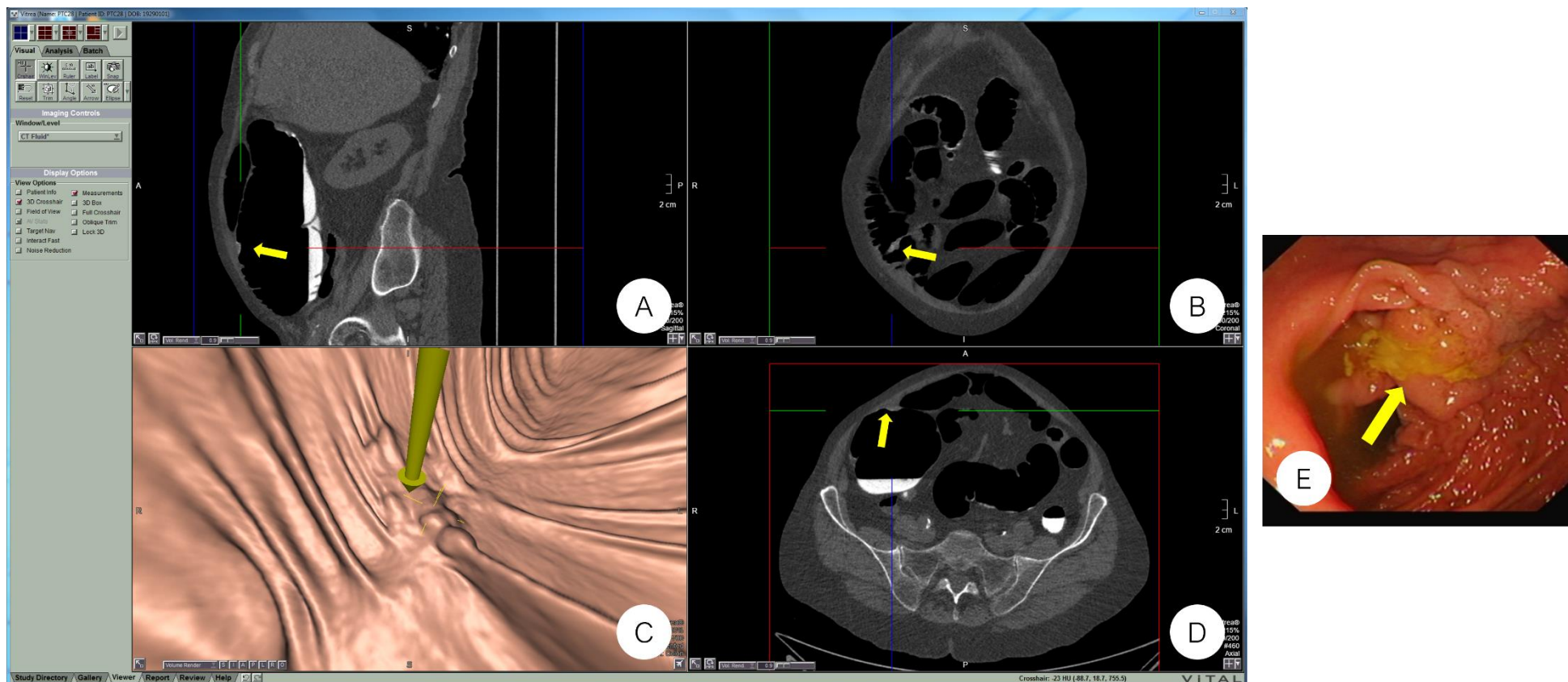
Development of a 'Training CTC Trainers Course' (TC3) allows the teaching process to be formalised, with due consideration appropriately given to preparation, learning objectives, cognitive overload, performance feedback, critical reflection, and take-home messages. Establishing a faculty of CTC trainers who have undergone such a course promotes sharing of best practice CTC training principles with subsequent improved learning experience of trainees. This concept

underpins the model developed and tested in Section C, where expert faculty delivered a one-day CTC training workshop to CTC reporting radiologists after attending a specifically designed TC3.

Clinically relevant content

Test cases and ideally all teaching cases used for CTC interpretation should have endoscopic (or follow up CTC) validation and where possible histological confirmation of the findings. Consensus opinion from a panel of experts on the CTC findings prior to using these cases to train and test readers ensures consistency. Learning principles of central importance to CTC interpretation include an appropriate use of multiplanar reformatting, competent use of 3D review with ability to correlate to the 2D data (Figure 7.3), methodical interpretation technique and knowledge of pitfalls.

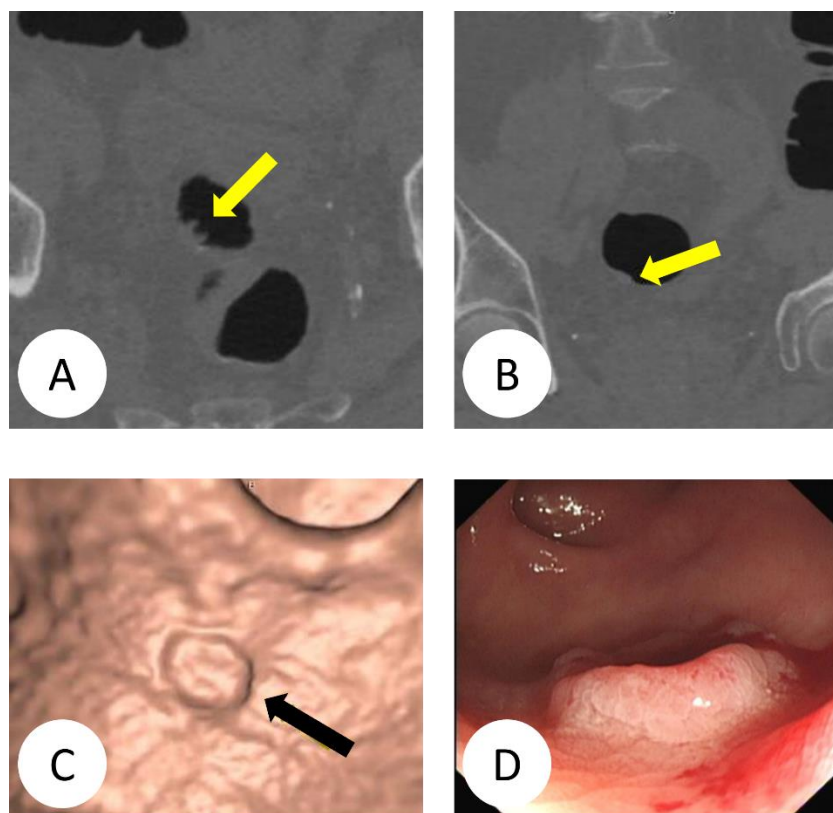
Figure 7.3: Screen capture from a CTC workstation showing correlation of the multiplanar reformats from the 2D acquisition and the 3D endoluminal view



2D multiplanar reformats: (A) – sagittal, (B) - coronal, (D) – axial, and 3D endoluminal view (C). The yellow arrows highlight a 22 mm nodular, sessile polyp in the ascending colon. Endoscopic view of the corresponding lesion (E), which is characterised as a granular laterally spreading tumour. Histology confirmed a tubular adenoma with low grade dysplasia

Interpretation technique forms the foundation of accurate CTC interpretation and familiarity with local CTC software allows manipulation of acquired images to maximise chances of polyp detection. Interpretation should be performed methodically using standard 2D images (in at least two different planes) and 3D endoluminal reformats (Figure 7.4).

Figure 7.4: Subtle rectal lesion on 2D axial views (A) which is less conspicuous on the coronal view (B)



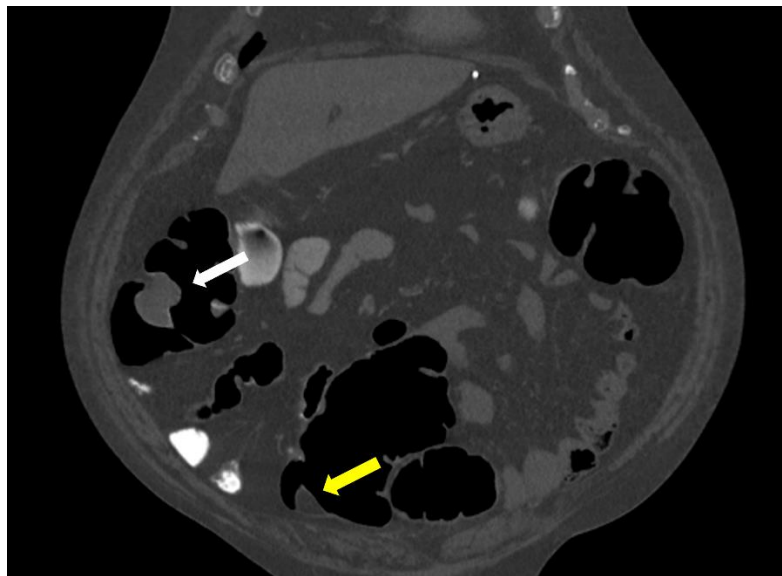
The lesion is best appreciated on the 3D endoluminal view where it appears as a flat 12mm rectal lesion with rolled edges (C). Colonoscopy confirmed a sessile lesion with depressed centre (D) and the lesion was found to be a moderately differentiated adenocarcinoma on histology

During the 2D review the reader scrolls through the colonic images, carefully scrutinising the circumference of each colonic segment to detect protrusions or irregularities which may appear momentarily in the field of view. The 3D review involves the endoluminal 'fly-through', and with the 'camera' orientation facing proximally the reader flies through the colon in a retrograde direction from rectum

to caecum, often then repeated in the anterograde direction with the camera facing distally.²¹⁷ This allows visualisation of both sides of the colonic folds. The 3D review requires the reader to be aware of blind spots behind folds, beneath tagged (or untagged) fluid and at colonic turns. Troubleshooting requires comparing the different views to fully interrogate the lesion and achieve accurate characterisation. All potential polyps identified should be evaluated for two criteria: a fixed position on the colonic mucosa and a soft tissue core (as opposed to air/fat density or the mottled texture of faecal residue).²¹⁷

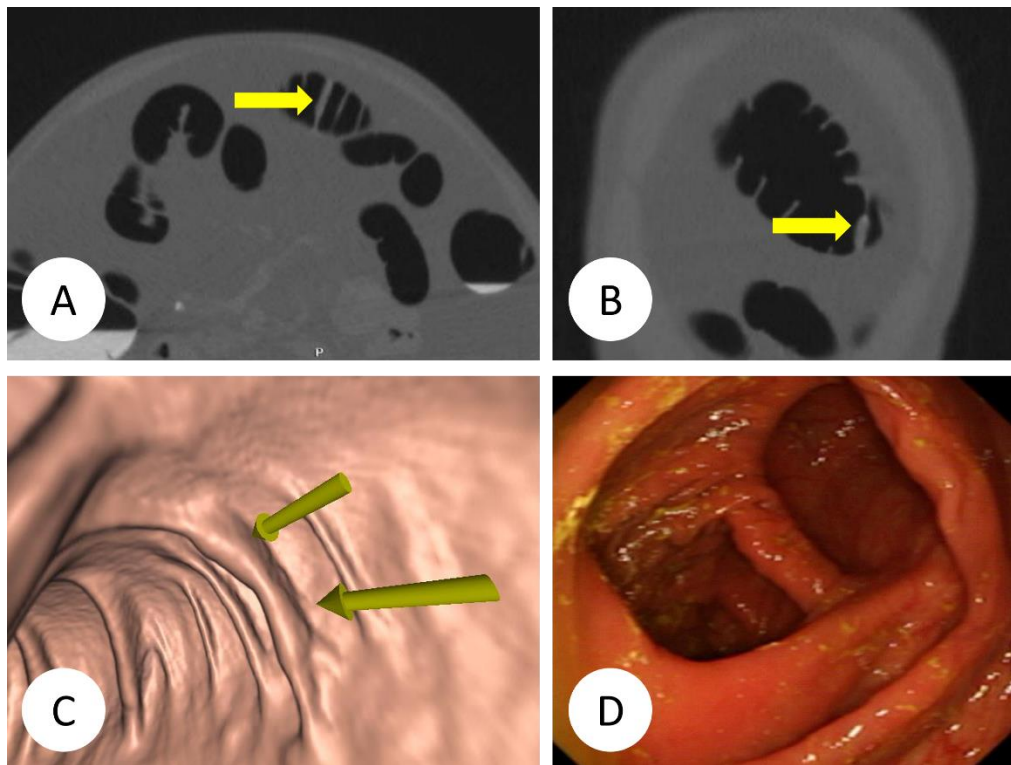
Teaching cases should be selected to present a spectrum of difficulty and disease, ranging from normal scans with non-neoplastic lesions (e.g. lipoma, haemorrhoids, diverticular disease; Figure 7.5) to scans with subtle, difficult to detect lesions (e.g. flat lesions, Figure 7.6).

Figure 7.5: A non-neoplastic lesion and polyp



2D coronal view on bone window demonstrates a 17 mm lipoma (fat attenuation) in the proximal ascending colon (yellow arrow), compare with a 36 mm polyp in the ascending colon (white arrow) which has soft tissue attenuation

Figure 7.6: Example of a subtle, 'hard to detect' lesion



On the 2D, bone window, there is a flat lesion on a fold in the distal transverse colon (A – axial, B – coronal). This fold is abnormally thickened in comparison to adjacent folds, appearing more conspicuous on the 3D endoluminal view (C). Colonoscopy confirmed a 17 mm tubular adenoma with low grade dysplasia (D)

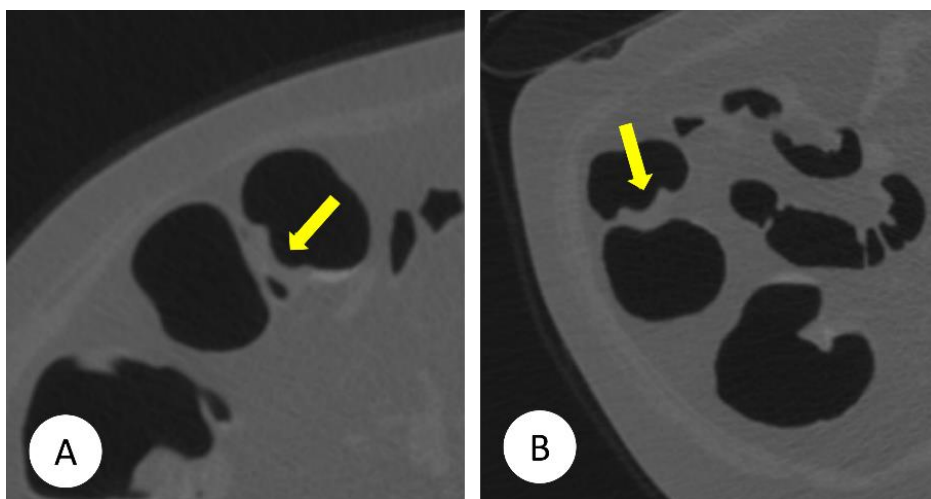
Differing morphologies e.g. pedunculated, semi-pedunculated, sessile, flat and malignant lesions should be highlighted.

Readers should be advised that current guidance recommends a CTC reporting time between 20 and 25 minutes per scan, performed in dedicated/uninterrupted sessions.¹²¹ As presented in Chapter 5, reporting too quickly and for too long is associated with reduced polyp detection, therefore a maximum of four sequential scans should be reported before taking a screen-break.²¹⁸

Pitfalls and error

The process of CTC interpretation requires the specific skill of luminal navigation of 2D and 3D images, in addition to those typically used to interpret abdominal CTs. This requirement and the additional time taken can result in reader fatigue and errors of detection and characterisation. Errors of detection occur when a polyp is not identified by the reader and the scan is incorrectly interpreted as negative. In comparison, errors of characterisation occur when a polyp is identified but disregarded due to improper assessment of its features (false negative) or a normal structure or residue with a polypoid appearance is reported as a polyp (false positive).²¹⁹ Both such errors can be considered perceptual errors and as described in Chapter 4 contribute to the majority of missed cancers. Figure 7.7 is an example of an error of perception when an abnormal fold was mistaken for spasm, resulting in a false negative study.

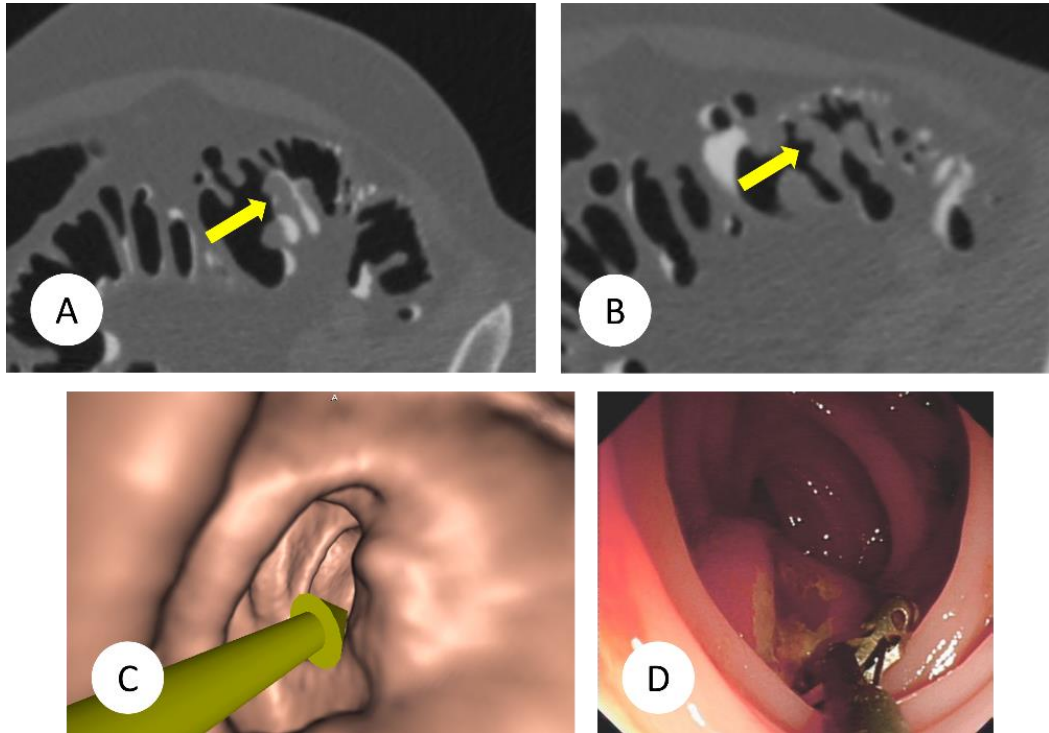
Figure 7.7: Example of a perceptual error



Supine (A) and prone (B) 2D axial images on bone window demonstrating a polyp with central depression on a fold in the transverse colon which was initially dismissed. The patient had a concurrent caecal polyp detected on this CTC and the additional transverse colon lesion was identified on colonoscopy and confirmed to be a malignancy. This case highlights cognitive errors of characterisation and satisfaction of search

Exposure to the spectrum of polyp and cancer morphology during teaching cases can increase awareness of such errors and mitigate against them (Figure 7.8).

Figure 7.8: Subtle lesion in a diverticular segment of sigmoid colon



2D axial supine (A) and prone (B) images on bone window demonstrate a 10 mm sigmoid polyp with central depression in diverticular segment. The presence of central depression is in keeping with malignancy and this morphology is confirmed on the 3D endoluminal view (C) and colonoscopy (D). This was histologically confirmed as an adenocarcinoma. This case highlights the importance of careful interrogation of poorly distended diverticular segments which can easily be dismissed as suboptimal for excluding pathology

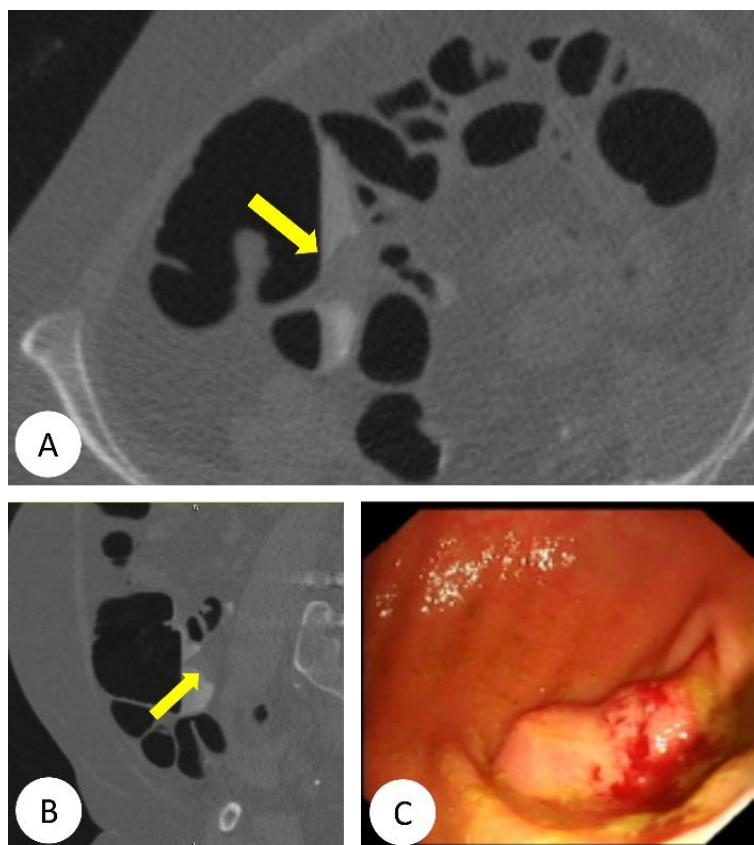
Pitfalls in CT colonography interpretation are well documented and can be broadly divided into pitfalls related to preparation and technique, review of 2D and 3D images, and anatomy (Table 7.1).^{217,220,221}

Table 7.1: Types of pitfalls in CTC interpretation with select examples

Preparation and technique
<ul style="list-style-type: none"> • Inadequate bowel preparation resulting in large volumes of tagged and untagged residue. Faecal residue can be misinterpreted as a polyp • Poor colonic distension makes it difficult to differentiate between spasm, stricture or tumour
Interpretation of 2D images
<ul style="list-style-type: none"> • Image quality degraded by movement artifact resulting in excessive noise and causing pseudolesions • Mobile colonic segments can cause misinterpretation of a polyp as mobile stool, equally pedunculated polyps on a long stalk can be misinterpreted as stool • Flat lesions (height \leq 3mm) are subtle and hard to detect
Interpretation of 3D images
<ul style="list-style-type: none"> • Inadequate visualisation of both sides of the colonic folds can obscure lesions • Presence of tagged fluid can submerge pathology visible on the 2D images • Submucosal lesions e.g. lipomas can appear as polyps on 3D images
Anatomy
<ul style="list-style-type: none"> • Internal haemorrhoids in the rectum can be mistaken for polyps • Pseudothickening of the colonic wall at the flexures can cause a pseudotumour appearance • Ileocaecal valve appearance on 3D images may mimic an intraluminal mass • The appendix may prolapse into the lumen mimicking a polyp, or the appendicular stump may appear as a smooth inverted polypoid mass.

CTC training cases should illustrate these pitfalls and provide troubleshooting mechanisms for avoiding them (Figure 7.9). Subsequently, understanding should be assessed with discriminatory test cases.

Figure 7.9: Example of a polyp submerged under tagged fluid, a common pitfall in CTC interpretation



2D images on bone window (A – axial, B – sagittal) demonstrate a 23mm caecal polyp submerged under tagged fluid (arrow) and corresponding endoscopic view (C). In cases with retained tagged fluid, the window level should be adjusted to increase conspicuity of lesions. Care should be taken to specifically interrogate the colonic segments with retained fluid to maximise lesion detection. The patient underwent a right hemicolectomy and histology confirmed a T2V0N2 adenocarcinoma

Individualised training and performance feedback

A novice learning to interpret CTC scans for the first time and an experienced reader each have different learning needs.²⁰² Typically, experienced readers will have little difficulty with commonly-encountered abnormalities and their mimics. Even so, the spectrum of disease identified will vary between even experienced individuals; however, many previous models of CTC training operate on a 'one size fits all' assumption, offering the same training to all readers. Several studies have observed that this approach has limited impact on improving reader sensitivity (Chapter 6). Interestingly, Fletcher et al (2010) found that acceptable reader sensitivity could be achieved after reviewing only 45 training cases; notably, 30 of

these cases were tailored to individual reader weaknesses.²¹¹ This contrasts with observations by Liedenbaum et al, who found that although novice readers reached the sensitivity of experienced readers after 164 cases, one third of readers did not reach competency even after 200 cases.¹⁹⁸ Their training model comprised self-directed reading, lectures, and training on pitfalls; however, independent hands-on practise was only delivered on four CTC cases.

It is intuitive that training will have more impact when it is targeted to the trainees needs. Indeed, Fidler et al suggest that formal CTC training must provide enough cases for readers to learn their own idiosyncratic weaknesses in interpretation.¹⁹⁵

Testing and assessment of performance

The type of lesion which appropriately assesses the ability of novice versus experienced readers will be different. For novice readers, teaching the recognition of large, protuberant lesions will allow them to appreciate obvious abnormal findings, providing the opportunity to practise luminal navigation and interpretation technique. For more experienced readers, focus should be directed towards more subtle, hard to detect lesions, especially if these readers are involved in reporting bowel cancer screening studies, where lesions are typically less conspicuous.²²² A suitable training programme will provide a variety of discriminatory test cases of varying difficulty to assess performance. Formative assessments, undertaken throughout the training are beneficial in consolidating learning, while summative tests, at the end of the training, assess reader understanding and ability.

Conclusion

If the full utility of CT colonography (CTC) as a sensitive diagnostic tool for colorectal cancer is to be established there must be high quality training in technique and interpretation.

Training cases should cover a spectrum of difficulty, with emphasis on recognising pitfalls and troubleshooting. Particular attention should be paid to developing methodical interpretation technique, with the opportunity for hands-on training to practise reading a wide variety of cases. Furthermore, regular testing and feedback on reader performance is essential to assessing understanding and embedding good practice.

Such CTC interpretation training should be delivered by experienced faculty, who have received specific guidance in how best to teach this subject. This may be difficult to achieve locally, therefore consideration must be given to the development and funding of national or international programmes which pool expertise and resource. Readers and services who have attained accreditation through completion of such a programme could benefit from better tariffs and reimbursement from insurance companies; thus, providing a financial incentive for participation.

Without a more considered approach to CTC interpretation training, readers will inevitably miss lesions which, if detected at an early stage, could prevent cancers. This observation should motivate regulating bodies to develop high quality teaching for those involved in delivering CTC services.

SECTION C: INTERVENTION TO IMPROVE CT COLONGRAPHY INTERPRETATION – THE PERFECTS STUDY: A MULTICENTRE, CLUSTER-RANDOMISED CONTROLLED TRIAL

The previous sections have summarised the burden of colorectal cancer (CRC), the purpose of screening to reduce incidence and mortality and the role that CT colonography (CTC) has in the diagnostic pathway. I subsequently discussed factors affecting CTC performance including the speed of reporting and established that most interval cancers are due to perceptual errors. The impact of CTC training on interpretation accuracy were reviewed, along with best practice training principles which have informed the design of the trial presented in the following chapters.

Section C presents a multi-centre, cluster, randomised controlled trial designed to test the hypothesis that one day of individualised training can improve CTC interpretation by radiologists.

Contribution statement

The following multi-centre, cluster-randomised trial was conceived and designed by Professor Steve Halligan and Associate Professor Andrew Plumb (UCL), in conjunction with Dr David Burling (St Mark's Hospital, Harrow) and me. Statistical analysis was provided by collaborators Professor Susan Mallett (University of Birmingham) and Mr Paul Bassett (Stats Consultancy). I obtained ethical approval, managed the trial (identified and recruited participants, performed case selection and coding, and wrote funding reports) and conducted all data collection. I designed and executed the pre-randomisation questionnaire with advice from Dr Plumb and Dr Burling on survey design. The design of the faculty training course for the intervention was led by Dr Burling, research radiographer, Ms Rachel Baldwin-Cleland (St Mark's Hospital, Harrow) and me. The one-day training intervention for participants was designed by me, Dr Burling and Dr Plumb. I organised and managed the training intervention along with administrator Ms Carmen Ugarte-Cano (St Mark's Hospital, Harrow) and Ms Baldwin-Cleland. I wrote the manuscript drafts which were modified with the above colleagues.

Versions of the following chapters have been published as follows:

Colorectal Cancer: Performance and Evaluation for CT Colonography Screening - A Multicenter Cluster-randomized Controlled Trial. Obaro AE, Plumb AA, Halligan S, Mallett S, Bassett P, McCoubrie P, Baldwin-Cleland R, Ugarte-Cano C, Lung P, Muckian J, Ilangovan R, Gupta A, Robinson C, Higginson A, Britton I, Greenhalgh R, Patel U, Mainta E, Gangi A, Taylor SA, Burling D (2022). Radiology. DOI: 10.1148/radiol.211456.

Performance and Evaluation in Computed Tomographic Colonography Screening (PERFECTS): Protocol for a Cluster Randomized Trial. Plumb AA, Obaro AE, Bassett P, Baldwin-Cleland R, Halligan S, Burling D (2020). medRxiv. DOI: 0.1101/2020.02.25.20027714

Funding sources: 40tude Curing Colon Cancer, the Edith Murphy Foundation, the Peter Stebbings Memorial Charity, and Public Health England (funds administered by the St Mark's Hospital Foundation).

Abstract

Aim:

To determine if a 1-day training intervention for CTC reporting radiologists can improve their sensitivity in detecting colorectal neoplasia.

Methods:

We conducted a multicentre, cluster-randomised controlled trial in the National Health Service (NHS) in England and Wales. Hospitals with established CTC services were cluster randomised into intervention (1-day training plus feedback) or control (no training or feedback) arms. Individual radiologists received the intervention; a 1-day hands-on workshop focussing on CTC reporting pitfalls supplemented by individualised peer coaching. Sensitivity for CRC and ≥ 6 mm polyps was tested at baseline and one, six and 12 months post-training (or post-recruitment for controls) via interpretation of 10 CTC examinations at each timepoint. The primary outcome was the between-arm difference in sensitivity at

the 1-month timepoint, analysed using multilevel regression after adjustment for baseline sensitivity.

Results:

Recruitment was April 2017 to Sept 2018 and follow-up completed by Jan 2020. 69 hospitals were randomised (intervention: 31 clusters, 80 radiologists; control: 38 clusters, 59 radiologists). Radiologists were experienced (median: 500-999 CTCs interpreted) and reported CTCs routinely (median: 151-200 cases/year). Baseline characteristics were similar between randomised arms. The primary outcome of 1-month sensitivity was significantly greater in the intervention arm (66.4% (659/992)) than control (42.4% (278/655)); difference 20.8%, 95% CI: 14.6 to 27.0; $p < 0.001$), an improvement maintained at 6- (66.4% (572/861) vs 50.5% (283/560); difference 13.0%, 95% CI: 7.4 to 18.5; $p < 0.001$) and 12-months (63.7% (310/487) vs 44.4% (187/421); difference 16.7%, 95% CI: 10.3 to 23.1; $p < 0.001$). This beneficial effect was independent of career experience, lesion location and morphology, and interpretation method.

Conclusion:

For radiologists routinely reporting CTC in the NHS, a simple training intervention produces a sustained 16.7% improvement in the detection of clinically-significant colorectal neoplasia. Such testing and training could be implemented to accredit radiologists reporting screening CTC.

Chapter 8 Introduction to the PERFECTS Trial

In Chapter 4, I established that most post-imaging colorectal cancers (PICRCs) are due to perceptual errors, which raises the possibility that these could be reduced by improved training in CTC interpretation. In Chapter 6, I reviewed the effectiveness of CTC training in previous studies and observed that the number of initial studies required for training before acceptable diagnostic accuracy was achieved was highly variable (50 to 175 cases),^{198,202,203,211} with up to a third of trainees unable to reach adequate sensitivity even with more prolonged training. This implies that many practitioners interpreting CTC in routine practice have been trained on an insufficient number of cases for them to have reached acceptable diagnostic accuracy.

To mirror the substantial improvements in screening mammography and colonoscopy achieved by assessment, training and monitoring,^{130,141,146,223} we hypothesised that radiologists' diagnostic accuracy for screening CTC could be improved similarly by using an individualised training programme with ongoing feedback. The principles and optimal design of such a training intervention were researched and summarised in Chapters 6 and 7. To test this hypothesis, we performed a cluster randomised trial of such training, aiming to establish:

- (a) whether it improves radiologist detection of CRC and ≥ 6 mm lesions;
- (b) the durability of such improvement, if any;
- (c) acceptance of said training;
- (d) variability in radiologist CTC reporting accuracy and associated factors

The trial was designed and is reported in accordance with the cluster extension of CONSORT recommendations (Appendix 1).²²⁴

Chapter 9 Materials and Methods

Ethical permissions

Permission was obtained from the University College London Research Ethics Committee (5967/003) and the Health Research Authority (HRA; IRAS ID 206876).

Registration: Clinical Trials (ClinicalTrials.gov Identifier: NCT02892721 – PERFormance and Evaluation in CT colonography Screening [PERFECTS]); NIHR Clinical Research Network (CPMS ID 32293).

Trial design summary

We conducted a parallel group, two-arm, cluster randomised superiority trial with a 1:1 allocation in 69 National Health Service (NHS) hospitals in England and Wales. Each cluster was a single hospital site undertaking CT colonography (CTC) in routine practice. A cluster randomised design was chosen because randomising and subsequently training individual radiologists at a given hospital would likely change practice among their colleagues, potentially contaminating any controls at the same site.

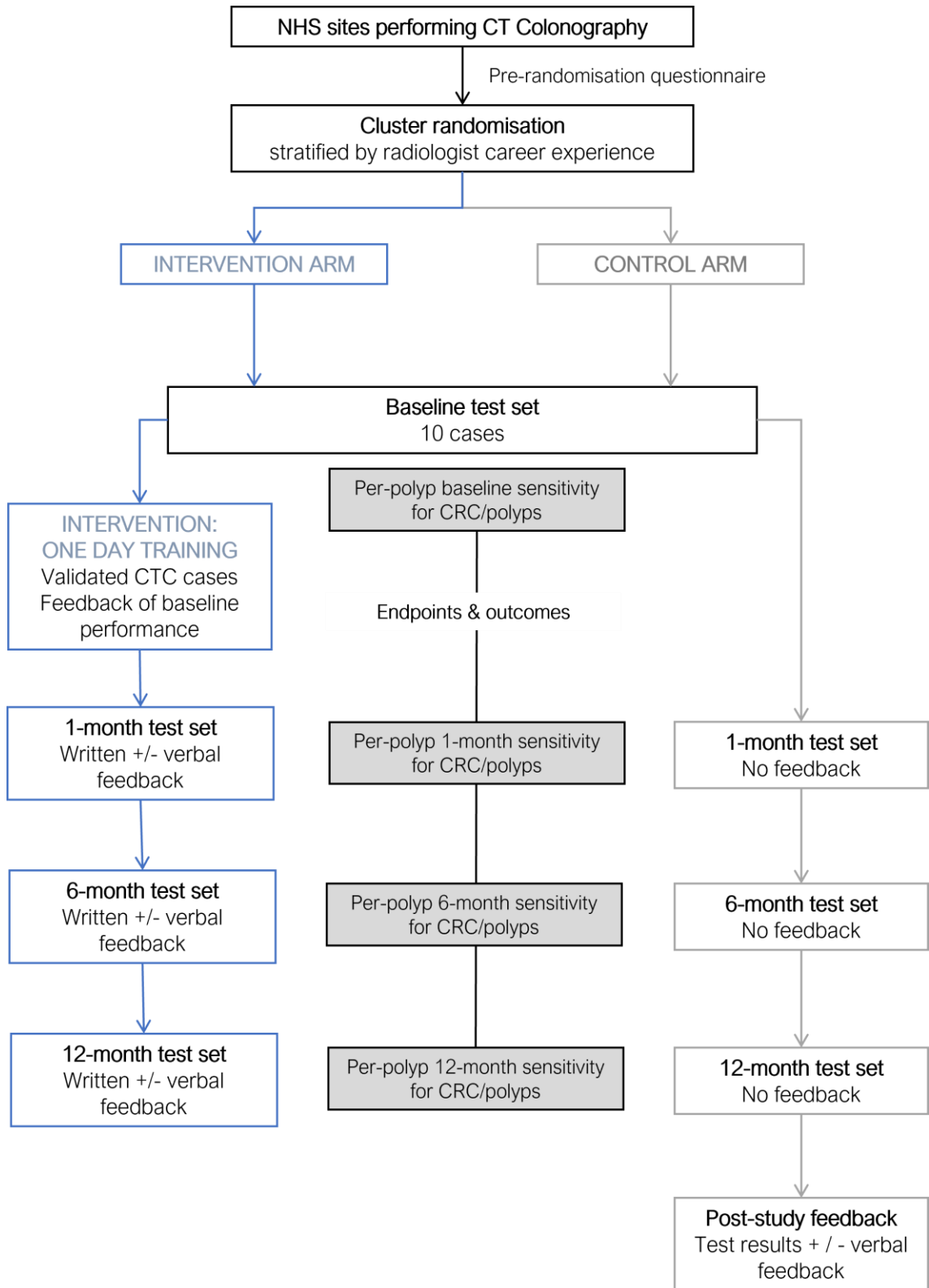
Following completion of a pre-randomisation questionnaire, radiologists were cluster randomised according to career experience. Radiologists in both arms then completed four assessments of their CTC interpretive performance at baseline, one month, six months and 12 months. The intervention of a one-day training workshop on CTC interpretation was delivered after the baseline test for the intervention arm. These radiologists received their individual test results and

supplementary written feedback after each test. Optional additional verbal feedback via telephone call was also available to the intervention arm.

The control arm did not receive any training, test results or feedback during the trial but underwent all four tests at the same intervals (Figure 9.1). They received their results for all four assessments at the end of the study and at that point were offered optional verbal feedback on their performance via telephone call.

Once randomised, individual radiologists were inevitably unblinded to arm allocation, since delivery of the training intervention required participants to know which trial arm they were in. Sham training as a comparator was deemed impossible and unethical.

Figure 9.1: Trial structure for PERFECTS



CRC: colorectal cancer. CTC: CT colonography

Eligibility of clusters and individual participants

NHS hospitals in England and Wales currently providing CTC services (both BCSP and non-BCSP sites) were eligible. Multi-hospital Trusts were eligible, provided the radiologists worked separately (to avoid cluster contamination). Eligible participants within each cluster were consultant NHS radiologists or senior specialty trainees (within 6 months of completing training) currently reporting CTC studies in their clinical practice. Exclusion criteria were radiologists working outside England and Wales, or who could not complete 12 months follow-up.

Recruitment was by advertisement at the annual British Society of Gastrointestinal and Abdominal Radiology (BSGAR) conference (Figure 9.2), project website (Appendix 2) and word of mouth.

Figure 9.2: Leaflet and online form created to promote recruitment to the PERFECTS trial

"How good am I at CT colonography?"

...is a question frequently asked of the
Bowel Cancer Screening Programme (BCSP) National Committee.




PERFECTS will help you answer this question.

PERFECTS
(Performance & Evaluation in CT colonography Screening)
is a BCSP/ BSGAR supported project which provides
structured training, assessment and individualised feedback
for Radiologists interpreting CT Colonography.

We will establish whether randomised structured training
and feedback helps Radiologists detect more lesions than those
undergoing assessments alone.

You are warmly invited to register your interest in this research project
if you are a Radiologist currently reporting CT colonography.

For further details please contact: LNWH-TR.PERFECTS@nhs.net

Register your interest

Please complete the following short form to register your interest in participating in the PERFECTS research project.

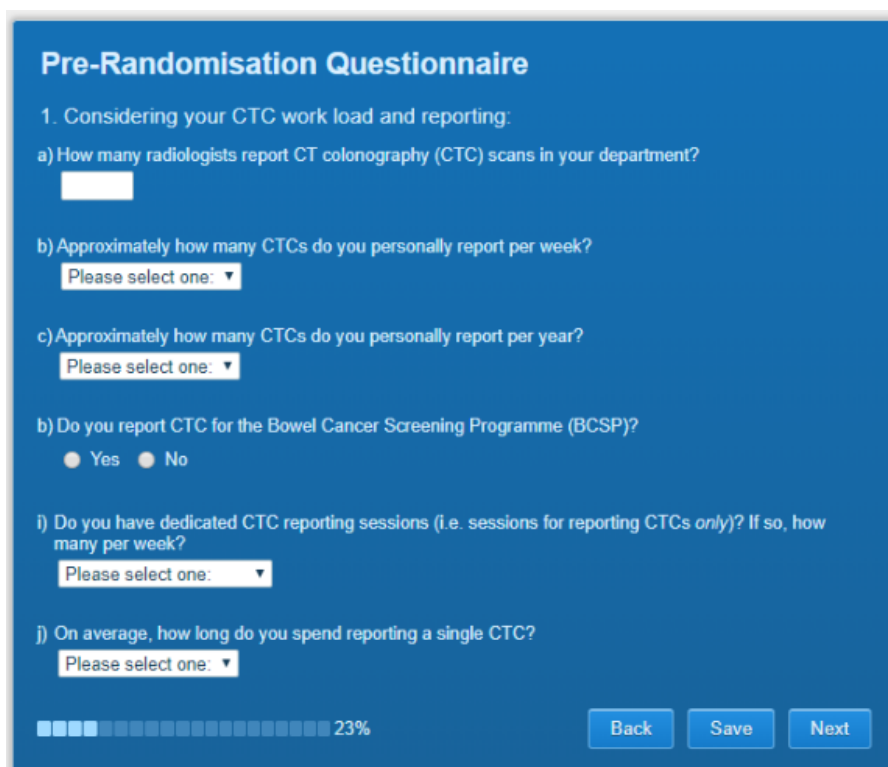
1. First Name:
2. Surname:
3. Email address:
4. Phone number:
5. Hospital Trust:
6. Do you routinely report CT colonography as part of the national Bowel Cancer Screening Programme?
 Yes
 No
7. How did you hear about the PERFECTS research project?
 British Society of Gastrointestinal & Abdominal Radiology (BSGAR) website
 Email
 Word of mouth
 Other (please state)

Once enrolled, questionnaire completion formed part of the pre-randomisation process, following which eligible participants were invited to take part in the main study. All participants were required to complete the CTC assessments in sequence to be eligible for the subsequent test.

Randomisation

Although randomisation was performed at cluster-level, I obtained informed written consent from individual radiologists. Following their expression of interest, they were sent the trial Participation Information Sheet and written consent form which were completed and returned by email (Appendix 3). Once enrolled on the trial, the online pre-randomisation questionnaire was administered, recording prior training, BCSP reporting status, career experience and workflow (Figure 9.3; Appendix 4). Radiologist attitudes to training and accreditation were also captured.

Figure 9.3: Excerpt from the online questionnaire



Pre-Randomisation Questionnaire

1. Considering your CTC work load and reporting:

a) How many radiologists report CT colonography (CTC) scans in your department?

b) Approximately how many CTCs do you personally report per week?
Please select one: ▼

c) Approximately how many CTCs do you personally report per year?
Please select one: ▼

b) Do you report CTC for the Bowel Cancer Screening Programme (BCSP)?
 Yes No

i) Do you have dedicated CTC reporting sessions (i.e. sessions for reporting CTCs *only*)? If so, how many per week?
Please select one: ▼

j) On average, how long do you spend reporting a single CTC?
Please select one: ▼

Progress: 23%

Buttons: Back, Save, Next

The questionnaire was distributed by unique link to each participant's email address. Responses were automatically collected within a password protected database (UCL Opinio v7.12) and subsequently extracted to an Excel spreadsheet. The questionnaire was designed to be completed within 5 to 10 minutes and divided into the following four main areas (i) CTC workload; (ii) CTC interpretation; (iii) previous training; and (iv) views on feedback. Response options were a combination of free text (with restrictions on field entries e.g., strictly numerical, or limited characters), tick boxes, drop down menus and Likert scale options.

Randomisation was stratified according to career experience of the first radiologist recruited to each cluster. I collapsed relevant questionnaire data into binary categories of 'less than' or 'more than 1000 CTCs reported in career so far' and the trial statistician Mr Paul Bassett subsequently performed the randomisation using software-generated pseudo-random numbers to allocate clusters to each of the two study arms.

Intervention

'Training the CT Colonography Trainers Course' faculty training

As per best practice in training principles discussed in Chapter 7, we designed and conducted a 'Training the CT Colonography Trainers Course' (TC3) to develop an 'Expert Faculty' who would teach at the PERFECTS 1-day training intervention. The course was based on a TC3 that had previously been developed and run by Dr David Burling and Ms Rachel Baldwin at St Mark's Hospital (part of the PERFECTS

central research team) and was adapted by us to suit the aims of the one-day training intervention. The purpose of the faculty training was to refine their teaching skills in CTC, highlighting key concepts behind learning including conscious competence and critical reflection and to ensure consensus when delivering the training intervention (course programme available in Appendix 5). Potential faculty members, included radiographers and radiologists, who fulfilled any of the following criteria were invited to participate in the TC3:

- (a) career experience of more than 3000 CTCs,
- (b) local/national role in CTC education or
- (c) position at a tertiary colorectal cancer referral centre.

During the course, faculty were introduced to the PERFECTS study and aims, the workshop topics they would be teaching, and the CTC practice case database.

The faculty TC3 training day was held in 2017 (Figure 9.4), and 13 faculty members were trained in total.

Figure 9.4: PERFECTS faculty training day



Agreement was reached on the optimum CTC interpretation strategy to ensure consistent messaging during the workshop regardless of which expert trainer a given participant was partnered. Each faculty member was asked to rank their three favoured CTC topics to teach, and I used these to organise the workshop timetables (shown later in Table 9.2).

The CTC training cases were compiled from anonymised, endoscopically-validated datasets retrieved from St Mark's Hospital, Harrow and University College London Hospitals NHS Foundation Trust. I created a case database with descriptive data of each case, including screenshots of lesions, colonoscopy and histology findings, teaching points and difficulty level (Figure 9.5). These 40 cases were divided into learning categories and used by the expert faculty to emphasise teaching points at the workshop (Appendix 5). The training cases were separate and distinct cases from those used in the subsequent CTC assessments and were specifically selected to highlight common pitfalls in CTC interpretation. Faculty received printed packs of the case bases at TC3, which they could then reference when delivering the workshop training.

Figure 9.5: Excerpt from case description pack provided to expert faculty

PTC10

Difficulty: MEDIUM

Findings:

- 3cm CRC proximal AC (S345/RLD306).
- 10mm distal SC polyp (S426/RLD374)

Endpoints = 2

Colonoscopy/Histology:
 12mm ls polyp 25 cm from the anal verge and just prior to an acute angulation (very awkward position), biopsied.
 In the right colon a 4-5 cm lesion taking over 60% of the luminal circumference, biopsied.
 HISTOLOGY: total colectomy. Synchronous cancers. T3NOV0, T1N1V0

Learning Category:
 Interpretation technique > Satisfaction of search

Learning Point(s):
 Remember to look for synchronous lesions

Teaching Notes:

One-day training workshop

Following the baseline test, intervention arm radiologists submitted a Personal Development Plan (PDP) detailing three CTC learning objectives they would like to address (Appendix 5). They then attended a 1-day, face-to-face training workshop delivered by the central research team and Expert Faculty at St Mark's Hospital, Harrow. The workshop day focused on practical 1:1 or 2:1 teaching, using the CTC training datasets described above (Figure 9.6).

Figure 9.6: Photos of PERFECTS one-day training



Given observations that most participants will have already received basic CTC interpretation training via attendance at some form of introductory CTC course,¹²² and most CTC training is general rather than targeted; the training intervention was designed to be individualised. It specifically addressed the submitted PDPs and declared areas of weakness of each participant, thereby allowing them to gain hands-on experience tailored to their learning needs.

The workshop also addressed general topics in CTC reporting (Table 9.1). Using an Objective Structured Clinical Examination (OSCE)-type workshop format with a single topic addressed at each station. Learning points were emphasised with specific cases selected from the training case database to support each participant's PDP.

Table 9.1: Workshop topics and learning objectives

Interpretation technique
<ul style="list-style-type: none"> - Use MPR and 3D endoluminal views for both primary detection and problem solving - Principles of 2D scrolling focused on the colon and polyp matching between scan positions - Awareness of advanced 3D visualisation tools (e.g., panoramic, unfolded cube and virtual dissection) - Employ techniques that improve detection of difficult lesions - Develop a process for evaluating review areas - Employ techniques to avoid 'satisfaction of search'
Non-neoplastic abnormalities
<ul style="list-style-type: none"> - Differentiate non-neoplastic abnormalities from neoplastic pathology - Features of haemorrhoids, diverticular change and colonic anastomoses - Characteristics of benign and malignant strictures - Hernia
Flat lesions
<ul style="list-style-type: none"> - Develop strategy to detect flat lesions more easily - Increase confidence in flat lesion identification - Use techniques that improve detection of difficult lesions
Fold-related lesions
<ul style="list-style-type: none"> - Develop strategy to detect subtle, fold-related lesions more easily - Increase confidence in fold-related lesion identification - Use techniques that improve detection of difficult lesions
Small/irregular polyps
<ul style="list-style-type: none"> - Develop strategy to detect small (6 to 9 mm) lesions more easily - Characterisation of polyp candidates with an irregular or atypical morphology - Understand the Paris Polyp Classification System

Additional tips on pitfalls involving anorectal junction lesions, ileocaecal valve variations and lesions, spasm and under-distension, tagging and faecal residue and appendix and appendiceal orifice were delivered during each station and when illustrated by specific cases.

Between each station, Expert Faculty held a five minute debrief to confidentially share feedback on their participant's performance and exchange tips and ideas to develop the participant's strengths and further address any weaknesses (Table 9.2).

Table 9.2: Sample workshop timetable, with five stations, allowing 1:1 teaching with an expert trainer and interval debriefing

0830-0900	Registration/Coffee				
0900-0915	Welcome & Introduction				
0915-0930	Software review				
	Small polyps – Trainer A	Interpretation technique 1 – Trainer B	Fold related lesions – Trainer C	Non-neoplastic abnormalities – Trainer D	Flat lesions – Trainer E
0930-1030	Participant A	Participant B	Participant C	Participant D	Participant E
1030-1035	5 min changeover				
1035-1135	Participant E	Participant A	Participant B	Participant C	Participant D
1135-1145	Coffee Break				
1145-1245	Participant D	Participant E	Participant A	Participant B	Participant C
1245-1330	LUNCH				
	Small polyps – Trainer E	Interpretation technique 1 – Trainer A	Fold related lesions – Trainer B	Non-neoplastic abnormalities – Trainer C	Flat lesions – Trainer D
1330-1430	Participant C	Participant D	Participant E	Participant A	Participant B
1430-1435	5 min changeover				
1435-1535	Participant B	Participant C	Participant D	Participant E	Participant A
1535-1545	Summary/Concluding comments				
1545-1645	<i>Optional session to review additional cases</i>				

I collected participants' views regarding the quality of the workshop training and format by subsequent online survey (Appendix 5). Following receipt of their

completed post-workshop survey they were issued with a formal course attendance certificate and Continued Professional Development (CPD) points.

Feedback on performance

At the workshop, each participant received written feedback of their baseline test performance, including details of any false positive lesions identified and anonymous benchmarking of their score against the rest of the group (Figure 9.7).

Figure 9.7: PERFECTS individualised written feedback on test performance

Participant Information

Name	Dr xxxx
Grade	Consultant
Trust	xxxxx
Lifetime experience	100 to 499 cases
BSCP reporter?	Yes
Primary read	2D
Routine 3D use?	Yes (25% of read time)
Routine CAD?	No
Average routine reporting time per case	16 to 20 mins
Personal development plan	1) Being more confident in dismissing benign lesions/faecal matter. 2) Using 3D more confidently as a primary reading tool. 3) Accurate measurements of polyps.

Overall Results

Category	Number	Explanation
Lesions correctly detected	12	There are a total of 16 lesions (>6mm) in the 6 month test as agreed by expert panel. Correctly detected lesions are highlighted in green . Your missed lesions are highlighted in red . Measurements that differ by more than 6mm from the panel's or lesions that were incorrectly matched are also highlighted in red . Non-neoplastic lesions are not scored.
Index lesions correctly detected	7	There are a total of 2 Index lesions in the 6 month test. Index lesion (in bold) = lesion with most advanced histology, or largest lesion where several have the same histology
False positive lesions	2	Polyp 5mm+ or cancer lesion recorded in a segment that is normal or has non-neoplastic abnormalities as per colonoscopy or repeat CT colonography are highlighted in orange .

Further breakdown and analysis of your results will be provided as the project advances.

PTC39 – 1 of 2 lesions detected

Your Response (diagnostic confidence = 6):

	Lesion Type	Size (mm)	Colonic Segment	Series 1	Image number	Series 2	Image number
Index lesion	Cancer - mass like	13.0	Ileocaecal valve	Supine	96	Prone	111

Management: Refer for consideration of endoscopic evaluation (for characterisation +/- biopsy or polypectomy)

Panel Response:

	Lesion Type	Size (mm)	Colonic Segment	Series 1	Image number	Series 2	Image number
Index lesion	Cancer - mass like	25.0	Ileocaecal valve	Supine	91-101	Prone	103-114
Lesion 2	Polyp - 5mm +	11.0	Ascending colon	Supine	89-93	Prone	100-103

Management: Refer for consideration of same day colonoscopy, biopsy and CT staging

PTC39

Comparison of results

	Baseline (19 lesions)		1 Month (16 lesions)		6 month (16 lesions)	
	#	%	#	%	#	%
Lesions correctly detected	10	52.6	12	75.0	12	75.0
Index lesions correctly detected	1	14.3	5	71.4	7	100.0
False positive lesions	1	-	3	-	2	-

Further breakdown and analysis of your results will be provided as the project advances.

Comparison of your performance to the average at each test

Test	User Performance (%)	Average Performance (%)
Baseline	52.6%	41.9%
1m	75.0%	66.3%
6m	75.0%	66.3%

At each topic station they also received verbal feedback from an expert trainer and reviewed relevant test cases to identify areas of improvement. Following each subsequent test (at 1-, 6- and 12-months), radiologists randomised to the intervention arm received their test results with written feedback and were invited to receive optional verbal feedback via a phone call (up to one hour) with a faculty member to discuss their performance.

Control arm radiologists did not attend a training workshop or receive any feedback on their test performance until after the trial was completed at 12 months. To encourage adherence to the protocol, participants in both arms were able to claim CPD points for trial participation as private study. Travel expenses to the workshop were reimbursed, and participants were offered a £20 gift voucher if they successfully recruited a colleague who contributed to the primary outcome. Participants received no financial incentives for study participation.

Assessments

Selection of CT colonography imaging datasets

The CTC cases that were compiled into each test were specifically chosen to represent the spectrum of luminal colorectal lesions encountered in screening practice.²²² A prevalence of 50-70% abnormal cases per test set was used, at the upper range of that seen among screenees with positive faecal immunochemical testing (FIT).³⁵ A relatively high prevalence had two effects – firstly providing multiple endpoints, thereby increasing statistical power, and secondly, increasing

the likelihood of some lesions being missed, therefore avoiding ceiling effects due to all radiologists identifying all lesions.

Like the workshop training cases, the CTC test cases were identified from anonymised datasets retrieved from St Mark's Hospital, Harrow and University College London Hospitals NHS Foundation Trust. True negative (normal) scans were identified similarly and defined as those in which both initial CTC and subsequent colonoscopy (or repeat CTC occurring at least 24 months later) showed no lesion, of any size.

All CTC studies had been performed according to published guidelines, i.e thin slice (≤ 2 mm) CT, universal faecal tagging, images acquired in at least two positions, automated carbon dioxide insufflation via rectal catheter and use of a spasmolytic unless contraindicated.¹²¹ I divided possible test cases into true positives (i.e. depicting a cancer and/or ≥ 6 mm lesion) and true negatives (i.e. normal). All true positive lesions were confirmed with subsequent colonoscopic and/or histological proof and scrutinised by a minimum of three experienced (>1000 career CTCs) members of the research team (Associate Professor Andrew Plumb, Dr David Burling, Dr Raj Ilagovan and Mrs Janice Muckian). They reached consensus on lesion size, colonic segmental location, CT location (range of axial slice numbers over which the lesion was visible) and level of difficulty (graded out of 100 and based on lesion conspicuity). If consensus was not reached on lesion size and location, then I excluded the case from the test bank.

Cases of varying difficulty were evenly spread across each of the four tests and true negative cases were added to make test sets of 10 CTC cases each.

CT colonography test delivery

I compiled all agreed cases onto a separate Excel database and applied a unique study code to each one. The cases were then further coded according to possible teaching points and lesion morphology (flat (height ≤ 3 mm) and non-flat lesions).⁷⁴ Each case contained only the best quality two views e.g. supine and prone, or supine and decubitus to minimise fatigue and optimise chances of test completion.

I considered several different options to capture the test case interpretation by study participants and performed a comparison and risk analysis of various factors including cost, convenience, licensing, and technical challenges. Each option was scored accordingly (Appendix 6). The options considered were as follows:

1. Online CTC viewer – using a ‘thin client’ and image processing/rendering server in the cloud
2. Downloadable CTC viewer programme – using a ‘thick client’ with integrated cases to download from a server and install on participants own device
3. Hardcopies of cases on USB or DVD distributed by post and uploaded to hospital CTC workstations
4. Mobile laptops with installed CTC viewing software and uploaded test cases distributed
5. Image Exchange Portal (IEP) - download CTC cases only from imaging exchange server to local server
6. Physical training hubs in central locations with CTC workstations available for testing

Based on best overall score, ease of accessibility and ability to track participant access to the cases, an agreement was reached with Vital Images, Toshiba to provide an online platform for case review. Participants were able to access the

CTC software 'Vitrea' via a dedicated link to the Vital servers on which the test cases had been preloaded. A limited number of users (10 at a time) could access the platform between pre-specified hours to complete their tests. Unfortunately, due to insufficient technical support available to provide timely troubleshooting and a complicated workflow, only 13 participants of 38 (34%) were able to successfully view cases in the first rounds of testing.

Following the failure of direct online access to the test cases, the second highest scoring alternative (downloading the CTC viewer onto participant devices) was explored as an additional option. Vital Images proposed a process for this via access to a remote desktop and I created a guide detailing installation and use of Vitrea using either the direct online link or the remote desktop for software download (Appendix 7).

In parallel, to mitigate further difficulties accessing the CTC tests and to minimise participant drop out, the test cases were made also available as hardcopies on Digital Versatile Disc (DVD) and posted to participants at their request. Due to ease of delivery and ongoing technical challenges, the decision was eventually made to transition completely to providing cases on DVD for local upload to the participant's usual CTC workstation. Participants were therefore able to use their usual CTC workstation, including access to computer aided detection (CAD) if provided by their local software.

CT colonography test data collection

Participants were informed that each test set combined normal and abnormal cases but were unaware of the prevalence of abnormality or any clinical

information. Both trial arms received the same 10 test cases at each time point, and were only required to perform a colonic assessment for each case (i.e. ignoring any other abnormalities in the scanned volume outside of the colon).

Participants were provided with a unique 7-digit participant identification (ID) code, which became their anonymous identifier for the duration of the trial. Using a central database, Unique UCL Opinio v7.12, I generated email links inviting participants to a specifically designed online electronic Case Report Form (eCRF) (Appendix 8). The 7-digit ID and unique email link provided two points of verification to identify each participant's responses.

Participants used the eCRF to record their assessment of each test case specifying:

- a) case-level diagnosis. Defined as normal (no lesion of ≥ 6 mm) or abnormal (CRC and/or lesion(s) ≥ 6 mm)
- b) the type of lesion(s) and its maximum dimension
- c) the colonic segment and slice location of each abnormality (denoted at the epicentre of the lesion)
- d) best management option
- e) the proportion of time spent using 2D vs 3D visualisation for each case
- f) diagnostic confidence

To allow for measurement error, participants were asked to document any lesions measured at ≥ 5 mm, but only lesions with the reference standard size of ≥ 6 mm were included for analysis. Participants were encouraged to keep their test answers confidential during the trial and were advised not to discuss the test cases with colleagues.

At the end of the eCRF a free text section was included for participants to list three learning objectives. These formed the personal development plan (PDP) for the intervention arm radiologists and were addressed during the one-day workshop.

Participants were given a two- to three-week window within which to complete each CTC test. Compliance and retention were encouraged by up to five automatically generated reminder emails from the eCRF database. If no responses were received for the relevant test, then I sent up to three personal reminders before the participant was considered lost to follow up.

Anonymous data from the completed eCRFs were exported into a password protected Microsoft Excel spreadsheet and the tests were manually classified according to pre-specified criteria discussed below. Outcome data were collected for every completed test, even if a participant discontinued the study before the final assessment at 12 months. Original participant eCRFs were downloaded and archived as study source data.

Classification of radiologist interpretations

I manually classified radiologist interpretations from each eCRF and approximately 40% were also classified by additional readers: Associate Professor Andrew Plumb (thesis supervisor) or Dr David Burling to ensure reproducibility. We agreed detailed, pre-specified criteria which were universally applied to all tests and used to create individual written feedback for each participant (Figure 9.7).

As any given CTC study may depict more than one lesion or cancer, *a priori* we decided to classify cases on both a per-lesion and a per-patient basis. For the per-

lesion analysis, an individual lesion or cancer was regarded as detected by the interpreting radiologist if the correct slice number(s) within the pre-specified range for that lesion was stated, and at least two of the following three parameters were correct:

- a) lesion type
- b) colonic segmental location (to within one colonic segment of the reference standard)
- c) size measurement (to within 50% of the reference standard)⁵⁷

For the per-patient analysis, a pre-specified 'index' lesion was agreed for each CTC dataset (i.e. corresponding to a single individual patient's scan), which was defined as the neoplasm with the most advanced histology or, where there were several neoplasms with equivalent histology, the largest of these.²²⁵ In all cases except one (in which a 14mm carcinoma (index lesion) co-existed with a 40mm sessile serrated lesion), the most histologically-advanced lesion was also the largest. Correct identification of the index lesion, using the same criteria as above, denoted a true positive finding for the per-patient analysis.

Correctly identified normal cases (i.e. true negative interpretations) were those in which no false positive lesions were documented by the radiologist. A false positive lesion was defined as a lesion or CRC of any size identified by a participant in a case defined as normal by the reference standard. Benign findings (e.g. lipomas or haemorrhoids) were not regarded as false positives if correctly described as such by the participant.

Intervention arm participants were sent feedback documents after each completed test and were invited for an optional telephone feedback call with an expert faculty member. Each set of feedback documents contained the participant

demographics, total score (i.e. number of lesions correctly identified), number of index lesions identified, number of false positives, comparison of their findings compared to that of the expert faculty, benchmarking of their performance compared to the rest of the cohort and screenshots of the pathology (Figure 9.7).

Although eCRFs were classified at the time of completion, the control arm feedback documents were not distributed to control participants until trial completion.

Outcomes

Although randomisation was performed at cluster level, the intervention was targeted at individual radiologists; therefore, the study outcomes focus on individual-level outcomes.

The primary outcome was the mean difference in per-lesion sensitivity for CRC or ≥ 6 mm lesions between study arms at the 1-month test timepoint.

The secondary outcomes were:

1. Mean difference in per-lesion sensitivity at 6- and 12-months post-intervention. The results at 12-months are of particular importance as this represents the most realistic time point at which any repeat / refresher training would be administered in an established programme
2. Mean difference in per-patient sensitivity (as defined by identification of the index lesion) at each test timepoint
3. Difference in per-lesion sensitivity pre- and post-intervention

- a. According to the following sub-groups: percentage of time spent performing 3D read, morphology, colonic segment, BCSP status
4. Number of false positives per case at each test timepoint
5. Association between lesion detection and radiologist characteristics: career experience and use of 3D read
6. Association between lesion detection and polyp characteristics e.g. size, morphology and colonic location

Although not a pre-specified per-protocol secondary outcome measure, participant acceptance of the training intervention was sought via post-workshop feedback.

Sample size and statistical analysis

Sample size calculation was based on the primary outcome of difference in sensitivity between study arms for ≥ 6 mm polyps or CRC at the 1-month timepoint. We assumed a sensitivity of 70% for the control arm,⁶⁶ and assigned a 10% increase as being clinically important. Under an assumption of independent data points, then with 5% significance level and 80% power, 294 lesions (i.e. polyps or cancers) were required per arm. The inflation factor (i.e. the design effect to account for the clustered design) was taken to be $1 + ICC(n-1)$,²²⁶ where ICC = Intraclass Correlation Coefficient and n = number of positive cases interpreted by each radiologist. Data from previous CTC reader performance studies suggest an ICC of 0.092.²²⁷ At mean 60% prevalence of abnormality per test ($n=6$), the design effect was 1.46. Therefore, we required 429 abnormal CTC cases per study arm, totalling 715 cases (429 abnormal, 286 normal) at the 1-month test, corresponding to 72 radiologists per arm reaching 10 scans each. Accounting for

10% drop-out, we aimed to recruit 80 radiologists to each arm. A previous national UK survey identified an average of 3 CTC reporting radiologists per hospital.¹²² Therefore we anticipated a median cluster size of 2 (assuming not all radiologists in a given centre would participate), thus aiming to recruit from approximately 40 clusters per arm.

All statistical analyses were performed by Paul Bassett (Stats Consultancy) and Dr Susan Mallett (University of Birmingham) using multilevel methods. A cross-classified model with radiologist crossed with lesion at the higher level, and individual measurements at the lowest level was performed with separate analyses for each test timepoint. Multilevel logistic regression was used for the analysis of lesion/patient level sensitivity and specificity outcomes, whilst multilevel Poisson regression was used for the number of false positives. In all analyses, the average outcome at baseline for each radiologist was included as a covariate in the model. For all outcomes, secondary analyses were also performed with the outcome being the sensitivity/specificity/number of false positives calculated for each radiologist at each timepoint. These analyses were performed in order to obtain the absolute differences in outcome between arms. Linear regression using one observation per radiologist per timepoint was used for these analyses.

For the primary outcome, lesion-level sensitivity, additional analyses were performed to examine if the intervention effect varied dependent on radiologist/lesion factors. Separately, an interaction between each factor and the intervention was included in the model. If the interaction was significant, the effects of the intervention were quantified for each subgroup. All analyses were performed using Stata 15.1 (StataCorp, College Station, Texas, USA).

Chapter 10 Results

Participant characteristics

Between 20 April 2017 and 27 Sept 2018, 139 radiologists (134 Consultants, 5 senior trainees) from 72 NHS hospital sites were recruited and completed the pre-randomisation questionnaire (Figure 10.1). The full list of hospital sites represented is included in Appendix 9. Three sites were subsequently excluded from the main trial as they were outside England and Wales.

Figure 10.1: Hospital sites of questionnaire respondents



Due to time constraints, recruitment closed prior to reaching our target sample number and follow up was completed by January 2020.

Radiologist attitudes to CT colonography performance and training

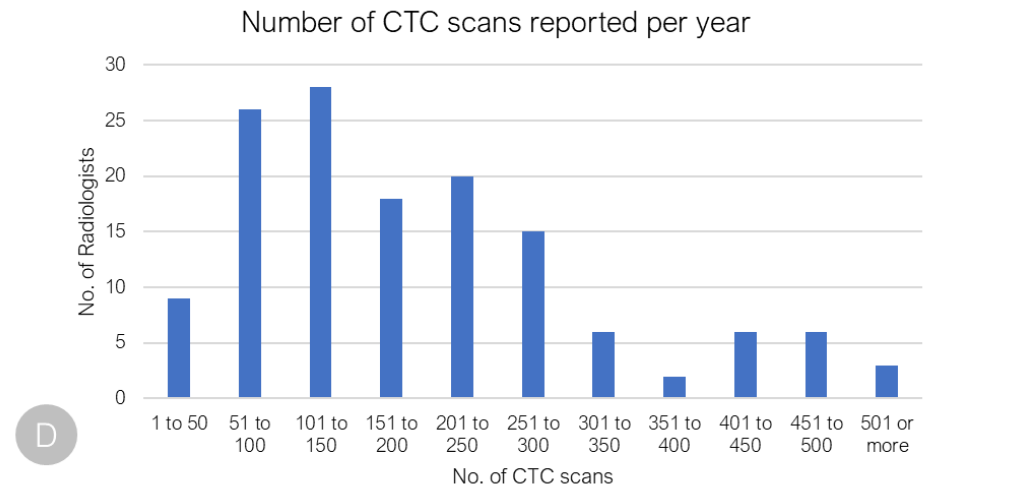
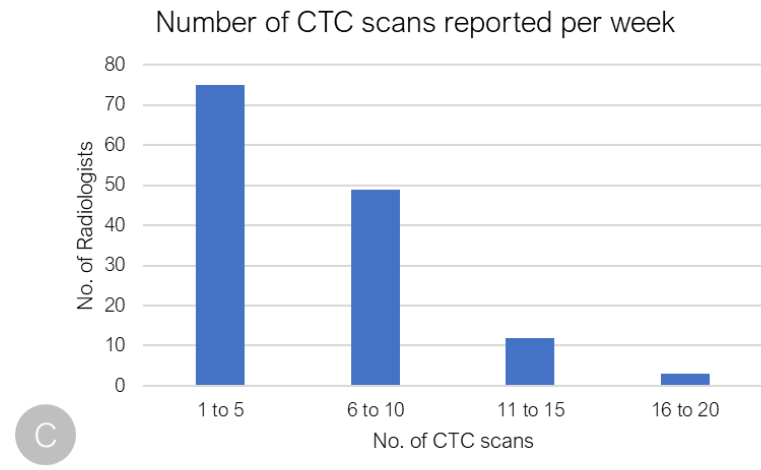
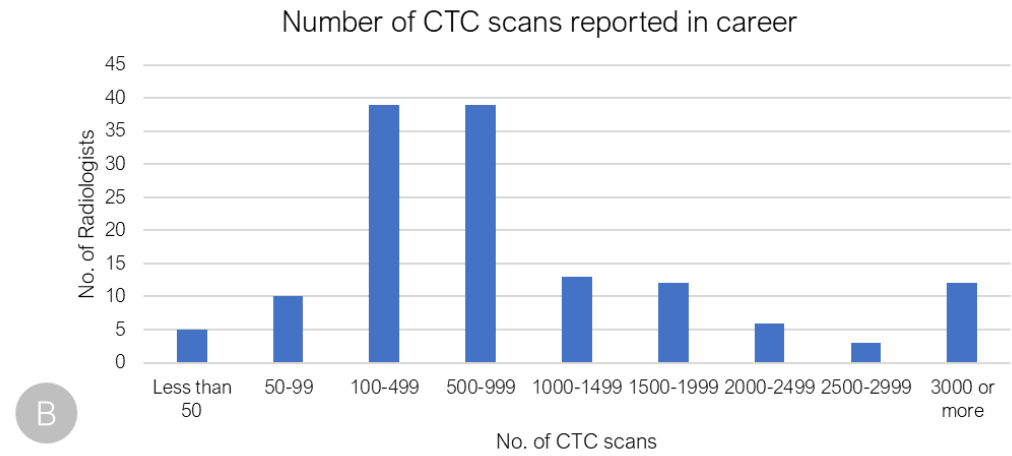
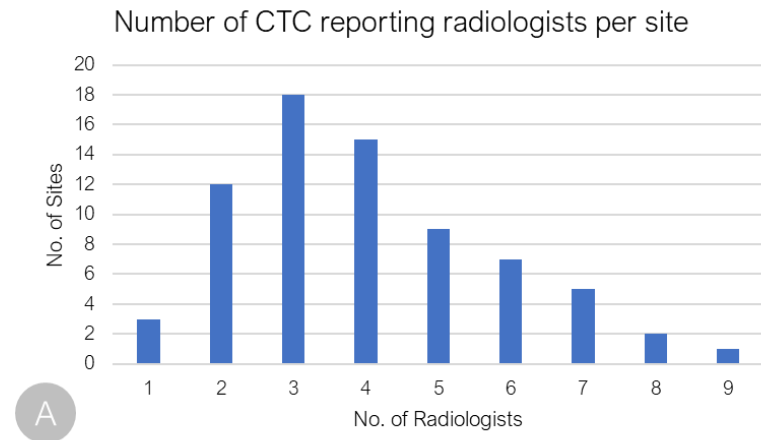
The pre-randomisation questionnaire captured reader experience and training, service organisation and CTC reporting characteristics. Response rate was necessarily 100%, as completion of the questionnaire was required for subsequent enrolment in the PERFECTS trial. There were 139 respondents.

CT colonography service organisation and workload

The number of radiologists reporting CTC per site ranged from one to nine, with most sites (25% [18/72]) having three readers (Figure 10.2A). Just over two-thirds of respondents (68% [95/139]) report for the BCSP, and there was a median career experience of 500 to 999 CTC scans (Figure 10.2B).

Most recruited radiologists do not have dedicated CTC reporting sessions (73% [101/139]), while 23% (33/139) had one session per week and 4% (5/139) had two sessions. Despite this, 54% (75/139) of radiologists report one to five scans a week, while 2% (3/139) report 16 to 20 scans (Figure 10.2C). The median number of scans reported per year was 151 to 200 scans, with 17% (23/139) reporting more than 300 scans per year.

Figure 10.2: Questionnaire responses regarding CT colonography workload



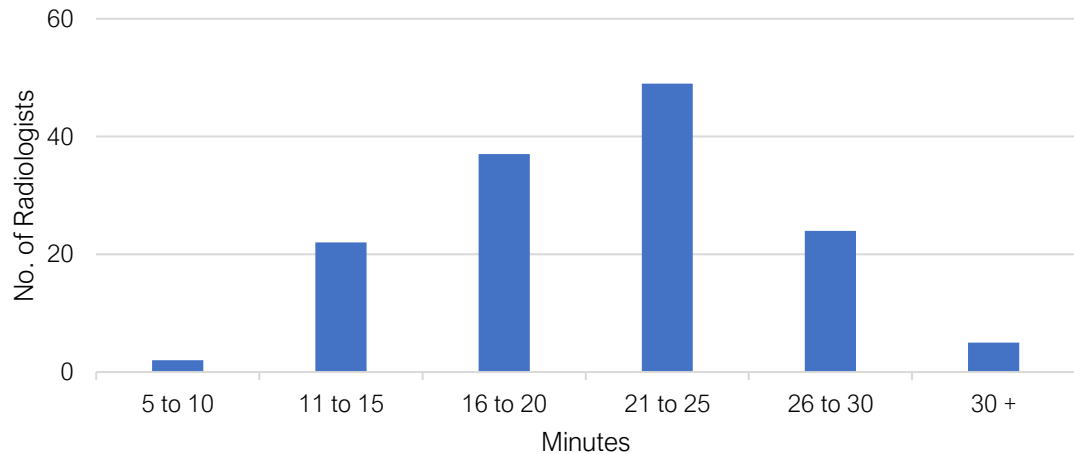
CT colonography interpretation

Ninety-nine percent (137/139) of radiologists reported using CTC software for reporting. The three most popular software providers were Siemens (Syngo.via) 29% (40/139), General Electric Healthcare (Advantage Windows Colon VCAR) 28% (39/139) and Vital Images (Vitreia) 24% (34/139). Eighteen (13%) radiologists used more than one different platform and two (1%) did not use dedicated CTC software at all, therefore only utilising a picture archiving and communication system (PACS) workstation. Forty-eight percent (67/139) of radiologists have one or more workstations in their department specifically for CTC interpretation.

Most radiologists described themselves as primary 2D readers (73% [101/139]) although 73% (102/139) also perform a 3D review. Time spent on the 3D read varied, with 17% (23/139) spending less than 10%, and 29% (41/139) spending more than 50% of their read time on a 3D fly-through.

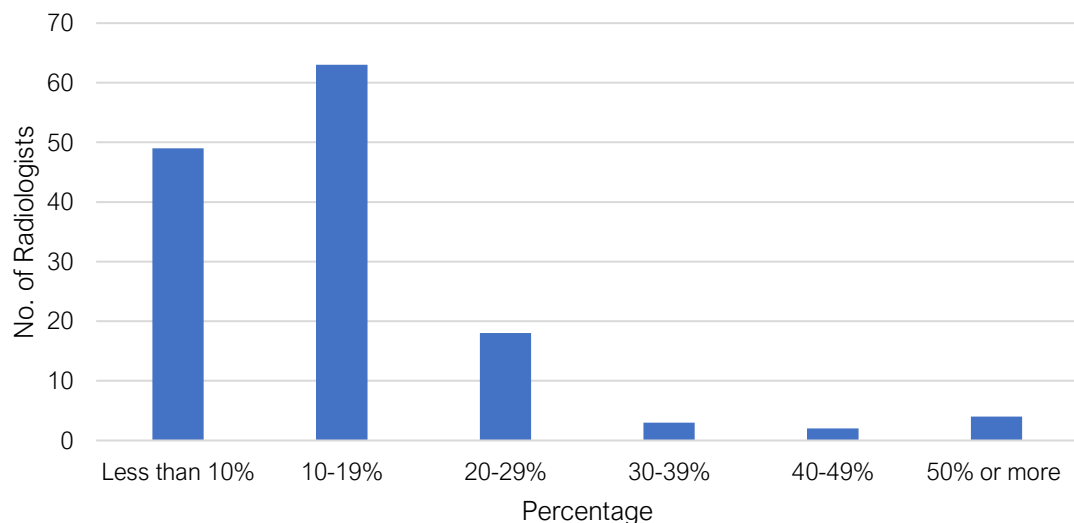
The median time spent reporting one CT scan was estimated at 21 to 25 minutes (Figure 10.3) and 75% (104/139) of recruited radiologists routinely use computer aided detection (CAD).

Figure 10.3: Time spent reporting one CTC scan



Regarding the direction of CTC interpretation, no radiologists performed their interpretation from caecum to rectum only; most read in both directions (60% [84/139]) and 40% (55/139) read from rectum to caecum only. A typical range of detected abnormalities (polyp detection rate; PDR) was 10 to 19% (45%; [63/139]; Figure 10.4).

Figure 10.4: Rate of abnormalities (polyp detection rate)



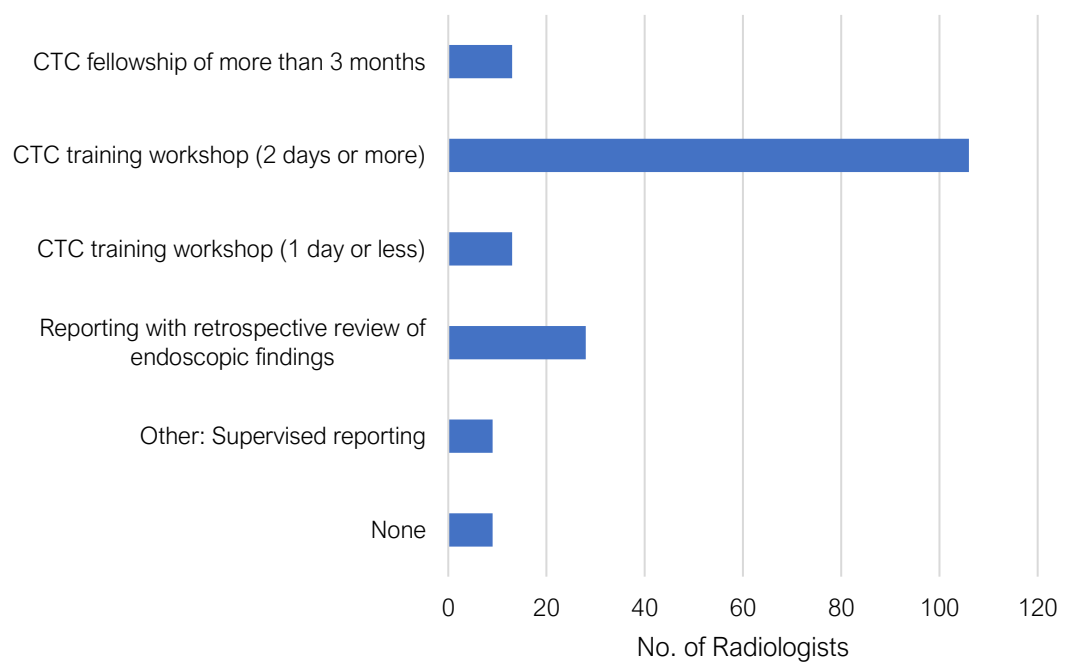
However, few radiologists (6% [9/139]) use audit with endoscopic correlation to calculate their PDR and 80% (111/139) were only able to estimate this rate, with

13% (18/139) using a combination of estimate and audit; one person did not know their PDR (0.7% [1/139]). Most radiologists (57% [79/139]) do not know what percentage of their reported cases are endoscopically validated, while 37% (52/139) report that up to 25% of their cases have endoscopic validation.

CT colonography training

Beyond routine reporting practice, 76% (106/139) of radiologists had attended a CTC training workshop of two days or longer, while a smaller number, 9% (13/139), had attended a workshop of one day or less. Reporting with retrospective review of endoscopy findings was used by 20% (28/139) and 9% had undertaken a dedicated CTC fellowship of three months or longer (Figure 10.5). Forty-three radiologists had undergone more than two different types of training. Nine radiologists (6%) had no previous CTC training.

Figure 10.5: Different types of previous CT colonography training



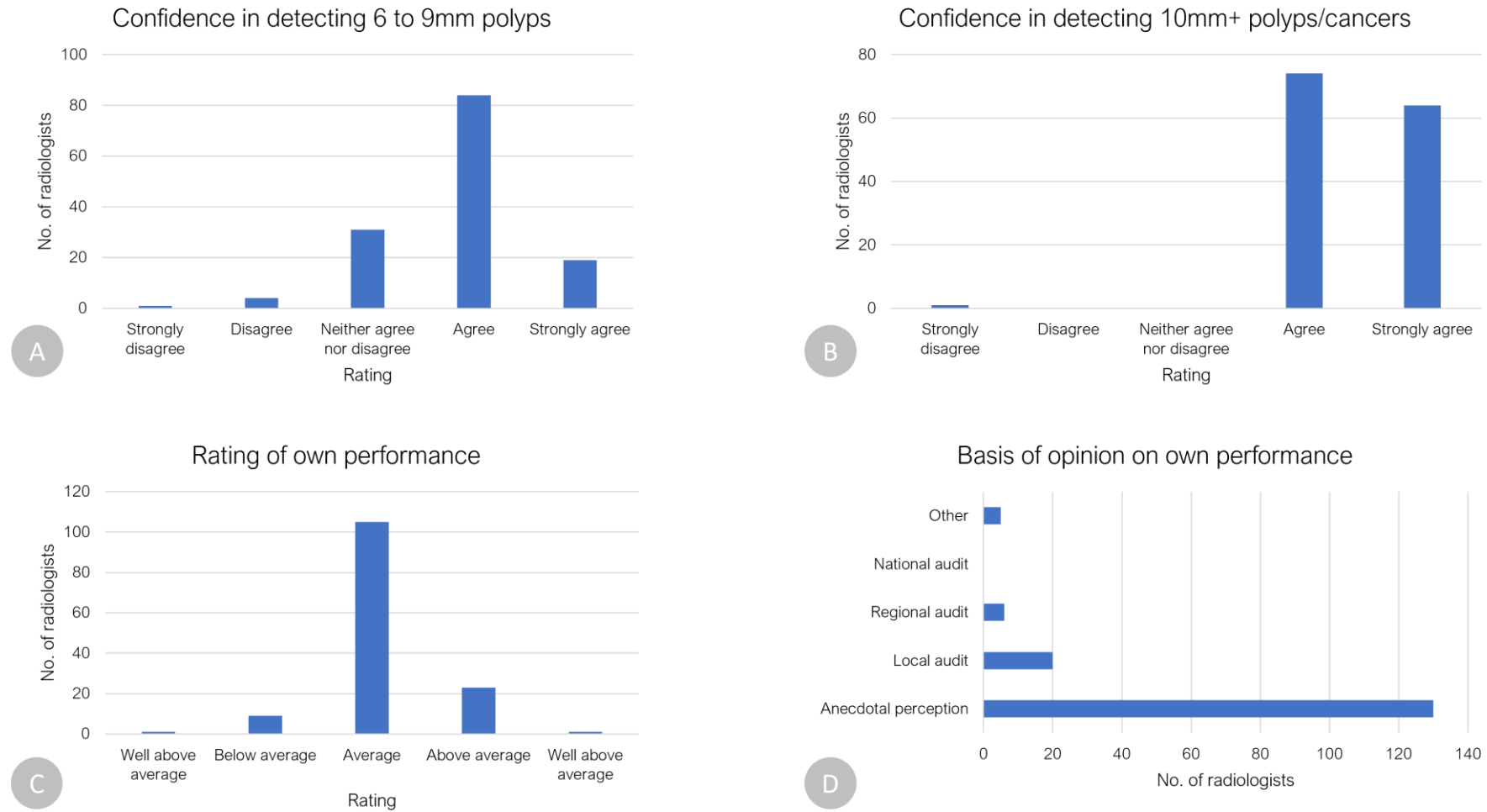
When rating their CTC interpretation training, 60% (83/139) of radiologists rated it as 'satisfactory', 29% (40/139) as 'very good' and 4% (5/139) as 'excellent'. One person reported their previous training as 'poor' (0.7%), and 10 radiologists rated it as 'not very good' (7%).

Of respondents who stated they report for the BCSP, 47% (50/107) felt satisfactorily prepared to interpret CTC in the programme, 35% (37/107) felt well prepared and 7% (7/107) felt very well prepared. One person felt very poorly prepared (1%), and 12 radiologists (11%) felt poorly prepared.

When considering confidence in lesion detection, most radiologists (60% [84/139] agreed that they were confident in detecting 6 to 9 mm polyps (Figure 10.6A) and 14% (19/139) stated they strongly agreed, while 4% disagreed or strongly disagreed and 22% (31/139) were uncertain. In comparison, 53% (74/139) agreed they were confident in detecting ≥ 10 mm polyps/cancers and 46% (64/139) strongly agreed (Figure 10.6B). Only one person (1%), stated they strongly disagreed that they were confident in detecting ≥ 10 mm lesions.

Respondents were also asked to benchmark their performance by answering the question, 'In comparison to other Radiologists reporting CTC, where do you think your performance lies?' and on what basis they formed their answer (Figure 10.6C, D). Most radiologists felt their performance was average (76% [105/139]) and this was overwhelming based on anecdotal perception (94% [130/139]) rather than objective measures.

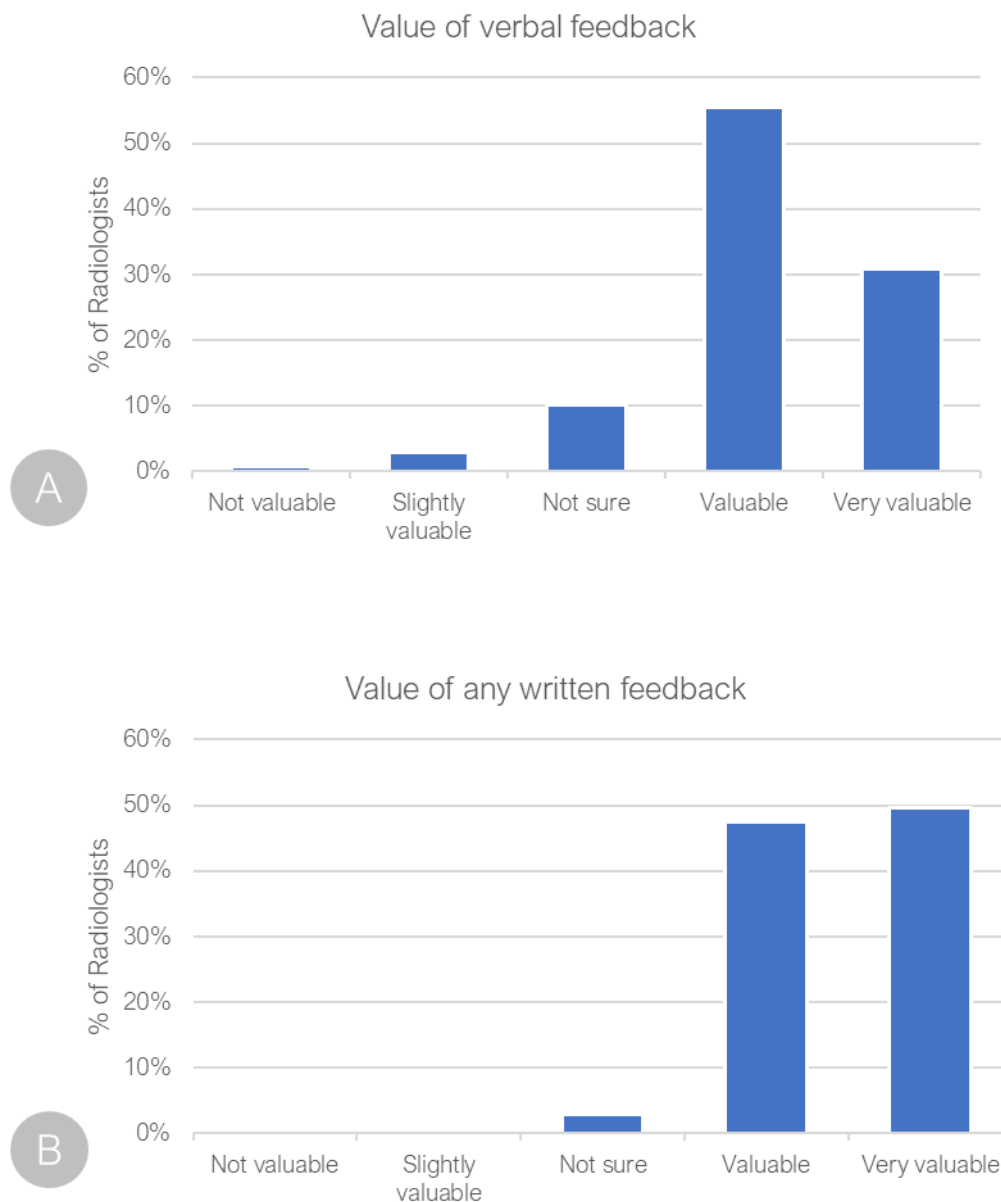
Figure 10.6: Confidence in lesion detection and rating of own performance

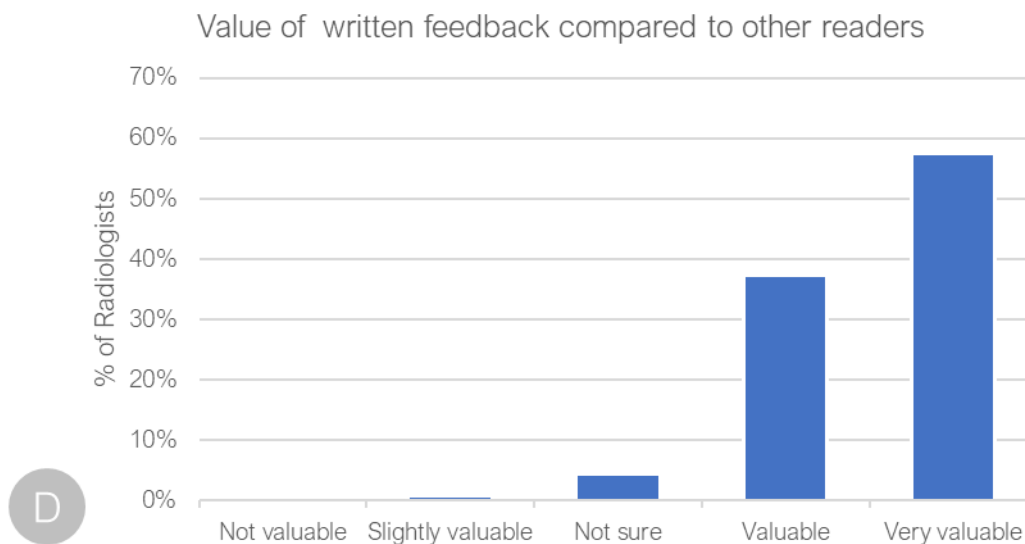
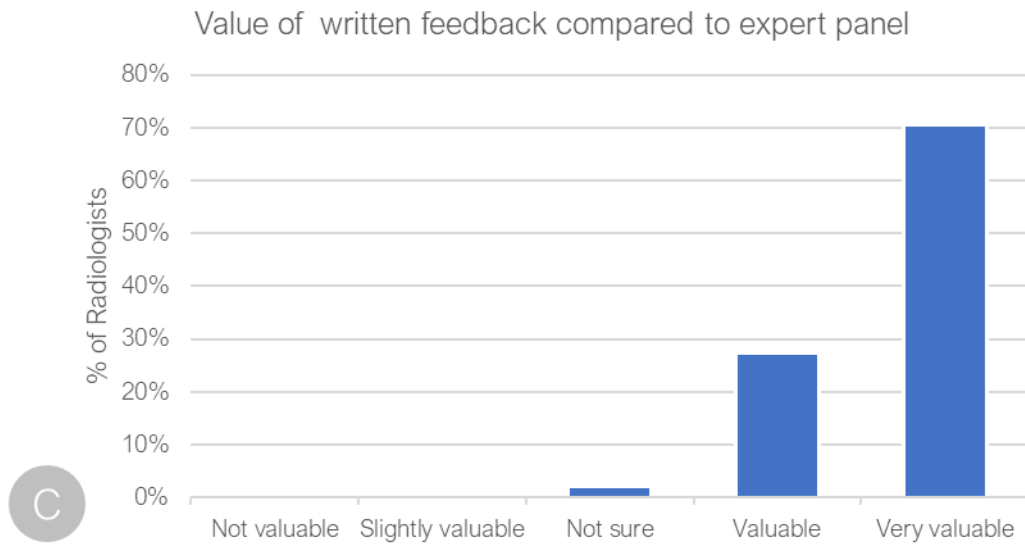


Views on performance feedback

Radiologists were asked their views on CTC reporting performance feedback and 86% (120/139) stated that verbal feedback is valuable (55%) or very valuable (31%). Generally, any written feedback was considered valuable (47% [66/139]) or very valuable (50% [69/139]), with 3% (4/139) stating they were unsure (Figure 10.7A and B).

Figure 10.7: Value of feedback on performance





If written feedback were provided with a comparison to expert panel reports, 71% (98/139) responded that this would be very valuable. In comparison 58% (80/139) responded that written feedback with benchmarking compared to other readers was very valuable and 37% (52/139) reported that this was valuable (Figure 10.7C and D).

Opinions on four different CTC performance metrics were collated; and for each more than 50% of radiologists responded that knowing these would be very valuable (Table 10.1)

Table 10.1: Reported value of knowing specific CTC performance metrics

		Performance metric			
		Polyp detection rate	Cancer detection rate	Positive predictive value	Negative predictive value
Perceived value (n of 139)	Not valuable	0% (0)	0% (0)	0% (0)	0% (0)
	Slightly valuable	1% (1)	1% (1)	0% (0)	0% (0)
	Not sure	6% (8)	3% (4)	4% (5)	4% (6)
	Valuable	35% (48)	24% (33)	32% (44)	31% (43)
	Very valuable	59% (82)	73% (101)	65% (90)	65% (90)

Following completion of the pre-randomisation questionnaire, 69 clusters were randomised into the two trial arms (Figure 10.8).

Baseline characteristics were well-balanced between the trial arms (Table 10.2) and BCSP status and career experience were comparable. Use of 3D visualisation was similar in both arms (control: 75% [45/59]; intervention: 71% [57/80]), as was use of computer-aided detection (CAD; control: 78% [46/59]; intervention: 73% [58/80]); with radiologists typically spending 15 to 25 minutes reporting one CTC study (control: 68% [40/59]; intervention: 58% [46/80]). When considering previous CTC training, 8% (5/59) of the control arm and 5% (4/80) of the intervention arm had received no training at all, however most had attended a CTC training workshop of two days or longer (73% (43/59) of control arm and 80% (64/80) of intervention arm).

Figure 10.8: Trial profile

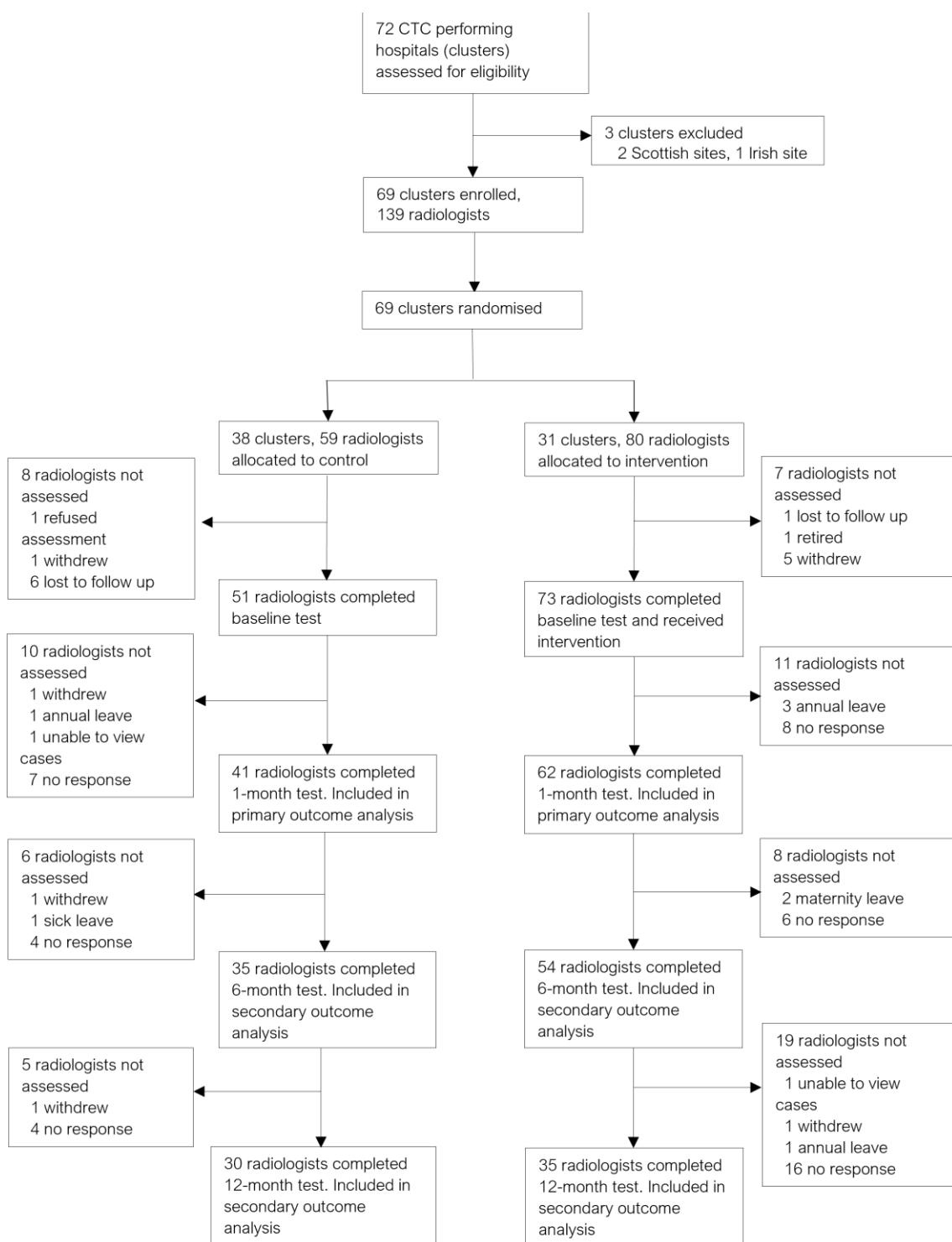


Table 10.2: Characteristics of radiologists included in the trial

	Control (n=59)	Intervention (n=80)	P-Value
Report for BCSP	36 (61%)	59 (74%)	0.11
Career experience			0.99
<500 CTC scans	23 (38%)	31 (39%)	
500-1499 CTC scans	22 (38%)	30 (38%)	
1500+ CTC scans	14 (24%)	19 (24%)	
Reporting characteristics			
3D read performed	45 (76%)	57 (71%)	0.51
Mean % of total read time spent on 3D read (range)	39% (5-100)	36% (5-80)	
Use of CAD	46 (78%)	58 (73%)	0.46
Time to report:			0.34
<15 mins	10 (17%)	14 (18%)	
15-25 mins	40 (68%)	46 (58%)	
26+ mins	9 (15%)	20 (25%)	
CTC training workshop			0.34
None	11 (19%)	8 (10%)	
CTC training workshop (1 day or less)	5 (8%)	8 (10%)	
CTC training workshop (2+ days)	43 (73%)	64 (80%)	
Other training			
Supervised reporting	5 (8%)	11 (14%)	0.34
Reporting with retrospective review of endoscopic findings	13 (22%)	15 (25%)	0.70
CTC fellowship (3 months or more)	4 (7%)	2 (3%)	0.22

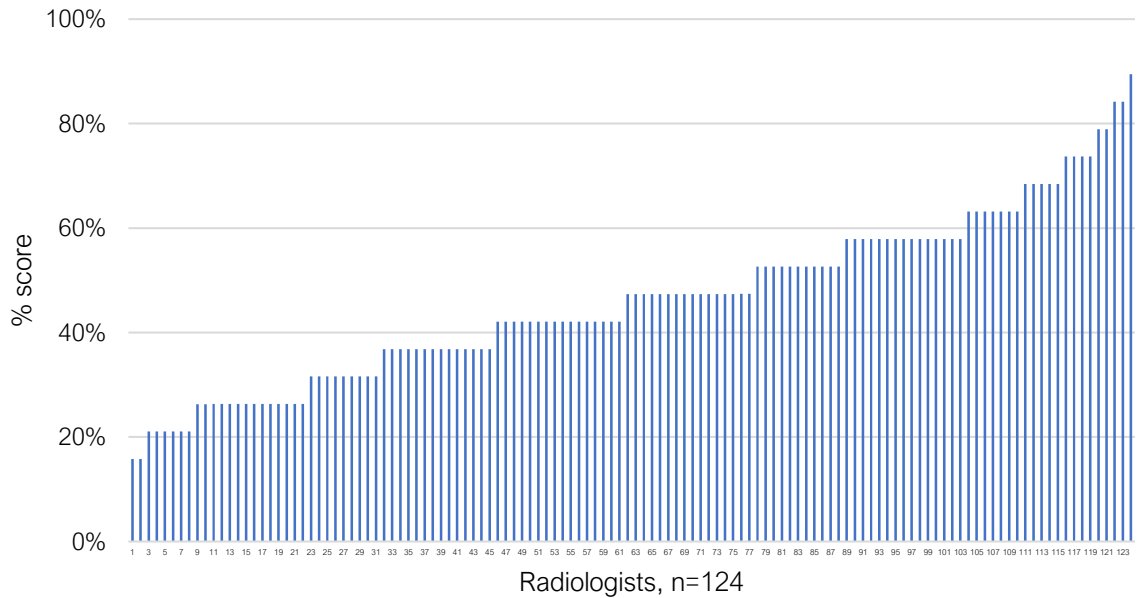
Proportions (%) have been rounded to the nearest whole number and may not total 100%. Some radiologists had more than one form of CTC training, so the total is greater than 100%. BCSP: Bowel Cancer Screening Programme. 3D: three dimensional. CAD: Computed Aided Detection.

Baseline performance

A total of 65 lesions were assessed across the four tests, comprising 12 cancers (measuring 10-60 mm), five serrated lesions (measuring 8-40 mm) and 48 adenomas (measuring 6-50 mm); 23 lesions (36%) were flat (<3 mm height) and 46 (72%) were ≥ 10 mm. At baseline testing, 1240 cases were interpreted by a total of 124 radiologists. Individual radiologist sensitivity varied widely, ranging from

15.8% (3 of 19 true positive lesions detected) to 89.5% (17/19) (mean 46.0%, interquartile range 35-58%; Figure 10.9).

Figure 10.9: Variability in radiologist performance at the baseline test (intervention and control arm data combined)



% score = number of lesions correctly detected out of 19 in the baseline assessment. Each bar represents one radiologists' score

Baseline per-lesion sensitivity was similar between intervention and control arms (intervention: 47.7% [661 of 1387 lesions detected] vs control: 43.3% [420/969]; difference 4.3%; 95% CI: -1.4 to 10.0; $p=0.13$; Table 10.3); and between BCSP and non-BCSP radiologists ($p=0.10$; Table 10.4).

Table 10.3: Difference in per-lesion detection, per-patient detection, and per-patient specificity between the two arms at the baseline test

Test timepoint	Control % (n/N)	Intervention % (n/N)	Odds Ratio (+) (95% CI)	% Difference (**) (95% CI)	P-value
Per-lesion sensitivity					
Baseline - All (*)	43.3% (420/969)	47.7% (661/1387)	1.37 (0.91, 2.05)	4.3 % (-1.4%, 10.0%)	0.13
Baseline (**)	43.4% (338/779)	49.4% (582/1178)	1.53 (0.99, 2.39)	6.0% (-0.2%, 12.3%)	0.06
Per-patient sensitivity (¥)					
Baseline - All (*)	29.4% (105/357)	35.2% (180/511)	1.65 (0.93, 2.94)	5.8% (-0.8%, 12.4%)	0.09
Baseline (**)	28.9% (83/287)	37.3% (162/434)	2.06 (1.07, 3.95)	8.4% (1.1%, 15.8%)	0.08
Per-patient specificity					
Baseline - All (*)	92.2% (141/153)	87.2% (191/219)	0.55 (0.23, 1.31)	-4.9% (-12.0%, 2.2%)	0.18
Baseline (**)	92.7% (114/123)	88.2% (164/186)	0.55 (0.19, 1.58)	-4.5% (-12.4%, 3.3%)	0.27

Differing denominators are a result of the different number of lesions per test and radiologist dropout.

(*) Including data from all radiologists, including those who took no further part in the trial

(**) Data only from radiologists who provided further data. (¥) Calculated by detection of the histologically most advanced lesion ('index' lesion)

(+) Odds ratio calculated as odds of detection intervention arm relative to the control arm, adjusted for baseline sensitivity or specificity as appropriate

n= number of lesions detected/N=total number of lesions for per-lesion sensitivity results; number of index lesions detected/total number of index lesions for per-patient sensitivity results and number of normal studies correctly identified/total number of normal studies for per-patient specificity

(++) % difference calculated as value intervention arm minus value in the control arm, adjusted for baseline sensitivity or specificity as appropriate

Table 10.4: Summary of baseline test results by BCSP reader status

Outcome	Dropouts(*)	Non-BCSP	BCSP	P-value
Per-lesion sensitivity	No	43.6% (323/741)	46.9% (758/1615)	0.37
	Yes	42.9% (269/627)	49.0% (651/1330)	0.10
Per-patient sensitivity	No	32.6% (89/273)	32.9% (196/595)	0.88
	Yes	32.5% (75/231)	34.7% (170/490)	0.74
Specificity	No	88.9% (104/117)	89.4% (228/255)	0.72
	Yes	90.9% (90/99)	89.5% (188/210)	0.84

(*) Data with and without radiologists who took no further part in the study

BCSP: Bowel Cancer Screening Programme

Per-patient sensitivity and per-patient specificity were also comparable between the trial arms at baseline (Table 10.3).

Trial Outcomes

Twelve one-day training workshops were conducted between 6th June 2017 and 7th November 2018. Eighteen radiologists in the control arm and 18 in the intervention arm were lost to follow-up before the primary outcome.

Primary outcome. The one-day training intervention significantly improved radiologist per-lesion sensitivity at 1 month. Radiologists randomised to the intervention had greater improvement in 1-month test scores (659/992 lesions detected, 66.4%) than control (278/655, 42.4%; difference 20.8%, 95% CI: 14.6 to 27.0; $p < 0.001$; Figure 10.10; Table 10.5).

Table 10.5: Difference in per-lesion detection, per-patient detection, and per-patient specificity between the two arms at each test timepoint

Test timepoint	Control % (n/N)	Intervention % (n/N)	Odds Ratio (+) (95% CI)	% Difference (++) (95% CI)	P-value
Per-lesion sensitivity					
Baseline (**)	43.4% (338/779)	49.4% (582/1178)	1.53 (0.99, 2.39)	6.0% (-0.2%, 12.3%)	0.06
1 month	42.4% (278/655)	66.4% (659/992)	3.85 (2.54, 5.83)	20.8% (14.6%, 27.0%)	<0.001
6 months	50.5% (283/560)	66.4% (572/861)	2.64 (1.79, 3.92)	13.0% (7.4%, 18.5%)	<0.001
12 months	44.4% (187/421)	63.7% (310/487)	4.29 (2.41, 7.64)	16.7% (10.3%, 23.1%)	<0.001
Per-patient sensitivity (¥)					
Baseline (**)	28.9% (83/287)	37.3% (162/434)	2.06 (1.07, 3.95)	8.4% (1.1%, 15.8%)	0.08
1 month	26.9% (77/286)	59.0% (256/434)	5.67 (3.40, 9.47)	29.0% (21.1%, 36.9%)	<0.001
6 months	72.2% (177/245)	84.0% (316/376)	2.05 (1.22, 3.46)	9.9% (2.2%, 17.6%)	0.007
12 months	59.8% (107/179)	75.9% (157/207)	8.01 (2.58, 27.1)	14.4% (8.2%, 20.7%)	<0.001
Per-patient specificity					
Baseline (**)	92.7% (114/123)	88.2% (164/186)	0.55 (0.19, 1.58)	-4.5% (-12.4%, 3.3%)	0.27
1 month	91.1% (112/123)	80.6% (150/186)	0.40 (0.19, 0.84)	-10.3% (-18.5%, -2.1%)	0.02
6 months	90.5% (95/105)	84.0% (136/162)	0.56 (0.21, 1.51)	-5.3% (-14.5%, 4.0%)	0.26
12 months	97.5% (117/120)	89.3% (125/140)	0.21 (0.06, 0.84)	-7.7% (-14.4%, -1.0%)	0.03

Differing denominators are a result of the different number of lesions per test and radiologist dropout.

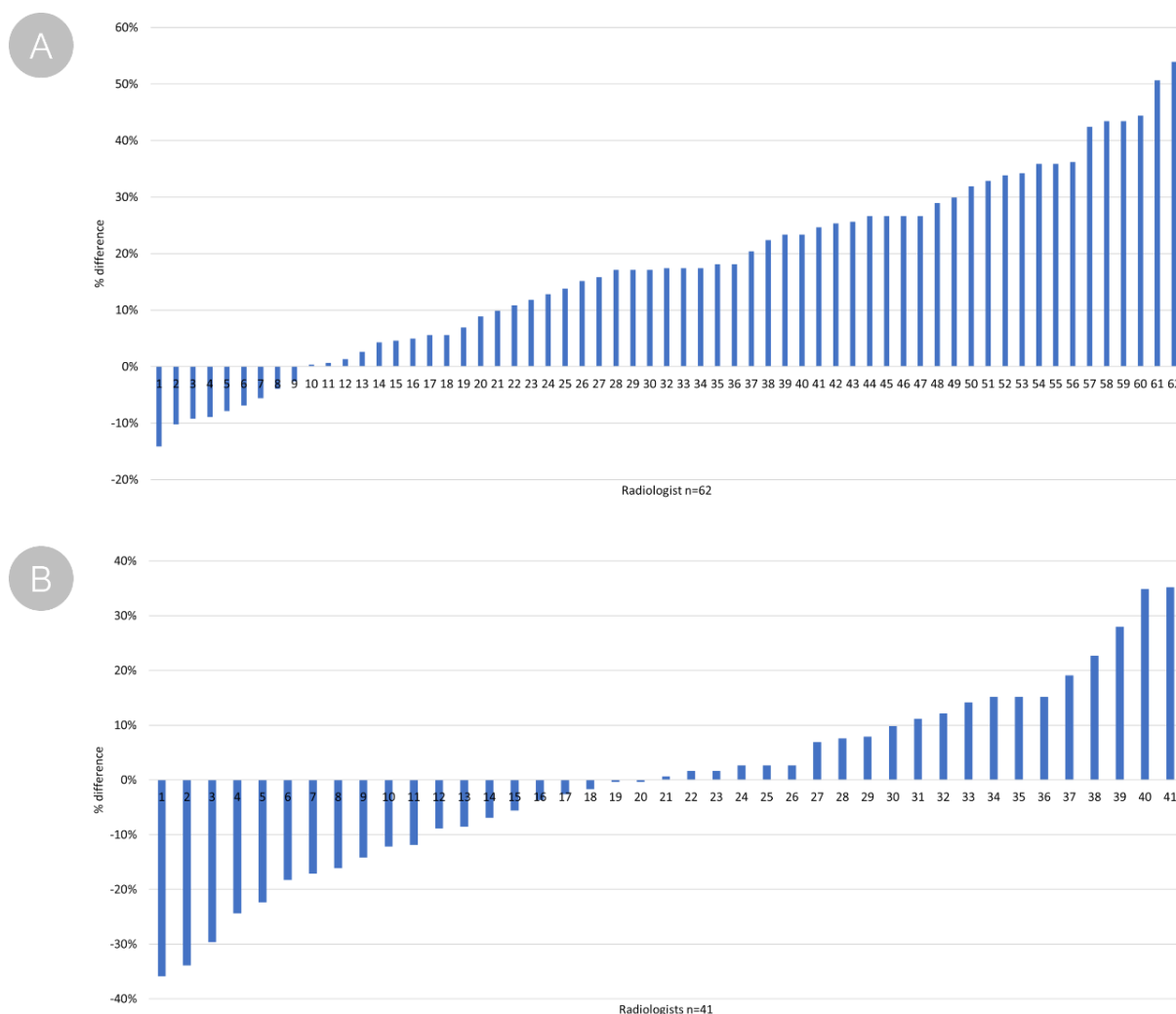
(**) Data from radiologists who provided further data. (¥) Calculated by detection of the histologically most advanced lesion ('index' lesion)

(+) Odds ratio calculated as odds of detection intervention arm relative to the control arm, adjusted for baseline sensitivity or specificity as appropriate

n= number of lesions detected/N=total number of lesions for per-lesion sensitivity results; number of index lesions detected/total number of index lesions for per-patient sensitivity results and number of normal studies correctly identified/total number of normal studies for per-patient specificity

(++) % difference calculated as value intervention arm minus value in the control arm, adjusted for baseline sensitivity or specificity as appropriate

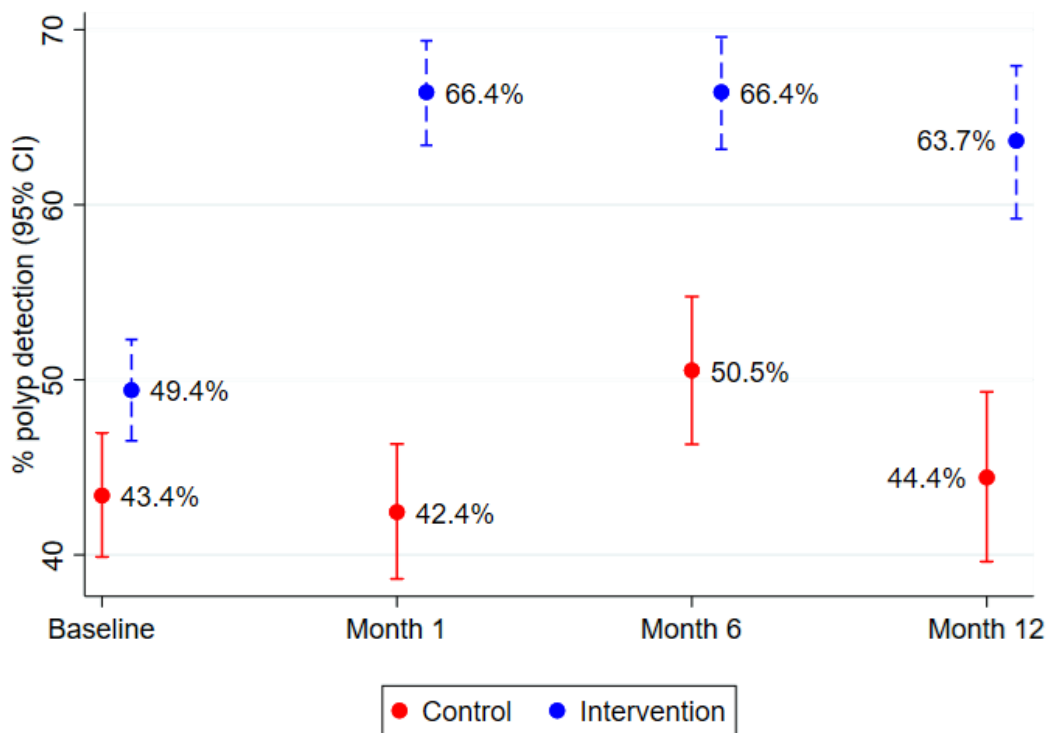
Figure 10.10: Differences in individual radiologist baseline and 1-month per-lesion sensitivity in detecting colorectal cancer/lesions ≥ 6 mm



(A) intervention arm, (B) control arm. Each bar represents the difference in a single radiologist's score

Secondary outcomes. The beneficial effect of the one-day workshop persisted at 6-months (intervention: 66.4% [572/861] vs control: 50.5% [283/560]; difference 13.0%; 95% CI: 7.4 to 18.5; $p < 0.001$) and 12-months (intervention: 63.7% [310/487] vs control: 44.4% [187/421]; difference 16.7%; 95% CI: 10.3 to 23.1; $p < 0.001$; Table 10.3). Overall, the intervention arm had an approximately 16.7% mean increase in per-lesion sensitivity relative to baseline over the three post-randomisation test points, compared to a 2.3% increase for controls (Figure 10.11).

Figure 10.11: Per-lesion detection of colorectal cancer/lesions ≥ 6 mm at each test timepoint for the control and intervention arms, with corresponding 95% CIs



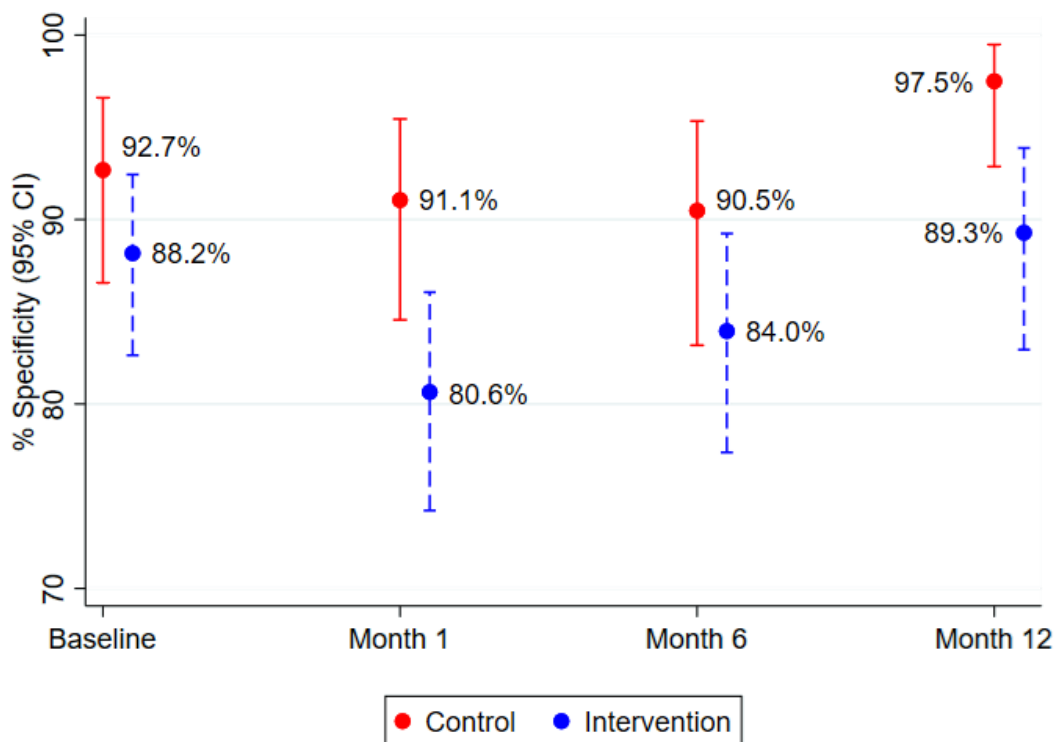
Radiologists who dropped out prior to reaching the 1-month timepoint were omitted from the baseline calculations

When considering per-patient analysis of sensitivity for the most histologically-advanced lesion, the intervention arm showed a significant improvement compared to control at all timepoints. At 1-month, per-patient sensitivity was 59.0% (256/434) in the intervention arm compared to 26.9% (77/286) for controls (difference 29.0%; 95% CI: 21.1 to 36.9; $p < 0.001$). This improvement was sustained at 6-months (intervention: 84.0% [316/376] vs control: 72.2% [177/245]; difference 9.9%; 95% CI: 2.2 to 17.6; $p = 0.007$) and 12-months (intervention: 75.9% [157/207] vs control: 59.8% [107/179]; difference 14.4%; $p < .001$; Table 10.5).

Patient-level specificity was similar between arms at baseline (intervention: 88.2% [164/186] vs control: 92.7% [114/123]; difference -4.5%; 95% CI: -12.4 to 3.3;

p=0.27). Following training, per-patient specificity was lower in the intervention arm at all time points (Table 10.5), with the difference being statistically significant at 1- (intervention: 80.6% [50/186] vs control: 91.1% [112/123]; difference -10.3%; 95% CI: -18.5 to -2.1; p=0.02) and 12-months (intervention: 89.3% [125/140], control: 97.5% [117/120]; difference -7.7%; 95% CI: -14.4 to -1.0; p=0.03). Overall, the intervention arm had an approximately 4% reduction in per-patient specificity relative to baseline over the three post-randomisation time points compared to a 0.4% increase for the control arm (Figure 10.12).

Figure 10.12: Per-patient specificity (denoted by identification of an 'index' lesion) at each test timepoint for the control and intervention arms, with corresponding 95% CIs



Radiologists who dropped out before the 1-month test were omitted from the baseline calculations

The number of false positive lesions detected at baseline, 1-month and 12-month tests was significantly higher in the intervention arm, although the magnitude of this

difference was small, averaging 0.27 false positives per-patient (intervention) versus 0.12 false positives per-patient (control) at 1-month (Table 10.6).

Table 10.6: Number of false positives at each test timepoint

Test timepoint	Control			Intervention			Ratio ⁽⁺⁾ (95% CI)	Difference ⁽⁺⁺⁾ (95% CI)	P-value
	N	N. FP	Mean ^(^) ± SD	N	N. FP	Mean ^(^) ± SD			
Baseline - All ^(*)	510	65	0.13 ± 0.35	730	147	0.20 ± 0.49	1.51 (1.04, 2.20)	0.07 (0.00, 0.15)	0.03
Baseline ^(**)	410	45	0.11 ± 0.33	620	130	0.21 ± 0.51	1.83 (1.04, 3.21)	0.10 (0.04, 0.18)	0.04
1 month	410	51	0.12 ± 0.43	620	169	0.27 ± 0.59	1.51 (1.04, 2.18)	0.14 (0.06, 0.21)	0.03
6 months	350	66	0.19 ± 0.50	540	143	0.26 ± 0.69	0.86 (0.62, 1.20)	0.05 (-0.05, 0.14)	0.37
12 months	300	24	0.08 ± 0.28	350	96	0.27 ± 0.56	2.05 (1.25, 3.36)	0.16 (0.07, 0.25)	0.004

(*) Including data from all radiologists, including those who took no further part in the trial

(**) Data only from radiologists who provided further data

(^) Mean number of false positives per case

(+) Ratio calculated as number of false positives in intervention arm relative to the control arm, adjusted for number of false positives at baseline

(++) Difference calculated as value intervention arm minus value in the control arm, adjusted for number of false positives at baseline

N: number of cases. N.FP: Number of False Positives

Radiologist experience and lesion size did not affect detection rates, therefore the effect of the intervention was not dependent on either of these two factors (Table 10.7).

Table 10.7: Association between radiologist or lesion characteristics and study group with per-lesion detection (all postintervention timepoints combined)

Factor	Factor x Group Interaction P-Value	Study Group	Category	% Detection (n/N)	Odds Ratio (95% CI)	P-value
Career experience	0.64	Both combined	< 500	55.8% (651/1167)	1	0.22
			500 – 1499	56.8% (955/1681)	0.92 (0.75, 1.12)	
			1500+	60.6% (683/1128)	1.09 (0.88, 1.36)	
Polyp size	0.25	Both combined	< 10 mm	44.2% (1080/2437)	1	0.35
			11 – 19 mm	53.9% (953/1769)	1.89 (0.54, 6.62)	
			20 mm	63.0% (1336/2122)	2.69 (0.63, 11.5)	

n = number of lesions detected/N = total number of lesions for per-lesion sensitivity results

In contrast, the intervention had a significant impact on the detection of lesions of any morphology, and irrespective of time spent using 3D visualisation (Table 10.8). Flat lesions were significantly more likely to be detected by radiologists in the intervention (55.1%, [458/832]) vs control arm (28.5% [164/575]; difference 22.7%; 95% CI: 15.5 to 29.9; $p < 0.001$), as were non-flat (i.e. elevated) lesions (intervention: 71.9% [1083/1506], control: 55.1% [582/1059]; difference 11.6%, 95% CI: 4.6 to 18.6; $p < 0.001$; Table 10.8). The training intervention had a significant impact on both BCSP and non-BCSP radiologists where test score improvements of 15.2% (95% CI: 9.8 to 20.6; $p < 0.001$) and 20.3% (95% CI: 12.8 to 27.8; $p < 0.001$) respectively, were observed (Table 10.8).

Table 10.8: Per-lesion detection according to subgroup (all post-intervention timepoints combined)

Subgroup	Control % (n/N)	Intervention % (n/N)	Odds Ratio ⁽⁺⁾ (95% CI)	P-value	% Difference ⁽⁺⁺⁾ (95% CI)
3D reporting					
< 20%	43.9% (329/750)	68.7% (365/531)	4.11 (3.04, 5.55)	<0.001	31.6% (20.3%, 42.9%)
20 - 49%	48.4% (171/353)	67.2% (721/1073)	2.67 (1.95, 3.67)	<0.001	17.9% (6.6%, 29.2%)
50+%	46.5% (248/533)	61.7% (442/717)	2.45 (1.82, 3.28)	<0.001	16.3% (5.5%, 27.2%)
Morphology					
Not flat	55.1% (583/1059)	71.9% (1083/1506)	2.46 (2.00, 3.03)	<0.001	11.6% (4.6%, 18.6%)
Flat	28.5% (164/575)	55.1% (458/832)	4.94 (3.63, 6.71)	<0.001	22.7% (15.5%, 29.9%)
Segment					
Caecum	36.9% (87/236)	58.8% (193/328)	2.82 (1.84, 4.30)	<0.001	14.2% (2.6%, 25.8%)
Ascending	25.8% (104/403)	53.5% (318/594)	4.78 (3.35, 6.83)	<0.001	25.4% (13.6%, 37.3%)
Transverse	24.6% (42/171)	53.4% (126/236)	4.64 (2.65, 8.11)	<0.001	22.7% (11.4%, 34.1%)
Descending	74.3% (26/35)	83.3% (45/54)	1.53 (0.52, 4.47)	0.44	4.1% (-9.1%, 17.2%)
Sigmoid	56.7% (284/501)	74.9% (531/709)	2.72 (2.02, 3.66)	<0.001	14.5% (4.7%, 24.3%)
Rectum	70.8% (204/288)	78.7% (328/417)	1.88 (1.19, 2.98)	0.007	7.3% (-3.6%, 18.1%)
BCSP reader					
No	41.0% (260/634)	62.2% (377/606)	3.90 (2.91, 5.24)	<0.001	20.3% (12.8%, 27.8%)
Yes	48.7% (488/1002)	67.1% (1164/1734)	2.69 (2.18, 3.31)	<0.001	15.2% (9.8%, 20.6%)

(+) Odds ratio calculated as odds of detection intervention group relative to the control arm, adjusted for baseline sensitivity

(++) % difference calculated as value intervention arm minus value in the control arm, adjusted for baseline sensitivity

In both trial arms, lesion detection varied according to segmental location, and was highest in the rectum and lowest in the ascending and transverse segments (Table 10.9). In the control arm, when radiologists used 3D visualisation for over 20% of their interpretation time, lesion detection was significantly higher (OR 1.48; 95% CI: 1.07 to 2.05; $p < 0.03$). Conversely, this was not true for the intervention arm, where 3D interpretation had little effect on odds of lesion detection ($p = 0.33$; Table 10.9). The morphology of lesions significantly affected detection by the control arm radiologists, and flat lesions were less likely to be detected (OR 0.20; 95% CI: 0.006 to 0.62; $p = 0.006$), whereas different lesion morphologies did not affect detection by the intervention arm ($p = 0.11$; Table 10.9).

Table 10.9: Association between radiologist or lesion characteristics and study group on per-lesion detection (all postintervention timepoints combined)

Factor	Factor x Group Interaction P-Value	Study Group	Category	% Detection (n/N)	Odds Ratio (95% CI)	P-Value	
Use of 3D reporting	.03	Control	< 20%	43.9% (329/750)	1	.03	
			20 - 49%	48.4% (171/353)	1.48 (1.07, 2.05)		
			50+%	46.5% (248/533)	1.37 (1.03, 1.82)		
		Intervention	< 20%	68.7% (366/532)	1		.33
			20 - 49%	67.0% (721/1073)	0.96 (0.73, 1.28)		
			50+%	61.7% (442/717)	0.81 (0.60, 1.11)		
Morphology	< .001	Control	Not flat	55.1% (583/1059)	1	.006	
			Flat	28.5% (164/575)	0.20 (0.06, 0.62)		
		Intervention	Not flat	71.9% (1083/1506)	1		.11
			Flat	55.1% (458/832)	0.39 (0.13, 1.22)		
Segmental location	.01	Control	Caecum	36.9% (87/236)	1	< .001	
			Ascending	25.8% (104/403)	0.46 (0.09, 2.34)		
			Transverse	24.6% (42/171)	0.42 (0.06, 2.90)		
			Descending	74.3% (26/35)	6.72 (0.20, 227)		
			Sigmoid	56.7% (284/501)	3.73 (0.80, 17.4)		
			Rectum	70.8% (204/288)	11.2 (1.99, 63.2)		
		Intervention	Caecum	58.8% (193/328)	1		< .001
			Ascending	53.5% (318/594)	0.79 (0.16, 3.89)		
			Transverse	53.4% (126/236)	0.69 (0.10, 4.55)		
			Descending	83.3% (45/54)	3.66 (0.11, 122)		
			Sigmoid	74.9% (531/709)	3.58 (0.78, 16.5)		
			Rectum	78.7% (328/417)	7.49 (1.34, 41.9)		

n = number of lesions detected/N = total number of lesions for per-lesion sensitivity results

The post-workshop feedback survey was completed by 97% (71/73) of radiologists randomised to the intervention arm. Almost all either 'agreed' (34% [24/71]) or 'strongly agreed' (65% [46/71]) that the workshop provided useful feedback regarding their performance (Figure 10.13). All respondents 'agreed' (27% [19/71]) or 'strongly agreed' (73% [52/71]) that workshop cases provided additional learning opportunities and 99% (70/71) would recommend it to their colleagues. Participation motivated 97% (69/71) of radiologists to improve their CTC reporting through independent study.

Figure 10.13: Sample of anonymous workshop feedback collected on post-workshop questionnaire (A) and, Email feedback received from a workshop attendee (B)



This was a difficult procedure.

At initial pass despite careful withdrawla after reaching the caecum I coudl not see the lesion on white light endoscopy. I then tried NBI and still coudl not identify the lesion despite position changes. Then on chromoscopy at first pass the lesion was not seen. At second pass with [REDACTED] help we identified the lesion. It is 50 mm in size and is type IIb with disporganised architecture on chromoscopy. Tes lifting with gelofusin showed only the edges to be lifting with the centre being adherent suggesting underlying malignancy.

Chapter 11 Conclusions of the PERFECTS trial

CTC is the first-choice radiological test for both CRC screening and symptomatic patients, and is recommended when colonoscopy is incomplete, contraindicated or undesirable.¹¹⁷ Although CTC is now widely available, and it is recognised that diagnostic accuracy for clinically relevant colonic neoplasia is impacted by the performance of the individual readers, radiologists are generally unaware of their poly detection rate (PDR). Coupled with the lack of standardised training this leads to inherent inconsistency in CTC quality, with pockets of good practice in high volume, experienced/academic centres, contrasting with areas of poorer performance due to either reduced resource or less local expertise.

Screening services are obliged to ensure competent interpretation is available nationally. For both endoscopy and breast screening, this is addressed in two main ways. Firstly, practitioners must undergo initial testing and accreditation processes before entry. Secondly, they must participate in ongoing accreditation via cycles of repeated performance monitoring, supported by quantitative metrics and (for mammographic screening) test cases to maintain accuracy. Illogically, there is no analogous mandatory testing, accreditation, or performance monitoring for CTC reporting in CRC screening. This is despite the observation that screen-detected lesions are both smaller and harder to detect at CTC than those encountered in routine (symptomatic) practice.²²² It is possible, indeed likely, that unregulated entry combined with absence of mandated training and assessment contributes to the lower detection rates for CTC and higher 3-year interval cancer rates reported in the English BCSP, in comparison to colonoscopy.^{63,228}

Therefore, we investigated whether testing, training and feedback analogous to that used for colonoscopy and breast screening, could address this deficiency. We recruited experienced radiologists already interpreting CTC in daily practice, most of whom were already reporting for the national BCSP. In total, 139 radiologists were recruited, from 69 hospital sites in England and Wales representing 29% (63 of 219)²²⁹ of NHS Trusts and 45% (63 of 139)⁵² of those performing CTC.

Only 28% had a weekly session dedicated to CTC reporting so invariably CTC scans are being reported within general reporting lists. This is suboptimal as it exposes the reader to external distractions and interruptions, and often requires moving between workstations to access CTC reporting software (used by 99%). Despite not having dedicated reporting sessions most radiologists (83%) manage to spend at least 16 minutes reporting each scan, which is in line with BSGAR recommendations.¹²¹ The value of longer reporting times has been discussed in Chapter 5.

Despite almost all radiologists responding that knowing their PDR would be valuable, most (80%) were only able to estimate this based on anecdotal evidence, rather than on objective local or regional audit data. Furthermore, most radiologists viewed their performance as 'average', again based on anecdotal perception only in the majority (94%). Without knowledge of objective performance metrics it is difficult to accurately assess the impact of previous CTC training, or identify areas of weakness that require further attention.

In the PERFECTS trial, 124 radiologists completed the baseline test and although it only comprised 10 CTC cases (with 19 lesions), initial sensitivity was extremely

variable. Worryingly, per-lesion sensitivity ranged from 15.8 to 89.5% (mean 45.95%), before our training intervention, with similar results between BCSP and non-BCSP radiologists, confirming widely ranging accuracy currently. We found that a 1-day training workshop and feedback model increased radiologist sensitivity for CRC and ≥ 6 mm polyps by 16.7%, and that this effect was sustained for at least 12 months ($p < 0.001$). The benefit was seen across the spectrum of neoplastic lesions encountered in screening, regardless of morphology, with a 22.7% improvement in detection of flat lesions ($p < 0.001$). Lesion detection in the intervention arm was higher across all colonic segments ($p < 0.01$; except descending colon: $p < 0.44$) and was irrespective of previous career experience ($p = 0.64$), use of 3-dimensional (3D) interpretation ($p = 0.33$) or BCSP reporting status. The training intervention was practical to deliver, lasting only one day, and 99% (70/71) of participants would recommend it to their colleagues.

Prior studies of CTC reader training and/or testing have used novices or small numbers (< 10) of experienced readers rather than large representative samples of current practitioners as we have.^{198,202,203,211} A study evaluating the effect of structured initial training found that approximately 175 CTC cases were required for most novices to achieve adequate sensitivity.¹⁹⁸ Even so, a third of readers failed to achieve adequate performance despite more prolonged training on over 200 cases. Many professional bodies set minimum standards for CTC training by simply stipulating a number of cases reported prior to independent practice and, thereafter, documentation of annual caseload.^{121,190} However, this is likely to have limited value as individuals achieve competence at different rates. Indeed, we found no association between career experience and lesion detection.

Our model of 1:1 and 2:1 training focused on individual areas of weakness, supplemented by written feedback, allowing us to target learning needs to each radiologist, thereby maximizing the relevance of their training. Although the per-lesion sensitivity of radiologists after training was 66.3%, lower than previous reports from unselected screening populations,⁶⁶ it is similar to the findings of another study of hard-to-detect polyps.¹⁹⁷

Our data suggest that this model of iterated testing with subsequent individualised feedback and (re)training when necessary will lead to far superior sustained performance versus relentlessly accumulating large caseloads without refresher training or feedback.

We found a large improvement in sensitivity coupled with a smaller loss of specificity. While improved detection rates might be partly offset by increased false-positive referrals to colonoscopy, we found sensitivity increased disproportionately (16.7% increased sensitivity vs. 7.7% reduced specificity at 12-months), meaning net benefit would be overwhelmingly positive. This is especially relevant because patients and their doctors value sensitivity gains disproportionately over loss of specificity.²³⁰

Study limitations

Naturally, there are limitations. Our test dataset was weighted to reflect the upper end of FIT prevalence and to include subjectively difficult-to-detect lesions. These cases do not mirror an unselected screening or symptomatic population exactly, so caution should be applied when extrapolating to settings with differing

prevalence and disease spectrum. Furthermore, we intentionally devised challenging test sets to avoid potential ceiling effects in a cohort of experienced radiologists, but this may mean our effect size is greater than that achievable in other settings. In addition, we did not make any provision for the Hawthorne effect – whereby participants modify their behaviour in response to being observed or studied.²³¹ This effect should have been distributed evenly between the randomised arms, however, may still affect generalisability. For example, participants performing a more thorough review for a test case to achieve a higher score than they may be able to do within the pressures and distractions of normal clinical practice. We also encouraged radiologists to report all lesions ≥ 5 mm, without providing any clinical history. This was to maximise detection rates, but does not necessarily accurately mirror typical practice, e.g. within the BCSP which advises against reporting diminutive polyps or symptomatic practice where polyps ≤ 10 mm are unlikely to be responsible for the clinical presentation.

We closed recruitment before reaching our pre-specified sample size, meaning 103 radiologists contributed data to the primary outcome compared to our initial target of 144. However, our observed effect size was 1.6 times larger than our *a priori* expectation. We also experienced moderate loss to follow-up, albeit relatively few prior to primary endpoint measurement. Some participants could not view cases in their preferred reporting environment due to technical reasons and felt unable to reach their full potential; however, such problems will be split randomly across both arms. As a follow-up to the study described in Chapter 5, we had intended to monitor time spent reporting each case and assessing how that may

impact detection; however, due to the failure of the online CTC viewer we were unable to objectively capture this data.

Due to the nature of the intervention, it was impossible to blind participants to their allocation; however, it is unlikely this introduced significant bias, as the outcome measures (i.e. lesion detection or not) were both pre-specified and objective, and applied equally across arms.²³² Seven more clusters were randomised to intervention than control despite attempts to balance this by including more control clusters. This probably occurred because once radiologists were aware their hospital had been randomised to the intervention arm, they were more likely to invite their colleagues to participate, the opposite being true for controls. Finally, although we observed a significant increase in sensitivity in a test environment, this may not generalise to real-world settings. Originally, we had intended to examine this via analysis of pre- and post-trial lesion detection rates and positive predictive values for recruited radiologists, comparing across arms, but the SARS-CoV-2 pandemic prevented this. This presents a clear avenue for future research when possible.

Given our results, which show a sustained benefit from a single day of individualised training supplemented with verbal and written feedback, we believe that training and ongoing assessment should be mandated for practitioners interpreting CTC. With the improvements we observed among BCSP radiologists, this should certainly be considered within the national screening programme. As discussed in Chapter 3, such accreditation is already stipulated for breast cancer screening which uses PERFORMS to evaluate performance on a range of difficult cases and provides individualised feedback.²³³ It would also align CTC with

colonoscopy within the same screening programme, resolving inequality for patients whose choice of test generally depends on factors beyond their control (primarily, co-existent medical conditions). Our data suggest radiologists would welcome this, as our participants found the training package beneficial and surveys have found radiologists favour accreditation and assessment.¹²²

SECTION D: DISCUSSION, SUMMARY AND FUTURE CONSIDERATIONS

In this final section I summarise the main findings and conclusions from the thesis and discuss future considerations and avenues of research.

Chapter 12 Discussion and future considerations

Introduction

This thesis describes the use of CT colonography (CTC) in colorectal cancer (CRC) screening and the role of reader performance in CTC accuracy. As the whole-colon investigation of choice when colonoscopy is contraindicated, CTC has the potential to improve population screening uptake as it is minimally invasive, does not require sedation, uses less onerous bowel preparation and is cost effective.

However, its applicability in population screening has been in part hampered by the absence of accreditation processes to maintain quality, and the lack of accepted performance metrics and consensus regarding training.

Summary of results

Section A: Literature background

The performance of readers (radiologists and reporting radiographers) who interpret CTC scans directly impacts the accuracy of the study and the subsequent detection of colonic pathology. While detection rates are comparable to colonoscopy in research studies, accuracy is variable in clinical practice within the Bowel Cancer Screening Programme (BCSP). The lack of mandatory training for CTC interpretation contrasts to processes in place for colonoscopy and may contribute to this variability. An analogous imaging-based screening programme

for breast cancer uses a centralised model to assess and monitor performance in screening radiologists. A similar model could be applied to CTC, thereby aligning it with colonoscopy, increasing quality and improving detection of early malignancy.

Section B: Reader performance in CTC and methods to improve it

Through systematic review and meta-analysis, the post-imaging CRC rate (PICRC) was established, and is at the lower (i.e. better) end of the published range for colonoscopy (4.4% for CTC vs 2.9-8.6% for colonoscopy). CTC is therefore reaffirmed as a safe and accurate alternative colonic investigation. Importantly, the majority of PICRCs are due to perceptual errors i.e. are visible in retrospect.

Improving training in CTC interpretation, with particular focus on subtle colonic lesions, could mitigate against such errors and increase neoplasia detection rates in CTC screening.

In general, CTC training is shown to increase reader sensitivity and specificity.

However, the size of the improvement is dependent on the type of training model applied and guidance on CTC training is variable between jurisdictions. As well as training prior to independent CTC interpretation, optimising reporting conditions can increase lesion detection. Radiologists who spend at least 20 minutes reviewing a scan detect more polyps than those who report faster. Furthermore, detection is highest when no more than four scans are reported sequentially.

Section C: Intervention to improve CT colonography interpretation

Most experienced CTC-reporting radiologists do not know their objective PDR and have only undergone short course, general CTC training prior to independent

reporting. Their performance at baseline was variable (15.8% to 89.5%), with significant and durable improvements in sensitivity observed after a day of individualised training (16.7% improvement in sensitivity at 12-months).

The use of an Expert Faculty to deliver training targeted at participant's individual Personal Development Plans and performance feedback are likely all contributing factors to the improvements observed. These results demonstrate that significant performance improvements are possible among a group of experienced radiologists if the training is tailored to their learning needs. Given the already widespread use of CTC, such an approach would be necessary if CTC standards are to be universally raised.

Suggestions for future research

1. Future research into CTC screening should focus on radiologist training and CTC quality assurance, with identification of evidence-based key performance indicators that are associated with clinically-relevant outcomes such as the incidence of post-imaging cancers. Establishing the true PICRC rate in clinical practice by linking CTC reports with cancer outcomes, via the national cancer registry would allow us to associate radiologist performance with PICRC rates. This could inform a national database collating performance metrics and permit testing of the hypothesis that readers with higher PDR have lower PICRC rates (similar to colonoscopy). Underperforming centres could be identified and additional targeted training focused on those sites.

2. Evaluation of the clinical impact of the PERFECTS training intervention in routine practice. By assessing PDR in the intervention arm radiologists, a year before and a year after their training, it would be possible to determine if the improvements observed in the trial translate into real-world increases in neoplasia detection.
3. Long term follow up of CTC screened patients to assess whether the screening interval can be extended beyond the currently-recommended 60 months.
4. In light of the SARS-CoV-2 pandemic, there are restrictions on face-to-face training, therefore evaluation of an online CTC training package to determine if large scale training can be delivered digitally would be of value.

Conclusion

CT colonography (CTC) is a safe and accurate investigation when performed well and has value in the bowel cancer screening programme. However, a lack of investment in ensuring CTC interpretation is of the highest quality leads to variable performance and lower neoplasia in comparison to colonoscopy. In order to minimise reader error and improve detection, evidence-based CTC interpretation training must be developed and deployed. Any such training requires adequate funding and infrastructure to ensure parity among geographical regions, with consideration for innovative digital delivery. While improving CTC performance is a small part of the overall landscape of colorectal cancer screening, it is an area in which substantial gains can be made with tangible improvements in patient outcome.

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APPENDICES

Appendix 1 CONSORT 2010 checklist of information to include when reporting a cluster randomised trial

Section/Topic	Item No	Standard Checklist item	Extension for cluster designs	Page No
Title and abstract				
	1a	Identification as a randomised trial in the title	Identification as a cluster randomised trial in the title	156
	1b	Structured summary of trial design, methods, results, and conclusions (for specific guidance see CONSORT for abstracts) ^{1,2}	See table 2	158-159
Introduction				
Background and objectives	2a	Scientific background and explanation of rationale	Rationale for using a cluster design	161
	2b	Specific objectives or hypotheses	Whether objectives pertain to the cluster level, the individual participant level or both	161-163
Methods				
Trial design	3a	Description of trial design (such as parallel, factorial) including allocation ratio	Definition of cluster and description of how the design features apply to the clusters	161
	3b	Important changes to methods after trial commencement (such as eligibility criteria), with reasons		N/A
Participants	4a	Eligibility criteria for participants	Eligibility criteria for clusters	164
	4b	Settings and locations where the data were collected		184; Appendix 9
Interventions	5	The interventions for each group with sufficient details to allow replication, including how and when they were actually administered	Whether interventions pertain to the cluster level, the individual participant level or both	166-173
Outcomes	6a	Completely defined pre-specified primary and	Whether outcome measures pertain to the	180-181

Section/Topic	Item No	Standard Checklist item	Extension for cluster designs	Page No
		secondary outcome measures, including how and when they were assessed	cluster level, the individual participant level or both	
	6b	Any changes to trial outcomes after the trial commenced, with reasons		N/A
Sample size	7a	How sample size was determined	Method of calculation, number of clusters(s) (and whether equal or unequal cluster sizes are assumed), cluster size, a coefficient of intracluster correlation (ICC or k), and an indication of its uncertainty	181-182
	7b	When applicable, explanation of any interim analyses and stopping guidelines		N/A
Randomisation:				
Sequence generation	8a	Method used to generate the random allocation sequence		166
	8b	Type of randomisation; details of any restriction (such as blocking and block size)	Details of stratification or matching if used	166
Allocation concealment mechanism	9	Mechanism used to implement the random allocation sequence (such as sequentially numbered containers), describing any steps taken to conceal the sequence until interventions were assigned	Specification that allocation was based on clusters rather than individuals and whether allocation concealment (if any) was at the cluster level, the individual participant level or both	165-166
Implementation	10	Who generated the random allocation sequence, who enrolled participants, and who assigned participants to interventions	Replace by 10a, 10b and 10c	
	10a		Who generated the random allocation sequence, who enrolled clusters, and who	165-166

Section/Topic	Item No	Standard Checklist item	Extension for cluster designs	Page No
			assigned clusters to interventions	
	10b		Mechanism by which individual participants were included in clusters for the purposes of the trial (such as complete enumeration, random sampling)	165-166
	10c		From whom consent was sought (representatives of the cluster, or individual cluster members, or both), and whether consent was sought before or after randomisation	166
Blinding				
	11a	If done, who was blinded after assignment to interventions (for example, participants, care providers, those assessing outcomes) and how		N/A
	11b	If relevant, description of the similarity of interventions		166-173
Statistical methods				
	12a	Statistical methods used to compare groups for primary and secondary outcomes	How clustering was taken into account	182
	12b	Methods for additional analyses, such as subgroup analyses and adjusted analyses		182-183
Results				
Participant flow (a diagram is strongly recommended)	13a	For each group, the numbers of participants who were randomly assigned, received intended treatment, and were analysed for the primary outcome	For each group, the numbers of clusters that were randomly assigned, received intended treatment, and were analysed for the primary outcome	195; Figure 10.8
	13b	For each group, losses and exclusions after randomisation, together with reasons	For each group, losses and exclusions for both clusters and individual cluster members	195; Figure 10.8

Section/Topic	Item No	Standard Checklist item	Extension for cluster designs	Page No
Recruitment	14a	Dates defining the periods of recruitment and follow-up		184
	14b	Why the trial ended or was stopped		184
Baseline data	15	A table showing baseline demographic and clinical characteristics for each group	Baseline characteristics for the individual and cluster levels as applicable for each group	196; Table 10.2
Numbers analysed	16	For each group, number of participants (denominator) included in each analysis and whether the analysis was by original assigned groups	For each group, number of clusters included in each analysis	195; Figure 10.8
Outcomes and estimation	17a	For each primary and secondary outcome, results for each group, and the estimated effect size and its precision (such as 95% confidence interval)	Results at the individual or cluster level as applicable and a coefficient of intracluster correlation (ICC or k) for each primary outcome	199-208
	17b	For binary outcomes, presentation of both absolute and relative effect sizes is recommended		199-208; Tables 10.5 to 10.9
Ancillary analyses	18	Results of any other analyses performed, including subgroup analyses and adjusted analyses, distinguishing pre-specified from exploratory		185-193
Harms	19	All important harms or unintended effects in each group (for specific guidance see CONSORT for harms ³)		N/A
Discussion				
Limitations	20	Trial limitations, addressing sources of potential bias, imprecision, and, if relevant, multiplicity of analyses		213-215
Generalisability	21	Generalisability (external validity, applicability) of the trial findings	Generalisability to clusters and/or individual participants (as relevant)	213, 215
Interpretation	22	Interpretation consistent with results, balancing		210-216

Section/Topic	Item No	Standard Checklist item	Extension for cluster designs	Page No
		benefits and harms, and considering other relevant evidence		
Other information				
Registration	23	Registration number and name of trial registry		161
Protocol	24	Where the full trial protocol can be accessed, if available	Plumb AA, Obaro AE, Bassett P, Baldwin-Cleland R, Halligan S, Burling D. Performance and evaluation in computed tomographic colonography screening: protocol for a cluster randomised trial. medRxiv 2020:2020.2002.2025.20027714	
Funding	25	Sources of funding and other support (such as supply of drugs), role of funders		158

¹ Hopewell S, Clarke M, Moher D, Wager E, Middleton P, Altman DG, et al. CONSORT for reporting randomised trials in journal and conference abstracts. *Lancet* 2008, 371:281-283

² Hopewell S, Clarke M, Moher D, Wager E, Middleton P, Altman DG at al (2008) CONSORT for reporting randomized controlled trials in journal and conference abstracts: explanation and elaboration. *PLoS Med* 5(1): e20

³ Ioannidis JP, Evans SJ, Gotzsche PC, O'Neill RT, Altman DG, Schulz K, Moher D. Better reporting of harms in randomized trials: an extension of the CONSORT statement. *Ann Intern Med* 2004; 141(10):781-788.

Appendix 2 PERFECTS website

The PERFECTS project website (<http://www.perfectsprogramme.com/>) designed to promote recruitment to the PERFECTS trial.

HOME CONTACT



How good am I at CT colonography?

This is a question frequently asked of the Bowel Cancer Screening Programme (BCSP) National Committee.

PERFECTS, a BSCP and ESGAR supported project, will help you answer this question.

Through a randomised trial we will determine if structured, individualised training and feedback improves diagnostic accuracy amongst radiologists reporting CT colonography (CTC).

Who is eligible?

Radiologists in England, who report CTC as part of their routine clinical practice and are either a:

- Consultant or;
- Specialty Trainee or Clinical Fellow within one year of CCT/post-CCT

What is involved?

Radiologists will be randomised, in clusters, to a control or intervention group and both groups will remotely interpret 40 CTCs over 12 months.

The intervention group will receive feedback after each test and will be invited to attend a one-day workshop at St Mark's Hospital, Harrow, focusing on subtle, easily missed lesions.

The control group will receive their test results and feedback at the end of the year and if the workshop is of proven benefit, will be offered this at a later date.

This study is Health Research Authority approved (16/01/2016)

“ It [the workshop] was wonderful. A very good opportunity to have 1:1 session with the trainers and get individual feed back. The workshop was organised and run very well.



Why should I participate?



CPD Points
Free CT colonography CPD Points for workshop attendance and personal reflection



Feedback
Receive individualised feedback about your performance



Improvement
Improve your CTC interpretation skills

How can I sign up?

To register your interest in participating, please click below

REGISTER ME

HOME CONTACT

Get in touch

email PERFECTS Research Team lnwh-tr.perfects@nhs.net **phone** 0208 235 4184 **address** Intestinal Imaging Dept., Level 4
St Mark's Hospital
London Northwest Healthcare NHS Trust
Watford Rd, Harrow, Middlesex
HA1 3UJ



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Appendix 3 PERFECTS participant information sheet

PERFECTS Trial – Participant information sheet and consent form

Participant Information Sheet:

IRAS 206876. Study Number: RD16/055

Clinicaltrials.gov ID: NCT02892721

Version 1.1 1 March 2017

Study title: Performance and Evaluation in CT colonography Screening (PERFECTS)

We would like to invite you to take part in our research study. Before you decide we would like you to understand why the research is being done and what it would involve for you. One of our team will go through the information sheet with you and answer any questions you have.

This study has been approved by the Health Research Authority and UCL Research Ethics Committee (Project ID number 5967/003).

Please discuss the information above with others if you wish or ask us if there is anything that is not clear or if you would like more information.

It is up to you to decide whether to take part or not; choosing not to take part will not disadvantage you in any way. If you do decide to take part you are still free to withdraw at any time and without giving a reason.

All data will be collected and stored in accordance with the Data Protection Act 1998.

What is the purpose of the study?

To assess the impact of an intensive one-day workshop and online education module, with assessment and structured feedback, on CTC interpretation performance amongst Radiologists currently reporting CT colonography in their routine practise.

Why have I been invited?

You have been chosen because you are a Consultant or a non-consultant grade Radiologist e.g. specialty trainee or clinical fellow within one year of CCT date or post-CCT, who interprets CT colonography examinations as part of their current clinical practice

Do I have to take part?

It is up to you to decide to join the study. If you agree to participate, we will describe the study and go through this information sheet with you if necessary. If you still wish to take part, we will then ask you to sign a consent form. You are free to withdraw at any time, without giving a reason.

What will happen to me if I take part?

If you agree to participate you will be asked to complete an initial questionnaire about current working practices and then you will be randomized to join either the intervention

or control group. If you are part of the intervention group, you be invited to attend a one-day individualized training workshop at St Mark's Hospital, Harrow, Middlesex and also have access to an online education module. You will be assessed immediately before and after the workshop and then undergo repeat assessments at 6 and 12 months. The assessments will comprise ten CT colonography examinations for interpretation and review (intraluminal assessment only), supplemented by a short online test to assess knowledge. **All assessments will take place in your own hospital.** You will either complete the CT interpretation test cases on an online platform or we will send you the CT data via encrypted storage for upload to the software platform you prefer and/or use routinely. You will receive confidential, structured, individualised feedback after each assessment.

If you are randomized to the control group you will be invited to undertake the assessments and knowledge tests at the same time points, but you will not attend the one-day workshop and you will not have access to the online educational materials or receive feedback. At the end of the study you will receive results of your performance at each assessment and access to the online training materials.

Both groups will also receive short questionnaires at 6 months and again at the end of the study to assess their attitudes to intensive CTC training and accreditation.

Should the intervention (structured training and feedback programme) be shown to significantly improve performance, and is adopted into a national accreditation scheme, then priority enrollment into the new scheme will be first offered to control group participants.

Expenses and payment

There is no payment for participating beyond second class rail fare (or equivalent) travel expenses for the intervention group participants to attend the one-day workshop.

What will I have to do?

You will have to complete a pre-randomisation questionnaire (taking approximately 45 minutes). All participants will undergo all four assessments (approximately 3 hours each) and the short online test (approximately 30 minutes). If randomized to the intervention group, you will also be asked to attend the one-day workshop at St Mark's Hospital (approximately 8 hours). There will be two short questionnaires at 6 and 12 months for you share your views on the process (approximately 10 minutes).

What are the possible disadvantages and risks of taking part?

There are no safety concerns for participation. However, you will need to allocate sufficient time to participate and understand that, if part of the control group, results of assessments will only be made available at the end of the study.

What are the possible benefits of taking part?

The study may benefit you by improving your CT colonography interpretation and also enabling you to benchmark your performance against other participants. Please note your individual performance will not be identifiable either to other participants or in any publication. The one-day workshop will be CPD credited.

What happens when the research study stops?

We will analyse the data and publish the results. We will let you know when this happens and email you a copy of findings.

What if there is a problem?

We will address any complaint about the way you have been dealt with during the study.

Will my taking part in the study be kept confidential?

Yes. We will follow ethical and legal practice and all information about you will be handled in confidence.

Part 2. Additional information:

What will happen if I don't want to carry on with the study?

If you withdraw from the study, we will delete all your identifiable data. You may withdraw your data from the project at any time until it has been analysed for use in the final report.

What if there is a problem?

If you have a concern about any aspect of this study, you should ask to speak to the researchers who will do their best to answer your questions [0208 235 4180].

Will my taking part in the study be kept confidential?

All information that is collected about you during the course of the research will be kept strictly confidential, and any information about you that leaves our research unit will have your details removed so that you cannot be recognised. You will not be identified in any subsequent research paper. Data will be retained for 5 years.

What will happen to the results of the research study?

We intend to publish the results of our research in indexed medical journals. We will tell you when this has happened. You will not be identified in any report or summary of this research.

Who has reviewed the study?

This research has been assessed by the Health Research Authority, to protect your interests. This study has been also reviewed and given a favourable opinion by the UCL Research Ethics Committee.

Please keep this information sheet for your records.

Further information and contact details

Dr Anu Obaro, Radiology Department, St Mark's Hospital, London North West
Healthcare NHS Trust, Watford Rd, Harrow, Middlesex, HA1 3UJ / [REDACTED]
/ [REDACTED]

Name of Researchers:

Dr Anu Obaro (Radiology Research Fellow St Marks Hospital)
Dr Andrew Plumb (Consultant Radiologist UCLH)
Dr David Burling Consultant Radiologist St Marks Hospital)
Prof Steve Halligan (Professor of Radiology UCL)
Mrs Rachel Baldwin-Cleland (Research Radiographer St Marks Hospital)
Mr Paul Bassett (StatsConsultancy)

IRAS 206876. Study Number: RD16/055
Clinicaltrials.gov ID: NCT02892721
Version 1.0. 28 March 2017
Patient Identification Number for this trial:

CONSENT FORM

Performance and Evaluation in CT colonography Screening (PERFECTS)

Name of Researcher: Dr Anu Obaro
Supervisors: Dr Andrew Plumb & Dr David Burling

Please initial box

1. I confirm that I have read and understand the information sheet dated 28 March 2017 (version 1.1) for the above study and have had the opportunity to ask questions.
2. I understand that my participation is voluntary and that I am free to withdraw at any time without giving any reason, without my medical care or legal rights being affected.
3. I understand that my anonymised personal information will be used during the study and that such information will be treated as strictly confidential and handled in accordance with the provisions of the Data Protection Act 1998.
4. I agree to take part in the above study.

Name of Radiologist

Date

Signature

Name of Person taking consent
(if different from researcher)

Date

Signature

Researcher

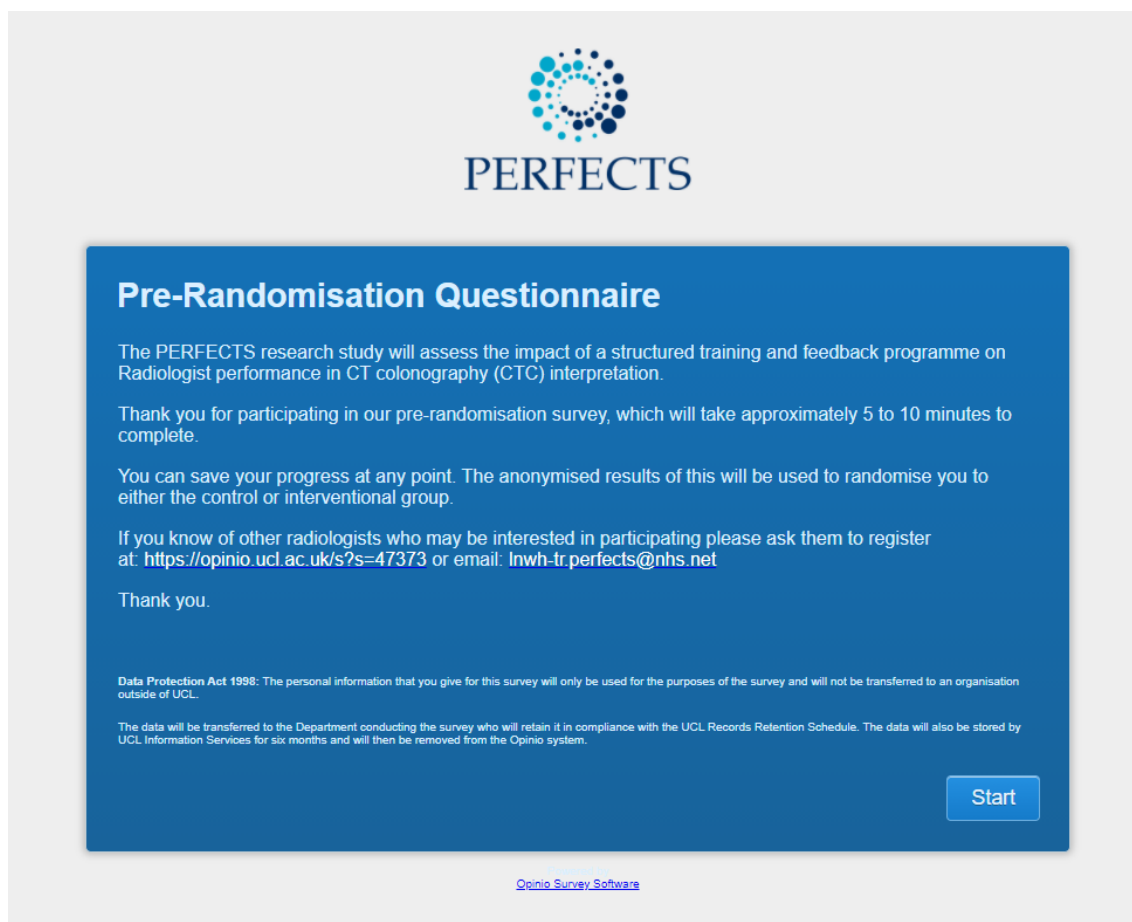
Date

Signature

1 copy for Radiologist; 1 copy for Researcher

Appendix 4 Pre-randomisation questionnaire

Pre-randomisation questionnaire administered to radiologists recruited for the multi-centre randomised controlled trial (0 and Chapter 9)



The image shows a screenshot of a web-based questionnaire interface. At the top center is the PERFECTS logo, which consists of a circular arrangement of blue and teal dots of varying sizes, with the word "PERFECTS" in a blue serif font below it. The main content is contained within a blue rectangular box with rounded corners. The title "Pre-Randomisation Questionnaire" is displayed in white bold text at the top of this box. Below the title, there are several paragraphs of white text providing information about the study, including a thank you message and a "Start" button. At the bottom of the blue box, there is a small link for "Opinio Survey Software".

PERFECTS

Pre-Randomisation Questionnaire

The PERFECTS research study will assess the impact of a structured training and feedback programme on Radiologist performance in CT colonography (CTC) interpretation.

Thank you for participating in our pre-randomisation survey, which will take approximately 5 to 10 minutes to complete.

You can save your progress at any point. The anonymised results of this will be used to randomise you to either the control or interventional group.

If you know of other radiologists who may be interested in participating please ask them to register at: <https://opinio.ucl.ac.uk/s?s=47373> or email: lnwh-tr.perfects@nhs.net

Thank you.

Data Protection Act 1998: The personal information that you give for this survey will only be used for the purposes of the survey and will not be transferred to an organisation outside of UCL.

The data will be transferred to the Department conducting the survey who will retain it in compliance with the UCL Records Retention Schedule. The data will also be stored by UCL Information Services for six months and will then be removed from the Opinio system.

[Start](#)

[Opinio Survey Software](#)

Pre-Randomisation Questionnaire

Please state the hospital that you are currently working in:

Please state which NHS Trust this hospital is in:

5%

Back

Save

Next

[Opinio Survey Software](#)

Pre-Randomisation Questionnaire

1. Considering your CTC work load and reporting:

a) How many radiologists report CT colonography (CTC) scans in your department?

b) Approximately how many CTCs do you personally report per week?

Please select one: ▾

c) Approximately how many CTCs do you personally report per year?

Please select one: ▾

b) Do you report CTC for the Bowel Cancer Screening Programme (BCSP)?

Yes No

i) Do you have dedicated CTC reporting sessions (i.e. sessions for reporting CTCs *only*)? If so, how many per week?

Please select one: ▾

j) On average, how long do you spend reporting a single CTC?

Please select one: ▾

23%

Back

Save

Next

Pre-Randomisation Questionnaire

2. Considering CTC interpretation:

a) Does your department have one or more workstations dedicated to CTC interpretation?

- Yes No

b) Which software platform do you use? *Please select all that apply*

- Philips
 Siemens
 Vital
 GE Healthcare
 Cadens
 TeraRecon
 Other. Please state:

c) Do you perform a 3D flythrough the colon?

- Yes No

d) Do you generally perform a primary 2D or primary 3D read?

- Primary 2D read Primary 3D read

e) If you use a combination of 2D and 3D visualisation, what percentage of time do you spend performing the 3D read?

f) Do you use computer-aided detection (CAD)?

- Yes No

g) In which direction do you perform your CTC interpretation?

- Rectum to caecum
 Caecum to rectum
 Both

h) What is the approximate rate of abnormalities that you report (6mm+ polyp to cancer), i.e. your polyp detection rate (PDR)?

Please select one:

i) Are these audit figures or estimates?

- Audit – with correlation to endoscopy findings.
 Estimate
 Combination of audit and estimate
 Other. Please state:

50%

Back

Save

Next

Pre-Randomisation Questionnaire

3. Considering CTC training:

a) Approximately, how many CTC cases have you reported so far in your career (symptomatic plus screening cases)?

Please select one:

b) Of these, how many were endoscopically validated cases?

Please select one:

c) Beyond routine reporting practise, what was your training for CTC interpretation? *Tick all that apply*

- None
- Reporting with formal, regular retrospective review of endoscopic findings
- Attended formal CTC training workshop (1 day or less)
- Attended formal CTC training workshop (2 days or more)
- CTC training fellowship for more than 3 months
- Other. Please state:

d) How do you rate the quality of your training for CTC interpretation, to date?

Poor Not very good Satisfactory Very good Excellent

Please rate your level of agreement with the following statements:

e) I am confident at detecting 6 to 9mm polyps after my previous CTC training

Strongly disagree Disagree Neither agree nor disagree Agree Strongly agree

f) I am confident at detecting 10mm+ polyps/cancers after my previous CTC training

Strongly disagree Disagree Neither agree nor disagree Agree Strongly agree

g) How well-prepared were you to interpret CTC in the Bowel Cancer Screening Programme (BCSP)?

Very poorly prepared Poorly prepared Satisfactorily prepared Well prepared Very well prepared I do not report as part of the BCSP

h) In comparison to other Radiologists reporting CTC, where do you think your performance lies?

Well below average Below average Average Above average Well above average

i) What is your answer to the above question based on? *Please tick all that apply*

- Anecdotal perception
- Local Audit
- Regional Audit
- National Audit
- Other. Please state:

76%

Back

Save

Next

Pre-Randomisation Questionnaire

4. Regarding feedback of your CTC interpretation, how valuable would you find the following?

a) Verbal feedback

Not valuable Slightly valuable Not sure Valuable Very valuable

b) Written feedback of any type

Not valuable Slightly valuable Not sure Valuable Very valuable

c) Written feedback with comparison of your interpretation to that of an expert panel

Not valuable Slightly valuable Not sure Valuable Very valuable

d) Written feedback with anonymised comparison of your results to other radiologists

Not valuable Slightly valuable Not sure Valuable Very valuable

How valuable is it to know your:

e) Polyp detection rate (PDR)

Not valuable Slightly valuable Not sure Valuable Very valuable

f) Cancer detection rate

Not valuable Slightly valuable Not sure Valuable Very valuable

g) Positive predictive value (PPV)

Not valuable Slightly valuable Not sure Valuable Very valuable

h) Negative predictive value (NPV)

Not valuable Slightly valuable Not sure Valuable Very valuable

100%

Back

Save

Finish

Appendix 5 PERFECTS one-day workshop resources

Training the CT Colonography Trainers Course (TC3) programme



FACULTY TRAINING DAY OVERVIEW

Date: Tuesday 16th May 2017 from 8.30 am to 3.30 pm

Location: Himsworth Hall, Medical Education Centre, St Mark's Hospital, Harrow,

SCHEDULE

830 – 900	Introduction & PERFECTS project overview (coffee)
900 – 1000	Method of Individualised Training <ul style="list-style-type: none">• Review Participant Training Programme• Review of TC3 principles (Train the Trainers)• Workshop topics (see below) & Teaching Points
1000 – 1100	Putting Theory into Practice
1100 – 1120	Coffee break
1120 – 1245	Baseline Test Case Review – 7 cases
1245– 1320	Lunch
1320 – 1330	Allocation of Faculty to Training Topics
1330 – 1500	Further Cases with Practice Training
1500 – 1530	Discussion of post-test feedback and Q & A

WORKSHOP TOPICS

Topics	Subtopics
Review of baseline test	<i>Each test case is integrated into the topic groups</i>
Flat polyps	Flat lesions, laterally spreading tumours
Small/irregular polyps	Satisfaction of search
Fold related lesions	Normal fold morphology, complex folds
Interpretation technique	Use of MPR, assessing tagged fluid, review areas, cancer morphology
Non-neoplastic abnormalities	Haemorrhoids, vessels, lipoma

Case category table for expert faculty to select studies from at each workshop station

Case ID	Main teaching point	Subtopic	site of main lesion	size of main lesion (mm)	2ry teaching point (subtopic)	Difficulty	endpoints	Test	Notes
PTC02	flat	morphology	AC	18	3D	hard	1	baseline	strength of 3D as adjunct. PTC47 f/up scan
PTC22	flat	LST	caecum	40	search	medium	2	baseline	
PTC27	flat	LST	caecum	60	review areas	medium	1	w/shop	
PTC69	flat	morphology	AC	13	search	hard	2	baseline	v. tough case (RCR1013)
PTC72	flat		TC	22		easy	1	w/shop	(RCR1016)
PTC73	flat		caecum	30	tagging	medium	1	w/shop	(RCR1012)
PTC01	fold	review areas	AC	22		medium	1	w/shop	medial apsect of AC often missed by OC
PTC04	fold	morphology	TC	20	search	hard	4	baseline	TC lesion most important
PTC11	fold	morphology	TC	25	search	easy	2	w/shop	also has AC tumour
PTC17	fold	LST	SC	50	MPR	easy	1	w/shop	
PTC26	fold	morphology	AC	16	morphology	easy	1	w/shop	
PTC29	fold	morphology	rectum	40	review areas	medium	1	w/shop	f/up, 2016 scan of PTC30
PTC35	fold	morphology	HF	10	MPR	hard	1	baseline	PTC34 initial case (2007), PTC36 f/up (2012)
PTC36	fold	morphology	HF	35		easy	1	w/shop	f/up scan of PTC35
PTC38	fold	morphology	rectosig	11	3D	hard	1	w/shop	
PTC47	fold	morphology	AC	28		easy	1	w/shop	f/up scan of PTC02
PTC03	non-neoplastic		SC	27	morphology	medium	3	w/shop	use as eg of benign SC thickening, AC cancer on
PTC23	non-neoplastic	haemorr	AR jn		review areas	medium	0	w/shop	FALSE POSITIVE
PTC45	non-neoplastic	morphology	SC	10	search	easy	2	w/shop	initial scan (Aug 2015), AC polyp, benign sigmoid,
PTC101	normal							baseline	confirmed NAD on multiple CTC
PTC54	normal							baseline	OC confirmed
PTC62	normal							baseline	confirmed NAD on multiple CTC
PTC05	small/irreg	search	TC	10	haemorr	hard	6	baseline	consider new dx polyposis, nb review of tagged
PTC09	small/irreg	search	SC	6		easy	3	w/shop	use 6mm SC polyp as main lesion
PTC25	small/irreg	search	HF	8	morphology	hard	3	baseline	HF polyp is tricky and was serrated
PTC34	small/irreg	morphology	HF	9	tagging	hard	1	w/shop	scan before PTC35
PTC40	small/irreg	review areas	caecum	9	tagging	medium	1	w/shop	
PTC44	small/irreg	search	HF	6	tagging	hard	13	w/shop	focus on right colon
PTC10	technique	search	SC	10		medium	2	w/shop	
PTC15	technique	search	caecum	14	tagging	medium	2	w/shop	
PTC16	technique	search	AC	10	MPR	medium	1	w/shop	looks smaller than it is
PTC18	technique	morphology	ICV	56	MPR	easy	1	w/shop	
PTC24	technique	review areas	AR jn	10	MPR	easy	1	w/shop	
PTC37	technique	review areas	rectum	16		easy	1	w/shop	
PTC41	technique	3D	TC	22	search	easy	2	w/shop	RTB58, PICRC CASE
PTC56	technique	morphology	SC	52	search	hard	4	w/shop	polyp in divertic seg (LLD284). Gd prep for PTC33
PTC58	technique	MPR	DC	16		medium	1	w/shop	adeno on histo. ?central depression
PTC61	technique	MPR	AC	21	flat	hard		w/shop	tough case. Polyp on a fold
PTC71	technique	tagging	TC	18	MPR	easy	1	w/shop	(RCR1015)

Participant personal development plan

Objectives were compiled from free-text responses at the end of the pre-randomisation questionnaire and transferred to an individualised PDP with cross references to appropriate cases to facilitate critical reflection during the one-day workshop

PERSONAL DEVELOPMENT PLAN & REFLECTION

NAME: Dr

Date: Tuesday 6th June 2017



Pre-course Personal Development Plan	1. 2.
SESSION	REFLECTION
Baseline test review	
Flat Polyps	
Small/ irregular polyps	
Fold related lesions	
Interpretation technique	
Non-neoplastic abnormalities	

Our job as Trainers is to assist you in reflecting on your performance. During this time, we will help you to identify any areas of improvement or development, which you can reflect on further after the course.

PERFECT post-workshop survey

Postworkshop survey questions were delivered by email as a unique link to an interactive online form.

	Strongly disagree	Agree	Neutral	Agree	Strongly agree
Question 1 Please select the response that best represents your opinion:					
The test answer form is representative of information I would normally include in my CTC reports					
Participating in this assessment has motivated me to independently improve my CTC interpretation					

	Very easy	Easy	Neither easy or difficult	Difficult	Very difficult
Question 2 The test cases have been specifically selected to represent subtle, easily missed lesions. How difficult did you find the baseline test assessment?					

	< 1 hour	1-2 hours	2-3 hours	3-4 hours	4-5 hours	> 5 hours
Question 3 Excluding installation and set-up, how long did it take you to complete the baseline test?						

	Free text
Question 4 In what areas do you think we could improve the CTC assessment?	

	Strongly disagree	Agree	Neutral	Agree	Strongly agree
Question 5 Please select the response that best represents your opinion. The objectives of the workshop were clear					
The instructional materials were clearly written and easy to use					
The workshop was well organised					
The workshop has provided useful feedback about my performance in the baseline test					
The workshop cases provided additional learning opportunities					
The workshop achieved the stated learning objectives					
I would recommend the workshop to my colleagues					
Question 6 Please select the response that best represents your opinion. The Trainers were knowledgeable about the session topics					
The Trainers were responsive to my needs/queries					
The Trainers were prepared and organised					

	Free text
Question 7 Which session did you find most useful?	

	Free text
Question 8 In what areas do you think we could improve the one-day workshop?	

Appendix 6 Comparison and risk assessment of different CTC test delivery options

	Online CTC viewer	Downloadable CTC viewer	Hardcopies for upload	Mobile laptops	IEP Link / Case download	Central Hub
Convenience & flexibility for user	Accessible from home or work by clicking link from PERFECTS website. Not dependent on user's device specifications. Unified user experience.	Minimum system requirements; ideally suitable for Windows and Mac OS. Dependent on user to install appropriately. Requires technical support for troubleshooting. Unified user experience.	Reliant on upload of cases by local PACS/IT team. Requires a contact or local radiologist to coordinate.	Reliant on PERFECTS team support to transport and monitor laptops. Unified user experience. Laptop will need to circulate to multiple sites four times/year.	Reliant on PACS team to access the IEP link and download cases. IEP usually reserved for clinical cases only so will need to overcome local policies.	Completely reliant on participants to travel to the hubs at specified time. May have issues with gaining study leave to leave site during test window.
					Similar to PERFORMS	But would only have to get cases to the hubs
<i>Score out of 5</i>	<i>5</i>	<i>4</i>	<i>2</i>	<i>1</i>	<i>2</i>	<i>1</i>
Cost	No idea – £10k++?	Prob at least £40k (Cadens estimate) – major costs would be software development + customisation (£20k)	Around £3k+ – need to cover postage (do we want the devices back??), cost of devices, packaging	Employ PERFECTS IT support person ?£20k+	Not sure - £3K++, but will probably be one of the cheaper options.	Depends on several factors. Do we need to book rooms? Are we providing software or just cases? Just cases probably
	Likely to need separate budget for cloud storage and support	??Aprox £10 if we can use Vital		Travel costs for them from site to site ?£2.5k	Needs software support	Travel costs for users? Unlikely
				Insurance for laptops???		Renumerate hubs????
<i>Score</i>	<i>3</i>	<i>3</i>	<i>4</i>	<i>2</i>	<i>5</i>	<i>3</i>
Licensing	Shouldn't be an issue, since license will be held centrally at STM	Will be most up to date version of Vitrea. Use will be limited to that computer only and only for the installed test cases	Zero issues since users will be using their local CTC software.	?10 laptops already at STM, but older versions of Vitrea and not recently tested. Vitrea may oppose licensing. Alternatively, PERFECTS staff take the CTC workshop server too – could use the newer laptops, BUT insurance issue, and its large and unwieldy!	None, since users are only downloading cases	None if we allow sites to use their own software
<i>Score</i>	<i>5</i>	<i>5</i>	<i>5</i>	<i>2</i>	<i>5</i>	<i>5</i>
Technical challenges	Multiple users viewing cases at the same time may slow down server but could limit people to a specific time slot.	Time to develop and test programme, with no guarantee that it will work on the majority of user computers.	Need a PACS contact for each cluster – could get this during pre-randomisation questionnaire. How will we prevent users doing the wrong cases or viewing before appropriate time?	Minimal since all cases already preloaded onto appropriate spec PC. PERFECTS support would need be skilled at dealing with any software issues and ideally have an understanding of CTC interpretation to answer questions on site.	If using cloud option we must ensure use of a provider that can be accessed by all sites, with robust enough server to allow multiple sites downloading simultaneously	Unless we plan to visit all the hubs we would need to reply on local PACS to provide any software support and manage initial set up

	Online CTC viewer	Downloadable CTC viewer	Hardcopies for upload	Mobile laptops	IEP Link / Case download	Central Hub
	All companies have concerns with server/cloud capabilities and we can't afford to have poor 3D etc	Need to ensure installing to a PC with suitable spec. How do we get all the spec details??	Will need someone at our end to provide support for troubleshooting	Any updates or tweaks may be difficult to achieve if person is on the road and laptops are not connected to wifi	Need to explore IEP limitations and terms of use. Would it be best to send all cases in one go?	
		Would potentially need most robust IT support/helpline. (if we use Vital, this already exists)	Each test will need to be password protected on the USB and ?send password when next test due. Maybe easier to upload all in one go.	Not sure how old version of Vitrea is yet, ?functionality	IEP links cases to PACS. Sites may not be using PACS machines as their CTC work stations. How do we get cases from PACS to workstation??	
<i>Score</i>	<i>1</i>	<i>2</i>	<i>2</i>	<i>3</i>	<i>2</i>	<i>2</i>
Timeline	Very quick to set up	Once programme is developed and tested it should be relatively easy to stick to assessment timeline	Reliant on Royal Mail (!) , local PACS to setup and maintain, on participant to ensure cases are ready to view for first assessment. We could try and manage this step remotely	Getting the laptops to each site, in time for the assessment will be challenging.	Relying on local PACS team to access cases and get them onto workstation	Relies on cases getting to central hub and uploaded, AND on users going to sites to do the cases
	Since everything is online, it should be easy to monitor and encourage users to stick to assessment timeline	Vital already have this platform. Would just need tweaking	Would email users to remind them to do tests at the appropriate time	Multiple potential unexpected issues may arise – traffic/breakdowns/ unexpected user absence etc	Once cases are loaded we rely on users to participate	Must somehow get users to commit to the times, esp if there are space limitations at the hub
<i>Score</i>	<i>4</i>	<i>3</i>	<i>1</i>	<i>1</i>	<i>1</i>	<i>2</i>
Central control	Excellent, would be easy to update software and monitor progress	Can update software easily if there are any faults – would just re-upload the programme and users can download new version	None really re setup. Once cases are sent out we have no control over postage, if they're received, how quickly they are uploaded and tested. Reliant on participant to liaise with their local PCAS to ensure this happens	Very little once PEFECTS support is on the road.	Would only have control prior to sending out cases electronically	Very little. We are at the mercy of the users! Would have to impress upon them the importance of committing to travelling to Hub sites
	But may end up being time consuming ?delegate	BUT not as reactive as online option		Would be relying heavily on the support to maintain control/standards		
	<i>5</i>	<i>4</i>	<i>1</i>	<i>1</i>	<i>1</i>	<i>1</i>
Monitoring results	Can send reminders when deadline for tests is approaching.	If answer proforma is integrated into software, users would have to send proformas to us manually after completion OR complete proforma online on the PEFECTS website.	Since they will be completing their answers online we can monitor results easily.	PEFECTS assistant will be onsite to ensure tests completed satisfactorily	Since they will be completing their answers online we can monitor results easily.	Since they will be completing their answers online we can monitor results easily.
	Can track progress, and ?time spent on cases but may require robust software support	Monitoring wouldn't be possible until forms are submitted	Will also be able to see when people have logged in and started, therefore can send reminders and track progress	This assumes answer proforma is built into the software, otherwise users also have to get online to complete answers on PEFECTS website	Will also be able to see when people have logged in and started, therefore can send reminders and track progress	Will also be able to see when people have logged in and started, therefore can send reminders and track progress

	Online CTC viewer	Downloadable CTC viewer	Hardcopies for upload	Mobile laptops	IEP Link / Case download	Central Hub
<i>Score</i>	4	3	5	4	5	5
Uptake	Most easily accessible, so uptake should be good BUT may not be timely or complete. Users can choose to start/stop etc.	Getting users to actually download programme onto suitable PC may be a challenge. They're likely to give up at the first sign of difficulty. How could we streamline this?	Users may feel more comfortable using their usual software and we can package this to make it v attractive – "report at your usual workstation in your usual manner, with familiar tools etc."	Radiologists must be available on the day PERFECTS support arrives with laptop, would we have provision for inevitable cancellations? Arranging this will be tricky.	IEP link would be great as it's an already established system	Likely to be poor unless there is some sort of massive incentive
	Will be able to send reminders and encouragement tho.	If downloading onto PC at work they will need administrator access via IT – LABOURIOUS process!	Marketing the assessments as v similar to usual working practise will be advantageous	Alternatively, would people be more likely to make themselves available if they know someone is coming??	Uptake likely to be similar yo option C, as users get to use familiar work station.	I suspect users will be resistant to any travel, presenting another obstacle to participation
	Users can complete tests at home or in own time (less interruptions)	Again would need great tech support.	But need CTC workstation <i>plus</i> PC with online access to complete answer proforma OR proforma easy to complete on mobile device	Users will have to complete each assessment in one sitting, preferably with no interruptions	Would also need workstation and PC, unless integrated already.	Need to be sure hub is big enough to cater to all users within a limited time frame
	This model most closely simulates a possible future accreditation scheme.					
<i>Score</i>	4	3	4	3	3	1
Other Potential obstacles	PC requirements of user computers – possible that spec necessary is not available on most home/work computers.	PC requirements of user computers – possible that spec necessary is not available on most home/work computers.	Lose consistency of having all users using the same software. Loss of case library	LOGISTICS!!!! Eg. We have 2 or 3 radiologists in 40 sites (20 control, 20 intervention). PERFECTS support would need to go to all 40 sites four times in 12 months. Assessments spaced at baseline, 1m, 6m, 12m. So at least for the first two tests they would have to visit at least one site per day, ideally two. Before starting the cycle again almost immediately.	Lose consistency of having all users using the same software	We have maintained that all research will be at STM. Creating hubs for the assessments would make them research sites I think - amendment necessary to IRAS form (to be avoided at all costs!). Also how many hubs do we need? Would we mix up the intervention and control groups?
	Internet speed issues, CTCs will need to render each time on server so could get overloaded, jerking scrolling etc.	But less issues re: server and rendering than online solution		Site access! Would need several contacts on the ground.		Remuneration to users for travelling and/or hubs??
Total Scores	31/40	27/40	24/40	17/40	24	20

PACS: Picture Archiving and Communication System. IT: Information Technology. OS: Operating System

Appendix 7 Vitrea installation/user guide and CTC test guide

PERFECTS
Performance & Evaluation in CT Colonography Screening

We are pleased to be using the Vitrea Enterprise Suite, by Vital Images, as the platform to allow remote viewing of our CT colonography test cases.

You can access their software by either establishing a direct connection to their server (Windows only) or through the use of a remote desktop connection (Windows and Macs).

Please follow the appropriate step-by-step instructions on the following pages.

The test cases will be accessible between 7am and 11pm daily.

Contents

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Establishing a direct connection to server

STEP 1: Enabling Microsoft .NET Framework

- You only need to download and install the VES software on first use.
- On a Windows 7, Windows 8.1 or Windows 10 System you may need to also install the ActiveX component to enable viewing of the CTC studies.
- This is achieved by enabling the **‘.Net Framework 3.5’** feature on your computer

STEP 1: Enabling Microsoft .NET Framework

- Press the **Windows Key** and **F** key simultaneously
- In the pop up box, type: **‘appwiz.cpl’**

STEP 1: Enabling Microsoft .NET Framework

- The **‘Program and Features’** window will open.
- On the left, click **‘turn windows features on or off’**
- Scroll down to **‘.Net Framework 3.5 (includes .NET 2.0 and 3.0)’** and check the box.
- Click **‘OK’**.

STEP 1: Enabling Microsoft .NET Framework

- Click **‘Download files from Windows Update’** and once completed click **‘Close’**.
- Click **‘connect’** and then **‘Yes’** on the following screen.

STEP 2: Installation of Vitrea Enterprise Suite

- Using **Internet Explorer** type in the web address: <http://cloud.vitalema.eu/>
- Click **‘Install’**, when it appears.

Please note: You will need **‘admin rights’** on the computer, so may be unable to do this at work without IT clearance.

STEP 2: Installation of Vitrea Enterprise Suite

If you get this error message, then shut the window and retry from the beginning, by retying <http://cloud.vitalema.eu/> into Internet Explorer. Make sure you have enough rights to install software (local administrator rights)

STEP 2: Installation of Vitrea Enterprise Suite

- When successful, the following message will be displayed:
- Then please click **‘OK’**

Logging in to Vitrea Enterprise Suite

You are now ready to run the Vitrea Enterprise Suite:

- Using **Internet Explorer** go to the link: <http://cloud.vitalema.eu/>
- Input your 7 digit user ID and password and click **‘Sign in’**. You may be asked for an email address on the first login

Installing a Remote Desktop Connection

WINDOWS USERS

For Windows users: Establishing the Remote Desktop Connection

- Open the **‘Client_xx’** attachment, and then double-click the icon.
- Click **‘Yes’** on the alert box and check **‘Don’t ask me again’**.
- Your computer will now try and establish the remote connection. Check **‘Don’t ask me again’** and then click **‘Connect’**

Establishing the Remote Desktop Connection

- You will now see the remote desktop with the VitreaCore icon displayed. Double-click this to launch the Vitrea Enterprise Suite.

Establishing the Remote Desktop Connection

- Add the Vitrea website to the trusted sites
- Uncheck server verification box
- Add the Vitrea website to the trusted sites (make the website box may go blank, don’t worry!)
- Click **‘Close’**

Proceed to page 14

Installing a Remote Desktop Connection

MAC USERS

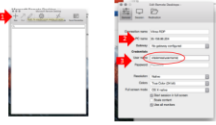
For Mac Users: Establishing the Remote Desktop Connection

In order to access the remote desktop you must first download the free app from the App Store. Search for **Microsoft Remote Desktop** and select the app from the list.

Once downloaded, double-click to open.


Establishing the Remote Desktop Connection

1. Click 'New'
2. Enter the IP address provided in your email e.g. 35.158.86.204
3. Enter 'vitalema' and add your user ID or username at the end
4. Enter your password and then close the window




Establishing the Remote Desktop Connection

1. The new desktop will be visible in the main screen. Double-click it to launch.
2. Press continue to accept the certificate



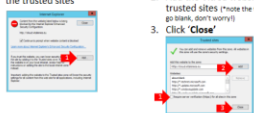
Establishing the Remote Desktop Connection

1. You will now see the remote desktop with the VitreaCore icon displayed. Double-click this to launch the Vitrea Enterprise Suite.



Establishing the Remote Desktop Connection

1. Add the Vitrea website to the trusted sites
1. Uncheck server verification box
2. Add the Vitrea website to the trusted sites (note the website box may go blank, don't worry)
3. Click 'Close'




Vitrea Enterprise Suite

HOW TO LOGIN & OPEN CASES

Logging in to Vitrea Enterprise Suite

You are now ready to run the Vitrea Enterprise Suite (1):

Input your 7 digit user ID or username and password and click 'Sign in'. You may be asked for an email address on the first login




Opening & Viewing Cases

Once you have logged in, a work list will appear on the screen (if not, select 'All Studies')

To filter studies for your test please type 'baseline' or '1m' in the institution field to the right of the screen and press enter. Each test has 10 cases only.


1. To put the cases in numerical order click on the 'Patient name' tab once
2. To select a case, highlight the name e.g. DEMO_PTC74 in the 'Patient name' column by clicking on it once



Opening & Viewing Cases

1. Patient DEMO_PTC74 is now selected and a toolbar has opened at the bottom of the screen.
2. Select the 'Series' tab


NOTE:
If you accidentally double click the case name, the study will load in a default view, which does not have full CT functionality. Close this window and return to the patient list screen.



Opening & Viewing Cases


Left-click on the first series, then holding down 'Ctrl' on the keyboard, left-click the second series.

1. When both sequences are highlighted, right-click on one of them and a menu will appear.
2. Select 'Load in Advanced Viewer'



Opening & Viewing Cases

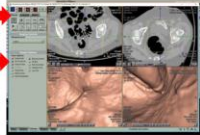
1. Select the 'Colon CT' examination protocol.
2. Allow the study to load by waiting until the purple bar at the bottom right corner of the screen has loaded.
3. Click the bottom right hand 'Pick' button.



Opening & Viewing Cases – Visual Tab

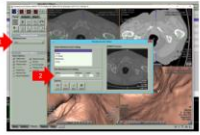
1. To maximise your viewing area and reduce distractions, you can turn off the patient information and the yellow guide lines. Go to the 'Visual' tab.
2. Deselect 'Patient info' and 'Yield of view'

* Please ensure that you are reading the corresponding case to your answer sheet.



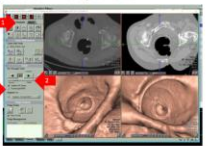
Opening & Viewing Cases – Visual Tab

1. To change the window levels, select the drop down menu in the 'Window/Level' box and select the window you require.
2. You can also add a window – e.g. 'Bone', by clicking 'New' and filling in the values (e.g. 3500/400).



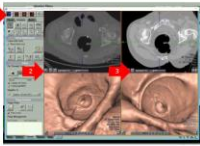
Opening & Viewing Cases – Analysis Tab

1. In the 'Analysis' tab select 'Update all views' and deselect 'Register to'. This will make your image interpretation experience smoother.
 - You will need to do this for each case you load.
2. If you perform a 3D read, you can adjust the speed by moving the slider.



Opening & Viewing Cases


1. To change the layout of your windows, select one of the options at the top left.
2. To maximise a series click the diagonal arrow. To minimise, click it again.
3. To view coronal or sagittal reformats, click the 'MRP' button



Mouse Controls

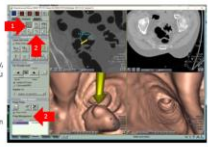
2D and MPR mouse functions

3D mouse functions



Opening & Viewing Cases

1. To measure a lesion select the ruler tool. To delete the measurement, click on it again and press delete on your keyboard.
2. To mark lesions for further review, or keep track of your findings, you can label them with the arrow tool.
 - These arrows will automatically appear in the 3D endoluminal view.
 - A list of arrowed lesions will appear in the 'Physio Management' box at the bottom left.




Troubleshooting

If you get an error stating 'Advanced profile not available', please try and log in again later.

This is because all the user slots are filled at that time. Please email us if this happens more than once.

Please remember that cases will only be available for review between 7am and 11pm.

Do not use the VitreaCore application as this has less functionality and no endoluminal options

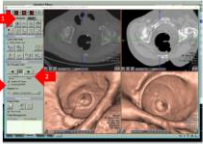


Further information and detailed Vitrea User Guide is available from:

<http://vitreaebus.vitalimages.com/vital/Help/en/pdf/VitreaAdvancedGeneralGuide.pdf>

Opening & Viewing Cases – Analysis Tab

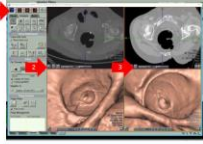
- In the 'Analysis' tab select 'Update all views' and deselect 'Register to'. This will make your image interpretation experience smoother.
 - You will need to do this for each case you load.
- If you perform a 3D read, you can adjust the speed by moving the slider.



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Opening & Viewing Cases

- To change the layout of your windows, select one of the options at the top left.
- To maximise a series click the diagonal arrow. To minimise, click it again.
- To view coronal or sagittal reformats, click the 'MPR' button.



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Mouse Controls

2D and MPR mouse functions



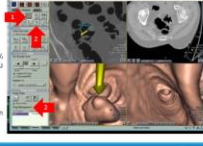
3D mouse functions



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Opening & Viewing Cases

- To measure a lesion select the ruler tool. To delete the measurement, click on it again and press delete on your keyboard.
- To mark lesions for further review, or keep track of your findings, you can label them with the arrow tool.
 - These arrows will automatically appear in the 3D endoluminal view.
 - A list of arrowed lesions will appear in the 'Pose Management' box at the bottom left.



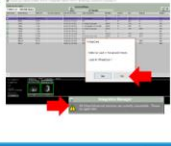
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Troubleshooting

If you get an error stating 'Advanced profile not available', please try and log in again later. This is because all the user slots are filled at that time. Please email us if this happens more than once.

Please remember that cases will only be available for review between 7am and 11pm.

Do not use the VitreaCore application as this has less functionality and no endoluminal options.



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Further information and detailed Vitrea User Guide is available from:

<http://vitreaweb.vitalimages.com/vital/help/en/pdf/VitreaAdvancedGeneralEaUserGuide.pdf>

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Appendix 8 PERFECTS case report form


PERFECTS


Baseline Test

This web based form is used to record your findings for the PERFECTS baseline test, comprising ten CT colonography cases. Each of the ten cases is either normal or abnormal and, where abnormal, one or more abnormal findings are present. You can save your answers at any time and return to complete the test at any point until the assessment window closes. Please read the cases in the order stated on the form, ensuring that when inputting your answers you are reviewing the corresponding CTC.

Instructions:

- Please review the cases as you would in your routine practice.
- You are only required to record colonic findings for each case, documenting each individual abnormal finding; polyp (neoplastic and appears benign), cancer (either polypoid or mass-like) or other (such as diverticular stricture, haemorrhoid or lipoma).
- To allow for measurement error, please report any lesions measuring **5mm maximal diameter** or more.
- Please record the location of the epicentre of the polyp or cancer according to series acquisition and image slice numbers.
- Whilst all 10 cases do not have to be completed in one go, please endeavour to complete each case in a single sitting.
- A demo case is included, DEMO-PTC74, on which you can practise using the Vitrea software tools. This case is **not** part of the assessment.
- Please do not discuss the cases or share your answers with colleagues at any time.

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PERFECTS

Baseline Test

Please enter your 7 digit user ID

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Baseline Test

1. CASE PTC02

a. Is this a normal study?

- Yes (ie no size significant polyp >5mm or colorectal cancer)
 No

Back

Save

Next

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Genie Survey Software

Baseline Test

b. Please record the lesions you have detected:

Note:

Lesion type, 'Other', should be selected if you detect a presumed non-malignant lesion eg. diverticular stricture, lipoma etc

If a lesion is unmatched on Series 2, please put the slice number as 0 in the final column

*RLD- right lateral decubitus. **LLD- left lateral decubitus

	Lesion Type	Size (mm)	Colonic Segment	Series 1	Image number	Series 2	Image number
Lesion 1	Select: <input type="text"/>	<input type="text"/>	Select: <input type="text"/>	Select <input type="text"/>	<input type="text"/>	Select: <input type="text"/>	<input type="text"/>
Lesion 2	Select: <input type="text"/>	<input type="text"/>	Select: <input type="text"/>	Select <input type="text"/>	<input type="text"/>	Select: <input type="text"/>	<input type="text"/>
Lesion 3	Select: <input type="text"/>	<input type="text"/>	Select: <input type="text"/>	Select <input type="text"/>	<input type="text"/>	Select: <input type="text"/>	<input type="text"/>
Lesion 4	Select: <input type="text"/>	<input type="text"/>	Select: <input type="text"/>	Select <input type="text"/>	<input type="text"/>	Select: <input type="text"/>	<input type="text"/>
Lesion 5	Select: <input type="text"/>	<input type="text"/>	Select: <input type="text"/>	Select <input type="text"/>	<input type="text"/>	Select: <input type="text"/>	<input type="text"/>
Lesion 6	Select: <input type="text"/>	<input type="text"/>	Select: <input type="text"/>	Select <input type="text"/>	<input type="text"/>	Select: <input type="text"/>	<input type="text"/>
Lesion 7	Select: <input type="text"/>	<input type="text"/>	Select: <input type="text"/>	Select <input type="text"/>	<input type="text"/>	Select: <input type="text"/>	<input type="text"/>
Lesion 8	Select: <input type="text"/>	<input type="text"/>	Select: <input type="text"/>	Select <input type="text"/>	<input type="text"/>	Select: <input type="text"/>	<input type="text"/>
Lesion 9	Select: <input type="text"/>	<input type="text"/>	Select: <input type="text"/>	Select <input type="text"/>	<input type="text"/>	Select: <input type="text"/>	<input type="text"/>
Lesion 10	Select: <input type="text"/>	<input type="text"/>	Select: <input type="text"/>	Select <input type="text"/>	<input type="text"/>	Select: <input type="text"/>	<input type="text"/>

Back

Save

Next

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Genie Survey Software

Baseline Test

c. Considering the case PTC02 overall, which of the following is the best management option?

- Repeat CT colonography as the current study is suboptimal
- No additional colonic investigation required
- CT colonography surveillance within 3 years
- Refer for consideration of endoscopic evaluation (for characterisation +/- biopsy or polypectomy)
- Refer for consideration of same day colonoscopy, biopsy and CT staging

d. Please select your diagnostic confidence for case PTC02:

0 1 2 3 4 5 6 7 8 9 10
No abnormality Definite abnormality

e. If you performed a 2D and 3D read, what percentage of time did you spend performing the 3D read?

%

If you would like to provide us with any feedback on this case, please enter it below:

Appendix 9 Radiologists from 72 hospital sites completed the PERFECTS pre-randomisation questionnaire

Barnet Hospital	Royal Hampshire County Hospital
Barts and The London	Royal Lancaster Infirmary
Basingstoke and North Hampshire Hospital	Royal Liverpool University Hospital
Bristol Royal Infirmary	Royal Preston Hospital
Broomfield Hospital	Royal Stoke Hospital
Charing Cross Hospital	Royal Surrey County Hospital
Chelsea and Westminster Hospital	Royal Sussex County Hospital
Croydon University Hospital	Royal Victoria Infirmary
Ealing Hospital	Salisbury District Hospital
Fairfield General Hospital	Sandwell general hospital
Freeman Hospital	Scarborough General Hospital
Hinchingbrooke Hospital	South Tyneside District General Hospital
Huddersfield Royal Infirmary	Southampton General Hospital
Ipswich Hospital	Southmead Hospital
James Cook University hospital	St George's Hospital
Kent and Canterbury Hospital	St James's University Hospital
Kettering General Hospital	St Mark's Hospital
Leicester General Hospital	St Peter's Hospital
Leighton Hospital	Torbay Hospital
Maidstone Hospital	Tunbridge Wells Hospital
Medway Maritime Hospital	University College London
New Cross Hospital	University Hospital Lewisham
North Tees hospital	University Hospital of North Midlands
North Tyneside General Hospital	University Hospital of South Manchester
Northern General and Royal Hallamshire hospitals	University Hospital of Wales
Northern General Hospital	University Hospital Southampton
Nottingham City Hospital	University Hospitals Leicester
Pinderfield Hospital	Wansbeck General Hospital
Princess Royal Hospital, Telford	Watford General Hospital
Queen Alexandra, Portsmouth	West Middlesex University Hospital
Queen Elizabeth Hospital	Weston general hospital
Queens Medical Centre	Wexham Park hospital
Royal Berkshire Hospital	Worcestershire Royal Hospital
Royal Bolton Hospital	Worthing Hospital
Royal Cornwall hospital	Wythenshawe Hospital
Royal Free Hospital	York Teaching Hospital