



National
Cancer
Screening
Service

Guidelines for
**Quality Assurance in
Colorectal Screening**

First edition

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Foreword

The National Cancer Screening Service (NCSS), which is part of the Health Service Executive's National Cancer Control Programme (NCCP), has gained significant expertise over many years in designing, implementing and managing successful population-based call, re-call screening programmes in Ireland. The NCSS governs BreastCheck – The National Breast Screening Programme and CervicalCheck – The National Cervical Screening Programme. It is also responsible for developing and implementing a national diabetic retinopathy screening programme.

Definition of screening

According to 'A Strategy for Cancer Control in Ireland, 2006', screening is a means of detecting disease before it has developed to the point where it results in symptoms. In screening for cancer, cancers can be detected at an early stage of invasiveness or even before invasiveness has occurred. Screening aims to improve survival rates, limit morbidity and improve the quality of life of those who have developed cancer.

Screening can be appropriate for conditions other than cancer. Screening does not diagnose illness; its purpose is risk reduction. Screening is not a guarantee of diagnosis and cure; those who have a positive test require confirmatory diagnostic testing before definitive diagnoses can be established and appropriate treatment planned.

Population-based screening

Population-based call, re-call screening programmes provide a consistent, high-quality and standardised approach to identifying the population most at risk from a particular disease right through to diagnosis and referral for treatment. This begins with developing a register of clients in the identified population, inviting participation in the programme, offering defined referral and treatment pathways within set time limits and developing a mechanism to re-call clients at defined intervals.

The particular value of an organised call, re-call screening programme is in the repeat nature of the test at determined intervals rather than the actual test itself because no screening test can be considered to be 100 per cent accurate. It is important, therefore, that the individuals continue to participate each time they are called. It is this continued uptake that leads to early detection and ultimately to achieving the objective of reducing mortality from the disease in the screened population. This means that it is incumbent on the programme to ensure that the high-quality, consistent approach is maintained throughout the lifetime of the programme.

The relationship between a screening programme and its clients is unique in that clients may interact many times with the programme over a significant period of time. For example, when the colorectal screening programme is available to the entire age cohort of 55-74 years, some individuals may interact with the programme up to 10 times over a 20-year period.

Colorectal cancer in Ireland

In Ireland, colorectal cancer is the second most common newly diagnosed cancer among men and women. Each year over 2,000 new cases of colorectal cancer are reported. The number of new cases is expected to increase significantly over the next 10 years, due mainly to an increasing and ageing population. Colorectal cancer is currently the second most common cause of cancer death in Ireland, and about 50 per cent of colorectal cancer patients die from the disease.

Colorectal screening

The primary objective of colorectal cancer screening is to detect pre-cancerous adenomas in the lining of the bowel, thereby making colorectal cancer screening a truly preventative health measure. This has the effect of potentially reducing the burden of treatment on both the individual and the health system. It reduces the stress, disruption and anguish that cancer diagnoses and subsequent treatment can bring to the individual, their family and community.

The programme

The colorectal screening programme will offer free screening to men and women aged 55-74 on a two-yearly cycle. To develop capacity for the full population, the programme will be implemented on a phased basis, starting with men and women aged 60-69. This age group has the highest incidence of cancer within the wider age range. The maximum benefit in terms of reduction in mortality and cost-effectiveness will occur only when the programme targets the full 55-74 age population.

As its primary screening tool, the programme will use the faecal immunochemical test (FIT), which operates on an automated testing platform. This is one of the first international population-based screening programmes for colorectal cancer that utilises this technology as the primary screening tool.

One of the particular advantages of this test to population-based screening is that it can be self-administered in the privacy of the individual's own home. For the vast majority (approximately 94 per cent) of the population, this will be the only test required. For a small minority (5 to 6 per cent), a further test (colonoscopy) at a hospital-based screening colonoscopy unit will be necessary.

No screening programme exists in isolation from other health services. As part of the preparation for the commencement of the colorectal screening programme, a number of quality initiatives are underway across publically funded endoscopy facilities nationwide. These quality improvement schemes will benefit all users of endoscopy, whether for screening, colorectal cancer or any of the other benign conditions diagnosed and monitored through endoscopic procedures.

In preparation for building the capacity of the screening programme over the long term, 20 new service posts were granted for clinical nurse specialists to train for future roles as advanced nurse practitioners. Following the achievement of a master's qualification and practical training, successful candidates will, in time, be qualified to carry out colonoscopies.

Population-based screening for colorectal cancer has the potential to be one of the most effective public health interventions in the Irish healthcare system. To ensure its effectiveness and that it adheres to the highest international standards, each step of the colorectal screening programme must be fully quality assured and monitored.

We would like to thank all those involved in the implementation and introduction of the colorectal screening programme for their dedication to the project. We would also like to thank those involved in developing these guidelines for their valuable time and expertise.



Majella Byrne,
Acting Director, National
Cancer Screening Service



Dr Susan O'Reilly,
Director, National Cancer
Control Programme

Preface

The primary goal of the National Cancer Screening Service (NCSS) national colorectal screening programme is to reduce mortality from colorectal cancer in men and women aged 55-74 in Ireland. Organised population-based screening for colorectal cancer is a layered, complex process involving a number of steps, including the identification of the target population, recruitment of the target population into the programme, delivery of a suitable screening test, analysis of the screening test, the re-call of people whose initial screening test indicates an abnormality and the provision of diagnosis and referral for treatment where required.

Each aspect of the screening process must be fully quality assured. Quality assurance is process-driven, and specific steps help define and achieve screening goals.

Prior to the NCSS being tasked by the Minister for Health and Children in January 2010 to begin preparations for the introduction of a national programme, a number of actions and activities had taken place. In 2007, the Minister asked the former Board of the NCSS to explore the potential for a national, quality-assured colorectal cancer screening programme in Ireland. Chaired by Professor Niall O'Higgins, an expert group evaluated the clinical and organisational elements required to introduce a programme and presented its first (interim) report to the Board of the NCSS in December 2007.

An independent peer review of the report was sought from an international panel of experts in colorectal cancer screening (Professor Wendy Atkin and Professor Robert Steele (UK), Professor Jean Faivre (France) and Professor Michael O'Brien (USA)). On completion of this review, the expert group submitted its final report to the Board of the NCSS in October 2008.

The Board of the NCSS requested the Health Information and Quality Authority (HIQA) to undertake a Health Technology Assessment (HTA) so that the cost-effectiveness of the proposed programme could be measured. The outcome of the HIQA report supported the recommendations made by the Board of the NCSS.

The recommendations of the Board of the NCSS on the organisation and implementation of a national, population-based, quality-assured colorectal cancer screening programme were provided to the Minister for Health and Children in December 2008.

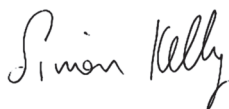
A significant aspect of the preparations for the introduction of the programme was the establishment of the NCSS Quality Assurance (QA) Committee for Colorectal Screening. Its purpose was to review international standards, recommend best practice, monitor and evaluate achievement of the recommended standards and monitor and support adherence by service providers. The QA Committee reports to the Director of the NCSS, who has overall responsibility for quality assurance in NCSS programmes.

To ensure continual adherence to quality assurance across every aspect of the colorectal screening programme, a set of written, auditable QA standards needed to be developed against which the performance of the programme could be monitored. A multidisciplinary process to agree QA processes and standards was developed. In addition to my appointment as QA chairperson, the NCSS appointed chairpersons for designated specialist QA subgroups (Programme and Administration; Endoscopy and Radiology; Histopathology; and Surgery) and members of each subgroup representing experts in each field. Together these subgroups developed the suite of QA standards contained in these guidelines.

One of the main principles of developing quality assurance standards is to focus on the delivery of optimal outcomes for all users of the programme. Quality assurance standards, although subject to intermittent review and revision, must be sufficiently robust to stand alone over time. It was imperative, therefore, that the members of the QA Committee and subgroups disregard current constraints or difficulties in the area when developing standards. It is important to note that some of the standards will not be measurable until at least one round of the programme has been completed.

Before publication, the standards were reviewed and approved by an international peer review panel that included leading experts and practitioners in the delivery of colorectal cancer screening, endoscopy, cytology, pathology and surgery. The international peer review panel recommended that the NCSS must be satisfied that a number of criteria are fully met before the screening programme commences so that the programme can consistently and reliably deliver best outcomes for the men and women who participate in the programme.

This first edition of 'Guidelines for Quality Assurance in Colorectal Screening' represents best practice. Rigorous adherence to best practice will ensure that the colorectal screening programme has a significant impact on reducing mortality from colorectal cancer in Ireland.

A handwritten signature in black ink that reads "Simon Kelly". The signature is written in a cursive, flowing style.

Mr Simon Kelly
Chairperson of the NCSS Quality Assurance Committee
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International peer review

As part of the development of the Guidelines for Quality Assurance in Colorectal Screening, an external international peer review took place in March 2011.

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1

Introduction

The colorectal screening programme will offer free screening nationally to men and women aged 55-74 on a two-yearly cycle. To develop the capacity to cater for the full 55-74 population, the programme will be implemented on a phased basis, starting with men and women aged 60-69. The programme will be expanded over time until the full 55-74 age group is reached.

The purpose of the screening programme is to identify the population most at risk of colorectal cancer and most likely to benefit from early detection and treatment. The maximum benefit in terms of reduction in mortality and cost-effectiveness will occur when the programme targets the full 55-74 age population.

The National Cancer Screening Service (NCSS) is working with colleagues in the Special Delivery Unit, Department of Health and the Health Service Executive so that colonoscopy services nationwide will have the capacity to support the introduction of the screening programme while maintaining and enhancing the capability of the symptomatic endoscopy service.

Strategic planning for the development and implementation of the programme is provided by the NCSS's Colorectal Executive Management Team. The NCSS's Quality Assurance Committee for Colorectal Screening developed the guidelines contained in this document. A Clinical Advisory Group has been established to support the ongoing development of the programme and to provide medical policy and clinical advice to the NCSS.

Establishing an organised population-based screening for colorectal cancer is a complex and layered process. This programme is based on international evidence.

The programme will be introduced on a call, re-call basis. A number of steps will be involved including the identification of the target population, recruitment of the target population into the programme by a proactive call, delivery of a suitable screening test, analysis of the screening test, the re-call of people whose initial screening test indicates an abnormality and the provision of diagnosis and referral for treatment where required. A freephone information line, materials and a comprehensive website will be provided to support clients of the screening programme.

Eligible men and women who indicate they wish to take part in the screening programme will be sent a screening test kit called a faecal immunochemical test (FIT). The test looks for the presence of blood in the bowel motion. The simple and easy-to-use test kit will include step-by-step instructions for self-administration of the test at home. The completed test can then be sent by Freepost to an accredited laboratory for analysis. Approximately 94 per cent of people will receive a normal test result and will be sent another home test kit in two years' time while they remain within the eligible age range.

Five to six per cent of people will receive an abnormal result following the home test kit and will require an additional test. They will be offered a screening colonoscopy (an investigation of the lining of the bowel) at a hospital-based unit contracted by the NCSS to provide this service. Each person will be contacted by a suitably qualified nurse, who will assess the person's suitability for colonoscopy and then guide them through the colonoscopy process. In the event that further treatment or surgery is required, defined pathways have been developed in conjunction with the National Cancer Control Programme (NCCP).

The following chapters set out the key performance indicators against which the screening programme will be measured and standards for all aspects of the screening programme, including administration, FIT, endoscopy and radiology, histopathology and surgery.

Each part of the screening process must be fully quality assured and monitored to ensure it adheres to the highest international standards and gives rise to best outcomes.

2

Summary of key performance indicators

For ease of reference, a summary table of key performance indicators (KPIs) from the guidelines specified throughout this report is given below. Please note that the numbering of the indicators is not indicative of importance. In any case, all targets should be constantly reviewed in the light of experience and revised accordingly with respect to results achieved and best clinical practice. As far as possible, targets given refer to people aged 55-74 years of age attending the colorectal screening programme. At least one full round of screening or a number of years will be required to measure some of these standards.

This chapter includes a summary of:

- Key performance indicators (KPI)
- Other measurable standards. The colorectal screening programme will also monitor other measurable standards that are included in these guidelines. While these may not be KPIs, they will have an impact on the overall performance of the programme.

Each KPI specified in the tables to follow is cross-referenced in superscript to a section number in the relevant chapter where the KPI can be seen in context.

2.1 Key performance indicators

	Key performance indicators	Minimum standard	Achievable standard
2.1.1	Reduction of mortality from colorectal cancer among the target population ^{3.2.1}	≥15%	≥25%
2.1.2	Proportion of eligible population on register invited for screening every two years ^{3.2.2}	≥90%	100%
2.1.3	Proportion of eligible individuals screened in the period (screening round) every two years ^{3.2.4}	≥45%	≥55%
2.1.4	Proportion of individuals responding positively to invitations to screening ^{3.2.3}	≥50%	≥60%
2.1.5	Proportion of FIT test kits and instructions despatched to clients who request them within five working days ^{3.5.1}	≥90%	100%
2.1.6	Proportion of unacceptable tests received by laboratory (related to 2.2.6 below) ^{4.5.4}	≤3%	≤1%
2.1.7	Proportion of results of FIT samples tested by laboratory made available to NCSS within three working days of receipt of samples in laboratory ^{4.5.1}	100%	

	Key performance indicator	Minimum standard	Achievable standard
2.1.8	Proportion of positive FIT results notified to screening colonoscopy unit by the NCSS within five working days of result received from laboratory ^{3.5.3}	≥90%	100%
2.1.9	Proportion of FIT result letters to clients printed and posted to clients within five working days of date result received from laboratory ^{3.5.4}	≥90%	100%
2.1.10	Proportion of clients offered colonoscopy within 4 weeks from when deemed clinically suitable following pre-assessment ^{3.5.7}	≥90%	100%
2.1.11	Minimum number of screening colonoscopies undertaken annually by each screening colonoscopist ^{5.2.2} <ul style="list-style-type: none"> • Colonoscopies (symptomatic and screening) per annum • Screening colonoscopies (auditable after programme is running at full capacity) 		>300 >150
2.1.12	Response rate (acceptance rate) for colonoscopy after positive FIT ^{5.2.4.1}	>85%	>90%
2.1.13	Unadjusted caecal intubation rate (CIR) with photographic evidence ^{5.2.7}	≥90%	≥95%
2.1.14	Perforation rate of colonoscopy ^{5.3.2.1}	<1 per 1,000 colonoscopies	
2.1.15	Post-polypectomy perforation rate ^{5.3.2.2}	<2 per 1,000 colonoscopies where polypectomy is performed	
2.1.16	Post-polypectomy bleeding requiring transfusion (PPB) ^{5.3.3}	<1% colonoscopies where polypectomy is performed	
2.1.17	Percentage of individuals scheduled for surveillance colonoscopy who undergo that procedure within 3 months of scheduled date ^{5.2.4.2}	>85%	>90%
2.1.18	Cancer detection rate ^{5.2.8.1}	≥2 per 1,000 screened	≥5 per 1,000 screened
2.1.19	Adenoma detection rate (ADR) ^{5.2.8.2}	25% of colonoscopies	35% of colonoscopies
2.1.20	Proportion of CT colonography performed on clients within 30 working days of receipt of referral ^{5.10, 5.14.10}	≥95%	100%
2.1.21	Completion rates of CT colonography ^{5.14.2}	≥95%	

	Key performance indicator	Minimum standard	Achievable standard
2.1.22	Perforation rate of CT colonography ^{5.13.1, 5.14.4}	<1 per 3,000 CT colonography examinations	
2.1.23	Turnaround time for report being issued to the programme after CT colonography examination is performed ^{5.14.11}	≤15 working days	≤10 working days
2.1.24	Median number of lymph nodes retrieved in non-neoadjuvant treated cases ^{6.2.15, 6.3.9, 6.9}	>12	
2.1.25	Proportion of lesions reported as high-grade dysplasia ^{6.2.16, 6.3.10, 6.9}	≤10%	
2.1.26	Proportion of polyp cancer identified as poor differentiation ^{6.3.11, 6.7.3.2}	≤20%	
2.1.27	Proportion of histopathological biopsy reports authorised and relayed to referrer within 5 working days of receipt of specimen in laboratory ^{6.3.1}	≥90%	100%
2.1.28	Proportion of colon cancer referrals to a designated cancer centre taken place within 10 working days of histological diagnosis ^{7.2.1}	≥90%	100%
2.1.29	Proportion of colon cancer patients offered an admission date for surgery within 20 working days of histological diagnosis ^{7.2.2}	≥90%	100%
2.1.30	Minimum number of colon cancer resections per surgeon per annum ^{7.2.3}	≥20	
2.1.31	Proportion of rectal cancer referrals to designated cancer centre that have taken place within 10 working days of histological diagnosis ^{7.3.1}	≥90%	100%
2.1.32	Proportion of rectal cancer patients offered admission date for surgery within 20 working days of histological diagnosis where surgery is primary treatment ^{7.3.2}	≥90%	100%
2.1.33	Minimum number of rectal resections per surgeon per annum ^{7.3.3}	≥20	
2.1.34	Proportion of rectal cancer patients whose neoadjuvant therapy is initiated within 30 working days of histological diagnosis where surgery is not initial treatment ^{7.3.5}	≥90%	100%

2.2 Other measurable standards

The colorectal screening programme will also monitor other measurable standards that are included in these guidelines. While these may not be KPIs, they will have an impact on the overall performance of the programme.

	Standard	Minimum standard	Achievable standard
2.2.1	Acquire and maintain demographic details for the eligible population ^{3.3.1}	Within 95% of census figures	
2.2.2	Proportion of invited population who do not respond to invitations within eight weeks that are sent at least one reminder ^{3.4.3}	≥90 %	100%
2.2.3	Proportion of clients who request and receive test kits that are sent a reminder if test kit is not received at laboratory within four weeks ^{3.5.2}	≥95%	100%
2.2.4	Proportion of FIT samples tested within 2 working days of receipt in laboratory ^{4.4.5}	100%	
2.2.5	Proportion of FIT result letters to general practitioners following test printed and posted within five working days of date result is received from laboratory ^{3.5.5}	≥90%	≥95%
2.2.6	Proportion of repeat test kits despatched to clients within 10 working days where unacceptable test kits are received at laboratory (related to 2.1.6 above) ^{3.5.6}	≥90%	≥95%
2.2.7	Bowel cleanliness at colonoscopy: excellent or adequate ^{5.2.3}	≥90%	≥95%
2.2.8	Colonoscopic comfort ^{5.2.6}	Auditable outcome	
2.2.9	Medication used for comfort during lower gastrointestinal (GI) endoscopy ^{5.2.6.1}	Auditable outcome	
2.2.10	Use of reversal agents ^{5.2.6.2}	Auditable outcome	
2.2.11	Colonoscopic cancer detection rate ^{5.2.8.1}	≥11 per 100 colonoscopies	
2.2.12	Colonoscope withdrawal time ^{5.2.9}	≥6 mins inspection time on withdrawal ≥90% of negative procedures	≥6 mins inspection time on withdrawal ≥95% of negative procedures
2.2.13	Retrieval rate of polypectomy specimens for histological analysis ^{5.2.10}	≥90%	≥95%

	Key performance indicator	Minimum standard	Achievable standard
2.2.14	Proportion of “no abnormality detected” following colonoscopy result letters printed and posted to clients within 10 working days of colonoscopy date ^{3.5.8}	≥90%	≥95%
2.2.15	Proportion of result letters to general practitioners following colonoscopy printed and posted within 10 working days from date of result received from screening colonoscopy unit ^{3.5.9}	≥90%	≥95%
2.2.16	Other adverse events of colonoscopy ^{5.3.4}	Auditable outcome	
2.2.17	Referral rates for CT colonography referred for colonoscopy following a positive FIT ^{5.11.2, 5.14.1}	≤10%	
2.2.18	Minimum number of CT colonography cases read per consultant radiologist per year ^{5.8.2}	≥100	
2.2.19	Adequacy of preparation and distension ^{5.14.3}	≥95%	
2.2.20	Other major complication rate of CT colonography ^{5.14.5}	Auditable outcome	
2.2.21	Proportion of clients with abnormal CT colonography report with CRADs classification of C4 or equivalent who have follow-up colonoscopy or are referred to MDT within 15 working days ^{5.14.12}	≥95%	100%
2.2.22	Proportion of clients with abnormal CT colonography report with CRADs classification of C3 or equivalent who have follow-up colonoscopy or are referred to MDT within 30 working days ^{5.14.13}	≥95%	100%
2.2.23	CT colonography radiation dose ^{5.14.6}	Auditable outcome	
2.2.24	Large adenomas (≥10 mm) detected on CT colonography ^{5.14.7}	Auditable outcome	
2.2.25	Cancers detected on CT colonography ^{5.14.8}	Auditable outcome	
2.2.26	Prevalence of extracolonic lesions that warrant additional investigation ^{5.14.9}	Auditable outcome	
2.2.27	Proportion of histopathology reporting consistent with Faculty of Pathology, RCPI guidelines and including a clear indication of main diagnosis ^{6.3.2}	≥95%	100%
2.2.28	Proportion of pathologists participating in a national external quality assurance scheme ^{6.3.3}	100%	

	Standard	Minimum standard	Achievable standard
2.2.29	Proportion of histopathology laboratories holding or working towards CPA accreditation or equivalent ^{6.3.4}	100%	
2.2.30	Proportion of histopathology laboratories participating in national histopathology quality assurance scheme ^{6.3.5}	100%	
2.2.31	Proportion of histopathology screening results validated by a named screening pathologist ^{6.3.6}	100%	
2.2.32	Proportion of polyp cancers with double reporting ^{6.3.7}	100%	
2.2.33	Overall proportion of resectable rectal cancer treated by abdomino-perineal excision (APR) ^{7.3.6.1}	<30%	<25%
2.2.34	Anastomotic leakage rate ^{7.3.6.2}	<8%	<5%
2.2.35	Crude length of stay (date of admission to date of discharge) ^{7.4}	Auditable outcome	
2.2.36	Unadjusted operative and procedural 30-day mortality from date of patient's operation or stent ^{7.4}	Auditable outcome	
2.2.37	Margin positivity ^{7.4}	Auditable outcome	
2.2.38	Nodal harvest (number of positive nodes/total number of nodes) ^{7.4}	Auditable outcome	
2.2.39	Return to theatre rate during hospital stay ^{7.4}	Auditable outcome	
2.2.39	Neo-adjuvant and adjuvant radiotherapy use ^{7.4}	Auditable outcome	
2.2.41	Re-admission rate within 30 days of operation ^{7.4}	Auditable outcome	

3

Programme and administration standards

3.1 Programme overview

The aim of the national colorectal screening programme is to reduce mortality from colorectal cancer in the target population.

The achievement of this aim requires the management and co-ordination of complex activities, some of which are directly within the control of the programme and some of which are contracted or provided to the programme from external sources, organisations and institutions.

The role of the Programme and Administration Quality Assurance subgroup is to take a holistic view of the screening programme and consider the way in which each aspect relates to the programme as a whole. In particular, the subgroup takes into account the needs of the target population and its subsets and their communication and interaction with each stage of the screening programme.

The service provided must be safe, equitable and effective. To ensure this, appropriate standards must be assigned to each facet of programme delivery. Such standards must be measured, interpreted, reported and reviewed.

The National Cancer Screening Service (NCSS) has the benefit of lessons learned from its other population-based screening programmes and encourages a culture of continual improvement, which will enhance the colorectal screening programme.

The standards are categorised as follows:

- Programme standards
- Population register
- Call, re-call process
- Screening process
- Communications
- Information communications technology (ICT)

3.2 Programme standards

The colorectal screening programme standards are set to ensure overall quality in a national population-based screening programme. To maintain and monitor programme quality, a number of activities will be established, including cancer audit and risk management.

Cancer audit: The programme will collaborate with relevant national bodies in relation to the collection and investigation of cancer cases.

Risk management: A programme risk register will be monitored and updated regularly and steps will be taken to mitigate or lessen the impact of identified risks. All incidents will be reported and escalated according to established protocols.

	Criterion	Measurement	Standard
3.2.1	Mortality	To reduce mortality from colorectal cancer among the target population	Minimum $\geq 15\%$ ¹ Achievable $\geq 25\%$ ¹
3.2.2	Coverage by invitation	The eligible population on the register will be invited for screening every two years.	Minimum $\geq 90\%$
3.2.3	Uptake	The numbers of individuals responding to invitations to screening is maximised. Screening promotion efforts are focused on local populations and special "harder to reach" groups and minority communities.	Minimum $\geq 50\%$ Achievable $\geq 60\%$
3.2.4	Coverage by screening	The number of eligible individuals screened in the period (screening round) every two years	Minimum $\geq 45\%$ Achievable $\geq 55\%$
3.2.5	Complaints	All complaints pertaining to the programme will be recorded and responded to within the timeframes set out in the NCCS client feedback process.	HSE Your Service, Your Say
3.2.6	Failsafe	Failsafe measures appropriate to the outcome of each stage of the screening programme will be in place.	Yes

3.3 Population register

A population register – one of the key elements of an effective screening programme – is required to ensure that the eligible population is invited for screening. In order that the population database is complete and accurate, a minimum demographic dataset will be collected and recorded on each eligible client. The population register will maintain details in agreement with the Data Protection Acts 1988 and 2003.

	Criterion	Measurement	Standard
3.3.1	Population registration	Completeness of population register.	Validation within 95% of census figures*
3.3.2	Unique identifier number	Each client registered will have a unique identifier number.	Minimum $\geq 90\%$ Achievable 100%
3.3.3	Matching of client clinical data	Client clinical data details will be matched to the correct client record.	Minimum 100%

3.4 Call, re-call process

	Criterion	Measurement	Standard
3.4.1	Consent process	Consent for screening will be obtained and recorded from the screened population prior to screening taking place.	Minimum 100%
3.4.2	Opt-off process	A process will exist for clients who wish to opt off from screening and should be recorded. Clients will be given information about re-instatement.	Yes
3.4.3	Reminder process	The invited population who do not respond to invitations within eight weeks will be sent at least one reminder.	Minimum $\geq 90\%$ Achievable 100%

* In any defined period of time the number of eligible women listed on the register (numerator) expressed as a percentage of relevant Central Statistics Office (CSO) census data (denominator).

3.5 Screening process

There are a number of key steps in the screening process. The eligible population who respond to the invitation to take part will be offered screening by a test (the FIT test) that is self-administered in their own home.

Approximately 94 to 95 per cent of people screened as part of the programme will receive a normal FIT test result and will be invited for routine screening again in a further two years. (See 3.5.1 to 3.5.6.)

Approximately 5 to 6 per cent of people screened will receive a result that will require a screening programme colonoscopy for which they will be referred to one of the screening colonoscopy units (3.5.7 to 3.5.9).

	Criterion	Measurement	Standard
3.5.1	Test kits despatched to clients	Test kits and instructions will be despatched to clients who request them within five working days.	Minimum $\geq 90\%$ Achievable 100%
3.5.2	Test kits despatched to clients but not received at laboratory	Clients who request and receive test kits will be sent a reminder when the test kit is not received at laboratory within four weeks.	Minimum $\geq 95\%$ Achievable 100%
3.5.3	Positive FIT results to screening colonoscopy units	Positive FIT results will be notified to screening colonoscopy unit within five working days of result being received from laboratory.	Minimum $\geq 90\%$ Achievable 100%
3.5.4	Result letters to clients following test	Result letters following test will be printed and posted within five working days of the date the result is received from laboratory.	Minimum $\geq 90\%$ Achievable 100%
3.5.5	Result letters to clients' general practitioners following test	Result letters following test will be printed and posted within five working days of the date the result is received from laboratory.	Minimum $\geq 90\%$ Achievable $\geq 95\%$
3.5.6	Unacceptable test kits received at laboratory	Repeat test kits will be despatched to clients within 10 working days of when unacceptable test kits are received at laboratory.	Minimum $\geq 90\%$ Achievable $\geq 95\%$
3.5.7	Colonoscopy appointment	Clients will be offered colonoscopy within 4 weeks from when deemed clinically suitable following pre-assessment.	Minimum $\geq 90\%$ Achievable 100%
3.5.8	"No abnormality detected" result letters to clients following colonoscopy	"No abnormality detected" result letters following colonoscopy will be printed and posted within 10 working days of colonoscopy date.	Minimum $\geq 90\%$ Achievable $\geq 95\%$
3.5.9	Result letters to clients' general practitioners following colonoscopy	Result letters following colonoscopy will be printed and posted within 10 working days from date result is received from screening colonoscopy unit.	Minimum $\geq 90\%$ Achievable $\geq 95\%$

3.6 Communications

One of the hallmarks of an effective population-based screening programme is the quality, clarity, availability and access of information for the eligible population, the general population and other stakeholders. Information should be easy to understand, available in a number of formats, relevant and timely.

	Criterion	Measurement	Standard
3.6.1	Standard written communications to individual clients	All standard written communications (letters and information leaflets) from the programme to individual clients will be approved by the NCSS Communications Department and link with National Adult Literacy Association.	Yes
3.6.2	Review of written communications	All written communications will be reviewed on a periodic basis by the NCSS Communications Department.	Yes
3.6.3	Informed consent	All individuals invited for screening will be given standardised information explaining the benefits and risks of screening and the significance of both positive and negative screening test results.	Yes
3.6.4	Information in other formats	Information will be made available in different formats appropriate to the needs of the eligible population.	Yes
3.6.5	Website	Information about the screening programme will be available on a specific site and will be updated regularly.	Yes
3.6.6	Client support	A freephone information line will be available during normal working hours for clients and general enquiries.	Yes
3.6.7	Freephone information line: staff	All staff answering the freephone information line will receive appropriate training.	Yes
3.6.8	Freephone information line: monitoring	The freephone information line will be audited and monitored regularly.	Yes

3.7 Information communications technology

The security of the ICT systems in place to support the screening programme is of paramount importance as personal and health data are collected and stored.

	Criterion	Measurement	Standard
3.7.1	Network	All data will be held in a secure manner.	Evidence of annual network audit
3.7.2	Secure transfer of personal health data	All personal health data transferred between the programme and third-party service providers will use virtual private network (VPN) or secure email systems. All data transferred will be encrypted and subject to file transfer protocols (FTPs).	Yes

3.8 References

1. Hewitson P, Glasziou P, Irwig L, Towler B, Watson E. Screening for colorectal cancer using the faecal occult blood test, Hemoccult. *Cochrane Database Syst Rev* 2007;1:CD001216
<http://www.ncbi.nlm.nih.gov/pubmed/17253456>.

4

Faecal immunochemical test standards

4.1 Faecal immunochemical test standard subgroups

The colorectal screening programme will use the faecal immunochemical test (FIT) to carry out biochemical testing for colorectal cancer. The test is designed to detect faecal occult blood.

FIT standards are grouped into four sections:

- Standards for pre-laboratory processes
- Standards for laboratory organisation
- Standards for the analytical method
- Standards for post-laboratory processes

4.2 Standards for pre-laboratory processes

4.2.1 Faecal sampling/collection system for the client

The design of the collection device/kit should be acceptable to the target population. It should produce reliable sample collection with a reproducible sample size. The kit should include a clear and simple instruction sheet.

The collection device should minimise contact with the sample when being handled by the client or laboratory staff.

4.2.2 Sample identity

The sample identity should unambiguously identify the client by name, barcode and other means (such as health number).

4.2.3 Stability

The stability characteristics for samples collected in the test device should be known and subject to periodic assessment by monitoring population positivity rates and stability checks using agreed methodology. The stability of biological samples stored at 20°C should show no more than 30 per cent loss of analyte within two days of sample collection. No patient samples should be assayed if the time between sample collection and analysis is greater than 10 days.

4.2.4 Transport

The proposed sample should be safe and acceptable for the chosen method of transport and should comply with EU/Irish postal regulations.

4.2.5 Electronic test ordering

Using barcode or similar technology, the laboratory should be able to enter the test order electronically on the laboratory information system.

4.2.6 Interferences

Dietary restriction should not be a requirement for testing.

The proposed method should be free from analytical interference from drugs.

It is noted that biological interference may occur due to gastrointestinal bleeding with drugs such as aspirin, NSAIDs and anticoagulants.

4.3 Standards for laboratory organisation

4.3.1 Laboratory accreditation

The faecal occult blood testing service will be carried out in a clinical laboratory that is accredited to the ISO15189 ("Medical laboratories - Particular requirements for quality and competence") or the CPA standard.

4.3.2 Overall laboratory direction

The service should be led by a consultant chemical pathologist or an appropriately qualified clinical chemist/scientist who is trained and experienced in the techniques used for analysis and clinical quality assurance procedures.

4.3.3 Operational management

A senior member of the scientific staff should be designated to operate the service on a day-to-day basis and should be required to participate in structured appraisal and appropriate continuing professional development schemes.

All staff should receive relevant training in the colorectal screening programme, including induction training and periodic updates. There should be no access to client data (protected by password) until trained. Regular and recorded updates ('top-up' training) should be provided.

4.3.4 Quality manual

The faecal occult blood testing service should be described in a quality manual. The manual should cover all pre-laboratory, intra-laboratory and post-laboratory processes and should be supported by detailed standard operating procedures.

The overall service should be documented in a screening algorithm.

4.4 Standards for the analytical method

4.4.1 Analytical principle

The analytical principle of the method for the determination of blood in stool specimens should be immunochemical.

4.4.2 Method validation

The method should be easy and reliable to undertake. It should be quantitative and should demonstrate adequate analytical sensitivity, specificity and reproducibility.

Be aware that although the analytical method should be quantitative, the measurement by the faecal occult blood test (FOBT) should not be regarded as quantitative because the sampling process lacks rigour.

Before commissioning for routine use, the proposed method should be validated with respect to analytical accuracy, precision, recovery and extent of prozone (hook) effect (if any) to ensure that actual performance is within acceptable limits for these parameters. The validation procedure should be recorded along with the outcome data.

4.4.3 Cut-off point

The laboratory must be able to specify and adjust the concentration at which a positive test is reported. This level will be determined by the National Cancer Screening Service (NCSS).

4.4.4 Automation

The method should be capable of automation on an automated analyser from a reliable commercial provider that can handle the numbers of samples expected in a population-based screening programme.

Results should be authorised for release by a senior member of the scientific staff and subsequently stored on a laboratory information system.

4.4.5 Turnaround time (TAT)

The samples should be analysed without delay to prevent further sample denaturation and an increase in false negative results. An intra-laboratory and whole-process TAT should be specified and agreed with laboratory service providers.

All samples received by the laboratory are tested within two working days of receipt in the laboratory. If a sample is not tested within one day of receipt, it should be stored in the fridge.

4.4.6 Internal quality control (IQC)

The assay should be controlled using readily available internal quality control materials at a number of clinically significant levels including the chosen cut-off point for positivity. Rigorous IQC procedures should be adopted for all analytical batches. Given the difficulty in providing good biological data for quality control/quality assurance (QC/QA), duplicate measurements for a selected few samples should be carried out. Acceptance testing for all products should be carried out as follows:

- Population positivity rates should be monitored regularly (for example, weekly).
- Mean and a dispersion parameter SD (standard deviation) of SEM (standard error of the mean) for the measured Hb concentration should be calculated.
- Measuring and monitoring the CUSUM (or cumulative sum control chart) should be considered.

4.4.7 External quality assurance

The laboratory should be an active participant and demonstrate satisfactory performance in approved clinical chemistry external quality assurance schemes and, when developed, specific EU/international faecal occult blood schemes.

Using secure electronic circulation and review of QA data, the laboratory team should participate in a multidisciplinary QA review that includes the NCSS and other representatives.

4.5 Standards for post-laboratory processes

4.5.1 Reporting

Protocols should be implemented to facilitate rapid, standardised and reliable classification of the test result into negative and positive categories.

The results of all FIT samples tested by the laboratory should be made available to the NCSS within three working days of receipt of the samples in the laboratory.

4.5.2 Electronic reporting

The laboratory should be capable of providing electronic reports in a format agreed with the NCSS.

4.5.3 Clinical advice

Clinical advice should be readily available in the host laboratory.

4.5.4 Technical audit

The proportion of unacceptable tests received for measurement should not exceed 3 per cent of all kits received, and less than 1 per cent is desirable.

Horizontal and vertical audits should be conducted in a manner and frequency compatible with laboratory accreditation or on specific request, including:

- Turnaround time (TAT) – intra-laboratory
- TAT – overall process
- Uptake
- Undelivered mail
- Analytical performance
- Lost and spoilt kits
- Technical failure rate
- Proportion of unacceptable tests
- Patient compliance rate
- Number to “scope” (to find one cancer or one adenoma)

4.5.5 Clinical Audit

Multidisciplinary clinical audits should be conducted on a regular basis. In particular, the following metrics should be monitored in relation to selected cut-off points against agreed targets: clinical sensitivity, specificity, predictive value of a positive and overall clinical efficiency.

5

Endoscopy and radiology standards

5.1 Colonoscopy

Colonoscopy quality standards form a central part of the National Cancer Screening Service (NCSS) colorectal screening programme. The standards described in this section have emerged following detailed critical appraisal of best international practice with particular reference to UK¹ and European guidelines². The Endoscopy and Radiology Quality Assurance subgroup comprised individuals with considerable experience in this area.

Colonoscopy is an invasive procedure and can potentially cause serious and significant adverse events. To optimise the benefit-to-risk ratio of screening, colonoscopy services in Ireland must be delivered to national standards and underpinned by a robust QA framework. The aim is to help ensure that colonoscopy is safe, effective and comfortable and adheres to best practice.

The Paris endoscopic classification³ should be used to describe the gross appearance of lesions. See Appendix 1.

As part of a screening investigation, colonoscopy requires public and professional acceptance to ensure the ongoing success of the screening programme. Quality assurance in colonoscopy is supported through the United Kingdom JAG (Joint Advisory Group on Gastrointestinal (GI) Endoscopy) accreditation process¹. In addition the Royal College of Physicians of Ireland (RCPI) and the Royal College of Surgeons in Ireland (RCSI) are undertaking a National Quality Assurance Programme in Gastrointestinal Endoscopy in collaboration with the Health Service Executive's National Cancer Control Programme (NCCP), the National Cancer Screening Service (NCSS), the HSE Quality and Patient Safety Directorate and the Department of Health. This initiative aims to ensure the provision of a high quality endoscopy service throughout the health service in Ireland.

5.2 Quality indicators

5.2.1 Quality assurance guidelines

Colonoscopy quality assurance guidelines set out:

- The objective to be achieved in each area of activity
- The measure used to evaluate whether that objective is being achieved
- The minimum standard expected of each screening colonoscopy unit (or, for certain standards, each colonoscopist)

It is recognised that there are many reasons why performance might fall below the minimum standard. Where this happens closer monitoring or support may be needed.

The quality standards presented apply to the prevalent screening round only. Quality standards for incident screening rounds will be developed once such data become available. In the interim, incident round quality measures will be reported as auditable outcomes. It is anticipated that the collection and monitoring of data from the colorectal screening programme will help to identify areas for quality improvement and will provide evidence for revising and consolidating future quality standards and key performance indicators.

5.2.2 Minimum number of screening colonoscopies

To support the maintenance of colonoscopists' clinical competence, a minimum number of screening colonoscopies should be undertaken each year^{4,5}.

Quality measure	Minimum number of screening colonoscopies undertaken annually by each screening colonoscopist
Objective	Minimise harm and maximise benefit to screening population
Standard	>300 colonoscopies (symptomatic and screening) per annum >150 screening colonoscopies (Note: this standard will only be auditable after the programme is running at full capacity.)
Accountability	Colonoscopist
Comments	<ul style="list-style-type: none"> • Equates to 1 or 2 lists per week • Supports other key performance indicators

5.2.3 Bowel preparation

Effective bowel preparation is crucial to detailed interrogation of the bowel. Many published data support a variety of regimens with variable tolerability. Good bowel preparation supports improved polyp detection and caecal intubation. Poor bowel preparation is associated with failure to reach the caecum and hinders the detection of lesions^{6,7}.

Quality measure	Bowel cleanliness at colonoscopy
Objective	Maximise pathology detection and minimise need for additional procedures
Standard	Bowel preparation described as excellent or adequate <ul style="list-style-type: none"> • Minimum $\geq 90\%$ • Achievable $\geq 95\%$
Accountability	Screening colonoscopy unit
Comments	<ul style="list-style-type: none"> • Reasons for poor preparation should be documented in patient's care plan. • Bowel preparation definitions: <ul style="list-style-type: none"> Excellent: No or minimal solid stool and only clear fluid requiring suction Adequate: Collections of semi-solid debris that are cleared with washing/suction Complete despite poor prep: Solid or semi-solid debris that cannot be cleared effectively but still permits intubation to caecum Failed due to poor prep: Solid debris that cannot be cleared effectively and prevents intubation to caecum

5.2.4 Response rate (acceptance rate) for colonoscopy

The projected response rate will be 90 per cent of patients with positive FIT test results. Maximising the response for colonoscopy in this cohort will be a core challenge for the programme as a whole. The effectiveness of screening programmes is compromised by low uptake, which makes monitoring and optimising colonoscopy attendance rates a key priority. Each screening colonoscopy unit will be responsible for documenting compliance/non-compliance.

5.2.4.1 Index screening programme colonoscopy

Quality measure	Response rate (acceptance rate) for colonoscopy after positive FIT
Objective	Investigate individuals with positive FIT results
Standard	Percentage of individuals with positive FIT results who undergo colonoscopy: <ul style="list-style-type: none"> • Minimum >85% • Achievable >90%
Accountability	Screening colonoscopy unit

5.2.4.2 Surveillance colonoscopy

Quality measure	Surveillance attendance ⁸
Objective	Optimise attendance for surveillance procedures
Standard	Percentage of individuals scheduled for surveillance colonoscopy who undergo that procedure within 3 months of scheduled date: <ul style="list-style-type: none"> • Minimum >85% • Achievable >90%
Accountability	Screening colonoscopy unit
Comments	<ul style="list-style-type: none"> • Reasons for non-attendance should be recorded. • Clock starts following last complete colonoscopy in previous episode.

5.2.5 Consent for colonoscopy

The process starts after a positive FIT test. The nurse will contact individuals by phone and will co-ordinate the written consent process as part of the colonoscopy pre-assessment process, taking into account:

- Comorbidity (for example, insulin-dependent diabetes mellitus (IDDM), chronic obstructive pulmonary disease (COPD))
- Use of anticoagulants or antiplatelet drugs
- Allergies
- A clear and realistic explanation of the procedure
- Possible discomfort, the risks and benefits and a discussion of potential adverse events
- The possibility of late adverse events and how to seek help
- The right of the patient to withdraw consent at any stage of the colonoscopy process

5.2.6 Sedation

It is essential that colonoscopy is performed to a high standard and is both safe and comfortable. This requires appropriate sedation. All sedation used should be recorded to permit later audit.

Quality measure	Colonoscopic comfort ⁹
Objective	Minimise harm to screening population and optimise patient experience
Standard	Auditable outcome
Accountability	Colonoscopist
Comments	<p>To add objectivity to this scale, the following Modified Gloucester comfort score could be used:</p> <p>No: No discomfort – resting comfortably throughout</p> <p>Minimal: One or two episodes of mild discomfort, well tolerated</p> <p>Mild: More than two episodes of discomfort, adequately tolerated</p> <p>Moderate: Significant discomfort, experienced several times during the procedure</p> <p>Severe: Extreme discomfort, experienced frequently during the procedure</p>

All screening colonoscopy units should conduct rolling audits of sedation practice, patient comfort scores and the use of reversal agents in line with Global Rating Scale (GRS – Ireland) requirements.

5.2.6.1 Medications used

Quality measure	Medication used for comfort during lower GI endoscopy ⁹
Objective	Minimise harm to screening population and optimise patient experience
Standard	Auditable outcome
Accountability	Colonoscopist
Comments	Proportion of all patients undergoing lower GI endoscopy who are receiving: <ul style="list-style-type: none"> • Intravenous sedative/opioid medication • Intravenous propofol (not recommended without anaesthesia cover)

5.2.6.2 Use of reversal agents

Quality measure	Use of reversal agents ⁹
Objective	Minimise harm to screening population and optimise patient experience
Standard	Auditable outcome
Accountability	Colonoscopist
Comments	Proportion of patients who receive intravenous sedative/opioid medication who are then given flumazenil/naloxone reversal agents (respectively)

5.2.7 Caecal intubation rate (CIR)

Complete examination of the colon is a fundamental objective of colonoscopy and a key performance indicator. An unadjusted (intention to scope) figure of 90 per cent or more has been set as the programme standard. This is consistent with the performance standards adopted by the US Multi-Society Task Force on Colorectal Cancer of a 95 per cent completion rate but adjusted for poor bowel preparation and structural lesions^{10,11}. The CIR is a marker of full colonoscopy; when supported by the other performance measures, it contributes to a high-quality patient-centred outcome. Photographic evidence of either the ileo-caecal valve (ICV) or the appendix orifice must be available to support completion colonoscopy.

Quality measure	Caecal intubation rate (CIR)
Objective	To ensure that the entire colon is visualised; marker of quality of colonoscopy
Standard	90% unadjusted CIR with photographic evidence: <ul style="list-style-type: none"> • Minimum $\geq 90\%$ • Achievable $\geq 95\%$
Accountability	Colonoscopist
Comments	<ul style="list-style-type: none"> • Caecal intubation is defined as passage of the scope beyond the ICV into the caecal pole or terminal ileum (passage of scope to anastomosis with small intestine also accepted). • Photographic evidence of appendix orifice and/or ICV and/or terminal ileum and/or anastomosis is required to document complete intubation.

5.2.8 Neoplasia detection rates

5.2.8.1 Cancer detection rate

The principal aim of the NCSS colorectal screening programme is to reduce the number of deaths from bowel cancer by detecting cancer or advanced adenomas at an asymptomatic stage rather than later on at symptomatic presentation. Standards for cancer detection are being set at least ≥ 2 per 1,000 people screened by FIT and at least 11 per 100 screening colonoscopies. Cancer detection rate is probably less accurate than adenoma detection rate as a measure of colonoscopist quality.

Quality measure	Cancer detection rate
Objective	Identification of pathology in patients undergoing screening
Standard	<ul style="list-style-type: none"> • Minimum ≥ 2 per 1,000 screened by FIT/≥ 11 per 100 colonoscopies • Achievable ≥ 5 per 1,000 screened by FIT
Accountability	Screening colonoscopy unit

5.2.8.2 Adenoma detection rate (ADR)

ADR is a robust and key metric for the quality of colonoscopy^{10,12,13,14,15,16,17}. Standards for detection have been set at an ADR of 25 to 35 per cent (based on Tallaght colorectal screening programme) compared with a 25 per cent polyp ADR in men and 15 per cent in women in US screening studies. There are reported differences between endoscopists' rates of small and large adenoma detection. Tandem studies demonstrated a miss rate for advanced adenomas (greater than 1 cm) of up to 6 per cent and as high as 27 per cent in adenomas less than 5 mm in size. In studies that compare CT colonography and optical colonoscopy¹⁴ using segmental un-blinding, a discrepancy of 12 per cent was identified between the two techniques in detecting lesions greater than 1 cm. Withdrawal time clearly influences and informs ADR.

Quality measure	Adenoma detection rate (ADR)
Objective	Identification of polyps, prevention of cancer; marker of quality of colonoscopy
Standard	Histologically confirmed adenomas detected in 25-35% of colonoscopies
Accountability	Colonoscopist
Comments	<ul style="list-style-type: none"> • Surveillance procedures and repeat endoscopic procedures are excluded. • ADR is a more important quality standard than withdrawal time. • ADR standards may need reviewing for incident rounds of screening.

5.2.9 Withdrawal time in negative colonoscopies

In the setting of a negative colonoscopy (no pathology detected), withdrawal time should take a minimum of six minutes. Two large studies have supported withdrawal times of six minutes or longer and demonstrated significant variability in adenoma detection amongst experienced colonoscopists. A linear relationship between withdrawal time and adenoma detection was observed. These studies demonstrate a clear correlation between withdrawal time and the detection of both small and large adenomas. The studies strongly support the concept of withdrawal time as a surrogate marker of the quality of colonoscopy^{13,14,15,16,17}.

Quality measure	Colonoscope withdrawal time
Objective	Maximise pathology detection; marker of colonoscopy quality
Standard	<p>≥6 minutes inspection time on withdrawal from caecal pole to anus</p> <ul style="list-style-type: none"> • Minimum ≥90% of negative procedures • Achievable ≥95% of negative procedures
Accountability	Colonoscopist

5.2.10 Polyp recovery

This standard requires the retrieval of 90 per cent of all excised polyps.

Quality measure	Polyp retrieval rate
Objective	Availability of polyps for histological evaluation
Standard	Retrieval of polypectomy specimens for histological analysis <ul style="list-style-type: none"> • Minimum $\geq 90\%$ • Achievable $\geq 95\%$
Accountability	Colonoscopist
Comments	<ul style="list-style-type: none"> • Denominator = number of polyps excised during lower GI endoscopies • Numerator = number of polyps with histological tissue retrieved for analysis

5.2.10.1 Polypectomy and endoscopic mucosal resection (EMR)

The Endoscopy and Radiology QA subgroup recognises that considerable therapeutic expertise exists within the wider endoscopy community. However, some endoscopists may not wish to provide conventional screening but instead may provide an enhanced therapeutic endoscopic service (tertiary referral). It is recommended that each screening colonoscopy unit has Level 3 EMR expertise to hand^{17,18}. Competencies and training in EMR are being developed in specialised centres, and this expertise needs to be made available nationally as much as possible. Level 4 EMR should only be performed in a designated centre where such expertise is available.

5.2.10.2 Tattooing of suspected malignant polyps

Tattooing is an important technique for locating lesions at surgery and identifying colonic lesions (suspected malignancy) or resection sites at future colonoscopy (repeat therapeutic colonoscopy or incomplete/suspected incomplete removal of lesions). Tattooing sites or lesions with sub-mucosal injection that may require later surgical or endoscopic localisation is recommended^{18,19}.

5.2.11 Cases for discussion at multidisciplinary team meetings

Cases where cancers or medium or high risk adenomas are detected during colonoscopy will be discussed at multidisciplinary team meetings. This may be reviewed at a future date when the actual numbers involved become fully apparent.

5.3 Harm reduction and adverse effects

5.3.1 Adverse events in colonoscopy

The American Society for Gastrointestinal Endoscopy (ASGE) sponsored a workshop to devise a lexicon for adverse events and approved the report²⁰. This lexicon forms the basis of that to be used in the screening programme.

5.3.1.1 Definition

An 'adverse event' is defined as one that prevents completion of the planned procedure (excluding technical failure or poor preparation) and/or results in:

- Admission to hospital or prolongation of existing hospital stay
- Another interventional procedure (endoscopic, radiological or surgical) or
- Subsequent medical consultation

Adverse events may occur prior to the procedure (as a result of bowel preparation, for example), during the procedure and recovery period, or afterwards. Post-procedural events may present within minutes or many days or even years after the procedure (such as a stricture at the site of a previous endoscopic mucosal resection). The post-procedure timescale should be recorded.

5.3.1.2 Attribution of adverse events

It is not always clear if an adverse event relates to the procedure. After root cause analysis by the appropriate QA team, attribution of events should be recorded as definite, probable, possible or unlikely.

5.3.1.3 Capturing adverse events

Consideration should be given to a proactive and robust mechanism for detecting and recording adverse events, especially those that occur after patients leave the unit. More trivial events, called 'incidents' (such as minor bleeding that is adequately controlled during the procedure or intravenous cannula site phlebitis), should also be documented so that quality improvement processes can be applied and to assess if the incidents predict subsequent adverse events. The standards described in this document provide an indication of complication rates and do not capture all adverse events. However, all adverse events should still be recorded and the reporting processes followed.

5.3.2 Colonic perforation

Perforation is defined as evidence of air, luminal contents or instrumentation outside the GI tract²⁰. It may result from direct mechanical trauma to the bowel wall during insertion, over-insufflation of the colon (barotrauma) or therapeutic procedures (hot biopsy, polypectomy, dilatation). Results from a study in the 1970s (25,000 colonoscopies and 1,000 polypectomies) revealed a perforation rate of 0.2 per cent for diagnostic colonoscopy and 0.32 per cent for polypectomy. A study published in 2008 of 97,091 people undergoing colonoscopy aged 50 to 75 years revealed a perforation rate of 0.6 per cent²¹. In one series involving 1,172 patients and 1,555 polypectomies, there was one perforation²². These low adverse event rates must be viewed against a population-based study of Medicare patients aged 65 years or older (39,286 colonoscopies), where the overall perforation risk was 1:500; however, the incidence of perforation in the screening group was 1:1,000. Risk factors identified for perforation were increasing age and diverticulosis²³.

In the British Society of Gastroenterology (BSG) colonoscopy audit, the perforation rate was 1:769. It is clear that widely varying perforation rates have been reported²⁴. The perforation rate in the screening group in the Medicare series (1:1,000) does not translate to the UK screening population in England because of the high polyp burden of faecal occult blood positive patients (more than 35 per cent require polypectomy). Anecdotal experience suggests that the risk of perforation with hot biopsy is high. Perforation is more likely to occur in larger right-sided sessile polyps. Submucosal injection to raise polyps is potentially protective by limiting thermal injury from electrocautery: because most colonic perforation is associated with polypectomy as a result of thermal injury from electrocautery, a clear understanding of technique and equipment is essential. The current standards for perforation will remain under review and amended as performance data accumulate. The risks associated with EMR will become clearer, but for now all therapeutic perforations will be counted.

Note: It is recommended that surgical backup be available on site or within an adjacent unit as per standard of care for symptomatic population.

5.3.2.1 Perforation rate

Quality measure	Perforation rate
Objective	Minimise harm to screening population
Standard	<1 per 1,000 colonoscopies
Accountability	Colonoscopist
Comments	<ul style="list-style-type: none"> • Includes all colonoscopy, whether diagnostic or therapeutic • Perforation rate needs to be interpreted carefully as some colonoscopists will appropriately perform advanced therapeutic procedures (which may carry higher perforation rates).

5.3.2.2 Post-polypectomy perforation rate

Quality measure	Post-polypectomy perforation rate
Objective	Minimise harm to screening population
Standard	<2 per 1,000 colonoscopies where polypectomy is performed
Accountability	Colonoscopist
Comments	Perforation rate needs to be interpreted carefully as some colonoscopists will appropriately perform advanced therapeutic procedures (which may carry higher perforation rates).

5.3.3 Post-polypectomy bleeding (PPB)

Bleeding is the most frequent adverse event following polypectomy. Blended or pure cut diathermy is said to be associated with more immediate bleeding²¹, whereas pure coagulation electrocautery is associated with more delayed bleeding. PPB due to the removal of small polyps is the most frequent cause of bleeding and is usually related to complications of electrocautery. An emerging expert consensus supports the position that small polyps that are not pedunculated should be cold snared, thus preventing the development of late bleeding, which is a complication of electrocautery. Bleeding associated with cold snaring is usually immediate and of no clinical significance. Immediate bleeding allows the endoscopists the opportunity for endoscopic management.

A variety of studies have reported polypectomy bleeding rates of 0.3 to 6.1 per cent^{21, 25, 26}. The risk of bleeding increases with the size of polyp and location, with some series reporting up to 10 per cent bleeding rates for polyps larger than 2 cm located in the right colon. There is evidence that removable snares (endoloops) placed on pedunculated polyp stalks reduce early bleeding. Adrenaline injection into the polyp base may decrease immediate bleeding. While it is not clear if clipping and apposing mucosal defects following polypectomy reduces bleeding, the practice is intuitively appealing.

All colonoscopists should be comfortable with a range of therapeutic interventions aimed at controlling PPB. They should be familiar with the techniques, maintain staff competencies and support ongoing training to ensure seamless application of these therapies. Approximately 90 per cent of PPB should be amenable to conservative management without the need for surgical intervention. However, surgical backup needs to be available on site or within an adjacent unit as per standard of care for symptomatic population.

Quality measure	Post-polypectomy bleeding (PPB) requiring transfusion
Objective	Minimise harm to screening population
Standard*	<1% colonoscopies where polypectomy is performed
Accountability	Colonoscopist
Comments	<ul style="list-style-type: none"> • Includes endoscopic mucosal resection (EMR), endoscopic submucosal dissection and all other polypectomies at colonoscopy • Sub-categorisation of bleeding severity will permit more robust analysis and revision of standards. • Data will be measured up to 30 days post-colonoscopy.

* Individual performance standard

5.3.4 Other adverse events

Adverse events may occur anywhere in the patient journey. The causes are multiple and varied; they include pain, post-polypectomy syndrome, vasovagal events and arrhythmia, all of which may result in unplanned admissions. These events require clear standard documentation, collection of outcomes and discussion at screening colonoscopy unit governance meetings.

Quality measure	Rate of other adverse events
Objective	Minimise harm to screening population
Standard	Auditable outcome
Accountability	Individual colonoscopist and screening colonoscopy unit
Comments	Report should be stratified according to severity (100%).

5.4 Interval cancer

In the first instance, it is recommended that interval symptoms are dealt with within the symptomatic service.

There are three types of interval cancer^{27,28,29,30,31,32,33} – FIT, colonoscopy (non-surveillance) and surveillance.

5.4.1 FIT interval cancer

FIT interval cancer is diagnosed in the two-year interval between a negative FIT and the next proposed FIT. If the patient is 70 years of age (later to be 75 or over), an interval cancer will be defined as a cancer diagnosed within two years of the patient's last screening episode.

5.4.2 Colonoscopy interval cancer (non-surveillance)

Non-surveillance colonoscopy interval cancer is diagnosed in the two-year interval between a negative screening colonoscopy (where colonoscopic surveillance is not required) and the next proposed episode of a standard FIT (if aged under 70; later to be under 75).

5.4.3 Surveillance interval cancer

Surveillance interval cancer is diagnosed in any surveillance interval, whether one year (high risk) or three years (intermediate risk).

Note: Cancers detected at a surveillance colonoscopy are not considered to be interval cancers.

Cancers detected following a negative screening colonoscopy may represent missed lesions and qualitative concerns. However, some cancers may be a facet of aggressive tumour biology. No standard has been set but the goal is to minimise the number of interval cancers. Once monitoring processes have been established, it is anticipated that monitoring interval cancers will become an important component of quality assurance.

5.5 Failure to meet agreed quality standards

A process for dealing with suboptimal performance and mechanisms will be in place for the screening programme.

The local clinical lead/director will be the individual managing compliance with QA guidelines for all colonoscopists and will, in the first instance, address non-compliance issues. Endoscopists who fail to achieve agreed standards after an implementation plan has been agreed will have their practice reviewed by the hospital clinical governance risk committee/endoscopy lead clinician and the NCSS as appropriate.

5.6 Computed tomography colonography

Computed tomography (CT) colonography is widely regarded as the imaging test of choice for total colorectal evaluation and should replace barium enema in this regard. It is, however, a relatively new technique and involves varying local practice with regard to study technique and interpretation. It is widely accepted that the accuracy of CT colonography is heavily dependent on good technique and reader training and expertise. Accepting these factors, clear guidelines as to how the test should be performed and how studies should be read are an absolute requirement for a quality programme. The provision of this service, therefore, requires strict adherence to quality assurance standards and performance monitoring to maximise clinical expertise and best outcomes for patients.

The sections to follow summarise quality standards for CT colonography in the proposed NCSS colorectal screening programme. These guidelines are based on international best practice³⁴, published recommendations from the international CT Colonography Standards document (which was developed through a collaboration of expert groups involved in CT colonography in the UK, Canada, Australia and New Zealand³⁵) and the combined personal experience of over 5,000 CT colonography examinations of the consultant radiologist members of the Endoscopy and Radiology QA subgroup.

5.7 Role of computed tomography colonography in screening programme

In the context of the screening programme, CT colonography should be available as the completion test following an incomplete or unsuccessful colonoscopy and offered to patients for whom a repeat colonoscopy is unlikely to be successful or who are medically unfit for colonoscopy.

5.8 Staffing requirements

5.8.1 Consultant radiologist requirements

Consultant radiologists involved in the provision of CT colonography within the colorectal cancer programme will be required to:

- Assist in establishing the service
- Agree referral and scanning protocols
- Put in place standard operating procedures
- Assist in training ancillary staff
- Supervise examinations
- Address issues of radiation protection
- Interpret and report examinations
- Liaise with consultant radiology colleagues to provide second opinion
- Liaise with endoscopists regarding abnormal or incomplete studies
- Attend and/or prepare weekly colorectal multidisciplinary team meetings
- Attend and/or prepare regular audit and review meetings of CT colonography
- Assist in monitoring key performance indicators and participate in quality assurance activities

The service should be delivered by consultant radiologists who are fully trained in CT colonography performance and interpretation (see 5.8.2).

Specific and protected consultant radiology sessions should be assigned to the provision of this service. CT colonography examinations should be batch read during sessions specifically allocated for this activity and separate to routine CT scan interpretation.

Specific details relating to what is considered safe and achievable in a given consultant radiology session in CT colonography are given in Appendix 2.

Single-person practices are to be avoided. At least two consultant radiologists who are adequately trained in CT colonography will be required per reading centre, and a portion of their sessions should be ring-fenced per week for CT colonography reading as part of the screening programme. This is essential to allow for adequate access to second opinion and to facilitate activities such as internal audits and the review of interval cancers. The total number of sessions required per centre will depend on the total number of centres and volumes per centre.

5.8.2 Training and continuing medical education (CME) requirements

Each consultant radiologist is required to:

- Be on the Irish Register of Medical Specialists
- Hold a Fellowship of the Faculty of Radiologists of the Royal College of Surgeons in Ireland (FFR, RCSI) or equivalent
- Have cross-sectional fellowship training or equivalent
- Have completed at least one accredited CT colonography training course, including the evaluation of 50 CT colonography cases with full colonoscopic correlation or mentored-double-reading of 100 cases with formal tuition and instruction
- Read a minimum of 100 CT colonography cases per year
- Maintain annual CME credits as per RCSI Faculty of Radiologists guidelines
- Take part in regular national audits as well as local colorectal multidisciplinary team (MDT) activities in their hospital³⁶

5.8.3 Evolving guidelines on reader training and interpretation

International guidelines for CT colonography training, interpretation and accreditation have evolved over the past five years and continue to do so. Taking this into account, ongoing review of standards and targets will be required by the national screening programme.

In the event that a diploma in CT colonography interpretation is developed by ESGAR (European Society of Gastrointestinal and Abdominal Radiology) or the ESR (European Society of Radiology), reporting radiologists should comply with the diploma's requirements.

5.8.4 Ongoing assessment of reader performance

The following are recommended as part of a more comprehensive quality assurance programme for reporting radiologists:

- Regular review at each centre of a series of test cases, such as those developed by the Faculty of Radiologists at two-yearly intervals
- Review of CT colonography examinations of patients who are subsequently diagnosed with colorectal cancer (interval cancer review)
- Attendance at multidisciplinary team meetings with endoscopy and pathology services for endoscopic and pathologic correlation of abnormalities reported on CT colonography

Each centre should undergo regular (annual) peer review of 10 randomly selected cases by another centre. Comment will be required on both image quality and interpretation.

5.8.5 Ancillary staffing requirements

For reasons of safety and efficiency, the following requirements will typically apply:

- Radiographers with appropriate training in CT colonography performance will be required in each centre. The number of radiographers required will depend on volumes per centre.
- Nursing support must be available for tagging agent administration and attending to patients if required during data acquisition.
- Secretarial support must be available for data documentation and collation.

5.9 Preparation, scanning and reading protocols

Standard and up-to-date protocols for patient preparation, scanning technique and interpretation are required for a quality screening programme. As CT colonography technology rapidly evolves, these protocols will need to be regularly reviewed and updated.

Details relating to the preparation of patients for CT colonography are given in Appendix 3. These include both full cathartic and stool-tagging regimens.

Image acquisition protocols are listed in Appendix 4. Particular attention must be paid to the use of multislice CT (four or more slices), dual positioning, thin section reconstructions and low dose techniques. Effective doses should be monitored locally and dose modulation should be used where available. Smooth muscle relaxants may be used if required, and the use of IV contrast is not regarded as routine. Colonic distension can be performed manually with room air or by using automated systems for CO₂ delivery (preference for CO₂ with automated delivery).

A workstation with facilities for two-dimensional (2D) and three-dimensional (3D) displays and multiplanar reformations is considered standard for the interpretation of CT colonography examinations. Consideration should be given to computer-assisted diagnosis (CAD) as the technology develops. Double reading is regarded as desirable but may not be feasible; CAD may assist in this regard. Easy access to a second trained consultant radiologist for second opinion is essential.

A standardised reporting system should be used (such as CT Colonography Reporting and Data System (C-RADS) or equivalent), which will require agreement on threshold polyp size for reporting and follow-up and protocols for reporting and work-up of extracolonic findings.

5.10 Access requirements

If at all possible, a same-day or next-day CT colonography is the ideal next step following an incomplete colonoscopy. When same-day imaging is not possible, patients must be scheduled for CT colonography within 30 working days of receipt of referral (see section 5.14.10).

5.11 Patient eligibility for Computed tomography colonography

5.11.1 Patient referral

Patients will be referred for CT colonography in the event of an incomplete colonoscopy following a positive FIT and for whom a repeat colonoscopy is unlikely to be successful.

Patients who have been deemed medically unfit for colonoscopy may be referred directly for CT colonography. Such patients include:

- Those with significant cardiovascular or respiratory comorbidity
- Those deemed to be too frail to undergo laxative preparation but who would tolerate reduced laxative faecal tagging for limited-prep CT colonography (to be considered in centres with expertise in limited-prep CT colonography)
- Those taking warfarin or other anticoagulants (Plavix) that cannot be stopped
- Those with a history of failed colonoscopy

5.11.2 Referral protocols

Clear referral protocols should govern the direct referrals from the screening programme at the point of colonoscopy pre-assessment. Referral rates for CT colonography should be less than 10 per cent of all those referred for colonoscopy following a positive FIT.

Patients who are unlikely to be fit for CT colonography or further intervention such as surgery should not automatically be referred for imaging. Instead, the options should be explained to the patient and appropriate further management decided at this time.

5.12 Patient information and consent

- Written consent for CT colonography should be obtained by a suitably qualified practitioner (such as a physician or nurse) in the screening colonoscopy unit.
- So that they can address patient queries, the physician or nurse who obtains the consent should be fully informed about the risks and benefits of CT colonography.
- Contact details for an experienced CT colonography team member should be made available so that any additional questions that the patient may have can be answered prior to the day of the examination.
- Patient referral forms for CT colonography should include completed information regarding suitability for bowel preparation (such as allergy to iodine).

5.13 Safety, risks and patient experience

5.13.1 Colonic perforation

The most serious adverse effect of CT colonography is colonic perforation, which occurs in 1 in 3,000 CT colonography examinations. This figure is lower in screening populations. The radiologist and adequately trained radiographer performing the examination should review the 2D images before the patient leaves the CT table. If a perforation is detected, the reviewer should contact the appropriate surgical team to request a timely assessment. Staff inserting rectal tubing should have appropriate training regarding anatomy and safe methods of tube insertion. A thin rectal catheter should be utilised for gas insufflations.

5.13.2 Other complications

All members of the CT colonography team must be trained to recognise and deal appropriately with complications arising before, during and after procedures and should follow clearly documented protocols for documenting and managing complications. In addition to colonic perforation, complications can include:

- Severe abdominal pain
- Cardiovascular complications (angina, hypotension and bradycardia)
- Anaphylaxis (to oral iodinated contrast material)
- Glaucoma (related to buscopan use)

A history of allergy to iodine should be sought at the time of referral by an experienced practitioner before prescribing bowel preparation.

After the procedure, patients should be provided with information regarding common minor symptoms that they may experience, including advice on what to do if symptoms persist or worsen. Patients should be advised to seek medical attention if they develop painful blurred vision (possible glaucoma).

5.13.3 Radiation doses

Mindful of both an individual patient's radiation exposure and population radiation doses in a screening programme, low dose techniques must be adhered to. Effective doses should be monitored locally and dose modulation should be used where available.

5.14 Quality assurance in CT colonography

Key performance indicators (KPIs), which may include the following, will be required of each centre:

	Key performance indicator	Standard
5.14.1	Referral rates for CT colonography (amongst all clients) referred for colonoscopy following a positive FIT	≤10%
5.14.2	Completion rates of CT colonography	≥95%
5.14.3	Adequacy of preparation and distension	≥95%
5.14.4	Perforation rate of CT colonography	<1 in 3,000 CT colonography examinations
5.14.5	Other major complication rate	Auditable outcome
5.14.6	Radiation dose	Auditable outcome
5.14.7	Large adenomas (≥10 mm) detected	Auditable outcome
5.14.8	Cancers detected	Auditable outcome
5.14.9	Prevalence of extracolonic lesions that warrant additional investigation	Auditable outcome
5.14.10	CT colonography will be performed on all clients referred from the screening programme within 30 working days of receipt of referral.	Minimum ≥95% Achievable 100%
5.14.11	Turnaround time for report being issued after CT colonography examination being performed	Minimum ≤15 working days Achievable ≤10 working days
5.14.12	Clients in receipt of abnormal CT colonography report with a CRADs classification of C4 (or other equivalent classification) will have follow-up colonoscopy or referred to MDT within 15 working days.	Minimum ≥95% Achievable 100%
5.14.13	Clients in receipt of abnormal CT colonography report with a CRADs classification of C3 (or other equivalent classification) will have follow-up colonoscopy or referred to MDT within 30 working days.	Minimum ≥95% Achievable 100%
5.14.14	Patients with C3 and C4 CT colonography findings who subsequently have biopsy at colonoscopy should be discussed at multidisciplinary team meetings.	Minimum ≥95% Achievable 100%

5.15 RCSI Faculty of Radiologists

The Faculty of Radiologists has developed operational guidance on the use of CT colonography that captures current best practice in the provision of this service and outlines how the service should be structured and delivered by hospitals interested in providing a CT Colonography service as part of the population screening programme. This operational guidance called Guidelines for use of CT Colonography (CTC) as part of the National Colorectal Screening Programme in Ireland³⁷ should be read by service providers in conjunction with this QA document.

5.16 Appendices

Appendix 1: Paris classification³

A newer classification system (the Paris classification) was proposed at a consensus development meeting held in Paris in 2002. Superficial lesions (Type 0) are sub-classified as:

- Polypoid (0-I, subdivided as protruded pedunculated, 0 p, or protruded sessile, 0-I_s)
- Non-polypoid (slightly elevated [0-II_a], flat [II_b], slightly depressed [II_c], and excavated [0-III])

According to the Paris classification, depressed lesions may have invasion into the submucosa even when they are small. Deep invasion should be considered a strong contraindication to EMR: it can be predicted when:

- Lesions are greater than 15mm
- The border of an elevated and depressed (type 0-II_a and II_c) lesion presents as a smooth circle without indentations
- The lesions fail to lift after injection with saline into the submucosa

Appendix 2: Sessional activities for CT colonography

In a typical session designated for CT colonography, it is estimated that a consultant radiologist could:

- Supervise, interpret and report approximately five CT colonography examinations, provide second opinion for complex cases and liaise with gastroenterologists in relation to abnormalities detected

or

- Prepare/attend colorectal multidisciplinary team meetings

or

- Prepare/attend audit meetings

or

- Attend to issues related to quality assurance, radiation protection, protocol review and ancillary staff training

Appendix 3: Patient preparation for CT colonography

The following bowel preparations are regarded as suitable:

- If patients are scanned on the same day as a failed colonoscopy, options include no additional preparation or addition of an oral contrast agent for stool tagging one hour prior to CT.
- If patients are scanned on a day other than the day of the incomplete colonoscopy, a combination of a cathartic agent and tagging agent is recommended.
- In frail and medically unfit patients, a limited preparation approach with purgation may be used if the examination is read by experienced personnel in reduced preparation CT colonography.

Appendix 4: Image acquisition protocols for CT colonography

All scans should be performed using accepted scanning protocols, including:

- Multislice CT (four or more slices)
- Dual positioning
- Thin section reconstructions (collimation less or equal to 3 mm and slice thickness greater or equal to 1.0 mm) with a reconstruction interval of 0.5 to 0.8 (x slice width)
- Low dose techniques (effective doses monitored locally and dose modulation used where available)
- Use of smooth muscle relaxants if required
- Manual colonic distension with room air or (preferably) automated delivery of CO₂.

The use of intravenous (IV) contrast is not regarded as routine.

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6

Histopathology standards

6.1 Pathology

Colorectal cancer screening by faecal occult blood testing has been shown to reduce mortality in randomised trials. Screening programmes aim to routinely achieve a similar level of reduction in mortality in the target population. Pathology plays a very important role in screening because the management of participants in the programme depends on the accuracy and quality of the diagnosis. Pathology impacts on the decision to undergo further local and/or major resection as well as surveillance after screening. The adoption of formal screening programmes leads to improvement not only in the management of early but also advanced disease by the introduction of guidelines, quality standards, external quality assurance and audit. In screening programmes, the performance of individuals and programmes must be assessed, and it is advantageous if common diagnostic standards are developed to ensure quality, recognise areas where sufficient evidence is still lacking and initiate high-quality studies to answer these questions.

This chapter is based on chapter 7 of 'European Guidelines for Quality Assurance in Colorectal Cancer Screening and Diagnosis'¹, which suggests practical guidelines for pathology within a colorectal screening programme. The European guidelines concentrated on the areas of clinical importance in the hope of standardising these across the European Union. Annex 1 deals with some of the more difficult areas and suggests topics for future research. Guidelines for the reporting and management of resected specimens have been included in an attempt to move towards agreed minimum European standards of pathology in these areas. This is the first edition of what will be a continuing process of revision as new data emerge on the pathology, screening and management of colorectal cancer. It is hoped that minimum standards will be set that will be followed in all programmes, and the development of higher standards in the pathology community and screening programmes will be encouraged. 'Reporting Lesions in the National Health Service (NHS) Bowel Screening Programme'² is recommended reading.

Many lesions are found within a screening programme, some of which are of little or no relevance to the aim of lowering the burden of colorectal cancer in the population. The range of pathology differs between the different approaches, with faecal occult blood programmes yielding later, more advanced disease than flexi-sigmoidoscopy and colonoscopy screening. Programme activities must focus on the identification and appropriate management of invasive colorectal cancer and its precursors. The management of pre-invasive lesions involves surveillance to allow the prevention of future disease, whereas the management of adenocarcinoma focuses on immediate treatment and decisions on local removal or radical surgery with the potential for operative mortality. Overuse of radical surgery must be avoided, and recommendations for its use must be balanced with the risks to the patient.

There are a number of lesions, especially in the serrated pathway leading from hyperplastic polyps to other serrated lesions and, in some cases, to adenocarcinoma, which may be difficult to diagnose and for which knowledge of their natural history and clinical implications is limited³. Further work is required in this area, but until there is a greater understanding of these lesions, it is recommended that all serrated lesions, with the exception of hyperplastic polyps, are fully removed. The literature does not contain much data on this issue. This paucity of data is caused in part by a lack of standardisation in terminology. Furthermore, a lack of prospective studies precludes a clear indication of the optimal treatment and surveillance strategy for lesions in the serrated pathway. See Annex 1 for more information. The screening programme will also identify other, non-serrated neoplastic and non-neoplastic lesions, and our knowledge of the optimum treatment of these should increase over time.

6.2 Recommendations for histopathology

- 6.2.1** A modification of the revised Vienna classification is recommended for screening and diagnosis to ensure consistent international communication and comparison of histopathology of biopsies and resection specimens. In the screening programme, the term dysplasia will be used in place of neoplasia. To minimise intraobserver and interobserver error, only two grades of colorectal dysplasia (low grade and high grade) should be used. The terms intra-mucosal adenocarcinoma or in-situ carcinoma should not be used.
- 6.2.2** The WHO (World Health Organisation) definition of colorectal adenocarcinoma should be used: “an invasion of neoplastic cells through the muscularis mucosae into the submucosa”.
- 6.2.3** Adenocarcinomas should be reported according to the TNM classification⁴. The edition of TNM to be used should be agreed by the Faculty of Pathology (currently edition 7) and should be stated as, for example, pT1NoMx (TNM edition 7).
- 6.2.4** The WHO classification of adenomas into tubular, tubulo-villous and villous should be used.
- 6.2.5** Flat lesions and/or depressed lesions should be called non-polypoid lesions and further classified by the Paris classification⁵ if this classification system is used by the endoscopist.
- 6.2.6** Substaging of T1 cancers should be performed to determine the risk of residual disease. Consideration should be given to the appropriate method, which may vary depending on the morphology of the lesion (using Kikuchi⁶/Haggitt⁷ where possible, or measurement). High-risk features for residual or nodal disease, such as margin less than or equal to 1mm, poor differentiation and/or lymphovascular invasion, should be reported. The multidisciplinary team should be consulted on whether or not surgical resection of pT1 adenocarcinomas is recommended; if surgical resection is recommended, a second histopathologic opinion is highly recommended as variation exists in evaluating high-risk features. A panel of gastrointestinal pathologists will be available for second opinion. All cases should be discussed as part of a multidisciplinary team meeting.
- 6.2.7** The size of lesions should be measured by the pathologist to the nearest mm on the haematoxylin and eosin slide or on the fixed specimen when the largest dimension of the lesion cannot be reliably measured on the slide.
- 6.2.8** Hyperplastic polyps are benign and require neither removal (unless greater than or equal to 10mm in diameter) nor surveillance. All other lesions in the serrated pathway should be excised, and serrated lesions with dysplasia should be followed up (surveillance) as if they were adenomas, even though many of these lesions do not contain adenomatous tissue.
- 6.2.9** Dissection of all specimens should be according to national guidelines and reported with a proforma. If national guidelines do not exist, they should be created or adopted from elsewhere.
- 6.2.10** There should be good communication between the members of the screening team, including agreed terminology, regular meetings and clinical discussions.

- 6.2.11** Pathologists must ensure that their proformas are received by the screening programme co-ordinators or a cancer registry for the purposes of clinical management, audit and quality assurance.
- 6.2.12** Pathologists reporting specimens in the screening programme must participate in a national external quality assurance scheme for colorectal screening pathology.
- 6.2.13** Histopathology departments and individual pathologists should audit their own reporting practices for key features and should fulfil nationally set criteria.
- 6.2.14** Pathologists reporting in the screening programme must be registered on the Specialist Register of the Medical Council of Ireland.
- 6.2.15** Histopathology departments and pathologists taking part in the screening programme should audit the number of lymph nodes retrieved, the frequency of circumferential margin involvement (CMI) and the frequency of high-risk features such as extramural vascular invasion and peritoneal invasion reported. In the UK, national standards suggest that the number of nodes retrieved should be above a median of 12 (in non-neoadjuvant treated cases), CMI positivity in rectal cancer below 15 per cent, extramural vascular invasion reported in more than 25 per cent, and peritoneal invasion in greater than 20 per cent. These percentages refer to non-screening cases only. It is recognised that there will be variability in these parameters depending on local prevalence of disease and shifting staging patterns (stage migration as the programme evolves).
- 6.2.16** Pathologists should not report high-grade dysplasia in more than 10 per cent of lesions in a faecal immunochemical test (FIT) programme.
- 6.2.17** Pathologists should attend one refresher training course every year on the pathology of colorectal dysplasia.
- 6.2.18** Laboratories participating in the screening programme must be able to demonstrate participation in a laboratory technical external quality assurance programme and hold external accreditation for their services.
- 6.2.19** All laboratories reporting screening programme pathology should have at least two designated GI pathologists.
- 6.2.20** Any cases where cancers or medium or high risk adenomas are detected during colonoscopy will be discussed at multidisciplinary team meetings. This may be reviewed at a future date when actual numbers involved become fully apparent.

6.3 Histopathology standards

	Criterion	Measurement	Standard
6.3.1	Turnaround time	Histopathology biopsy reports are authorised and relayed to the referrer within five working days of receipt of the specimen in the laboratory.	Minimum $\geq 90\%$ Achievable 100%
6.3.2	Recognised professional standards	Histopathology reporting is consistent with the Faculty of Pathology, RCPI guidelines as applicable to the specimen type being reported and should include a clear indication of the main diagnosis. All specimens should be identified using the unique identifier of the screening participant.	Minimum $\geq 95\%$ Achievable 100%
6.3.3	External quality assurance	Pathologists reporting specimens must participate in a national external quality assurance scheme for colorectal screening pathology.	Minimum 100%
6.3.4	Accreditation	All histopathology laboratories participating in the screening programme must hold or be working towards achieving CPA/INAB* accreditation or equivalent within the agreed time limit and must retain CPA/INAB accreditation. All laboratory procedures must be undertaken in an appropriate laboratory.	Minimum 100%
6.3.5	Accreditation	All histopathology laboratories participating in the screening programme must be active participants in the RCPI national histopathology QA programme.	Minimum 100%
6.3.6	Validation of results	All screening results must be validated by a named screening pathologist.	Minimum 100%
6.3.7	Double reading	There should be double reporting on all specimens where there is a diagnosis of polyp cancer or any uncertainty over the histological diagnosis.	Minimum 100%
6.3.8	Difficult to interpret polyps	There must be a pathway for discussion of polyps or other lesions that are difficult to interpret.	Minimum 100%

* Clinical Pathology Accreditation/Irish National Accreditation Board

	Criterion	Measurement	Standard
6.3.9	Nodes (see 6.2.15 & 6.9)	Number of nodes retrieved (in non-neoadjuvant treated cases)	> median 12
6.3.10	High-grade dysplasia (see 6.2.16 & 6.9)	Percentage of high-grade dysplasia	≤10%
6.3.11	Tumour grade in pT1 lesions (see 6.7.3.2)	Proportion of polyp cancer identified as poor differentiation	≤20%

6.4 Classification of lesions in the adenoma-carcinoma sequence

A colorectal adenoma is defined as a lesion in the colon or rectum containing unequivocal epithelial dysplasia. In the screening programme, the term dysplasia will be used in place of neoplasia. Classification of adenomas should include grading of dysplasia according to the revised Vienna classification, which has been modified for the European guidelines to obtain a two-tiered system of low-grade and high-grade dysplasia (see Table 6.1 and Kudo et al. 2008⁸). This modified grading system aims to minimise intraobserver and interobserver variation and facilitate management of endoscopically detected lesions.

Classically, adenomas are divided into tubular, tubulo-villous or villous types and demarcation between the three is based on the relative proportions of tubular and villous components according to the '20 per cent rule' described in the WHO classification of tumours in the digestive tract⁹. At least 20 per cent of the estimated volume of an adenoma should be villous to be classified as a tubulo-villous adenoma and 80 per cent villous to be defined as a villous adenoma. All other lesions are classified as tubular⁹. The reproducibility of villousness increases when collapsing the categories into only two: tubular versus any villous component. Adenomas can be endoscopically polypoid, flat or depressed. The Paris endoscopic classification⁵ of superficial neoplastic lesions should be used to describe the gross appearance of colorectal adenomas. Key features to be able to report in a programme are size, villousness, the grading of intraepithelial dysplasia, the recognition of invasion and features suggesting the need for further local or radical intervention. While the size of adenomas is important for their risk of containing an adenocarcinoma, it is also related to the need for subsequent surveillance or colonoscopy.

The two-tiered system for grading colorectal dysplasia recommended in the European guidelines (see Table 6.1 and Kudo et al. 2008⁸) is based on the revised Vienna classification, which has substantially improved interobserver and intraobserver reproducibility^{10,11}. The recommended two-tiered grading system also permits translation of histopathologic findings of Western and Japanese pathologists into a uniform system for classification of colorectal neoplastic lesions.

The hyperplastic polyp must be distinguished from other serrated lesions due to its extremely low malignant potential. The significance of other lesions in the serrated spectrum is controversial and our knowledge is still developing; traditional serrated adenomas should be considered as adenomas for the purpose of follow-up (surveillance). More details are provided in Annex 1.

6.4.1 Measurement of size of adenomas

Size is an important objective measurement best performed by the pathologist¹² from the slide, as is recommended in the EU guidelines for breast cancer screening¹³. This method is auditable, accurate and simple to perform. Although the quality of evidence is low, there are some indications that different modalities of advanced adenoma measurement (endoscopic measurement versus pathologist's measurement – before and after fixation, slide preparation) can affect diagnostic reproducibility and the detection rate of advanced adenomas. An overestimation or underestimation of a large or small polyp is more likely to be important when the misjudgement crosses the 1 cm threshold. It seems that the use of the pathologist's measurement would be more accurate. If the lesion is too large for the maximum dimension to be measured by this method because it cannot be represented on a single slide, the measurements taken at the time of specimen dissection should be used. If a biopsy is received or the specimen is fragmented, it should be stated that it cannot be accurately assessed for size by the pathologist and the endoscopy measurements should be used. Measurements should exclude the stalk if it is composed of 'normal mucosa'. However, the distance to the excision margin should be noted. The size of adenomas is used to determine the need for surveillance and therefore must be measured accurately to the nearest millimetre (and not 'rounded up' to the nearest 5 or 10 mm). Where the lesion is mixed or only part of a lesion is adenomatous, measurement should be performed on the adenomatous component.

6.4.2 Grading of villousness

The 20 per cent rule only applies to wholly excised polyps and to intact sections of lesions large enough to provide reliable proportions. For small fragmented lesions or superficial polyp biopsies, the presence of at least one clearly identifiable villus merits classification as "at least tubulo-villous".

6.4.3 Non-polypoid adenomas

The role of the pathologist in the evaluation of non-polypoid adenomas is to confirm the adenomatous nature of the lesion and to determine the grade of dysplasia as well as the depth of depression in the case of a depressed non-polypoid lesion. Since the expression "flat adenoma" is not well defined, it is recommended to group together all adenomatous lesions other than polypoid into the category of "non-polypoid adenomas" and avoid the term 'flat'. According to the Paris classification⁵, non-polypoid adenomas correspond to an endoscopic diagnosis of dysplasia in the subtypes IIa, IIb and IIc. Completely flat adenomas (type IIb) and depressed lesions (type IIc) are rarely found in the colon and rectum, while slightly elevated lesions (type IIa) are frequent. In the literature, the height of non-polypoid adenomas has been described histologically as not exceeding twice the height of normal mucosa, thus measuring less than 3 mm in height. This definition may be difficult to apply due to fixation artefacts or if submucosal injection is employed and in slightly depressed lesions since the adjacent mucosa may be thinner than the normal epithelium. The endoscopic diagnosis of a non-polypoid lesion should be reported according to the Paris classification^{5,8,14}. It was not possible to retrieve studies that specifically address the topic of the differences in the detection rates of non-polypoid colorectal neoplasms among the different types of screening programmes (FOBT vs FS (flexible sigmoidoscopy) vs TC (total colonoscopy)), although a prevalence of 9 to 10 per cent of non-polypoid colorectal neoplasm (flat and depressed) was recently reported by Western pathologists in a large cross-sectional study¹⁴.

Depressed lesions (type IIc) should be mentioned in the histological report for clinico-pathological correlation. Special care should be taken for centrally depressed lesions, particularly when the depression is deeper than half of the adjacent lesion. These are reported to have a higher frequency of high-grade dysplasia and invasion at a smaller size than other flat or depressed lesions⁸. Non-polypoid adenomas can show so-called lateral spread with poor delineation of the margins, thus making endoscopic removal difficult.

6.4.4 Serrated lesions

6.4.4.1 Terminology

Serrated lesions have in common a serrated morphology but, depending on other characteristics, the potential to develop into invasive adenocarcinoma differs considerably. Serrated lesions vary from the hyperplastic polyp, which, although relatively frequent, has no implications for the screening programme unless very numerous or of a large size (greater than 10 mm), to sessile serrated lesions (sometimes referred to as sessile serrated polyps/sessile serrated adenomas), traditional serrated adenomas, or mixed lesions/mixed polyps. Serrated lesions are infrequent, the evidence base is poor and recommendations are not well established. However, until further evidence is forthcoming, the European guidelines offered the recommendations below.

6.4.4.2 Hyperplastic (metaplastic) polyp

Hyperplastic polyps (HPs) are often small lesions (less than 5 mm in diameter) frequently found in the left (distal) colon. They are composed of simple elongated crypts with a serrated structure in the upper half. These polyps usually show some proliferation in the basal (non-serrated) part of the crypts (regular proliferation). Nuclei are small, regular and basally orientated. There is no hyperchromasia, and stratification of the upper half of the crypts has a serrated appearance without cytological atypia. Hyperplastic polyposis should be excluded in cases with giant hyperplastic polyps (more than 10 mm) or hyperplastic polyps in the right colon or in first-degree relatives of individuals with hyperplastic polyposis.

6.4.4.3 Sessile serrated lesions

The use of the term sessile serrated lesion (SSL) is recommended for serrated lesions with structural alterations that do not show intraepithelial dysplasia. This term should replace the use of sessile serrated polyp and sessile serrated adenomas until better definitions are created. It is not recommended to use the latter terms in screening programmes because it would add additional ill-defined categories that may confuse practitioners.

The term sessile serrated polyp has been proposed elsewhere for serrated lesions that cannot be definitely classified into the category of hyperplastic polyps or serrated adenomas³, especially in cases with technical inconsistencies, such as tangential cuts or superficial biopsies. The same terminology has been proposed for lesions with minimal and focal structural alterations in the absence of cytological atypia¹⁵.

6.4.4.4 Traditional serrated adenomas

If the lesion shows a serrated morphology as well as intraepithelial dysplasia (cytological abnormalities), it is considered to be a traditional serrated adenoma (TSA)¹⁶. It should be reported as such (TSA), and treatment and surveillance should be the same as for adenomas. See Annex 1 for details. This pragmatic recommendation recognises the neoplastic nature of these lesions. The non-serrated features found in such lesions (such as size and grade of dysplasia) and characteristics of respective patients (number of neoplastic lesions) should be taken into account when selecting an appropriate surveillance protocol.

6.4.4.5 Mixed polyp

These are lesions with combinations of more than one histopathologic type in the serrated spectrum (hyperplastic polyps, sessile serrated lesions, traditional serrated adenomas) or at least one type in combination with adenoma¹⁷. The important feature to recognise for the screening programme is the presence of dysplasia. The respective histopathologic types in a mixed polyp should be reported, and the term mixed polyp should only be used in brackets after the diagnosis of the histopathologic components (for example, adenoma and hyperplastic polyp, or traditional serrated adenoma plus adenoma). Mixed polyps should be completely removed. If there is an adenomatous component, the lesion should be followed up (surveillance) in the same manner as for adenomas.

6.5 Grading of dysplasia

In the revised Vienna classification, the term neoplasia is used, which is synonymous with the formerly used term dysplasia. As previously mentioned, the screening programme will use the term dysplasia in place of neoplasia.

In relation to the grading of dysplasia, the revised Vienna classification has been adopted, but in a simplified form suitable for screening and diagnosis, by removing the indefinite category between “negative for intraepithelial dysplasia” and “low-grade intraepithelial dysplasia”. This category has no clinical value and, unlike inflammatory bowel disease, is likely to be chosen very infrequently. Excluding it reduces the number of categories and simplifies the subsequent management choices. The advantages of the revised Vienna classification, on which the European classification is based, are that it minimises interobserver variation, encompasses the diagnostic categories used in the Eastern and Western schools and includes a clinical consequence for each level. In the two-tiered classification recommended in the European guidelines, mucosal low-grade dysplasia corresponds to low-grade intraepithelial dysplasia in the revised Vienna classification; likewise, mucosal high-grade dysplasia corresponds to high-grade intraepithelial dysplasia in the revised Vienna classification. Invasive submucosal dysplasia in the European classification corresponds to carcinoma invading the submucosa or beyond (see Table 6.1).

Table 6.1: Modification of revised Vienna classification for colorectal cancer screening

No dysplasia	Category 1 of the original Vienna classification
Mucosal low-grade dysplasia	Category 3; mild and moderate dysplasia; low-grade dysplasia; low-grade intraepithelial dysplasia ⁹
Mucosal high-grade dysplasia	Category 4 and 5.1; severe dysplasia; high-grade dysplasia; high-grade intraepithelial dysplasia; carcinoma in situ; intramucosal carcinoma
Invasive submucosal carcinoma	Category 5.2; carcinoma invading the submucosa or beyond

6.5.1 Low-grade dysplasia

Low-grade dysplasia is an unequivocal intraepithelial neoplastic condition. It should not be mistaken for inflammatory or regenerative changes. Alterations characteristic for low-grade dysplasia start from one gland and develop into a microadenoma, which then grows to become macroscopically visible. Caution should be exercised in patients with chronic inflammatory bowel disease where the diagnosis of a neoplastic sporadic adenoma has different implications to that of dysplasia in colitic mucosa.

6.5.2 High-grade dysplasia

The changes of high-grade dysplasia should involve more than just one or two glands (except in tiny biopsies of polyps) and should therefore be identifiable at low-power examination. Caution should be exercised in over-interpreting isolated surface changes that may be due to trauma, erosion or prolapse.

High-grade dysplasia is diagnosed on architecture, supplemented by an appropriate cytology. Hence its presence is nearly always suspected by the low-power appearances where complex architectural abnormalities are present in structures whose epithelium looks thick, blue, disorganised and "dirty". High-grade dysplasia also contains the subgroup of intramucosal carcinoma used by some pathologists but not recommended here. For details, see Annex 1.

The structural features of high-grade dysplasia are:

- Complex glandular crowding and irregularity. (Note that the word "complex" is important and excludes simple crowding of regular tubules that might result from crushing.)
- Prominent glandular budding
- A cribriform appearance and "back to back" glands
- Prominent intraluminal papillary tufting

While many of these features often coexist in high-grade dysplasia, individually they are neither necessary nor usually sufficient. Indeed, they may occasionally occur in lower grades of dysplasia, which is why it is necessary to go on to scrutinise the cytological features for signs of high-grade dysplasia.

The cytological features of high-grade dysplasia are:

- Loss of cell polarity or nuclear stratification. High-grade dysplasia should show at least two to five nuclear rows and preferably a variable number of rows within individual glands. The nuclei are haphazardly distributed within all three thirds of the height of the epithelium. No maturation of the epithelium is seen towards the luminal surface.
- Neoplastic goblet cells (retronuclear goblet cells)
- Cytology includes vesicular or/and irregular round nuclei with loss of polarity, whereas spindle-like palisading nuclei are a sign of low-grade intraepithelial dysplasia.
- Markedly enlarged nuclei, often with a dispersed chromatin pattern and a prominent nucleolus
- Atypical mitotic figures
- Prominent apoptosis, giving the lesional epithelium a "dirty" appearance

Again, these features usually coexist in high-grade dysplasia, and caution must be exercised in using just one. It should be emphasised again that they should occur in a background of complex structural abnormality. Marked loss of polarity and nuclear stratification sometimes occurs on the surface of small, structurally regular, tubular adenomas that otherwise have a lower grade of dysplasia, probably as a result of trauma, and must not be used to

classify a lesion as high grade. The only exception to the rule is when the specimen consists of just a small biopsy from a polyp, when there is insufficient tissue to assess the architecture properly. In this situation it is permissible to label florid cytological abnormalities alone as high-grade dysplasia, but this will usually lead to re-excision of the whole polyp, when it will be possible to assess the whole lesion properly.

Also included within high-grade dysplasia is the presence of definite invasion into the lamina propria of the mucosa but not invasion through the muscularis mucosae.

6.6 Other lesions

6.6.1 Inflammatory polyps

Experience from the UK faecal occult blood pilot sites has shown that inflammatory-type polyps are relatively common. While they are most usually seen as a complication of chronic inflammatory bowel disease, particularly ulcerative colitis, they are also seen in association with diverticulosis, mucosal prolapse and at the site of ureterosigmoidostomy. Furthermore, sporadic, single inflammatory-type polyps are well described in the colorectum. As the reporting pathologist may not know the true context of such polyps, the European guidelines recommend that all such polyps are classified as "post inflammatory polyp". The term inflammatory pseudopolyp should be avoided. Cases of mucosal prolapse syndrome should be identified and reported as such and not as neoplastic conditions.

6.6.2 Juvenile polyps

Juvenile polyps are spherical in shape, show an excess of lamina propria and have cystically dilated glands. The expanded lamina propria shows oedema and mixed inflammatory cells. Experience from the UK faecal occult blood pilot sites suggests that occasional juvenile-type polyps are identified, even in the screening age group¹⁸. Juvenile polyps are most common in children but occasional examples are seen in adults. The European guidelines advise that any polyp showing juvenile polyp-type features should be classified as "juvenile polyp" for the purposes of diagnostic reporting in a screening programme. Juvenile polyps often show epithelial hyperplasia but dysplasia is very rare. Single sporadic juvenile polyps have a smooth surface and can be found in all age groups and are often eroded. So-called "atypical juvenile polyps" show different morphological features, with a multilobated architecture, intact surface mucosa and (usually) a much more pronounced epithelial component. They are a characteristic feature of juvenile polyposis.

6.6.3 Peutz-Jeghers polyps

While these polyps are usually seen in the Peutz-Jeghers syndrome, occasional examples are demonstrated as single, sporadic polyps in the colon. There remains uncertainty as to whether "inflammatory myoglandular polyp" represents a similar entity. As with juvenile polyposis, it would seem most unlikely, given the rarity of the syndrome and the age of the screening population, that Peutz-Jeghers syndrome would be diagnosed as part of a screening programme. Although Peutz-Jeghers polyps are classified as hamartomas, they have a very organised structure. They have a central core of smooth muscle with conspicuous branching, each branch being covered by colorectal-type mucosa that appears hyperplastic but not neoplastic. As with sporadic juvenile polyps, solitary Peutz-Jeghers-type polyps are most unlikely to demonstrate foci of dysplasia.

6.6.4 Hyperplastic polyposis

This condition is characterised by one or more of the following conditions¹⁹:

- At least five histologically diagnosed serrated polyps proximal to the sigmoid colon, of which two are greater than 10mm
- Any number of serrated polyps occurring proximal to the sigmoid colon in an individual who has a first-degree relative with hyperplastic polyposis
- More than 30 serrated polyps of any size, but distributed throughout the colon

As mentioned in section 6.4.4.2, hyperplastic polyposis should be excluded in cases with giant hyperplastic polyps (more than 10mm) or hyperplastic polyps in the right colon or in first-degree relatives of individuals with hyperplastic polyposis.

6.6.5 Cronkhite-Canada syndrome

It is most unlikely that such cases will present via the screening programme, and the true diagnosis may not be recognised by pathological assessment. However, if Cronkhite-Canada syndrome is suspected, contact the endoscopist and ask for clinical details to ensure the diagnosis.

6.6.6 Carcinoids

It is recommended to use the term endocrine tumour in accordance with the WHO classification. These lesions are usually benign, small and do not give rise to diagnostic difficulty.

6.6.7 Colorectal intramucosal tumours with epithelial 'entrapment' and surface serration

Entrapment and pseudoinvasion of glands into the submucosal layer has to be distinguished from invasive carcinoma. If in doubt, the respective findings should be stated in the written report. If evaluation is problematic, step sections, a second opinion and further biopsies from the polypectomy ulcer should be considered.

6.6.8 Non-epithelial polyps

- Lipoma
- Leiomyoma of the muscularis mucosae
- Ganglioneuroma
- Gastrointestinal schwannoma
- Neurofibroma
- GIST (gastrointestinal stromal tumour)
- Various forms of vascular tumour
- Perineurioma
- Fibroblastic polyp
- Epithelioid nerve sheath tumour
- Inflammatory fibroid polyp

6.7 Assessing invasion of pT1 colorectal cancer

pT1 cancers are those showing invasion through the muscularis mucosae into the submucosa but not into the muscularis propria.

6.7.1 Definition of invasion

The European guidelines recommend the use of the WHO definition^{20,9} of an adenocarcinoma: "An invasion of neoplastic cells through the muscularis mucosae into the submucosa".

The term intramucosal carcinoma should be substituted by mucosal high-grade dysplasia according to the WHO classification and the modified classification of dysplasia recommended in the European guidelines based on the revised Vienna classification (see Table 6.1). The European guidelines recognise that this will not allow detailed comparison with Japanese series where, contrary to the previous US and European literature, a diagnosis of carcinoma can be made on cases of dysplasia without submucosal invasion, or even on the basis of marked intraepithelial atypia. The TNM classification allows carcinoma in situ (Tis), but this does not improve on the revised Vienna classification and should not be used. Please see Annex 1 for details.

Careful consideration should be given to the potential for surgical overtreatment of misclassified early T1 cancers. Screening programmes require explicit criteria for the diagnosis and staging of early adenocarcinoma because unnecessary radical resection will raise the morbidity and mortality in colorectal cancer screening programmes. Refer to Annex 1 for further discussion of this point. Postoperative mortality (within 30 days) varies between 0.6 per cent and 4.4 per cent in T1 cancers and varies depending on the population and quality of services available. Achieving the optimum balance between removing all disease by resection and minimising harm is very important.

6.7.2 Epithelial misplacement

Epithelial misplacement of adenomatous epithelium into the submucosa of a polyp is a well recognised phenomenon²¹. It is commonly seen in prolapsing polyps in the sigmoid colon. Experience suggests that this will be one of the most difficult areas of pathological diagnostic practice in FOBT screening. Sigmoid colonic polyps are particularly prone to inflammation, a feature that tends to enhance the neoplastic changes present. When associated with epithelial misplacement, the potential for misdiagnosis of these lesions as early carcinoma becomes much greater. In cases of epithelial misplacement, surrounding lamina propria and haemosiderin-laden macrophages are found. Submucosal mucinous lakes may be seen. These do not warrant an immediate diagnosis of invasion and must be interpreted in association with the surrounding features.

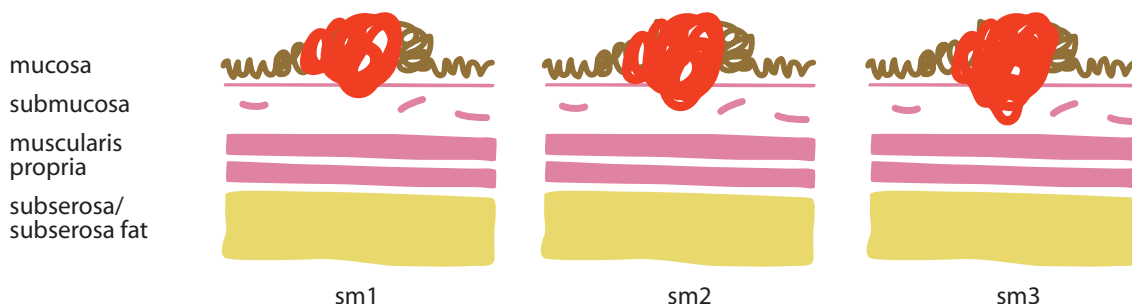
6.7.3 High-risk pT1 adenocarcinoma

pT1 tumours provide many difficulties in a screening programme, and the current evidence base for management of these lesions is poor,^{22,23,24,25}. With regard to the correlation between clinical outcomes and tumour pathologic features (poor grade of histologic differentiation, venous and lymphatic invasion), a clear indication of an increased risk of residual disease, lymph node metastasis, hematogenous metastasis and mortality in poorly differentiated tumours was observed after endoscopic polypectomy and surgical resection. Other pathologic features, such as tumour budding, lymphatic and venous invasion, appeared as possible prognostic factors for increased risk of lymph node metastasis, but a clear guideline cannot be drawn as this correlation was not statistically significant in all studies. The available methods for sub-staging and differentiation grading are addressed below. The most appropriate method depends on the morphology of the lesion (for example, sessile – Kikuchi⁶ and polypoid – Haggitt⁷). It would be preferable to move to more quantitative measurements in the future.

6.7.3.1 Sub-staging pT1

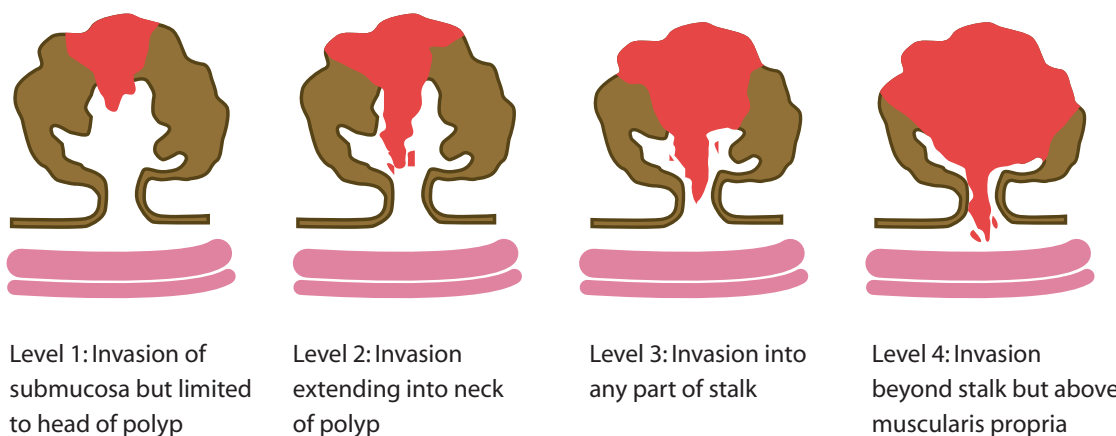
In pT1 tumours, the frequency of lymph node metastasis in tumours that involve the superficial, middle and deep thirds of the submucosa – so-called Kikuchi⁶ levels sm1, sm2 and sm3 (Figure 6.1) – has been reported to be 2 per cent, 8 per cent and 23 per cent, respectively²⁶.

Figure 6.1: Kikuchi levels of submucosal infiltration (from Nascimbeni et al. 2002)²⁶



In polypoid lesions (Figure 6.2), Haggitt⁷ identified the level of invasion into the stalk of the polyp as being important in predicting outcome and found that ‘level 4’ invasion, in which the tumour extended beyond the stalk of the polyp into the submucosa but did not invade the muscularis propria, was an adverse factor.

Figure 6.2: Haggitt levels of invasion in polypoid carcinomas



However, neither the Kikuchi⁶ (for sessile tumours) nor the Haggitt⁷ (for polypoid tumours) system is always easy to use in practice, especially if there is fragmentation or suboptimal orientation of the tissue, and one study found lymph node metastases in 6/24 Haggitt level 3 lesions. More recently, Ueno et al. (2004)²⁷ proposed that the depth (greater than 200 µm) and width (greater than 4,000 µm) of invasion measured in microns beyond the muscularis mucosae provide a more objective measure, and this approach has been adopted in Japan. Each classification has advantages and disadvantages. Kikuchi cannot be used in the absence of muscularis propria; Haggitt is not applicable in sessile lesions, and measurement depends on a recognisable submucosa from which to measure. In view of the uncertainty and lack of consensus, a firm evidence-based recommendation for one method of assessing local invasion cannot yet be made. The European guidelines currently recommend the Kikuchi stage for flat mucosal lesions and Haggitt for polypoid lesions. All three approaches need to be evaluated in further large series from multiple programmes to derive adequately evidence-based recommendations.

6.7.3.2 Tumour grade in pT1 lesions

Poorly differentiated carcinomas are identified by either the presence of irregularly folded, distorted and often small tubules or the lack of any tubular formation. There is usually marked cytological pleomorphism. In the absence of good evidence, the European guidelines recommend that a grade of poor differentiation should be applied in a polyp cancer when any area of the lesion is considered to show poor differentiation. The frequency should not exceed 20 per cent. According to the WHO classification²⁸, budding of the tumour cells at the front of invasion should not influence grading of the tumour. Refer to Annex 1 for details.

6.7.3.3 Lymphovascular invasion in pT1 adenocarcinomas

Definite invasion of endothelium-lined vascular spaces in the submucosa is generally regarded as a significant risk for lymph node or distant metastasis. Sometimes retraction artefact around tumour aggregates can make assessment uncertain, in which case this uncertainty should be recorded and the observation should be interpreted in a multidisciplinary conference in the light of any other adverse histological features. There are currently no consistent data available on the additional use of immunohistochemistry, but this might be helpful in distinguishing retraction artefacts from lymphatic spread (such as LEM D 2-40).

6.7.3.4 Margin involvement in pT1 adenocarcinomas

It is important to record whether the deep (basal) resection margin is involved by invasive tumour (which may be a reason for further surgery) and whether the lateral mucosal resection margin is involved by carcinoma or the pre-existing mucosal dysplasia (in which case a further local excision may be attempted).

There has been considerable discussion and controversy in the literature over what degree of clearance might be regarded as acceptable in tumours that extend close to the deep submucosal margin²⁹. It is important that clearance is measured and recorded in the report. All would agree on 0 mm, most would regard a clearance of less than 1 mm as an indication for further therapy and others would use less than 2 mm. The European guidelines currently recommends that clearance of 1 mm or less indicates margin involvement.

6.7.3.5 Tumour cell budding in pT1 adenocarcinomas

Tumour cell budding – the presence of small islands or single infiltrating tumour cells at the front of tumour invasion – has been described in the Japanese literature as an unfavourable prognostic factor if present in a marked degree^{27,30,31}. Budding has been assessed as slight, moderate or marked; or as present/absent^{32,33}. However, its reproducibility has been criticised, the diagnostic criteria vary³⁴ and the ability to predict metastasis compared to the previously discussed factors is unproven. The European guidelines do not recommend use of this factor at this time. Further research is needed in this area.

6.7.3.6 Site

The site of origin of each specimen should be individually identified by the clinician and provided to the pathologist on the request form. This should preferably be in centimetres from the anus but at the very least the segment of the bowel. The pathologist should record this on the proforma. This is important information as the risk of lymph node metastases from a T1 adenocarcinoma has been reported to vary depending on the site of the lesion³⁵. Immunohistochemistry and special stains are not mandatory but could help to identify lymphovascular invasion in difficult cases. However, the value of these methods has not been studied effectively.

6.8 Specimen handling

Specimen handling is an important issue because poor handling and dissection procedures can impair diagnostic accuracy. Specimen handling starts with the endoscopic removal of the specimen and ends with the histopathological diagnosis and report. The necessity of a close relationship between endoscopy and histology is stressed.

6.8.1 Submission of specimens

It is recommended to place specimens in separate containers, one for each lesion, to avoid confusion about exact location. If lesions are small, individual cassettes or pots can be used. Biopsies from the same lesion can be placed in the same container. For endoscopic resections, it is helpful to pin out specimens by inserting pins through the periphery of the specimen onto cork or thick paper. Too much tension on the specimen could result in artificially thinned lesions. Needles should not be placed directly through a lesion but at the margin. For biopsies, it could be useful to use multi-cassette systems or acetate support to ensure that information on locations can also be given for all biopsies. Besides patient data, an exact description on location should be provided (centimetres from anocutaneous line, for example), as well as size and morphology (stalked polyp, sessile, non-polypoid – Paris classification, etc.). Additional information about central depression or focal erosion or ulceration or coexistent chronic inflammatory bowel disease can be useful. Endoscopic pictures can also be submitted with the specimen(s).

6.8.2 Fixation

Fixation should be by 10 per cent formalin – this equals a roughly 4 per cent paraformaldehyde concentration as formalin is 30-40 per cent paraformaldehyde. It has to be noted that specimen(s) can shrink due to formalin fixation. Biopsies shrink up to 50 per cent. Therefore, measurements taken after fixation can differ from that prior to fixation. Fixation in alcohol is not recommended. If any other fixatives are used, a comparative study of size of adenomas after fixation should be performed prior to use to avoid excessive shrinkage of adenomas (and therefore to avoid undertreatment).

6.8.3 Dissection

The pathologist should verify the complete removal of neoplastic lesions (clear margins) and the absence of submucosal invasion in biopsy specimens. The European guidelines currently recommend that clearance of 1 mm or less indicates margin involvement. Cases of incomplete removal or uncertainty about submucosal invasion should be highlighted in the pathology report. Lesion size should be given in millimetres. Size should be carefully measured to identify the maximum diameter of the adenomatous component as well as the distance to the margin of excision(s) to within a millimetre.

Given the small dimensions of the submucosal layer, infiltration into the submucosal level should be measured in microns from the bottom line of the muscularis mucosae.

6.8.3.1 Polypoid lesions

Polyps need to be sliced and totally embedded. Special caution needs to be paid to the resection margin. Firstly, the resection margin should be identified and described (dot-like, broad, stalked, etc.) and either dissected tangentially into an extra cassette or sliced in a way that allows complete assessment. If the polyp is small, it can be embedded intact and then cut into in the paraffin block. If it is large enough to consider bisection, the two “sides” should be trimmed off and embedded and the “central” portion embedded and subsequently cut into in the block.

6.8.3.2 Mucosal excisions

Mucosal excisions need to be pinned out on a cork board or on another suitable type of material and fixed, described and dissected, allowing the identification of involvement of the deep and lateral surgical margins. Particular attention should be paid to any areas of ulceration or induration for signs of invasion.

6.8.3.3 Piecemeal removal

It may be helpful to reconstruct the lesion but commonly it is not possible to do so. It is good practice to embed the entire lesion to allow exclusion of invasive malignancy. Frequently, whole embedding will not be possible.

6.8.4 Sectioning and levels

Levels should be cut through each block and stained with haematoxylin and eosin.

6.8.5 Surgically removed lesions

6.8.5.1 Classification

The staging of colorectal cancer can be undertaken by a number of different systems. The two used in Europe are TNM and the older Dukes classification. Originally, the Dukes classification system placed patients into one of three categories (stages A, B or C). This system was subsequently modified by dividing stage C into stage C1 and C2 and adding a fourth stage (stage D) – see Table 6.2.

Table 6.2: Modified Dukes stages

Dukes A	Tumour penetrates into, but not through, the muscularis propria (the muscular layer) of the bowel wall.
Dukes B	Tumour penetrates into and through the muscularis propria of the bowel wall but does not involve lymph nodes.
Dukes C	C1: There is pathological evidence of adenocarcinoma in one or more lymph nodes but not the highest node. C2: There is pathological evidence of adenocarcinoma in the lymph node at the high surgical tie.
Stage D	Tumour has spread to other organs (such as the liver, lung or bone).

More recently, the Union Internationale Contra le Cancer and the American Joint Committee on Cancer³⁶ has introduced the TNM⁴ staging system, which places patients into one of four stages (stages I-IV). While TNM is superior to Dukes because of the greater information it yields, there are currently major issues due to the periodic reclassification of this system that can lead to stage migration. Because TNM has a number of editions, the edition used should be noted in brackets (for example, v5, v6, v7).

Table 6.3: TNM classification of tumours of the colon and rectum

T – Primary tumour	Classification
TX	Primary tumour cannot be assessed
T0	No evidence of primary tumour
T1	Tumour invades submucosa
T2	Tumour invades muscularis propria
T3	Tumour invades through muscularis propria into subserosa or into non-peritonealised pericolic or perirectal tissues
T4	Tumour directly invades other organs or structures and/or perforates visceral peritoneum

N – Regional lymph nodes	Classification
NX	Regional lymph nodes cannot be assessed
N0	No regional lymph node metastasis
N1	Metastasis in 1 to 3 regional lymph nodes
N2	Metastasis in 4 or more regional lymph nodes

M – Distant metastasis	Classification
MX	Distant metastasis cannot be assessed
M0	No distant metastasis
M1	Distant metastasis

Stage grouping	Classification
Stage I	pT1T2N0M0
Stage II	pT3T4N0M0
Stage III	Any pT, N1-2, M0
Stage IV	Any pT, any N, M1

The above categories are common to the fifth and sixth versions of the TNM classification³⁷. However, these versions differ regarding the notes on T and N classification. There is variation between countries as to the TNM classification used. For example, TNM 5 is recommended in the UK and Belgium and is growing in popularity in other countries. In the USA, TNM 7 has been used since January 2010. TNM 6 appears to be more subjective than TNM 5 due to the notes on T and N classification and promotes stage migration from II to III^{38,39}. National results should be reported with the version of TNM used in a given country. The Faculty of Pathology, RCPI has recommended adoption of TNM 7; this is supported by the Irish Association of Coloproctology (IACP).

6.8.5.2 Practical issues

Dissection should be according to national guidelines, such as those of the Royal College of Pathologists, UK or Faculty of Pathology, RCPI.

Reporting should be by paper or computer proforma to the referring clinician, the relevant cancer registry and the screening programme for cases diagnosed through such a programme.

High-quality reporting of colorectal cancer is very important both to the clinicians treating the patients and to the Cancer Registry. The introduction of a 'minimum' data proforma template allows for more complete reporting compared with interpretation of free-text reports by medical staff^{40,41,42,43,44,45,46}.

Pathologists need access to a high-quality microscope and a computer for identifying previous material from a given patient and for filling in proformas online, if provided. Adequate time must be available for dissection and reporting and attendance at meetings of the screening team and the colorectal cancer multidisciplinary team. Time and funding is required for pathologists to attend national meetings on the screening programme and continued training in histopathology of colorectal neoplasia. Pathologists need to provide back to the programme comprehensive data on the pathology of the submitted lesions by proforma and also on any subsequently resected specimens.

6.9 Standards and quality indicators

There should be good communication between members of the screening team with agreed terminology, regular meetings and clinical discussions.

An external quality assurance programme of two slide circulations per year of an adequate number of slides should be put in place. This may be via clusters or cells of pathologists using glass slides or can be electronic using either distributed images via DVD or the web (see www.virtualpathology.leeds.ac.uk). There should be external oversight of such programmes. In the absence of evidence-based guidelines, the European guidelines recommend that pathologists reporting in a faecal immunochemical test (FIT) programme should not report high-grade dysplasia in more than 10 per cent of lesions.

The pathologists reporting in the programme must meet their national criteria for safety in reporting colorectal cancer. Departments and pathologists taking part in screening programmes should audit the number of lymph nodes retrieved, the frequency of circumferential margin involvement (CMI) and the frequency of high-risk features such as extramural vascular invasion and peritoneal invasion reported. In the UK, national standards suggest that the number of nodes retrieved should be above a median of 12 (in non-neoadjuvant treated cases), CMI positivity in rectal cancer below 15 per cent, extramural vascular invasion reported in more than 25 per cent and peritoneal invasion in greater than 20 per cent. These latter three percentages apply to non-screening resections only. The laboratory must be able to demonstrate participation in a laboratory technical external quality assurance programme (German Strukturvertrag, for example) and external accreditation by a recognised body (Clinical Pathology Accreditation UK, for example).

Data on lesions removed, both early lesions and subsequently resected carcinomas, should be returned to the screening programme or national tumour registries. This should occur in a minimum of 90 per cent of all cases.

6.10 Data collection and monitoring

Lesions reported in the screening programme should be reported by proforma or structured reporting and the data returned to the screening programme. This will include all lesions identified and the subsequent resection specimen.

Results from the key indicators of quality should be returned to the NCSS for analysis. Statistics should include the size distribution reported, frequency of reporting high-grade and villous lesions, frequency of high-risk lesions, frequency of adenocarcinoma and distribution of TNM stages.

6.11 Annex 1

Adapted from 'Annotations of colorectal lesions in Europe'⁴⁷

6A.1 Introduction

European guidelines for quality assurance in colorectal cancer screening and diagnosis should provide multidisciplinary standards and best practice recommendations which can be implemented routinely across the EU. The authors therefore chose to limit the scope of the histopathology chapter of the European guidelines and to describe in greater detail in an annex some issues raised in the chapter, particularly details of special interest to pathologists. We also felt that an annex would be the appropriate place to point out new insights not yet widely adopted in Europe in routine practice which may be included in future updates of the guidelines.

6A.2 Grading of dysplasia

In the present guidelines, a classification system for grading colorectal dysplasia has been recommended based on a two-tiered, modified version of the revised Vienna classification (section 6A.3). For readers not yet familiar with the Vienna classification, it may be helpful to note that it is the first classification including a clinical recommendation for each neoplastic category. Furthermore, the system was developed to reduce intraobserver and interobserver variation in the diagnostic interpretation of biopsy specimens and subsequent resection specimens^{48,49,50}. Strictly speaking, the Vienna classification is only valid for biopsy specimens since a clinical recommendation should follow. However, to avoid diagnostic inconsistencies, the Vienna classification can be used for resection specimens as well.

In the Vienna classification and hence in the European Guidelines, the term "dysplasia" has been replaced by "(intraepithelial) neoplasia". As previously mentioned, the Irish colorectal screening programme will use the term dysplasia in place of neoplasia. In accordance with the WHO classification, the terms moderate dysplasia and moderate intraepithelial dysplasia are obsolete. The pathologist must decide whether the lesion can be categorized as low or as high-grade intraepithelial dysplasia; for criteria, see Table 6A.1.

As always in dysplasia, the lesion should reach the mucosal surface (no epithelial maturation). Undermining edges of an adjacent carcinoma should be excluded.

The criteria in Table 6A.1 can be weighted. The most important criteria for the diagnosis of carcinoma are the lateral expansion and the number of nuclear rows. In carcinoma, the number of nuclear rows should change within a single gland. High-grade intraepithelial dysplasia is diagnosed when the nuclear rows do not exceed 2-5 nuclei, and the glands do not show lateral expansion. Low-grade intraepithelial dysplasia is diagnosed when the nuclear rows do not exceed 2-3 nuclei^{51,52,53}.

In histopathology, the entity of carcinoma in situ is generally defined as carcinoma confined to the epithelial layer. In squamous epithelium such an entity can be readily diagnosed. In columnar epithelium, an analogous entity should theoretically also exist. However, exact criteria are lacking to date which would permit diagnosis and which would enable the histopathologist to distinguish high-grade intraepithelial dysplasia from mucosal

carcinoma that is invasive in the lamina propria. Therefore, throughout the entire gastrointestinal tract, use of the term "carcinoma in situ" is not recommended for respective lesions in columnar epithelium. The term intramucosal carcinoma is widely introduced in the upper GI-tract but not yet in the lower GI tract (see also section 6A.4.5).

Table 6A.1: Grading of gastrointestinal neoplasia

	Normal	Low-grade intraepithelial dysplasia LGIEN	High-grade intraepithelial dysplasia HGIEN	Invasive Cancer
Glands	non-branching	villous	branching, cribriform, irregular, solid	branching, cribriform, irregular, solid
Expansion	up/down	till surface	till surface	lateral expansion
Epithelial differentiation	up/down	top-down	no maturation towards surface	
Goblet cells	++	(+)	-/(+) retronuclear, dysplastic	
Nuclear rows	1	2-3	2-5	Changing
Nuclear size	small, basal	palisading	enlarged	Vesicular
Chromatin	few	+	++	++ / +++
Nucleoli	none	none	few small	several/prominent

Modified from (Borchard et al. 1991; Borchard 2000; Vieth & Stolte 2005)^{54,55,56}

6A.3 Classification of serrated lesions

6A.3.1 Terminology

The terminology is still under discussion. Serrated lesions can be regarded as a continuous spectrum of colorectal lesions with increasingly more pronounced serrated morphology starting with a hyperplastic polyp, and progressing to sessile serrated lesions (SSLs, sometimes referred to as sessile serrated adenomas or sessile serrated polyps), traditional serrated adenomas (TSA), and leading, finally, to adenocarcinoma. Not only the adenomatous component but also other alterations associated with more pronounced serrated morphology may potentially progress to cancer.

The situation in sessile serrated lesions is complicated since these lesions only reveal complex structural abnormalities, not adenomatous changes. Therefore, these lesions are neither adenomas nor neoplastic. This is why Kudo et al. (2008)⁸ and Lambert et al. (2009)⁵⁷ recommended that these lesions no longer be called adenomas: instead they should be referred to as sessile serrated lesions (SSLs). Few of these lesions are reported to rapidly progress to invasive carcinoma⁵⁸. Those few cases which do progress rapidly, particularly in the right colon, may be expected to appear more frequently as interval cancers. Traditional serrated adenomas (TSAs),

unlike SSLs, do contain adenomatous alterations¹⁶. They are therefore termed correctly and treatment and surveillance should correspond to that of adenomas.

Due to the continuous spectrum in the serrated pathway to colorectal cancer, lesions with combinations of serrated morphology and adenomatous cytology can be observed. If more than one histopathologic type in the serrated spectrum (HP, SSL, TSA) is discernible in a given lesion or at least one type in combination with adenomatous tissue, such lesions are referred to as mixed polyps.

The different histopathologic types (e.g., HP and SSL; SSL and TSA, adenoma and SSL, etc.) must be stated in the diagnosis.

Table 6A.2: Continuous spectrum of serrated lesions and possible combinations of histopathologic types

(Note: Every polyp can give rise to adenocarcinoma. Most of the adenocarcinomas are believed to derive from adenomatous components.)

Lesion	Dysplasia	Risk of malignant transformation
Hyperplastic polyp	No	Minimal
Sessile serrated lesion	No	Slightly increased but exact data are missing (rapid transformation may be possible in a short time)
Traditional serrated adenoma	Yes	Increased and suggested worse prognosis than carcinomas in sessile serrated lesions
Mixed polyp	Yes	Increased, but exact data are not available
Adenoma (tub, vill)	Yes	Increased, 17 years on average

6A.3.2 Hyperplastic polyp

Hyperplastic polyps (HPs) are composed of elongated crypts (no complex architecture) with serrated architecture in the upper half of the crypt. These polyps usually show some proliferation in the basal (non-serrated) part of the crypts (regular proliferation). Nuclei are small, regular, basal orientated, lacking hyperchromasia, but with stratification of the upper (serrated) half of the crypts, and without cytological or structural signs of dysplasia.

Cytoplasmatic differentiation permits recognition of three types:

- Microvesicular type (MVHP)
- Goblet cell rich type (GCHP)
- Mucin poor type (MPHP)

Routine distinction of these types is difficult and subject to wide interobserver variation, especially in small lesions. Exact distinction is not possible in all cases. Sub-classification therefore cannot be recommended at this point. From a molecular point of view the microvesicular variant of HP may be the precursor lesion for sessile serrated lesion, and a goblet-cell-rich HP may be the precursor lesion for a traditional serrated adenoma^{59,60,61}.

6A.3.3 Sessile serrated lesion

Sessile serrated lesions are described in the literature as “sessile serrated adenoma” and often found in the right colon. This is a misnomer since sessile serrated lesions do not contain adenomatous changes^{8,57,62}.

To date, four synonymously used terms exist for these lesions: sessile serrated adenoma⁶³; superficial serrated adenoma⁶⁴, Type 1 serrated adenoma⁶⁵, and serrated polyp with abnormal proliferation⁶¹.

We recommend to use only the term “sessile serrated lesion” and to avoid use of any other terms for this entity. This recommendation is given in full awareness that sessile serrated lesions do not show histological signs of an adenoma, but, like adenomas, they should be excised if detected during an endoscopic examination.

The vast majority of SSLs will not progress to adenocarcinoma. Histological criteria of these sessile, usually larger lesions include an abnormal proliferation zone with structural distortion, usually most pronounced in dilatation of the crypts, particularly near the base. Abundant mucus production is usually also observed as pools of mucin in the lumen of the crypts and on the surface of the mucosa. SSLs are found mainly in the right colon and may be misdiagnosed as hyperplastic polyps. Clues to the correct diagnosis include location and large size. As discussed above, cytological signs of “dysplasia” are lacking, but structural abnormalities are present, i.e., glandular branching⁶².

Sessile serrated lesions have an elevated serration index, serration in the basal half of crypts with basal dilation of crypts (often with mucinous endoscopic appearance) due to parallel maturation towards the surface and the base. The epithelium/stroma-ratio is believed to be >50 per cent in SSL and there is crypt branching with horizontal growth (above muscularis mucosae; e.g., T- and L-shaped glands).

A well-oriented polypectomy is mandatory for the identification of such histological features. Correct assessment of the deepest portions of the mucosa is impossible in superficial or tangentially cut lesions^{59,60}.

Further criteria include an often asymmetrical expansion of the proliferation zone into the middle third of crypts. Often mild cytological atypia (slightly enlarged vesicular nuclei, nucleoli) is found without clear signs of dysplasia (otherwise called neoplasia).

BRAF-Mutations depend on the type and location of lesion (see Table 6A.3).

Table 6A.3: Prevalence of serrated lesions with BRAF Mutation: A prospective study of patients undergoing colonoscopy

Lesion	Number (n=414) (% of all lesions)	Proximal location (% BRAF mutations)	Distal location (% BRAF mutations)
Hyperplastic polyp	120 (29%)	35 (29%)	85 (71%)
Sessile serrated lesion	36 (9%)	27 (75%)	9 (25%)
Trad. serrated adenoma	3 (1%)	2 (66%)	1 (33%)
Mixed polyp	7 (2%)	4 (57%)	3 (43%)
Tubular adenoma	237 (57%)	176 (74%)	61 (26%)
Villous adenoma	11 (3%)	6 (55%)	5 (45%)

Source: modified from (Spring et al. 2006)⁶⁶

In conclusion, abnormalities include:

- Majority of SSL and TSA show CIMP and Promoter-Methylation of hMLH1
 - o CRC: CIMP+ MSI-H
 - o CRC: CIMP+ non-MSI-H
- BRAF mutations in 8-10% of all CRC (27-76% of CIMP and sporadic MSI-H CRC)
- BRAF mutations in the majority of SSL and TSA (also microvesicular variant of HP, especially proximal), but rarely (0-5%) in adenoma^{67,68,69,70,71,72,73,74,75,76,77,78}.

Table 6A.4: Comparison of proliferative activity in adenoma (AD), hyperplastic polyps (HP), sessile serrated lesion (SSL) and traditional serrated adenoma (TSA)

Ki-67	AD	HP	SSL	TSL
Upper 1/3	68.8%	0.1%	1.6%	27.9%
Middle 1/3	48.7%	9.1%	20.3%	30.6%
Lower 1/3	29.6%	60.3%	64.9%	38.2%

Source modified from (Higuchi, Sugihara & Jass 2005; Sheridan et al. 2006)^{79,80}

The frequency of sessile serrated lesions in small retrospective series is estimated at 2-11% of all mucosal lesions in the colon^{81,17}; between 8 and 23% are misdiagnosed as hyperplastic polyps with an interobserver variation of up to 40%^{61,79,82,83}.

The histological features separating HPs from SSLs constitute a continuous spectrum, and intermingled features can often be seen, particularly in small polyps. This could explain the moderate interobserver concordance ($k=0.47$) and the overlapping proliferative activity, and may justify establishing semi-quantitative criteria for diagnosis (e.g.: > 30% of undifferentiated cells)^{84,85}. Only a few immunohistochemical markers (Ki67, Ki67 + CK20, MUC6) have been tested for differentiating HPs and SSAs, and their usefulness in colorectal screening and diagnosis remains to be validated^{86,15}. At the present time, such an additional immunohistochemical analysis cannot be recommended.

In all likelihood, lesions formerly interpreted as “mixed hyperplastic and adenomatous polyp” are, in fact, SSLs complicated by conventional dysplasia⁸⁰. Special care must be taken in such cases to document the respective histopathologic components in such mixed polyps.

Prospective studies with risk stratification are needed to develop more precise methods of diagnosis and recommendations for classification. Sessile serrated lesions appear to take a long time (average 17 years) to develop into an invasive carcinoma. In contrast, an ill-defined, small subsample of SSLs seems to rapidly progress^{58,80}. Therefore, SSLs should be completely excised, particularly if they are located on the right side of the colon^{60,87}.

Bioptic diagnosis is not adequate to exclude SSL since the most severe histologic changes might only appear focally within a lesion which otherwise appears to be a hyperplastic polyp.

The German Guidelines for colorectal cancer⁸⁸ recommend complete removal and follow-up similar to adenomas. An intensive surveillance protocol is recommended for sessile serrated lesions (surveillance colonoscopy after 3-5 years subsequent to complete excision of non-neoplastic SSL, after one year following excision of SSL HGIEN⁸⁸).

Current UK guidelines recommend complete excision but classify these lesions in the same risk category as hyperplastic polyps. The evidence base does not exist to be definitive as to the level of risk, and follow up decisions should be decided locally until more evidence is forthcoming.

6A.3.4 Traditional serrated adenoma

Traditional serrated adenomas show neoplastic crypts with a serrated structure⁹. Compared to hyperplastic polyps, the most striking diagnostic feature of traditional serrated adenomas are the complex serrated morphology and the eosinophil, "dysplastic" cytoplasm that still can be identified in cases with invasive adenocarcinoma. These lesions also frequently show BRAF mutations and CIMP with hMLH1-Promoter-Methylation. Additionally, so-called "intraepithelial microacini" can be observed in the upper half of the mucosa (ectopic crypt formation). Often these lesions are located in the distal colon and can be found more frequently in elderly female individuals^{16,62,15}.

6A.3.5 Mixed polyp

A mixed polyp may contain partially hyperplastic, classical adenomatous or traditional serrated components. Rather than a continuous spectrum such lesions most probably represent several evolutionary lines, depending on the order of certain abnormalities in genes such as APC, BRAF and KRAS^{59,60}.

Focal, hyperplastic-like narrowing of the basal region of a few crypts in SSL and the findings of flat sectors or ectopic crypt formation in SSL/TSA¹⁵ are examples of combinations of serrated and adenomatous components. However, these features add no information of further diagnostic value; they probably result from the continuous developing nature of serrated lesions. We therefore recommend that the diagnosis of mixed polyp should be restricted to the above definition given in section 6A.3.1. Mixed polyps are serrated lesions in which more than one histopathologic type in the serrated spectrum (HP, SSL, TSA) is discernible in a given lesion or at least one type in combination with classical (unserrated) adenomatous tissue. The different histopathological types must be mentioned in the diagnosis, e.g.: mixed polyp (HP and SSL, adenoma and SSL).

6A.3.6 Risk of progression

The vast majority of hyperplastic polyps and serrated lesions will not undergo malignant transformation. Only a fraction, especially in the group of sessile serrated lesions, may progress to rapidly aggressive carcinoma^{66,81}.

Hyperplastic polyps rarely progress to carcinoma. A single case report can be found in the literature⁸⁹ and a second (unpublished) case has been reported in Southern Germany. Interestingly, these carcinomas are of gastric differentiation.

Little evidence is available on which the risk of colorectal cancer associated with serrated lesions other than hyperplastic polyps could be reliably judged. The risk assessment for sessile serrated lesions is not yet defined, but a subset of these lesions appears to give rise to carcinoma often less than a few mm in size. In a series of 110 traditional serrated adenomas, 37% exhibited foci of significant dysplasia and 11 per cent contained areas of intramucosal carcinoma¹⁶. Mixed polyps (e.g., HP/TSA/SSL or HP/adenoma) seem to have at least the same rate of progression to colorectal carcinoma as adenomas, and the risk might be higher^{90,91}.

6A.4 Assessment of T1 adenocarcinoma

Careful assessment in T1 adenocarcinoma is mandatory because a decision is required on local excision versus operation.

6A.4.1 Size

Firstly, accurate measurement is very important, and measurement must be to the nearest mm (and not rounded-up to the nearest 5 or 10 mm). The maximum size of the lesion should be measured from the formalin-fixed macroscopic specimen or from the histological slide. If a biopsy is received then "n/a" should be entered in the size box.

6A.4.2 Tumour grade

Poorly differentiated carcinomas are identified by the presence of either irregularly folded, distorted and often small tubules; or the lack of any tubular formation and showing marked cytological pleomorphism. In the absence of good evidence, we recommend that a grade of poor differentiation should be applied in a pT1 cancer when ANY area of the lesion is considered to show poor differentiation. It has to be noted that this is not in accordance with the WHO classification that recommends a certain proportion of lesion showing poor differentiation before diagnosing a lesion as G3.

6A.4.3 Budding

Budding describes the biological behaviour of the tumour at the front of invasion⁹². Budding or tumour cell dissociation⁹² can be divided into slight, moderate and marked and is known from the Japanese literature of the 1950s⁹³.

At this time, evidence is lacking concerning reproducibility of the numerous methods for tumour budding measurement (see table 6A.5). We recommend it is good practice but not mandatory to document the presence or absence of single tumour cells at the front of invasion and to give this additional information in the written report with an explanatory comment since it has been suggested that budding may be a prognostic factor in colorectal cancer⁹⁴.

Table 6A.5: Measurement of tumour budding

Author	Year	pT	Count	Magnif.	Object.	Area (mm ²)	Classification	Cut-off	Notes
Ueno	2004		H&E		20x	0,785	negative/positive	5	
Ueno	2002		H&E		25x	0,385	<10/>10	10	degree of grading agreement
Ueno	2004		H&E	250	25x	0,385	low (<10)/high (>10)	10	
Shinto	2005		IHC:MNf 116		20x		low (<10)/high (>10) moderate (10-19), severe (>20)		identification of cytoplasmic fragments
Shinto	2006	3	IHC:MNf 116		20x		low (<10)/high (>10) moderate (10-19), severe (>20)		scoring of cytoplasmic fragments called now podia
Okuyama	2002	1 & 2	H&E	n.a.	n.a.	n.a.	present/absent	1	endoscopically resected tumours were excluded
Okuyama	2003	3	H&E	n.a.	n.a.	n.a.	present/absent	1	
Okuyama	2003	3	H&E	n.a.	n.a.	n.a.	present/absent	1	
Prall	2005		IHC:MNf 116	250		0,785	low/high	25	ROC metastatic progression; 0-120 buds range; 14 median 20,46 mean
Kazama	2006	1	IHC: CAM5.2 and AE1/AE3	n.a.	n.a.	n.a.	present/absent	1	
Kanazawa	2007		H&E	n.a.	n.a.	n.a.	none/mild/ moderate/marked		
Nakamura	2008		H&E	n.a.	n.a.	n.a.	None/mild/ = low moderate/ marked=high		
Choi	2007	≥2	H&E		20x		(0-3)/(4-5)/(6-10)/(11-38)		
Park	2005	≥2	H&E		20x		(0-3)/(4-5)/(6-9)/(10-38)		mean intensity: (+/-SD) 6,6+/-5,6
Hori	2005		H&E	200	40x			0,05	5% of the horizontal length of the invasive front
Yasuda	2007		H&E				present/absent		
Ishikawa	2008		IHC:MNfIb	400			negative/positive	5	

Source: modified from (Cooper et al. 1995; Coverlizza et al. 1989; Haggitt et al. 1985; Kikuchi et al. 1995; Konishi & Morson 1982; Nakamura et al. 2008; Nascimbeni et al. 2002; Ueno et al. 2004; Volk et al. 1995)^{95, 22, 7, 6, 96, 94, 26, 27, 25}

6A.4.4 Site

The site of origin of each specimen should be individually identified by the clinician and reported to the pathologist on the histopathology request form. The pathologist should record this on the proforma. This is important information because the risk of lymph node metastasis from a T1 adenocarcinoma varies depending on the site and size of the lesion (rectum versus other locations)⁹⁷.

6A.4.5 Definition of invasion

In columnar epithelium, it is difficult to define the onset of invasive carcinoma and reliably distinguish it from high-grade intraepithelial dysplasia. Criteria such as single tumour cells are more likely to be seen in more advanced carcinomas, but not in early carcinomas. Desmoplastic stromal reactions are also seldom seen in very early carcinomas. However, basal membrane structures are frequently discernible in well-differentiated early carcinomas^{54,55,56}.

The WHO definition of colonic adenocarcinoma does not yet permit diagnosis of intramucosal carcinoma in the colon or rectum, in contrast to the accepted WHO definitions for the stomach, oesophagus and small bowel. All such cases in the colon have to be diagnosed as high-grade intraepithelial dysplasia by definition because according to the WHO classification, a carcinoma in the colon is defined by infiltration of the submucosa. Within the respective WHO working groups there is an ongoing discussion about this definition due to the request of some pathologists to allow intramucosal carcinoma in the colon, also within the next reprint of the WHO classification of gastrointestinal tumours. Pathologists should report on what version of WHO classification and TNM their diagnosis is based.

Concern about potential overtreatment of early T1 carcinomas in a screening programme has been expressed as a reason to exclude the diagnosis of intramucosal colonic carcinoma. This concern may be legitimate, but it is inconsistent with accepted WHO standards and practice in all other locations in the GI-tract. In the latter cases, a decision on surgical versus local therapy is made based on respective protocols.

In those cases in which intramucosal colorectal cancer is suspected, and particularly in countries in which this diagnosis is documented in addition to the WHO terminology, explicit comments by the pathologist are recommended. Based on the cytologic characteristics of the case, the pathologist should indicate whether local or surgical removal is recommended, and the recommendation should be discussed in a multidisciplinary conference prior to operation. The Japanese criteria for such stratification have been published by Watanabe & Suda (1984)⁸⁹. The updated Paris classification based on a workshop in Feb 2008 in Kyoto permits such subclassification⁸ based on improved grouping and explains in detail the grading criteria⁵⁷.

The use of the term colonic carcinoma in situ introduced by the TNM system is inadequate because the criteria are too vague and cannot be used for columnar epithelium.

A subclassification of all carcinomas into low risk and high risk based on risk of lymph node involvement should always be undertaken. For exact criteria, please see the Histopathology chapter and the updated Paris classification^{8,57}.

6A.4.6 Genetic instability

Colorectal carcinomas are believed to develop through several potential pathways: the classical adenoma-carcinoma sequence described by Vogelstein. These tend to show chromosomal instability (CIN). Such tumours have marked structural changes within their DNA showing translocations or numerical chromosomal aberrations. Other pathways that show an increased level of promoter methylation of a number of key genes: the so-called CpG-island methylation pathway (CIMP) exist. Some of these cases may also show the effects of methylation of

the promoter and loss of expression of a key mismatch repair gene hMLH1. This leads to microsatellite instability (MIN) where there is expansion or shortening of repetitive sequences within the genome leading to defective gene function. Such cases tend to be diploid without a high frequency of chromosomal aberrations. Both forms of genetic instability tend to be exclusive.

6A.4.7 Microsatellite-instability – MIN

Besides mutational inactivation, methylation of DNA can lead to gene inactivation. Immuno-histochemically these microsatellite inactivations can be detected through specific reactions against hMLH1, MSH2, MSH6 and PSM2.

In 14 per cent of sporadic colorectal cancer MIN can be detected, and somatic mutations of DNA-repair system are not seen. The most frequent cause for inactivation of the MLH1-gene can be seen in methylation of regulatory DNA-sequences of the MLH1 gene (promoter methylation), e.g. due to somatic BRAF mutation.

The BRAF-protein is part of the signal pathway that transmits the extracellular signal of growth factors via tyrosine-kinase receptors of the epidermal growth factor (EGFR) into the intracellular compartment. Besides BRAF, KRAS is also part of this signalling way. Mutations of BRAF (V600E) and KRAS (Gly12,13,61) can lead to an activation of the signalling pathway independently of growth factor signalling. Tumour cells with oncogenic activation of the signalling cascade cannot be influenced by antibodies against growth factor receptors.

Mutations in the BRAF gene lead to a partial methylation of MLH1-promotor and ca. 50 per cent inactivation of both MLH1 gene copies. Therefore, methylation has nearly the same functional effect than a direct mutation of MLH1-gene copies. This leads to a DNA repair gene defect. This mechanism is a major part of the CIMP-pathway.

Mutations of the KRAS gene also lead to methylational events. Methylation of KRAS seem to lead to a little different consequences since MLH1 is not affected that much compared to BRAF but other genes such as p16, MINT1, MINT2, MINT31. Therefore, slight or no microsatellite instabilities can be detected (MSI-L and MSS).

CpG-islands include between 100-2000 nucleotides with predominantly Cytosine and Guanine (C and G) nucleotides. Within the DNA, these are combined with phosphate ("p") = CpG-island. Quite often these CpG-islands undergo methylation close to or in promoters that activate or inactivate certain genes. Methylation on normal promoters leads to inactivation of genes since contact areas for activating proteins are less accessible. This mechanism underlies the CpG-island methylation pathway (CIMP- CpG- ISLAND METHYLATION PATHWAY, CIMP).


Depending on the degree of methylation within the CIMP-pathway, tumours can be subclassified as CIMP-H (high) and CIMP-L (low) status.

CIMP-H tumours show numerous methylations and often a BRAF-mutation that lead via methylation of MLH1 promotor to a high degree of microsatellite instability. CIMP-L tumours show in 92 per cent a KRAS-mutation. The pattern of methylation is locally more dense than in CIMP-H tumours; in total there are less proteins methylated. Mutation of KRAS does activate the same signal cascade induce via methylation of other genes than MLH1 such as MGMT (Methylguanine-DNA-Methyltransferase: delivers Nucleotides for DNA-Repair), a slight or no microsatellite instability. Within the CIMP-pathway, tumours with MSI-H, MSI-L and MSS need to be differentiated.

6.12 Appendices

Appendix 1: Faculty of Pathology, Royal College of Physicians of Ireland Dataset for Colorectal Cancer

Available at <http://www.rcpi.ie/Faculties/Pages/FacultyofPathology.aspx>. (Adapted from Royal College of Pathologists Dataset for Colorectal Cancer⁹⁸)

	FACULTY OF PATHOLOGY <small>ROYAL COLLEGE OF PHYSICIANS OF IRELAND</small>	Colorectal Dataset	Revision: 1
		Date:	
		Author:	

REPORTING TEMPLATE FOR COLORECTAL CANCER REPORTS

Surname: Forenames: Date of Birth:

Sex: Case ID: Hospital:

Pathologist: Surgeon:

Instructions: If completing form by hand, fill in blank spaces & circle required text as appropriate. If completing form online, fill in blank spaces & delete non-required text as appropriate. Optional data fields are denoted with C, all other data fields are required.

Specimen type: Total colectomy / Right hemicolectomy / Left hemicolectomy / Sigmoid colectomy / Anterior resection / Abdominoperineal excision / Other (specify)

Macroscopy:

Site of tumour: Maximum tumour diameter:mm

Distance of tumour to nearer cut endmm Tumour perforation (pT4): Yes / No

If yes, perforation is: serosal / retro / infra peritoneal

For rectal tumours,
 relation of tumour to peritoneal reflection: Above / Astride / Below

Plane of surgical excision: Mesorectal fascia / Intramesorectal / Muscularis propria

For abdominoperineal resection specimens: Distance of tumour from dentate line:mm

Microscopy

Histology:

Type: Adenocarcinoma: Yes / No If No, specify type:

Differentiation by predominant area: Well / Moderate / Poor

Local Invasion:	No carcinoma identified (pT0):	Yes / No
	Submucosa (pT1):	Yes / No
	Muscularis propria (pT2):	Yes / No
	Beyond muscularis propria (pT3):	Yes / No
	Perforates visceral peritoneum (pT4a) :	Yes / No
	Directly invades other organs or structures (pT4b):	Yes / No

Maximum distance of spread beyond muscularis propria:mm

Neoadjuvant therapy given: Yes / No

If Yes, circle as appropriate

No residual tumour cells, mucus lakes only (TRG 1)

Minimal residual tumour/fibrosis outgrows tumour (TRG 2)

No marked regression/tumour outgrows fibrosis (TRG 3)

Tumour involvement of margins:

Doughnuts: Yes / No / Not Applicable Margin (cut end): Yes / No / Not Applicable

Non-peritonealised 'circumferential' margin: Yes / No / Not Applicable

Histological measurement from tumour to non-peritonealised margin: mm



Colorectal Dataset	Revision: 1
Date:	
Author:	

METASTATIC SPREAD

No of lymph nodes present:

No of involved lymph nodes:	Metastasis in 1 regional LN (N1a):	Yes / No
	Metastasis in 2-3 regional LNs (N1b):	Yes / No
	Tumour deposit(s), i.e., satellites, in the subserosa, or in non-peritonealised pericolic or perirectal soft tissue without lymph node metastasis (N1c):	Yes / No
	Metastasis in 4-6 regional LNs (N2a):	Yes / No
	Metastasis in 7 or more regional LNs: (N2b)	Yes / No
	Extramural venous invasion:	Yes / No
Distant metastases:	No distant metastases:	Yes / No
	Microscopically confirmed metastases confined to one organ (M1a):	Yes / No
	Microscopically confirmed metastases in more than one organ or the peritoneum (M1b):	Yes / No

Background abnormalities: Yes / No

If yes: No of Adenomas:

Type of Adenoma (circle appropriate):

Familial adenomatous polyposis / Ulcerative colitis/ Crohn's disease / Diverticulosis / Synchronous carcinoma(s) (complete a separate form for each cancer) / Other:

Pathological Staging:

Complete resection at all surgical margins:	Yes (R0) / No (R1 or R2)
UICC, TNM Classification 7th Edition:	pT N..... M..... (Delete pM if unknown) (y for neoadjuvant cases)

Dukes Stage:

Signature:	Date:	SNOMED codes: T	M
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FACULTY OF PATHOLOGY
ROYAL COLLEGE OF PHYSICIANS OF IRELAND

Colorectal Dataset	Revision: 1
Date:	
Author:	

REPORTING TEMPLATE FOR LOCAL EXCISION SPECIMENS

Surname: Forenames: Date of Birth:
 Sex: Case ID: Hospital:
 Pathologist: Surgeon:

Instructions: If completing form by hand, fill in blank spaces & circle required text as appropriate. If completing form online, fill in blank spaces & delete non-required text as appropriate. Optional data fields are denoted with ¢, all other data fields are required.

Specimen type:

Polypectomy /Endoscopic mucosal resection /Transanal endoscopic microsurgical (TEM) excision / Other

Comments:

Macroscopy:

Site of tumour: Maximum tumour diameter (if known):mm

Microscopy

Histology:

Type: Adenocarcinoma: Yes / No If No, specify type:

Differentiation: Well / Moderate / Poor

Local Invasion:	No carcinoma identified (pT0):	Yes / No
	Submucosa (pT1):	Yes / No
	Muscularis propria (pT2):	Yes / No
	Beyond muscularis propria (pT3):	Yes / No
	Perforates visceral peritoneum (pT4a) :	Yes / No
	Directly invades other organs or structures (pT4b):	Yes / No

For pT1 tumours, Maximum thickness of invasive tumour from muscularis mucosa mm

Haggitt level (polypoid tumours): 1 / 2 / 3 / 4	Kikuchi level (for sessile/flat tumours): sm1 / sm2 / sm3
Lymphatic or vascular invasion:	None / Possible / Definite
Background adenoma:	Yes / No

Margins (circle as appropriate): Not involved / Involved by adenoma only / Deep margin involved by carcinoma / Peripheral margin involved by carcinoma

Histological measurement from carcinoma to nearest deep excision margin: mm

Pathological Staging:

Complete resection at all surgical margins:	Yes (R0) / No (R1 or R2)
UICC, TNM Classification 7th Edition:	pT N M (Delete pM if unknown) (y for neoadjuvant cases)

Signature: _____ Date: _____ SNOMED codes: T _____ M _____



FACULTY OF PATHOLOGY
ROYAL COLLEGE OF PHYSICIANS OF IRELAND

Colorectal Dataset	Revision: 1
Date:	
Author: Colorectal Pathology subgroup	

REPORTING TEMPLATE FOR BIOPSY/ POLYPECTOMY SPECIMENS

Surname: Forenames: Date of Birth:
 Gender: Lab No: Hospital & MRN:
 Pathologist: Clinician: Programme ID:

Specimen type:

Biopsy/ Polypectomy /Endoscopic mucosal resection /Other

Comments: This may include description at endoscopy.....

Macroscopy:

Site of lesion:

Free text: description of tissue received.

Microscopy

Mucosal site:

Polyp type: adenoma/sessile serrated lesion/hyperplastic polyp/other

Architecture (for adenomas): tubular / tubulovillous / villous/ traditional serrated

Dysplasia grade (for adenomas): low / high

Evidence of invasion:

Size: mm.

Excision: Complete/incomplete/not assessable

Note: Multiple polyps require separate reporting



Colorectal Dataset	Revision: 1
Date:	
Author:	

HANDLING AND CUT-UP GUIDELINES

Please refer to Royal College of Pathologists Dataset for Colorectal Cancer (2nd Edition) for assistance in completing the above dataset. This document presents recommendations on specimen handling, notes on macroscopic and microscopic assessment, pathological staging and reporting. The Faculty Colorectal Cancer review group has advised the use of the 7th edition TNM; therefore the current dataset has been updated to reflect these changes.

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7

Surgery standards

7.1 Management of screen-detected colorectal cancer

The management of screen-detected colon and rectal cancer is not materially different from that of the management of symptomatic disease. In May 2008, at the request of Professor Tom Keane (the then Director of the National Cancer Control Programme), the Irish Association of Coloproctology (IACP) established a working group to develop a common framework for the management of patients with colorectal cancer. This framework has been published as 'Recommendations for the Future Development of Colorectal Cancer Surgery in Ireland and Guidelines for the Management of Rectal Cancer in Ireland'¹.

The standards to follow are based on this framework and on evidence-based international guidelines^{2,3}.

7.2 Colon cancer

There is increasing evidence that outcomes after surgery for colon cancer are dependent on the degree of specialisation and experience of the surgeon⁴. In that context, together with the multidisciplinary components of care required, it would seem appropriate that screen-detected cancers should be managed in designated cancer centres in Ireland.

Colon cancer surgery should be performed in designated cancer centres within defined timeframes, as follows:

	Criterion	Measurement	Standard
7.2.1	Referral to surgeon	All patients will be referred to a surgeon at a designated cancer centre within 10 working days of the histological diagnosis.	Minimum $\geq 90\%$ Achievable 100%
7.2.2	Offered admission date for surgery	All patients will be offered an admission date for surgery within 20 working days of the histological diagnosis.	Minimum $\geq 90\%$ Achievable 100%
7.2.3	Appropriate specialist hospital	Minimum number of colon cancer resections per surgeon per annum	≥ 20

7.2.4 Pre-operative staging

Once the diagnosis of colon cancer has been made at colonic screening, the whole colon must be visualised for second primaries or adenomas. Synchronous cancers will occur in 5 per cent, and adenomas will require removal. Appropriate evaluation of the entire colon is required if colonoscopy is not possible.

Screening for metastatic disease is required using CT of the chest, abdomen and pelvis. This should be carried out on site at the designated cancer centre.

7.2.5 Colon cancer surgery

The quality of surgery for screen-detected cancers is central to the outcome: safe high-quality surgery is essential.

All cases should be discussed at a multidisciplinary team meeting both prior to and after surgery (see Appendix 4 of the IACP framework¹). The meeting should be attended by a named surgeon working within a team, a colorectal nurse and, where appropriate, a stoma therapist. The designated cancer centre will collect a minimum data set of information and will follow the IACP framework (see Appendix 1). The designated cancer centre providing the surgery will also take part in the audit of the Association of Coloproctology of Great Britain and Ireland (ACPGBI).

While the exact colon resection performed will depend on the anatomical location of the tumours, the most common operations will be a right hemicolectomy for tumours in the caecum and ascending colon, an extended right hemicolectomy for tumours in the transverse colon up to the splenic flexure, a left hemicolectomy for tumours between the splenic flexure and the sigmoid colon and a sigmoid colectomy or high anterior resection for tumours in the sigmoid colon.

There is accumulating evidence that radical surgery is associated with a better long-term outcome^{5,6}, and all these operations should be carried out with a full lymphadenectomy, with flush ligation of the feeding vessels at the superior mesenteric artery or aorta. A complete mesocolic resection/excision should be performed.

Centres providing surgery for screen-detected colon cancers should be able to offer laparoscopic surgery to appropriate patients. Surgeons providing laparoscopic surgery for such cancers should have undergone appropriate training in these techniques and should provide surgery with the same oncological principles as outlined above⁷. Laparoscopic surgery can offer better short-term results in well-selected patients. The colonoscopist and surgeon should ensure that malignant polyps and small or soft tumours are tattooed to enable identification at surgery, on-table endoscopy and in the histopathology laboratory. Bowel preparation should be considered for those lesions that may require on-table endoscopy.

7.3 Rectal cancer

Rectal cancers are those tumours where the lower margin is 15 cm or less from the dentate line.

Rectal cancer surgery should only be performed in designated cancer centres provided they meet the criteria laid down by the IACP¹. Rectal cancer surgery should not be performed by individuals performing fewer than 20 rectal resections per annum.

	Criterion	Measurement	Standard
7.3.1	Referral to surgeon	All patients will be referred to a surgeon at a designated cancer centre within 10 working days of the histological diagnosis.	Minimum $\geq 90\%$ Achievable 100%
7.3.2	Offered admission date for surgery	Where surgery is primary treatment, all patients will be offered an admission date for surgery within 20 working days of the histological diagnosis.	Minimum $\geq 90\%$ Achievable 100%
7.3.3	Appropriate specialist hospital	Minimum number of rectal resections per surgeon per annum	≥ 20

The management of small rectal cancers is very relevant to screen-detected lesions and requires special consideration. Multidisciplinary team (MDT) review before and after surgery is mandatory with screen-detected rectal cancers.

7.3.4 Pre-operative staging

Accurate determination of the position of a rectal cancer is a critical step in selecting an appropriate operative strategy. Every patient with rectal cancer should have a rigid sigmoidoscopy performed by a consultant colorectal surgeon to measure the distance of the tumour from the anal verge prior to any therapeutic intervention. This distance should be clearly recorded to the nearest centimetre and the circumferential orientation noted.

High-resolution MRI scanning should be undertaken to assess pelvic and mesorectal nodal involvement and the proximity of the tumour to the circumferential resection margin. Rectal endo-sonography is particularly valuable in early tumours and where local excision is being considered. These investigations should be performed at the designated rectal cancer specialist centre for quality assurance and audit purposes. This will enable the development of specialist radiologic expertise and will facilitate the personal involvement of the consultant radiologist in the pre-operative MDT meeting, where the treatment strategy will be agreed.

Pre-operative staging with CT scanning of the thorax, abdomen and pelvis should be routine practice. PET scanning may be required for patients with indeterminate lesions or atypical primary rectal cancer as well as those requiring extensive "en bloc" resections, such as sacrectomy or pelvic extenteration.

7.3.5 Neoadjuvant therapy

	Criterion	Measurement	Standard
7.3.5.1	Initiation of neoadjuvant therapy	Where surgery is not initial treatment, all patients' neoadjuvant therapy will be initiated within 30 working days of the histological diagnosis.	Minimum $\geq 90\%$ Achievable 100%

Local recurrence of rectal cancer is reduced by adjuvant chemoradiotherapy, which, when given pre-operatively, is superior to post-operative treatment⁸. All cases of rectal cancer should be considered for pre-operative radiotherapy, plus or minus concomitant chemotherapy. The appropriate therapy may well vary with the staging of the tumour and the age and fitness of the patient.

7.3.6 Rectal cancer surgery

Appropriate patient selection, consent and preparation for surgery are paramount. Patients with rectal cancer undergoing elective surgery should receive pre-operative counselling from a stoma nurse specialist, and the stoma site should be marked. The risks attached to operative treatment include, but are not limited to, bleeding, infection, deep vein thrombosis (DVT) and pulmonary embolism (PE). In addition, the risk of an unplanned stoma, urinary or sexual dysfunction should be discussed. Functional outcome should form part of the general discussion about the outcomes of treatment. It may be appropriate to discuss mortality risk, and validated risk models are available to counsel patients requiring this level of information.

A blood type and screen should be performed on every patient undergoing rectal cancer surgery; cross-matching is essential when extensive surgery is planned. Bowel preparation may be used in some cases. Patients undergoing surgery for rectal cancer have an increased risk of DVT and PE, and prophylactic measures should be employed. All patients undergoing surgery for colorectal cancer should have antibiotic prophylaxis before incision in accordance with hospital guidelines. With modern antibiotic prophylaxis, the rates of wound infection (presence of wound discharge with positive microbiology) following elective rectal cancer surgery should be less than 10 per cent. Designated rectal cancer centres should establish locally relevant enhanced recovery programmes.

It is essential that surgeons treating rectal cancer are trained and experienced in all relevant operative techniques and that they perform enough operations annually to maintain their expertise, work in a team with other colorectal surgeons and participate in audit and continuing medical education (CME) activities.

Whether the operation is open or laparoscopic, the aim of surgery is a negative circumferential resection margin and complete excision of potentially involved lymph nodes. It is recommended that total mesorectal excision should be performed for tumours in the lower two-thirds of the rectum, either as part of low anterior resection or an abdomino-perineal excision (APR). In tumours of the upper rectum, the mesorectum should be divided no less than 5 cm below the lower margin of the tumour. When this is done, care must be taken to preserve the autonomic nerves and plexuses on which sexual potency and bladder function depend. Perforation of the tumour during resection is associated with local recurrence, and its occurrence should be documented in the operation note.

	Criterion	Measurement	Standard
7.3.6.1	APR	Overall proportion of resectable rectal cancer treated by APR	Minimum <30% Achievable <25%

APR should be avoided where possible in favour of anterior resection but it is necessary in certain low rectal cancers, especially where the sphincter is involved or where an insufficient distal resection margin exists. It is recommended that the overall proportion of resectable rectal cancer treated by APR should be between 25 and 30 per cent. Particular care is required to ensure clear margins in these cases, and cylindrical, extra-levator excision should be considered⁵. The colorectal surgeon should indicate on the operation record whether the operation is intended to be curative or not. If residual tumour is thought to remain, it should be biopsied if possible.

Pathology plays a key role in quality assurance of rectal cancer surgery, and for this reason the provision of a high-quality pathology service in every rectal cancer centre is mandatory. Margin positivity and tumour perforation should be audited. The Royal College of Pathologists Dataset for Colorectal Cancer⁹ provides detailed guidelines for pathologists. The term curative resection should be based on surgical and histological confirmation of complete excision. Every rectal cancer histopathology report should contain the agreed rectal cancer minimum dataset. Surgeons should expect to achieve an overall curative resection rate of 60 per cent, but this will depend at least in part on the stage at which patients present.

	Criterion	Measurement	Standard
7.3.6.2	Leak rate	Audit each surgeon's leak rate.	Minimum <8% Achievable <5%

The ACPGBI recommends that surgeons should audit their leak rate, which should be less than eight per cent³. Anastomotic leakage is associated with poorer survival and a significant increase in the local recurrence rate. There is evidence that a defunctioning stoma can ameliorate the consequences of leakage, decreasing the risk of death and need for a permanent stoma. Post-operative function should be considered in choosing the mode of anastomosis, and rectal cancer surgeons must be familiar with techniques such as colonic J-pouch, coloplasty and side-to-end anastomosis. The use of cytotoxic washout prior to anastomosis is generally accepted as a sensible precaution. Irrespective of the type of surgery, operation notes should follow standard hospital protocols and should contain the agreed minimum dataset¹.

7.3.7 Management of small rectal cancers

A major effect of the screening programme is to increase the number of small primary cancers detected, and because the rectum can be accessed transanally, this occasionally opens up the possibility of local excision for small primary tumours and rectal adenomas. This can be done using a standard bivalve retractor or, for tumours in the mid and upper rectum, transanal microsurgery (TEMS)¹⁰. Rectal cancers discussed at the MDT and deemed appropriate for TEMS should be managed in a smaller number of centres to allow for the development of sub-specialised skills and audit.

pT1 (sm1) rectal cancers may occasionally be safely treated by local excision. Careful studies of these pT1 tumours have shown that by radiological and then by further histological subdivision, selection of those sm1 lesions that are curable by local excision alone is possible. However, pT1 (sm3) and pT2 tumours are more likely to have lymph node involvement and to develop local recurrence without further treatment and are not suitable for local excision¹¹. While pre-operative chemoradiation may modify this, further trials are required. Radical rectal excision remains the standard for small rectal cancers, but in the case of pT1 (sm1) lesions, the risk benefit of radical versus local excision should be discussed at the MDT and then with the patient.

Subsequent histopathological examination of cancers treated by local excision may identify a proportion requiring more radical surgery.

7.3.8 Summary of evidence

- The quality of surgery for rectal cancer, particularly with respect to circumferential margin involvement and the plane of surgery, is strongly associated with outcome in terms of local recurrence and survival.
- Although the evidence is not as strong as for colon cancer, there is evidence that laparoscopic surgery for rectal cancer may be associated with better short-term outcomes without significant detriment.
- Pre-operative radiotherapy is associated with improved local recurrence rates and improved survival in appropriate patients undergoing radical surgery for rectal cancer.
- Although small rectal cancers can be excised locally, local recurrence rates are higher than with radical surgery with the exception of early (sm1) T1 cancers.

7.3.9 Management of complications of colonoscopy

Screening colonoscopy units should be able to deal with the complications that may occur. These units should be able to (i) provide emergency admission with general surgical service and operating theatre availability; (ii) cross match and provide blood for transfusion; and (iii) provide emergency angiographic and radiology services.

7.4 Appendices

Appendix 1: Minimum key performance indicators for colorectal cancer surgery

(Adapted from Appendix 5 of 'Recommendations for the Future Development of Colorectal Cancer Surgery in Ireland and Guidelines for the Management of Rectal Cancer in Ireland'¹)

A. Core data:

1. Number of patients diagnosed with colorectal cancer
2. Age of patient at diagnosis
3. Gender of patient
4. Radiologic stage of cancer at time of presentation based on CT and/or MRI
5. ASA grade (American Society of Anesthesiologists)
6. Mode of presentation (emergency, urgent or elective)
7. Position of tumour at rigid sigmoidoscopy (0-5, 6-10, 11-15 cm)*

B. Key performance indicators:

1. Crude length of stay (date of admission to date of discharge)
2. Unadjusted operative and procedural 30-day mortality (all causes of mortality in the 30 days from the date of patient's operation or stent)
3. Margin positivity (Yes/No/Not reported)
4. Nodal harvest (number of positive nodes/total number of nodes)
5. APR (abdomino-perineal excision) rate*
6. Return to theatre rate (return to theatre during hospital stay for any reason, including central line insertion)
7. Clinical leak rate
8. Radiotherapy use (% neoadjuvant, % adjuvant)
9. Readmission rate within 30 days of operation for any reason apart from planned readmissions for chemotherapy or radiotherapy

*For rectal cancer only

7.5 References

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