An Roinn Sláinte
Department of Health

Diagnosis, staging and treatment of patients with colon cancer

National Clinical Guideline No. 24

December 2020

National Patient Safety Office
Oifig Náisiúnta um Shábháilteacht Othar

NATIONAL CLINICAL EFFECTIVENESS COMMITTEE

This National Clinical Guideline has been developed by the National Cancer Control Programme Guideline Development Group, within the Health Service Executive (HSE).

Using this National Clinical Guideline

This National Clinical Guideline applies to adults (18 years or older) with newly diagnosed colon cancer, or, those that have a suspected diagnosis of colon cancer in a hospital setting.

This guideline is intended for all health professionals involved in the diagnosis, staging and treatment of patients with colon cancer. While the CEO, General Manager and the Clinical Director of the hospital have corporate responsibility for the implementation of the recommendations in this Clinical Guideline, each member of the multidisciplinary team is responsible for the implementation of the individual guideline recommendations relevant to their discipline.

This guideline is also relevant to those involved in clinical governance, in both primary and secondary care, to help ensure that arrangements are in place to deliver appropriate care for the population covered by this guideline.

Whilst the guideline is focused on clinical care, it is expected to be of interest to patients with colon cancer and their significant others. Effort has been made to make this document more user friendly a list of medical abbreviations used throughout the guideline can be found in Appendix 9: Glossary of terms and abbreviations.

Disclaimer

NCEC National Clinical Guidelines do not replace professional judgment on particular cases, whereby the clinician or health professional decides that individual guideline recommendations are not appropriate in the circumstances presented by an individual patient, or whereby an individual patient declines a recommendation as a course of action in their care or treatment plan. In these circumstances the decision not to follow a recommendation should be appropriately recorded in the patient's healthcare record.

Users of NCEC National Clinical Guidelines must ensure they have the current version (hardcopy or softcopy) by checking the relevant section in the National Patient Safety Office on the Department of Health website: https://www.gov.ie/en/collection/c9fa9a-national-clinical-guidelines/

Whilst every care has been taken to ensure that all information contained in this publication is correct, the Department of Health cannot accept responsibility for any errors or omissions which may have occurred.

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Membership of the Guideline Development Group

The Guideline Development Group was chaired by Professor Deborah McNamara, Consultant Colorectal Surgeon, Beaumont Hospital. This National Clinical Guideline is supported by the National Cancer Control Programme (NCCP).

Membership nominations were sought from a variety of clinical and non-clinical backgrounds so as to be representative of all key stakeholders within the Health Service Executive. Guideline Development Group members included those involved in clinical practice, research and library services, and health economics.

The NCCP recognise the importance of patient input and their role as key stakeholders in informing quality improvements in our healthcare system. Patients were engaged via patient's support & advocacy groups and charities and invited to contribute to the development of the guideline from a patient's perspective. This approach assisted in capturing the patient experience which encompassed important quality of life issues and patient's values.

Name	Title/Position	Role on guideline group
Professor Deborah McNamara	Consultant Colorectal Surgeon, BH	Chair and Member
Radiology		
Professor Martina Morrin	Consultant Radiologist, BH	Member
Dr Marie Staunton	Consultant Radiologist, MUH	Member
Dr Caitriona Logan	Radiology Specialist Registrar, BH	Member
Dr Stephen Power	Radiology Specialist Registrar, CUH	Member
Dr Nicola Hughes	Radiology Specialist Registrar, CUH	Member
Dr David Ryan	Radiology Specialist Registrar, CUH	Member
Dr David Woodlock	Radiology Specialist Registrar, GUH	Member
Dr Aileen O'Shea	Radiology Specialist Registrar, BH	Member
Dr Damien O'Neill	Radiology Specialist Registrar, BH	Member
Pathology		
Dr Michael Bennett	Consultant Histopathologist, CUH	Member
Professor Elaine Kay	Consultant Histopathologist, BH	Member (until October 2019)
Dr Cian Muldoon	Consultant Histopathologist, SJH	Member
Professor Kieran Sheahan	Consultant Histopathologist, SVUH	Member
Gastroenterology		
Professor Padraic MacMathuna	Consultant Gastroenterologist, MMUH	Member
Dr Martin Buckley	Consultant Gastroenterologist, MUH	Member
Dr Subhasish Sengupta	Consultant Gastroenterologist, OLOLH	Member
Dr Barbara Ryan	Consultant Gastroenterologist, TUH	Member

Name	Title/Position	Role on guideline group
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Ms Ann Hanly	Consultant Colorectal Surgeon, SVUH	Member
Mr Eddie Myers	Consultant Colorectal Surgeon, PH	Member
Ms Ann Brannigan	Consultant Colorectal Surgeon, MMUH	Member
Mr Jurgen Mulsow	Consultant Colorectal Surgeon, MMH	Member (from October 2019)
Mr John Burke	Consultant Colorectal Surgeon, BH	Member (from October 2019)
Mr Emmet Andrews	Consultant Colorectal Surgeon, CUH	Member (from October 2019)
Mr Paul McCormick	Consultant Colorectal Surgeon, SJH	Member (from October 2019)
Professor Fiachra Cooke	Consultant Colorectal Surgeon, UHW	Member (from October 2019)
Professor Calvin Coffey	Consultant Colorectal Surgeon, UL	Member (from October 2019)
Mr Myles Joyce	Consultant Colorectal Surgeon, GUH	Member (from October 2019)
Professor Ronan O' Connell	Consultant Colorectal Surgeon, SVUH	Member (from October 2019)
Dr Gemma Solon	Colorectal Specialist Registrar, MMUH	Member
Dr Ailin Rogers	General Surgery Specialist Registrar, BH	Member
Dr Cillian Clancy	General Surgery Specialist Registrar, MMUH	Member
Dr Babak Meshkat	General Surgery Specialist Registrar, BH	Member
Radiation Oncology		
Dr Brian O'Neill	Consultant Radiation Oncologist, SLRON	Member
Dr Cormac Small	Consultant Radiation Oncologist, GUH	Member
Dr Charles Gillham	Consultant Radiation Oncologist, SLRON	Member
Dr Martin Higgins	Radiation Oncology Specialist Registrar, SLRON	Member (from October 2019)
Palliative Care		
Dr Karen Ryan	Consultant in Palliative Medicine, SFH	Member
Project Management		
Ms Keira Doherty-McCullough	Project Manager, NCCP	Project manager and Member (from January 2017)
Ms Deirdre Love	Project Manager, NCCP	Project manager and Member (July 2014 – December 2016)
Ms Angela Clayton-Lea	Project Manager, NCCP	Project manager and Member (December 2012 – May 2014)
Evidence and Research		
Dr Eve O'Toole	Head of Evidence and Quality Hub, NCCP	Methodology Chair and Member
Ms Louise Murphy	Research Officer, NCCP	Research and Member
Dr Helena Gibbons	Senior Research Officer, NCCP	Research and Member (from September 2017)
Library		
Ms Margaret Morgan	HSE Librarian, HSE East	Information services
Ms Maura Flynn	HSE Librarian, HSE Midlands	Information services
Ms Nicola Fay	HSE Librarian, HSE Midlands	Information services
Mr Gethin White	HSE Librarian, HSE East	Information services
Mr Brendan Leen	HSE Librarian, HSE South	Information services
Health Economist		
Ms Rebecca Moore	Health Economist, TCD	Health Economist and Member
Patient Representative Groups		
Irish Cancer Society Colorectal Cancer Group		
Mayo Stoma Support Group		
Waterford Stoma Support Group		
Southeast Ostomates		

Key:

BH	Beaumont Hospital
CUH	Cork University Hospital
MMUH	The Mater Misericordiae University Hospital
MUH	Mercy University Hospital
NCCP	National Cancer Control Programme
OLOLH	Our Lady of Lourdes Hospital, Drogheda
PH	Portiuncula Hospital, Ballinasloe
SFH	St. Francis Hospice
SJH	St. James's Hospital
SLRON	St. Lukes Radiation Oncology Network
SUH	Sligo University Hospital
SVUH	St Vincents University Hospital
TCD	Trinity College Dublin
TUH	Tallaght University Hospital
GUH	Galway University Hospital
UHW	University Hospital Waterford
UL	University Hospital Limerick

Credits

The role of the NCEC is to prioritise, quality assure and recommend clinical guidelines to the Chief Medical Officer for endorsement by the Minister for Health. It is intended through Ministerial endorsement that full implementation of the guideline will occur through the relevant service plans.

The NCEC and the Department of Health acknowledge and recognise the Chair and members of the Guideline Development Group for development of the guideline. The NCEC and Department of Health wish to express thanks and sincere gratitude to all persons contributing to this National Clinical Guideline; especially those that give of their time on a voluntary basis.

Acknowledgments

The following credits and acknowledgements are made by the Chair of the Guideline Development Group. The Chair, Professor Deborah McNamara wishes to acknowledge all members of the Guideline Development Group as full contributors credited with having given substantial intellectual leadership to the National Clinical Guideline.

Ms Deirdre Love and Dr Eve O' Toole successfully submitted the guideline for NCEC prioritisation. The Guideline Development Group clinical members, methodology chair, research members and project manager agreed the scope and developed the clinical questions. The Guideline Development Group librarians and research members carried out the systematic searches for evidence. The Guideline Development Group research members reviewed the evidence, appraised the literature and performed the data extraction. The Guideline Development Group led by Professor Deborah McNamara and Dr Eve O'Toole carried out the evidence synthesis including formulation of the evidence summaries and recommendations. Ms Keira Doherty-McCullough, Dr Helena Gibbons and Ms Louise Murphy conducted the budget impact analysis. Professor Deborah McNamara, Ms Keira Doherty-McCullough and Dr Eve O'Toole successfully submitted the guideline for NCEC quality assurance. All Guideline Development Group writing members approved the final guideline. Ms Louise Murphy and Dr Helena Gibbons edited the document and prepared it for publication.

The external review was carried out by Professor Maria A. Hawkins (Professor of Radiation Oncology, University College London), Professor Paul Horgan (Professor of Surgery, University of Glasgow), Mr Fergal Fleming (Assistant Professor of Surgery and Oncology, University of Rochester Medical Center, Rochester, New York), Professor Brian Saunders (Professor of Endoscopy Practice, London North West Hospitals University Healthcare Trust), Dr David Burling (Consultant Radiologist, St. Mark's Hospital, Harrow, UK) and Dr Amitabh Srivastava, (Associate Professor of Pathology, Harvard Medical School).

A full list of members of the Guideline Development Group is available in the previous page/s.

Signed by the Chair:
Professor Deborah McNamara

Date: December, 2020

National Clinical Guidelines

Providing standardised clinical care to patients in healthcare is challenging. This is due to a number of factors, among them diversity in environments of care and complex patient presentations. It is self-evident that safe, effective care and treatment are important in ensuring that patients get the best outcomes from their care.

The Department of Health is of the view that supporting evidence-based practice, through the clinical effectiveness framework, is a critical element of the health service to deliver safe and high quality care. The National Clinical Effectiveness Committee (NCEC) is a Ministerial committee set up in 2010 as a key recommendation of the report of the Commission on Patient Safety and Quality Assurance (2008). The establishment of the Commission was prompted by an increasing awareness of patient safety issues in general and high profile health service system failures at home and abroad.

The NCEC on behalf of the Department of Health has embarked on a quality assured National Clinical Guideline development process linked to service delivery priorities. Furthermore, implementing National Clinical Guidelines sets a standard nationally, to enable healthcare professionals to deliver safe and effective care and treatment while monitoring their individual, team and organisation's performance.

The aim of these National Clinical Guidelines is to reduce unnecessary variations in practice and provide an evidence base for the most appropriate healthcare in particular circumstances. As a consequence of Ministerial mandate, it is expected that NCEC National Clinical Guidelines are implemented across all relevant services in the Irish healthcare setting.

The NCEC is a partnership between key stakeholders in patient safety. NCEC's mission is to provide a framework for national endorsement of clinical guidelines and clinical audit to optimise patient and service user care. The NCEC has a remit to establish and implement processes for the prioritisation and quality assurance of clinical guidelines and clinical audit so as to recommend them to the Minister for Health to become part of a suite of National Clinical Guidelines and National Clinical Audit. The aim of the suite of National Clinical Guidelines is to provide guidance and standards for improving the quality, safety and cost-effectiveness of healthcare in Ireland. The implementation of these National Clinical Guidelines will support the provision of evidence-based and consistent care across Irish healthcare services.

NCEC Terms of Reference

1. Provide strategic leadership for the national clinical effectiveness agenda.
2. Contribute to national patient safety and quality improvement agendas.
3. Publish standards for clinical practice guidance.
4. Publish guidance for National Clinical Guidelines and National Clinical Audit.
5. Prioritise and quality assure National Clinical Guidelines and National Clinical Audit.
6. Commission National Clinical Guidelines and National Clinical Audit.
7. Align National Clinical Guidelines and National Clinical Audit with implementation levers.
8. Report periodically on the implementation and impact of National Clinical Guidelines and the performance of National Clinical Audit.
9. Establish sub-committees for NCEC workstreams.
10. Publish an annual report.

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1 Background

1.1 Impact of colon cancer in Ireland

Cancer is a major healthcare challenge. Each year in Ireland, approximately 24,793 people are diagnosed with invasive cancer (excluding non-melanoma skin cancer (NMSC)) (National Cancer Registry Ireland (NCRI), 2020). Cancer is the second leading cause of death in Ireland after diseases of the circulatory system. Deaths from cancer averaged 9,063 deaths per year during 2015-2017 (NCRI, 2020).

Cancer incidence data from the NCRI and population projections from the Central Statistics Office (CSO) have been combined by the NCRI to estimate the number of new cancer cases expected in five year bands from 2020 to 2045. Assuming that average age-standardised rates during 2011-2015 continue to apply ('demographic' projection), annual numbers of cases of all cancers combined (excluding NMSC) are projected to increase in males from 11,460 in 2015 to 24,160 in 2045 (+111%) and in females from 10,240 in 2015 to 18,840 in 2045 (+84%) — a doubling of numbers overall (+98%) (NCRI, 2019b).

Colorectal cancer is the second most common newly diagnosed cancer among men and the third most common among women. Each year approximately 2,800 new cases of colorectal cancer are reported (2018-2020) (NCRI, 2020). The incidence of colon cancers (ICD-10, C18) in Ireland is projected to rise. By 2045 the incidence of colon cancer is projected to increase by 114% in females and 129% in males based on demographic changes alone (NCRI, 2019b).

1.2 The National Cancer Control Programme, cancer centres and multidisciplinary teams

The National Cancer Control Programme (NCCP) was established in 2007 to implement the recommendations of the 2006 National Cancer Strategy (Department of Health and Children (DoHC), 2006). In Ireland, there are nine hospitals designated as cancer centres which includes one paediatric cancer centre.

Recommendation 13 of the National Cancer Strategy 2017-2026 (Department of Health, 2017) states "Patients diagnosed with cancer will have their case formally discussed at a multidisciplinary team meeting. The NCCP, working with the Hospital Groups, will oversee and support multidisciplinary team composition, processes and reporting of outcomes"

A multidisciplinary team consists of clinicians' representative of the specialities required to diagnose and treat a specific disease. For the implementation of this guideline the multidisciplinary teams must have representation from diagnostic and treatment specialities with experience in colon cancer.

1.3 Centralisation of services

Cancer patients should have access to high quality care staffed by appropriate specialists to ensure optimal treatment and improve patient outcomes. Recommendation 21 of The National Cancer Strategy 2017-2026 states "The NCCP will draw up a plan setting out which number/location of designated cancer centres in which surgery will take place for the various tumour types. Timescales for the implementation of the plan will be included for each tumour type" (Department of Health, 2017).

The National Cancer Strategy 2017-2026 has set a target that 95% of cancer surgeries performed in public hospitals will be conducted in approved centres by 2020. The NCCP is working together with the Department of Health and the HSE Acute Hospital Division to achieve this goal. It is acknowledged in the implementation plan for this guideline, that centralisation of colon cancer services is required in order to implement a number of its recommendations. Funding for centralisation of cancer surgeries will be sought through normal service planning processes.

1.4 Colorectal Cancer National Clinical Leads Group

The purpose of the Colorectal Cancer National Clinical Leads Group is to advise on the governance arrangements for colon and rectal cancer services nationally, ensuring it operates as a cohesive national clinical network for the purpose of clinical audit, sharing of good practice and problem solving. Membership of this group includes; clinicians with expertise in colorectal surgery, radiation oncology and medical oncology. Importantly, there is cross over between those involved in the clinical leads group and membership of the colon Guideline Development Group which is key for the implementation of this guideline.

1.5 Context and scope of this National Clinical Guideline

The National Cancer Strategy (Department of Health and Children (DoHC), 2006) recommended that national, tumour site-specific, multidisciplinary groups be convened to develop national evidence-based clinical guidelines for cancer care. The purpose of developing these guidelines is to improve the quality of care received by patients.

The National Cancer Strategy 2017-2026 (Department of Health, 2017) recommendation 37 states that "the NCCP will develop further guidelines for cancer care in line with National Clinical Effectiveness Committee (NCEC) standards".

A Guideline Development Group was established to develop evidence-based guidelines for the diagnosis, staging and treatment of patients with colon cancer. The guideline development process is described in detail in Section 3: Development of this National Clinical Guideline. This National Clinical Guideline integrates the best current research evidence with clinical expertise and patient values.

This guideline includes recommendations on the diagnosis, staging, and treatment of patients with colon cancer. It focuses on areas of clinical practice that are known to be controversial or uncertain, where there is variation in practice, where there is new or emerging evidence, and where there is potential for most impact for the patient and services. It does not include recommendations covering every aspect of diagnosis, staging, and treatment. The aims, objectives and the scope of the guideline are outlined Section 3.3 Aims and objectives.

2 National Clinical Guideline recommendations

2.1 Summary of clinical recommendations, practical considerations around patient care and summary of budget impact analysis

Here follows a list of all the recommendations in this guideline, along with the grade of that recommendation. The grade reflects the level of evidence upon which the recommendations were based, the clinical significance of the evidence, and whether further research is likely to change the recommendation. The levels of evidence and grading systems used are documented in Appendix 10: Levels of evidence and grading systems.

A list of practical considerations around patient care was generated through collaboration with patients and patient representative organisations. The NCCP recognises the importance of patient input and of their role as key stakeholders in informing quality improvements in our healthcare system. This approach assisted in capturing the patient experience and aided discussion on important quality of life issues and patient values.

Recommendation	Grade
Diagnosis and staging	
2.2.1.1 **Initial staging** Contrast enhanced CT-TAP should be employed for the initial staging of patients diagnosed with colon cancer.	**C**
2.2.1.2 **Hepatic metastases** Hepatocyte specific contrast enhanced MRI of the liver is the modality of choice for evaluation of liver metastases in patients with colon cancer being considered for surgical resection.	**A**
2.2.1.3 **Extrahepatic metastases** Currently, PET-CT is not a first-line imaging modality for staging colon cancer and can be considered as a problem solving tool in patients with equivocal imaging findings following discussion at a multidisciplinary team meeting.	**C**
2.2.2.1 **Imaging for further liver lesions** Hepatocyte specific contrast enhanced MRI of the liver is the imaging modality of choice in patients with colon cancer with a potentially resectable liver lesion to detect further liver lesions.	**A**
2.2.2.2 **Imaging for further liver lesions** PET-CT can be considered in patients with colon cancer with potentially resectable liver lesion with equivocal imaging findings following discussion at a multidisciplinary team meeting.	**C**
2.2.3.1 In patients diagnosed with colon cancer whose tumour cannot be endoscopically passed, preoperative CT colonography should be considered to look for synchronous lesions and to allow for surgical planning. CT colonography should only be performed when local expertise is available.	**D**
2.2.4.1 In patients with left-sided colon cancer, complete visualisation of the entire colon by colonoscopy or CT colonography is recommended prior to surgery. CT colonography should only be performed in centres experienced in the technique.	**C**
2.2.4.2 In patients diagnosed with colon cancer whose tumour cannot be endoscopically passed, preoperative CT colonography should be considered to look for synchronous lesions and to allow for surgical planning. CT colonography should only be performed when local expertise is available.	**D**

Recommendation	Grade
Diagnosis and staging	
2.2.5.1 For patients with colon cancer, lesions should be tattooed at colonoscopy.	**C**
2.2.5.2 For patients with colon cancer, the tattoo should be placed 1-2 cm distal to the lesion and ideally at three points in the circumference.	**D**
2.2.6.1 In patients undergoing surgery with colon cancer, it is recommended to identify as many nodes as possible, all of which should be submitted for microscopic examination/evaluation. Overall, the median for the laboratory should be at least 12.	**C**
2.2.7.1 In patients diagnosed with colon cancer, Haggitt and Kikuchi classification systems may be considered where deemed applicable	**D**
2.2.8.1 In patients with colon cancer tumours ≤1 mm from the peritoneal surface if tumour does not demonstrate serosal involvement after additional evaluation, it should be categorised as pT3, additional comment should be made in the report.	**C**
2.2.9.1 In patients with early stage colon cancer treated with local excision, lesions should be assessed for depth of submucosal invasion, lymphovascular invasion, budding, grade of differentiation, and margin status.	**B**
2.2.9.2 Local resection colon cancer specimens both en-bloc and piecemeal resections, should be of sufficient quality to enable such assessment and should be discussed at a multidisciplinary team meeting.	**D**
2.2.9.3 Patient factors such as performance status, comorbidities, and informed patient preferences should be taken into consideration following multidisciplinary team discussion for decisions on further management.	**D**
Treatment: Emergency presentations	
2.3.1.1 In patients with obstructing colon cancer colonic stenting as a bridge to surgery may be considered in selected patients	**C**
2.3.1.2 Colonic stenting should be considered for the palliation of patients with obstructing colon cancer (i.e. In those who are not fit for immediate resection or in those with advanced disease).	**C**
Treatment: Surgical techniques	
2.4.1.1 In patients diagnosed with colon cancer minimally invasive colectomy/partial colectomy by an experienced laparoscopic surgeon should be considered in appropriate patients.	**A**
2.4.2.1 In patients with colon cancer dissection in the mesocolic plane is essential for good oncologic outcomes.	**B**
2.4.2.2 In patients with colon cancer undergoing curative resection the role of extended lymphadenectomy remains uncertain.	**C**

Recommendation	Grade
Treatment: Surgical techniques	
2.4.3.1 Patients with metastatic disease deemed unresectable, and a colon primary, should be discussed at a multidisciplinary team meeting with appropriate surgical expertise prior to undergoing any treatment except in the presence of a surgical emergency.	**D**
Treatment: Late stage/Palliative care	
2.5.1.1 For patients with cancer, early provision of palliative care can improve patient outcomes.	**C**
2.5.1.2 Assessment of palliative care needs should be an ongoing process throughout the course of a patient's cancer illness and services provided on the basis of identified need.	**D**

Practical considerations around patient care
• Patients with colon cancer should have access to a stoma care/clinical nurse specialist to co-ordinate patients' education and care requirements that impact on quality of life.
• Consider referral of patients with colon cancer to psycho-oncology and/or a medical social worker for psychological support.
• Patients with colon cancer should be made aware of voluntary cancer support groups, charities and organisations to contact for support inside and outside the hospital setting.
• Patients with colon cancer should be fully informed of the side effects of different treatment types they may undergo.
• All healthcare professionals who provide care to patients with colon cancer should use patient friendly language when communicating with patients about their diagnosis, staging and treatment.
• Patients should be referred for a prehabilitation and preoperative assessment to identify what supports the patient requires.

Summary of budget impact analysis†				
Cost	**2020**	**2021**	**2022**	**Total cost**
Total operational for implementing recommendations	€905,410	€905,410	€905,410	€2,716,230
Total staff costs of implementing the recommendations	Awaiting outcome of surgical centralisation and workforce planning			
Total cost of implementing the guideline				€2,716,230 + Total Revenue cost (TBC)

† See Table 14 Budget impact analysis of expected operational costs (excluding staff costs) in implementing recommendations for more information.

2.2 Diagnosis and staging

The following are responsible for implementation of recommendations regarding diagnosis and staging:
While the CEO, General Manager and the Clinical Director of the hospital have corporate responsibility for the implementation of the recommendations in this National Clinical Guideline, each member of the multidisciplinary team is responsible for the implementation of the individual guideline recommendations relevant to their discipline.

Clinical question 2.2.1

In patients with newly diagnosed colon cancer, is CT-TAP the most suitable imaging modality for initial staging?

Evidence summary

Initial staging

An UpToDate review (Macrae and Bendell, 2020) and a clinical guideline (NCCN Clinical Practice Guidelines In Oncology (NCCN Guidelines®), 2020) addressed the most suitable imaging modality for initial staging of newly diagnosed colon cancer.

The NCCN (2020) panel recommends that all patients with stage II, III, or IV colorectal cancer undergo chest, abdomen, and pelvic CT before resection. In general, it is preferable to obtain these scans prior to, rather than after surgery, as the scan results will occasionally change surgical planning. (Macrae and Bendell, 2020)

The NCCN panel's consensus is that a PET-CT scan is not indicated at baseline for preoperative workup. In fact, PET-CT scans are usually done without contrast and multiple slicing and do not obviate the need for a contrast-enhanced diagnostic CT scan. If, however, abnormalities are seen on CT or MRI scan that are considered suspicious but inconclusive for metastases, then a PET-CT scan may be considered to further delineate that abnormality, if this information will change management. (NCCN, 2020)

Hepatic metastases

Three meta-analyses (Niekel et al., 2010, Floriani et al., 2010, Maffione et al., 2015) addressed the issue of the most suitable imaging modality for diagnosing hepatic metastases.

The best meta-analysis from a methodological point of view was deemed to be Niekel et al. (2010). The authors concluded that MRI is the preferred first-line imaging study for evaluating colorectal cancer liver metastases in patients who have not previously undergone therapy (Table 1) (Niekel et al., 2010).

Table 1 Mean sensitivity (on a per lesion basis) of MRI and CT in the detection of colorectal liver metastases based on lesion size and study year (Niekel et al., 2010)

	Mean sensitivity (%)	
Subgroup	**MRI**	**CT**
Lesion size		
<10mm	60.2 (54.4, 65.7) [n=8]	47.3 (40.1, 54.5) [n=5]
≥10mm	89.0 (81.7, 93.7) [n=8]	86.7 (77.6, 92.5) [n=5]
Study year		
Before January 2004	70.2 (63.2, 76.3) [n=34]	73.4 (61.0, 83.0) [n=20]
After January 2004	84.9 (79.3, 89.2) [n=27]	74.9 (69.1, 79.9) [n=18]
Numbers in parentheses are the 95% CIs, numbers in brackets are numbers of data sets		

Current practice dictates that hepatocyte specific contrast enhanced MRI of the liver is generally reserved for patients who have suspicious but not definitive findings on CT scan, particularly if better definition of hepatic disease burden is needed in order to make decisions about potential hepatic resection (Macrae and Bendell, 2020).

The NCCN (2020) panel strongly discourages the routine use of PET-CT scanning for staging, baseline imaging, or routine follow-up. However, the panel recommends consideration of a preoperative PET-CT scan at baseline in selected cases if prior anatomic imaging indicates the presence of potentially surgically curable M1 disease. The purpose of this PET-CT scan is to evaluate for unrecognised metastatic disease that would preclude the possibility of surgical management.

Extrahepatic metastases

Currently there is no strong evidence to address the best imaging modality for extrahepatic metastasis, international guidelines (SIGN, 2016) suggest that CT-TAP is the imaging modality of choice for the identification of extrahepatic metastases.

Recommendation 2.2.1.1	Grade
Initial staging Contrast enhanced CT-TAP should be employed for the initial staging of patients diagnosed with colon cancer.	C

Recommendation 2.2.1.2	Grade
Hepatic metastases Hepatocyte specific contrast enhanced MRI of the liver is the modality of choice for evaluation of liver metastases in patients with colon cancer being considered for surgical resection.	A

Recommendation 2.2.1.3	Grade
Extrahepatic metastases Currently, PET-CT is not a first-line imaging modality for staging colon cancer and can be considered as a problem solving tool in patients with equivocal imaging findings following discussion at a multidisciplinary team meeting.	C

Good Practice Point
If CT with IV contrast is contraindicated, then a non-contrast CT thorax, abdomen and pelvis in addition to an MRI liver should be considered.

Clinical question 2.2.2

In patients diagnosed with colon cancer with a potentially resectable liver lesion, is MRI of the liver superior to PET-CT in determining the presence of further liver lesions?

Evidence summary

Hepatic metastases

Three meta-analyses (Niekel et al., 2010, Floriani et al., 2010, Maffione et al., 2015), an UpToDate review (Macrae and Bendell, 2020) and a clinical guideline (NCCN, 2020) addressed the issue of the imaging modality of choice for diagnosing hepatic metastases.

The best meta-analysis from a methodological point of view was deemed to be Niekel et al. (2010). The authors concluded that as there was a limited number of FDG PET/CT studies, no check for heterogeneity could be performed and the number of studies was small, MRI is the preferred first-line imaging study for evaluating colorectal cancer liver metastases in patients who have not previously undergone therapy (Table 2) (Niekel et al., 2010).

Table 2 Mean sensitivity (on a per patient basis) of MRI and FDG PET-CT in the detection of colorectal liver metastases (Niekel et al., 2010)

Modality	Mean sensitivity (%)	Mean specificity (%)
MRI (n=6)*	88.2 (64.8, 96.8) †	92.5 (89.5, 94.6) †
PET-CT (n=3)*	96.5 (94.2, 97.9) †	97.2 (92.8, 99.0) †
* Numbers in parentheses are numbers of data sets † Numbers in parentheses are 95% CIs		

Current practice dictates that hepatocyte specific contrast enhanced MRI of the liver is generally reserved for patients who have suspicious but not definitive findings on CT scan, particularly if better definition of hepatic disease burden is required in order to make decisions about potential hepatic resection (Macrae and Bendell, 2020)

The NCCN (2020) panel strongly discourages the routine use of PET-CT scanning for staging, baseline imaging, or routine follow-up. However, the panel recommends consideration of a preoperative PET-CT scan at baseline in selected cases if prior anatomic imaging indicates the presence of potentially surgically curable M1 disease. The purpose of this PET-CT scan is to evaluate for unrecognised metastatic disease that would preclude the possibility of surgical management.

Recommendation 2.2.2.1	Grade
Imaging for further liver lesions Hepatocyte specific contrast enhanced MRI of the liver is the imaging modality of choice in patients with colon cancer with a potentially resectable liver lesion to detect further liver lesions.	**A**

Recommendation 2.2.2.2	Grade
Imaging for further liver lesions PET-CT can be considered in patients with colon cancer with potentially resectable liver lesion with equivocal imaging findings following discussion at a multidisciplinary team meeting.	**C**

Good Practice Point

PET-CT scans should only be requested after discussion at a multidisciplinary team meeting.

Clinical question 2.2.3

In patients diagnosed with colon cancer whose tumour cannot be endoscopically passed, is CT colonography always necessary prior to surgery?

Evidence summary

One prospective study (Mulder et al., 2011) and two retrospective studies (Flor et al., 2020, Park et al., 2012) addressed this clinical question. All newly diagnosed colorectal cancer patients (n=13,683) were obtained from the Rotterdam Cancer Registry, and studied for synchronous colorectal cancer between 1995 and 2006. There was a large sample size and the study sample was representative of both the study population and target population (Mulder et al., 2011).

Of 5,985 patients with a primary left colon cancer 4.4% were found to have a synchronous colorectal lesion and of 4,530 patients with a primary right colon cancer 4.3% were found to have a synchronous colorectal lesion (Table 3) (Mulder et al., 2011). Patients with a primary left colon cancer had 22.3% of those synchronous neoplasms located in a different surgical segment and patients with a primary right colon cancer had 31.1% of those synchronous neoplasms located in a different surgical segment. Therefore the detection of a synchronous lesion(s) may change management in a number of patients (Mulder et al., 2011).

Table 3 Tumour localisation and the prevalence of synchronous colorectal cancer (Mulder et al., 2011)

	Sample size (n)	Solitary cancer	Synchronous cancer
Rectum	3,168 (23.1%)	3,088	80 (2.5%)
Left colon	**5,985 (43.7%)**	**5,724**	**261 (4.4%)**
Right colon	**4,530 (33.2%)**	**4,337**	**193 (4.3%)**
Total	13,683	13,149	534 (3.9%)

In obstructing colorectal cancer, pre-operative CT colonography is technically feasible and allows detection of synchronous colonic neoplasms with a high sensitivity. Suboptimal bowel preparation can occur in approximately 3 to 3.6% (Park et al., 2012, Flor et al., 2020) of patients; however the CT colonography completion rate across studies has been greater than 95%.

Park et al. (2012) evaluated CT colonography examinations in 284 patients with stenosing colorectal cancer. The per-patient CT colonography sensitivity for detecting patients harbouring synchronous colorectal cancer and advanced neoplasia in the proximal colon was 100% (6/6 patients) and 88.6% (39/44 patients), respectively. The corresponding per-patient NPV was high, 100% (194/194 patients) for proximal synchronous colorectal cancers and 97.4% (189/194) for advanced neoplasia. Therefore, negative CT colonography findings in the proximal colon exclude the need for additional surgical procedures in the proximal colon with high confidence.

Flor et al. (2020) showed that CT colonography is a highly accurate test for detecting synchronous colonic lesions in patients with occlusive colorectal cancer. The prevalence of advanced neoplasia in their patient cohort was high (23%). They evaluated 70 patients with stenosing colorectal cancer of whom 27 (39%) had at least one 6-mm or larger synchronous lesion, and four patients (6%) had a total of five synchronous colorectal cancers. The overall per-patient CT colonography sensitivity in detecting synchronous lesions 6 mm or larger was 0.93 (25/27); specificity, 0.98 (42/43); PPV, 0.96; and NPV, 0.95. Per-patient sensitivity in the diagnosis of synchronous colorectal cancer was 1.00 (4/4). Per-patient sensitivity for the diagnosis of synchronous advanced neoplasia (advanced adenoma and colorectal cancers) was 0.94 (15/16). Per-lesion CT colonography sensitivity for detecting synchronous lesions 6 mm or larger was 0.88 (37/42), all adenomatous lesions was 0.89 (55/62) and advanced neoplasia, 0.92 (22/24). Per-lesion sensitivity of CT colonography for detecting colorectal cancers was 100% (5/5).

Recommendation 2.2.3.1	**Grade**
In patients diagnosed with colon cancer whose tumour cannot be endoscopically passed, preoperative CT colonography should be considered to look for synchronous lesions and to allow for surgical planning. CT colonography should only be performed when local expertise is available.	**D**

Good Practice Point

CT colonography should only be performed and interpreted by appropriately trained radiologists.

Clinical question 2.2.4

In patients diagnosed with left-sided colon cancer, is complete colonoscopy always necessary prior to surgery?

Evidence summary

One meta-analysis (Pickhardt et al., 2011) three randomised controlled trials (Halligan et al., 2015, Atkin et al., 2013, von Wagner et al., 2012) and one prospective study (Mulder et al., 2011) addressed this clinical question.

An important aspect of preoperative staging is complete visualisation of the colon. When a cancer has been diagnosed a complete colonoscopy or CT colonography should be carried out prior to surgery, if possible, to detect synchronous tumours.

Synchronous colorectal lesions were found in 4.4% of patients with a primary left colon cancer and 4.3% of patients with a primary right colon cancer (Mulder et al., 2011) (Table 4).

Table 4 Tumour localisation and the prevalence of synchronous colorectal cancer (Mulder et al., 2011)

	Sample size (n)	Solitary cancer (n)	Synchronous tumour prevalence (%)
Rectum	3,168 (23.1%)	3,088	80 (2.5%)
Left colon	**5,985 (43.7%)**	**5,724**	**261 (4.4%)**
Right colon	**4,530 (33.2%)**	**4,337**	**193 (4.3%)**
Total	13,683	13,149	534 (3.9%)

The detection of synchronous tumours is important because of the implications for change of surgical management.

CT colonography and colonoscopy detect a similar proportion of cancers (96.1 vs. 94.7%; (Pickhardt et al., 2011) and their costs are also similar according to Halligan et al. (2015). Colonoscopy has the facility to take a biopsy from any suspected lesion and also permits complete removal of most benign lesions during the same procedure.

Non-completion rates for diagnostic colonoscopy in symptomatic patients are approximately 11-12% (Atkin et al., 2013). Reasons for incompleteness include the inability of the colonoscope to reach the tumour or to visualise the mucosa proximal to the tumour for technical reasons (e.g., partially or completely obstructing cancer, tortuous colon, poor preparation) and patient intolerance of the examination.

In non-emergent obstructing lesions or in the presence of an impending obstruction, where a colonoscopy may not be possible, CT colonography provides a non-invasive alternative (see Clinical Question 2.2.3). CT colonography is more tolerable and acceptable to patients (von Wagner et al., 2012).

Recommendation 2.2.4.1	**Grade**
In patients with left-sided colon cancer, complete visualisation of the entire colon by colonoscopy or CT colonography is recommended prior to surgery. CT colonography should only be performed in centres experienced in the technique.	**C**

Recommendation 2.2.4.2	**Grade**
In patients diagnosed with colon cancer whose tumour cannot be endoscopically passed, preoperative CT colonography should be considered to look for synchronous lesions and to allow for surgical planning. CT colonography should only be performed when local expertise is available.	**D**

Clinical question 2.2.5

In patients diagnosed with colon cancer, should the lesion be routinely tattooed at colonoscopy, prior to laparoscopic surgery? If so, should they be tattooed proximally or distally?

Evidence summary

A systematic review (Reynolds et al., 2017), a cohort study (Conaghan et al., 2011), a multicentre observational study (Johnstone and Moug, 2014) and an UpToDate review (Adler et al., 2020) addressed this clinical question.

The goal of tattooing is to facilitate accurate localisation of a gastrointestinal mucosal lesion (or the site of an endoscopic resection) during a follow-up surgical or endoscopic procedure. (Adler et al., 2020)

Tattooing has the potential to improve the oncological safety of resections, ensure high quality resections and reduce operative time for patients (Reynolds et al., 2017).

In a study by Conaghan et al. (2011) tattoos were judged to be visible and accurate in 70% of patients, visible but inaccurate in 7% and not visible in 15%. It was significantly easier to see the tattoo in women (19/21 women vs. 21/29 men; p=0.03) but there was no relationship between tattoo visibility and body mass index (BMI). An accurate tattoo did not reduce the conversion rate (p=0.71). No tattoo-related complications were encountered.

Johnstone and Moug (2014) found that five out of 15 inaccurately located patients required on-table alteration in planned surgical management. Pre-operative imaging was unable to visualise the primary tumour in 23.1% of cases, a finding that was more prevalent amongst bowel screened patients compared to symptomatic patients (45.8% vs. 13%; p=0.003).

Carbon black is a permanent ink that is used in the gastrointestinal tract, and it is available in two formulations:

- Pure carbon black: A sterile and prediluted suspension of carbon black particles (Spot endoscopic marker) is commercially available for endoscopic injection and results in a permanent stain.
- India ink: The India ink formulation of carbon black has been traditionally used for tattooing, and the stain persists for a minimum of 10 years without fading (Park et al., 2008, Yeung et al., 2009). India ink is black drawing ink made with carbon particles. However, India ink contains several other substances that are immunologically active (eg, carriers, stabilizers) and may be associated with rare complications (e.g. sterile abscess formation, focal peritonitis, and inflammatory pseudotumor) (Rex, 2018). (Adler et al., 2020)

Other types of dye that are used for marking a mucosal lesion include:

- Methylene blue: Methylene blue is not a permanent marker and is not used for tattoos for future localization or clinical surveillance. This temporary marker may be used during endoscopic resections of large colon polyps (ie, endoscopic mucosal resection, endoscopic submucosal dissection) or to aid in the detection of esophageal dysplasia.
- Indocyanine green: We do not use indocyanine green because this dye does not leave a permanent mark, and therefore, its clinical use is limited. In addition, indocyanine green has been reported to cause inflammation at injection sites in a rabbit model (Price et al., 2000). While an injection with indocyanine green provides staining of the serosal surface for up to eight days, the subsequent surgical or endoscopic intervention may not occur for several weeks, at which time the dye will have been absorbed and no tattoo remains visible (Miyoshi et al., 2009, Hammond et al., 1993). (Adler et al., 2020)

Location of tattoo

The Guideline Development Group agreed that there is a clear preference for distal rather than proximal location of the tattoo and that the injection of permanent marker solutions is at 1-2 cm distal to the lesion (not at the lesion) and ideally at three points in the circumference. Consensus is that tattooing of the caecum is not necessary.

Recommendation 2.2.5.1	**Grade**
For patients with colon cancer, lesions should be tattooed at colonoscopy.	**C**

Recommendation 2.2.5.2	Grade
For patients with colon cancer, the tattoo should be placed 1-2 cm distal to the lesion and ideally at three points in the circumference.	D

Good practice point
The location of the tattoo should be documented in the colonoscopy report.

Clinical question 2.2.6

In patients diagnosed with colon cancer, is there a minimum number of lymph nodes that need to be identified in a resection specimen and, if so, what is that number?

Evidence summary

Current guidelines (NCCN, 2020, Royal College of Pathologists (RCPath), 2018); addressed this clinical question.

It is very important to emphasise that all of the lymph nodes that can be found in a specimen are examined histologically as the number of lymph nodes identified in resection specimens from patients with stage II and stage III colon cancer has been positively correlated with survival (Chang et al., 2007). The setting of a standard of 12 for the median number of lymph nodes examined per specimen in no way means that pathologists should stop searching for lymph nodes once 12 have been identified. Placing the specimen in a fat-clearing agent for 24 hours, after initial dissection, may be used to help increase nodal yield. Other methods such as GEWF (glacial acetic acid, ethanol, distilled water, formaldehyde) fixation have also been used for this purpose. This approach is not routinely recommended but should be considered if the laboratory has low lymph node yields or in the context of preoperative therapy. Judgement of quality should be on the median number of lymph nodes found by an individual dissector interpreted in the light of the material reported by the individual pathologist. (RCPath, 2018)

For stage II (pN0) colon cancer, if fewer than 12 lymph nodes are initially identified, it is recommended that the pathologist go back to the specimen and resubmit more tissue of potential lymph nodes. If 12 lymph nodes are still not identified, a comment in the report should indicate that an extensive search for lymph nodes was undertaken. The pathologist should attempt to retrieve as many lymph nodes as possible. (NCCN, 2020)

The number of lymph nodes retrieved can vary with age of the patient, gender, tumor grade, and tumor site (Sarli et al., 2005). (NCCN, 2020)

Recommendation 2.2.6.1	**Grade**
In patients undergoing surgery with colon cancer, it is recommended to identify as many nodes as possible, all of which should be submitted for microscopic examination/evaluation. Overall, the median for the laboratory should be at least 12.	**C**

Good Practice Point

Where fewer than 12 nodes are identified, additional effort should be made to identify further lymph nodes, particularly in the area adjacent to the tumour (primary nodal basin).

Good Practice Point

There are many factors which may reduce the number of nodes retrieved in individual cases, including neoadjuvant treatment, patient age and surgical technique.

Clinical question 2.2.7

In patients diagnosed with colon cancer, are the Haggitt and Kikuchi classification systems sufficiently applicable to recommend their use?

Evidence summary

An international guideline (RCPath, 2018) addressed this clinical question.

Neither Kikuchi (for sessile tumours) nor Haggitt (for polypoid tumours) systems are always easy to use in practice, especially if there is fragmentation or suboptimal orientation of the tissue, and one study found lymph node metastatic disease in 6/24 Haggitt level 3 lesions (Ueno et al., 2004). Kikuchi level requires division of the submucosa into thirds and this is not possible to do accurately unless muscularis propria is included in the specimen, which is rare in most local excision specimens with the exception of some transanal resection specimens. (RCPath, 2018)

Given these difficulties, and resultant limitations on clinical utility of Haggitt and Kikuchi levels, they should be reported as applicable and where possible, in the absence of good evidence as yet to recommend alternative measures. (RCPath, 2018)

Recommendation 2.2.7.1	Grade
In patients diagnosed with colon cancer, Haggitt and Kikuchi classification systems may be considered where deemed applicable but are not routinely recommended.	D

Clinical question 2.2.8

In patients diagnosed with colon cancer, should tumours ≤1 mm from the peritoneal surface be separately identified from standard pT3 tumours?

Evidence summary

An international guideline (International Collaboration on Cancer Reporting (ICCR), 2020) and a narrative review (Dawson et al., 2019) addressed this clinical question.

Involvement of the peritoneal surface (pT4a) is defined as tumour breaching the serosa with tumour cells visible either on the peritoneal surface, free in the peritoneal cavity or separated from the peritoneal surface by inflammatory cells only (Petersen et al., 2002). Should tumour pass close to the serosal surface and elicit a mesothelial reaction but no clear invasion, additional sections and/or multiple levels should be examined. (ICCR, 2020). For illustrations see Dawson et al. (2019).

If tumour does not demonstrate serosal involvement after additional evaluation, it should be categorised as pT3. Assessment of this scenario remains prone to interobserver variation (Kirsch et al., 2018). Several studies advocate the application of elastic stains to evaluate peritoneal elastic lamina invasion, as a staging or prognostic tool, but others have not found this useful (Liang et al., 2013, Kojima et al., 2010, Grin et al., 2013, Puppa et al., 2011). (ICCR, 2020)

Cases with perforation through tumour should also be classified as pT4a, even in the absence of microscopic documentation of tumour cells on the peritoneal surface. This does not apply to colonic or rectal perforation distant from the tumour, for example secondary to distal obstruction. (ICCR, 2020)

Recommendation 2.2.8.1	**Grade**
In patients with colon cancer tumours ≤1 mm from the peritoneal surface if tumour does not demonstrate serosal involvement after additional evaluation, it should be categorised as pT3, additional comment should be made in the report.	**C**

Clinical question 2.2.9

In patients with early-stage colon cancer treated with local excision, what pathological features indicate that radical surgery is required?

Evidence summary

Three systematic review and meta-analyses (Rogers et al., 2016, Wada et al., 2015, Choi et al., 2015), two prospective studies (Saraste et al., 2013, Blumberg et al., 1999), a retrospective study (Ozturk et al., 2015) and three guidelines (CAP, 2017, NCCN, 2020, RCPath, 2018) addressed this clinical question.

Following the introduction of the National Bowel Screening Programme in Ireland, early colon cancers are being diagnosed with increased frequency. Such cancers are expected to have a good prognosis. Local resection of early malignant lesions may be sufficient as the only management. There is a risk of local recurrence or metastatic spread, particularly to local lymph nodes.

Factors which are known to influence lymph node status or prognosis in early colon cancer include poor differentiation (Saraste et al., 2013), lymphovascular invasion (Saraste et al., 2013), and tumour budding (Rogers et al., 2016), and should be accounted for when making treatment plans. As yet, perineural invasion and mucinous histology have not demonstrated prognostic potential in this specific subset, but they should be considered due to their association with negative outcomes in all stages of colorectal cancers (Ozturk et al., 2015, Blumberg et al., 1999, NCCN, 2020).

A number of meta-analyses have identified risk factors associated with recurrent malignancy or lymph node metastasis following local resections. Choi et al. (2015) revealed that submucosal invasion (≥ SM2 or ≥ 1,000 µm) (OR 3.00, 95% CI 1.36-6.62, p=0.007), vascular invasion (OR 2.70, 95% CI 1.95-3.74; p<0.001), lymphatic invasion (OR 6.91, 95% CI, 5.40-8.85; p<0.001), poorly differentiated carcinomas (OR 8.27, 95% CI, 4.67-14.66; p<0.001) and tumour budding (OR 4.59, 95% CI, 3.44-6.13; p<0.001) were significantly associated with lymph node metastases. The authors concluded that a more extensive resection accompanied by a lymph node dissection is necessary. Similarly, Wada et al. (2015) revealed two factors significantly associated with T1 colorectal cancer lymph node metastasis: lymphatic vessel invasion identified by an anti-human podoplanin antibody (Mantel–Haenszel OR 5.19, 95% CI 3.31–8.15, p=0.01) and tumour budding (OR 7.45, 95% CI 4.27–13.02, p=0.0077).

The completeness of the endoscopic excision appears to be the most reliable predictor of tumour recurrence and, although publications vary, current consensus is that a distance of less than 1 mm from the tumour to the margin of excision is associated with a high risk of cancer recurrence (CAP, 2017, RCPath, 2018).

Even when local excision margins are clear, a number of pathological features indicate a higher risk of recurrence or lymph node metastasis, and in such cases radical resection should be considered.

Local excision should only be performed in patients being treated with curative intent when a specimen of sufficient diagnostic quality can be obtained. The specimen should allow detailed pathologic examination including the criteria specified above, and should be discussed at a multidisciplinary team meeting (for both en-bloc and piecemeal resections). Availability of endoscopic photography may assist the multidisciplinary team meeting in evaluating the polyp.

Recommendation 2.2.9.1	**Grade**
In patients with early stage colon cancer treated with local excision, lesions should be assessed for depth of submucosal invasion, lymphovascular invasion, budding, grade of differentiation, and margin status.	**B**

Recommendation 2.2.9.2	**Grade**
Local resection colon cancer specimens both en-bloc and piecemeal resections, should be of sufficient quality to enable such assessment and should be discussed at a multidisciplinary team meeting.	**D**

Recommendation 2.2.9.3	Grade
Patient factors such as performance status, comorbidities, and informed patient preferences should be taken into consideration following multidisciplinary team discussion for decisions on further management.	D

Good Practice Point
Complex suspicious lesions should be discussed at a multidisciplinary team meeting, this may be required prior to endoscopic treatment depending on the individual lesion.

Good Practice Point
An attempt should be made to retrieve all resected tissue and the need for endoscopic reassessment should be discussed at a multidisciplinary team meeting.

2.2.10 Staging algorithm for patients with colon cancer and suspected hepatic metastases

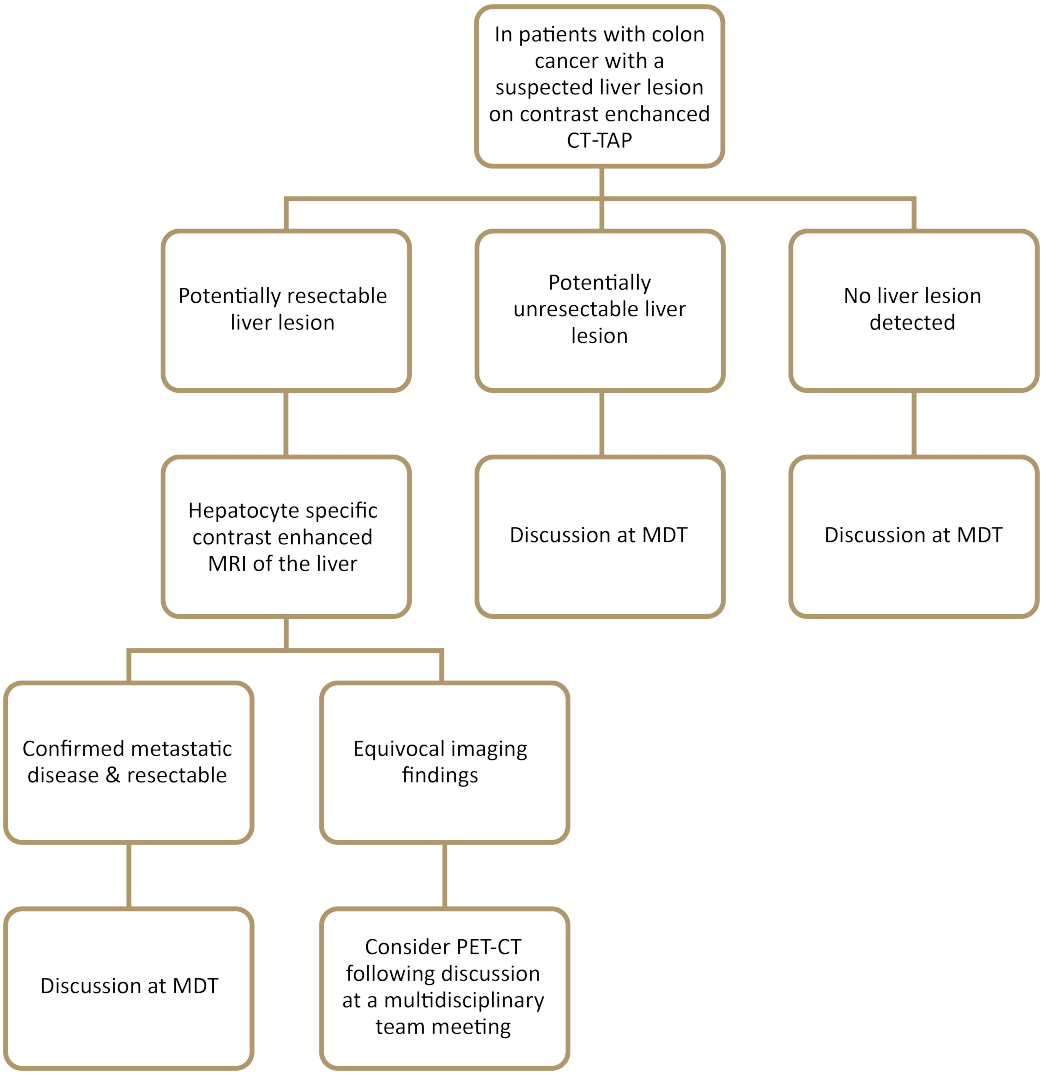


Figure 1 Staging algorithm recommended by the Guideline Development Group for patients with colon cancer and suspected hepatic metastases

2.3 Treatment: Emergency presentation

Responsibility for the implementation of recommendations regarding emergency presentation
While the CEO, General Manager and the Clinical Director of the hospital have corporate responsibility for the implementation of the recommendations in this National Clinical Guideline, each member of the multidisciplinary team is responsible for the implementation of the individual guideline recommendations relevant to their discipline.

Clinical question 2.3.1

In patients diagnosed with obstructive colon cancer, what is the role of stenting:

(i) when intention of treatment is curative?

(ii) when intention of treatment is palliative?

Evidence summary

Three meta-analyses (Allievi et al., 2017, Ceresoli et al., 2017, Ribeiro et al., 2018), an UpToDate review (Rodriguez-Bigas et al., 2020a) and three clinical guidelines (van Hooft et al., 2014, NCCN, 2020, NICE, 2020) addressed this clinical question.

In patients with colorectal cancer there are two major indications for colonic stenting:

- preoperative decompression in patients being treated with curative intent, and
- palliation in patients with advanced disease.

(i) Curative intent

An updated meta-analysis, including seven randomised controlled trials, found no difference in the mortality rate between the stent group and the emergency surgery group (Allievi et al., 2017). The incidence of postoperative complications was significantly reduced in the stent group compared to the emergency surgery group (37.84% vs. 54.87%, RR 0.6, 95% CI 0.38-0.96, p=0.02). Primary anastomosis rate was not significantly different between the groups but stoma rate was significantly reduced in the stenting as a bridge to surgery group (28.8% vs. 46.02%, p<0.0001). Technical and clinical success rate was reported at 78.83% and 75.23% respectively and the perforation rate was 5.89% (Allievi et al., 2017). Perforation of the tumour has led to two trials being closed prematurely (van Hooft et al., 2011, Pirlet et al., 2011). Stenting has no effect on mortality or recurrence (Ceresoli et al., 2017).

NICE (2020) recommend that either stenting or emergency surgery are offered to patients presenting with acute left-sided large bowel obstruction if potentially curative treatment is suitable. Patients need to be counselled regarding the risk of tumour perforation.

(ii) Palliative intent

Endoscopic or radiographic placement of self-expanding metal stent (SEMS) may achieve successful palliation of an obstructing or nearly obstructing tumour.

A meta-analysis including four randomised controlled trials (n=125 patients) in the palliative setting found no significant difference in 30-day mortality, mean survival days or adverse events between the emergency surgery and SEMS group (Ribeiro et al., 2018). Clinical success was higher in the emergency surgery group (96%) than in the SEMS group (84%) (Risk Difference (RD), −0.13, 95% CI −0.23 to −0.02, I^2: 51%). Permanent stoma rate was 84% in the emergency surgery group and 14.3% in the SEMS group (RR, 0.19, 95% CI 0.11-0.33, I^2: 28%).

Among the other advantages of SEMS over palliative surgery are a faster recovery time (permitting earlier administration of chemotherapy) and a shorter hospital stay (Tilney et al., 2007, Karoui et al., 2007, Vemulapalli et al., 2010). (Rodriguez-Bigas et al., 2020a)

SEMS are not appropriate in patients with right-sided colonic obstructions because of high complication rates, low success rate and more complicated stent insertion and they are contraindicated where there is evidence of perforation or peritonitis because these patients need immediate surgery.

Another potential complication includes stent migration. According to the European Society of Gastrointestinal Endoscopy (ESGE) SEMS placement is strongly discouraged for patients who are being treated or considered for further treatment with antiangiogenic drugs (bevacizumab) due to the risk of perforation (van Hooft et al., 2014). The NCCN (2020) panel also cautions that the use of bevacizumab in patients with colon or rectal stents is associated with a possible increased risk of bowel perforation (Small et al., 2010, Cennamo et al., 2009).

Recommendation 2.3.1.1	Grade
Curative intent In patients with obstructing colon cancer colonic stenting as a bridge to surgery may be considered in selected patients.	C

Recommendation 2.3.1.2	Grade
Palliative intent Colonic stenting should be considered for the palliation of patients with obstructing colon cancer (i.e. In those who are not fit for immediate resection or in those with advanced disease).	C

Good Practice Point
Every patient presenting with obstructing colon cancer should have access, through inter hospital referral where necessary, to an emergency service to provide colonic stenting where appropriate.

Good Practice Point
The risk of colonic perforation should be taken into account in every patient undergoing stenting.

2.4 Treatment: Surgical techniques

Responsibility for the implementation of recommendations regarding surgical techniques
While the CEO, General Manager and the Clinical Director of the hospital have corporate responsibility for the implementation of the recommendations in this National Clinical Guideline, each member of the multidisciplinary team is responsible for the implementation of the individual guideline recommendations relevant to their discipline.

Clinical question 2.4.1

In patients diagnosed with colon cancer, what is the evidence for specific surgical techniques and the effectiveness of these techniques on patient outcomes?

Evidence summary

Five meta-analyses (Theophilus et al., 2014, Di et al., 2013, Rondelli et al., 2012, Chang et al., 2015, Lim et al., 2016), a randomised trial (Deijen et al., 2017) and a guideline (NCCN, 2020) addressed this clinical question.

Laparoscopic versus open approach

In appropriate patients, minimally invasive and open colectomy are equivalent in terms of cancer outcome. Both approaches provide similar long-term outcomes with respect to local recurrence and 5-year survival in patients with colon cancer (Theophilus et al., 2014, Di et al., 2013).

Di et al. (2013) found no significant differences between minimally invasive colectomy and open colectomy in terms of overall mortality (RR, 0.94, 95% CI 0.82-1.09, p=0.23, I^2 = 21%), total recurrence rate (RR, 0.94, 95% CI 0.81-1.10, p=0.24, I^2 = 27%), 5-year tumour free survival rate (RR, 1.00, 95% CI 0.94-1.06), p=0.96, I^2 = 0%) and overall 5-year survival (RR, 1.02, 95% CI 0.97-1.07, p=0.55, I^2 = 0%).

Similarly, Theophilus et al. (2014) demonstrated that overall survival was equivalent (HR, 0.93, 95% CI 0.80–1.07). With each of the cancer stages, I–III, there was no difference in 5-year survival.

The 10 year follow up of Dutch patients from the COLOR trial was reported (Deijen et al., 2017) and found that overall survival rates were 48.4 in the laparoscopic group and 46.7 %, in the open group (difference 1.7 %, 95 % CI -10.6 to 14.0, p=0.83). However it must be noted that this study was not powered for a 10-year follow-up period.

Minimally invasive right colectomy results in less blood loss, a shorter length of hospital stay and lower postoperative short-term morbidity compared with open right colectomy (Rondelli et al., 2012).

The NCCN panel recommends that minimally invasive colectomy be considered only by surgeons experienced in the techniques. A thorough abdominal exploration is required as part of the procedure. Routine use of minimally invasive colon resection is generally not recommended for tumors that are acutely obstructed or perforated or tumors that are clearly locally invasive into surrounding structures (i.e., T4). Patients at high risk for prohibitive abdominal adhesions should not have minimally invasive colectomy, and those who are found to have prohibitive adhesions during exploration should be converted to an open procedure (Ota et al., 1994, Nelson et al., 1995, Wishner et al., 1995). (NCCN, 2020)

Robot-assisted laparoscopic versus conventional laparoscopic resection

A meta-analysis has demonstrated that where the technology is available, robotic surgery appears to provide similar short term advantages to laparoscopic surgery – shorter hospital stay, reduced morbidity and quicker return of GI function (Chang et al., 2015). In several studies, length of stay appears to be shorter in the robotic surgery group (Chang et al., 2015), however, time in theatre was significantly longer (Lim et al., 2016). Long term outcomes comparisons, including cancer related outcomes, are not yet available for robotic surgery.

Recommendation 2.4.1.1	Grade
In patients diagnosed with colon cancer minimally invasive colectomy/partial colectomy by an experienced laparoscopic surgeon should be considered in appropriate patients.	A

Good Practice Point

Surgeons undertaking colon cancer surgery should participate in a multidisciplinary team meeting and should audit surgical morbidity and mortality.

Good Practice Point

In patients undergoing minimally invasive colectomy/partial colectomy oncological outcomes should be the subject of a national audit.

Good Practice Point
Patients with colon cancer should have access to a colorectal clinical nurse specialist.

Good Practice Point
Minimally invasive surgery requires HD laparoscopic equipment and an experienced theatre team.

Clinical question 2.4.2

In patients diagnosed with colon cancer, what is the evidence for complete mesocolic excision (CME) during curative resection?

Evidence summary

The Guideline Development Group defines complete mesocolic excision as a careful sharp dissection in a plane that ensures an intact mesocolon. The potential benefit of an extended lymphadenectomy (D3) versus less extensive (D2) lymphadenectomy remains to be defined.

Three meta-analyses (Killeen et al., 2014, Kontovounisios et al., 2015, Wang et al., 2017) and two retrospective cohort studies (Bertelsen et al., 2016, Bertelsen et al., 2019) addressed this clinical question.

Meta-analyses by Killeen et al. (2014), Kontovounisios et al. (2015) and Wang et al. (2017) have stated similar conclusions that there is insufficient, consistent high quality evidence to recommend widespread adoption of CME.

Of the evidence that is available, some show trends towards increased survival and decreased recurrence but others fail to demonstrate a difference. A recent cohort study identified a possible survival advantage of CME (Bertelsen et al., 2019), however the study design and lack of adequate controls challenge such a conclusion. Future studies may more clearly define the role of D2 vs D3 lymphadenectomy in CME.

A population-based study by Bertelsten et al. (2016) analysing 529 patients who underwent laparoscopic CME surgery and 1,701 patients who underwent laparoscopic 'conventional' resection were not consistent. Despite higher risk of injury to the superior mesenteric vein (1.7% vs. 0.2%, $p<0.001$), spleen (3.2% vs. 1.2%, $p=0.004$) and other organs (9.1% vs. 3.6%, $p<0.001$) as well as the risk of postoperative respiratory failure (8.1% vs. 3.4%, $p<0.001$) and sepsis (6.6% vs. 3.2%, $p=0.001$) in patients undergoing CME, the study did not show a statistically significant increased risk in 30-day (4.2% vs. 3.7%, $p=0.605$) or 90-day (6.6% vs. 4.9%, $p=0.219$) mortality after CME compared with 'conventional' surgery.

A systematic review by Kontovounisios et al. (2015) found that some studies demonstrate that CME is associated with increased lymph node harvest (Bertelsen et al., 2011, West et al., 2010) and others report an improvement in the quality of the specimen as assessed by histopathological examination (Hashiguchi et al., 2011, West et al., 2008), implying a survival advantage.

In summary, there is some evidence of an increased tendency for morbidity following CME and a potentially long-term survival advantage however the quality of the evidence is weak and inconsistent. A more definitive evidence base is awaited.

Recommendation 2.4.2.1	**Grade**
In patients with colon cancer dissection in the mesocolic plane is essential for good oncologic outcomes.	**B**

Recommendation 2.4.2.2	**Grade**
In patients with colon cancer undergoing curative resection the role of extended lymphadenectomy remains uncertain.	**C**

Good Practice Point

The number of patients receiving a complete mesocolic excision and their oncological outcomes and morbidity may be an appropriate subject for national audit.

Good Practice Point

Morphology of the operative specimen should be recorded (i.e. photography).

Clinical question 2.4.3

In patients with unresectable metastases from colon cancer, does resection of the primary tumour improve life expectancy and/or quality of life?

Evidence summary

A meta-analysis (Clancy et al., 2014) and an UpToDate review (Rodriguez-Bigas et al., 2020b) addressed this clinical question.

Initial management of the primary site in patients who present with unresectable metastases should be individualised. Patients with a right-sided colonic tumour and metastatic disease present a particular challenge as endoscopic stenting is often not possible.

Evidence for this question was found in the largest meta-analysis of studies to date, comparing resection to chemotherapy alone, in stage IV disease (Clancy et al., 2014). The results suggested that patients with stage IV disease undergoing primary resection of colonic and rectal tumours may have a survival benefit. While the evidence specific to tumour site is lacking the Guideline Development Group has extrapolated its findings from pooled data.

The meta-analysis, which included 21 studies (44,226 patients), demonstrated a six month survival advantage in patients undergoing resection of a primary colorectal tumour when compared to chemotherapy alone. The authors of the meta-analysis suggest a selection bias towards resection of primary colon tumours versus rectal resection. Patients undergoing resection were more likely to have metastatic disease confined to the liver, single metastases, and tumors located in the colon. Patients with multiple metastases in locations other than the liver were more likely to receive only chemotherapy. It was also likely that those with advanced rectal tumors more commonly underwent palliative surgical procedures such as stoma formation rather than resection (Clancy et al., 2014).

Resection of the primary tumour in patients with unresectable metastases compared with chemotherapy alone was associated with a lower mortality risk (OR 0.28, 95% CI 0.165–0.474, p<0.001), translating into a difference in mean survival of 6.4 months in favour of resection (95% CI 5.025–7.858, p<0.001). Patients who underwent resection of the primary tumour were more likely to have liver metastasis only (OR 1.551, 95 % CI 1.247–1.929, p<0.001), were less likely to have ≥2 metastasis (OR 0.653, 95 % CI 0.508–0.839, p=0.001), and were less likely to have rectal cancer (OR 0.495, 95 % CI 0.390–0.629, p<0.001). The authors indicate that significant cross-study heterogeneity was observed and a selection bias may be present. (Clancy et al., 2014)

Regardless of the method of surgical palliation, the laparoscopic approach to colorectal resection is preferred to minimise the risk of postoperative complications (Hida et al., 2012). (Rodriguez-Bigas et al., 2020b)

The Guideline Development Group agree that there is a body of literature on both sides of this issue (pro and con resection of the primary colonic tumour) and inherent case selection bias, tumor heterogeneity, differences in metastatic burden etc makes it impossible to have a uniform policy for resection.

Recommendation 2.4.3.1	Grade
Patients with metastatic disease deemed unresectable, and a colon primary, should be discussed at a multidisciplinary team meeting with appropriate surgical expertise prior to undergoing any treatment except in the presence of a surgical emergency.	D

Good Practice Point

Shared decision making approach should be undertaken with the patient, especially in the setting of metastatic disease.

2.5 Treatment: Palliative care

Responsibility for the implementation of palliative care recommendations
While the CEO, General Manager and the Clinical Director of the hospital have corporate responsibility for the implementation of the recommendations in this National Clinical Guideline, each member of the multidisciplinary team is responsible for the implementation of the individual guideline recommendations relevant to their discipline.

Clinical question 2.5.1

When should palliative care be introduced for patients with cancer?

Evidence summary

Palliative care is an approach that improves the quality of life of people and their families facing the problems associated with life-limiting illness, through the prevention and relief of suffering by means of early identification and impeccable assessment and treatment of pain and other problems, physical, psychosocial and spiritual (World Health Organization, 2014). It is a vital and integral part of all clinical practice.

When combined with standard cancer care or as the main focus of care, palliative care leads to better patient and caregiver outcomes. These include improvement in symptoms, quality of life (QOL), and patient satisfaction, with reduced caregiver burden. Earlier involvement of palliative care also leads to more appropriate referral to and use of hospice, and reduced use of futile intensive care (Smith et al., 2012). No trials to date have demonstrated harm to patients and caregivers from early involvement of palliative care (Smith et al., 2012).

A 2013 literature review on the cost and cost-effectiveness of palliative care found that despite wide variation in study type, characteristics and study quality, there are consistent patterns in the results. Palliative care is most frequently found to be less costly relative to comparator groups, and in most cases, the difference in cost is statistically significant. (Smith et al., 2014)

Good clinical practice dictates that assessment of palliative care needs should be an ongoing process throughout the course of a patient's illness; assessments should be carried out at key transition points in the patient pathway, for example:

- At diagnosis of a life-limiting condition
- At episodes of significant progression/exacerbation of disease
- A significant change in the patient's family/social support
- A significant change in functional status
- At patient or family request
- At end of life. (HSE, 2014)

Palliative care services should be structured in three levels of ascending specialisation according to the expertise of the staff providing the service (Department of Health, 2001):

- Level one (Palliative Care Approach): Palliative care principles should be appropriately applied by all healthcare professionals.
- Level two (General Palliative Care): At an intermediate level, a proportion of patients and families will benefit from the expertise of healthcare professionals who, although not engaged full time in palliative care, have had some additional training and experience in palliative care.
- Level three (Specialist Palliative Care): Specialist palliative care services are those services whose core activity is limited to the provision of palliative care.

All patients should be able to engage easily with the level of expertise most appropriate to their needs.

Recommendation 2.5.1.1	**Grade**
For patients with cancer, early provision of palliative care can improve patient outcomes.	**C**

Recommendation 2.5.1.2	**Grade**
Assessment of palliative care needs should be an ongoing process throughout the course of a patient's cancer illness and services provided on the basis of identified need.	**D**

Good Practice Point

Palliative care specialist services should be an integral part of the colorectal cancer multidisciplinary team meeting.

3 Development of this National Clinical Guideline

3.1 Epidemiology

3.1.1 Incidence

The estimated annual average incidence for colorectal cancer in Ireland between 2018 and 2020 was 2,818 cases per annum (Table 5), which represents 11.4% of invasive cancers (excluding non-melanoma skin cancer) (NCRI, 2020).

Table 5 Estimated annual average incidence for colorectal cancer in Ireland, 2018-2020 (NCRI, 2020)

Colorectal Cancer	Cases		
	Males	Females	Total
Colon C18*	1,038	853	1,891
Rectosigmoid junction C19*	108	79	187
Rectum C20*	487	253	740
Total	1,633	1,185	2,818

*C18 – malignant neoplasm of colon; C19 – malignant neoplasm of rectosigmoid junction; C20 – malignant neoplasm of rectum.

In 2020, the European Cancer Information System (ECIS) estimated that the age-standardised incidence rate of colorectal cancer in males in Ireland of 68.1 per 100,000 was 17% higher than the EU27 rate of 58.2 per 100,000, while the estimated age-standardised incidence rate in females in Ireland of 43.7 per 100,000 was 19.7% higher than the EU27 rate of 36.5 per 100,000 (ECIS, 2020).

Table 6 shows the annual average estimated percentages and rank of the most commonly diagnosed invasive cancers in Ireland from 2018-2020. Excluding non-melanoma skin cancer, colorectal cancer was the 2nd most common cancer in males, making up 12% of all cancers (age-standardised rate per 100,000 was 58.3), and the 3rd most common cancer in females making up 10% of all cancers (age-standardised rate per 100,000 was 38.3)(NCRI, 2020).

Table 6 Estimated percentage and ranking among total cancer incidences of the most commonly diagnosed invasive cancers (excluding non-melanoma skin cancers) in Ireland, 2018-2020 (NCRI, 2020)

Invasive Cancer	Males		Females	
	%	Rank	%	Rank
Prostate	29.6	1	-	-
Breast	-	-	31.5	1
Colorectal	12.4	2	10.1	3
Lung	11.4	3	10.7	2

3.1.2 Mortality

The annual average number of deaths from colorectal cancer (C18-21) in Ireland from 2015-2017 was 1,025 (605 males; 420 females), which represented 11.0% of all registered cancer deaths (Table 7) (NCRI, 2020).

Table 8 shows the average annual estimated percentages and rank of the most common causes of cancer death in Ireland from 2015-2017. Colorectal cancer was the second most common cancer death in males and the third most common cancer death in females (NCRI, 2020).

Table 7 Annual average mortality rate from colorectal cancer, 2015-2017 (NCRI, 2020)

	Death		Rate/100,000*	
	Males	**Females**	**Males**	**Females**
Colorectum and anus (C18-21)	605	420	23.5	13.4

*Rates are standardised to the 1976 European standard population

Table 8 Percentage and ranking of the most common cancer deaths in Ireland, 2015-2017 (NCRI, 2019a)

	Males		Females	
	%	Rank	%	Rank
Lung	22.1	1	19.7	1
Colorectal	12.3	2	9.7	3
Prostate	11.0	3	-	-
Breast	-	-	16.9	2

In 2020, the estimated age-standardised mortality rate of colorectal cancer in males in Ireland of 26.5 per 100,000 was 7.7% higher than the EU27 rate of 24.6 per 100,000, while the estimated age-standardised mortality rate in females in Ireland of 15.7 per 100,000 was 12.1% higher than the EU27 rate of 14.0 per 100,000 (ECIS, 2020).

3.1.3 Survival

According to the latest NCRI statistics, the estimated complete prevalence of colorectal cancer at the end of December 2018 was 22,738 (12,427 males; 10,310 females) (Table 9). Overall, colorectal cancer is the third most common cancer in the prevalent cancer population (12% of all cancer survivors) after breast (23%) and prostate (21%) (NCRI, 2020).

The estimated five-year net survival (age-standardised) for patients with colorectal cancer during the period 2012-2016 was 64% (NCRI, 2020).

Table 9 Estimated complete prevalence of colorectal cancer on 31st December 2018, by age and sex (NCRI, 2020)

	Males		Females		All	
Age	n	%	n	%	n	%
<50	677	5	894	9	1,570	7
50+	11,751	95	9,417	91	21,167	93
All	12,427	100.0	10,310	100.0	21,738	100.0

3.1.4 Cancer trends and projections 2020-2045

Annual numbers of cases of colon cancer are projected to increase in males from 1,021 in 2015 to 2,196 in 2045 (+115%) and in females from 776 in 2015 to 1,617 in 2045 (+108)- an increase of 3,813 overall (+112) (NCRI, 2019b).

Compared to the demographic projections, the median projections suggest a similar increase for both males and females. For males, cases are projected to increase to 2,338 in 2045 (+129%) and for females to 1,662 (+114%) which is a 123% increase (to 4,000 cases) for both sexes combined (NCRI, 2019b).The median age-standardised rates are projected to increase by 5% by 2045, giving a rate of 42 per 100,000.

Table 12 shows the projected numbers of incident cases of colon cancer up to the year 2045, estimating increased incidence rates of 129% and 114% for males and females respectively by the year 2045 compared to 2015, based on the median of five models projection estimates and demographic estimates (NCRI, 2019b).

Table 12 Projected numbers of incident cases 2020-2045 (with % increase compared to 2015): cancer of the colon (NCRI, 2019b)

Cancer of the Colon (C18)				
Year	Projected numbers of incident cases 2020-2045 (based on median of 5 models and demographic projections)		% increase compared to 2015	
	Males	**Females**	**Males**	**Females**
2020	1,183	897	16	16
2025	1,399	1,034	37	33
2030	1,628	1,184	59	53
2035	1,866	1,341	83	73
2040	2,104	1,501	106	93
2045	2,338	1,662	129	114

3.2 Rationale for this National Clinical Guideline

The National Cancer Strategy (Department of Health and Children (DoHC), 2006) recommended that national tumour site-specific multidisciplinary groups be convened to develop national evidence-based clinical guidelines for cancer care.

The National Cancer Strategy 2017-2026 (Department of Health, 2017) recommends: *The NCCP will develop further guidelines for cancer care in line with National Clinical Effectiveness Committee (NCEC) standards.*

The purpose of developing these guidelines is to improve the quality of care delivered to patients.

Colon cancer is distinct from rectal cancer, with different aetiologies and risk factors. The treatment for colon cancer can require highly specialised care and can cause a number of cancer specific issues for patients which require expert management to provide the best outcomes. The diagnosis, staging, and treatment of patients with colon cancer requires multidisciplinary care in an acute hospital setting. The majority of patients will require diagnostic tests (radiology, pathology) and depending on the treatment plan may require surgery, radiotherapy and chemotherapy. When centralisation of surgical services takes place, colon cancer surgery will be performed in a number of designated cancer centres who will provide the multidisciplinary team expertise and poses the specialist facilities required to manage this type of cancer. As a result, the Guideline Development Group made the decision to develop an individual guideline which dealt specifically with colon cancer.

3.3 Aims and objectives

The overall objectives of the NCCP's National Clinical Guideline 'Diagnosis, staging and treatment of patients with colon cancer' are outlined below, along with the clinical question number that addresses the specific aim. The recommendations within this guideline relate to the clinical treatment of cancer and do not provide specific guidance on nutritional intervention, physical rehabilitation or full multidisciplinary management of patients with colon cancer. The guideline is based on the best research evidence in conjunction with clinical expertise, and developed using a clear evidence-based internationally used methodology.

- Improvement in patient outcomes including potential for reduction in morbidity and mortality, improvement in quality of life (Clinical Questions 2.3.1, 2.4.1, 2.4.2, 2.4.3),
- Promotion of interventions of proven benefit and discouragement of ineffective interventions,

improvement in standard of care (Clinical Questions 2.2.1, 2.2.2, 2.2.3, 2.2.4, 2.2.5, 2.2.6, 2.2.7, 2.2.8, 2.2.9),
- Improvement in consistency of care, and reduce variation in practice (Clinical Questions 2.2.5, 2.2.6, 2.2.7, 2.2.8, 2.2.9),
- To address areas of clinical care with new and emerging evidence (Clinical Questions 2.2.6),
- Potential to have the most impact (on patients and resources) (Clinical Questions 2.2.2, 2.5.1).

3.4 Financial impact of colon cancer

A population-based cost analysis (Luengo-Fernandez et al., 2013) illustrated the economic burden of cancer on the European Union (EU). In 2009, cancer is estimated to have cost the EU €126 billion, with healthcare costs accounting for €51 billion (40%). Across the EU, the cost of cancer healthcare was equivalent to €102 per person, but varied substantially from €33 per person in Lithuania to €171 per person in Germany.

In Ireland, inpatient care costs were estimated to account for €417 million of cancer-related healthcare costs out of a total of €619 million. Drug expenditure accounted for a further €127 million while primary, outpatient and emergency care were estimated at €32 million, €30 million and €13 million respectively (Luengo-Fernandez et al., 2013). Across the EU, healthcare costs per person were estimated to cost between €1 and €22 for colorectal cancer (€15 per person in Ireland) (Luengo-Fernandez et al., 2013). With colon cancer incidence expected to increase by 129 % in males and 114 % in females by 2045 (NCRI, 2019b), there could be a significant increase seen in healthcare costs per person in Ireland.

The costs of colorectal cancer related informal care and productivity losses were estimated at €2.84 billion and €3.77 billion, respectively (Luengo-Fernandez et al., 2013).

A recent productivity loss analysis carried out in an Irish context (Pearce et al., 2016) projected that by 2030, premature death as a result of colorectal cancer will cause a value of €237,664 lost production per household and an overall productivity loss per population of 1.3 billion.

The resource implications of implementing the recommendations within the guideline were identified by the clinicians during meetings to discuss and develop the recommendations (Appendix 6: and Appendix 7: Implementation plan).

Healthcare investment of €2.7 million over three years is required to implement the recommendations of this guideline. However, this estimate does not include the cost for centralisation of cancer surgical services and workforce planning. The NCCP in partnership with the Department of Health and the HSE Acute Hospital Services will be in a position to provide more accurate costing for this area once the project to centralise cancer services is complete in late 2020.

A number of the recommendations made within the surgical section can be implemented by centralising the service which would take into consideration staffing, expertise, infrastructure and equipment requirements. By adopting novel surgical techniques as recommended, length of hospital stay could be reduced resulting in a cost-saving, which is currently unknown.

Much of the budget is required to ensure adequate availability of the different radiological modalities to appropriately diagnose stage and restage disease in patients with colon cancer. €1,418,250 is required for contrast enhanced CT-TAP, €753,480 is required to adequately finance the use of MRI while CT colonography requires €544,500 in funding for this patient population.

Importantly, by implementing the recommendations of this guideline, the misuse of PET-CT as a first line staging modality for colon cancer can be reduced, resulting in a potential cost-saving. The recommendations relating to pathology, gastroenterology, and radiation oncology are mostly current practice and do not require any further healthcare investment outside of what is already provided via normal service planning.

3.5 Guideline scope

3.5.1 Target population

Patients that are covered by this guideline are:

- Adults (18 years or older) that have a suspected diagnosis of colon cancer
- Adults with newly diagnosed colon cancer, early and locally advanced colon cancer.

3.5.2 Target audience

This guideline is intended for all health professionals involved in the diagnosis, staging and treatment of patients with colon cancer. While the CEO, General Manager and the Clinical Director of the hospital have corporate responsibility for the implementation of the recommendations in this Clinical Guideline, each member of the multidisciplinary team is responsible for the implementation of the individual guideline recommendations relevant to their discipline.

This guideline is also relevant to those involved in clinical governance, in both primary and secondary care, to help ensure that arrangements are in place to deliver appropriate care for the population covered by this guideline.

Whilst the guideline is focused on clinical care, it is expected to be of interest to patients diagnosed with colon cancer and their significant others. A list of medical abbreviations used throughout the guideline can be found in Appendix 9: Glossary of terms and abbreviations.

3.6 Conflicts of interest statement

A conflict of interest form developed by the NCEC was signed by all Guideline Development Group members and the national/international reviewers. The Guideline Development Group was managed by the Chair to promote the highest professional standard in the development of this guideline.

Any member of the Guideline Development Group who declares a COI is not permitted to attend a recommendation meeting where their stated conflict is relevant to the evidence being reviewed or which may influence any recommendation being generated. All research evidence along with an assessment of its quality is presented to the Guideline Development Group members by the research members. Membership of colleges or professional bodies do not represent a conflict in this guideline. No specific pharmaceutical devices, products or equipment are specified in these guidelines and no items were discussed which where relevant to any conflicts declared. Conflicts of interests declared by members of the Guideline Development Group are described in Table 10.

Table 10 Conflicts of interests declared by members of the Guideline Development Group

Guideline Development Group Member	Detail of conflict declared
Professor Debbie McNamara	RCSI Council member and Co-Lead National Clinical Programme for Surgery.
Professor Padraic MacMathuna	Member of BowelScreen Clinical Advisory Group.
Dr Brian O' Neill	Principal investigator of a national rectal cancer trial TRILARC with cancer trials Ireland. This is a randomised trial comparing 3D-CRT with IMRT for locally advanced rectal cancer.
Professor Kieran Sheahan	Consultancy work for Roche Diagnostics, research sponsorship by Roche Diagnostics, research sponsorship by Genomics Medicine Ireland.

3.6.1 Governance

Governance of the guideline development process was provided by a multidisciplinary Guideline Steering Group which was chaired by the Director of the NCCP. Details of Guideline Development Group members are provided at the beginning of the document and details of the Guideline Steering Group members are available in Appendix 1: Guideline Development Group terms of reference.

The Guideline Development Group was responsible for the development and delivery of the National Clinical Guideline and included representatives from relevant professional groups (radiology, pathology, surgeons, gastroenterologists, and radiation oncologists) with expertise in the diagnosis, staging and treatment of patients with colon cancer. The Guideline Development Group also included a project manager, a methodologist, research officers, a health economist and a number of clinical librarians.

3.7 Sources of funding

The guideline was commissioned and funded by the NCCP; however, the guideline content was not influenced by the NCCP or any other funding body. This process is fully independent of lobbying powers. All recommendations were based on the best research evidence integrated with clinical expertise.

3.8 Guideline methodology

The methodology for the development of the guideline was designed by a research methodologist and is based on the principles of Evidence-Based Practice (EBP)(Sackett et al., 2000). The methodology is described in detail in the NCCP Methodology Manual for guideline development and is available on the NCCP website. This manual adheres to the standards outlined in the NCEC Guideline Development Manual. Figure 2 outlines the stages of guideline development.

3.8.1 Step 1: Formulate the clinical questions

Guideline Development Group members met and through clinician led experience identified areas of new and emerging evidence or areas where there was variance in practice and formulated the list of clinical questions. These questions then formed the basis for the types of evidence being gathered, the search strategy, and the inclusion and exclusion criteria.

To formulate the clinical questions they were broken down into their component parts using the PICO(T) framework:

- Participant/Population
- Intervention/Exposure
- Control/Comparison
- Outcome
- Time

This process was carried out by discipline specific sub-groups. The Guideline Development Group signed off the entire list of clinical questions to ensure a comprehensive guideline. The resulting 13 clinical questions are listed in Appendix 2: Clinical and economic questions in PICO format.

3.8.2 Step 2: Search methodology

The clinical questions formulated in step one were used to conduct literature searches of the primary literature. The systematic literature review protocol was developed for the guideline development process by the HSE librarians in conjunction with the NCCP (Appendix 4: Systematic literature review protocol). The following bibliographic databases were searched in the order specified below using keywords implicit in the PICO(T) question and any identified subject headings:

- Cochrane Library
- Point-of-Care Reference Tools

- Medline
- Embase (where available)
- Other bibliographic databases such as PsycINFO, CINAHL, as appropriate.

The literature was searched based on the hierarchy of evidence. The search strategies for all clinical questions and the five economic questions in the budget impact assessment are available on request by contacting the NCCP at guidelines@cancercontrol.ie

3.8.3 Step 3: Screen and appraise the evidence

International guidelines were appraised using the international, validated tool the AGREE II instrument (Brouwers et al., 2010). Primary papers were appraised using validated checklists developed by the Scottish Intercollegiate Guideline Network (SIGN).

Economic papers included in the Budget Impact Assessment (Appendix 6: Economic assessment) were appraised by a health economist using validated economic checklists developed by SIGN. There were three main points considered when appraising all the research evidence:

- Are the results valid? (internal validity)
- What are the results? (statistical and clinical significance)
- Are the results applicable/generalisable to the patient/population of this guideline? (external validity)

After literature appraisals were completed, the data selected for possible inclusion in the guideline were compiled in the data extraction tables by the research officers. The data extraction tables are available upon request.

3.8.4 Step 4: Formulation and grading of recommendations

The evidence which addressed each clinical question, both from international guidelines and primary literature, was extracted into evidence tables. Recommendations were formulated through a formal structured process. A 'considered judgment form' (adapted from SIGN) was completed for each clinical question.

The following items were considered and documented:

- What evidence is available to answer the clinical question?
- What is the quality of the evidence?
- Is the evidence consistent?
- Is the evidence generalisable to the Irish population?
- Is the evidence applicable in the Irish context?
- What is the potential impact on the health system?
- What is the potential benefit versus harm to the patient?
- Are there resource implications?

The evidence summaries and recommendations were then written. Each recommendation was assigned a grade by the Guideline Development Group. The grade reflected the level of evidence upon which the recommendations were based, the directness of the evidence, and whether further research is likely to change the recommendation. The levels of evidence tables and grading systems used are documented in Appendix 10: Levels of evidence and grading systems.

Good Practice Points are intended to assist guideline users by providing short pieces of advice which may not have an evidence base, but which are seen as essential to good clinical practice (SIGN, 2015). The Good Practice Points presented in this clinical guideline were based on the clinical expertise of the Guideline Development Group. For the economic literature, key messages are presented in boxes entitled 'relevance to the guideline recommendations'.

Practical considerations around patient care are statements developed through collaboration with patients and patient representative organisations on issues that were important to them with regards to their own experience of the diagnosis and staging of their cancer.

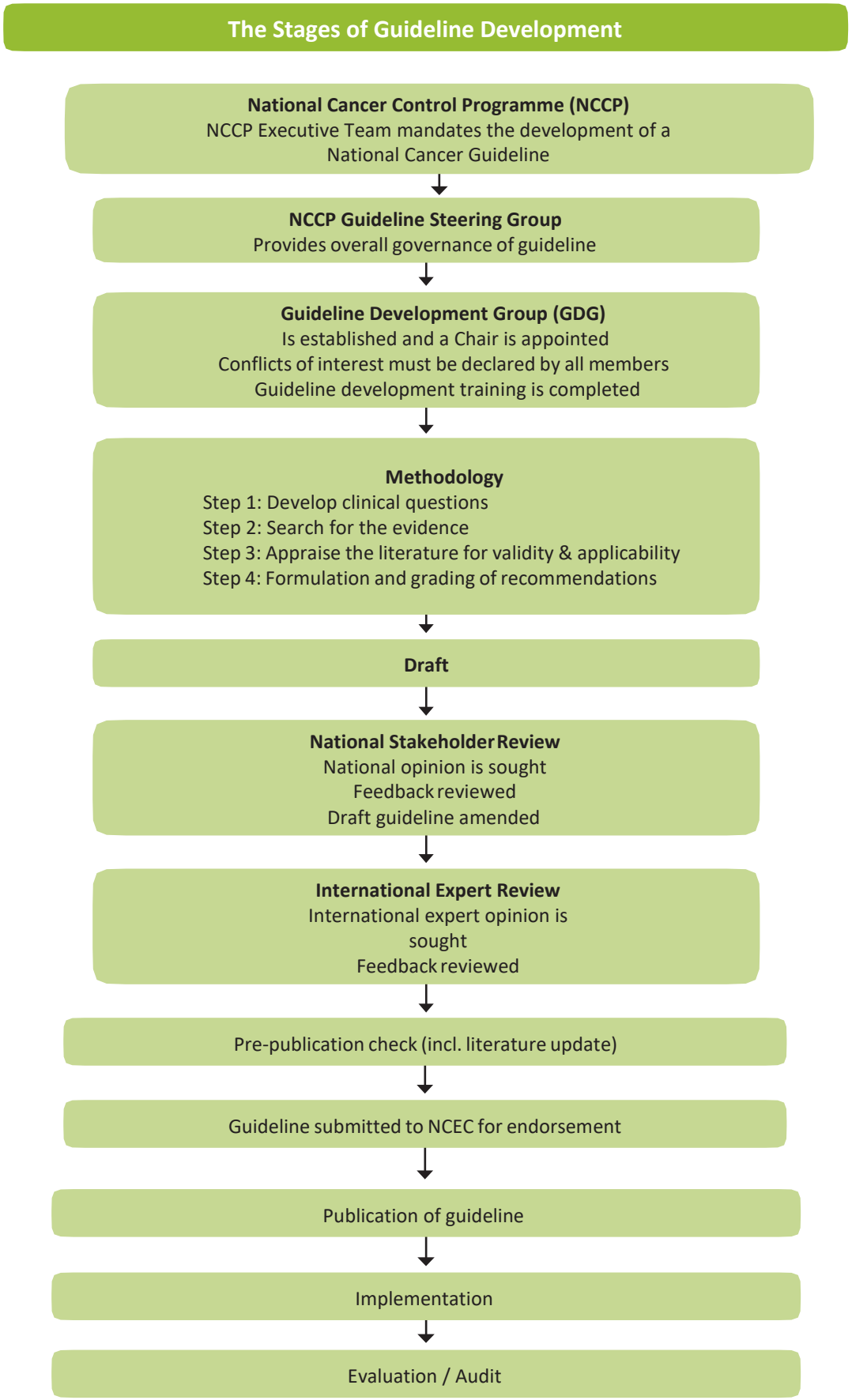


Figure 2 The stages of guideline development

3.9 Consultation process

The guideline was placed on the NCCP website and circulated for comment from the 17th of February 2020 to March 16th 2020. Stakeholders were asked to comment on the comprehensiveness of evidence used to form the recommendations. Stakeholders were required to submit feedback with supporting evidence on a form provided (see NCCP Methodology Manual) along with a completed conflict of interest form. A time-period of four weeks was allocated to submit comments. A list of stakeholders including groups, organisations and committees can be found in Appendix 5: Details of consultation process.

All feedback received was reviewed by the project managers and research team. Suggested amendments and supporting evidence were reviewed by the discipline specific subgroup and consensus reached to accept or reject the amendments. Amendments were rejected following discussion between members of the relevant subgroup(s) and in instances where no superior evidence was provided or no conflict of interest form was provided. All modifications were documented and the report is available upon request.

3.9.1 Patient involvement

The views and preferences of the target population were sought by inviting patient advocacy groups (HSE Patient Forum, Irish Cancer Society, Cancer Care West, Marie Keating Foundation, Gary Kelly Cancer Support Centre Purple House Support Centre and a number of nationwide stoma support groups) to engage in the National Stakeholder Review process (Appendix 5: Details of consultation process).

A number of cancer patients groups and charitable organisations were contacted and their patient representatives and family members were invited to engage with the NCCP and asked to provide feedback on issues important to them with regards to their own experiences of the diagnosis, staging and treatment of their colon cancer.

Three patients from various patient cancer organisations and charities provided feedback which included issues around quality of life and patient dissatisfaction. A list of practical considerations from a patient perspective was developed and this can be found in Section 2.1 Summary of clinical recommendations, practical considerations around patient care and summary of budget impact analysis.

3.9.2 Patient advocacy

A collaborative approach is used in the development of the NCCP patient information, clinical guidelines and other national projects. All NCCP booklets are submitted to the National Adult Literacy Agency (NALA) (www.nala.ie) for the Plain English Award. This is to ensure comprehension and readability is in line with health literacy best practice standards. Service user testing is a key part of the process, and includes liaising with the HSE Patient Forum, online surveys, and engaging with other relevant patient groups e.g. Irish Cancer Society, Marie Keating Foundation.

The NCCP in partnership with the Irish Cancer Society has commenced a cancer survivorship programme. The main goal for the NCCP Survivorship Programme is to empower patients to achieve their best possible health while living with and beyond a diagnosis of cancer. This involves providing information, guidance and support to survivors and their families and healthcare professionals in relation to healthy lifestyle, disease prevention and control. It aims to promote a good quality of life and prolonged survival for people who experience cancer.

3.10 External review

The draft guideline was submitted for international expert review. The Guideline Development Group nominated six international reviewers to provide feedback on the draft guideline. These reviewers were chosen based on their in-depth knowledge of the subject area and guideline development processes. The review followed the same procedure as the National Stakeholder Review. The guideline was circulated for comment from from 17th of February 2020 to March 16th 2020.

All feedback received was reviewed by the project managers and research team. Suggested amendments and supporting evidence were reviewed by the discipline specific subgroup and consensus reached to accept or reject the amendments. Amendments were rejected following discussion between members of the relevant subgroup(s) and in instances where no superior evidence was provided or no conflict of interest form was provided. All modifications were documented. A log was recorded of all submissions and amendments from the national stakeholder review and international expert review process and is available on request from the Guideline Development Group.

3.11 Plan to update this National Clinical Guideline

This guideline was published in December 2020 and will be considered for review by the NCCP in three years. Surveillance of the literature base will be carried out periodically by the NCCP. Any updates to the guideline in the interim period or as a result of three year review will be subject to the NCEC approval process and noted in the guidelines section of the NCCP and NCEC websites.

3.12 Implementation

The implementation plan (Appendix 7: Implementation plan) was developed based on the NCEC implementation guide (Department of Health, 2018). The implementation plan outlines the actions required to implement the recommendations, who has lead responsibility for delivering the action, the timeframe for completion and the expected outcomes of implementation.

This National Clinical Guideline including the implementation plan should be reviewed by the multidisciplinary team and senior management in the hospital to plan the implementation of the recommendations.

The CEO, General Manager and the Clinical Director of the hospital have corporate responsibility for the implementation of the National Clinical Guideline and to ensure that all relevant staff are appropriately supported to implement the guideline. A Cancer Network Manager from the NCCP meets with each cancer centre on a quarterly basis for performance monitoring and service planning.

The Colorectal Cancer Clinical Leads group will also have an important role in implementation of the recommendations contained in this guideline with regards to local clinical arrangements, clinical audit, sharing of good practice and problem solving.

All medical staff with responsibility for the care of patients with colon cancer are required to:

- Comply with this National Clinical Guideline and any related procedures or protocols.
- Adhere to their code of conduct and professional scope of practice guidelines as appropriate to their role and responsibilities.
- Maintain their competency for the management and treatment of patients with colon cancer.

This National Clinical Guideline will be circulated and disseminated through the professional networks who participated in developing and reviewing this document. The guideline will also be available on the NCEC and NCCP websites. A multidisciplinary team is responsible for the implementation of the guideline recommendations.

A summary of tools to assist in the implementation of this National Clinical Guideline are available in Appendix 3: Supporting tools.

3.12.1 Dissemination and communication plan

The National Clinical Guideline will be circulated and disseminated through the professional networks who participated in developing and reviewing this guideline (HSE Clinical Programmes in Surgery, Radiology, and Palliative Care, RCSI, HSE Patient Forum, Irish Cancer Society, Cancer Care West etc.). The guideline will also be available via the NCEC and NCCP websites.

The NCCP will co-ordinate with HSE Communications to distribute, share and disseminate through the media (HSE Broadcast, Health Matters, and Twitter). The guideline will be officially launched and circulated to all relevant faculties and colleges for dissemination to their members. The implementation of the guideline will also be supported by communication, training and education.

Potential dissemination and communication strategies:

- Create slide for inclusion in presentations by clinical leads, subgroup chairs, NCCP Director around published guidelines.
- Included link to guidelines in NCCP email signatures.
- Liaise with cancer voluntary support groups, organisations and charities to ensure guidelines are represented in their patient and public information.

- Promote through NCCP website and social media.
- Direct communication from NCCP Director/CCO/Acute Operations to hospital managers raising awareness and setting out expectations/actions.
- Include discussion on implementation at launch.

3.13 Monitoring and audit

The NCCP engages regularly with the individual cancer centres and with Hospital Group structures. Discussion of performance data, improvement plans, resources including manpower, service planning and development takes place at regular review meetings between the NCCP and senior management at cancer centre and Hospital Group level.

It is important that both the implementation of the guideline and patient outcomes are audited to ensure that this guideline positively impacts on patient care. For audit criteria see Appendix 8: Monitoring and audit.

3.14 Recommendations for research

The following areas have been identified by the Guideline Development Group that requires further research:

Recommendation 2.2.6.1
In patients undergoing surgery with colon cancer, it is recommended to identify as many nodes as possible, all of which should be submitted for microscopic examination/evaluation. Overall, the median for the laboratory should be at least 12.

4 Appendices

Appendix 1: Guideline Development Group terms of reference and logic model

Membership of the Guideline Development Group is outlined at the beginning of this document.

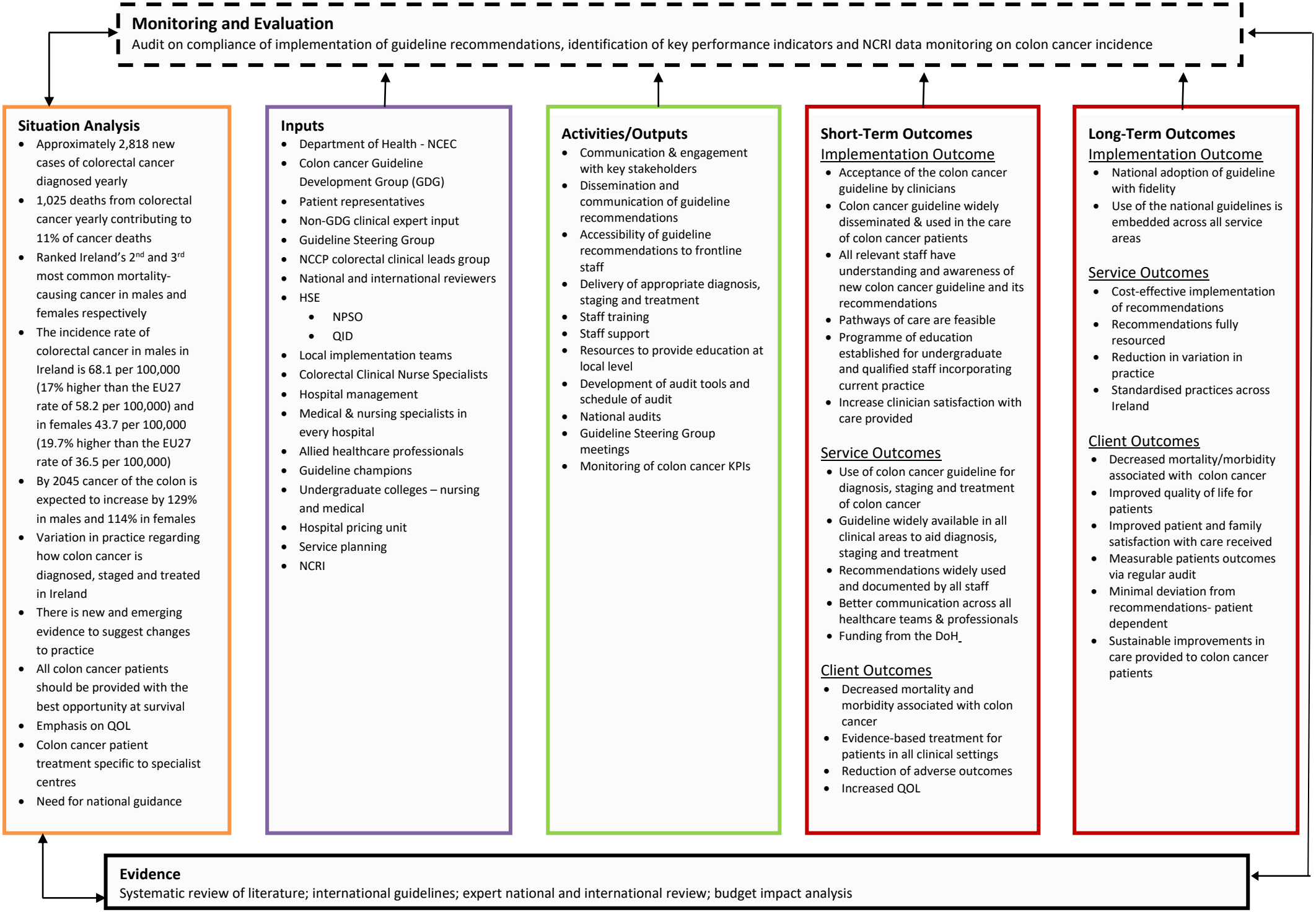
Terms of Reference**:** To develop a national evidence-based clinical guideline for the diagnosis, staging, and treatment of patients with colon cancer. Full terms of reference are available in the NCCP Methodology Manual for guideline development.

Table 11 Membership of the NCCP Guideline Steering Group

Name	Title/Position	Role on guideline group
Professor Risteárd Ó Laoide	National Director, NCCP	Chair
Ms Fiona Bonas	Interim Deputy Director, NCCP	Member
Dr Eve O'Toole	Head of Evidence and Quality Hub, NCCP	Member
Dr Deirdre Murray	Health Intelligence, NCCP	Member
Ms Patricia Heckmann	Assistant National Director, NCCP	Member
Professor Arnold Hill	NCCP Surgical Advisor & BH	Member
Dr Aileen Flavin	NCCP Radiation Oncology Advisor & CUH	Member
Professor Maccon Keane	NCCP Medical Oncology Advisor & GUH	Member
Mr Brendan Leen	Regional Librarian, HSE South-East	Member
Mr David Galvin	Chair Prostate GDG, SVUH	Member
Dr Marcus Kennedy	Chair Lung GDG, CUH	Member
Professor John Reynolds	Chair Gastrointestinal GDG, SJH	Member
Professor Deborah McNamara	Chair Lower GI GDG, BH	Member
Mr Justin Geoghegan	Chair Hepatobiliary GI GDG, SVUH	Member
Dr Josephine Barry	Co-chair Ovarian GDG, CUH	Member
Dr Ciarán Ó Riain	Co-chair Ovarian GDG, SJH	Member
Mr Martin O Sullivan	Chair Breast GP GDG, CUH	Member
Mr John Coulter	Chair Gestational trophoblastic disease GDG, CUH	Member
Dr Brian Creedon	Clinical Lead Clinical Programme for Palliative Care, UHW	Member

Table 12 Guideline contributors

Name	Title/Position	Role
Mr Rory Kennelly	Consultant Colorectal Surgeon, SVUH	Contributor
Professor Mike Clarke	Director of MRC Methodology Hub, QUB	Methodology advisor
Mr Robin Harbour	Lead Methodological, SIGN	Contributor
Dr Aisling Daly	Radiology Specialist Registrar, NI ST2	Contributor
Dr Colin McQuaid	Radiology Specialist Registrar, TUH	Contributor
Dr Michael Durand	Radiology Specialist Registrar, SJH	Contributor
Ms Michelle O'Neill	Senior Health Economist, HIQA	Contributor
Dr Paul Patrick Healy	Clinical Lecturer, RCSI	Contributor
Ms Laura Currie-Murphy	Postdoctoral Research Fellow, SJH	Contributor
Ms Elaine Scanlon	Library Assistant, Dr Steevens' Library	Contributor
Dr Sandra Deady	Data Analyst, NCRI	Contributor
Dr Niamh Kilgallen	Senior Research Officer, NCCP	Contributor
Dr Aoife McErlean	Consultant Radiologist, BH	Contributor


Monitoring and Evaluation
Audit on compliance of implementation of guideline recommendations, identification of key performance indicators and NCRI data monitoring on colon cancer incidence
Situation Analysis
Approximately 2,818 new cases of colorectal cancer diagnosed yearly
1,025 deaths from colorectal cancer yearly contributing to 11% of cancer deaths
Ranked Ireland's 2nd and 3rd most common mortality-causing cancer in males and females respectively
The incidence rate of colorectal cancer in males in Ireland is 68.1 per 100,000 (17% higher than the EU27 rate of 58.2 per 100,000) and in females 43.7 per 100,000 (19.7% higher than the EU27 rate of 36.5 per 100,000)
By 2045 cancer of the colon is expected to increase by 129% in males and 114% in females
Variation in practice regarding how colon cancer is diagnosed, staged and treated in Ireland
There is new and emerging evidence to suggest changes to practice
All colon cancer patients should be provided with the best opportunity at survival
Emphasis on QOL
Colon cancer patient treatment specific to specialist centres
Need for national guidance
Inputs
Department of Health - NCEC
Colon cancer Guideline Development Group (GDG)
Patient representatives
Non-GDG clinical expert input
Guideline Steering Group
NCCP colorectal clinical leads group
National and international reviewers
HSE
NPSO
QID
Local implementation teams
Colorectal Clinical Nurse Specialists
Hospital management
Medical & nursing specialists in every hospital
Allied healthcare professionals
Guideline champions
Undergraduate colleges – nursing and medical
Hospital pricing unit
Service planning
NCRI
Activities/Outputs
Communication & engagement with key stakeholders
Dissemination and communication of guideline recommendations
Accessibility of guideline recommendations to frontline staff
Delivery of appropriate diagnosis, staging and treatment
Staff training
Staff support
Resources to provide education at local level
Development of audit tools and schedule of audit
National audits
Guideline Steering Group meetings
Monitoring of colon cancer KPIs
Short-Term Outcomes
Implementation Outcome
Acceptance of the colon cancer guideline by clinicians
Colon cancer guideline widely disseminated & used in the care of colon cancer patients
All relevant staff have understanding and awareness of new colon cancer guideline and its recommendations
Pathways of care are feasible
Programme of education established for undergraduate and qualified staff incorporating current practice
Increase clinician satisfaction with care provided
Service Outcomes
Use of colon cancer guideline for diagnosis, staging and treatment of colon cancer
Guideline widely available in all clinical areas to aid diagnosis, staging and treatment
Recommendations widely used and documented by all staff
Better communication across all healthcare teams & professionals
Funding from the DoH
Client Outcomes
Decreased mortality and morbidity associated with colon cancer
Evidence-based treatment for patients in all clinical settings
Reduction of adverse outcomes
Increased QOL
Long-Term Outcomes
Implementation Outcome
National adoption of guideline with fidelity
Use of the national guidelines is embedded across all service areas
Service Outcomes
Cost-effective implementation of recommendations
Recommendations fully resourced
Reduction in variation in practice
Standardised practices across Ireland
Client Outcomes
Decreased mortality/morbidity associated with colon cancer
Improved quality of life for patients
Improved patient and family satisfaction with care received
Measurable patients outcomes via regular audit
Minimal deviation from recommendations- patient dependent
Sustainable improvements in care provided to colon cancer patients
Evidence
Systematic review of literature; international guidelines; expert national and international review; budget impact analysis

Appendix 2: Clinical and economic questions in PICO format

Diagnosis and staging

Clinical question 2.2.1 In patients with newly diagnosed colon cancer, is CT-TAP the most suitable imaging modality for initial staging?	
Population:	Patients with newly diagnosed colon cancer
Intervention:	CT-TAP
Comparison:	Chest X-ray, ultrasound, MRI, PET-CT
Outcome:	Sensitivity, specificity, diagnosis of hepatic & extrahepatic metastases
Clinical question 2.2.2 In patients diagnosed with colon cancer with a potentially resectable liver lesion, is MRI of the liver superior to PET-CT in determining the presence of further liver lesions?	
Population:	Patients diagnosed with colon cancer with a potentially resectable liver lesion
Intervention:	MRI
Comparison:	PET-CT
Outcome:	Sensitivity, specificity, diagnosis of additional liver lesions
Clinical question 2.2.3 In patients diagnosed with colon cancer whose tumour cannot be endoscopically passed, is CT colonography always necessary prior to surgery?	
Population:	Patients diagnosed with non-emergent obstructing colon cancer
Intervention:	CT colonography
Comparison:	No CT colonography
Outcome:	Clinical effectiveness (diagnosis, treatment), sensitivity, specificity, safety and harm
Clinical question 2.2.4 In patients diagnosed with left-sided colon cancer, is complete colonoscopy always necessary prior to surgery?	
Population:	Patients diagnosed with left-sided colon cancer
Intervention:	Complete pre-operative colonoscopy
Comparison:	Incomplete pre-operative colonoscopy
Outcome:	Clinical effectiveness (diagnosis, treatment), sensitivity, specificity, safety and harm
Clinical question 2.2.5 In patients diagnosed with colon cancer, should the lesion be routinely tattooed at colonoscopy, prior to laparoscopic surgery? If so, should they be tattooed proximally or distally?	
Population:	Patients diagnosed with colon cancer
Intervention:	Tattoo at index colonoscopy prior to laparoscopic surgery
Comparison:	No tattoo at index colonoscopy prior to laparoscopic surgery
Outcome:	Complete excision, recurrence, overall survival, location of tattoo

Clinical question 2.2.6 In patients diagnosed with colon cancer, is there a minimum number of lymph nodes that need to be identified in a resection specimen and, if so, what is that number?	
Population:	Patients diagnosed with colon cancer
Intervention:	Minimum threshold of lymph nodes sampled
Comparison:	Any number of lymph nodes sampled
Outcome:	Accuracy of staging, survival benefit
Clinical question 2.2.7 In patients diagnosed with colon cancer, are the Haggitt and Kikuchi classification systems sufficiently applicable to recommend their use?	
Population:	Patients diagnosed with colon cancer
Intervention:	Application of Haggitt (polypoid tumours) and Kikuchi (sessile tumours) classification systems
Comparison:	Non-application of Haggitt and Kikuchi classification systems
Outcome:	Accuracy of assessing local invasion
Clinical question 2.2.8 In patients diagnosed with colon cancer, should tumours ≤1 mm from the peritoneal surface be separately identified from standard pT3 tumours?	
Population:	Patients diagnosed with colon cancer
Intervention:	Sub-division of pT3 tumours (≤1mm, >1mm)
Comparison:	Standard classification (all pT3 tumours)
Outcome:	Prediction of serosal penetration, recurrence, prognosis, staging
Clinical question 2.2.9 In patients with early-stage colon cancer treated with local excision, what pathological features indicate that radical surgery is required?	
Population:	Patients with suspected early-stage colon cancer (T1)
Intervention:	Local excision
Comparison:	-
Outcome:	Pathological features indicating a requirement for radical surgery

Treatment: Emergency presentation

Clinical question 2.3.1 In patients diagnosed with obstructive colon cancer, what is the role of stenting: (i) when intention of treatment is curative? (ii) when intention of treatment is palliative?	
Population:	Patients diagnosed with obstructive colon cancer
Intervention:	Stenting
Comparison:	Immediate surgery
Outcome:	Bridge to surgery, tumour dissemination, palliation, safety, stoma rates, curative resection, mortality, perforation

Treatment: Surgical techniques

Clinical question 2.4.1 In patients diagnosed with colon cancer, what is the evidence for specific surgical techniques and the effectiveness of these techniques on patient outcomes?	
Population:	Patients diagnosed with colon cancer
Intervention:	Laparoscopic surgery, colonic resection
Comparison:	Radical surgery
Outcome:	Lymph node harvest, pathology scoring in macroscopic specimens, survival, recurrence - locoregional and distant
Clinical question 2.4.2 In patients diagnosed with colon cancer, what is the evidence for complete mesocolic excision (CME) during curative resection?	
Population:	Patients diagnosed with colon cancer
Intervention:	Complete mesocolic resection during curative resection
Comparison:	Curative resection alone
Outcome:	Recurrence, overall survival, morbidity
Clinical question 2.4.3 In patients with unresectable metastases from colon cancer, does resection of the primary tumour improve life expectancy and/or quality of life?	
Population:	Patients diagnosed with right-sided colon cancer and unresectable metastases
Intervention:	Resection of primary tumour ± adjuvant chemotherapy
Comparison:	Palliation or palliative chemotherapy
Outcome:	Overall survival, quality of life

Treatment: Palliative care

Clinical question 2.5.1 When should palliative care be introduced for patients with cancer?	
Population:	Patients with metastatic cancer
Intervention:	Timing of palliative care
Comparison:	-
Outcome:	Quality of life

Economics

Radiology What is the cost-effectiveness of various imaging modalities in staging patients with colorectal cancer?	
Population:	Patients diagnosed with colon or rectal cancer
Intervention:	Complete colonoscopy, CT colonography, CT-TAP (thorax, abdomen, pelvis), chest radiography, ultrasound, MRI, PET-CT
Comparison:	-
Outcome:	Cost-effectiveness analysis, cost-benefit analysis, cost-utility analysis, economic evaluation
Pathology What is the cost-effectiveness of processing lymph nodes or classifying pathological specimens in patients with colorectal cancer?	
Population:	Patients diagnosed with colon or rectal cancer
Intervention:	Processing lymph nodes (≤12 vs. 12) Classifying pathological specimens (Haggitt, Kikuchi, 3-point TRG system, 5-point TRG system)
Comparison:	-
Outcome:	Cost-effectiveness analysis, cost-benefit analysis, cost-utility analysis, economic evaluation
Gastroenterology What is the cost-effectiveness of gastroenterology services in patients with colorectal cancer?	
Population:	Patients diagnosed with colon or rectal cancer
Intervention:	Tattooing lesions during colonoscopy, preoperative colonoscopy, CT colonography, endoscopic mucosal resection, endoscopic submucosal dissection
Comparison:	-
Outcome:	Cost-effectiveness analysis, cost-benefit analysis, cost-utility analysis, economic evaluation
Surgery What is the cost-effectiveness of various surgical techniques in patients with colorectal cancer?	
Population:	Patients diagnosed with colon or rectal cancer
Intervention:	Laparoscopic surgery, colonic resection, mesocolon excision, complete mesocolic excision, stenting, abdomino-perineal excision, total mesorectal excision, robotic surgery, radical/open surgery, open low anterior surgery, endoscopic mucosal resection, endoscopic submucosal dissection, transanal excision, mesocolic section, curative resection, decompression, local resection
Comparison:	-
Outcome:	Cost-effectiveness analysis, cost-benefit analysis, cost-utility

Appendix 3: Supporting tools

Downloading this guideline

This National Clinical Guideline will be available to download on the following websites:

- NCCP: https://www.hse.ie/eng/services/list/5/cancer/profinfo/guidelines/
- NCEC: https://health.gov.ie/national-patient-safety-office/ncec/national-clinical-guidelines/

Clinician information

- GP Referral Pathway for Suspected Colorectal Cancer https://www.hse.ie/eng/services/list/5/cancer/profinfo/resources/gpreferrals/gp-referral-pathway-for-suspected-colorectal-cancer.pdf
- NCCP Website: Information for Health Professionals https://www.hse.ie/eng/services/list/5/cancer/profinfo/
- Algorithms available in this guideline for clinicians:
    - **Figure 1** Staging algorithm recommended by the Guideline Development Group for patients with colon cancer and suspected hepatic metastases

Patient information booklets/website

- Booklet - Sexual Wellbeing after breast or pelvic cancer treatments- a guide for women https://www.hse.ie/eng/services/list/5/cancer/patient/leaflets/sexual-wellbeing-after-breast-or-pelvic-cancer-treatment.pdf
- Booklet - Information for men on sexual wellbeing after pelvic cancer treatment- What you should know https://www.hse.ie/eng/services/list/5/cancer/profinfo/resources/booklets/pelvic%20cancer.pdf
- Booklet-Good bone health after cancer treatment- What you should know https://www.hse.ie/eng/services/list/5/cancer/patient/leaflets/good-bone-health-after-cancer-treatment.pdf
- Booklet - Irish Cancer Society. (2019) Understanding bowel (colorectal) and anal cancer booklet https://www.cancer.ie/cancer-information-and-support/cancer-types/bowel-cancer
- Irish Cancer Society. (2017). Diet and Cancer – a guide for patients and families. https://www.cancer.ie/sites/default/files/content-attachments/diet_and_cancer_2017.pdf
- NCCP Colorectal cancer patient passport https://www.hse.ie/eng/services/list/5/cancer/profinfo/cancer-nursing-programme/patient%20passport.html
- NCCP Website: Patient Information https://www.hse.ie/eng/services/list/5/cancer/patient/

Service quality

- Department of Health (2017) National Cancer Strategy 2017-2026 https://health.gov.ie/blog/publications/national-cancer-strategy-2017-2026/
- Department of Health (2018) Framework for Public Involvement in Clinical Effectiveness Processes https://health.gov.ie/wp-content/uploads/2018/03/Final-WEB-COPY_PI-Framework-Feb-2018-1.pdf
- Department of Health (2018) NCEC Implementation Guide and Toolkit for National Clinical Guidelines https://www.gov.ie/en/collection/cd41ac-clinical-effectiveness-resources-and-learning/
- Health Information and Quality Authority (2012) National Standards for Safer Better Healthcare www.hiqa.ie/standards/health/safer-better-healthcare

Publications to assist with Implementation of this guideline

- Department of Health (2017) Working Together for Health- A National Strategic Framework for Health and Social Care Workforce Planning https://health.gov.ie/blog/publications/working-together-for-health-a-national-strategic-framework-for-health-and-social-care-workforce-planning/
- Health Service Executive (2017) Palliative Care Services- Three Year Development Framework 2017-2019 https://www.hse.ie/eng/services/publications/clinical-strategy-and-programmes/palliative-care-services-development-framework.pdf

- Department of Health (2017) Framework for Safe Nurse Staffing and Skill Mix in General and Specialist Medical and Surgical Care settings in Adult Hospitals in Ireland 2018 https://health.gov.ie/blog/publications/framework-for-safe-nurse-staffing-and-skill-mix-in-general-and-specialist-medical-and-surgical-care-settings-in-ireland-2018/
- Department of Health (2014) Strategic Review of Medical Training and Career Structure https://www.gov.ie/en/publication/572ede-strategic-review-of-medical-training-and-career-structure-ninth-prog/?referrer=http://www.health.gov.ie/blog/publications/strategic-review-of-medical-training-and-career-structure-final-report/
- Kumarasinghe et al., (2020) Pathological assessment of endoscopic resections of the gastrointestinal tract: a comprehensive clinicopathologic review. Mod Pathol ;33(6):986-1006. doi: 10.1038/s41379-019-0443-1.

Appendix 4: Systematic literature review protocol

National Cancer Control Programme

HSE Library Services
NCCP Guideline Development

SYSTEMATIC LITERATURE REVIEW PROTOCOL

Literature searches to answer clinical questions identified by the relevant tumour group will be conducted using the following procedure. Questions should only be submitted if they have not been adequately answered in the guidelines adopted by the tumour group, or where guidelines need to be updated. Guidelines should be identified in consultation with library services.

Tumour Group	1	PICO(T)		Analyse the clinical question using PICO(T) and complete a Clinical Query Request form. See below Annex 1: Clinical Query Request.
Tumour Group or Library Services	2	Question Category		Assign a question category, if appropriate: Therapy/Intervention ☐ Aetiology/Risk Factors ☐ Diagnosis ☐ Prognosis/Prediction ☐ Frequency/Rate ☐ Phenomena ☐ Other ☐
Library Services	3	Literature Search		Conduct searches of the following bibliographic databases in the order specified below using keywords implicit in the PICO(T) strategy and any identified subject headings:
		Cochrane	3.1	**Cochrane Library** Comprising: the Cochrane Database of Systematic Reviews; the Cochrane Central Register of Controlled Trials (Central); the Database of Abstracts of Reviews of Effects; the Health Technology Assessment Database; the NHS Economic Evaluation Database. Use MeSH and keyword searches to identify systematic reviews and other relevant studies.
		Point-of-Care	3.2	**Point-of-Care Reference Tools** One or more of the following point-of-care reference tools: BMJ Best Practice; DynaMed; UpToDate.
		Medline	3.3	**Medline** Use MeSH and keyword searches. Limit results using the 'Human' search filter. Unless otherwise specified by the tumour group or warranted by the specific clinical question, limit results to studies from the previous 5 years. Where appropriate, limit intervention questions according to the following priority: Medline clinical queries; Cochrane systematic reviews; other systematic reviews or meta-analyses; RCTs; systematic reviews of cohort or cross-sectional studies; cohort or cross-sectional studies; general Medline or other sources. Where appropriate, limit diagnosis, prognosis or aetiology questions according to the following priority: Medline clinical queries; systematic reviews of cohort or cross-sectional studies; cohort or cross-sectional studies; general Medline or other sources.
		Embase	3.4	**Embase** Repeat the Medline search strategy above using Embase, if available.
		Other Databases	3.5	**Other Bibliographic Databases** Repeat the Medline search strategy above using the Cumulative Index to Nursing and Allied Health Literature and/or PsycINFO, as appropriate.
		Other Sources	3.6	**Other Sources** Use any other sources for background or additional information, as appropriate. Other sources may include: PubMed, particularly for in-process or ahead-of-print citations; quality-assured, subject-specific Internet resources; clinical reference books; patient information materials; etc.
		Trial Registers	3.7	**Trial Registers** When a relevant trial is identified through searching the bibliographic databases, a search of trial registers should be carried out to identify any related trials which have been completed but whose findings have not been published or made available. The tumour group should be alerted to the presence of these unpublished trials. The following sources may be included:
			3.7.1	**ClinicalTrials.gov**: http://clinicaltrials.gov/

3.7.2 **Cochrane Central Register of Controlled Trials (Central)**: http://www.thecochranelibrary.com/

3.7.3 **EU Clinical Trials Register**: https://www.clinicaltrialsregister.eu/

3.7.4 **International Prospective Register of Systematic Reviews (Prospero)**: http://www.crd.york.ac.uk/prospero/search.asp

3.7.5 **WHO International Clinical Trials Registry**: http://apps.who.int/trialsearch/

3.8 For questions relating to economic evaluations, use the SIGN economic studies filter for Medline as a basis for the search strategy: http://www.sign.ac.uk/methodology/filters.html#econ. The following source may also be consulted, if available: HEED: Health Economic Evaluations Database: http://onlinelibrary.wiley.com/book/10.1002/9780470510933.

Library Services **4** **Reference Management**

Retain an electronic record of the search strategy and all search results using the Zotero reference management utility.

Library Services **5** **Search Results**

Respond to the tumour group using the Clinical Query Response form to include:

- a copy of the search strategy
- bibliographic details of all search results identified
- optionally, a note of studies that seem to the librarian to be of particular relevance to the clinical question

See below Annex 2: Clinical Question Response.

Library Services **6** **Retracted Publications**

6.1 Set up an alert to review results lists returned to the tumour group to rapidly capture any articles that are subsequently retracted or withdrawn, and notify the tumour group accordingly.

Tumour Group or Library Services **Retracted Publications**

6.2 Review all articles included in recommendations of the completed guideline to confirm that they have not been subsequently retracted or withdrawn.

Library Services **7** **Summary of Search Strategy**

A summary of the search strategy is included as an addendum to the completed guideline. Complete the Clinical Question: Summary of Search Strategy form and return to the tumour group.

See below Annex 3: Clinical Question: Summary of Search Strategy.

Library Services **8** **[Pre-External Review] Update of Literature Search**

Once internal review of the guideline has been completed, literature searches for all clinical questions should be updated to capture articles published in the interim between the original literature search and the final draft of the guideline. Updated literature searches should be conducted prior to submission of the guideline for external review.

Respond to the tumour group as previous using the Clinical Query Response form to include:

- a copy of the search strategy
- bibliographic details of all search results identified
- optionally, a note of studies that seem to the librarian to be of particular relevance to the clinical question

See below Annex 2: Clinical Question Response.

Annex 1 - Clinical Question Request to Library

Your Contact Details	
Name	
Job Title	
Work Address	
Telephone	
Email	
Employee Number	
Please state your clinical question	
… and list any relevant keywords	
… or (optional) enter keywords under the following headings (PICO)	
PICO	
Population/Problem	
Intervention/Indicator	
Comparator/Control	
Outcome	

Is your question specific to any of the categories below?		
GENDER	AGE GROUP	DATE OF PUBLICATION
Male ☐ Female ☐	Infant (0 – 23 months) ☐ Child (2 – 12 years) ☐ Adolescent (13 – 18 years) ☐ Adult (19 – 65 years) ☐ Aged (> 65 years) ☐	Current year only ☐ 0 – 5 years ☐ > 5 years ☐

Question Type
Therapy/Intervention ☐
Aetiology/Risk Factors ☐
Diagnosis ☐
Prognosis/Prediction ☐
Frequency/Rate ☐
Phenomena ☐
Other ☐

Additional Information

Annex 2 - Clinical Question Response from Library

Dear_____,

Thank you for your email. Please see attached in response to your clinical query and, below, details of the search strategy applied to your question. If you wish to source any of the references contained in these results, or to search further, please do not hesitate to contact us.

Best wishes,

_____.

[ATTACH CLINICAL QUESTION REQUEST HERE]

Search Strategy		
Primary Database(s) Searched		
Search Strategy		
Other/Secondary Resources Searched		
Comments		
Contact		
Your Library Staff Contact		
Date		

Annex 3 - Clinical Question: Summary of Search Strategy

<table>
<tr><td colspan="4">Clinical Question</td></tr>
<tr><td colspan="4"></td></tr>
<tr><td colspan="4">PICO</td></tr>
<tr><td>Population/Problem</td><td colspan="3"></td></tr>
<tr><td>Intervention/Indicator</td><td colspan="3"></td></tr>
<tr><td>Comparator/Control</td><td colspan="3"></td></tr>
<tr><td>Outcome</td><td colspan="3"></td></tr>
<tr><td colspan="4">Is your question specific to any of the categories below?</td></tr>
<tr><td>GENDER</td><td>AGE GROUP</td><td colspan="2">DATE OF PUBLICATION</td></tr>
<tr><td>Male □
Female □</td><td>Infant (0 – 23 months) □
Child (2 – 12 years) □
Adolescent (13 – 18 years) □
Adult (19 – 65 years) □
Aged (> 65 years) □</td><td colspan="2">Current year only □
0 – 5 years □
> 5 years □</td></tr>
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<tr><td colspan="2">Prognosis/Prediction □</td><td colspan="2"></td></tr>
<tr><td colspan="4">Search Strategy</td></tr>
<tr><td>Primary Database(s) Searched</td><td colspan="3"></td></tr>
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<tr><td>Date</td><td colspan="3"></td></tr>
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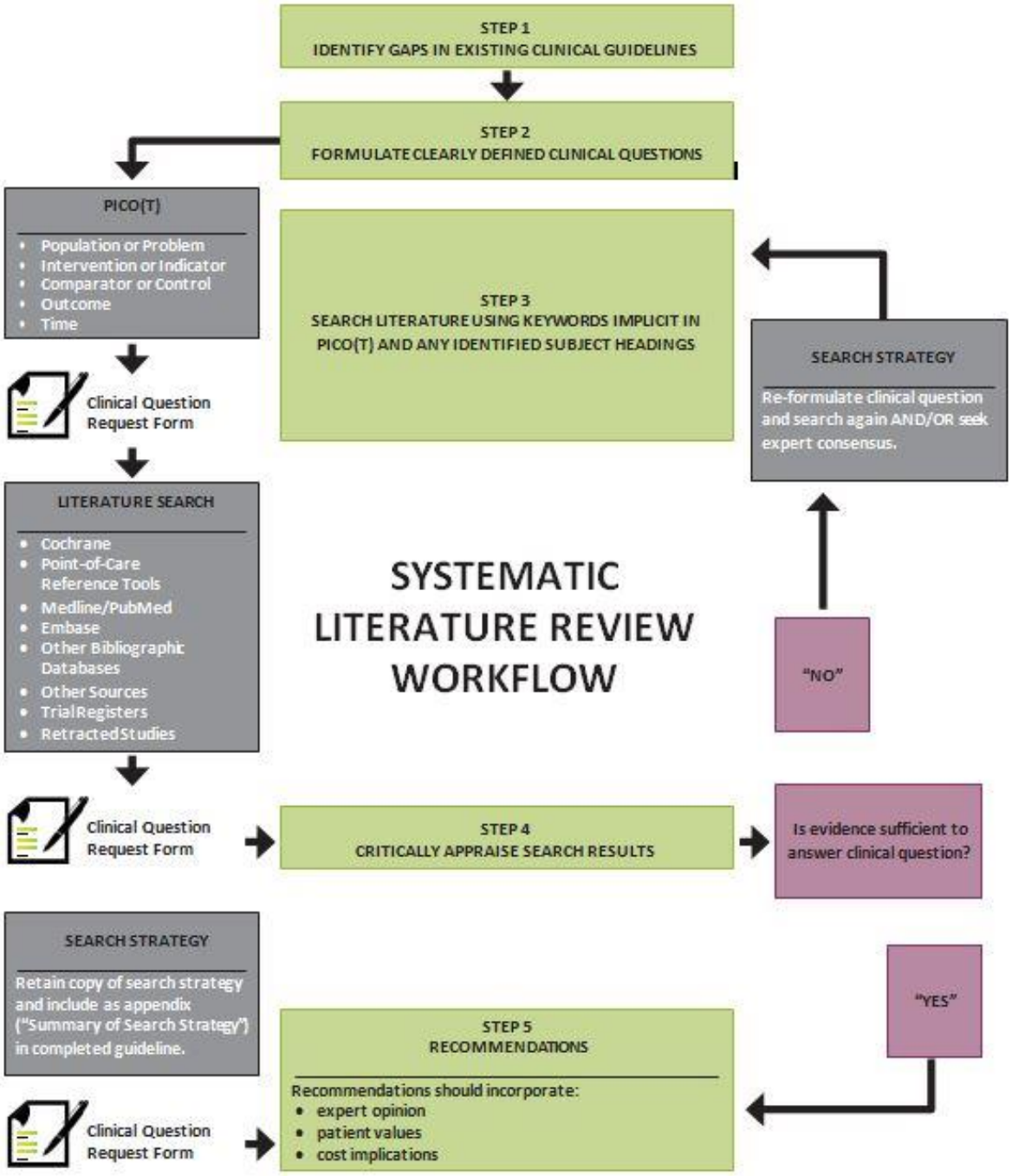
*Annex 4 - Systematic Literature Review Workflow**



* Based in part on "Figure 10: Systematic Literature Review" of SIGN 50: A Guideline Developer's Handbook. - Scottish Intercollegiate Guidelines Network (2011). SIGN 50: A Guideline Developer's Handbook. Revised ed. Edinburgh: Scottish Intercollegiate Guidelines Network.

Protocol designed by the HSE/hospital librarians in conjunction with the NCCP.

Appendix 5: Details of consultation process

As part of the consultation process, the draft guideline was circulated for review to this list of groups, committees and organisations. The guideline was also available on the NCCP website so it was accessible to all who wished to comment and feedback. All submissions and amendments from the national stakeholder and international expert review process are available on request from the Guideline Development Group. Further information regarding the consultation process can be found in Section 3.10 External review.

Clinical leaders and healthcare managers	National Colorectal Clinical Leads group HSE Clinical Programme in Surgery HSE Clinical Programme in Radiology HSE Clinical Programme in Palliative Care HSE Clinical Programme in Medicines management & pharmacological interventions HSE Clinical Programmes in Renal Failure HSE Clinical Programme in Primary Care CEOs of the Hospital Groups CEOs of the designated cancer centres CEO/managers of the Cancer Network Hospitals
National groups, organisations, faculties & committees	Faculty of Surgery, RCSI Faculty of Radiology, RCSI Faculty of Pathology, RCSI Irish Society for Medical Oncologists (ISMO) Irish Association for Nurses in Oncology (IANO) Irish Stoma Care and Colorectal Nurses Association (ISCCNA) Irish College of General Practitioners (ICGP) Irish Association of Emergency Medicine Irish Association of Directors of Nursing and Midwifery Hospital Pharmacists Association of Ireland Oncology Pharmacists Special Interest Group Irish Association of Physicists in Medicine (IAMP)
Patient support and advocacy groups	HSE Patient Forum Irish Cancer Society Cancer Care West Marie Keating Foundation Gary Kelly Cancer Support Centre Purple House Support Group All Ireland Institute of Hospice and Palliative Care The Irish Hospice Foundation The Irish Association for Palliative Care ASH Ireland Stoma Support Groups nationwide
International Expert Review	Dr David Burling, Consultant Radiologist, St. Mark's Hospital, Harrow, UK Professor Brian Saunders, Professor of Endoscopy Practice, London North West Hospitals University Healthcare Trust, UK Professor Paul Horgan, Professor of Surgery, University of Glasgow, UK Mr Fergal Flemming, Assistant Professor of Surgery and Oncology, University of Rochester Medical Center, Rochester, New York, USA Dr Maria A. Hawkins, Professor of Radiation Oncology, University College London, UK Dr Amitabh Srivastava, Associate Professor of Pathology, Harvard Medical School, USA

Appendix 6: Economic assessment

This budget impact assessment of the diagnosis, staging and treatment of colon cancer is covered in two sections (Part A: Economic evidence summary and Part B: Budget Impact Analysis)

The report was compiled by:
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The following people are thanked for the input they contributed:
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Part A: Economic evidence summary

The Guideline Development Group undertook a literature search for evidence of clinical- and cost-effectiveness, cost and resource impact, including primary (research studies) and secondary (reviews) sources.

Methods

The literature sources searched are specified in the literature search strategy and include relevant resources, such as trial/guideline registries and relevant citation databases. The NCCP identified four economic questions pertaining to relevant areas within the guideline requiring cost-effectiveness analysis. Literature searches were carried out by HSE librarians and sifted by NCCP research staff. Selected literature was reviewed and quality appraised by the Guideline Development Group Health Economist to determine the cost of diagnosis, treatment and staging options. Using the SIGN economic literature checklist, a paper was determined to be too low quality to be used if the process of ensuring internal validity could not be established. A clearly focused question with an appropriate study design and measurable outcomes were important items considered in the overall assessment of study quality.

The estimated costs per quality adjusted life year (QALY) or life years gained (LYG) given in the following summaries are those reported within each study for the given year and national currency. These cost-effectiveness ratios have been complemented in brackets by euro estimates to correct for the purchasing power parity (PPP) between countries and health inflation to 2016-2017 costs as per the Health Information and Quality Authority's Economic Evaluation Guidelines (Health Information and Quality Authority (HIQA), 2014).

The following summaries report the conclusions regarding cost-effectiveness made by the authors of the reviewed literature. It is important to note that the thresholds of cost-effectiveness in other countries differ from that in Ireland and that statements of cost-effectiveness made in another context therefore may not be applicable to Ireland. While Ireland has no explicit cost-effectiveness threshold for non-drug interventions, cost-effectiveness ratios falling within the region of €45,000/QALY are conventionally considered cost-effective in Ireland.

Despite the conversion of the reported costs to PPP-adjusted 2016-2017 euro values it is also important to remember that there may still be a number of other factors which mean that cost-effectiveness ratios from other countries are not necessarily directly applicable to the Irish setting. For example, Ireland's discount rate is higher than that applied in the UK, so many interventions assessed in the UK would have less favourable ratios if the Irish discount rate was applied. Similarly, some analysis are conducted from the societal perspective and may account for more costs than are considered in Irish cost-effectiveness analyses (CEAs), which only account for costs to the health sector. Accordingly, the euro-adjusted ratios reported here should only be considered broadly indicative of the level of cost-effectiveness rather than precisely adjusted estimates for the Irish health system.

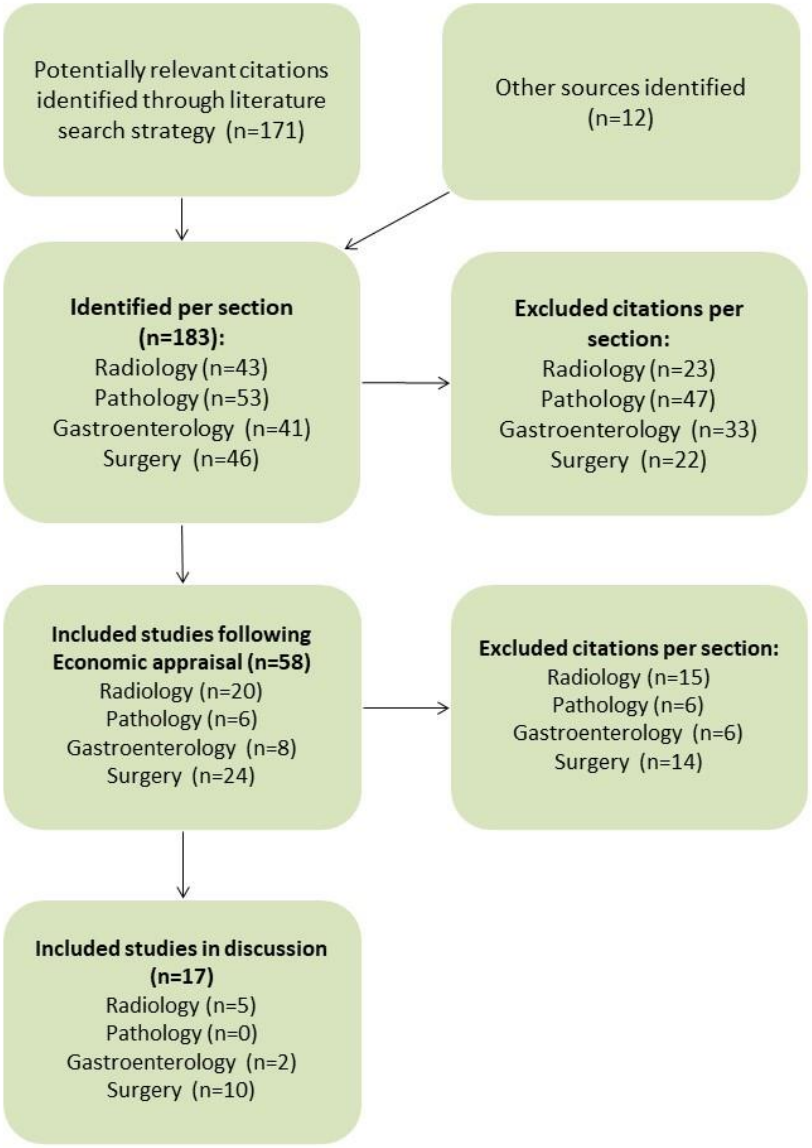

Figure 3 Economic literature review results breakdown

***Inclusion criteria**
Economic study
Applicable to the Irish healthcare system
Applicable to patient population/intervention/outcome
English Language
Relevant to guideline recommendations

***Exclusion criteria**
Not an economic study
Not in English language
Methodological or quality issues
Not applicable to Irish healthcare system
Not applicable to patient population/intervention/outcome
Not relevant to guideline recommendations

Table 13 Economic literature review protocol

ID	Search
1	Economics/
2	“costs and cost analysis”/
3	Cost allocation
4	Cost-benefit analysis/
5	Cost control/
6	Cost savings/
7	Cost of illness/
8	Cost sharing/
9	“deductibles and coinsurance”/
10	Medical savings accounts/
11	Health care costs/
12	Direct service costs/
13	Drug costs/
14	Employer health costs/
15	Hospital costs/
16	Health expenditures/
17	Capital expenditures/
18	Value of life/
19	Exp economics, hospital/
20	Exp economics, medical/
21	Economics, nursing/
22	Economics, pharmaceutical/
23	Exp “fees and changes”/
24	Exp budgets/
25	(low adj cost).mp.
26	(high adj cost).mp.
27	(health?care adj cost$).mp.
28	(fiscal or funding or financial or finance).tw.
29	(cost adj estimate$).mp.
30	(cost adj variable).mp.
31	(unit adj cost$).mp.
32	(economic$ or pharmacoeconomic$ or price$ or pricing).tw.
33	Or/1-32

Radiology

What is the cost-effectiveness of various imaging modalities in staging patients with colorectal cancer?

Of the 20 articles identified only five were relevant high quality economic studies assessing the cost-effectiveness of various imaging modalities in staging patients with colon or rectal cancer. The diagnostics included in the search were complete colonoscopy, CT colonography, CT-TAP, chest radiography, ultrasound, MRI, PET-CT.

The first study included was a very high quality health technology assessment from the UK under the NHS National Institute for Health Research Health Technology Assessment Programme. This study, "Brush et al. (2011) *The value of FDG positron emission tomography/computed tomography (PET/CT) in pre-operative staging of colorectal cancer: a systematic review and economic evaluation*" is a very comprehensive 192 page document. The research objectives were to "evaluate the diagnostic accuracy and therapeutic impact of PET-CT for the pre-operative staging of primary, recurrent and metastatic cancer using systematic review methods; undertake probabilistic decision-analytic modelling; and construct a value of information analysis". The systematic review did not find sufficient evidence for the use of PET-CT in primary colorectal cancer and only little supportive evidence in the use of PET-CT in pre-operative staging for recurrent and metastatic disease. The review judged the quality of the data identified to be generally of poor quality. The authors concluded that they could not support the use of PET-CT in staging primary colorectal cancer. The economic evaluations demonstrated a cost-effectiveness ratio of £21,409/QALY for recurrent rectal cancer, £6,189/QALY for recurrent colon cancer and £21,434 for metastatic disease.

Conclusions: PET-CT as an add-on imaging device is cost-effective in the preoperative staging of recurrent rectal and metastatic disease but not in primary colon or rectal cancer.

The second study by Halligan et al. (2015) "*Computed tomographic colonography compared with colonoscopy or barium enema for diagnosis of colorectal cancer in older symptomatic patients: two multicenter randomised trials with economic evaluation (the SIGGAR trials)"* is a 134 page long NHS National Institute for Health research health technology assessment. The cost-effectiveness is based on the SIGGAR trials and compares CT colonography with colonoscopy or barium enema in diagnosing symptomatic elderly patients. The objective was to examine the diagnostic efficacy, acceptability, safety and cost-effectiveness of CT colonography compared with barium enema or colonoscopy. The authors concluded that CT colonography detects more cancers and large polyps then barium enema and misses fewer cancers and improves patient experience but does increase follow-up investigations. The way in which results were delivered, quicker and face to face favoured colonoscopy however CT colonography improved patient experience in the short term. Compared to barium enema, CT colonography detected an extra serious colonic neoplasm for approximately £4,000. However detection rates were similar for CT colonography and colonoscopy and costs were also similar so there was not enough evidence for a solid recommendation.

Conclusions: No conclusions were possible.

In Huppertz et al. (2010) "*Whole-body MRI imaging versus sequential multimodal diagnostic algorithm for staging patients with rectal Cancer: Cost Analysis*", the direct and fixed costs of 33 patient were compared. Algorithm A included rectoscopy, endoscopic and abdominal ultrasound, chest x-ray, thoracic/abdominal CT in the case of positive findings in abdominal ultrasound or x-rays. The comparator was Algorithm B which consisted of rectoscopy followed by whole body MRI scanner. The study concluded that substantial savings are achievable with the use of whole-body MRI in pre-operative TNM staging of patients with rectal cancer compared to conventional work-up. The MRI option was deemed preferable to patients due to faster definitive diagnostic and to hospitals as the method involved less planning, personnel, steps and procedures and was thus easier to control. However, this study was a cost-minimisation study as the evidence for the superiority of the MRI scanner was not in the scope of the paper and was only based on one study Brown et al., (2003).

Conclusions: There is not enough evidence to conclude recommendations based on this study.

Yip et al. (2014) in "*Optimal imaging sequence for staging colorectal liver metastasis: Analysis of three hypothetical imaging strategies*" assessed inappropriate over investigations which can lead to delays in treatment and additional costs. Based on cost-analyses they concluded that a specialist multidisciplinary team should assess the initial CT of all patients with liver limited metastatic colorectal cancer, who are deemed fit for consideration for hepatectomy, prior to further radiological assessment by both PET-CT and MRI.

Conclusions: The most cost-effective option would be a specialist multidisciplinary team assessing the initial CT of all patients with liver limited metastatic colorectal cancer, who are deemed fit for consideration for hepatectomy, prior to further radiological assessment by both PET-CT and MRI.

In Zech et al. (2009)"*Health economic evaluation of three imaging strategies in patients with suspected colorectal liver metastasis: Gd-EOB-DTPA-enhanced MRI vs. extra cellular contrast-media enhanced MRI and 3-phase MDCT in Germany, Italy and Sweden*" the authors performed an economic evaluation of PV-MRI, ECCM-MRI and three-phase-MDCT as initial modalities in the work up of patients with metachronous colorectal liver metastasis. The authors concluded that PV-MRI with the lowest rate of further imaging needed can lead to cost-savings.

Conclusions: PV-MRI can lead to cost-savings.

Relevance to the guideline recommendation

The literature above discussed the cost-effectiveness of radiological modalities and techniques addressed within guideline recommendations 2.2.1.3, 2.2.2.1, 2.2.2.2, 2.2.3.1, and 2.2.4.2.

Recommendations 2.2.1.3 and 2.2.2.2 discusses how PET-CT can be used as an imaging modality for patients with suspected liver metastases or used as a problem solving tool in patients with equivocal imaging results. These are supported by evidence from three meta-analyses, an international guideline and an UpToDate review. The use of PET-CT in this cohort of patients should only be used after careful consideration of the patient at a multidisciplinary team meeting. PET-CT was deemed as cost-effective in the preoperative staging of recurrent rectal and metastatic disease but not in primary colon or rectal cancer and thus cannot conclude its economic benefit in the context of these recommendations.

Cost-effectiveness literature was available for recommendations 2.2.3.1 and 2.2.4.2 which recommends that where colonoscopy cannot be utilised, full colonic evaluation should be carried out by CT colonography to detect a synchronous tumour or prior to surgical intervention. A meta-analysis, a number of RTCs plus two prospective studies where amongst the evidence used to support these recommendations. According to the available economic literature, cancer and polyp detection rates were similar between colonoscopy and CTC as were costs but concluded there wasn't enough evidence to make a valid recommendation on its cost-effectiveness.

Recommendation 2.2.2.1 relates to the utility of MRI and its role in the evaluation and resectability of liver metastases. The cost-effectiveness literature is specific to rectal cancer and is a cost minimisation study related to whole body MRI as a staging tool so its applicability to colon cancer and the context of this recommendation is largely uncertain.

Pathology

What is the cost-effectiveness of processing lymph nodes or classifying pathological specimens in patients with colorectal cancer?

We were unable to include any studies in this section. Of the six articles found in the literature that were included for full text extraction, there was no high quality cost-effectiveness studies relevant to the key question.

Relevance to the guideline recommendation
N/A

Gastroenterology

What is the cost-effectiveness of gastroenterology services for colorectal cancer?

Of the eight articles found in the literature search that were included for full text extraction only two were high quality cost-effectiveness studies relevant to our interventions of interest.

Law et al. (2016) compared the cost-effectiveness of endoscopic resection (ER) versus laparoscopic resection (LR) in the management of complex colon polyps. The two strategies ER versus LR were compared in a hybrid Markov model with a 10 year time horizon. In the first strategy the patient underwent ER followed by surveillance colonoscopy at three, six and 12 months any failed ER and residual adenoma at 12 months were referred for LR. Under strategy two, patients underwent LR as primary treatment. Performance was obtained for a systematic review of the literature. Medicare and Medicaid services were used to obtain costs and loss of utility. The results showed that LR was more costly and yielded fewer QALYs compared with ER. The cost of ER was $5,570 per patient with an average QALY of 9.64 while a LR was $1, 8717 and yielded fewer QALYs (9.577). The authors concluded that ER is a cost-effective strategy for removal of complex colon polyps.

The second study to be included, Jayanna et al. (2016) undertook a cost-analysis of endoscopic mucosal resection versus surgery for large laterally spreading colorectal lesions. The authors concluded that EMR for large laterally spreading colorectal lesions is safer than surgery and savings of AU$8,839 and 2.81 inpatient nights can be achieved with a primary EMR strategy for large laterally spreading colorectal lesions in comparison with hypothetical ideal survival outcome. Event specific costs were derived from Australian Refined Diagnostic Related Groups (AR-DRG).

Relevance to the guideline recommendation
The literature above discussed the cost-effectiveness of gastroenterology services, in particular it relates to the treatment of patients that have a colorerectal lesion or polyp.

There are no recommendations related to the treatment of colorerectal polyps in the guideline.

Surgery

What is the cost-effectiveness of various surgical techniques in patients with colorectal cancer?

Of the 24 articles identified, 10 were relevant high quality economic studies assessing the cost-effectiveness of various surgical procedures in colon and rectal cancer. The procedures included for the health economics section were laparoscopic surgery, colonic resection, mesocolon resection, complete mesocolic excision, stenting, abdomino-perineal excision, total mesorectal excision, robotic surgery, radical surgery, open low anterior resection, endoscopic mucosal resection, endorectal submucosal dissection and transatlantic excision. Seven of the articles included focused on the cost-effectiveness of laparoscopic surgery.

The cost-effectiveness of laparoscopy in rectal cancer was assessed by authors Keller at al. (2014) in "*Cost-effectiveness of Laparoscopy in Rectal Cancer*". This was a case-matched study from the US conducted at a tertiary referral setting. 250 patients were included in the study through a review of a prospective database for elective laparoscopic rectal cancer resection which were matched to open cases. There was no significant difference in TNM stage, tumour distance from the anal verge or neoadjuvant therapy received between the two groups. The two groups were oncologically equivalent and there were no significant difference in postoperative complications, 30-day readmission, re-operation or mortality. However the laparoscopic group had significantly shorter stay and lower total hospital costs and more patients in the open resection group required intensive care. The average total cost for open surgery was USD$21,803 versus USD$17,214 for laparoscopic surgery in this tertiary hospital setting.

Another study, "*Cost-savings for elective laparoscopic resection compared with open resection for colorectal cancer in a region of high uptak*e" by Thompson et al. (2014) also looked at the cost-effectiveness of laparoscopic surgery versus open resection. This study used hospital data from public hospitals in Queensland, Australia between 2009-2011. The results showed that the crude mean cost for laparoscopic resection was AUS $20,036 and for open resection was AUS$22,780. The two procedures had the same length of surgery in this study but patients in the laparoscopic surgery group had shorter length of stay and fewer admissions to the ICU.

Norwood et al. (2011) assessed the nursing and financial implications of laparoscopic colorectal surgery in a paper titled "*The nursing and financial implications of laparoscopic colorectal surgery: data from a randomised controlled trial".* They looked at the cost of the nursing staff as according to the authors this topic was unaddressed. They included patients from the Australasian Laparoscopic Colon Cancer Study from one hospital in Australia. Of the 44 patients in the open surgery group an average of 80 hours nursing was needed and in the 53 patients in the laparoscopic arm 58.5 hours of nursing had been utilised. The cost of open surgery was AUS $9,698 and laparoscopic surgery AUS$10,951.

In a study from the US, "*Cost-effectiveness of Laparoscopic vs Open Resection for Colon and Rectal Cancer*", Jensen et al (2012) constructed a decision model with data from previously published studies. The results showed that laparoscopic surgery yielded average savings of USD$4,283 per patient. There was no difference in QALYs (0.001 more QALY than open surgery). The only issue that would not make laparoscopic surgery more cost-effective was the post-operative hernia rates which needed to be equivalent or less than that of open surgery rates to ensure cost-effectiveness of laparoscopic resection. The study from 2012 concluded that more surgeons, nurses and operating room staff needed to be trained in this procedure.

Jordan et al. (2014) assessed quality of life in the first six weeks after surgery to assess cost-effectiveness of laparoscopic surgery versus open surgery in "*Laparoscopic versus Open colorectal resection for cancer polyps: a cost-effectiveness study*" as all other comparators of the two procedures according to the authors suggested the methods were equivalent. Using the EQ-5D quality of life measurement the laparoscopic group gained an average of 0.011207 QALYs. Incremental cost-effectiveness ratios showed the cost per QALY gained in the laparoscopic surgery group was GBP£12,375 compared to the open surgery group.

In a study, "*Clinical effectiveness and cost-effectiveness of laparoscopic surgery for colorectal cancer: systematic reviews and economic evaluation*" Murray et al. (2006) pooled 20 different studies on laparoscopic surgery and pooled them into a Markov model. The results did not find laparoscopic surgery to be more cost-effective as the outcomes were similar, except for a quicker recovery time with laparoscopic surgery but the laparoscopic method was more costly and surgery times were also longer with laparoscopy. They concluded that laparoscopy yielded an extra cost of GBP£250-300 per patient. The authors suggested that long term follow up of the RCT patients would make the results more robust.

Another study from the UK by Hernandez et al. (2008) "*Systematic review of economic evaluations of laparoscopic surgery for colorectal cancer*" undertook a systematic review of economic evaluations of laparoscopic surgery using published papers form 2000-2005. Five studies were included and the results were inconsistent. The authors concluded that laparoscopic surgery was generally more expensive but the effectiveness data was not consistent and unreliable.

Using the NHS perspective Roberts et al. (2015) paper "*Cost-Utility of operative versus non-operative treatment for colorectal liver metastasis*" wanted to find out if surgery was more cost-effective than non-surgical interventions (palliative care, including chemotherapy) for treating colorectal liver metastasis. Results were conclusive and surgery had a mean survival of 41 months versus 21 months in the non surgical group. In addition, surgery was less costly €22,200 compared to €32,800 and yielded 4.017 QALYS versus 1.111 QALY.

The cost-effectiveness of robotic surgery for rectal cancer focusing on short term outcomes was analysed by Kim et al. (2015). Two patient groups were retrospectively compared to ascertain the cost-effectiveness of robotic surgery versus laparoscopic surgery in patients with rectal cancer. Propensity matched scoring was used to reduce bias between the robotic surgery group and the laparoscopic surgery group. Costs and short-term outcomes were compared. The short-term outcomes were similar between the groups and 30-day post-surgery complications were not significantly different. In patients with robotic surgery with complications the post-operative course seemed to be milder. However the costs were $3,137 higher on average in the robotic surgery group.

Van den Broeck et al. (2009) in "*Transvaal endoscopic microsurgery (TEM) versus endoscopic mucosal resection (EMR) for large rectal adenomas*" studied TEM versus EMR for large rectal adenomas in the randomised controlled TREND trial. The costs and effects from a Dutch healthcare perspective were collected alongside the trial. The trial was not able to demonstrate statistical non-inferiority of EMR. There was no difference in quality of life. Nevertheless EMR could be considered a primary method because of a tendency of lower complication rates and a better cost-effectiveness ratio.

Conclusion: Laparoscopy is cost-effective for rectal cancer surgery, improving patient outcomes and lowering costs in a US tertiary hospital setting when the technique is widely adopted and the surgeons are experienced in the technique. It is more cost-effective than open resection under almost all conditions and reduces nursing intensity compared to open resection.

Surgery to treat colorectal liver metastasis is cost-effective as it is less costly and more effective than non-surgical intervention while EMR saved approximately €3,000 per patient without any difference in QALYs and is thus the preferable treatment in terms of cost-effectiveness.

Relevance to the guideline recommendation

The literature above discussed the cost-effectiveness of surgical interventions and techniques which are addressed in guideline recommendations. Some of the economic literature is specific to rectal cancer and therefore its applicability to the recommendations for this guideline is uncertain.

Recommendation 2.4.1.1 uses evidence from three high quality meta-analyses and a recent international guideline as evidence to support the use of minimally invasive surgical techniques in colorectal cancer. This technique should be carried out by an experienced surgeon and used in patients deemed clinically appropriate. The cost-effectiveness literature associated with this recommendation demonstrates that laparoscopic surgery is more cost-effective with fewer adverse patient outcomes, shorter length of stay and in one study reduced the intensity of nursing interventions than open procedures. Jensen et al (2012) concluded that more clinical, nursing staff and operating room staff required specialist training in this type of procedure.

Cost-effectiveness studies: Evidence tables

Radiology

Authors (year), country	Intervention and comparator(s)	Population	Analysis details	Costs	Clinical outcomes	Methods for dealing with uncertainty	Results (ICERs)
Brush et al. (2011) *The value of FDG positron emission tomography/computed tomography (PET/CT) in pre-operative staging of colorectal cancer: a systematic review and economic evaluation* (United Kingdom)	FDG Positron emission tomography-computed tomography (FDG PET-CT).	HTA Systematic review of 5 studies. Unknown patient population.	**Model type:** Probabilistic decision-analytic model **Perspective:** UK NHS **Time horizon:** Not provided **Discount rate:** 3.5%	The economic evaluations demonstrated a cost-effectiveness ratio of £21,409/QALY for recurrent rectal cancer, £6,189/QALY for recurrent colon cancer and £21,434 for metastatic disease.	PET-CT as an add-on imaging device is cost-effective in the preoperative staging of recurrent rectal and metastatic disease but not in primary colon or rectal cancer.	A lower confidence interval was used to calculate the standard error for use in the probabilistic analysis as it represented the widest range of uncertainty.	The recurrent models found FDG PET-CT as an add-on device to have an incremental cost-effectiveness ratio (ICER) of £21,409 per QALY in the rectal model and £6,189 per QALY in the colon model. The metastatic model produced an ICER of £21,434 per QALY. Considering the NICE monetary threshold of £20,000-£30,000 per QALY, these ICERs can be considered cost-effective.
Halligan et al. (2015) *Computed tomographic colonography compared with colonoscopy or*	CT colonography and colonoscopy vs. CT colonography and barium enema.	5,384 patients from 21 NHS hospitals.	**Model type:** Markov model **Perspective:** NHS Secondary	CT colonography detected an extra serious	CT colonography detected an extra serious	Costs were analysis in relation to the benefits	Detection rates in BE trial were 7.3% for CT colonography

Authors (year), country	Intervention and comparator(s)	Population	Analysis details	Costs	Clinical outcomes	Methods for dealing with uncertainty	Results (ICERs)
barium enema for diagnosis of colorectal cancer in older symptomatic patients: two multicenter randomised trials with economic evaluation (The SIGGAR Trials) (United Kingdom)			care **Time horizon:** 5.2 years **Discount rate:** Not provided	colonic neoplasm for approximately £4,000.	large polyps then barium enema and misses fewer cancers and improves patient experience but does increase follow-up investigations.	of detecting extracolonic lesions separately from colonic lesions. Bootstrapping was used to estimate costs and cost differences. ICERS and their CI and a scatterplot was produced based on 1000 replicates.	compared to 5.6% for barium enema. CT colonography was better at detecting large polyps with no significant differences for cancer. CT colonography was associated with higher healthcare costs. The cost per large polyp or cancer detected as £4,235. ICERS amongst the studies varied from USD$2,144-USD$498,668 with a tendency for more recent studies to yield more favourable results.
Huppertz et al. (2010) *Whole-body MRI imaging versus sequential multimodal diagnostic algorithm for*	**Algorithm A:** included rectoscopy, endoscopic and abdominal ultrasound, chest x-	33 people with rectal cancer.	**Model type:** Cost minimisation **Perspective:** Not provided	This study was a cost-minimisation study as the evidence for	The MRI option was deemed preferable to patients due to faster	Activity based costing was used as the framework	Costs could be substantially reduced by replacing the current sequential

Authors (year), country	Intervention and comparator(s)	Population	Analysis details	Costs	Clinical outcomes	Methods for dealing with uncertainty	Results (ICERs)
staging patients with rectal Cancer: Cost Analysis (Germany)	ray, thoracic/abdominal CT in the case of positive findings in abdominal ultrasound or x-rays. **Algorithm B:** which consisted of rectoscopy followed by whole body MRI scanner.		**Time horizon:** Not provided **Discount rate:** Not provided	the superiority of the MRI scanner was not in the scope of the paper.	definitive diagnostics and to hospitals as the method involved less planning, personnel, steps and procedures and was thus easier to control.	for cost analysis.	multimodal diagnostic algorithm with the novel algorithm based on whole body MRI for the preoperative staging of rectal cancer.
Yip et al. (2014) *Optimal imaging sequence for staging colorectal liver metastasis: Analysis of three hypothetical imaging strategies* (United Kingdom)	CT, PET-CT and MRI and the use of appropriate imaging sequencing models.	644 patients with colorectal cancer.	**Model type:** Not provided **Perspective:** Not provided **Time horizon:** Not provided **Discount rate:** Not provided	Upfront imaging pathway £2,700 compared to £2,440.73 for a sequential pathway and £2,381 for the hybrid pathway.	The most-cost effective option would be a specialist MDT assessing the initial CT of all patients with liver limited metastatic colorectal cancer, who are deemed fit for consideration for hepatectomy, prior to further	Not provided	Based on cost analysis, assessment with initial CT followed by MDT with subsequent PET-CT and MRI imaging thereafter, was associated with shortest time to decision making and lowest cost.

Authors (year), country	Intervention and comparator(s)	Population	Analysis details	Costs	Clinical outcomes	Methods for dealing with uncertainty	Results (ICERs)
					radiological assessment by both PET-CT and MRI.		
Zech et al. (2009) *Health economic evaluation of three imaging strategies in patients with suspected colorectal liver metastasis: Gd-EOB-DTPA-enhanced MRI vs. extra cellular contrast-media enhanced MRI and 3-phase MDCT in Germany, Italy and Sweden* (Germany, Italy & Sweden)	PV-MRI, ECCM-MRI and three-phase-MDCT	26 pairs of clinicians (One liver surgeon and one radiologist) from Germany, Italy and Sweden	**Model type:** Decision tree model **Perspective:** Health care Payer **Time horizon:** Not provided **Discount rate:** Not provided	A strategy starting with PV-MRI was €959 and was cost-saving compared to ECCM-MRI (€1,123) and MDCT (€1,044) in Sweden. In Italy PV-MRI was cost-saving compared to ECCM-MRI and had total costs similar to MDCT.	According to the estimates, the proportion of high risk resectable, unresectable and non malignant categories were higher in the PV-MRI in comparison to ECCM-MRI and MDCT. In patients considered eligible for hepatic resections and scheduled for low risk resections, the proportion of "confirmed surgical plans" were	Results were presented to a third party where any areas in the uncertainty of the results were discussed and resolved.	PV-MRI with the lowest rate of further imaging needed can lead to cost-savings.

Authors (year), country	Intervention and comparator(s)	Population	Analysis details	Costs	Clinical outcomes	Methods for dealing with uncertainty	Results (ICERs)
					estimated to be higher and the proportion of "modified surgical plans" lower following initial imaging with PV-MRI compared with ECCM-MRI and MDCT.		

Pathology

Authors (year), country	Intervention and comparator(s)	Population	Analysis details	Costs	Clinical outcomes	Methods for dealing with uncertainty	Results (ICERs)
N/A							

Gastroenterology

Authors (year), country	Intervention and comparator(s)	Population	Analysis details	Costs	Clinical outcomes	Methods for dealing with uncertainty	Results (ICERs)
Law et al. (2016) *Endoscopic resection is cost-effective compared with laparoscopic resection in the management of complex Colon polyps: an economic analysis* (United States)	Endoscopic resection (ER) vs laparoscopic resection (LR)	ER vs LR were evaluated in a hypothetical cohort of patients with complex colon polyps (CCPs). Reference case: a healthy 50-year-old patient who underwent an initial colonoscopy with identification of a complex, sessile colon polyp without features of deep submucosal invasion (>1000 mm).	**Model type:** Hybrid Markov model **Perspective:** Third-party payer **Time horizon:** 10 year **Discount rate:** None provided	The cost of ER of a CCP was $5,570. The cost of LR of a CCP was $18,717 per patient.	The probability of an adverse event with ER was 9.1%; however, the probability that an adverse event would require surgical intervention was 1.0%. After the index resection and routine surveillance colonoscopies at 3 to 6 months and 12 months, the probability of persistent adenomatous tissue was 7.2%	Baseline estimates and costs were varied by using a sensitivity analysis through the ranges.	The cost of ER of a CCP was $5,570 per patient and yielded 9.640 QALYs. LR of a CCP cost $18,717 per patient and yielded fewer QALYs (9.577).
Jayanna et al. (2016) *Cost-analysis of endoscopic mucosal resection vs*	Endoscopic mucosal resection versus surgery for large laterally spreading colorectal lesions.	Endoscopic mucosal resection performed on 1489 colorectal lesions in 1253	**Model type:** Surgical Management model **Perspective:** Not provided	EMR for large LSL is safer than surgery and savings of AU$8839 and 2.81 inpatient nights.	EMR performed at an appropriately experienced and resourced tertiary centre	Data was compared from patients who underwent EMR with those from a model where	Endoscopic management produced a total cost-saving of US $10,284,909;

Authors (year), country	Intervention and comparator(s)	Population	Analysis details	Costs	Clinical outcomes	Methods for dealing with uncertainty	Results (ICERs)
surgery for large laterally spreading colorectal lesion (Australia)		patients.	**Time horizon:** Not provided **Discount rate:** Not provided		should be first line treatment for patients with large laterally spreading colorectal lesion.	all patients had surgery without complication. Event specific costs based on Australian refined diagnosis related group codes were used to estimate average costs per patient.	the mean cost difference per patient was US $7602. In patient hospitalisation length of stay was reduced by 2.81 nights. This approach is likely to deliver substantial overall health expenditure savings.

Surgery

Authors (year), country	Intervention and comparator(s)	Population	Analysis details	Costs	Clinical outcomes	Methods for dealing with uncertainty	Results (ICERs)
Roberts et al. (2015) *Cost-Utility of operative versus non-operative treatment for colorectal liver metastasis* (United Kingdom)	Resection for colorectal liver metastasis (CRLMs) compared with non-operative treatment (palliative care including chemotherapy).	Observational study of two patient cohorts. Operative cohort comprised consecutive patients undergoing CRLM resection between 1992 and 2001 (n=286). The non-operative cohort was identified from a review of patients who presented to a dedicated liver surgery multidisciplinary team between 2008 and 2010 (n=46).	**Model type:** Markov model **Perspective:** Healthcare provider perspective (UK NHS) **Time horizon:** Lifetime time horizon **Discount rate:** 3.5%	Non-operative treatment mean cost: €32,800 Operative strategy mean cost: €22,200	Median survival was 41 and 21 months in the operative and non-operative cohorts respectively (p<0.001).	Probabilistic sensitivity analysis was carried out to examine the impact of uncertainties in the model parameters on the robustness of the model results. One-way sensitivity analysis was carried out to provide further insight into the impact of specific parameters on the model results.	The operative strategy dominated non-operative treatments, being less costly (€22,200 vs. €32,800) and more effective (4.017 vs. 1.111 QALYs gained). The results of extensive sensitivity analysis showed that the operative strategy dominated non-operative treatment in every scenario.
Kim et al. (2015) *Cost effectiveness of robotic surgery*	Robotic surgery (RS) compared with laparoscopic surgery (LS).	From January 2007- December 2011, 311 patients underwent	**Model type:** Cost-effectiveness analysis **Perspective:**	**RS:** Total hospital charges: $15,965.10 Operation: $1,0375.40	Most perioperative outcomes were similar between the groups	To reduce the selection bias, propensity score matching with a 1:1 ratio	Total hospital charges and patients' bill were higher in RS than in LS.

Authors (year), country	Intervention and comparator(s)	Population	Analysis details	Costs	Clinical outcomes	Methods for dealing with uncertainty	Results (ICERs)
for rectal cancer focusing on short term outcomes (Korea)		totally RS and 560 patients conventional LS for rectal cancer in a single large-volume institution in Korea. As a result of the propensity score-matching, both groups included 251 patients.	Not provided **Time horizon:** 30 days **Discount rate:** Not provided	Anaesthesia: $1,028.50 Preoperative diagnosis: $1,175.70 Postoperative management: $3,317.00 Other: $56.40 **LS:** Total hospital charges: $11,933.00 Operation: $6,796.30 Anaesthesia: $875.30 Preoperative diagnosis: $1,184.80 Postoperative management: $3,010.20 Other: $66.50	except for the OT. The OT was longer in RS than in LS, and the time to soft diet was earlier in RS than in LS. Complications and readmission rates within 30 days of surgery were not different between the 2 groups.	was performed according to a number of variables such as sex, age, year of operation, smoking status, BMI etc. Continuous variables were compared using Student t tests or Mann-Whitney U tests and categorical variables were compared using X^2 or fisher exact tests.	The total hospital charges for patients who recovered with or without complications were higher in RS than in LS, although their short-term outcomes were similar. In patients with complications, postoperative course after RS appeared to be milder than that of LS. Total hospital charges for patients who were readmitted due to complications were similar between the groups.

Authors (year), country	Intervention and comparator(s)	Population	Analysis details	Costs	Clinical outcomes	Methods for dealing with uncertainty	Results (ICERs)
Keller at al (2014) *Cost-effectiveness of Laparoscopy in Rectal Cancer* (United States)	Elective laparoscopic rectal cancer resection versus open resection.	Case matched study from the United States. n=254 patients undergoing elective rectal cancer resection (n=125 laparoscopic rectal cancer resections, n=129 open cases).	**Model type:** Cost-effectiveness analysis **Perspective:** Not provided **Time horizon:** Not provided **Discount rate:** Not provided	The average total cost for open surgery was USD $21,803 versus USD $17,214 for laparoscopic surgery in this tertiary hospital setting.	The two groups were oncologically equivalent and there were no significant difference in postoperative complications, 30-day readmission, re-operation or mortality. However the laparoscopic group had significantly shorter stay and lower total hospital costs and more patients in the open resection group required intensive care.	Data analysis was completed by using Student t test, the X2 test or fisher exact tests.	Laparoscopy is cost-effective for rectal cancer surgery improving patient outcomes and lowering costs. The average total cost for open surgery was USD $21,803 versus USD $17,214 for laparoscopic surgery.
Thompson et al (2014) *Cost-savings for elective laparoscopic*	Laparoscopic surgery versus open resection.	1,391 patients who received an elective resection for colorectal cancer	**Model type:** Regression Model **Perspective:** Not provided	The results showed that the crude mean cost for laparoscopic resection was AUS$20,036 and for	The two procedures had the same length of surgery in this study but		Laparoscopic surgery cost lower than open procedures but

Authors (year), country	Intervention and comparator(s)	Population	Analysis details	Costs	Clinical outcomes	Methods for dealing with uncertainty	Results (ICERs)
resection compared with open resection for colorectal cancer in a region of high uptake (Australia)			**Time horizon:** Not provided **Discount rate:** Not provided	open resection was. AUS$22,780.	patients in the laparoscopic surgery group had shorter length of stay and less admissions to the ICU. Laparoscopic resection for CRC was shown to be cost-saving when the technique is widely adopted and the surgeons are experienced in the technique.		this could be due to a number of confounder factors.
Norwood et al. (2011) *The nursing and financial implications of laparoscopic colorectal surgery: data from a randomised*	Laparoscopy versus open surgery.	Participants from the Australasian Laparoscopic Colon Cancer Study (ALCCaS). Data from 97 patients were analysed (laparoscopy, 53; open	**Model type:** Cost-effectiveness analysis **Perspective:** Healthcare **Time horizon:** Not provided **Discount rate:** Not provided	The total cost of the procedure from admission to discharge was AUS$ 9,916⁄£5,631 (Aus$ 4,694–90,397) in the open surgery group and AUS $10,951⁄£,6219 (AUS$6,505–66,236)	There was no statistical difference in the median LOS between the two groups. The median number of nursing hours per patient for	Subgroup analysis was performed according to anatomical resection which showed no significant differences in LOS, nursing	The median number of nursing hours required per patient was 80 in the open group and 58.5 in the laparoscopic group which

Authors (year), country	Intervention and comparator(s)	Population	Analysis details	Costs	Clinical outcomes	Methods for dealing with uncertainty	Results (ICERs)
controlled trial (Australia)		surgery, 44).		in the laparoscopy group.	their total hospital stay was 80 (27.5–907) h in the open surgery group and 58.5 (15–684.5) h in the laparoscopy group (a saving of approximately 10 min per patient per hour).	time in minutes or cost.	represents a time saving of 10 minutes per patient. Nursing costs were less for laparoscopic procedures.
Jensen et al. (2012) *Cost-effectiveness of Laparoscopic vs Open Resection for Colon and Rectal Cancer* (United States)	Laparoscopy versus open surgery.	Data from previously published studies (randomised controlled trails where possible). Included sources of cost and QOL data related to laparoscopic and open resection of colon and rectal cancer.	**Model type:** Decision analysis model **Perspective:** Societal **Time horizon:** 5 years **Discount rate:** 3%	The results showed that laparoscopic surgery yielded average savings of USD $4,283 per patient. There was no difference in QALYs (0.001 more QALY than open surgery).	Laparoscopic resection is cost-effective versus open resection under almost all conditions. The only issue that would not make laparoscopic surgery more cost-effective was the postoperative hernia rates which needed to	Sensitivity analyses were performed on all variables input into the model. A sensitivity model was also performed in which patients whose surgeries were converted from laparoscopic to open had higher costs	Laparoscopic resection resulted in a cost savings of $4,238 and no difference in QALYS (0.001 more QALYS than open resection). Postoperative hernia rates needed to be equivalent or less than that of open

Authors (year), country	Intervention and comparator(s)	Population	Analysis details	Costs	Clinical outcomes	Methods for dealing with uncertainty	Results (ICERs)
					be equivalent or less than that of open surgery rates to ensure cost-effectiveness of laparoscopic resection.	related to the use of both laparoscopic and open equipment and additional operating room time.	surgery rates to ensure cost-effectiveness of laparoscopic resection.
Jordan et al. (2014) *Laparoscopic versus Open colorectal resection for cancer polyps: a cost-effectiveness study* (United Kingdom)	Laparoscopic versus open colorectal resection for cancer or polyps.	95 patients with either cancer or polyps requiring either laparoscopic (n=68) or open colorectal resection (n=27).	**Model type:** Multivariate regression model **Perspective:** National Health Service **Time horizon:** Not provided **Discount rate:** Not provided	Using the EQ-5D quality of life measurement the laparoscopic group gained an average of 0.011207 QALYs. Incremental cost-effectiveness ratios showed the cost per QALY gained in the laparoscopic surgery group was GBP £12,375 compared to the open surgery group. Cost-effective acceptability curves showed that at a willingness to pay threshold of GBP£30,000 there	The cost of the laparoscopic procedure was £1,037 higher than open due to cost of equipment. Staff cost were £190 lower due to shorter operative times. The open group had a longer mean length of stay which incurred a £897 higher bed day cost compared with a laparoscopic procedure. There was no	Uncertainty in the ICER point estimates are represented using confidence intervals, on the cost - effectiveness plan (CEP).	At 28 days the ICER calculated as the difference in adjusted means cost divided by the difference in adjusted mean QALYs, and showing the cost per QALY gained from laparoscopic compared to open surgery, was £12,375. Given the mean difference with QALYs (0.011207) and

Authors (year), country	Intervention and comparator(s)	Population	Analysis details	Costs	Clinical outcomes	Methods for dealing with uncertainty	Results (ICERs)
				was a >65% chance that laparoscopic surgery would be cost-effective in the NHS.	significant difference in total cost between procedures because higher cost for laparoscopic surgery was offset by shorter length of stay.		costs (£139) observed, laparoscopic procedure times could be increased by 55 minutes (£197) and still achieve an ICER ≤ £30,000.
Murray et al. (2006) *Clinical effectiveness and cost-effectiveness of laparoscopic surgery for colorectal cancer: systematic reviews and economic evaluation* (United Kingdom)	Laparoscopically assisted and hand-assisted laparoscopic surgery (HALS) in comparison with open surgery for the treatment of colorectal cancer.	Systematic review involving 4,568 patients. (laparoscopic n=2,429 and open surgery n=2,139)	**Model type:** Markov model **Perspective:** Healthcare **Time horizon:** 25 years **Discount rate:** Not provided	Laparoscopy yielded an extra cost of GBP £250-300 per patient.	The results did not find laparoscopic surgery to be more cost-effective as the outcomes were similar, except for a quicker recovery time with laparoscopic surgery but the laparoscopic method was more costly and surgery times were also longer with	Beta distribution and triangular distribution was used to help evaluate uncertainty around the cost estimates. CECGs have also been used to illustrate uncertainty and these curves help show if a strategy or intervention is cost-effective.	Incremental cost per life-year, laparoscopic surgery appeared more costly and no more effective than open surgery. With respect to incremental cost per QALY, few data were available to differentiate between laparoscopic and open

Authors (year), country	Intervention and comparator(s)	Population	Analysis details	Costs	Clinical outcomes	Methods for dealing with uncertainty	Results (ICERs)
					laparoscopy.		surgery. The results of the base-case analysis indicate that there is an approximately 40% chance that laparoscopic surgery is the more cost-effective intervention at a threshold willingness to pay for a QALY of £30,000.
Hernandez et al (2008) *Systematic review of economic evaluations of laparoscopic surgery for colorectal cancer* (United Kingdom)	Laparoscopic surgery versus open surgery for the treatment of colorectal cancer.	Systematic review (five studies were included and the results were inconsistent)with 1,421 participants in total.	**Model type:** Different models used per study **Perspective:** Societal and hospital **Time horizon:** Not provided **Discount rate:** Not provided	Most studies reported longer operational times and shorter length of stay with laparoscopic surgery but had similar long-term outcomes compared with open procedures.	Laparoscopic surgery was generally more expensive but the effectiveness data was inconsistent.	NHS-EED guidelines for reviewers were used to assess uncertainty across included studies. Data from all included studies were summarised and appraised	The evidence on cost-effectiveness was not consistent. Laparoscopic resection was generally more costly than open procedures. ICERs were

Authors (year), country	Intervention and comparator(s)	Population	Analysis details	Costs	Clinical outcomes	Methods for dealing with uncertainty	Results (ICERs)
						in order to identify common results, variations and weaknesses. Where ICERs were not included but sufficient data was available, ICERS were estimated.	calculated for a number of outcomes.
Van den Broek (2009) *Transanal endoscopic microsurgery versus endoscopic mucosal resection for large rectal adenomas (TREND-study)* (Netherlands)	Transanal endoscopic microsurgery versus endoscopic mucosal resection.	178 patients with large rectal adenomas.	**Model type:** Randomised control trial protocol **Perspective:** Dutch healthcare **Time horizon:** 24 months **Discount rate:** Included in sensitivity analysis	Direct medical costs, out of-pocket expenses, and the indirect non-medical costs of production loss.	NA	Sensitivity analysis is planned – sampling variability, unit cost of surgery and endoscopic treatment, discount rates, rectal adenoma diameter and distances of the adenoma from the anal verge.	NA

Part B: Budget Impact Analysis

For recommendations which affect resource requirements, the budget impact was calculated where data on cost was available. Additional resources where required will be sought through the HSE service planning process.

The burden of cancer is growing, and the disease is becoming a major economic expenditure for all developed countries. In 2008, the worldwide cost of cancer due to premature death and disability (not including direct medical costs) was estimated to be US$895 billion. This is not simply due to an increase in absolute numbers, but also the rate of increase of expenditure on cancer. Several drivers of cost, such as over-use, rapid expansion, and shortening life cycles of cancer technologies (such as medicines and imaging modalities), and the lack of suitable clinical research and integrated health economic studies, have converged with more defensive medical practice, a less informed regulatory system and a lack of evidence-based socio-political debate. (Sullivan et al., 2011)

“The cancer profession and industry should take responsibility and not accept a substandard evidence base and an ethos of very small benefit at whatever cost.” (Sullivan et al., 2011)

Sullivan et al. (2011) believe that value and affordable cancer care can be introduced into the cancer policy lexicon without detracting from quality, and that the management tools, evidence, and methods are available to affect this transformation across all developed countries.

A population-based cost analysis illustrated the economic burden of cancer on the European Union (EU). In 2009, cancer was estimated to have cost the EU €126 billion, with healthcare costs accounting for €51 billion (40%) (Luengo-Fernandez et al., 2013). In Ireland, inpatient care costs were estimated to account for €417 million of cancer-related healthcare costs out of a total of €619 million. Drug expenditure accounted for a further €127 million, while primary, outpatient and emergency care were estimated at €32 million, €30 million and €13 million, respectively. Across the EU, lung cancer had the highest economic cost (€18.8 billion) when compared to breast (€15 billion), colorectal (€13.1 billion) and prostate (€8.43 billion) cancer.

A recent productivity loss analysis carried out in an Irish context (Pearce et al., 2016) projected that by 2030, premature death as a result of colorectal cancer will cause a value of €237,664 lost household per death and an overall productivity loss per population of €2.5 billion.

Information on the expected future trends of colon cancer can be found in the epidemiology section of this guideline (Section 3.1 Epidemiology). Although some patients with colon cancer may be treated in the private sector, all costing have been calculated on the assumption that all patients diagnosed annually with colon cancer will attend publically and be treated within that system. This budget impact assessment focused on those recommendations considered to affect resource requirements, as determined by the Guideline Development Group at recommendation meetings held for each clinical question.

The National Cancer Strategy 2017-2026 (DOH, 2017) made a number of recommendations on how Irish cancer services should be organised, including hospital admissions policies, the organisation of hospital care including palliative care, infrastructure and staffing. The strategy encompasses a range of areas within cancer control, prevention, primary care from treatment to post treatment care and patient involvement, facilitating our healthcare system to operate to its full capacity. A number of recommendations (Table 17) made within the cancer strategy are relevant to the implementation of some of the guideline recommendations.

Measuring the performance and quality of cancer services is essential. The strategy also outlines a number of Key Performance Indicators (KPIs) (Table 18) that are relevant to how the NCCP proposes to evaluate the level of implementation of a number of recommendations made within the guideline.

All salaries used to calculate costs within this BIA, are based on the midpoint of the 2019 salary scale and are

adjusted for pension (4%), pay related social insurance (10.95%) and overheads (25%). Salaries are rounded to the nearest thousand.

Salaries for consultant posts were calculated based on new entrants from 1st October 2012 and are based on the midpoint of contract type B on the 2019 salary scale for adjusted for pension (4%), pay related social insurance (10.95%) and overheads (25%). Salaries are rounded to the nearest thousand.

Budget impact analysis

The resource implications of implementing the recommendations were identified by the clinicians during meetings to discuss and develop the clinical recommendations. The Guideline Development Group complied with HIQA guidance on conducting this budget impact analysis.

The implementation plan (Appendix 7: Implementation plan) based on the NCEC Implementation Guide (Department of Health, 2018) details the guideline recommendation(s), the implementation barriers/enablers and gaps, the actions/tasks to implement the recommendation, which group/unit/organisation has lead responsibility for the task; an indicative timeframe for completion; some detail on expected outcomes and how they will be verified or measured. The implementation plan also details if there is an additional cost related to implementing the guideline in the context of a colon cancer patient.

The operation costs (excluding staff) of implementing the recommendations in the guideline are summarised in Table 14 and the staff costs are summarised in Table 15. Each table details the additional resources required, the unit cost, unit of analysis, total cost per annum (2020-2022), and the total cost. In areas where additional resources are required these will be sought through the service planning process. Figures for funding approved by the National Service Plan may differ to those quoted below.

Table 14 Budget impact analysis of expected operational costs (excluding staff costs) in implementing recommendations

Operational costs (excluding staff costs)							
Recommendation	**Additional resource required**	**Unit cost**	**Number required**	**2020**	**2021**	**2022**	**Total cost**
Recommendation 2.2.1.1 **Initial staging** Contrast enhanced CT-TAP should be employed for the initial staging of patients diagnosed with colon cancer.	CT-TAP (potential revenue costs for staffing included in Table 15)	€250 (SJH)	1,891[1]	€472,750	€472,750	€472,750	€1,418,250
Recommendation 2.2.1.2 **Hepatic metastases** Hepatocyte specific contrast enhanced MRI of the liver is the modality of choice for evaluation of liver metastases in patients with colon cancer being considered for surgical resection.	MRI (potential revenue costs for staffing included in Table 15)	€138 (SJH)	1,456[2]	€200,928	€200,928	€200,928	€602,784
Recommendation 2.2.1.3 **Extrahepatic metastases** Currently, PET-CT is not a first-line imaging modality for staging colon cancer and can be considered as a problem solving tool in patients with equivocal imaging findings following discussion at a multidisciplinary team meeting.	PET-CT (potential revenue costs for staffing included in Table 15)	€1,199 (SJH)	Unknown[3]	TBD	TBD	TBD	TBD

[1] Estimated annual average incidence for colon cancer (C18) in Ireland, 2018-2020 (NCRI, 2020)

[2] Based on the percentage of colon cancer patients treated with surgery within the first year (77%) (NCRI, 2018) and the estimated annual average incidence for colon cancer (C18) in Ireland, 2018-2020 (NCRI, 2020).

[3] The number of PET-CTs required is unknown, this is due to the nature of this recommendation which states that PET-CT is not a first line imaging modality.

Operational costs (excluding staff costs)							
Recommendation	**Additional resource required**	**Unit cost**	**Number required**	**2020**	**2021**	**2022**	**Total cost**
Recommendation 2.2.2.1 **Imaging for further liver lesions** Hepatocyte specific contrast enhanced MRI of the liver is the imaging modality of choice in patients with colon cancer with a potentially resectable liver lesion to detect further liver lesions.	MRI (potential revenue costs for staffing included in Table 15)	€138	364[4]	€50,232	€50,232	€50,232	€150,696
Recommendation 2.2.2.2 **Imaging for further liver lesions** PET-CT can be considered in patients with colon cancer with potentially resectable liver lesion with equivocal imaging findings following discussion at a multidisciplinary team meeting.	PET- CT (potential revenue costs for staffing included in Table 15)	€1,199	Unknown[5]	TBD	TBD	TBD	TBD
Recommendation 2.2.3.1 In patients diagnosed with colon cancer whose tumour cannot be endoscopically passed, preoperative CT colonography should be considered to look for synchronous lesions and to allow for surgical planning. CT colonography should only be performed when local expertise is available.	CT Colonography (potential revenue costs for staffing included in Table 15)	€550 (HIQA HTA)	165[6]	€90,750	€90,750	€90,750	€272,250
Recommendation 2.2.4.1 In patients with left-sided colon cancer, complete visualisation of the entire colon by colonoscopy or CT colonography is recommended prior to surgery. CT colonography should only be performed in centres experienced in the technique.	Nil (No additional resource required as current practice)	N/A	N/A	N/A	N/A	N/A	N/A
Recommendation 2.2.4.2 In patients diagnosed with colon cancer whose tumour cannot be endoscopically passed, preoperative CT colonography should be considered to look for synchronous lesions and to allow for surgical planning. CT colonography should only be performed when local expertise is available.	CT Colonography (potential revenue costs for staffing included in Table 15)	€550 (HIQA HTA)	165	€90,750	€90,750	€90,750	€272,250

[4] Based on the estimated annual average incidence for colon cancer (C18) in Ireland, 2018-2020 (NCRI, 2020) and adjusted for the number of patients expected to undergo surgery (77%) (NCRI, 2018) and of those the number expected to have a metastases (25%) (NCRI, 2019a).

[5] The number of PET-CTs required is unknown, this is due to the nature of this recommendation which states PET-CT should be used in patients with equivocal imaging findings.

[6] Based on the estimated annual average incidence for colon cancer (C18) in Ireland, 2018-2020 (NCRI, 2020) and adjusted for the number of patients expected to undergo surgery (77%) (NCRI, 2018) and of those the number of patients expected to have a failed colonoscopy (11.3%) (Atkin et al., 2013).

Operational costs (excluding staff costs)							
Recommendation	**Additional resource required**	**Unit cost**	**Number required**	**2020**	**2021**	**2022**	**Total cost**
Recommendation 2.2.5.1 For patients with colon cancer, lesions should be tattooed at colonoscopy.	Nil (No additional resource required as current practice)	N/A	N/A	N/A	N/A	N/A	N/A
Recommendation 2.2.5.2 For patients with colon cancer, the tattoo should be placed 1-2 cm distal to the lesion and ideally at three points in the circumference.	Nil (No additional resource required as current practice)	N/A	N/A	N/A	N/A	N/A	N/A
Recommendation 2.2.6.1 In patients undergoing surgery with colon cancer, it is recommended to identify as many nodes as possible, all of which should be submitted for microscopic examination/evaluation. Overall, the median for the laboratory should be at least 12.	Nil (No additional resource required as current practice)	N/A	N/A	N/A	N/A	N/A	N/A
Recommendation 2.2.7.1 In patients diagnosed with colon cancer, Haggitt and Kikuchi classification systems may be considered where deemed applicable	Nil (No additional resource required)	N/A	N/A	N/A	N/A	N/A	N/A
Recommendation 2.2.8.1 In patients with colon cancer tumours ≤1 mm from the peritoneal surface if tumour does not demonstrate serosal involvement after additional evaluation, it should be categorised as pT3, additional comment should be made in the report.	Nil (No additional resource required as current practice)	N/A	N/A	N/A	N/A	N/A	N/A
Recommendation 2.2.9.1 In patients with early stage colon cancer treated with local excision, lesions should be assessed for depth of submucosal invasion, lymphovascular invasion, budding, grade of differentiation, and margin status.	Nil (No additional resource required as current practice)	N/A	N/A	N/A	N/A	N/A	N/A
Recommendation 2.2.9.2 Local resection colon cancer specimens both en-bloc and piecemeal resections, should be of sufficient quality to enable such assessment and should be discussed at a multidisciplinary team meeting.	Nil (No additional resource required as current practice)	N/A	N/A	N/A	N/A	N/A	N/A
Recommendation 2.2.9.3 Patient factors such as performance status, comorbidities, and informed patient preferences should be taken into consideration following multidisciplinary team discussion for decisions on further management.	Nil (No additional resource required as current practice)	N/A	N/A	N/A	N/A	N/A	N/A

Operational costs (excluding staff costs)							
Recommendation	**Additional resource required**	**Unit cost**	**Number required**	**2020**	**2021**	**2022**	**Total cost**
Recommendation 2.3.1.1 In patients with obstructing colon cancer colonic stenting as a bridge to surgery may be considered in selected patients	Nil (potential revenue costs for staffing included in Table 15)	N/A	N/A	N/A	N/A	N/A	N/A
Recommendation 2.3.1.2 Colonic stenting should be considered for the palliation of patients with obstructing colon cancer (i.e. In those who are not fit for immediate resection or in those with advanced disease).	Nil (potential revenue costs for staffing included in Table 15)	N/A	N/A	N/A	N/A	N/A	N/A
Recommendation 2.4.1.1 In patients diagnosed with colon cancer minimally invasive colectomy/partial colectomy by an experienced laparoscopic surgeon should be considered in appropriate patients.	Nil (potential revenue costs for staffing included in Table 15)	N/A	N/A	N/A	N/A	N/A	N/A
Recommendation 2.4.2.1 In patients with colon cancer dissection in the mesocolic plane is essential for good oncologic outcomes.	Nil (potential revenue costs for staffing included in Table 15)	N/A	N/A	N/A	N/A	N/A	N/A
Recommendation 2.4.2.2 In patients with colon cancer undergoing curative resection the role of extended lymphadenectomy remains uncertain.	Nil (No additional resource)	N/A	N/A	N/A	N/A	N/A	N/A
Recommendation 2.4.3.1 Patients with metastatic disease deemed unresectable, and a colon primary, should be discussed at a multidisciplinary team meeting with appropriate surgical expertise prior to undergoing any treatment except in the presence of a surgical emergency.	Nil (potential revenue costs for staffing included in Table 15)	N/A	N/A	N/A	N/A	N/A	N/A
Recommendation 2.5.1.1 For patients with cancer, early provision of palliative care can improve patient outcomes.	Nil (potential revenue costs for staffing included in Table 15)	N/A	N/A	N/A	N/A	N/A	N/A
Recommendation 2.5.1.2 Assessment of palliative care needs should be an ongoing process throughout the course of a patient's cancer illness and services provided on the basis of identified need.	Nil (potential revenue costs for staffing included in Table 15)	N/A	N/A	N/A	N/A	N/A	N/A
						Total revenue costs of implementing the recommendations	€2,716,230

Table 15 Budget impact assessment of expected staff costs of implementing recommendations

Profession	Relevant Recommendation(s)	Additional staff required	Unit cost	Number required	2020	FYC 2021	FYC 2022	Total cost
Radiology	2.2.1.1, 2.2.1.2, 2.2.1.3, 2.2.2.1, 2.2.2.2, 2.2.3.1, 2.2.4.2	Consultant radiologist	€204,944[7]	x WTE[8]				
Surgery	2.3.1.1, 2.3.1.2, 2.3.1.3, 2.4.1.1, 2.4.2.1	Consultant Colorectal surgeon	€204,944[7]	x WTE[8]				
Palliative	2.8.1.1, 2.8.1.2	Palliative Care Consultant	€204,944[7]	x WTE[8]				
Pathology	2.2.9.1, 2.2.9.2	Consultant Histopathologist	€204,944[7]	x WTE[8]				
	2.2.9.1, 2.2.9.2	Medical laboratory scientist	€61,953	x WTE[8]				
Nursing	2.8.1.1, 2.8.1.2	Palliative care CNS	€74,057	x WTE[8]				
Admin	All	Administrator (MDT, data management)	€64,453	x WTE[8]				
Total revenue costs of implementing the recommendations:								TBD

Table 16 Total cost of implementing the guideline recommendations

Cost	2020	2021	2022	Total cost
Total expected operational costs in implementing recommendations	€905,410	€905,410	€905,410	€2,716,230
Total expected staff costs for implementing recommendations	Await outcome of surgical centralisation and workforce planning			
Total cost of implementing the guideline				€2,716,230 +Revenue cost TBC

[7] Salaries for consultant posts were calculated based on new entrants from 1st October 2012 and are based on the mid-point of contract type B on the 2019 salary scale for adjusted for pension (4%), pay related social insurance (10.95%) and overheads (25%). Salaries are rounded to the nearest thousand.

[8] Await outcome of surgical centralisation and workforce planning

Appendix 7: Implementation plan

Diagnosis and staging

Guideline recommendation or number(s)	Implementation barriers /enablers/gaps	Action / intervention / task to implement recommendation	Lead responsibility for delivery of the action	Timeframe for completion			Expected outcome and verification
				Year 1	Year 2	Year 3	
Rec. 2.2.1.1 **Initial staging** Contrast enhanced CT-TAP should be employed for the initial staging of patients diagnosed with colon cancer. **Rec. 2.2.1.2** **Hepatic metastases** Hepatocyte specific contrast enhanced MRI of the liver is the modality of choice for evaluation of liver metastases in patients with colon cancer being considered for surgical resection. **Rec. 2.2.1.3** **Extrahepatic metastases** Currently, PET-CT is not a first-line imaging modality for staging colon cancer and can be considered as a problem solving tool in patients with equivocal imaging findings following discussion at a multidisciplinary team meeting. **Rec. 2.2.2.1** **Imaging for further liver lesions** Hepatocyte specific contrast enhanced MRI of the liver is the imaging modality of choice in patients with colon	**Barrier:** Access to equipment. **Enabler:** National Cancer Strategy recommendation 14 (Capital investment plan).	Secure funding through the HSE service planning process for equipment. **National Cancer Strategy recommendation No. 14.** The NCCP, working with the other Directorates in the HSE and with the Department of Health, will develop a rolling capital investment plan, to be reviewed annually, with the aim of ensuring that cancer facilities meet requirements.	NCCP as per National Cancer Strategy recommendation no. 14.			X	**Outcome:** All patients with colon cancer will have access to diagnostic equipment. **Verification:** Completed capital investment plan. Current programme of work by the NCCP based on National Cancer Strategy recommendation 14.

Guideline recommendation or number(s)	Implementation barriers /enablers/gaps	Action / intervention / task to implement recommendation	Lead responsibility for delivery of the action	Timeframe for completion			Expected outcome and verification
				Year 1	Year 2	Year 3	
cancer with a potentially resectable liver lesion to detect further liver lesions. **Rec 2.2.2.2** **Imaging for further liver lesions** PET-CT can be considered in patients with colon cancer with potentially resectable liver lesion with equivocal imaging findings following discussion at a multidisciplinary team meeting. **Rec. 2.2.3.1** In patients diagnosed with colon cancer whose tumour cannot be endoscopically passed, preoperative CT colonography should be considered to look for synchronous lesions and to allow for surgical planning. CT colonography should only be performed when local expertise is available. **Rec. 2.2.4.2** In patients diagnosed with colon cancer whose tumour cannot be endoscopically passed, preoperative CT colonography should be considered to look for synchronous lesions and to allow for surgical planning. CT colonography should only be							

Guideline recommendation or number(s)	Implementation barriers /enablers/gaps	Action / intervention / task to implement recommendation	Lead responsibility for delivery of the action	Timeframe for completion			Expected outcome and verification
				Year 1	Year 2	Year 3	
performed when local expertise is available.							
Rec. 2.2.4.1 In patients with left-sided colon cancer, complete visualisation of the entire colon by colonoscopy or CT colonography is recommended prior to surgery. CT colonography should only be performed in centres experienced in the technique.	**Barrier:** Limited availability of appropriately trained radiology staff/personnel. **Enabler:** National Cancer Strategy recommendation 10, recommendation 16, recommendation 50 (Radiology training, consultant staffing, workforce planning).	**National Cancer Strategy recommendation no. 10.** The Department of Health will liaise with the Health and Education authorities with a view to increasing places in Third Level Institutions for the training of radiographers and sonographers.	DoH as per National Cancer Strategy recommendation no. 10.			X	**Outcome:** All patients with colon cancer will have access to diagnostics by appropriately trained staff. **Verification:** Training provided/Staff training records. Current programme of work by NCCP based on National Cancer Strategy recommendation no. 10.
		National Cancer Strategy recommendation no. 16. The NCCP will ensure that consultant appointments for radiology, endoscopy and histopathology, where necessary, are made in conjunction with appointments in other disciplines such as surgery and medical oncology.	NCCP as per National Cancer Strategy recommendation no. 16.			X	**Verification:** Staff in place. No additional resources required. Current programme of work by NCCP based on National Cancer Strategy recommendation no. 16.

Guideline recommendation or number(s)	Implementation barriers /enablers/gaps	Action / intervention / task to implement recommendation	Lead responsibility for delivery of the action	Timeframe for completion			Expected outcome and verification
				Year 1	Year 2	Year 3	
		National Cancer Strategy recommendation no. 50. The NCCP, aided by a crosssector group, will draw up a comprehensive workforce plan for cancer services. This will include an interim assessment of staffing needs at medical, nursing and health & social care professional levels by mid-2018[9].	NCCP as perNational Cancer Strategy recommendation no. 50.			X	**Verification:** Completed workforce assessment. No additional resources required. Current programme of work by NCCP based on National Cancer Strategy recommendation no. 50.
Rec. 2.2.5.1 For patients with colon cancer, lesions should be tattooed at colonoscopy. **Rec. 2.2.5.2** For patients with colon cancer, the tattoo should be placed 1-2 cm distal to the lesion and ideally at three points in the circumference. **Rec. 2.2.6.1** In patients undergoing surgery with colon cancer, it is recommended to identify as many nodes as possible, all of which should be submitted for microscopic examination/evaluation. Overall, the median for the laboratory should be at least 12. **Rec. 2.2.7.1** In patients diagnosed with colon cancer, Haggitt and	Current practice	Not applicable	Clinician				Not applicable

[9] Direct wording taken from the National Cancer Strategy (2017). Time frame for completion may differ.

Guideline recommendation or number(s)	Implementation barriers /enablers/gaps	Action / intervention / task to implement recommendation	Lead responsibility for delivery of the action	Timeframe for completion			Expected outcome and verification
				Year 1	Year 2	Year 3	
Kikuchi classification systems may be considered where deemed applicable **Rec. 2.2.8.1** In patients with colon cancer tumours ≤1 mm from the peritoneal surface if tumour does not demonstrate serosal involvement after additional evaluation, it should be categorised as pT3, additional comment should be made in the report. **Rec. 2.2.9.1** In patients with early stage colon cancer treated with local excision, lesions should be assessed for depth of submucosal invasion, lymphovascular invasion, budding, grade of differentiation, and margin status. **Rec. 2.2.9.2** Local resection colon cancer specimens both en-bloc and piecemeal resections, should be of sufficient quality to enable such assessment and should be discussed at a multidisciplinary team meeting. **Rec. 2.2.9.3** Patient factors such as							

Guideline recommendation or number(s)	Implementation barriers /enablers/gaps	Action / intervention / task to implement recommendation	Lead responsibility for delivery of the action	Timeframe for completion			Expected outcome and verification
				Year 1	Year 2	Year 3	
performance status, comorbidities, and informed patient preferences should be taken into consideration following multidisciplinary team discussion for decisions on further management.							

Treatment: Emergency presentation

Guideline recommendation or number(s)	Implementation barriers /enablers/gaps	Action / intervention / task to implement recommendation	Lead responsibility for delivery of the action	Timeframe for completion			Expected outcome and verification
				Year 1	Year 2	Year 3	
Rec. 2.3.1.1 In patients with obstructing colon cancer colonic stenting as a bridge to surgery may be considered in selected patients **Rec. 2.3.1.2** Colonic stenting should be considered for the palliation of patients with obstructing colon cancer (i.e. In those who are not fit for immediate resection or in those with advanced disease).	**Barrier:** Availability of trained surgical staff. **Enabler:** National Cancer Strategy recommendation 14, recommendation 21 (Capital plan, centralisation).	**National Cancer strategy recommendation no. 14.** The NCCP, working with the other Directorates in the HSE and with the Department of Health, will develop a rolling capital investment plan, to be reviewed annually, with the aim of ensuring that cancer facilities meet requirements.	NCCP as per National Cancer Strategy recommendation no. 14.				**Outcome:** All patients diagnosed with colon cancer will have access to surgical expertise. **Verification:** Completed capital investment plan. Current programme of work by the NCCP based on National Cancer Strategy recommendation no. 14 and 21.
		National Cancer Strategy recommendation no. 21. The NCCP will draw up a plan setting out the number/location of designated cancer centres in which surgery will take place for the various tumour types. Timescales for the implementation of the plan will be included for each tumour type.	NCCP as per National Cancer Strategy recommendation no. 21.				**Verification:** Designated cancer centres with surgical expertise in place for colon cancer. **KPI 11** Complete centralisation of cancer surgical services

Treatment: Surgical techniques

Guideline recommendation or number(s)	Implementation barriers /enablers/gaps	Action / intervention / task to implement recommendation	Lead responsibility for delivery of the action	Timeframe for completion			Expected outcome and verification
				Year 1	Year 2	Year 3	
Rec. 2.4.1 1 In patients diagnosed with colon cancer minimally invasive colectomy/partial colectomy by an experienced laparoscopic surgeon should be considered in appropriate patients. **Rec. 2.4.2.1** In patients with colon cancer dissection in the mesocolic plane is essential for good oncologic outcomes. **Rec. 2.4.2.2** In patients with colon cancer undergoing curative resection the role of extended lymphadenectomy remains uncertain. **Rec. 2.4.3.1** Patients with metastatic disease deemed unresectable, and a colon primary, should be discussed at a multidisciplinary team meeting with appropriate surgical expertise prior to undergoing any treatment except in the presence of a surgical emergency.	**Barrier:** Limited availability of appropriately trained surgical staff **Enabler:** National Cancer Strategy recommendation 14, recommendation 15, recommendation 16, recommendation. 21 & recommendation 50 (Capital investment plan, Consultant staffing centralisation & workforce planning).	**National Cancer strategy recommendation no. 14.** The NCCP, working with the other Directorates in the HSE and with the Department of Health, will develop a rolling capital investment plan, to be reviewed annually, with the aim of ensuring that cancer facilities meet requirements. **National Cancer strategy recommendation no. 15.** The Department of Health will ensure that investment in infrastructure, facilities, personnel and programmes in the designated cancer centres will have a goal of ultimately developing at least one comprehensive cancer care centre that will optimise cancer prevention, treatment, education and research during the Strategy period. **National Cancer strategy recommendation no. 16.** **T**he NCCP will ensure that consultant appointments for radiology, endoscopy and histopathology, where necessary, are made in conjunction with appointments in other disciplines such as surgery and medical oncology. **Cancer strategy recommendation No. 21.** The NCCP will draw up a plan setting out the number/location of	NCCP as per National Cancer Strategy recommendation no. 14.				**Outcome:** All patients diagnosed with colon cancer will have access to surgical equipment. **Verification:** Equipment available. Current programme of work by the NCCP based on National Cancer Strategy recommendation no.14, 15, 16, 21 and 50.
			NCCP as per National Cancer Strategy recommendation no. 21.				**Verification:** Designated cancer centres in which surgery will take place for colon cancer available. **KPI 11** Complete centralisation of cancer surgical services

Guideline recommendation or number(s)	Implementation barriers /enablers/gaps	Action / intervention / task to implement recommendation	Lead responsibility for delivery of the action	Timeframe for completion			Expected outcome and verification
				Year 1	Year 2	Year 3	
		designated cancer centres in which surgery will take place for the various tumour types. Timescales for the implementation of the plan will be included for each tumour type. **Cancer strategy recommendation no. 50.** The NCCP, aided by a crosssector group, will draw up a comprehensive workforce plan for cancer services. This will include an interim assessment of staffing needs at medical, nursing and health & social care professional levels by mid-2018*.					

Treatment: Palliative care

Guideline recommendation or number(s)	Implementation barriers /enablers/gaps	Action / intervention / task to implement recommendation	Lead responsibility for delivery of the action	Timeframe for completion			Expected outcome and verification
				Year 1	Year 2	Year 3	
Rec. 2.5.1.1 For patients with cancer, early provision of palliative care can improve patient outcomes.For patients with cancer, early provision of palliative care can improve patient outcomes. **Rec. 2.5.1.2** Assessment of palliative care needs should be an ongoing process throughout the course of a patient's cancer illness and services provided on the basis of identified need.	**Barrier:** Insufficient availability of specialist palliative care staff. **Enabler:** National Cancer Strategy recommendation 31, recommendation 32 (Specialist palliative care, identification of palliative care needs).	**National Cancer Strategy Recommendation no. 31.** Designated cancer centres will have a sufficient complement of specialist palliative care professionals, including psycho-oncologists, to meet the needs of patients and families (such services will be developed on a phased basis to be available over seven days a week.	HSE & designated cancer centres as per National Cancer Strategy recommendation no. 31.			X	**Outcome:** All patients with colon cancer have access to palliative care. **Verification:** Staff in place. National Cancer Strategy KPI 19 - Increase the proportion of patients receiving specialist palliative care. Current programme of work based on National Cancer Strategy recommendation no. 31 (HSE and designated cancer centres) and 32 (HSE).
		National Cancer Strategy Recommendation no. 32. Oncology staff will have the training and education to ensure competence in the identification, assessment and management of patients with palliative care needs and all patients with cancer will have regular, standardised assessment of their needs.	HSE as per National Cancer Strategy recommendation no. 31.			X	**Verification:** Training and education provided. Staff training records.

A list of National Cancer Strategy (2017) recommendations, KPIs and NCCP KPIs that are mentioned in the implementation plan are detailed below:

Table 17 Cancer strategy recommendations relevant to implementation (DoH, 2017)

No.	National Cancer Strategy Recommendations Relevant to Implementation
Recommendation 10	The Department of Health will liaise with the Health and Educational authorities with a view to increasing places in third level institutions for the training of radiographers and sonographers.
Recommendation 13	Patients diagnosed with cancer will have their case formally discussed at a multi-disciplinary team meeting. The NCCP, working with the Hospital Groups, will oversee and support MDT composition, processes and reporting of outcomes.
Recommendation 14	The NCCP, working with the other directorates in the HSE and with the department of Health, will develop a rolling capital investment plan, to be reviewed annually, with the aim of ensuring that cancer facilities meet requirements
Recommendation 16	The NCCP will ensure that consultant appointments for radiology, endoscopy and histopathology where necessary, are made in conjunction with appointments in other disciplines such as surgery and medical oncology.
Recommendation 21	The NCCP will draw up a plan setting out the number/location of designated cancer centres in which surgery will take place for the various tumour types. Timescales for the implementation of the plan will be included for each type.
Recommendation 31	Designated cancer centres will have a sufficient complement of specialist palliative care professionals, including psycho-oncologists, to meet the needs of patients and families (such services will be developed on a phased basis to be available over seven days a week).
Recommendation 32	Oncology staff will have the training and education to ensure competence in the identification, assessment and management of patients with palliative care needs and all patients with cancer will have regular, standardised assessment of their needs.
Recommendation 50	The NCCP, aided by a cross- sector group, will draw up a comprehensive workforce plan for cancer services. This will include an interim assessment of staffing needs at medical, nursing and health & social care professional levels by mid-2018

Table 18 Key Performance Indicators relevant to implementation (DoH, 2017)

No.	Key Performance Indicators relevant to implementation
Cancer strategy KPI 11	Complete centralisation of cancer surgical services
Cancer Strategy KPI 19	Increase proportion of patients receiving specialist palliative care

Appendix 8: Monitoring and audit

It is important that both the implementation of the guideline and patient outcomes are audited to ensure that this guideline positively impacts on patient care. A number of recommendations have been identified by the Guideline Development Group as areas suitable for audit, some specifically due to variation in practice Table 19.

There is a five stage approach to clinical audit which include planning for audit, standard/criteria selection, measuring performance, making improvements and sustaining improvements. Each audit carried out will be expected to follow this process (HSE, 2019). Two key performance indicators from the National Cancer Strategy 2016-2026 are outlined in Table 20 which can be used to monitor the implementation of a number of guideline recommendations.

The audit criteria detailed in Table 20 will be monitored as KPIs from the National Cancer Strategy.

Table 19 Recommendations identified by the Guideline Development Group as areas suitable for audit

Diagnosis and staging
Recommendation 2.2.1.1 **Initial staging** Contrast enhanced CT-TAP should be employed for the initial staging of patients diagnosed with colon cancer. **Recommendation 2.2.1.2** **Hepatic metastases** Hepatocyte specific contrast enhanced MRI of the liver is the modality of choice for evaluation of liver metastases in patients with colon cancer being considered for surgical resection. **Recommendation 2.2.1.3** **Extrahepatic metastases** Currently, PET-CT is not a first-line imaging modality for staging colon cancer and can be considered as a problem solving tool in patients with equivocal imaging findings following discussion at a multidisciplinary team meeting. **Recommendation 2.2.2.1** **Imaging for further liver lesions** Hepatocyte specific contrast enhanced MRI of the liver is the imaging modality of choice in patients with colon cancer with a potentially resectable liver lesion to detect further liver lesions. **Recommendation 2.2.2.2** **Imaging for further liver lesions** PET-CT can be considered in patients with colon cancer with potentially resectable liver lesion with equivocal imaging findings following discussion at a multidisciplinary team meeting. **Recommendation 2.2.3.1** In patients diagnosed with colon cancer whose tumour cannot be endoscopically passed, preoperative CT colonography should be considered to look for synchronous lesions and to allow for surgical planning. CT colonography should only be performed when local expertise is available. **Recommendation 2.2.4.1** In patients with left-sided colon cancer, complete visualisation of the entire colon by colonoscopy or CT colonography is recommended prior to surgery. CT colonography should only be performed in centres experienced in the technique. **Recommendation 2.2.5.1** For patients with colon cancer, lesions should be tattooed at colonoscopy. **Recommendation 2.2.5.2** For patients with colon cancer, the tattoo should be placed 1-2 cm distal to the lesion and ideally at three points in the circumference.

Recommendation 2.2.6.1 In patients undergoing surgery with colon cancer, it is recommended to identify as many nodes as possible, all of which should be submitted for microscopic examination/evaluation. Overall, the median for the laboratory should be at least 12. **Recommendation 2.2.8.1** In patients with colon cancer tumours ≤1 mm from the peritoneal surface if tumour does not demonstrate serosal involvement after additional evaluation, it should be categorised as pT3, additional comment should be made in the report. **Recommendation 2.2.9.1** In patients with early stage colon cancer treated with local excision, lesions should be assessed for depth of submucosal invasion, lymphovascular invasion, budding, grade of differentiation, and margin status.
Treatment: Surgical techniques
Recommendation 2.4.3.1 Patients with metastatic disease deemed unresectable, and a colon primary, should be discussed at a multidisciplinary team meeting with appropriate surgical expertise prior to undergoing any treatment except in the presence of a surgical emergency.
Treatment: Late stage/Palliative Care
Recommendation 2.5.1.1 For patients with cancer, early provision of palliative care can improve patient outcomes. **Recommendation 2.5.1.2** Assessment of palliative care needs should be an ongoing process throughout the course of a patient's cancer illness and services provided on the basis of identified need.

Table 20 National Cancer Strategy Key Performance Indicators relevant to implementation

No.	Key Performance Indicators Relevant to Implementation
Cancer Strategy KPI 11	Complete centralisation of cancer surgical services
Cancer Strategy KPI 19	Increase proportion of patients receiving specialist palliative care

Appendix 9: Glossary of terms and abbreviations

Glossary

Definitions within the context of this document

Case Control Study	The observational epidemiologic study of persons with the disease (or other outcome variable) of interest and a suitable control (comparison, reference) group of persons without the disease. The relationship of an attribute to the disease is examined by comparing the diseased and non-diseased with regard to how frequently the attribute is present or, if quantitative, the levels of the attribute, in each of the groups. (CEBM website)
Case Series	A group or series of case reports involving patients who were given similar treatment. Reports of case series usually contain detailed information about the individual patients. This includes demographic information (for example, age, gender, ethnic origin) and information on diagnosis, treatment, response to treatment, and follow-up after treatment. (CEBM website)
Clinician	A healthcare professional such as a doctor involved in clinical practice.
Cohort study	The analytic method of epidemiologic study in which subsets of a defined population can be identified who are, have been, or in the future may be exposed or not exposed, or exposed in different degrees, to a factor or factors hypothesised to influence the probability of occurrence of a given disease or other outcome. The main feature of cohort study is observation of large numbers over a long period (commonly years) with comparison of incidence rates in groups that differ in exposure levels. (CEBM website)
Validity	The extent to which a variable or intervention measures what it is supposed to measure or accomplishes what it is supposed to accomplish. The internal validity of a study refers to the integrity of the experimental design. The external validity of a study refers to the appropriateness by which its results can be applied to non-study patients or populations. (CEBM website)
Meta-analysis	A systematic review may or may not include a meta-analysis, which is a quantitative summary of the results. (CEBM website)
Randomised trial	An epidemiological experiment in which subjects in a population are randomly allocated into groups, usually called study and control groups, to receive or not receive an experimental preventive or therapeutic procedure, manoeuvre, or intervention. The results are assessed by rigorous comparison of rates of disease, death, recovery, or other appropriate outcome in the study and control groups. (CEBM website)
Systematic review	The application of strategies that limit bias in the assembly, critical appraisal, and synthesis of all relevant studies on a specific topic. Systematic reviews focus on peer-reviewed publications about a specific health problem and use rigorous, standardised methods for selecting and assessing articles. A systematic review differs from a meta-analysis in not including a quantitative summary of the results. (CEBM website)

Abbreviations

2DCRT	Two-Dimensional Conformal radiotherapy
3DCRT	Two-Dimensional Conformal radiotherapy
5FU	Fluorouracil
AGREE II	Appraisal of Guidelines for Research and Evaluation II
AR-DRG	Australian refined diagnostic related groups
ALCCaS	Australian Laparoscopic Colon Cancer Study
BH	Beaumont Hospital
BIA	Budget Impact Analysis
BMJ	British Medical Journal
BMI	Body Mass Index
CAP	College of American Pathologists
CCO	Chief Communications Officer
CCP	Complex colon polyps
CDR	Clinical Decision Rule
CEA	Cost-Effectiveness Analysis
CEBM	Centre for Evidence-Based Medicine
CEO	Chief Executive Officer
CEP	Cost-Effectiveness Plan
CI	Confidence Interval
CINAHL	Cumulative Index to Nursing and Allied Health Literature
CME	Complete Mesocolic Excision
CNS	Clinical Nurse Specialist
CQ	Clinical Question
CRC	Colorectal cancer
CRT	Chemoradiotherapy
CRLM	Colorectal liver metastasis
CSO	Central Statistics Office
CT	Computed Tomography
CTC	Computed Tomographic Colonography
CT-TAP	Computed Tomography of Thorax, Abdomen and Pelvis
CUH	Cork University Hospital
DCCG	Dutch Colorectal Cancer Group
DFS	Disease-Free Survival
DoH	Department of Health
DoHC	Department of Health and Children
ECCM-MRI	Extracellular contrast media-enhanced MRI
ECIS	European Cancer Information system
EBP	Evidence-Based Practice
EED	Economic Evaluation Database
EMR	Endoscopic mucosal resection
ER	Endoscopic resection
EU	European Union
EQ-5D	EuroQol-5D
GBP	Great British Pound
GDG	Guideline Development Group
GEWF	Galcial acetic acid, ethanol, distilled water, formaldehyde
GP	General practitioner
GUH	Galway University Hospital
FA	Folinic Acid
FDA	Food and Drug Administration
FDG	Fluorodeoxyglucose
HALS	Hand assisted laparoscopic surgery
HEED	Health Economics Evaluation Database

HIQA	Health Information and Quality Authority
HR	Hazard Ratio
HSE	Health Service Executive
HTA	Health Technology Assessment
IAMP	Irish Association of Physicists in Medicine
IANO	Irish Association for Nurses in Oncology
ICER	incremental cost-effectiveness ratio
ICU	Intensive Care Unit
ICD-O	International Classification of Diseases for Oncology
ICGP	Irish College of General Practitioners
IMRT	Intensity Modulated Radiotherapy
ISCCNA	Irish Stoma Care and Colorectal Nurses Association
ISMO	Irish Society for Medical Oncologists
IV	Intravenous
KPI	Key Performance Indicators
LOS	Length of Stay
LR	Laparoscopic resection
LS	Laparoscopic surgery
LSL	laterally spreading colonic lesions
LYG	Life Years Gained
LV5FU	Leucovorin/Fluorouracil
LV	Leucovorin
MDCT	Multidetector computed tomography
MDT	Multidisciplinary team meeting
MeSH	Medical Subject Headings
MMUH	Mater Misericordiae University Hospital
MUH	Mayo University Hospital
MRC	Medical Research Council
MRI	Magnetic Resonance Imaging
MUH	Mayo University Hospital
n/a	Not applicable
NALA	National Adult Literacy Agency
NCCN	National Comprehensive Cancer Network
NCCP	National Cancer Control Programme
NCEC	National Clinical Effectiveness Committee
NCRI	National Cancer Registry Ireland
NHS	National Health Service
NICE	National Institute for Health and Care Excellence
NMSC	Non-Melanoma Skin Cancer
NPSO	National Patient Safety Office
NSS	National Screening Service
OLOLH	Our Lady's of Lourdes Hospital
OR	Odds Ratio
OS	Overall Survival
OT	Operation time
PET-CT	Positron Emission Tomography-Computed Tomography
PFS	Progression-Free Survival
PH	Portunicula Hospital
PICO	Population/Patient; Intervention; Comparison/Control; Outcome
PICO(T)	Population/Patient; Intervention; Comparison/Control; Outcome, Time
PPP	Purchasing power of parity
PV-MRI	Primovist® MRI
QALY	Quality-Adjusted Life Year
QID	Quality Improvement Division
QOL	Quality Of Life

QUB	Queens University Belfast
RCPath	The Royal College of Pathologists
RCSI	Royal College of Surgeons in Ireland
RCT	Randomised Controlled Trial
RR	Risk Ratio
RS	Robotic surgery
SEMS	Self-Expanding Metal Stent
SFH	St. Francis Hospice
SIGN	Scottish Intercollegiate Guideline Network
SJH	St. James' Hospital
SLRON	St Luke's Radiation Oncology Network
SUH	Sligo University Hospital
SVUH	St. Vincent's University Hospital
TEM	Transanal endoscopic mircosurgery
TCD	Trinity College Dublin
TNM	Tumor, Node, Metastasis
TUH	Tallaght University Hospital
USA	United States of America
USD	United States Dollar
US	United States
UK	United Kingdom
UCD	University College Dublin
UHW	University Hospital Waterford
UL	University Hospital Limerick
WHO	World Health Organization

Appendix 10: Levels of evidence and grading systems

Table 21 Levels of evidence for diagnostic studies (Oxford CEBM, 2009)

1a	Systematic review (with homogeneity*) of Level 1 diagnostic studies; clinical decision rule (CDR") with 1b studies from different clinical centres.
1b	Validating** cohort study with good reference standards" " "; or CDR tested within one clinical centre.
1c	Absolute SpPins (specificity) and SnNouts (sensitivity)" ".
2a	Systematic review (with homogeneity*) of Level >2 diagnostic studies.
2b	Exploratory** cohort study with good reference standards; CDR after deviation, or validated only on split-samples§§§ or databases.
3a	Systematic review (with homogeneity*) of 3b and better studies.
3b	Non-consecutive study; or without consistently applied reference standards.
4	Case-control study, poor or non-independent reference standard.
5	Expert opinion without explicit critical appraisal, or based on physiology, bench research or first principles.

* By homogeneity we mean a systematic review that is free of worrisome variations (heterogeneity) in the directions and degrees of results between individual studies. Not all systematic reviews with statistically significant heterogeneity need be worrisome, and not all worrisome heterogeneity need be Statistically significant. As noted above, studies displaying worrisome heterogeneity should be tagged with a "-" at the end of their designated level.

" Clinical Decision Rule (these are algorithms or scoring systems that lead to a prognostic estimation or a diagnostic category).

** Validating studies test the quality of a specific diagnostic test, based on prior evidence. An exploratory study collects information and trawls the data (e.g. using a regression analysis) to find which factors are 'significant'.

" " " Good reference standards are independent of the test, and applied blindly or objectively to applied to all patients. Poor reference standards are haphazardly applied, but still independent of the test. Use of a non-independent reference standard (where the 'test' is included in the 'reference', or where the 'testing' affects the 'reference') implies a level 4 study.

" " An "Absolute SpPin" is a diagnostic finding whose Specificity is so high that a positive result rules-in the diagnosis. An "Absolute SnNout" is a diagnostic finding whose Sensitivity is so high that a negative result rules-out the diagnosis.

§§§ Split-sample validation is achieved by collecting all the information in a single tranche, then artificially dividing this into "derivation" and "validation" samples.

Table 22 Grades of recommendations for diagnostic studies (Oxford CEBM, 2009)

A	Consistent level 1 studies.
B	Consistent level 2 or 3 studies; or Extrapolations from level 1 studies.
C	Level 4 studies; or Extrapolations from level 2 or 3 studies.
D	Level 5 evidence; or Troublingly inconsistent or inconclusive studies of any level.

Extrapolations are where data is used in a situation that has potentially clinically important differences than the original study situation.

Table 23 Levels of evidence for interventional studies (SIGN grading system 1999-2012)

1++	High quality meta-analyses, systematic reviews of RCTs, or RCTs with a very low risk of bias.
1+	Well conducted meta-analyses, systematic reviews, or RCTs with a low risk of bias.
1-	Meta-analyses, systematic reviews, or RCTs with a high risk of bias.
2++	High quality systematic reviews of case control or cohort studies. High quality case control or cohort studies with a very low risk of confounding or bias and a high probability that the relationship is causal.
2+	Well conducted case control or cohort studies with a low risk of confounding or bias and a moderate probability that the relationship is causal.
2-	Case control or cohort studies with a high risk of confounding or bias and a significant risk that the relationship is not causal.
3	Non-analytic studies (e.g. case reports, case series).
4	Expert opinion.

Table 24 Grades of recommendations for interventional studies (SIGN grading system 1999-2012)

A	At least one meta-analysis, systematic review, or RCT rated as 1++, and directly applicable to the target population; or A body of evidence consisting principally of studies rated as 1+, directly applicable to the target population, and demonstrating overall consistency of results.
B	A body of evidence including studies rated as 2++, directly applicable to the target population, and demonstrating overall consistency of results; or Extrapolated evidence from studies rated as 1++ or 1+.
C	A body of evidence including studies rated as 2+, directly applicable to the target population and demonstrating overall consistency of results; or Extrapolated evidence from studies rated as 2++.
D	Evidence level 3 or 4; or Extrapolated evidence from studies rated as 2+.

Note: the grade of recommendation does not necessarily reflect the clinical importance of the recommendation.

Good Practice Point
Recommended best practice based on the clinical experience of the Guideline Development Group.

Practical considerations around patient care
Are statements developed with patients on issues that were important to them with regards to their own experience of the diagnosis, staging and treatment of their cancer.

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