Somerset, Wiltshire, Avon and Gloucestershire (SWAG) Cancer Services

Colorectal Cancer Clinical Advisory Group

Clinical Guidelines

June 2022

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VERSION CONTROL

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VERSION	DATE ISSUED	SUMMARY OF CHANGE	OWNER'S NAME
Draft 0.1	April 2015	First draft	SWAG Colorectal SSG
Draft 0.2	9th April 2015	Pathology guideline update	N Wong
Draft 0.2	22nd June 2015	Addition of Chemotherapy for Liver Mets Guidelines	M Williams
Draft 0.3	2nd July 2015	Removal of RAS flow diagram and points 1-5 from section 4.4 and retrospective update of version control.	N Wong / H Dunderdale
1.0	31st July 2015	Finalised	Colorectal MDT Leads
1.1	April 2017	Biennial Review	Colorectal MDT Leads
1.2	22nd May 2017	Change funding of RAS test	N Wong
1.3	30th June 2017	Finalised	H Dunderdale
1.4	2nd January 2018	Addition of TATME guidelines (p.13), screening for HPV virus for anal cancer (p.19) and advice on aspirin for all CRC patients (p.6).	M Thomas/ H Dunderdale
1.5	30th May 2019	Biennial Review. Rebranding of documents from Site Specific Groups to Clinical Advisory Groups	H Dunderdale
1.6	28th June 2019	Addition of Lynch Syndrome follow up guidelines. Finalised	J Burton / H Dunderdale
1.7	5th August 2019	Pathology update	N Wong
1.8	June 2022	Biennial Review. Change of link to website	H Dunderdale
1.9			

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Colorectal CAG Clinical Guidelines Contents

1. Introduction

The following guidelines pertain to the local management of colorectal malignancies for the Somerset, Wiltshire, Avon and Gloucestershire (SWAG) Network Colorectal Oncology Clinical Advisory Group (CAG).

The CAG refers to the National Institute for Health and Care Excellence (NICE) Colorectal Cancer clinical guidelines (December 2014):

https://www.nice.org.uk/guidance

Primary care clinicians should refer to the NICE guidelines *Suspected Cancer: recognition and management of suspected cancer in children, young people and adults* (2015) for the signs and symptoms relevant when referring to colorectal oncology services, and the CAG suspected cancer guidelines developed during the COVID-19 pandemic, found here. The CAG is committed to offering all eligible patients entry into clinical trials where available. Consent to provide tissue for research purposes will also be sought wherever appropriate.

All patients with colorectal cancer are recommended to take long term low dose aspirin (75mg) if tolerated.

2. The CAG Agreed Clinical Guidelines for Colorectal Cancer (NS/SCS/CC-16-008)

2.1 Investigations for patients suspected of having colorectal cancer

Patients with high-risk symptoms are fast tracked to an urgent 'two-week' clinic appointment or straight to a diagnostic test where appropriate.

Investigations for patients suspected of having colorectal cancer will vary according to the symptomatic presentation. The investigations should be performed as expediently as possible to allow treatment within recognised target times.

Change of Bowel Habit

- Colonoscopy is the recommended investigation and allows biopsy to better confirm the diagnosis, remove polyps and to extend the diagnostic yield for non-cancer diseases
- CT colonography is an alternative investigation, especially when colonoscopy has already failed or in elderly and comorbid patients using the minimal prep versions
- If colorectal cancer is confirmed, a CT of the chest, abdomen and pelvis will be requested.

Bleeding

Flexible sigmoidoscopy to splenic flexure; full colonoscopy if appropriate If colorectal cancer is confirmed, a full colonoscopy or CT colonogram will be requested to exclude disease in unseen colon. If colorectal cancer is confirmed a CT of the chest, abdomen and pelvis will be requested.

Iron-deficiency Anaemia

- Colonoscopy and consider gastroscopy with D2 duodenal biopsy
- Minimal prep CT colonography is an alternative in elderly and comorbid patients
- If colorectal cancer is confirmed a CT of the chest, abdomen and pelvis will be requested.

Abdominal Mass

- Two-week wait outpatient for clinical examination/confirmation
- Abdominal & pelvic (consider chest) CT scan
- Colonoscopy if the mass is likely to be related to the colon or after confirmation on CT.

Rectal Mass

- Two-week wait outpatient for clinical examination/confirmation
- If suspected rectal cancer, a colonoscopy and biopsy or CT colonography (after biopsy in clinic) will be requested to exclude synchronous disease
- If suspected rectal cancer, a CT of the Chest/Abdomen/Pelvis will be requested
- If suspected rectal cancer, an MRI Pelvis will be requested.

2.2 Imaging Guidelines

Colonoscopy: The endoscopist should biopsy / remove lesions as appropriate. Patients will be informed about the possibility of discomfort, risks of perforation and bleeding. Doctors performing colonoscopies must audit their results and aim to have high completion (>90% caecal intubation) and low perforation (0.1%) rates.

CT colonography: Allows diagnosis of colon lesions with similar specificity and sensitivity to colonoscopy but does not allow biopsy. It is particularly useful in cases where colonoscopy cannot be completed. It is a useful and safer alternative to colonoscopy in patients who cannot tolerate full bowel prep and is best performed using long oral prep.

CT Chest, abdomen & pelvis: All non-allergenic patients should receive oral and intravenous contrast. Examinations should be performed to the highest specificity of the local machine. Images will be taken of the liver in the portal venous phase of contrast enhancement.

Barium Enema: This is no longer regarded as a good alternative to colonoscopy or even CT colonography due to the relative lack of sensitivity and specificity compared to alternatives. It may be used when there is no alternative because of local issues with supply and demand in the interests of meeting targets.

MRI Rectum: Scanning protocols should comprise sagittal T2 3mm and axial T2 5mm slices of the whole pelvis with additional axial-oblique T2 high resolution slices perpendicular to the plane of the rectal tumour.

2.3 Histopathology guidelines for colorectal specimens

The CAG guidelines for the examination and reporting of colorectal cancer specimens refer to the following publications:

- Dataset for colorectal cancer histopathology reports (4th Edition). The Royal College of Pathologists, 2018. https://www.rcpath.org/uploads/assets/c8b61ba0-ae3f-43f1-85ffd3ab9f17cfe6/G049-Dataset-for-histopathological-reporting-of-colorectal-cancer.pdf
- TNM classification of malignant tumours (8th Edition). AJCC, 2018
- WHO Classification of Tumours: Digestive System Tumours. 5th ed. IARC Press, 2019
- Bowel cancer screening: pathology guidance on reporting lesions. Updated 31 May 2021. https://www.gov.uk/government/publications/bowel-cancer-screening-reporting-lesions/bowel-cancer-screening-guidance-on-reporting-lesions

Specimen Types

Colon: Endoscopic biopsies, Polypectomy specimens, Colectomy specimens.

Rectum: Endoscopic biopsies, Polypectomy specimens, TEM specimens, Anterior Resection specimens, Abdomino-perineal Resection specimens.

Colorectal Cancer Specimen Examination

Refer to: Dataset for colorectal cancer histopathology reports (4th edition). The Royal College of Pathologists, 2018: https://www.rcpath.org/uploads/assets/c8b61ba0-ae3f-43f1-85ffd3ab9f17cfe6/g049-dataset-for-histopathological-reporting-of-colorectal-cancer.pdf

Grading and Staging of Colorectal Cancers

Refer to: As above

In particular, the Colorectal Lead Pathologists should ensure that completed staging data is reported for all 'cancer polyps', i.e. invasive adenocarcinoma arising within a locally resected adenoma/polyp. This data is outlined in the Royal College of Pathologists dataset for colorectal cancer histopathology reports (4th Edition), 2018.

Clinical Governance

Pathologists reporting colorectal cancer resection specimens will undertake the following tasks:

- Participate in relevant EQA schemes.
- Have access to and be familiar with the abovementioned publications 1)-3) and, if participating in the Bowel Cancer Screening Programme, publication 4).

Bowel Cancer Screening Programme (BCSP)

Pathologists examine, dissect and report specimens derived from BCSP patients according to the 'Bowel cancer screening: pathology guidance on reporting lesions' (updated 31 May 2021).

BCSP pathologists should participate in the National BCSP EQA scheme.

Proforma for Reporting of Colorectal Cancer Resections

Refer to the Proforma for Colorectal Cancer Resections as published by the Royal College of Pathologists.

Proforma for Reporting of Colorectal Local Excision Specimens

Refer to the Proforma for Local Excision Specimens as published by the Royal College of Pathologists.

Reflex MSI/MMR testing of colorectal carcinoma

The NICE diagnostics guidance document '**Molecular testing strategies for Lynch syndrome in people with colorectal cancer**', reviewed in 2022, recommends reflex testing by MMR or MSI analysis for all new diagnoses of colorectal cancers:
https://www.nice.org.uk/guidance/dg27/chapter/1-Recommendations

This is to be addressed by cellular pathology departments according to the level of local resource available to cover this extra activity. MSI testing is available, via the National Test Directory

(https://www.england.nhs.uk/publication/national-genomic-test-directories/), at the South West Genomics Laboratory Hub (SWGLH) in Bristol.

An example of a reflex MSI testing pathway for colorectal cancer is provided by the following standard operating protocol from the Cellular Pathology Department of the North Bristol NHS Trust:

SOP for reflex testing of colorectal carcinomas (CRC)

1. Only large, surgically resected carcinomas will be subjected to this reflex testing. This does NOT include 'small' local resections such as polypectomy and TEM/TAMIS specimens.
2. At routine cut up of a CRC resection specimen, the pathologist will nominate a tumour block which macroscopically contains > 20% viable carcinoma.
3. This block number is recorded on Cerebro.
4. When the blocks are being cut for standard H&E sections, tissue from the nominated block will be prepared for MSI testing as per the SWGLH MSI guidelines.
5. The SWGLH lab has agreed to accept, for reflex MSI CRC cases, a copy of the original cellular pathology request form rather than a completed genetics request form.
6. A copy of the cellular pathology request form will be sent with the tissue sample to the SWGLH lab.
7. The MSI +/- BRAF +/- hMLH1 results will be added as supplementary reports to the specimen cellular pathology report so they are then available on ICE.
8. The supplementary report will be put in the sign out queue of the pathologist who originally reported the CRC resection specimen. If this pathologist is away, the report should be signed out instead by the pathologist manning the GIPathology@nbt.nhs.uk inbox that week.

NOTES

A. If the pathologist is doubtful at cut up that the specimen shows > 20% viable carcinoma in any block (e.g. due to neoadjuvant therapy), no tumour block will be nominated at this stage.

   a. Should histological assessment subsequently show > 20% viable carcinoma/neoplastic cell content (NCC) in a block, this can be requested via Access Further Requesting using the request code: **Reflex MSI** (the lab will understand this to follow the same tissue preparation and submission with a copy of the cell path request form as in steps 4-6 above).

b. Should histological assessment subsequently show viable carcinoma but < 20% NCC in a block, the pathologist will complete the standard SWGLH molecular pathology form because an H&E section will need to be marked and mounted unstained sections sent to SWGLH instead. This scenario should be uncommon.

B. If the pathologist finds that the nominated block does not microscopically show > 20% viable carcinoma/NCC, the pathologist will email this fact to nbn-tr.SWGLHcancer@nhs.net The pathologist will decide whether another specimen block has > 20% viable carcinoma/NCC and then follow one of the alternative pathways of Note A.

C. While the NBT cellular pathology department will record the genetic findings, it is NOT the responsibility of this department and its staff to action these findings, e.g. request referral to Clinical Genetics.

D. There may be rare cases which fail MSI testing. MMR testing may be considered for these cases.

SOP for reflex MSI testing of colorectal carcinomas (Newton Wong, 10 June 2020).

2.4 Management of Rectal Cancer

Defined as tumours below the sacral promontory/within 18 cms of anal verge.

2.4.1 Investigation and staging:

- Assessment of patient's general health and operative risk: ASA and PPOSSUM score if available. Record ASA and WHO Performance Status for NBOCAP database
- Digital examination (consider EUA in difficult cases)
- Bloods (FBC, U&E, LFT), baseline CEA
- Colonoscopy or CT colonography to visualise the colon (or within 6 months of potentially curative surgery performed as an emergency)
- CT chest, abdomen & pelvis to exclude metastatic disease
- MRI rectum to assess operability / at risk CRM
- MRI liver if liver metastases to assess suitability for hepatic resection. All patients with liver metastases will be referred to a regional hepatobiliary MDT for their opinion about optimal management
- All patients with potentially resectable lung metastases on CT will be referred to the regional lung MDT for their opinion about optimal management
- Early rectal cancer assessed by high quality MRI and EUS as stage T1 should be considered for local resection. Patients considered suitable for Transanal Endoscopic Microsurgery (TEMs) should be referred to UH Bristol or Cheltenham. All surgeons undertaking TEMS are accredited to perform this procedure
- PET will be considered when there is a high clinical or biochemical suspicion of systemic, metastatic or local recurrence in the context of negative or equivocal CT where there are further treatment options

- All investigations and histopathology results are discussed at the local MDT before treatment.

2.4.2 Treatment Options

Patients with rectal cancer are managed by surgeons with appropriate training who have completed the national TME, MDT Development Programme or equivalent, LOREC, and have fully audited outcome measures, and are working within a multidisciplinary team.

For patients with locally advanced cancer with multivisceral involvement of bladder, bone and or vascular structures consider referral to local centre with expertise for multiple specialists management

Preoperative long course chemo-radiotherapy is indicated if clinical examination (fixed, tethered) and/or MRI indicate that circumferential margins are potentially at risk i.e. R1 or R2 resections.

Preoperative short course radiotherapy should be considered if MRI indicates that margins are likely to be clear but there is a higher than usual risk of loco-regional recurrence i.e. major lymph node involvement.

Careful consideration should be given to the relative merits of palliative resection for rectal cancer, as should treatment with endoluminal stenting and palliative radiotherapy.

When a stoma is required or considered a possibility, all patients should see an accredited stoma nurse, ideally prior to admission, to allow adequate time for preparation.

The first definitive treatment is normally the first intervention intended to remove or shrink the tumour. Where there is no anti-cancer treatment, palliative intervention/best supportive care will be recorded.

2.4.3 Surgery

Preparation for Surgery – refer to Appendix 1

Upper third rectal cancer: Anterior Resection

- Excision outside mesorectum with pelvic autonomic nerve preservation aiming for minimum of 5cms clearance below the lower edge of the cancer
- Cytocidal washout of rectal stump & peritoneal cavity is recommended
- Covering stoma only when necessary.

Middle & lower third rectal cancer: Low Anterior resection

- Total Mesorectal Excision (TME) with pelvic autonomic nerve preservation
- Cytocidal washout of rectal stump & peritoneal cavity is recommended
- Consider a colonic pouch
- Temporary covering stoma should be considered in most cases.

Low rectal cancer: Where distal clearance <1cm, sphincter involvement, poor anal tone

The consensus on Transanal Total Mesorectal Excision (TATME) for low rectal cancer:

Due to concerns raised by the ACPBGI and while awaiting results from the COLOR III trial and Getting It Right First Time, CRC CAG make the following recommendations:

1. Temporary closure of the proctoring programme to new sites;
2. Extending the number of proctored cases from the current recommendation of 5–10 where sites are still completing the proctoring process;
3. Individual institutions to reconsider whether to continue transanal TME after review of local data, and subject to formal notification to local clinical governance authorities and permission of the medical director;
4. Transanal TME should only be carried out in institutions that undertake more than 40 rectal cancer resections (with rigorous exclusion of rectosigmoid cancer resections) each year, to allow sufficient ongoing experience to maintain surgical competency in the procedure;
5. Transanal TME should only be carried out in institutions that undertake more than 25 transanal rectal resections each year for rectal cancer and benign disease, to allow sufficient ongoing experience to maintain surgical competency in the technique;
6. Concentration of institutional experience in transanal TME by limiting performance of the procedure to two or three colorectal surgeons. Isolated practitioners are discouraged in order to ensure adequate local service delivery;
7. Use of procedure-specific enhanced patient consent;
8. Mandatory entry of data about patient demographics, patient selection, operative details and outcomes on the International Transanal TME Registry;
9. Updating the international registry with long-term oncological outcomes in patients who underwent resection for rectal cancer;
10. Independent review of the data held by the International Transanal TME Registry;
11. Assessment of the level of English and Welsh case ascertainment and data completeness in the International Transanal TME Registry through cross-referencing with NHS Digital data;
12. Collection of transanal TME as a data item in the National Bowel Cancer Audit for England and Wales, and by the Scottish Colorectal Cancer networks.

<u>Intersphincteric Abdomino-Perineal Excision</u> (APERi):

For low but early rectal cancer where the anal sphincter cannot be preserved (consider entering patients into a trial of local excision). For rectal cancer in patients with poor anal tone as an alternative to TME Hartmann's (see below).

<u>Standard abdomino-perineal Excision</u> (APERs):

For low rectal cancer within or just beyond the rectal wall in whom intersphincteric dissection would risk an involved margin.

Extra-Levator Abdominal Perineal Excision (ELAPE):

For locally advanced low rectal cancers (within 6cm from the anal verge) there is a national drive to promote extra-levator technique of abdominal perineal excision (ELAPE). This process has gained popularity because of the associated low intra-operative tumour perforation rates and subsequent local recurrence. It involves excision of the anus outside the levator plate to ensure enough clear tissue around the tumour.

TME Hartmann's:

Frail, elderly or incontinent patients with rectal cancer technically suitable for restorative surgery in whom there is a desire to avoid restoration of bowel continuity. An alternative to APERi.

Metastatic / Disseminated Disease:

- Unexpected/suspicious metastases within the abdomen should be biopsied. Biopsy/FNA liver lesions within the liver substance should not be undertaken without prior discussion with regional hepatobiliary surgeons.

Early rectal cancer - local excision – see 2.5 below

- Following pre-operative T1 stage assessment by EUS & MRI
- Performed by an adequately trained surgeon after discussion at MDT.

2.4.4 Neo-adjuvant chemotherapy and radiotherapy

Discussion about the use of neo-adjuvant chemo/radiotherapy takes place at the MDT meeting.

Preoperative

Long course chemo-radiotherapy will be considered when:

- MRI predictive of positive circumferential margin (R2) or threatened <1mm margin (R1)
- Schedule: 45-50 Gy in 25-28 fractions in 5 weeks given to a planned volume using a 3 - 4 field technique covering the tumour and an adequate margin
- Chemotherapy (5 Fluorouracil and folinic acid) is given daily in the first and fifth weeks of treatment
- Patients are reassessed after 2 - 4 weeks with further imaging ± PR or EUA.

Short-course radiotherapy will be considered when:

- MRI predictive of R0 resection but advanced T3 tumour / major lymph node involvement
- Schedule: 25 Gy in 5 fractions in 1 week. Surgery is scheduled within 7 days of completion. Delay to surgery for 4 to 8 weeks may be considered.

Post-Operative Multidisciplinary Team (MDT) Meeting

- Surgical treatment must be judged as curative or palliative
- Consider the best management options for beyond TME resection when indicated.
- Consider the place of post-operative radiotherapy or chemotherapy:

Postoperative Radiotherapy

MDT to consider long-course chemo-radiotherapy when:

- Circumferential margin is +ve (R2) or threatened <1mm (R1)
- The schedule is a 5 week course of 45-50 Gy and 25 fractions using a 3-4 field technique covering the posterior pelvis
- Chemotherapy (5 Fluorouracil and folinic acid) is given daily in the first and fifth weeks of treatment
- Patients with co-morbidity may receive radiotherapy as above or as a short course, both without chemotherapy.

Postoperative adjuvant chemotherapy

- Adjuvant chemotherapy usually recommended for all T4 NX tumours and TX N1-2, also for high risk T3 N0 tumours as judged by extramural vascular invasion. Patients should be counselled on the relative risks and benefits of treatment and understand that a "no chemotherapy" approach is an option
- Patients with favourable T3 tumours less than 80 years of age may be offered a discussion with the oncologist to discuss the potential but small benefits of therapy
- Chemotherapy may not be appropriate for patients with significant co-morbidity (WHO performance status), high frailty index or extremes of age when unacceptable toxicity a high probability, or their likelihood of death from those diseases affects any reduction in the risk of cancer recurrence or death.

Palliative chemotherapy

Patients who have un-resectable disease or undergo palliative surgery should be considered for palliative chemotherapy and offered the opportunity to meet with an oncologist. Patients unfit for chemotherapy should receive best supportive care.

2.5 Management of Early Rectal Cancer

2.5.1 Investigation and Staging

Preoperative staging includes:

- Digital rectal examination
- Endoscopic evaluation with biopsy
- CT chest / abdomen / pelvis
- MRI rectum
- Endoscopic ultrasound is highly recommended.

Accurate staging will determine which patients may be candidates for local excision.
In 'fit' patients local excision by TART or preferably TEMS (or equivalent technique) may be considered for early rectal cancers with good prognostic features:

- T1 (sm1) cancer on TRUS or high resolution MR rectum
- Small (<4 cm) tumours
- Good histological prognostic features (well to moderately differentiated adenocarcinoma)
- Mobile.

In patients unfit for major resection local excision of more advanced early rectal cancers, with or without radiotherapy, may be considered to try and achieve local control.

2.5.2 Post-operative MDT

Discovery of poor prognostic features on histopathology, including deeper or margin involvement, poor differentiation, and or vascular or perineural invasion, should lead to a discussion about the merits of a formal resection or post-operative chemo-radiotherapy.

Most early rectal cancers are diagnosed when a local excision is performed for a benign lesion and incidental cancer is found. If TEMS/ TAMIS / TART/ ESD or EMR has achieved a clear margin with good prognostic histological features, no further intervention will be necessary.

Mr Mike Thomas (UH Bristol), Ms Caroline Burt and Ms Ann Lyons (NBT) and Mr Neil Borley (Cheltenham) provide the Network TEMS/TAMIS service.

2.6 Management of Colon Cancer

2.6.1 Diagnosis

Diagnosis usually occurs after a colonoscopy and a biopsy. Histological confirmation of radiologically diagnosed cancer is desirable but not essential; however, every effort should be made when radiology is equivocal and especially for right-sided cancers.

2.6.2 Investigation and Staging

- Patient's general health and operative risk (ASA, WHO PS & PPOSSUM)
- Bloods (FBC, U&E, LFT) Baseline CEA
- Colonoscopy or CT colonography to visualise the non-visualised colon prior to surgery (or within 6 months of potentially curative surgery performed as an emergency)
- CT scan chest, abdomen & pelvis to exclude metastatic disease
- MRI liver if liver metastases to assess suitability for hepatic resection. All patients with liver metastases will be referred to the regional hepatobiliary MDT for their opinion about optimal management
- All patients with potentially resectable lung metastases will be referred to the regional lung MDT for their opinion about optimal management
- PET will be considered when there is a high clinical or biochemical suspicion of systemic, metastatic or local recurrence in the context of negative or equivocal CT where there are further treatment options
- All investigations and histopathology results are discussed at the local MDT before treatment.

2.6.3 Surgery

Preparation for surgery – refer to Appendix 1

Colonic resection

- Laparoscopy is offered to every suitable patient in the CAG in accordance with NICE Guidelines
- For most fit patients, excision will be by segmental resection to include high ligation of feeding arterial supply with associated lymph nodes
- Biopsy any suspicious lesions within the abdomen
- Do not biopsy / FNA liver lesions within liver substance unless discussed with the regional hepatobiliary MDT
- De-functioning stomas may be required (consider if cancer not resectable or bypass not possible).

Colonic Stenting (SEMS)

- Consider this option to ameliorate obstructive symptoms where disseminated disease is present or the patient is too unfit for surgical resection
- SEMS as a bridge-to-surgery in patients with acute bowel obstruction by probable cancer should be discussed with the patient as an alternative to Hartmann's procedure and you are encouraged to enter patients in an accredited randomised trial.

2.6.4 Post-Operative Multidisciplinary Team (MDT) Meeting

Surgical treatment must be judged as curative or palliative.

Consider the place of post-operative chemotherapy:

2.6.4.1 Postoperative adjuvant chemotherapy

- Adjuvant chemotherapy usually recommended for all T4 NX tumours and TX N1-2, also high risk T3 N0 tumours as judged by extra-mural vascular invasion. Patients should be counselled on the relative risks and benefits of treatment and understand that a "no chemotherapy" approach is an option
- Patients with favourable T3 tumours less than 80 years of age may be offered a discussion with the oncologist to discuss the potential but small benefits of therapy
- Chemotherapy may not be appropriate for patients with significant co-morbidity (WHO performance status), high frailty index or extremes of age when unacceptable toxicity is a high probability, or their likelihood of death from those diseases affects any reduction in the risk of cancer recurrence or death.

2.6.4.2 Palliative chemotherapy

Patients who have un-resectable disease or undergo palliative surgery should be considered for palliative chemotherapy and offered the opportunity to meet with an oncologist. Patients unfit for chemotherapy should receive best supportive care.

3. The CAG agreed Clinical Guidelines for Anal Cancer (14-1C-108d)

This service is centralised at University Hospitals Bristol NHS Foundation Trust and Gloucestershire Royal Hospitals NHS Foundation Trust.

3.1 Diagnosis

- Achieved by biopsy - histological confirmation is essential
- Consider examination under anaesthesia in difficult cases
- FNAC any palpable or radiologically enlarged inguinal lymph nodes.

3.2 Investigation and Staging

- Patient's general health (WHO performance status)
- CT scan chest, abdomen & pelvis
- Consider the role of pelvic MRI to aid staging
- Serology screening for the human papillomavirus.

3.3 Multidisciplinary Team Meeting (MDT) Meeting, UHBW

Radiotherapists and surgeons who are part of the specialist MDT at UH Bristol and GLOS treat anal cancer. The SWAG CAG recognises that the principle management of anal squamous cell carcinoma (SCC) is chemo-radiotherapy rather than resectional surgery.

Individual Trust based MDTs should confirm the histological diagnosis and stage of the disease, and then refer on to the Network Anal Cancer MDT (Consultant Clinical Oncologist and /or his Deputy) for discussion about the various options (radical chemo-radiotherapy or palliative radiotherapy) in light of the local extent of the tumour, the patient's co-morbidities and wishes.

Patients requiring pre-treatment stomas are to be referred back to the referring surgeon and CNS.

3.4 Treatment Options

- Histologically confirmed complete excision of an early lesion may be the sole treatment
- Radical chemo-radiotherapy will be the standard treatment
- Consider palliative radiotherapy for advanced disease / comorbid patients
- Consider palliative defunctioning stoma for advanced disease / comorbid patients
- Eligibility of entry into the national portfolio of clinical trials
- Salvage surgery: consider other specialities e.g. plastic surgery, urology and gynaecology

- Where palliative treatment is performed or best supportive care advised consider further supportive therapies and follow-up by the Palliative Care Team
- MDT decision and follow-up plan to be documented in patient's notes & conveyed to the patient/carers, referring surgical team/CNS, and the patient's GP.

3.5

These specimens should be prepared, processed and reported as per the Dataset for histopathology reporting of anal cancer. The Royal College of Pathologists, 2018.

https://www.rcpath.org/uploads/assets/d2782fd6-d58b-4b92-b147f8fe3af40a64/G165-Dataset-for-histopathological-reporting-of-anal-cancer.pdf

4. Management of Liver Metastases

Colorectal MDTs should refer patients with liver metastases, selected according to the network guidelines, to the liver resection MDT.

All patients with potentially curable liver metastases from colorectal cancer will be considered for liver resection, and referred for discussion to the regional hepatobiliary MDT at UHBW (Basingstoke from RUH Bath, Birmingham from Cheltenham/Gloucester)

Unsuitable cases for referral include patients with uncontrollable extra-hepatic disease defined as:

- Non-treatable primary tumour
- Wide-spread pulmonary disease
- Loco-regional recurrence
- Peritoneal disease
- Retroperitoneal, mediastinal or portal nodes
- Bone or CNS metastases.

Or, the patient is unwilling to have further treatment or is unfit for further treatment. Whilst patients with more than 5 multifocal metastases are less likely to benefit from surgery, each case will be looked at individually.

All patients with liver metastases with a performance status appropriate for chemotherapy +/- surgery will be referred to the regional hepatobiliary MDT. Patients with unresectable liver disease should be considered for chemotherapy +/- cetuximab as per the NICE Guidelines. The decision to undertake RAS testing will usually be made at the local MDT.

4.1 Staging investigations at presentation of primary cancer

All patients will have undergone a staging CT scan of the chest, abdomen and pelvis with intravenous contrast (ideally at a maximum collimation of 5mm), the whole colon visualised (barium enema or colonoscopy) and a baseline CEA measurement performed. Increasingly, PET scanning is requested and can be requested by the HPB MDT or the local MDT if the indication is

obvious.

4.2 Synchronous liver metastases

Colorectal cancer and liver resection are not normally performed synchronously. Patients found to have synchronous liver metastases at the time of their initial presentation should undergo a contrast enhanced liver MRI scan and be referred to/discussed at the designated Network HPB MDT (Bristol Royal Infirmary / Basingstoke / Birmingham).

Patients with potentially resectable disease, who have undergone radical resection of their primary bowel cancer, should be considered for 3 months of adjuvant chemotherapy (FOLFOX 4) prior to any liver resection. These patients will be restaged at 3 months by MRI. A further 3 months of chemotherapy will be considered post any potentially curative liver resection.

4.3 Metachronous liver metastases

Follow-up after resection of the primary colorectal cancer will be according to local protocol. The CAG recommends that a CT scan of the chest, abdomen and pelvis are performed as a minimum in the 2 years following completion of treatment of the primary tumour. Patients found to have liver metastases during follow up will have a treatment plan discussed at the Network HPB MDT.

If there is no extrahepatic disease on axial CT scanning, all patients will have a contrast enhanced MRI scan. Biopsy of liver lesions would not be performed without prior discussion at the Network HPB MDT. Patients should be considered for 3 months of neoadjuvant chemotherapy before any liver resection.

4.4 Chemotherapy

All patients with liver only metastases with a performance status appropriate for surgery +/- chemotherapy will be referred to the regional hepatobiliary MDT.

In all cases of metastatic colorectal cancer, molecular analyses to determine the presence of mutations in KRAS and NRAS (collectively known as RAS) should be performed as soon as the diagnosis is made and treatment is being considered.

RAS Mutation – Anti-EGFR targeted therapy should not be incorporated into the treatment algorithm of patients with RAS mutations

RAS Wild type – Anti-EGFR targeted therapy can be incorporated into the treatment algorithm of patients with wild-type RAS

The decision to undertake RAS testing will usually be taken at the CRC MDT.

Patients with potentially resectable liver metastases without unresectable extrahepatic disease should be considered for neoadjuvant chemotherapy (+/- cetuximab as per the NICE Technology Appraisal 176 Guidelines):

Algorithmhttp://www.eastmidlandscancernetwork.nhs.uk/Library/NeoadjuvantColorectal.pdf

Patients with unresectable liver metastases +/- extrahepatic disease should be considered for palliative chemotherapy. RAS mutation testing is requested via the CDF for these patients by an oncologist. The following metastatic colorectal cancer patient treatment algorithms are routinely funded by NHS England via the cancer drug fund (12 March 2015 V4.0):

Algorithm http://www.eastmidlandscancernetwork.nhs.uk/Library/mCRC.pdf

Genomic Testing Guidelines for CRC

- Genomic tests for colorectal cancer are available via the National Test Directory (https://www.england.nhs.uk/publication/national-genomic-test-directories/), at the South West Genomics Laboratory Hub (SWGLH) in Bristol.
- Genomic test requests for CRC will typically be initiated by oncologists at the CRC MDT.
- Systematic and robust testing pathways should ensure that every patient who qualifies for a test is offered one in a timely manner, with results being accessible by the treating oncologist at the time of the patient's first line treatment consultation
- Clear and unambiguous local responsibilities for genomic test requests, tissue sample handling, and reporting of the results should exist within each local Trust to ensure that necessary tests are requested timely and avoid unnecessary delays to patient access to treatment.

4.5 Ablative therapy

Patients not suitable for liver resection (e.g. extensive co-morbidity, patient choice, irresectable disease) may be offered ablative treatment (radiofrequency ablation). This would be discussed at the HPB MDT.

4.6 Follow up after liver resection

Follow up will be agreed in collaboration with the HPB MDT according to HPB and Colorectal MDT guidelines, in order to direct follow up for both liver and colorectal disease. CEA levels should be monitored at least 6 monthly.

Six monthly reviews should be considered for 3 years and then on an annual basis thereafter. Follow up will be shared between either the HPB team and the oncology team or base colorectal team. In patients who develop a local liver recurrence it may be appropriate to consider referral for re-resection and/or ablation as well as chemotherapy.

Patients will remain under the care of the local colorectal team for surveillance colonoscopy according to local protocol.

Patients with potentially treatable lung disease will be referred directly to the Lung Cancer MDT.

5. Management of Advanced Colorectal Cancer

5.1 Presentation

- Inoperable primary disease
- Inoperable metastatic disease
- Loco-regional recurrence.

5.2 Treatment

For patients with inoperable rectal cancer, (fixed or tethered on clinical examination and/or MRI indicates that margins are potentially at risk i.e. R1 or R2 resections) without evidence of metastatic spread, preoperative long course chemo-radiotherapy should be offered to downstage the cancer in the hope of making it resectable for potential cure.

Although there is less good evidence, for patients with apparently inoperable colonic cancer on CT scanning, without evidence of metastatic spread, preoperative chemotherapy may be offered to downstage the cancer in the hope of making it resectable for cure or could become palliative.

5.3 Metastatic Disease

- Colorectal MDTs should refer patients with liver metastases, selected according to the network guidelines, to the liver resection MDT (see above)
- Colorectal MDTs should refer patients with lung metastases, selected according to the network guidelines, to the appropriate chest MDT.

Lung resection to be considered in patients where:

- Primary disease has been radically removed
- Resectable colorectal metastases confined to the lung and/or liver.

5.4 Chemotherapy

Patients with incurable disease, and who are fit enough, should be offered the opportunity to discuss the benefits and disadvantages of chemotherapy with palliative intent.

5.5 Radiotherapy

Radiotherapy can be an effective form of treatment for palliation of rectal bleeding, tenesmus and rectal pain. It should be considered for patients with inoperable advanced disease and recurrent disease (not suitable for resection).

5.6 Palliative Care

Palliative care is an integral component of the management of incurable cancer and should be practised by all the members of the MDT. The key components are:

- A focus on quality of life, which includes good symptom control
- A whole person approach, taking into account past experiences and current situation
- Respect for patient autonomy and choice
- Open and sensitive communication between patients, carers and professional colleagues.

5.7 Referral for Specialist Palliative Assessment

The patient should meet one or both of the following criteria:

- Incurable disease with the focus being on quality of life
- The patient has one or more of the following needs, which cannot be met by the referring team:
    - Uncontrolled / complicated symptoms
    - Complex psychological / emotional issues
    - Complex social / family issues
    - Difficult decision making about appropriate future carers.

6. Follow up Guidelines

Colon Cancer & Rectal Cancer

It is expected that most Trusts in the SWAG Network will adhere to the NICE guidelines on follow-up after resection of colon and rectal cancer. There is a national move towards 'remote' surveillance programmes minimising the need for patient attendance at clinic. Consideration may be given to specialist nurse lead clinics and telephone follow-up.

6.1 NICE Guidance: Follow-up after apparently curative resection

Offer follow-up to all patients with primary colorectal cancer undergoing treatment with curative intent. Start follow-up at a clinic visit 4–6 weeks after potentially curative treatment.

Offer patients regular surveillance with:

- a minimum of two CTs of the chest, abdomen, and pelvis in the first 3 years **and**
- regular serum carcinoembryonic antigen tests (at least every 6 months in the first 3 years).

Offer a surveillance colonoscopy at 1 year, then 3 years, then 5 yearly thereafter as per BSG guidelines: https://www.bsg.org.uk/wp-content/uploads/2019/09/201.full .pdf

Start reinvestigation if there is any clinical, radiological or biochemical suspicion of recurrent disease.

Stop regular follow-up:

- when the patient and the healthcare professional have discussed and agreed that the likely benefits no longer outweigh the risks of further tests **or**
- when the patient cannot tolerate further treatments.

6.2 Follow up of Patients with Anal Cancer

Follow-up of patients with anal cancer is the responsibility of the anal cancer MDT at UH Bristol. The majority of these patients will be under the follow-up of the Lead Clinical Oncologist. Patients with disease relapse will be discussed at the UH Bristol Colorectal Cancer MDT (de facto Anal Cancer MDT) for the consideration of salvage surgery. The CAG salvage surgery service is run by Mr M Thomas and his colleagues in UH Bristol.

6.3 Risk Assessment and Clinical Surveillance in patients with a Family History of colorectal cancer

Referral for screening colonoscopy and / or specialist genetic counselling will be considered for the following patients:

- CRC in single first degree relative (FDR) <50 years or 2 FDR of any age.

  Risk 1 in 12. Once-only colonoscopy at age 55

- CRC in 2 FDR mean age <60 years or 3 FDR with **first degree kinship***

  Risk between 1 in 6 and 1 in 10 – suggest referral to geneticist

  Colonoscopy age 50 then 5 yearly colonoscopy to age 75

- Less strong family history of CRC. Risk >1 in 12. No colonoscopy offered

  (UK background population risk for colorectal cancer is 1 in 18).

N.B. first degree kinship* - affected relatives who are first-degree relatives of each other AND at least one is a first degree relative of the patient

- Colorectal cancer associated with other characteristic tumours in same individual/ family (ovary, urothelium, small bowel, biliary tree)

- Surveillance and genetic testing should be offered to all Familial Adenomatous Polyposis (FAP) families and Hereditary Non-polyposis Colorectal Cancer (HNPCC) / Lynch families that either meet the Amsterdam or Amsterdam II criteria (3 affected relatives in 2 successive generations of which one is under the age of 50) or have confirmed mismatch repair gene mutations.

7. Appendices

7.1 Appendix 1

Preparation for Surgical Procedures

- Informed consent, detailing the benefits and risks of the procedure versus alternatives including no surgery, will be obtained by the operating surgeon or delegated trainee with sufficient knowledge and training
- Appropriate treatment options will be discussed fully with all patients including laparoscopic intervention
- Consider iron infusion to restore iron deficiency anaemia prior to elective surgery
- Bowel preparation according to the local surgeon's preference / mechanical bowel preparation provided there is no incipient obstruction
- Anti-thrombotic & antibiotic prophylaxis according to local policy
- Group and save will be sufficient for most colorectal cancer resections dependent upon local transfusion facilities. Consider cross-match for pelvic resections and pre-operative transfusion if haemoglobin level (Hb) < 8 or if the patient is symptomatic)
- Counselling, guidance and support
- Stoma marking if applicable
- HDU / ITU facilities if required.

7.2: Appendix 2

SWAG Management and Surveillance Guidelines for people with a Lynch syndrome mutation

Background: Lynch syndrome is an autosomal dominant cancer predisposition syndrome that affects around 1:300 people. Of these 95% are unaware of their diagnosis. Individuals with Lynch syndrome are at an increased risk of developing colorectal, endometrial, ovarian, urinary tract, prostate and other cancers, depending on which gene is malfunctioning.

- All people with a Lynch syndrome mutation are referred to a clinical geneticist for genetic counselling and provision of information to families about the condition
- All people identified as being at high risk of Lynch syndrome on MMR IHC and/or MSI testing (as described in NICE Diagnostic Guidance 27 for example) are referred to a clinical genetics service for further assessment
- All people with a Lynch syndrome mutation are recommended to take long term low dose aspirin (75-100mg) if tolerated. Consider proton pump inhibitor cover in those at increased risk of gastrointestinal bleeding.
- All people with Lynch syndrome should have Helicobacter pylori screening and eradication
- All people with Lynch syndrome should be asked and consented to join the Southwest Lynch syndrome registry to enable co-ordination of their care and research
- People with Lynch syndrome should be told to modify their lifestyle (stop smoking, reduce alcohol intake, maintain a healthy weight and diet, keep active etc) as these interventions reduce the risk of Lynch syndrome associated cancers.
- An individual's risk of cancer is dependent on which gene, which cancer is in question and which mutation they carry. It can be estimated with the use of http://www.plsd.eu
- Clinicians should familiarise themselves with:
    - The Mallorca Guidelines: https://academic.oup.com/bjs/article/108/5/484/6287132
    - The Manchester Guidelines: https://pubmed.ncbi.nlm.nih.gov/30918358/

Site of Cancer:	Examination	Age range	Interval (years)
Colorectum	• All people with a Lynch syndrome	• Colonoscopy is recommended	• 1-2

	mutation are to be offered total colonic surveillance • Patients should be educated as to the symptoms of CRC • In those undergoing colorectal surgery, extended surgery should be considered on a patient-to-patient basis with reference to the Mallorca guidelines • Chromoendoscopy is equivalent to high-definition white-light endoscopy in specialist centres. It may be an adjunct to be considered in the absence of high-definition endoscopy or in centres with lower adenoma detection rates.	every 2 or 3years for path_MLH1, path_MSH2 and path_MSH6 carriers, unless they have had colorectal cancer before, after which biennial colonoscopy is recommended. • Path_PMS2 carriers may be considered for 5 yearly colonoscopy. • Colonoscopy surveillance is recommended starting at age 25yrs for path_MLH1 and path_MSH2 carriers, and at age 35 yrs for path_MSH6and path_PMS2 carriers. • The recommended surveillance for colorectal cancer does not differ between men and women. • If an individual has a family history of a CRC diagnosed before 25 years, colonoscopy should commence -5 years before the youngest age	• 1-2

		of diagnosis of CRC	
Uterus	• All women diagnosed with a Lynch syndrome should be referred to the gynaecology service for discussion of potential risks • Gynaecological screening should be discussed by a gynaecologist with a specialist interest in Lynch syndrome. The following article outlines the issues around gynaecological surveillance in Lynch syndrome. https://doi.org/10.1136/bmj.n2020 • Those with gynaecological organs should be offered risk reducing surgery once their family is complete or around the age of 40 years • The use of hormonal contraception should be discussed as to potentially reduce the risk of endometrial cancer • Patients should be educated as to the symptoms of gynaecological cancer		
Stomach	• Upper gastrointestinal endoscopy is only recommended in Lynch syndrome families from countries with high	• 25 years	• 1-2

	incidence of gastric cancer, preferably in a research setting • All people with a Lynch syndrome mutation are to be screened for H pylori infection • Patients should be educated as to the symptoms of stomach/hepatobiliary cancer		
Urinary tract	• Surveillance (by urine cytology and ultrasound) of MSH2 carriers should only be performed in a research setting or if results are systematically collected in a Lynch syndrome registry • Patients should be educated as to the symptoms of urinary track cancer.	• 30-35	• 1-2

References:

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