GUIDANCE ON LONG-TERM CONSEQUENCES OF TREATMENT FOR COLORECTAL AND ANAL CANCER

Guidance overview

This document is aimed at specialist oncology professionals but will also be useful to any healthcare professional involved in care of patients following treatment for colorectal and anal cancer. It has been endorsed by [input once endorsement process complete].

Its main purpose is to ensure people diagnosed with colorectal and anal cancer are offered appropriate information on the signs and symptoms of long-term consequences of their treatment and that they, and the professionals caring for them, are aware of pathways of care that should be available to help them manage them.

Within the eight sections of this guidance, professionals will be signposted to (a) ways of supporting people living with and beyond colorectal and anal cancer to self-manage and (b) key advice and source documents for clinical management.

If you are seeking guidance for a patient who is about to commence a particular treatment regime for colorectal or anal cancer please refer to *Part 1: Good practice recommendations prior to treatment,* then refer to the particular treatment section for detailed information on its long-term consequences.

If you wish to provide information and support to a patient who has completed treatment who may need informing of the likely consequences please refer to the relevant treatment section and then *Part 6: Assessment and symptom management*, *Part 7: Post-treatment advice*, and *Part 8: Good practice recommendations after treatment*.

If you require guidance of the management of a specific long-term consequences please refer to *Part 6: Assessment and symptom management*.

Guidance development group and methods

Robust evidence for the management of the consequences of colorectal and anal cancer treatment is lacking, but data and evidence are emerging, including the work of Dr Jervoise Andreyev at the Royal Marsden[1] and the Macmillan Survivorship Research Group at the University of Southampton[2]. This guidance has been developed through the compilation of published guidance and, where possible evidence, along with consensus opinion on best practice agreed by the expert group listed below. References are cited where appropriate.

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The group welcome all comments and suggestions for future editions via the Macmillan Consequences of Treatment Programme at consequences@macmillan.org.uk.

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Disclaimer: No reader should assume that this guidance represents the only management option. There are other reasonable care strategies and there is no duty of care for any healthcare worker to follow these recommendations. Each patient is an individual and holistic care is paramount and there may be many good reasons why this guidance may not be implemented. The group believes that all people at risk of developing consequences of their cancer are entitled to receive information that enables them to make informed choices about their cancer treatment and follow-up care. The group accept shared responsibility for the publication of this guidance

Contents

Introduction

Approximately 41,600[3] people a year are diagnosed in the UK with colorectal cancer, of whom over 60% will survive more than five years[4,5]. For males, European age-standardised incidence rates have increased by 29% over the last four decades and for females by 7% during this time.

Squamous cell carcinoma of the anus accounts for approximately 2% of all UK[6] lower gastrointestinal tract malignancies with an average of 1,200 new cases diagnosed annually. The incidence of anal cancer is almost twice as high in women as it is in men and while still rare, overall incidence has increased by nearly 300% over the last four decades.

Treatment for colorectal cancer includes surgery, chemotherapy and radiotherapy, either alone or in combination. It is estimated that a third of those diagnosed with rectal cancer will receive pelvic radiotherapy[4] (radiotherapy is very rarely used to treat people with colon cancer), two-thirds of people with colorectal cancer will have surgery and up to half will receive chemotherapy[7]. For people diagnosed with anal cancer, first-line treatment is chemo-radiation with pelvic surgery being held in reserve for recurrent or resistant disease.

As length of survival after diagnosis increases, there is growing recognition for the need to understand the consequences of cancer treatment to support patient recovery and optimise health-related quality of life[8]. While many cancer survivors develop acute consequences from cancer treatment, the majority will not experience any long-term effects. Nonetheless, all patients should be informed of the possible long-term consequences that can appear months to years after treatment.

Macmillan estimates that up to a quarter of all people diagnosed and treated for cancer will experience long-term ill health or disability, and that these effects may last for 10 years or more, with some risks (e.g. a second primary cancer, osteoporosis) lasting a lifetime. Recent analysis of responses to the first national cancer survey for Patient Reported Outcome Measures[9] (PROMs) showed 21,802 respondents with colorectal cancer (but not anal cancer) indicated the following 'frequently occurring challenges' within three years of diagnoses:

- The emotional impact of cancer and treatment.
- Ongoing social and financial problems that made life difficult.
- Long-term and age-related illnesses that could exacerbate, or be exacerbated by, problems associated with cancer treatment.
- Unpleasant physical side effects of treatment.

While this guidance focuses on the physical and psychosocial consequences of colorectal and anal cancer treatment, the associated financial implications are also acknowledged.

This guidance contains good practice recommendations when supporting people before and after treatment for colorectal and anal cancer. It considers the long-term consequences of the three main treatment modalities – surgery, chemotherapy and radiotherapy – plus the implications of receiving combined treatment modalities.

Where possible, care should aim to prevent or minimise any long-term consequences (see table 1) so within the treatment sections we discuss how these symptoms may be predicted and also prevented. For example, there is growing evidence supporting the benefits of a healthy lifestyle in managing treatment effects such as fatigue. Where consequences are unavoidable, the aim should be to inform all patients of this possibility and identify those most at risk of the consequences of treatment.

Table 1: Principles of care for approaching the consequences of cancer and its treatment

Principles	**Approach**
Prevent or minimise consequences	Promote healthier lifestyle choices where possible Review and correct co-morbidity where possible Review an aim to reduce unnecessary medication usage. Assess if patient may be eligible for minimally invasive surgery Consider targeted radiotherapy and therapies Plan treatment based on highest quality and most recent imaging available Promote self-monitoring to enable early identification
Inform patients of potential consequences	Introduce possibility of long-term consequences during treatment discussions Targeted information in Treatment Summary
Identify potential patients at risk	Identify patients who might be at high-risk of long-term consequences Empower patients to self-identify symptoms and seek prompt help, as needed
Assess potential consequences	Regular holistic needs and symptom assessment Consider using patient-reported outcome measures
Support patients through local care pathways	Support patients to self-manage Link patients in to appropriate local services GP follows the guidance in the Treatment Summary Stratified cancer treatment follow-up Establish specialist referral pathways Co-ordination of care may be required if complex
Monitor patients at risk of long-term consequences	Support patients in self-monitoring for long-term consequences to enable early identification and prompt referral GP follows the guidance in the Treatment Summary Stratified cancer treatment follow-up

In the last three parts of this document, guidance is offered to help patients manage common consequences, focusing on both the physical and psychosocial issues which can be experienced as well as good practice recommendations for all patients following treatment cessation.

When applying this guidance in practice, practitioners should refer to *A competence framework for nurses: Caring for patients living with and beyond cancer* (endorsed by UKONS and RCN) for advice on how to develop specific skills and confidence in managing consequences of cancer treatment.

Part 1: Good practice recommendations prior to treatment

Good practice, prior to treatment, is the prevention or minimisation of consequences of treatment where possible, by:

- Adopting a personalised approach when deciding upon and planning colorectal cancer treatment.
- Advocating minimally invasive treatments where available and appropriate, e.g. laparoscopic surgery and treatments targeted at the tumour.
- Using the most up-to-date, accurate information and imaging available when making decisions for treatment.
- Promoting a healthier way of life to ameliorate several common consequences of cancer and its treatment, as well as improving overall survival and reducing the probability of relapse.[10]

The following sections offer specific recommendations prior to treatment, aimed at helping identify and inform those potentially at risk of the consequences of colorectal and anal cancer treatment.

Assessment pre-treatment

A pre-treatment Holistic Needs Assessment (HNA) is a means to ensure that concerns or problems are identified prior to commencing treatment so that attempts can be made to resolve them through further exploration and care planning. Holistic needs assessment is not exclusively the role and responsibility of clinical nurse specialists. Other professional groups, including doctors, professionals allied to healthcare (AHPs), community nurses and social care professionals may be well placed to undertake part or all of the assessment.

Pre-treatment psychosocial factors such as confidence to manage problems (self-efficacy), anxiety and depression or degree of social support may be important predictors of recovery following treatment and could be included in to pre-treatment assessments[11].

A HNA can be incorporated into a broader assessment of an individual's health including overall fitness, current medications and presence of any comorbidities (*diabetes, cardiac, respiratory, renal, neurological and mental health disease)* to medically optimise the patient in preparation for treatment. These conditions can otherwise become problematic as they are placed under additional stress during treatment potentially contributing to a spectrum of longer-term consequences[12].

It is particularly important to gather information on an individual's sexual, bowel and urinary function prior to treatment to allow for comparison with functional changes which may occur over time after treatment. There are a range of specific symptom assessment tools available (see *Part 6: Assessment and symptom management*).

Other assessment tools (such as Functional Status Questionnaire or Nottingham Health Profile) measure functional or subjective health status to support a more structured and systematic assessment[13]. When planning care for an older person (80 years and beyond.), consider using a specialised tool such as the Comprehensive Geriatric Assessment (CGA[14]), or a Frailty index which can offer a clinical management strategy for those who may be frail and more at risk of long-term consequences of any planned interventions. More than half of older cancer patients have some degree of frailty which puts them at increased risk of chemotherapy intolerance, postoperative complications and mortality[15]. By identifying those at an increased risk of poorer recovery, care can be planned to proactively address potential concerns and subsequent support tailored to meet needs early on.

Information-giving

Offer accurate, clear information about acute side effects and potential long-term consequences in both verbal and written formats as part of the consent to treatment process. Verbal information should be tailored to individual needs during consultations with the clinical team. Information should also be explained in terms of what this might mean practically, on a day-to day basis for that individual. For example, 'you may suffer urgency of bowel movements' may become more meaningful when explained alongside advice such as 'it can be helpful to carry spare underwear and wipes when you leave the house'.

More than one in four people living with cancer say they would have found it helpful to receive more advice or information on the long-term physical and emotional effects of cancer[16] . There can be a disjuncture between what specialists think they have told patients to expect after treatment and what patients think they have been told, so it is important to assess comprehension at regular intervals. There is also evidence to indicate people like to be informed about late effects prior to starting treatment, and for this information to be repeated over time, even following the end of treatment[17]. Some survivors report that prior knowledge of whether symptoms would affect their lives 'a lot' would have changed their treatment decisions[18]. Thus information-giving on the likely consequences needs to be presented alongside guidance on how they can be managed and advisable adjustments which can be made.

Supplement verbal information with written patient information; the Macmillan resources listed below should be offered as appropriate:

- *Pelvic radiotherapy in men – managing side effects during treatment*.
- *Pelvic radiotherapy in women – managing side effects during treatment*.
- *Managing the late effects of pelvic radiotherapy in men*.
- *Managing the late effects of pelvic radiotherapy in women*.
- *Managing the late effects of bowel cancer treatment*.
- *Late effects of pelvic radiotherapy; symptom checklist and toilet card*.

In addition, offer information that will encourage people about to start treatment to make healthier lifestyle choices, in the hope that they will sustain them both during and beyond treatment (see Appendix 1).

Signpost to useful sources of support; such as:

- Macmillan website: colorectal cancer, anal cancer and late effects of pelvic radiotherapy
- Beating Bowel Cancer
- Bowel Cancer UK
- The HPV and Anal Cancer Foundation
- Oncolink (search for anal cancer)
- Pelvic Radiation Disease Association and patient stories
- Local patient support organisations and groups.

Consent to treatment

As part of the consent process, individuals need to be made aware that all treatment modalities carry risks of long-term consequences which can be made more manageable if given prompt and appropriate attention. Any ongoing post-treatment symptoms or concerns should be reported to health professionals immediately.

Personalised information should be provided, where available and stated, on the consent form so that each person is clear of the risk of short-term and long-term effects of their particular treatment. For this reason, it is important that a health care professional with a good knowledge of these effects carries out the consent process with the patient.

Part 2: Long-term consequences of surgery

What are the causes of long-term consequences following surgery for colorectal or anal cancer?

Surgery is the main treatment for primary colorectal cancer, offered with curative or palliative intent. The principle of potential surgical cure demands that the cancer be excised completely with an adequate margin of surrounding tissue and clearance of associated lymphatic tissue and blood vessels. Meticulous handling of tissues surrounding the bowel and careful dissection techniques are required to achieve optimal outcomes.

Surgery will often be the treatment of choice for management of both local and distant disease recurrence. Increasingly, surgery plays a role in the treatment of liver and lung metastases. When complete resection is achieved, survival outcomes improve considerably.

Colon cancer surgery typically requires a segment of large bowel to be resected. Rectal surgery is more complex due to the proximity of other pelvic structures to the rectum (prostate, bladder, sacrum and uterus) that become involved in the tumour mass and need to be partially or fully resected to achieve cure.

Currently, just under half of patients in the UK are offered a laparoscopic (minimally invasive) resection to surgically treat their colorectal cancer[8]. Laparoscopic surgery for colon cancer demonstrates better short-term outcomes and equivalent long-term results to open surgery. Long-term benefits for the patient may include preservation of their immunologic function which might translate into a longer post-operative survival, fewer incidences of abdominal adhesions and also of incisional hernia. In rectal cancer surgery, laparoscopic surgery can be more difficult to perform (depending on the tumour location) but safety and short-term benefits have been confirmed[19].

Long-term consequences will depend on a number of factors including cancer stage; type, urgency and extent of the procedure; experience and skill of the surgeon; and age and general health of the patient (including ASA (American Society of Anaesthesiologists) grade and co-morbidity[20]).

Surgery is no longer the standard option for a new diagnosis of anal cancer (unless it is a very small early stage cancer that can be removed by local excision). An abdominoperineal resection or pelvic exenteration will only be required to salvage disease that persists or recurs following a course of chemo-radiation.

What are the long-term consequences following surgery for colorectal or anal cancer?

Following surgery there may be a range of consequences experienced (see Figure 1) including:

- Pain
- Changes to bowel function and control
- Stoma formation
- Hernia development
- Phantom rectum syndrome
- Sexual concerns
- Urinary symptoms

- Lymphoedema
- Fatigue
- Psychological effects
- Changes in body image.

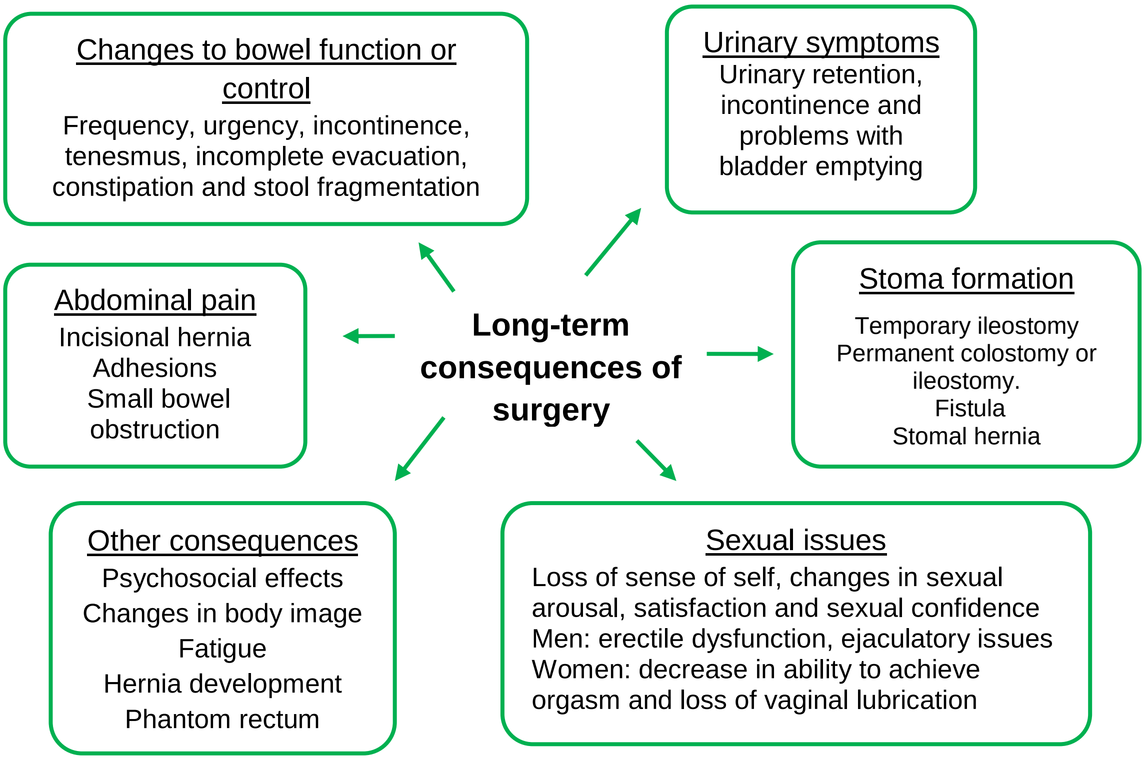


Figure 1: Possible long-term consequences following surgery for colorectal or anal cancer

Abdominal pain

Chronic abdominal pain is uncommon after laparoscopic primary colorectal cancer surgery. However a high proportion of patients may suffer from pelvic pain several years after treatment for rectal cancer. In one study more than half of patients (55%) reported their pain to be moderate to severe, and 41% reported daily pain[21]. Chronic pain can be associated with mood disturbance, sleep problems, and disruptions in many aspects of quality of life.
Occasionally, referred pain can develop, and persist, after more complex rectal or anal cancer surgery, particularly if there has been pelvic nerve removal. More often, post-surgical pain is acute in nature.

Causes of pain also include incisional hernia and abdominal adhesions. While adhesions may be considered an inevitable consequence of abdominal and pelvic surgery, most people who develop them are asymptomatic. Over time, abdominal and pelvic adhesions can cause serious consequences such as small bowel obstruction and bowel strangulation or infertility problems from pelvic scarring. A very small proportion (2–3%) of this patient group will require admission to hospital for adhesion-related intestinal obstruction and a third of these patients will require further surgery[22].

Changes to bowel function or control

Up to 90% of people who have had rectal cancer surgery involving sphincter-saving techniques (that aim to avoid a permanent stoma by preserving the normal route of defecation) will subsequently experience a change in bowel function[23]. One or more of the following bowel symptoms – often experienced as a cluster of symptoms known as Anterior Resection Syndrome (ARS) – may result: frequency, urgency, incontinence, incomplete evacuation and fragmentation of stool. Symptoms generally improve over time but cause distress due to their unpredictable nature that can limit daily activities[24]. There are multiple causes of ARS such as anal sphincter damage, a reduced neo-rectal reservoir altered colonic motility[19] and changes resulting from radiotherapy.

Large numbers of patients with rectal cancer undergoing a planned restorative anterior resection for rectal cancer will have a ‘temporary’ stoma[8]. It may be several months before the ileostomy is reversed – interim changes within the defunctioned large bowel can also affect post-reversal bowel function. However, individuals who undergo a pelvic dissection (integral to surgery such as an anterior resection) without stoma formation also report significant long-term changes in their bowel function[25,10].

Measurable compromises in long-term bowel function can also be experienced after colonic surgery, particularly for extended resections for a colonic malignancy (due to presence of other polyps, second colonic malignancy or Lynch syndrome) with the likelihood of a higher daily stool frequency than a segmental colonic resection[26].

As a consequence, many will undertake substantial dietary and behavioural adjustments to maintain bowel function, and these adjustments have implications for long-term health-related quality of life[27].

Stoma formation

Colon cancer surgery is less likely than rectal cancer surgery to involve a temporary or permanent stoma. A stoma formation may only be required if there is any concern regarding the integrity of the anastomosis (to allow time for the area to heal) and/or the health of the patient.

Formation of a temporary ileostomy or permanent colostomy is likely to be considered a possibility as part of a rectal cancer procedure (unless the tumour is amenable to a local excision), and will primarily be determined by how close the tumour is located to the anus. Cancers in the bottom third of the rectum may necessitate formation of a permanent stoma, a procedure described as an abdominoperineal excision of the rectum (APER) or alternatively a cylindrical or extralevator APER [ELAPER] which involves resection of the levator muscle *en bloc* with the anal canal and lower rectum,

Surgery to resect a cancer in the top third of the rectum, termed an anterior resection, carries a 5% risk of temporary stoma formation. The risk of stoma formation if greater if the patient presents as an emergency: in which case a Hartmann’s operation may be performed, resulting in a potentially reversible end-colostomy leaving a patent anus (from which there will be mucus discharge). For cancers in the mid to low rectum, a total mesorectal excision is considered the gold standard treatment. Since this is associated with a higher risk of anastomotic leak, it is considered safer to fashion an ileostomy than risk this acute, potentially fatal complication. However, despite intentions to reverse this stoma, 18 months after primary surgery, up to a third of individuals may still have an ileostomy[8]. Chemotherapy may be required after surgery and often necessitates a delay in ileostomy reversal.

In the National Colorectal Cancer Survivorship PROMs survey subset analysis of the 43% of respondents in this large sample (over 21,000) who were at least one year following colorectal cancer revealed: 21% reported the presence of a stoma; for 10%, their primary cancer site was the colon; for 20%, their primary cancer site was the recto-sigmoid; and 43% of respondents in this large sample had their primary cancer site in the rectum[10].

Formation of a urinary stoma, or both a urostomy and colostomy, to treat rectal cancer is rare, and only necessary when the disease has advanced beyond the mesorectum (peritoneal tissue supporting the rectum) requiring total pelvic clearance (or exenteration).

A stomal hernia, also known as parastomal hernia, is reportedly the most common complication[28] of permanent stoma. The incidence of a parastomal hernia increases over time, with most occurring within two years of stoma construction. Parastomal hernias have a postoperative incidence rate of up to 30% for end ileostomy and approximately 50% for colostomy at 10 years, which is higher than that of other types of incisional hernia (see below).

One in three patients may develop a hernia after stoma closure, and around half of hernias that are detected require repair. Risk of hernia is greater after colostomy closure than after ileostomy closure[29].

Hernia development

Incisional hernias indicate a defect of the fascia of the abdominal wall that can occur following any incision, months or years after surgery. Hernias form in up to 20% of patients after colorectal surgery when an abdominal incision is made[30]. Despite advances in surgical techniques with laparoscopic surgery, an incision is still required for specimen retrieval; thus, port and retrieval site hernias are reported[31].

One in three patients may develop a hernia after stoma closure, and around half of hernias that are detected require repair. Risk of hernia is greater after colostomy closure than after ileostomy closure[29].

Hernias do not get better or disappear without treatment and generally increase in size (usually over a period of months or years, but may occur more suddenly after sudden exertion), causing pain and body image issues that have a negative impact on quality of life. Complications of incisional hernias such as incarceration, strangulation and obstruction can occur and will require emergency surgery.

Phantom rectum syndrome

Phantom-related phenomena can occur following an abdominoperineal resection to remove very low rectal cancer, or in salvage surgery for recurrent anal or rectal cancer that involves excision of the pudendal nerve supply to the lower rectum.

Individuals with phantom rectum syndrome report continuing to feel that their rectum is still present and may also experience sensations of phantom flatus or phantom faeces which are discomforting and can be painful. One recent study suggests nearly all patients (96% of their sample) experience a sensation of a missing rectum in the months after rectal amputation and for most (60%), this will be a painful sensation characterised as pins and needles, pain in the perineal area, stinging and burning – occurring mostly in sitting positions[32].

Sexual concerns

Changes in sexual desire and function after colorectal and anal surgery will depend on the type of surgery performed, either as a result of direct structural change or as a consequence of how surgery makes that person feel about their body and ability to engage in sexual relations.

While nerve preservation is a priority during pelvic dissection, a percentage of men will still experience erectile and ejaculatory difficulties. Pelvic autonomic nerves are especially at risk in cases of low rectal cancer and during any major perineal resection. Sexual problems extending to loss of desire and loss of sexual satisfaction may occur in as many as half of all men treated by rectal cancer surgery by abdominoperineal excision[33]. Often issues such as the embarrassment of associated changes in body image and having a stoma can cause difficulties with arousal and desire.

Women experience difficulties with sexual arousal, vaginal lubrication, pain during intercourse and ability in achieving orgasm after pelvic surgery[34]. Sexual consequences are inevitable if the planned surgery necessitates removal of the posterior vaginal wall, a hysterectomy and/or oophorectomy to treat a locally advanced rectal cancer.

While pelvic nerve trauma is much less likely to occur during colon surgery, it cannot be assumed that at an individual level, fewer sexual concerns will be experienced.

Urinary dysfunction

Urinary dysfunction may result from damage to the pelvic autonomic nerve supply during surgery or by the anatomical changes created by altering the physical structure in the pelvis.

The true incidence of urinary problems is unknown as it is under-reported by those recovering from rectal cancer treatments. In the first three months after surgery, there is incidence of bladder dysfunction in half of patients following abdominoperineal resections and up to a quarter after a low anterior resection[35]. Long-term problems with bladder emptying, incontinence and chronic urinary retention occur in less than 15% of rectal cancer patients overall[19].

Pre-existing urinary incontinence in older people should be medically reviewed for reversible causes (e.g. polyuria from diabetes, diuretic treatment for hypertension etc.).

Lymphoedema

Pelvic cancer surgery necessitates lymphadenectomy or removal of lymph glands that can cause damage to the pelvic lymphatic system. This is a rare consequence of colorectal and anal surgery, yet if undiagnosed and untreated; it can progress to chronic pelvic dysfunction within a few months of surgery[36]. Unlike the common clinical skin signs that characterise other sites of lymphoedema, pelvic lymphoedema is usually ‘hidden’ or silent, with no skin changes or any single symptom but damaged lymphatic vessels manifest as pelvic muscular deficiency. Since the perineum is particularly vulnerable to damage caused by lymphadenectomy, any disruption may make the risks of this symptom higher.

Lymphoedema to the lower body typically occurs within the first 12 months following treatment; however, onset can also occur many years later[37]. Visible signs include swelling to the genitals, legs and feet. This can lead to loss of mobility and swelling severe enough to make it difficult to fit into a pair of trousers or even socks.

Fatigue

Postoperative fatigue encompasses both physical and psychological symptoms that delay return to normal activity. Preoperative and short-term postoperative optimisation of comorbidities in older patients including anaemia, delirium prevention, sepsis management and any others barriers to physical rehabilitation will reduce risk of long-term difficulties with fatigue and functional decline.

Many patients who undergo open colorectal surgery have a high level of fatigue in the first three months after surgery with significant reduction in work capacity, muscular strength and lean body mass[38]. If muscular endurance and cardiac fitness decline as a consequence, patients may need more energy to perform a physical task, leading to lasting sensations of fatigue[39].

Studies examining the impact of enhanced recovery (a fast-track care programme) on individuals treated by surgery for colorectal cancer show that fatigue can be clinically significant, but only in the short-term. After more extensive and morbid surgery, fatigue may have a longer-lasting consequence (one study shows by a duration of nine months) before functioning returns to pre-treatment levels. There is little evidence on the long-term incidence of fatigue in those who have uncomplicated colorectal or anal surgery alone[40].

Psychosocial effects

Any of the above symptoms may lead to psychological distress and impact on resuming normal roles and responsibilities, such as returning to work. Also, any experience of urinary and bowel incontinence after surgical treatment is likely to limit how much people socialise and adversely affect quality of life.

Body image

Body image and body confidence are particularly affected following surgery due to body shape changes, including abdominal scars and weight loss, and stoma formation, any of which may require specialist attention[41].

Can the long-term consequences after surgery be predicted?

Predicting long-term consequences after surgery helps to improve patient preparation, enhance informed consent and develop an infrastructure to support early management should any problems occur.

Generally speaking, the more extensive the surgery, the greater the risk of developing long-term consequences, since more organs and structures will be removed or be directly affected. Use of extensive pelvic dissection techniques to achieve the best oncological outcomes (such as a total mesorectal excision) means rectal cancer surgery carries greater risk of stoma formation and changes to pre-morbid pelvic function. Predictive factors for a temporary stoma becoming permanent (after an anterior resection) include anastomotic leak, change in patient health and disease status[42]. At the time of primary surgery, a definitive stoma, even when reconstruction is possible, may be more likely in older patients with significant co-morbidities or advanced cancer[43].

Procedures such as APER carry risk of delayed perineal wound healing. An extralevator abdominoperineal excision (ELAPER) requiring additional pelvic dissection, may be undertaken in patients with a low advanced rectal cancer, possibly resulting in more perineal wound complications, such as wound infection, sinus and perineal hernia formation[44] although reported outcomes remain controversial[45].

For patients undergoing sphincter-saving surgery for rectal cancer, the level and type of anastomosis provides an indication of functional outcome; the lower the anastomosis, the higher the likelihood of anterior resection syndrome[46]. In the first 12 months, a side-to-end anastomosis or colopouch formation is likely to result in better functional outcome than a straight colo-anal anastomosis, though functional differences are less clear in the long-term[47].

A third of those with colorectal cancer who responded to the national PROMs cancer survey (one to three years after their diagnosis) indicated they had no, little or only some control of their bowel function[10]. A 2012 Cochrane review concluded that health-related quality of life may not be better in rectal cancer survivors reconstructed without an ostomy when compared with those who have an ostomy[48]. Special attention should be paid to individuals reporting more physical symptoms, co-morbidities and in the presence of a new stoma three months post-surgery, as they are at greater risk of poor outcomes including low mood[49]. Patients with functional limitations or frailty may need more assistance and support in managing their stoma and this should be arranged before problems become overwhelming.

The most common aetiology for urinary and sexual dysfunction is autonomic nerve disruption during abdominoperineal or low anterior resections. Major urinary dysfunction after mesorectal excision for rectal cancer is associated with an incomplete nerve-sparing technique. One study reports 3.8% of patients required long-term urinary catheterisation, all of whom had incomplete pelvic autonomic nerve preservation[50].

In predicting risk of long-term bowel, sexual or urinary long-term consequences, those with pre-existing functional alteration to the bowel, bladder or sexual organs may be more predisposed to developing long-term consequences after any pelvic surgery and should undertake preoperative assessments to identify developing problems.

Factors to consider for patients who may be at additional risk of developing incisional hernia post-surgery include increased body mass index (BMI), the chosen surgical approach, emergency presentation and wound infection[51,52].

Review of the evidence indicates the main predictor of postoperative fatigue is the level of preoperative wellbeing. The severity of fatigue and vigour after surgery were predicted mostly by the preoperative levels[53].

Can the consequences be prevented?

The 2013 National Bowel Cancer Audit data indicates that three out of five colorectal cancer patients underwent surgical resection. Much research has been conducted with the aim of improving health-related quality of life after colorectal surgery. Technical modifications have allowed surgeons to achieve oncologic control while preserving the autonomic nerves that innervate the bladder and sexual organs. However during surgery that requires low pelvic dissection the possibility of altering sexual and urinary function is such that it cannot be prevented[54].

Research examining how to minimise and prevent these consequences of treatment continues, concentrating on modifying surgical techniques to prevent their occurrence. In the prevention of stomal hernia and prolapses, current investigation involves evaluating the benefits of mesh insertion. While there is insufficient evidence to support hernia prevention, advice should be given for exercise and weight reduction, as both will be beneficial for ongoing health.

A faster functional recovery, including reduction in fatigue, can be achieved (certainly in the short-term) by decreasing the surgical stresses imposed on the body and application of laparoscopy. Further benefits may be gained by combining laparoscopic surgery with an enhanced recovery programme[55].

Part 3: Long-term consequences of chemotherapy

What are the causes of long-term consequences of chemotherapy in colorectal and anal cancer?

Chemotherapy is a systemic treatment commonly administered in colorectal and anal cancer. It can be given as adjuvant treatment in high-risk groups, as a palliative treatment in patients with metastatic disease and as neo-adjuvant treatment in combination with radiotherapy in anal cancer and to downstage locally-advanced rectal cancer. It is often administered as a combination of intravenous and oral medication.

Since cancer cells divide more often than most normal cells, chemotherapy can damage them and cause cell death. In doing so, chemotherapy also kills other rapidly dividing cells such as those found in the gastrointestinal tract (which can cause sore mouth, nausea, vomiting and diarrhoea) and bone marrow (which causes immune suppression and puts the patient at the risk of life-threatening complications), which results in the side effects experienced. The acute side effects of chemotherapy generally resolve fairly quickly as the affected cells repair and recover, and by administration of appropriate supportive medication such as antiemetics and antidiarrhoeals. Patient education is vital, so patients must be instructed to call Acute Oncology services for early intervention in order to avoid dehydration and other complications.

Most consequences of chemotherapy are temporary and disappear a few weeks after treatment. Some people do experience long-term changes in the body, which may arise months or many years after the chemotherapy has finished indicating there has been permanent tissue damage.

What are the long-term consequences following chemotherapy for colorectal or anal cancer?

This section considers the most common long-term side effects associated with colorectal and anal cancer chemotherapy (see Figure 2). It does not address the rarer consequences of treatment including possible impairment to other bodily systems such as changes in hormone or lung function.

Common long-term consequences include:

- Chronic fatigue
- Peripheral neuropathy
- Cognitive impairment
- Cardiac consequences
- Fertility
- Psychosocial and sexual concerns.

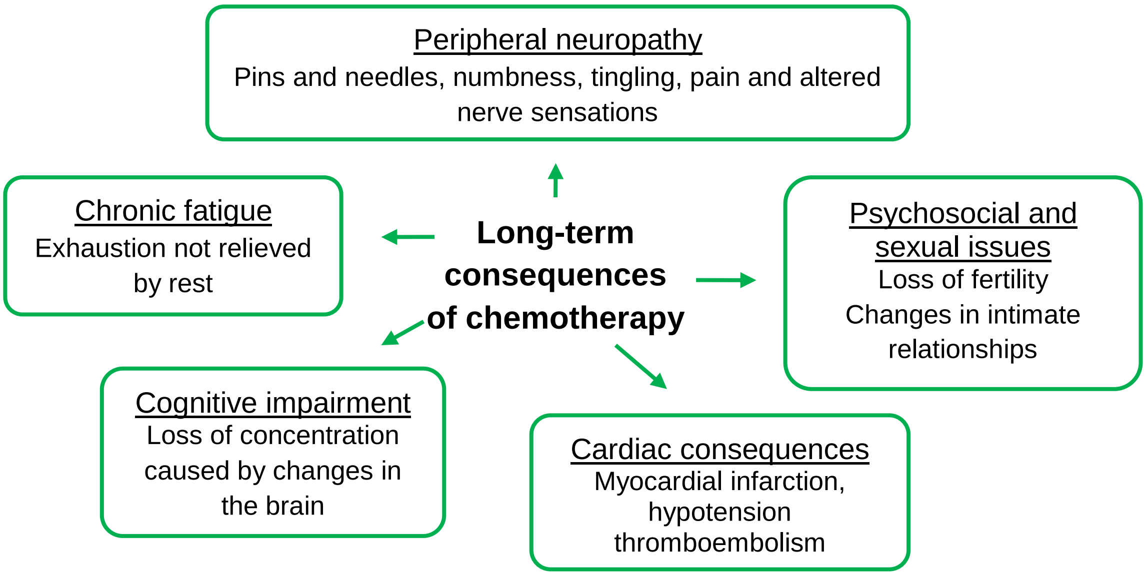


Figure 2: Possible long-term consequences following chemotherapy for colorectal or anal cancer

Fatigue

Chemotherapy-induced fatigue is experienced as a persistent, distressing, subjective sense of tiredness which is not proportional to recent activity and interferes with usual functioning[56].

Colorectal cancer is associated with a high incidence of cancer-related fatigue, especially among individuals older than 65 years. Its general prevalence may be as high as 75% but may reach up to 90% among some patients undergoing chemotherapy[57]. It may develop during and after any of the chemotherapy regimens commonly used to treat colorectal and anal cancers, with some suggestion that infusional 5-fluorouracil (5-FU) regimes give rise to more fatigue than oral derivatives such as capecitabine[58].

In general, the frequency of fatigue tends to increase during the course of chemotherapy, with a pattern of peaks and troughs through treatment cycles. One study reported nearly 40% of patients experience fatigue a year after chemotherapy with smaller numbers experiencing chronic fatigue for a number of years after treatment[59].

Its pathogenesis is unknown, but fatigue is assumed to be multifactorial, involving psychological, social and physiological components. The physical causes of fatigue can often be linked to imbalances in the blood such as anaemia, underactive thyroid or vitamin deficiency. Contributory psychological issues may be harder to discern than a physiological imbalance but chemotherapy-related fatigue often presents as a cluster of symptoms alongside depression, low mood or pain. Often a cycle of behaviour ensues where individuals take insufficient exercise due to feeling fatigued which is known as the fatigue cycle.

Experiencing chronic fatigue has huge implications for day-to-day life where simple tasks are exhausting and it may prevent some people from being able to socialise, work or engage in leisure pursuits.

Chemotherapy-induced peripheral neuropathy

Oxaliplatin, an agent integral to many of the current colorectal (and occasionally anal cancer) treatment chemotherapy regimens, is known to cause peripheral neuropathy by affecting the large sensory nerves. Most people receiving this drug in the adjuvant setting will experience transient symptoms of pins and needles, numbness and/or tingling (paraesthesias) in distal extremities which can appear during or within hours of infusion.

The signs and symptoms of sensory neuropathy may continue to develop for up to six months after treatment due to the cumulative effects of this drug. The long-term presence of neuropathy after chemotherapy treatment indicates a distinct and more chronic clinical syndrome which typically involves altered sensory perceptions, unpleasant sensations and numbness (dysaesthesia) in the hands and feet. Approximately 60% of patients will still have symptoms eight months after treatment[60].

When chemotherapy-induced peripheral neuropathy is more severe, it can cause disabling pain and numbness which affect a person’s ability to do things like walk, write, fasten buttons and pick up tiny objects. In many cases, these symptoms will resolve several months after completing treatment; yet, for some, peripheral neuropathy becomes a condition that severely affects quality of life.

Cognitive impairment

Post-chemotherapy cognitive impairment, also known as cognitive dysfunction or chemo brain, refers to the mental fog many people experience during or after chemotherapy treatment. Three-quarters of patients report cognitive decline or loss of mental acuity during chemotherapy: this may manifest as difficulties with multi-tasking or loss of short-term memory, word-finding, attention or concentration. At least a fifth to a third of individuals will continue to experience loss of language, slower processing time or reaction response and diminished organisational skills for some months after completion of treatment[61].

Older people, or people with known vascular disease, should have a screening questionnaire for short-term memory loss or previous episodes of acute confusion (delirium) at the start of treatment. If present, a baseline cognitive test should be done. Low vitamin B12 levels and hypothyroidism can cause reversible cognitive impairment and can be identified through simple blood tests.

These symptoms may resolve but some people are affected years after treatment with a significant impact on their responsibilities and social confidence. These often translate into lower health-related quality of life scores, especially when people experience difficulties when going back to work[62].

Many mechanisms have been suggested to explain cognitive dysfunction in patients with cancer and it is still subject to debate; however, it is evidently a complex phenomenon. There are two major theories as to the cause: the first is that chemotherapy has a direct neurotoxic effect and the second is the role of hormones in nervous system health. Other theories suggest there may be vascular injury, inflammation, auto-immunity and anaemia.

Integral to many colorectal and anal cancer chemotherapy regimes, 5-FU has been demonstrated in vivo to reduce the viability of cells that are precursors to both neurons and glia in the brain. Furthermore, when 5-FU is combined with oxaliplatin there appears, certainly in experimental conditions, to be a greater detrimental effect on hippocampal-dependent tasks[63].

Cardiac consequences

Some chemotherapy agents have serious long-term cardiac consequences including heart failure, myocardial ischaemia and arrhythmias; however, these risks are not strongly linked to the cytotoxic drugs commonly used to treat colorectal and anal cancer.

There are some known acute cardiac consequences with the risk that 5-FU can induce acute endothelial dysfunction, generally manifested as chest pain, but this rarely results in an acute myocardial infarction[64]. Similarly, therapy with capecitabine, a metabolite of 5-FU, has rarely resulted in acute myocardial infarction. However, it is known that individuals with pre-existing coronary artery disease are known to be at increased risk for this acute toxicity[65].

Fortunately, once therapy is complete, there does not appear to be any lasting cardiovascular risk attributable to these two agents. To date, there is no convincing evidence, beyond occasional case reports, of acute or long-term cardiotoxicity associated with oxaliplatin. Two commonly used biologics used in association with the above chemotherapy drugs may precipitate acute cardiac problems: cetuximab can induce hypotension whereas bevacizumab may promote severe hypertension and venous thromboembolism. It is important to check a patient’s blood pressure lying and then standing as those aged over 65 years, with diabetes and/or taking antihypertensive medication, are at greater risk of orthostatic hypotension during and after treatment. If this is present, antihypertensive medication should be reduced or stopped and good fluid intake during chemotherapy encouraged.

The long-term effects of both therapies are not known and based on findings from a large British cohort study which did not observe an excess risk of heart failure or coronary artery disease among colorectal cancer survivors, they may be small[66].

Fertility

Chemotherapy affects ovary and sperm function, and can induce an early menopause in women and decreased sperm production in men. There can be direct damage to spermatogenesis (sperm production) temporarily or permanently, since this process is highly sensitive to the effects of chemotherapy. The degree of gonadal stem cell damage varies according to the drugs used, dose, route of administration (oral versus intravenous), treatment regimen (e.g. combination therapies) and total doses of individual chemotherapeutic agents[67]. It is probable, although not well documented, that this also relates to pre-treatment sperm counts.

The ovary is equally chemo-sensitive and chemotherapy can result in loss of primordial and growing follicles, with consequent loss of hormone production and menstruation, and an early menopause. Ovarian toxicity varies depending on the regimen, with varying consequences: incomplete loss of follicles resulting in an early menopause, rapid and permanent ovarian failure, or no apparent effect. Although women must entertain the prospect of potential gonadal damage together with the possibility of early menopause as a direct consequence of chemotherapy treatment, the regimes commonly used for colorectal and anal cancer are not considered high risk for this to occur.

In summary, 5-FU alone may have little influence on fertility, but it is unknown whether agents such as oxaliplatin and irinotecan (the latter is only used in the metastatic setting) cause any gonadal failure in the long-term[68].

Sexual issues

The sexual issues experienced by colorectal cancer survivors may be akin to those recovering from similar chemotherapy regimes for other cancer types, but there is a lack of evidence on the incidence in either group and in the majority of cases, chemotherapy is given in combination with another treatment modality and treatment effects must therefore be considered in totality (see *Part 5: Long-term consequences of combined treatment modalities*).

Can long-term consequences after chemotherapy be predicted?

Pre-chemotherapy consultations can be used to identify co-morbidities which may result in a greater tendency to be affected by treatment. There are a number of pre-existing factors known to increase a person's risk for developing long-term consequences; for example, in chemotherapy-induced peripheral neuropathy, known risk factors include pre-existing neuropathy, alcoholism and diabetes mellitus[69]. Individuals with renal, hepatic and cardiac conditions will need to be more closely monitored during treatment. For instance, we know the risk of cardiac problems developing after treatment relates to any cardiovascular risk factors, particularly previous cardiovascular disease in the patient.

Age could be a factor as while there is much variation in the health status and functional reserve of individuals over the age of 70, it is generally suggested that this group of patients are more likely to experience long-term consequences of chemotherapy and for longer after the end of treatment, as their damaged cells take longer to repair[70]. In a prospective, population-based cohort of colorectal cancer survivors, chemotherapy was associated with worsening cognitive function, particularly for individuals younger than 70[71]. Other associated factors may contribute to long-term consequences such as potential interactions with current medications, impaired nutritional status and decreased functionality[72]. Older people with more than one comorbidity, multiple medications, any functional difficulty, history of falls or cognitive impairment, can benefit from multi-domain assessment and treatment from geriatric specialists[73]. Optimisation and support for an individual's wider health care needs can improve cancer treatment tolerance and survival[74].

We also know symptoms are dose related, severe neuropathy being observed with cumulated doses ranging from 510 to 765 mg/m^2 in up to 10% of patients, but affecting up to 50% of the patients receiving doses higher than 1000 mg/m^2 [75]. One small study reports neuropathy persistence in almost 35% of their sample five to six years after cessation of high-dose oxaliplatin treatment[76].

A post-chemotherapy treatment review to assess for any acute symptoms experienced during treatment can be predictive of potential long-term consequences due to the accumulation of toxicities.

Can these long-term consequences be prevented?

It is important that all chemotherapy treatment options, particularly in the adjuvant setting, are carefully discussed with each individual and a balance found between risk of recurrent disease (based on pathological staging) and likelihood of consequences which could cause a permanent effect on quality of life.

Dose reduction, delaying treatment and even modifying regimens are commonly used strategies in secondary prevention of treatment consequences. Ideally those most susceptible to chemotherapy side-effects will have been identified through assessment at the outset such as the frail elderly, and have been advised not to have treatment where risks outweigh any anticipated benefits[77].

Encourage any patients experiencing toxicity during their treatment to inform their treating team as soon as possible. By seeking help immediately if acute symptoms such as infection/ diarrhoea are suspected, the longer-term consequences can be much reduced[78].

In the case of oxaliplatin-induced peripheral neuropathy, several agents have been tested as neuro-protectants including anticonvulsants, antidepressants, vitamins, minerals, with currently insufficient evidence to support their prophylactic use. The intravenous administration of calcium gluconate and magnesium sulphate before and after an oxaliplatin infusion remains controversial.

Targeted therapies, which are agents specific for the deregulated proteins of cancer cells, offer the hope of greater treatment effect as they are more tumour specific and may be associated with less toxicity. In many cases the long-term consequences of these drugs are not yet known.

Currently, targeted therapies are given in combination with chemotherapy regimens for those with metastatic disease, but are administered in ‘general or average’ doses. In the future, personalised medicine may play a greater role in helping us preventing long-term consequences since its aim is to try to give the right treatment to the right patient in the right dose at the right time.

Part 4: Long-term consequences of radiotherapy

What are the causes of long-term consequences of radiotherapy?

Radiotherapy is used in the treatment of rectal and anal cancer; this section relates to the long-term consequences of external beam radiation given to the pelvis with curative intent.

Initial pathological changes from radiation can begin directly after the first exposure. Acute changes involve inflammation, oedema responses and the initiation of wound-healing processes. Long-term consequences tend to occur in tissues containing rapidly proliferating cells, such as subcutaneous or fatty tissue, muscle and the wall of the intestine[79].

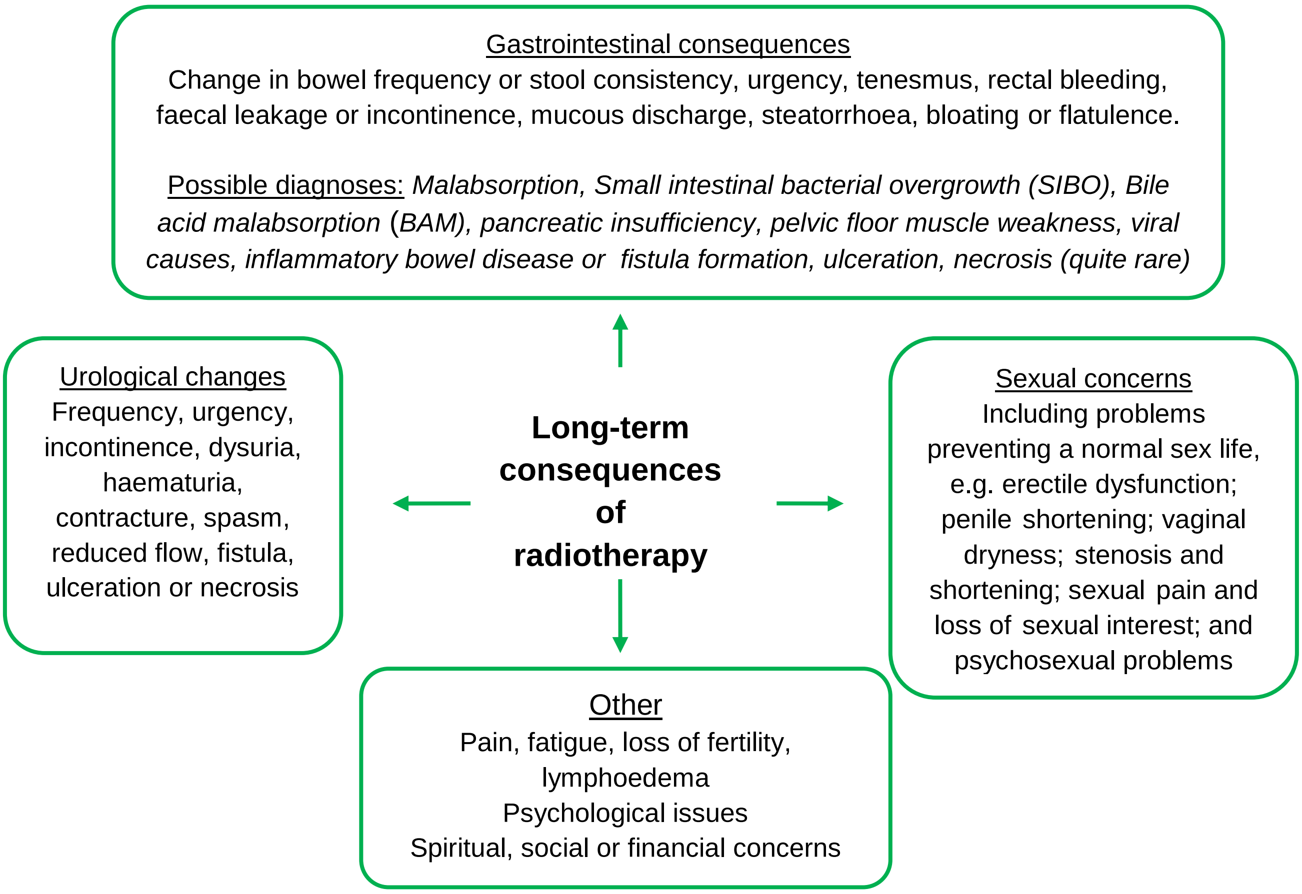
Fibrosis can develop in tissues exposed to radiation (similar to scarring) causing the architecture and function of the underlying organ or tissue to alter, developing atrophy, vascular damage or even tissue necrosis. These histological changes trigger clinical symptoms, yet may not become apparent for weeks, months or years after treatment[65,80].

The consequences of radiotherapy techniques traditionally used to treat rectal and anal cancer may include changes in gastrointestinal, bladder and sexual function, telangiectasia, lymphoedema, bone problems, hormonal changes, fatigue, infertility and pain[81,82,83,84]. A small percentage of people will develop a complex interplay of chronic symptoms following radiotherapy to the pelvis which is now termed Pelvic Radiation Disease (see Figure 3).

What are the long-term consequences after radiotherapy?

Following radiotherapy, consequences of treatment may include:

- Gastrointestinal effects
- Urinary changes
- Sexual changes
- Infertility
- Menopause
- Skin problems
- Bone health
- Lymphoedema
- Psychological effects



Gastrointestinal consequences
Change in bowel frequency or stool consistency, urgency, tenesmus, rectal bleeding, faecal leakage or incontinence, mucous discharge, steatorrhoea, bloating or flatulence.

Possible diagnoses: *Malabsorption, Small intestinal bacterial overgrowth (SIBO), Bile acid malabsorption (BAM), pancreatic insufficiency, pelvic floor muscle weakness, viral causes, inflammatory bowel disease or fistula formation, ulceration, necrosis (quite rare)*

Long-term consequences of radiotherapy

Urological changes
Frequency, urgency, incontinence, dysuria, haematuria, contracture, spasm, reduced flow, fistula, ulceration or necrosis

Sexual concerns
Including problems preventing a normal sex life, e.g. erectile dysfunction; penile shortening; vaginal dryness; stenosis and shortening; sexual pain and loss of sexual interest; and psychosexual problems

Other
Pain, fatigue, loss of fertility, lymphoedema
Psychological issues
Spiritual, social or financial concerns

Figure 3: Possible symptoms associated with pelvic radiation disease (adapted from the original designed by Lisa Punt, member of the guidance development group for *Guidance on long term consequences of treatment for gynaecological cancer*)

Gastrointestinal effects

Gastrointestinal effects are among the most common of the chronic consequences experienced following pelvic radiotherapy[1], with as many as 50% of patients reporting a worse quality of life[85,86,87] and up to 90% of patients developing a permanent change in their bowel habit[88]. The most common long-term consequences are increased stool frequency, urgency, spotting of blood and partial faecal incontinence. Other symptoms include tenesmus, rectal bleeding, mucous discharge, steatorrhoea, bloating and flatulence.

The main lasting effect of radiation damage is fibrosis in the large bowel accompanied by ischaemia in the submucosa and muscularis, telangiectasia and other vascular abnormalities. In addition, we know that there are physiological effects of radiotherapy on the rectum: rectal compliance, measured by the threshold volume and the maximum tolerated rectal volume, decreases after radiotherapy[89]. There are a variety of other reasons why a course of radiation to the pelvis causes these symptoms, including small intestinal bacterial overgrowth (SIBO), bile acid malabsorption (BAM), pancreatic insufficiency, viral causes, fistula formation and ulceration.

Although many people have mild to moderate gastrointestinal symptoms which can be relatively easily self-managed, a percentage will experience severe long-term changes in their bowel function requiring specialist assessment and advice. Severe gastrointestinal toxicity encompasses complications such as fistulation, transfusion-dependent bleeding and stricture formation and it seems that the incidence increases over time[90]. The incidence of chronic radiation proctopathy, caused by a progressive, obliterative arteritis and submucosal fibrosis, is estimated at 2%–20% of all those who have this treatment[91].

One recently published study of 94 long-term anal cancer survivors treated with curative intent radiotherapy without colostomy reports faecal frequency (87% of sample) incontinence for solid stools (31%), liquid stools (54%) and gas (79%) at least monthly[92].

Urinary effects

Around 20% of patients experience severe adverse urinary effects with up to 43% experiencing some change in their urinary function following pelvic radiotherapy[93]. Pelvic radiotherapy can cause scarring and hardening (fibrosis) of the bladder wall, and may also weaken the pelvic floor muscles and valve that holds the bladder closed. Blood vessels in the bladder may become fragile and bleed easily, and in some cases pelvic radiotherapy may cause the urethra to narrow. These changes can lead to long-term consequences, such as passing urine more often, leaking urine and blood in the urine.

Sexual effects

Both men and women report significant declines in sexual activity and significantly worse sexual function if they receive preoperative radiotherapy for rectal and anal cancer when compared to those who have surgery alone[94,95]. In men, erectile dysfunction after radiotherapy is an underdiagnosed, undertreated condition which can considerably affect the quality of life for men and their partners.

Changes in female sexual health are less well reported but a range of possible physical changes are known[96]. Vaginal narrowing, shortening and ultimately vaginal stenosis can occur with chemo-radiation or adjuvant radiation[97]. There may also be atrophic changes to the vaginal and perineal tissues, a decrease in vaginal lubrication and an increase in vaginal infection/irritation which can lead to loss of libido and impact on sexual function. There is convincing evidence to suggest that patients become significantly less active sexually following pelvic radiotherapy when compared to before treatment[98]. This change seems sustained with long-term follow-up studies reporting considerable impairment due to vaginal dryness, dyspareunia and reduced sexual enjoyment[99]. Pelvic radiotherapy can also cause hormone changes, precipitating early menopause and associated symptoms such as hot flushes, mood swings and low sexual desire.

Infertility

The primary therapy associated with infertility in women with rectal cancer is pelvic radiotherapy[100]. Women treated with abdominopelvic radiation have an increased rate of uterine dysfunction leading to miscarriage, preterm labour, low birth weight and placental abnormalities[101].

Pelvic radiotherapy has irreversible effects on testicular function and fertility. The testes may receive as much as 18.7% of the administered radiation in pelvic cancers, with rectal cancer being amongst the highest scatter doses to the testes[102]. This effect cannot be prevented and for most men seeking cryopreservation, a semen sample will need to be collected via masturbation prior to treatment. Cryopreservation induces a “suspended animation state” for storage as long as 15 years.

Lymphoedema

Pelvic lymph nodes can be damaged by radiotherapy causing fluid to build up in the lower limbs leading to long-term lymphoedema issues such as swelling, loss of mobility and body image issues.

Bone health

Pelvic bones can be damaged by radiotherapy; bone demineralisation and decreased bone elastic resistance can cause fine cracks and insufficiency (stress) fractures[103]. Symptoms of insufficiency fractures include pelvic pain, back pain and immobility, which can substantially affect quality of life. This constellation of symptoms can occur within two months of radiotherapy and up to 63 months post-treatment, with a median incidence of six to 20 months.

Skin problems

The majority of skin problems will heal within four weeks of treatment being complete since it takes this amount of time for the basal cells of the epidermis to recover and new skin to start to grow and heal[104]. Although the skin-sparing effect of modern linear accelerators ensures the maximum dose of radiotherapy is reached below the basal layer of the skin, basal cell loss has been found to begin once the radiation dose reaches 20–25 Gy, and their maximum depletion occurs when the patient receives a dose of 50 Gy.

The most common chronic changes associated with skin exposure to radiotherapy include atrophy, telangiectasia, pigmentation changes, fibrosis, ulceration and necrosis. Clinical manifestations indicative of atrophic changes of the skin and cutaneous appendages (e.g. absent sweat, dryness, thinning of epidermis) are directly related to the level of radiotherapy damage induced[105].

Telangiectasia is characterised by the presence of dilated, thin-walled capillaries, venules and lymphatics in the upper dermis resulting in reddish discolouration and tortuosity of vessels. Pigmentation changes may arise as a result of direct toxicity to the melanocytes, or as an effect of inflammatory changes resulting from contact dermatitis, radiation enhancement, radiation recall or photosensitivity reactions. Fibrotic changes characterised by induration, oedema formation and thickening of the dermis and subcutaneous tissues are dose dependent and most severe in areas previously affected by a moist reaction. Ulcerative and necrotic changes, although rare, may be induced by high doses of radiation[106].

Pain

The most important risk factor for development of chronic pain is pelvic irradiation resulting in chronic proctopathy.

Second cancer

It is generally believed that following pelvic radiotherapy, an individual is at an increased risk of developing cancer in the treatment field. After five years of follow-up, elevated risk has been observed in patients younger than 50[107]. Although, for this patient population, it is suggested that the risk is relatively small, with reported development of second cancer after radiotherapy being relatively infrequent when compared with the background incidence of spontaneous cancers. The incidence of second primary tumours within adjacent organs could represent a balance between the radiation-induction of tumours and the radiation-inhibition of spontaneously occurring tumours.

Psychosocial effects

A significant proportion of those living with and beyond colorectal and anal cancer will experience clinically meaningful levels of anxiety and depressive symptoms or reduced mental wellbeing across the trajectory of the illness[108]. Fear of recurrence is the concern that the cancer is going to come back following treatment completion, with studies suggesting that on average 74% of all cancer survivors experience this to some degree, and 49% have a moderate to high degree of fear of recurrence[109].

Many report difficulties in recovery and returning to 'normal' after treatment. Worries about bowel and urinary control are concerns for many individuals considering going out and when planning their return to work. It is not surprising that a third of all colorectal cancer survivors have difficulty engaging in leisure pastimes and particularly vigorous exercise due to such effects[110].

Further information on many of these symptoms can be found in *Part 6: Assessment and symptom management*.

Can long-term consequences after pelvic radiotherapy be predicted?

The risk of long-term consequences cannot entirely be predicted from the dose of radiotherapy delivered, since it also depends on a complex interaction of physical, patient-related, treatment and genetic factors.

Rates of bowel problems are significantly increased in rectal cancer survivors treated with pelvic radiation, regardless of whether it was administered pre- or postoperatively[111]. There can be greater risks from short-course preoperative radiotherapy, with one follow-up study showing relatively increased risk for postoperative hospitalisation due to bowel obstructions and other gastrointestinal complications[112].

The rate of development of consequences of treatment with radiotherapy does not necessarily plateau over time, indicating the potential to develop new symptoms many years after treatment[113]. This timescale highlights the importance of patients understanding from the outset and being regularly reminded of the risks for long-term problems, for example by offering the Macmillan symptom checklist or the patient booklets on pelvic radiotherapy for men and women.

It is nonetheless suggested that cumulative acute symptoms are more predictive of late symptoms[114]. Those with greater and particularly longer non-healing acute toxicity after radiotherapy are candidates for closer follow-up and possible prophylactic actions to reduce their risk of long-term problems. Currently, no reliable predictive marker of gastrointestinal toxicity after cancer treatment is available and there is no way to assess the levels of risk.

Can the long-term consequences be prevented?

Recent technical advances in radiotherapy and the introduction of more precise 3D-targeting, as used in Intensity Modulated Radiation Therapy (IMRT), will mean more normal tissue will be spared the toxic effects of radiotherapy, and thus long-term consequences will be minimised.

It is good practice to record the volume of small bowel receiving each dose between 5 and 40 Gy at 5-Gy intervals. While increased bladder volume has been associated with reduced small bowel volumes, this benefit decreases during delivery of treatment.

Preventive strategies such as minimising irritants to the irradiated skin may help ensure that the outer skin surface remains as intact as possible[115]. Please see *Guidance on the long-term consequences of treatment for gynaecological cancer*.

The number of women who develop vaginal stenosis is not well reported in rectal and anal cancer but it remains an important consideration[116,117] and women should be offered both verbal and written information about this potential problem. International guidance recommends the use of vaginal dilators from as soon as two to eight weeks after completing radiotherapy treatment once the active inflammatory response has settled. Dilation therapy may include the use of dilators, vibrators, fingers, or similar shaped devices. It may not be necessary to use a dilator if vaginal intercourse is resumed on a weekly basis (or more) following treatment. The need for dilation therapy should be reviewed regularly, as dilation therapy can be discontinued when no longer required; e.g. when sexually active or experiencing no discomfort during vaginal examinations at follow up 1-2 years post treatment. There is however currently little empirical evidence that dilators are of benefit.

For men with erection difficulties, there is some evidence to indicate that early penile rehabilitation during/after treatment may be beneficial. Penile corporal hypoxia due to the loss of daily and nocturnal erections leads to penile atrophy, penile scarring and fibrosis that limit further oxygenation. To break this vicious cycle, the concept of early intervention (ideally within weeks and certainly before a year from treatment) to oxygenate the penile corporal, termed penile rehabilitation[118] has been suggested through use of phosphodiesterase 5 inhibitor medication (PDE5-Is) such as Viagra and vacuum erection devices.

Another hope is that it may become possible to develop agents, with anti-fibrotic potential which can reverse the fibrosis, or at least prevent it at an early stage.

Part 5: Long-term consequences of combined treatment modalities

We have previously described the consequences of individual treatment modalities. However, it is important to acknowledge that treatment strategies depend on the type of cancer, location of the tumour, clinical assessment, staging and patient choice. The combination of different treatment modalities may influence the symptoms and long-term consequences that patients experience and need to be taken into account during assessment for recovery.

Rectal cancer

The addition of radiotherapy prior to surgery – as a neoadjuvant therapy - has an established role in reducing local recurrence in patients thought to be at risk (short-course preoperative radiotherapy the week prior to surgery) and can render inoperable tumours operable (downstaging or long-course combined pelvic chemo-radiation for those patients with tumours that are fixed and inoperable at presentation). Postoperative adjuvant chemotherapy is considered on the basis of individual risk of disseminated disease.

Surgery in combination with other treatment modalities (before or after surgery) can exacerbate the extent of many long-term consequences[119]. Pelvic radiotherapy treatment, with or without the addition of chemotherapy, before rectal cancer surgery results in a significantly greater risk of anterior resection syndrome, urinary problems and sexual dysfunction[120,121].

Neoadjuvant radiotherapy significantly increases perineal wound problems after an abdominoperineal resection for rectal cancer; if the perineum does not heal initially, secondary wound healing may prolong a patient's hospital stay, necessitate further surgical intervention and often requires intensive wound care for several months[122].

A locally-advanced rectal cancer is likely to be treated with surgery in combination with another treatment modality, resulting in greater risk of long-term treatment consequences. Both have a major impact on the severity of bowel dysfunction after restorative rectal cancer surgery. A recent study even suggests that no functional benefit is gained from having a rectal remnant once it has been irradiated[123].

In comparison to abdominal surgery for colon cancer, there is increasing evidence to show that with the greater use of pelvic radiotherapy and sphincter-preserving surgery in rectal cancer, long-term consequences are not uncommon[124]. There is increasing evidence that bowel function difficulties will be greatest in those patients who received radiotherapy before or after surgery[125]. Persistent problems of bowel frequency, faecal leakage, difficulty controlling flatus, dietary modification to control function and requirement to wear a protective pad have been reported, resulting in reduced quality of life[126,127,128]. Patients receiving preoperative radiotherapy also report reduced social functioning and financial difficulties, and in men, increased erectile function difficulties.

Colon cancer

There is no role for pelvic radiotherapy in the treatment of colon cancer, and postoperative adjuvant chemotherapy is considered on the basis of individual risk of disseminated disease.

Anal cancer

Combination chemo-radiation is the main treatment in anal cancer in an attempt to save sphincter function with pelvic surgery being held in reserve for persistent or recurrent disease[129,130]. There is no role for adjuvant chemotherapy post chemo-radiation[131]. Standard practice in the UK to treat primary anal cancer with 5-FU and 50.4 Gy radiotherapy in 28 daily fractions.

Similar to the rectal cancer data, persistent treatment-related issues are reported following pelvic chemo-radiation in a subset of patients, including bowel problems with moderate to severe faecal incontinence commonly experienced amongst anal cancer survivors following chemo-radiation[132]. Impaired sexual function in both men and women, reduced role and social functioning along with financial difficulties are also reported after anal cancer multi-modal treatment[105,133,134,135].

Can the long-term consequences after combined treatment modalities be predicted?

Though it is established that combined treatment regimes increase pelvic late effects, there is little evidence to indicate whether the use of combined modality therapy creates additional risk of long-term consequences. In each case, there will be a unique combination of factors which may play a part in determining this risk. Intrinsic factors include the patient characteristics such as general health condition, nutritional status, age, comorbid disease and ethnicity. Extrinsic factors include the dose, regime, other treatments and medications (plus in radiotherapy, the energy and fractionation).

Cancer-related fatigue is often more common, more severe and persistent in patients who receive more than one type of treatment[136,137]. The addition of chemotherapy may heighten the effect of radiation on bone density with associated medications and oestrogen deficiency further contributing to the risk of osteoporosis[138].

Two factors associated with increased risk of long-term consequences following chemo-radiation in anal cancer include large tumour size – with a size ≥4 to 5 cm to be a prognostic factor for defunctioning colostomy formation – and HIV-positive patients, linked independently to the occurrence of ulcers[139]. There is also some data which suggests that combined modality therapy should be performed with more caution in elderly patients with rectal cancer[140,141].

As indicated, a diagnosis of colorectal or anal cancer puts an individual at an increased risk of developing cancer at a number of other sites, especially those within the digestive system[142]. It is possible that multimodal therapy may increase this risk. In a large US-based study, radiotherapy was found to be related to a relatively small proportion (8%) of second cancers, although most second cancers were related to other factors[143].

Can the long-term consequences after combined treatment modalities be prevented?

As our understanding of health-related quality of life improves over time, we will be able to indicate more clearly what risk these treatments pose in the longer-term and to what extent other potential causes might also be affecting these consequences.

Existing late toxicity data is informed by patient cohorts receiving conventional radiotherapy techniques. Pelvic IMRT is increasingly being used, allowing sparing of normal tissues, such as genitalia, bowel and bladder, at least in terms of dose-volume data[144].

Overall, most long-term survivors of colorectal cancer report a psychological quality of life comparable to that of the general population, but a somewhat lower physical quality of life[145]. Our understanding of the quality of life issues of anal cancer patients treated with radio chemotherapy is currently limited by the QoL assessment measures used[146] which highlight difficulties experienced with bowel and sexual function but appear to be overlooking other treatment toxicities.

Part 6: Assessment and symptom management

Assessment

As many symptoms may be due to more than one underlying cause, effective assessment is important to identify all contributing factors and unmet needs.

Holistic Needs Assessment (HNA)
Patients should be asked at the end of treatment, at each follow-up appointment, telephone follow-up and during an HNA if they have any new or persisting problems following treatment. This also gives patients the opportunity to express any general concerns including fatigue, pain or psychological issues.

Detailed assessment of symptoms
Presence of symptoms and their severity can be assessed and recorded using instruments such as LENT SOMA[147], the modified GSRS for gastrointestinal symptoms[148] and MSKCC[149] although these can be lengthy and are usually designed for research rather than routine clinical care. LARS[150] a patient-reported questionnaire that seems to be both simple to complete and thorough enough to addresses the key symptoms.

Specific questions should include all of the following:

Do you have any changes in your bowel habits since your treatment that are causing you any problems? If so:

- → Have you noticed any bleeding from the bottom?
- → Are you ever woken up at night specifically to open your bowels?
- → Do you need to rush to the loo or not make it in time?
- → Do you have any other gastrointestinal symptoms that interfere with your daily activity?

Do you have any changes in your bladder function since your treatment causing you any problems?

Do you have any discomfort (dull/constant ache) in your pelvis?

Do you have any new concerns with your sexual health or with your sex life?

Do you have any changes/swelling in your lower limbs or pelvic region?

Do you have any changes in the condition, colour or comfort of your skin?

Patients may wish to keep a symptom diary to aid self-assessment of symptoms to share with professionals or identify patterns of symptoms. These can include food, pain, bowel or bladder diaries.

Symptom management

For each of the symptoms listed in this section, assess the person to identify the level of each problem (potentially using a visual analogue scale) to guide your decisions about signposting, referral or clinical management. Better assessment is a prelude to successful symptom treatment.

Level 1: Mild symptoms, no significant effect on quality of life

Advice and self-help, re-evaluate

Level 2: Moderate symptoms, mild effect on quality of life

Advice and self-help, consider complex management

Level 3: Severe symptoms, quality of life significantly affected

Complex: likely to need further investigations and specialist management depending on diagnosis

Figure 4: These levels of interventions use the suggested Model of Care Pathway[151].

Before proceeding, ask whether the person wants to undergo further investigations/referral, as some may not wish to continue at that point in time. If they decline a referral to a specialist, ensure:

- They have written information to help manage their own symptoms.
- They know who to contact if they change their mind at any time.
- Their GP is informed that the referral was declined.

The following consequences identified in the last three sections will now be discussed:

- Changes in bowel function
- Stoma care
- Bladder symptoms
- Peripheral neuropathy
- Dietary concerns
- Bone health
- Sexual concerns
- Fertility
- Menopause symptoms
- Lymphoedema
- Cognitive impairment
- Fatigue
- Pain
- Psychological issues.

Changes in bowel function

Firstly, assess for presence of any of the following symptoms: bleeding, pain, urgency, nocturnal defaecation, steatorrhoea, changes in bowel frequency or stool consistency, and reduced bowel control.

If rectal bleeding is present, this should always be endoscopically investigated to assess contributing factors and the need for treatment.

Some people will experience minimal functional changes after treatment; others may have symptoms which they are able to self-manage with possibly some dietary modifications, exercises and pharmacotherapy, although when more severe and/or persisting bowel symptoms occur, specialist input should be sought.

General guidance for changes in bowel function includes the following:

- Guided by a diagnosis and help from a specialist dietitian, consider dietary changes and/or assess dietary fibre intake to help modify bowel function. Good practice information for dietary advice is included later in this section.
- Use small doses of regular antidiarrhoeal medicines to slow down the bowel.
- Strengthen the muscles used for bowel control and good toileting habits.

Some patients find use of rectal irrigation helpful in addressing symptoms of incomplete evacuation of faecal incontinence. There is some evidence to suggest this can be effective[152].

There are options for the treatment of faecal incontinence, which include:

- Surgery
- Medical therapy, such as bulking agents or antidiarrheal medications to reduce stool frequency and improve stool consistency.
- Biofeedback therapy to improve control of the pelvic floor and abdominal wall musculature.

Biofeedback is a non-surgical, non-invasive therapy option which can help individuals retrain their bowels to normalise patterns of bowel function and lessen gastrointestinal symptoms.

Ensure the patient has relevant information such as *Managing the late effects of bowel cancer treatment* or print specific symptom advice and discuss with the patient. Offer other information as appropriate to support self-help. Identify the latest information by use of Information Prescriptions and signpost the patient to self-help groups and online resources or forums. The Bladder and Bowel Foundation is the largest UK continence charity and a valuable resource for patients.

Inform the GP of symptoms experienced by the patient and highlight *Managing lower gastrointestinal problems after cancer treatment: A quick guide for health professionals*, a non-specialist version of *Guidance: The practical management of the gastrointestinal symptoms of pelvic radiation disease* arising as a result of treatment for cancer.

If quality of life is significantly affected and the patient agrees, ask their GP to refer them to a gastroenterologist, ideally one who is known to have a special interest in GI consequences of cancer treatments. Key workers at the cancer unit/centre should be able to provide details of local services or signpost to central services. The British Society of Gastroenterology provide a resource pack to assist gastroenterologists who are developing a special interest.

Stoma care

Assessment for long-term stoma care consequences includes observing the stoma and the peristomal (surrounding) skin. There should also be a review of how that individual is coping practically and emotionally with their stoma.

Physical challenges include routine ostomy care; achieving bowel regularity; issues with leakage, gas and odour; and skin irritations at the ostomy site. Examples of dealing with the ostomy and appliances include finding the right equipment, equipment failures, dietary changes and adaptations.

Common issues may include sore skin, leaking appliances, output changes and body image issues – and can occur for people with either a temporary (closed after postoperative treatment) or permanent stoma[153].

- Sore skin can occur during treatment or as a result of the output from the stoma touching the skin. Careful appliance changes help avoid leakages and there are specific topical creams and powders for use under the stoma appliance to treat sore skin.

- Some patients will have difficulties affecting their ability to care for the stoma, such as peripheral neuropathy and tingling fingers from previous chemotherapy treatment. Seek advice from a stoma specialist nurse. If fatigue is an issue, consider prioritising appliance changes to times less affected by fatigue.

- Output changes from the colostomy or ileostomy can occur at any time following treatment, increasing the risk of dehydration for people with an ileostomy, particularly if there is associated nausea.
  - If bowel infection is excluded, medications to thicken the faecal output (such as loperamide) are recommended, as well as adding more salt to meals to replace the sodium lost in loose faeces.
  - A fluid intake of 1.5–2 litres is ideal. Large fluid intakes can worsen the problem.
  - Careful food choices which include eating a low-fibre diet can be useful in thickening the faecal output, as well as eating little and often to regulate the stoma output.

- Body image can be a long-term problem because of actual or perceived changes in the way the body looks or functions.
  - Actual changes can occur as a result of surgical scars, a stoma and/or weight loss.
  - Development of a parastomal hernia causes a change of abdominal contours and this bulge can be perceived to be unsightly. It is usually treated conservatively with a support belt fitted by a stoma specialist nurse.
  - Many people may perceive the stoma to be obvious to others: although this is not the case, it can have a significant impact on how people view of themselves.

Other problems that might occur with stomas include stenosis, blockages, prolapse and retraction: these are ideally assessed by the stoma specialist nurse.

From a psychological perspective, studies suggest that quality of life will improve within the first three months to a year for people with a stoma[154,155]. Nonetheless, there can be much anxiety and embarrassment about coping with the stoma in the presence of others which can delay socialising and returning to work.

If any problems with the stoma occur, the patient should be advised to contact their stoma specialist nurse for assessment. Although there is a lack of national guidance on caring for stomas, good-quality information is available from the Association of Stoma Care Nurses UK.

There are national and local support groups for people with stomas that may be of benefit to patients. The three main national groups are:

- The Colostomy Association.
- Ileostomy and Internal Pouch Support Group.
- Urostomy Association.

Bladder symptoms

Patients may experience long-term bladder effects such as urgency or incontinence, or even total incontinence (which may be the sign of a fistula). Check if the patient has a urinary tract infection and treat as appropriate.

NICE guidance should be followed for frequency (overactive bladder) or stress incontinence; however, general advice would, depending on symptoms, include:

  - Drink about 2–2.5 litres a day; avoid caffeinated drinks, alcohol and smoking.
  - Offer verbal/written information on pelvic floor exercise/bladder retraining.
  - GP may consider pharmacotherapy.

Specifically for men, refer to the recommendations in the *Integrative review on the non-invasive management of lower urinary tract symptoms in men following treatments for pelvic malignancies*, that is soon to become a quick guide for health professionals; offering a useful algorithm to follow when managing lower urinary tract symptoms (LUTS).

Inform the patient's GP of symptoms experienced by the patient to ensure appropriate community support such as a continence service referral, if appropriate.

If quality of life is significantly affected and the patient agrees, refer them to a urologist with special interest in effects of pelvic radiotherapy damage.

Ensure the individual has relevant information such as *Managing the late effects of bowel cancer treatment* or print specific symptom advice and offer other information as appropriate to support self-help. Identify the latest information by use of Information Prescriptions and signpost the patient to self-help groups and online resources/forums.

Peripheral neuropathy

High-grade chemotherapy-induced neurotoxicity can be predicted by clinical information obtained at mid-treatment. If there is acute toxicity then neurological assessment of the neuropathy symptoms and radial and dorsal sural nerves should be carefully monitored to predict and perhaps prevent the induction of more severe consequences.

Dietary changes

A patient's weight should be monitored and documented weekly during treatment. If weight loss or other symptoms (diarrhoea, nausea, constipation) affecting nutritional status are identified, first-line dietary advice should be given focusing on little and often snacks and nourishing fluids. If first-line advice does not improve nutritional intake, referral to a dietitian is recommended.

If dietary changes are made, they should be done in a systematic way and initially should always be for a trial period.

- Patients may develop carbohydrate intolerances; refer them to a dietitian if suspected.
- If patients have been prescribed fibre supplements then they should be advised to drink additional fluid every day.

There is little evidence-based guidance for diet following treatment for colorectal cancer. However, first-line dietary advice used for IBS (Irritable Bowel Syndrome) may be helpful:

- Have regular meals and take time to eat.
- Avoid missing meals or leaving long gaps between eating.
- Drink at least eight cups of fluid per day, especially water or other non-caffeinated drinks, for example herbal teas.
- Restrict tea and coffee to three cups per day.
- Reduce intake of alcohol and fizzy drinks.
- It may be helpful to limit intake of high-fibre food (such as wholemeal or high-fibre flour and breads, cereals high in bran, and whole grains such as brown rice).
- Reduce intake of 'resistant starch' (starch that resists digestion in the small intestine and reaches the colon intact), which is often found in processed or re-cooked foods.
- Limit fresh fruit to three portions per day (a portion is approximately 80 g).
- People with diarrhoea should avoid sorbitol, an artificial sweetener found in sugar-free sweets (including chewing gum) and drinks, and in some diabetic and slimming products.
- People with wind and bloating may find it useful to eat oats (such as oat-based breakfast cereals or porridge) and linseeds (up to one tablespoon per day).

In a prospective cohort study of colorectal cancer survivors, loss of taste and dry mouth were identified as significant late effects in patients who had received chemotherapy as late as five years post-treatment[65].

Bone health

Ensure underlying contributing conditions are managed appropriately. People with bile acid malabsorption or pancreatic insufficiency are not likely to absorb their fat-soluble vitamins such as vitamin D and require specialist input.

- Include on Treatment Summary (copy to GP and patient) that GP checks vitamin D levels yearly, especially as many elderly people treated for colorectal cancer will be at risk of vitamin D deficiency.
- Should pelvic insufficiency fractures occur, ask the GP to assess appropriate pain control and bisphosphonates to strengthen the bone. Physiotherapy or occupational therapy referrals should be arranged if necessary.
- A calcium-rich diet is important for people with a history of fracture in order to maintain and improve overall bone health. Adequate vitamin D is also important for the absorption of calcium, helping to keep muscles strong and prevent falls in older people. Daily calcium and vitamin D

supplements may be useful if calcium intake is low, and for those with little normal exposure to sunlight.

For further information, refer to National Osteoporosis Society guidance: *Vitamin D and bone health: A practical clinical guideline for patient management.*

Offer written information on bone health for patients: *A practical guide to living with and after cancer: Bone health.*

Sexual concerns

Sexual difficulties are often mentioned too late and be a low priority when other consequences of treatment are disrupting function, wellbeing or recovery – such as pain or urinary and bowel control difficulties. Ensure there is an opportunity to discuss sexual concerns once symptoms have improved or are resolved.

There is mixed evidence whether the presence of a stoma affects sexual function after rectal cancer surgery and it is generally agreed that there are a range of other factors causes[156,157].

In treatment of rectal cancer, the addition of chemotherapy to radiotherapy to downstage locally advanced disease is now standard practice. Additionally, the standard treatment for anal cancer is pelvic radiotherapy in combination with chemotherapy. These combined treatment modalities may have an impact on long-term sexual function (though further evidence is required).

Whilst it may be the Clinical Nurse Specialist (CNS) or GP who is best placed to explore sexual issues, all health professionals should give patients the opportunity to express any sexual function/health concerns[114]. Practitioners should recognise their own level of competency and ability to explore sexual issues and offer support to the level they are competent. See the NFGON level of interventions (presented at Liverpool ESGO[158]) Appendix 1. Using the PLISSIT model[159], the practitioner should establish and maintain a relationship with patients to allow them to discuss issues relating to sexuality, sexual function and body image.

The healthcare professional will need specialist knowledge and expertise to assess sexual function, and be able to analyse information to offer specific suggestions and, if necessary, interventions to address sexual dysfunction with patients and partners[160]. Education and information for for professionals include:

- Macmillan toolkit to help professionals talk to patients about the issues surrounding sexuality and cancer.
- Cancer Australia's online learning resource for healthcare professionals: *The psychosexual care of women affected by gynaecological cancers.*
- *Treating erectile dysfunction after surgery for pelvic cancers: A quick guide for health professionals supporting men with erectile dysfunction.*
- *Treating erectile dysfunction after radical radiotherapy and Androgen Deprivation Therapy (ADT) for prostate cancer: A quick guide for health professionals supporting men with erectile dysfunction.*

These guides cover the range of medication and interventions that exist to treat erectile dysfunction (ED). A range of strategies exist which include regimens of standard ED-specific therapies (e.g., oral, intracavernosal, and intraurethral pharmacotherapies; vacuum erection device therapy, which must be prescribed according to an specific treatment algorithm for that individual and carefully monitored.

Ask the GP to refer (unless the service is available within centre/unit) the patient to a psychosexual therapist for assessment when:

- There are pre-existing sexual problems and/or psychological vulnerability prior to diagnosis.
- There are sexual difficulties independently affecting the patient's partner, and thus the patient's sexual expression or recovery.
- Prior interventions offered (levels P to SS Appendix 1) have not improved the sexual difficulty and there is persistent or high level of distress.

Offer other information as appropriate to support self-help including Macmillan's *Sexuality and cancer* for men and women patient booklets, and identify the latest information using Information Prescriptions if appropriate.

Vaginal dilation information is locally produced/adapted from the *International guidelines on vaginal dilation after pelvic radiotherapy*[161].

Fertility

Prior to treatment, for patients of child-bearing age, patients should be offered counselling and fertility-conserving treatment such as egg harvesting and sperm banking. It is the recommendation that patients are advised to wait for a year after completion of treatment before trying for a family and seek the intervention of a specialist assisted conception unit before trying to conceive. It is still very important to advise patients on use of condoms, during and after chemotherapy.

Menopause symptoms

Discuss the appropriateness of HRT with colorectal oncologist, surgeon or specialist nurse and ask the GP to prescribe if applicable. Highlight the use of complementary therapies which may help with symptoms of the menopause. Signpost to support or self-help groups such as the Daisy Network and Menopause Matters. Complex cases should be referred to a menopause clinic.

Lymphoedema

Use of screening and assessment tools is advised but can be adapted to suit the individual's practice. Individuals should be informed how they can protect their skin and maintain optimum skin health in their lower limbs through regular inspection and moisturising etc. Any swelling noted in the genital area or legs should be promptly reported.

The assessment may include extent of visible and palpable tissue swelling, perception of fullness and heaviness in the affected limb and limb volume which can be measured in several ways, most commonly by using circumferential limb girth. There is a database of lymphoedema services on the British Lymphology Society website. Local service referral pathways should be available. Refer if the patient is agreeable.

Information should be given to the patient about lymphoedema prior to consent. It should be offered prior to treatment or if the patient presents with lymphoedema using Information Prescriptions or

Macmillan's *Understanding lymphoedema* booklet. Signpost the individual to self-help groups such as The Lymphoedema Support Network.

Cognitive impairment

Screen for cognitive problems and assess for depression and anxiety that might affect cognition and refer for treatment.

Fatigue

Cancer-related fatigue may have multiple causes, it is important to exclude any undiagnosed medical conditions through screening, which can be as simple as checking routine blood tests. Assess with a validated fatigue instrument, recommend physical activity similar to that recommended for the general population, and refer to specialists for psychosocial support or rehabilitation. Offer specific information such as the Macmillan booklet *Coping with fatigue* which can help individuals feel more confident to self-manage their fatigue.

Pain

Pain may continue after treatment and for a few, may get worse. It can affect sleep and have a significant impact on quality of life, requiring the use of prescription painkillers on a regular basis. Pain management encompasses a detailed assessment, followed by discussion with the patient of ways to improve their pain management including optimizing their analgesic regimen (using the 3-step WHO analgesic ladder) alongside use of non-pharmacological strategies. Complimentary treatments such as acupuncture and massage should be considered and ultimately a pain management specialist referral made if the pain becomes chronic.

Psychological issues

Provide opportunities to openly discuss the possibility of cancer recurrence, assess individual fears and offer suggestions to cope and reduce associated distress. Such supportive care is essential for helping people live well with and beyond this cancer. All patients completing colorectal and anal cancer treatment should be evaluated for symptoms of depression and anxiety periodically across the trajectory of care. Assessment should be performed using validated measures such as the HADS[162] score or at very least the Distress Thermometer.

Management depends on these screening results and should be guided by the NICE-approved four-tiered model of psychological response[163]. This model highlights the risk of harm to self and/or others, severe depression or agitation, or the presence of psychosis or confusion warrant immediate referral to a psychiatrist, psychologist, physician or equivalently trained professional.

The benefits of effective psychological support include reduced depression, anxiety and pain, improved self-management and coping skills, and help patients to feel more in control and that they can improve their quality of life[164].

Part 7: Post-treatment advice

Evidence suggests that half of patients reported they had not been told about the effects of treatment[165]; therefore, it is vital that all those completing treatment are offered the following:

- A combination of written and verbal information throughout their decision-making, treatment and after-care.
- A holistic needs assessment and care plan post-treatment.
- A Treatment Summary to inform the patient and their GP of potential effects.
- An opportunity to access health and wellbeing events and to be aware of resources, information and services offered.
- A way to reach specialist advice if long-term consequences develop.

All treatments carry risks of long-term consequences which can impact severely on quality of life unless given the required attention to prevent or reduce them.

General lifestyle recommendations – smoking cessation, reduce alcohol intake and increase physical activity – should be a part of routine clinical care within the context of health promotion, and seen as a strategy for preventing cancer recurrence, detailed in the Treatment Summary.

If the patient no longer has routine oncological follow-up, this information should be reinforced and included in the Treatment Summary and discharge summary that long-term consequences or late effects of treatment can occur **several years** or *even decades* following radiotherapy. Advice on what symptoms to look out for and who to contact should they arise should be given to both the patient and the primary healthcare team.

- People who develop long-term consequences can be signposted to supportive agencies, including the following:
    - Macmillan Cancer Support.
    - Beating Bowel Cancer.
    - Bowel Cancer UK.
    - Bladder and Bowel Foundation.
    - The Pelvic Radiation Disease Association (PRDA).
    - The Lymphoedema Support Network.
    - The Colostomy Association.
    - The Ileostomy and Internal Pouch Support Group.
    - The Urostomy Association.
    - Age UK.
    - The National Osteoporosis Society.

Healthy lifestyle advice

Smoking

Stopping smoking before or after cancer treatment can help the body respond positively to treatment and heal. Generally, non-smokers have fewer side effects from cancer treatment and the side effects they do have are less severe. Stopping smoking may also lower the risk of cancer returning.

Techniques and support are available to help people stop smoking, such as the NHS Stop Smoking services. There is also information on the Macmillan website.

Alcohol

The latest advice for alcohol consumption is up to fourteen units a week for women and men of all ages. There is no clear evidence as to whether drinking alcohol can cause cancer recurrence, but it can increase the risk of a second primary cancer. The risk of alcohol-related cancers increases with the amount of alcohol consumed.[166] Assess alcohol consumption and if people are drinking more than the recommended levels then discuss the benefits of drinking less alcohol.

Dietary advice and keeping a healthy weight

Eating a balanced diet is a good choice for keeping a healthy weight to maintain or regain strength, or have more energy. It can also reduce the risk of new cancer, heart disease, stroke and diabetes. Any diet changes should be made gradually; encourage patients to speak to their GP and ask for a referral to a dietitian or weight management programme for advice. It is important that this dietary advice is put in to context to guide individuals on how to find a sensible but also manageable diet after completing cancer treatment. For example, for some individuals many of the foods in the 'healthy eating' category may contribute to increased bowel frequency and discomfort and thus may have to be moderated or modified by only eaten in soups, smoothies or a slowly-cooked casserole.

Further dietary information can be found from World Cancer Research Fund International and Macmillan Cancer Support.

Physical activity

Physical activity is an important part of recovery after cancer treatment. Being active has many benefits, and can include short walks or gardening:

- Physical activity has been shown to reduce rates of local colorectal cancer recurrence[167,168,169] and overall survival
- It can reduce tiredness and some treatment side effects.
- It can reduce anxiety and depression.
- It can improve your mood and quality of life.
- It can strengthen your muscles, joints and bones.
- It can look after your heart and reduce the risk of other health problems.

Macmillan have information about the benefits of physical activity for people affected by cancer, and further information for health and social care professionals.

Find out about local exercise initiatives and rehabilitation opportunities in the local area which you can signpost people to.

A recent study reported colorectal cancer survivors, regardless of whether or not they were treated with adjuvant therapy, had significantly reduced exercise capacity[170]. This could be key when combined with other factors, such as pre-existing obesity and lifelong sedentary behaviours, in the development of cardiovascular disease. For further information about heart health and cancer treatment refer to Macmillan's guide for professionals on *Managing heart health during and after cancer treatment*, and additional information for patients *Heart health and cancer treatment*.

Support for psychosocial issues

Psychological

People often experience a range of psychological problems before, during or after treatment for cancer. Psychological and emotional support services play an important role in meeting the needs of people affected by cancer. They can promote self-management and coping skills, reduce depression, anxiety and pain; and potentially increase survival rates. A four-tier model of psychological support has been recommended by NICE for all patients with cancer and their families to enable those with the most complex needs to receive the most specialist support. Psychological interventions should be targeted immediately after treatment and patients may need to try more than one treatment types to find the one which is most effective.

There are many sources of support available such as the Macmillan Support Line, local information and support services including self-help and support groups. It may be appropriate to refer the patient for support from a counsellor, clinical psychologist or psychiatrist. Macmillan Cancer Support have further information around coping with emotions.

Financial

A cancer diagnosis often imposes a significant financial and economic burden on patients and their families. People experiencing long-term consequences following treatment for colorectal or anal cancers may also be experiencing financial difficulties such as loss of income or increased cost of daily living. Support is available to help people assess their finances, plan ahead and manage their money day-to-day, such as Macmillan's financial guidance tool and a whole range of information to support people experiencing financial difficulties during or after cancer treatment.

Be aware of benefit and welfare services which exist in the local area such as Citizens Advice Bureau, further details of which can be found through viewing the link on the Macmillan website which indicates what's on offer in the 'local area.'

Work and cancer

The long-term consequences of treatment may mean that people are unable to return to work or are unable to work in the same way they did prior to their treatment. Macmillan have a range of support and information available for people experiencing issues returning to or continuing work after cancer treatment.

Part 8: Good practice recommendations after treatment

The long-term consequences of colorectal and anal cancer and the related treatments are wide-ranging, covering physical, psychological and financial issues, with social and spiritual effects. Many of these determine quality of life for cancer survivors and highlight the importance of individualised patient-centred rehabilitation plans to support recovery.

Good after-care provision should include:

- Adoption of the Recovery Package (Holistic Needs Assessment, Treatment Summary, Cancer Care Review by GP, Health and Wellbeing Clinics).
- Systematic monitoring with the use of PROMs.
- Development of management pathways.

The Recovery Package

The Recovery Package has been designed to promote and sustain recovery, offering patients:

- A Holistic Needs Assessment and Care Plan.
- A Treatment Summary
- A Cancer Care Review.
- The opportunity to attend Health and Wellbeing Clinics.

When these interventions are delivered together, it has the potential to assist individuals by:

- Providing more tailored information about the consequences of their treatment.
- Helping identify potential problems through assessment and monitoring recommendations.
- Offering pre-emptive support for adapting.

The Recovery Package is framed by an ethos of supported self-management; our role is to help individuals to help themselves. Macmillan has developed a Recovery Package that includes information and guides for professionals and patients on all aspects of psychosocial issues for those living with and after cancer. These can be accessed electronically or in booklet form:

- www.macmillan.org.uk/recoverypackage.
- *What to do after cancer treatment ends: 10 top tips*.
- *Life after cancer treatment*.
- www.macmillan.org.uk/information-and-support/coping.

Monitoring

It is important to identify which patients are at risk and monitor closely for consequences after treatment to aid immediate identification. Should consequences occur, skilled management and support are needed to address not only their physical and psycho-emotional impact, but also minimise any further repercussions on people's lives.

The analysis of the 21,802 colorectal cancer survivors' responses in the PROMs survey has highlighted groups with lower health-related quality of life one to three years after diagnosis who may need closer monitoring, for example those aged under 55 or over 85 years, those with one or more other long-term conditions, those with active or recurrent disease, those with a stoma and those living in the most deprived areas[10].

There is growing acknowledgement that the current systems of hospital-based follow-up are not designed to meet the individual needs of those living with and beyond cancer but it continues to have a place in the follow-up of specific tumour groups, in particular anal cancer follow-up and in high-risk groups. Alternative models of follow-up, such as risk-stratified approaches and supported self-management, should be considered to give those living with and beyond cancer (and their GP) a more central role.

Good practice recommends a shift in the culture of after-care to one that supports self-management where the person completing their treatment is enabled and empowered to monitor their own health and take more control in their own care. In consultation with their clinician, they should jointly agree the best monitoring schedule as well as an action plan should new concerns or symptoms arise.

Such surveillance plans need to be communicated to the GP via the Treatment Summary. In addition, it is vital that the primary care team is made aware of all the consequences of treatment via the Treatment Summary; this should also be copied to the patient[171]. Patients who are going to be affected by long-term consequences cannot always be predicted, but end-of-treatment summaries will at least help to inform the patient and their GP of how to look out for anticipated consequences. It is important for GPs to READ code the cancer treatment modality and risks of consequences into the GP system, to help with future identification of problems.

Reiteration of long-term consequences is required to ensure that where possible, they are recognised early and are addressed in a timely manner. Importantly, people must be informed of where and how to seek help should such issues arise – however long ago treatment was.

Follow-up assessment

In order to assess the effectiveness of interventions and for future audit purposes, healthcare professionals may wish to keep a database of patients who report symptoms and the outcome of the recommended treatment.

Management pathways

Referral pathways to specialist services should be established to support prompt referral and support from relevant specialist rehabilitation agencies, including return to work or education.

The management of pelvic radiation symptoms are challenging and further complicated by inter-related problems. We do not currently have a broad intervention evidence base for managing all symptoms as there are various causes. One solution for the management of GI symptoms after pelvic radiotherapy is the development of clinical algorithms for patients experiencing these issues[56]. One such algorithm has been developed for pelvic radiation disease[1] and we need to develop further management pathways for the other common consequences. A continued focus on developing and agreeing pathways for the range of common problems that patients receiving combined treatment modalities may experience is now required.

In summary

In general, whilst studies may suggest that overall quality of life of long-term colorectal cancer survivors appears to be comparable to population norms[132], there is a great range in individual experiences with many people coping well whilst others suffer with a range of long-term consequences which affect their day-to-day lives. The different profiles experienced in the long-term will be the result of that person's own intrinsic risk factors as well as the different treatments. Those who have combined modality treatments may be more at risk of bowel, sexual and urinary problems. Many report transient episodes of anxiety and distress related to their cancer, yet only a minority have a significant mood disorder. These quality of life measures may fail to pick up on more subtle changes such as problems with self-confidence, difficulty in their social relations and delay in returning to work.

Appendix 1

NFGON psychosexual subgroup levels of intervention. *Adapted from Annon 1974.*

Level	PLISSIT	Who	Aim	Rationale
1	**P** Permission	All HCPs. Basic knowledge.	Woman is able to discuss sexual concerns/difficulties with a HCP.	First promoted when the woman is asked about her sexual concerns or suggests that it is an appropriate topic for discussion. Gives the patient permission to have (or not to have) sexual feelings.
2	**LI** Limited Information	Experienced HCP.	Woman is advised of the impact of treatment on sexual function to enable her to make informed choices about the proposed treatment.	Continues to convey willingness to discuss sexuality and provides specific factual information to clarify concerns and misconceptions and eliminate myths.
3	**SS** Specific Suggestion	Advanced CNS/HCPs with appropriate skills and knowledge.	To provide woman with specific suggestions promoting continued sexual satisfaction. Requires sexual history. • Suggestions include strategies for enhancing sexual expression. • Suggestions take into account the patient's and partner's values and attitudes towards sex. • Referral for intensive therapy is indicated if sexual concerns remain unresolved.	Provided when support and limited information alone are inadequate. Follow-up is necessary to monitor effectiveness.
4	**IT** Intensive Therapy	Psychological or psychosexual therapist.	Woman may need referral for more in-depth counselling if progress is not being made at other levels or if there are pre-existing sexual problems, dual dysfunctions or relationship distress.	Provides intensive therapy with appropriately qualified therapist to manage complex sexual and relationship issues that cannot be addressed at lower levels of interventions.

Glossary of terms

APER	Abdominoperineal excision of the rectum
ARS	Anterior resection syndrome
BAM	Bile acid malabsorption
BMI	Body mass index
CGA	Comprehensive geriatric assessment
CNS	Clinical nurse specialist
ED	Erectile dysfunction
ELAPER	Extralevator abdominoperineal excision of the rectum
FSQ	Functional status questionnaire
GSRS	A clinical rating scale for gastrointestinal symptoms in patients with irritable bowel syndrome and peptic ulcer disease
HADS	Hospital anxiety and depression scale
HNA	Holistic needs assessment
HRT	Hormone replacement therapy
IMRT	Intensity modulated radiation therapy
LARS	A patient reported questionnaire for Lower Anterior Resection syndrome (also known as anterior resection syndrome)
LENT SOMA	Late effects normal tissue and Subjective, objective, management, analytic scales
LUTS	Lower urinary tract symptoms
MSKCC	A bowel function instrument developed by the Memorial Sloan Kettering Cancer Centre
NBOCAP	National bowel cancer audit programme
NFGON	National Forum of Gynaecological Oncology Nurses
NHP	Nottingham health profile
NICE	The National Institute for Health and Care Excellence
PLISSIT	A modeling system used in the field of sexology to determine the different levels of intervention for individual clients
PRD	Pelvic radiation disease
PROMS	Patient reported outcome measures
QoL	Quality of life
SIBO	Small intestinal bacterial overgrowth
5-FU	5-fluorouracil

Online links for websites referenced in this guidance

- Competence framework for nurses
  www.macmillan.org.uk/competenceframework
- Pelvic radiotherapy in men: managing side effects during treatment
  http://be.macmillan.org.uk/be/p-20578-pelvic-radiotherapy-in-men-managing-side-effects-during-treatment.aspx
- Pelvic radiotherapy in women: managing side effects during treatment
  http://be.macmillan.org.uk/be/p-20579-pelvic-radiotherapy-in-women-managing-side-effects-during-treatment.aspx
- Managing the late effects of pelvic radiotherapy in men
  http://be.macmillan.org.uk/be/p-20085-managing-the-late-effects-of-pelvic-radiotherapy-in-men.aspx
- Managing the late effects of pelvic radiotherapy in women
  http://be.macmillan.org.uk/be/p-20086-managing-the-late-effects-of-pelvic-radiotherapy-in-women.aspx
- Managing the late effects of bowel cancer treatment
  http://be.macmillan.org.uk/be/p-19095-managing-the-late-effects-of-bowel-cancer-treatment.aspx
- Pelvic radiotherapy symptom checklist and toilet card
  http://be.macmillan.org.uk/be/p-22494-pelvic-radiotherapy-toilet-card-and-symptom-checklist.aspx
- Macmillan website information about colorectal cancer
  http://www.macmillan.org.uk/information-and-support/colon-and-rectal-colorectal
- Macmillan website information about anal cancer
  http://www.macmillan.org.uk/information-and-support/anal-cancer
- Macmillan website information about the late effects of pelvic radiotherapy~
  http://www.macmillan.org.uk/information-and-support/coping/side-effects-and-symptoms/late-effects-pelvic-radiotherapy
- Beating Bowel Cancer
  https://www.beatingbowelcancer.org/
- Bowel Cancer UK
  http://www.bowelcanceruk.org.uk/
- HPV and Anal Cancer Foundation
  http://www.analcancerfoundation.org/
- Oncolink
  http://www.oncolink.org/
- Pelvic Radiation Disease Association
  http://www.prda.org.uk/
- Macmillan website information about information and support groups
  http://www.macmillan.org.uk/information-and-support/coping/getting-support/talking-to-us/index.html
- Guidance for managing the long-term consequences of treatment for gynaecological cancer; Part 1 Pelvic Radiotherapy
  http://www.macmillan.org.uk/Documents/AboutUs/Health_professionals/MAC14942_GYNAE_GUIDE.pdf
- Be.Macmillan information on side effects and symptoms of cancer treatment
  http://be.macmillan.org.uk/be/s-614-side-effects-and-symptoms.aspx
- Macmillan pain diary
  http://www.macmillan.org.uk/Documents/Cancerinfo/Livingwithandaftercancer/Pain%20diary_2013.pdf
- Bowel Cancer UK bowel symptoms diary information
  http://www.bowelcanceruk.org.uk/media/74873/bcuk_factsheet_keeping_a_bowel_symptoms_diary.pdf
- Bowel and Bladder Foundation bladder symptoms diary information
  https://www.bladderandbowelfoundation.org/wp-content/uploads/2015/11/Bladder-Diary-2015.pdf

- Information Prescriptions
  http://www.nhs.uk/IPG/Pages/IPStart.aspx
- Managing lower gastrointestinal symptoms after treatment for cancer
  http://be.macmillan.org.uk/Downloads/CancerInformation/ResourcesForHSCP/COT/MAC15384GIquickguide.pdf
- Guidance: The practical management of the gastrointestinal symptoms of pelvic radiation disease
  http://www.macmillan.org.uk/Documents/AboutUs/Health_professionals/P215TRMGIBooklet_AW.pdf
- British Society of Gastroenterology resource pack
  http://www.bsg.org.uk/images/stories/docs/clinical/gi_effects_cancer_tment_resource_pack13.pdf
- Association of Stoma Care Nurses UK
  http://ascnuk.com/
- Colostomy Association
  http://www.colostomyassociation.org.uk/
- Ileostomy and Internal Pouch support group
  http://www.iasupport.org/
- Urostomy Association
  http://www.urostomyassociation.org.uk/
- NICE guidelines for urinary incontinence in women
  http://pathways.nice.org.uk/pathways/urinary-incontinence-in-women/urinary-incontinence-in-women-overview
- Integrative review on the non-invasive management of lower urinary tract symptoms following treatments for pelvic malignancies
  http://onlinelibrary.wiley.com/doi/10.1111/ijcp.12693/pdf
- National Osteoporosis Society - Vitamin D and Bone Health: A Practical Clinical Guideline for Patient Management
  https://www.nos.org.uk/document.doc?id=1352
- Macmillan booklet: Bone health
  http://be.macmillan.org.uk/be/p-19559-bone-health.aspx
- Macmillan's Learn Zone: Sex and Cancer course
  http://learnzone.org.uk/courses/course.php?id=68
- The psychosexual care of women affected by gynaecological cancers
  http://modules.cancerlearning.gov.au/psgc/
- Treating erectile dysfunction after surgery for pelvic cancers
  http://be.macmillan.org.uk/Downloads/ResourcesForHSCPs/InformationResources/MAC15226-2590PostsurgeryEDguideINTERACTIVE.pdf
- Treating erectile dysfunction after radical radiotherapy and androgen deprivation therapy (ADT) for prostate cancer
  http://be.macmillan.org.uk/Downloads/ResourcesForHSCPs/InformationResources/MAC15225-2960PosthormoneandradiotherapyEDguideINTERACTIVE.pdf
- Macmillan booklet: Sexuality and cancer, information for men
  http://be.macmillan.org.uk/Downloads/CancerInformation/LivingWithAndAfterCancer/MAC14767SexmenE01.pdf
- Macmillan booklet: Sexuality and cancer, information for women
  http://be.macmillan.org.uk/Downloads/CancerInformation/LivingWithAndAfterCancer/MAC14768SexwomenE01.pdf
- Daisy Network
  https://www.daisynetwork.org.uk/
- Menopause Matters
  http://www.menopausematters.co.uk/
- British Lymphology Society
  http://thebls.livepreview.co.uk/directory/

- Macmillan booklet: Understanding lymphoedema
  http://be.macmillan.org.uk/be/p-271-understanding-lymphoedema.aspx
- Lymphoedema Support Network
  http://www.lymphoedema.org/
- Macmillan booklet: Coping with fatigue
  http://be.macmillan.org.uk/be/p-284-coping-with-fatigue.aspx
- Distress Thermometer
  http://www.nccn.org/patients/resources/life_with_cancer/pdf/nccn_distress_thermometer.pdf
- Age UK
  http://www.ageuk.org.uk/
- National Osteoporosis Society
  https://www.nos.org.uk/
- NHS Smoke Free
  http://www.nhs.uk/smokefree
- Macmillan website information on smoking cessation
  http://www.macmillan.org.uk/information-and-support/coping/maintaining-a-healthy-lifestyle/giving-up-smoking/getting-support-to-reduce-cravings.html
- World Cancer Research Fund International
  http://www.wcrf.org/
- Macmillan website information on healthy eating
  http://www.macmillan.org.uk/information-and-support/coping/maintaining-a-healthy-lifestyle/healthy-eating
- Macmillan website information on physical activity
  http://www.macmillan.org.uk/information-and-support/coping/maintaining-a-healthy-lifestyle/keeping-active/index.html
- Managing heart health during and after cancer treatment (a guide for professionals)
  http://be.macmillan.org.uk/be/p-22855-heart-health-guide.aspx
- Macmillan booklet: Heart health and cancer treatment
  http://be.macmillan.org.uk/be/p-22060-heart-health-and-cancer-treatment.aspx
- Macmillan website information on emotional support
  http://www.macmillan.org.uk/information-and-support/coping/your-emotions
- Macmillan's financial guidance toolkit
  http://finance.macmillan.org.uk/
- Macmillan website information about financial support
  http://www.macmillan.org.uk/information-and-support/organising/your-finances?utm_source=thesun&utm_medium=newspapers&utm_content=money&utm_campaign=notalone2015
- Macmillan website information about work and cancer
  http://www.macmillan.org.uk/Aboutus/WhatWeDo/Howwework/Workandcancer/Workandcancer.aspx
- Macmillan website information about the Recovery Package
  http://www.macmillan.org.uk/Aboutus/Healthandsocialcareprofessionals/Macmillansprogrammesandservices/RecoveryPackage/RecoveryPackage.aspx
- Macmillan booklet: What to do after cancer treatment ends, 10 top tips
  http://be.macmillan.org.uk/be/p-20338-what-to-do-after-cancer-treatment-ends-10-top-tips.aspx
- Macmillan booklet: Life after cancer treatment
  http://be.macmillan.org.uk/be/p-18826-life-after-cancer-treatment.aspx

References

[1] Andreyev HJ, Davidson SE, Gillespie C, Allum W, Swarbrick E. Practice guidance on the management of acute and chronic gastrointestinal problems arising as a result of treatment for cancer. Gut 2012; 61(2): 179-192.

[2] Fenlon D, Richardson A, Addington-Hall J. A cohort study of the recovery of health and wellbeing following colorectal cancer (CREW STUDY): protocol paper. BMC Health Services Research 2012; 12:90.

[3] Cancer Research UK, Bowel cancer statistics, http://www.cancerresearchuk.org/health-professional/cancer-statistics/statistics-by-cancer-type/bowel-cancer, accessed 2 October 2015.

[4] Walters S, Benitez-Majano S, Muller P, Coleman MP, Allemani C, Butler J, Peake M, Gronlie Guren M, Glimelius B, Bergstrom S, Pahlman L, Rachet B. Is England closing the international gap in cancer survival? British Journal of Cancer 2015; 113: 848–860.

[5] Office of National Statistics, 10 most common cancers among males and females, http://www.ons.gov.uk/ons/rel/vsob1/cancer-statistics-registrations--england--series-mb1-/no--43--2012/info-most-common-cancers.html, accessed 2 October 2015.

[6] Information Services Division (ISD). 2012. Information Services Division, NHS National Services Scotland, http://isdscotland.org/health-topics/cancer/cancer-statistics, accessed 17 June 2015.

[7] National Bowel Cancer Audit Project (NBOCAP). 2012. Leeds: Health and Social Care Information Centre. http://www.ic.nhs.uk/bowel, accessed 21 June 2013.

[8] Richards A, Corner J and Maher J. The National Cancer Survivorship Initiative: New and emerging evidence on the ongoing needs of cancer survivors. British Journal of Cancer 2011; 105(1): 1-4.

[9] Public Health England Knowledge and Information Team (Northern and Yorkshire), University of Leeds and University of Southampton. 2015. Quality of life of colorectal cancer survivors in England: Report on a national survey of colorectal cancer survivors using Patient Reported Outcome Measures (PROMs). http://www.england.nhs.uk/wp-content/uploads/2015/03/colorectal-cancer-proms-report-140314.pdf, accessed 2 October 2015.

[10] Thomas RJ, Holm M and Al-Adhami A. Physical activity after cancer: An evidence review of the international literature. British Journal of Medical Practitioners 2014; 7(1): 708.

[11] Foster C, Haviland J, Grimmett C, Winter J, Fenlon D, Chivers-Seymour K, May CM, Smith PWF, Corner J, Richardson A and CREW Study Advisory Committee. Trajectories of quality of life, health and personal wellbeing up to two years following curative intent treatment for colorectal cancer: results from the UK Colorectal Wellbeing (CREW) cohort study. European Journal of Cancer Care 2015; 24(1): 24-82.

[12] Pallis AG, Ring A, Fortpied C, Wedding U, Van Nes MC, Penninckx B, Lacombe D, Monfardini S, Scalliet P and Wildiers H. EORTC elderly task force position paper: Approach to the older cancer patient. European Journal Cancer 2010; 46: 1502-1513.

[13] Richardson A, Medina J, Brown V and Sitzia J. Patients' needs assessment in cancer care: a review of assessment tools. Supportive Care in Cancer 2007; 15(10), 1125-1144.

---

[14] Welsh TJ, Gordon AL, Gladman JR. Comprehensive geriatric assessment – a guide for the non-specialist. International Journal of Clinical Practice 2014; 68(3): 290-293.

[15] Handforth C, Clegg A, Young C, Simpkins S, Seymour MT, Selby PJ and Young J. The prevalence and outcomes of frailty in older cancer patients: a systematic review. Annals of Oncology 2015; 26(6): 1091-1101.

[16] Department of Health. 2012. Quality of life of cancer survivors in England. Report on a pilot survey using Patient Reported Outcome Measures (PROMs). https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/213192/9284-TSO-2900701-PROMS.pdf, accessed October 2015.

[17] Adams E, Boulton MG, Horne A, Rose PW, Durrant L, Collingwood M, Oskrochi R, Davidson S and Watson E. The effects of pelvic radiotherapy on cancer survivors: Symptom profile, psychological morbidity and quality of life. Clinical Oncology 2013; 26(1): 10–17.

[18] Sanoff HK, Morris W L and Mitcheltree A-L. Lack of support and information regarding long-term negative effects in survivors of rectal cancer. Clinical Journal of Oncology Nursing 2015; 19(4): 444–448.

[19] Biondi A, Grosso G, Mistretta A, Marventano S, Toscano C, Drago F, Gangi S and Basile F. Laparoscopic vs. open approach for colorectal cancer: Evolution over time of minimal invasive surgery. Biomed Central Surgery 2013; 13(2): 12.

[20] Ascanelli S, Navarra G, Tonini G, Feo C, Zerbinati A, Pozza E and Carcoforo P. Early and late outcome after surgery for colorectal cancer: Elective vs emergency surgery. Tumori 2003; 89(1): 36–41.

[21] Feddern ML, Jensen TS and Laurberg S. Chronic pain in the pelvic area or lower extremities after rectal cancer treatment and its impact on quality of life: a population-based cross-sectional study. Pain 2015; 156(9):1765-71.

[22] Taylor GW, Jayne DG, Brown SR, Thorpe H, Brown JM, Dewberry SC, Parker MC and Guillou PJ. Adhesions and incisional hernias following laparoscopic versus open surgery for colorectal cancer in the CLASICC trial. British Journal of Surgery 2010; 97(1): 70-78.

[23] Haim N and Wexner S. Rectal cancer – associated urinary dysfunction: A review. Springer Science 2015; 10: 118–124.

[24] Taylor C and Bradshaw E. Tied to the toilet: Lived experiences of altered bowel function (anterior resection syndrome) after temporary stoma reversal. Wound Ostomy Continence Nursing 2013; 40(4): 415–421.

[25] Glaser AW, Fraser LK, Corner J, Feltblower R, Morris EJ, Hartwell G, Richards M and Wagland R. Patient-reported outcomes of cancer survivors in England 1–5 years after diagnosis: A cross-sectional survey. British Medical Journal 2013; 3(4): 10–11.

[26] Fingren J, Lindholm E and Carlsson E. Perceptions of phantom rectum syndrome and health-related quality of life in patients following abdominoperineal resection for rectal cancer. Wound Ostomy Continence Nursing 2013; 40(3): 280–286.

[27] Sun V, Grant M, Wendel CS, McMullen CK, Bulkley JE, Altschuler A, and Krouse RS. Dietary and Behavioral Adjustments to Manage Bowel Dysfunction After Surgery in Long-Term Colorectal Cancer Survivors. Annals of Surgical Oncology 2015; 22(13): 4317-4324.

---

[28] Carne PW, Robertson GM and Frizelle FA. Parastomal hernia. British Journal of Surgery 2003; 90(7): 784-793.

[29] Bhangu A, Nepogodiev D, Futaba K and West Midlands Research Collaborative. Systematic review and meta-analysis of the incidence of incisional hernia at the site of stoma closure. World Journal of Surgery 2012; 36(5), 973-983.

[30] Mudge M and Hughes LE. Incisional hernia: A 10 year prospective study of incidence and attitudes. The British Journal of Surgery 1985; 72(1): 70–71.

[31] Moran DC, Kavanagh DO, Sahebally S and Neary PC. Incidence of early symptomatic port-site hernia: A case series from a department where laparoscopy is the preferred surgical approach. Irish Journal of Medical Science 2012*;* 181(4): 463–466.

[32] Cancer Research UK. Sex and bowel cancer. 2015. http://www.cancerresearchuk.org/about-cancer/type/bowel-cancer/living/sex-and-bowel-cancer, accessed October 2015.

[33] Dowswell G, Ismail T, Greenfield S, Clifford S, Hancock B and Wilson S. Men's experience of erectile dysfunction after treatment for colorectal cancer: Qualitative interview study. British Medical Journal 2011; 343: 5824.

[34] Panjari M, Bell RJ, Burney S, Bell S, McMurrick PJ and Davis SR. Sexual function, incontinence, and wellbeing in women after rectal cancer—A review of the evidence. Journal of Sexual Medicine 2012; 9: 2749–2758.

[35] Chaudhri S, Maruthachalam K, Kaiser A, Robson W, Pickard RS and Horgan AF. Successful voiding after trial without catheter is not synonymous with recovery of bladder function after colorectal surgery. Diseases of the Colon and Rectum 2006; 49(7): 1066–1070.

[36] Vannelli A, Basilico V, Zanardo M, Caizzone A, Rossi F, Battaglia and Scaramuzza D. Pelvic lymphedema in rectal cancer: A magnetic resonance feasibility study: A preliminary report. European Review for Medical and Pharmacological Sciences 2013; 17: 929–935.

[37] Vannelli A, Battaglia L, Poiasina E and Leo E. Pelvic lymphedema: Truth or fiction? Med Hypotheses 2009; 72: 267–270.

[38] Jensen MB, Houborg KB, Nørager CB, Henriksen MG and Laurberg S. Postoperative changes in fatigue, physical function and body composition: An analysis of the amalgamated data from five randomized trials on patients undergoing colorectal surgery. Colorectal Disease 2011; 13: 588–593.

[39] Rubin GJ, Cleare A and Hotopf M. Psychological factors in postoperative fatigue. Psychosomatic Medicine; 2004; 66: 959–964.

[40] Young JM, Badgery-Parker T, Masya LM, King M, Koh C, Lynch AC, Heriot AG and Solomon MJ. Quality of life and other patient-reported outcomes following exenteration for pelvic malignancy. British Journal of Surgery 2014; 101: 277–287.

[41] Taylor C. Body image concerns after colorectal cancer surgery. British Journal of Nursing 2015*;* 24(10): 8–14.

---

[42] Lim SW, Kim HJ, Kim CH, Huh JW, Kim YJ and Kim HR. Risk factors for permanent stoma after low anterior resection for rectal cancer. Langenbeck's Archives of Surgery 2013; 398: 259–264.

[43] Tokode OM, Akingboye A and Coker O. Factors affecting reversal following Hartmann's procedure: Experience from two district general hospitals in the UK. Surgery Today 2011; 41: 79–83.

[44] West NP, Anderin C, Smith KJ, Holm T and Quirke P. Multicentre experience with extralevator abdominoperineal excision for low rectal cancer. British Journal of Surgery 2010; 97: 588-599.

[45] Zhou X, Sun T, Xie H, Zhang Y, Zeng H and Fu W. Extralevator abdominoperineal excision for low rectal cancer: a systematic review and meta-analysis of the short-term outcome. Colorectal Disease 2015; 17(6):474-81.

[46] Engel J, Kerr J, Schlesinger-Raab A, Eckel R, Sauer H and Holzel D. Quality of life in rectal cancer patients: A four-year prospective study. Annals of Surgery 2003*;* 238(2): 203–213.

[47] Tekkis PP, Fazio VW, Remzi F, Heriot A, Manilich E and Strong SA. Risk factors associated with ileal pouch-related fistula following restorative proctocolectomy. British Journal of Surgery 2005; 92(10): 1270–1276.

[48] Pachler J and Wille-Jørgensen P. Quality of life after rectal resection for cancer, with or without permanent colostomy. Cochrane Database of Systematic Reviews 2012, Apr 18; (2): CD004323.

[49] Foster C, Haviland JS, Grimmett C, Winter J, Fenlon D, Chivers Seymour K, May CM, Smith PWF, Corner J, Richardson A, and CREW Study Advisory Committee. Trajectories of quality of life, health and personal wellbeing up to two years following curative intent treatment for colorectal cancer: Results from the UK Colorectal Wellbeing (CREW) cohort study. European Journal of Cancer Care 2015; 24(1): 24–82.

[50] Kneist W, Heintz A and Junginger T. Major urinary dysfunction after mesorectal excision for rectal carcinoma. British Journal of Surgery 2005; 92: 230–234.

[51] Yamada T, Okabayashi K, Hasegawa H, Tsuruta M, Abe Y, Ishida T, Matsui S and Kitagawa Y. Age, preoperative subcutaneous fat area, and open laparotomy are risk factors for incisional hernia following colorectal cancer surgery. Annals of Surgical Oncology 2015.

[52] Sadava EE, Kerman Cabo J, Carballo FH, Bun ME and Rotholtz N. Incisional hernia after laparoscopic colorectal surgery. Is there any factor associated? Surgical Endoscopy 2014; 28(12): 3421–3424.

[53] Salmon P and Hall GMJ. Postoperative fatigue is a component of the emotional response to surgery: Results of multivariate analysis. Journal of Psychosomatic Research 2001; 50(6): 325–335.

[54] Doeksen A, Gooszen JA, Van Duijvendijk P, Tanis PJ, Bakx R, Slors JF and Van Lanschot JJ. Sexual and urinary functioning after rectal surgery: A prospective comparative study with a median follow-up of 8.5 years. International Journal of Colorectal Disease 2011; 26(12): 1549–1557.

[55] Paton F, Chambers D, Wilson P, Eastwood A, Craig D, Fox D, Jayne D and McGinnes E. Effectiveness and implementation of enhanced recovery after surgery programmes: A rapid evidence synthesis. British Medical Journal Open 2014; 4.

[56] Berger AM, Mooney K, Alvarez-Perez A, Breitbart WS, Carpenter KM, Cella D, Cleeland C, Dotan E, Eisenberger MA, Escalante CP, Jacobsen PB, Jankowski C, LeBlanc T, Ligibel JA, Loggers ET, Mandrell B,

---

Murphy BA, Palesh O, Pirl WF, Plaxe SC, Riba MB, Rugo HS, Salvador C, Wagner LI, Wagner-Johnston ND, Zachariah FJ, Bergman MA and Smith C. Cancer-related fatigue, version 2. Journal of the National Comprehensive Cancer Network 2015; 13(8): 1012-1039.

[57] Hofman M, Ryan JL, Figueroa-Moseley CD, Jean-Pierre P and Morrow GR. Cancer-related fatigue: The scale of the problem. Oncologist 2007; 12: 4–10.

[58] Berger AM, Grem JL, Visovsky C, Marunda HA and Yurkovich JM. Fatigue and other variables during adjuvant chemotherapy for colon and rectal cancer. Oncology Nursing Forum 2010; 37: 359–369.

[59] Thong MSY, Mols F, Wang XS, Lemmens VEPP, Smilde TJ and van de Poll-Franse LV. Quantifying fatigue in (long-term) colorectal cancer survivors: A study from the population-based PROFILES registry. European Journal of Cancer 2013; 49(8): 1957–1966.

[60] Argyriou P, Polychronopoulos P, Iconomou G, Chroni E and Kalofonos HP. A review on oxaliplatin-induced peripheral nerve damage. Cancer Treatment Review 2008; 34: 368–377.

[61] Ahles TA, Root JC and Ryan EL. Cancer- and cancer treatment-associated cognitive change: An update on the state of the science. Journal of Clinical Oncology 2012; 30(30): 3675–3686.

[62] Tannock, IF, Ahles TA, Ganz PA and Van Dam PS. Cognitive impairment associated with chemotherapy for cancer: Report of a workshop. Journal of Clinical Oncology 2004; 22: 2233–2239.

[63] Fardell JE, Vardy J, Shah JD and Johnston IN. Cognitive impairments caused by oxaliplatin and 5-flouroucail chemotherapy are ameliorated by physical activity. Psychopharmacology 2012; 2210(1): 183–193.

[64] Polk A, Vistisen K, Vaage-Nilsen M and Nielsen DL. A systematic review of the pathophysiology of 5-fluorouracil-induced cardiotoxicity. Biomed Central Pharmacology & Toxicology 2014; 15: 47.

[65] Polk A, Vaage-Nilsen M, Vistisen K and Nielsen DL. Cardiotoxicity in cancer patients treated with 5-fluorouracil or capecitabine: A systematic review of incidence, manifestations and predisposing factors. Cancer Treatment Review 2013; 39: 974–984.

[66] Khan NF, Mant D, Carpenter L, Forman D and Rose PW. Long-term health outcomes in a British cohort of breast, colorectal and prostate cancer survivors: A database study. British Journal of Cancer 2011; 105(1): 29–37.

[67] Royal College of Physicians, The Royal College of Radiologists, Royal College of Obstetricians and Gynaecologists. The effects of cancer treatment on reproductive functions: Guidance on management: Report of a Working Party. 2007. https://www.rcplondon.ac.uk/sites/default/files/documents/effects-of-cancer-treatment-reproductive-functions.pdf, accessed October 2015.

[68] Zbuk K, Sidebotham E, Bleyer A and La Quaglia MP. Colorectal cancer in young adults. Seminars in Oncology 2009; 36(5): 439–450.

[69] Krishnan AV, Goldstein D, Friedlander M and Kiernan MC. Oxaliplatin-induced neurotoxicity and the development of neuropathy. Muscle Nerve 2005; 32: 51–60.

[70] Kordatou Z, Kountourakis P and Papamichael D. Treatment of older patients with colorectal cancer: A perspective review. Therapeutic Advances in Medical Oncology 2014; 6(3): 128–140.

---

[71] Jansen L, Hoffmeister M, Chang-Claude J, Koch M, Brenner H and Arndt V. Age specific administration of chemotherapy and long-term quality of life in Stage I and II colorectal cancer patients: A population based prospective cohort. Oncologist 2011; 16(12): 1741–1751.

[72] Schmoll HJ. ESMO consensus guidelines for management of patients with colon and rectal cancer. A personalized approach to clinical decision making. Annals of Oncology 2012; 23: 2479–2516.

[73] Hurria A, Browner IS, Cohen HJ, Denlinger CS, deShazo M and Extermann M. Senior adult oncology: clinical practice guidelines in oncology. Journal of National Comprehensive Cancer Network 2012; 10(2): 162-209.

[74] McCorkle R, Strumph NE, Nuamah IF, Adler DC, Cooley ME, Jepson C, Lusk EJ and Torosian M. A specialized home care intervention improves survival among older post-surgical cancer patients. Journal of the American Geriatrics Society 2000; 48(12): 1707-1713.

[75] Beijers AJ, Mols F and Vreugdenhil G. A systematic review on chronic oxaliplatin-induced peripheral neuropathy and the relation with oxaliplatin administration. Supportive Care in Cancer 2014*;* 22: 1999–2007.

[76] Pietrangeli A, Leandri M, Terzoli E, Jandolo B and Garufi C. Persistence of high-dose oxaliplatin-induced neuropathy at long-term follow-up. European Neurology 2006; 56: 13–16.

[77] Extermann M, Boler I, Reich RR, Lyman GH, Brown RH, DeFelice J, Levine RM, Lubiner ET, Reyes P, Schreiber FJ 3rd and Balducci L. Predicting the risk of chemotherapy toxicity in older patients: the Chemotherapy Risk Assessment Scale for High-Age Patients (CRASH) score. Cancer 2012; 118(13): 3377-3386.

[78] Andreyev J, Ross P, Donnellan C, Lennan E, Leonard P, Waters C, Wedlake L, Bridgewater J, Glynne-Jones R, Allum W, Chau I, Wilson R and Ferry D. Guidance on the management of diarrhoea during cancer chemotherapy. The Lancet Oncology 2014; 15(10): 447–460.

[79] Stone HB, Coleman CN, Anscher MS and McBride WH. Effects of radiation on normal tissue: Consequences and mechanisms. The Lancet Oncology 2003; 4(9): 529–536.

[80] Shadad AK, Sullivan FJ, Martin JD and Egan LJ. Gastrointestinal radiation injury: Symptoms, risk factors and mechanisms. World Journal of Gastroenterology 2013; 19(2): 185–198.

[81] Andreyev H, Wotherspoon A, Denham JW and Hauer-Jensen M. Defining pelvic-radiation disease for the survivorship era*.* The Lancet Oncology 2010; 11(4): 310–312.

[82] Johnson N, Miles T and Cornes P. Dilating the vagina to prevent damage from radiotherapy: Systematic review of the literature. BJOG: An International Journal of Obstetrics & Gynaecology 2010; 117: 522–531.

[83] Wo J and Viswanathan A. The impact of radiotherapy on fertility, pregnancy, and neonatal outcomes of female cancer patients. International Journal of Radiation Oncology 2009; 73(5): 1304–1312.

[84] Pelvic Radiation Disease Association. What is Pelvic Radiation Disease. 2013. http://www.prda.org.uk/what-pelvic-radiation-disease, accessed October 2015.

[85] Andreyev HJ. Gastrointestinal problems after pelvic radiotherapy: The past, the present and the future. Clinical Oncology 2007; 19(10): 790–799.

---

[86] Henson CC, Andreyev HJ, Symonds RP, Peel D, Swindell R and Davidson SE. Late-onset bowel dysfunction after pelvic radiotherapy: A national survey of current practice and opinions of clinical oncologists. Clinical Oncology 2011; 23(8): 552–557.

[87] Nout R, van de Poll-Franse L, Lybeert M, Warlam-Rodenhuis C, Jobson J, Mens J, Lutgens L, Pras B, van Putten W and Creutzberg CL. Long-term outcome and quality of life of patients with endometrial carcinoma treated with or without pelvic radiotherapy in the post operative radiation therapy in endometrial carcinoma 1 (PORTEC-1) trial. Journal of Clinical Oncology 2011; 29(13): 1692–1700.

[88] Olopade FO, Norman AR, Blake P, Dearnaley DP, Harrington KJ, Khoo V, Tait D, Hackett C and Andreyev HJ. The inflammatory bowel disease questionnaire and the Vaizey incontinence questionnaire are useful to identify gastrointestinal toxicity after pelvic radiotherapy. British Journal of Cancer 2005; 92(9): 1663–1670.

[89] Putta S and Andreyev HJ. Faecal incontinence: A late side-effect of pelvic radiotherapy. Clinical Oncology 2005; 17: 469–477.

[90] Nostrant TT, Robertson J and Lawrence T. Radiation injury. Textbook of gastroenterology, 1995; 2524–2535.

[91] Kennedy GD and Heise CP. Radiation colitis and proctitis. Clinics in Colon and Rectal Surgery 2007; 20(1): 64–72.

[92] Sunesen KG, Norgaard M, Lundby L, Havsteen H, Buntzen S, Thorlacius-Ussing O and Laurberg S. Long-term anorectal, urinary and sexual dysfunction for anal cancer: A Danish multicentre cross-sectional questionnaire study. Colorectal Diseases 2015; 17(11): 230-239.

[93] Elliott SP and Malaeb B. Long-term urinary adverse effects of pelvic radiotherapy. World Journal of Urology 2011; 29(1): 35–41.

[94] Marijnen CA, van de Velde CJ, Putter H, van den Brink M, Maas CP, Martijn H, Rutten HJ, Wiggers T, Kranenbarg EK, Leer JW and Stiggelbout AM. Impact of short-term preoperative radiotherapy on health-related quality of life and sexual functioning in primary rectal cancer: Report of a multicenter randomized trial. Journal of Clinical Oncology 2005; 23(9): 1847–1858.

[95] Donovan KA, Thompson L and Hoffe SE. Sexual function in colorectal cancer survivors. Cancer Control 2010; 17(1): 41–51.

[96] White ID, Allan H and Faithfull S. Assessment of treatment-induced female sexual morbidity in oncology: Is this a part of routine medical follow-up after radical pelvic radiotherapy? British Journal of Cancer 2011; 1–8.

[97] Denton AS and Maher EJ. Interventions for the physical aspects of sexual dysfunction in women following pelvic radiotherapy. Cochrane Database of Systematic Reviews 2002; (1): CD003750.

[98] Lange MM, Marijnen CA, Maas CP, Putter H, Rutten HJ, Stiggelbout AM, Meershoek-Klein KE and van de Velde CJ. Risk factors for sexual dysfunction after rectal cancer. European Journal of Cancer 2009; 45: 1578–1588.

[99] Wiltink, LM, Chen TY, Nout RA, Kranenbarg EM, Fiocco M, Laurberg S, van de Velde CJ and Marijnen CA. Health-related quality of life 14 years after preoperative short-term radiotherapy and total mesorectal excision for rectal cancer: Report of a multicentre randomised trial. European Journal of Cancer 2014; 50: 2390–2398.

---

[100] Loren AW, Mangu PB, Beck LN, Brennan L, Magdalinski AJ, Partridge AH, Quinn G, Wallace WH, Oktay K and American Society of Clinical Oncology. Fertility preservation for patients with cancer: American Society of Clinical Oncology clinical practice guideline update. Journal of Clinical Oncology 2013; 31(19): 2500–2510.

[101] Goldfarb S, Mulhall J, Nelson C, Kelvin J, Dickler M and Carter J. Sexual and reproductive health in cancer survivors. Seminars in Oncology 2013; 40(6): 726–744.

[102] Osterberg EC, Ramasamy R, Masson P and Brannigan RE. Current practices in fertility preservation in male cancer patients. *Urology Annals*. 2014; 6(1):13-17.

[103] Higham CE and Faithfull S. Bone health and pelvic radiotherapy. Clinical Oncology 2015; 27(11): 668-678.

[104] Sitton E. Early and late radiation – induced skin alterations. Part 1: Mechanisms of skin changes. Oncology Nursing Forum 1992; 19(6): 907-912.

[105] Wells M and Macbride SK. Radiation skin reactions. In Faithfull S and Wells M (eds) Supportive Care in Radiotherapy. Elsevier Science, Edinburgh. 2003; 135-157.

[106] Gallagher J. Management of cutaneous symptoms. Seminars in Oncology Nursing 1995; 11: 239–247.

[107] Birgisson H, Påhlman L, Gunnarsson U and Glimelius B. Occurrence of second cancers in patients treated with radiotherapy for rectal cancer. Journal of Clinical Oncology 2005; 23: 6126–6131.

[108] Mosher CE, Winger JG, Given BA, Helft PR and O'Neil BH. Mental health outcomes during colorectal cancer survivorship: A review of the literature. Psycho-Oncology 2015.

[109] Simard S, Thewes B, Humphris G, Dixon M, Hayden C, Mireskandari S and Ozakinci G. Fear of cancer recurrence in adult cancer survivors: A systematic review of quantitative studies. Journal of Cancer Survivorship 2013; 7: 300–322.

[110] Elliott J, Fallows A, Staetsky L, Smith PWF, Foster CL, Maher EJ and Corner J. The health and well-being of cancer survivors in the UK: Findings from a population-based survey. British Journal of Cancer; 105(1): 11–20.

[111] Lange MM, Martz JE, Ramdeen B, Brooks V, Boachie-Adjei K, van de Velde CJ and Enker WE. Long-term results of rectal cancer surgery with a systematical operative approach. Annals of Surgical Oncology 2013; 20(6): 1806–1815.

[112] Birgisson H, Påhlman L, Gunnarsson U and Glimelius B. Adverse effects of preoperative radiation therapy for rectal cancer: Long-term follow-up of the Swedish Rectal Cancer Trial. Journal of Clinical Oncology 2005; 23(34): 8697–8705.

[113] Jung H, Beck-Bornholdt HP, Svoboda V, Alberti W and Herrmann T. Quantification of late complications after radiation therapy. Radiotherapy Oncology 2001; 61: 233–246.

[114] Wedlake L, Thomas K, Lalji A, Blake P, Khoo V, Tait D and Andreyev J. Predicting late effects of pelvic radiotherapy: Is there a better approach? International Journal of Radiation Oncology Biology Physics 2010; 78(4): 1163–1170.

---

[115] Chan R, Webster J, Battistutta D, Chung B and Brooks L. Interventions for preventing and managing radiation-induced skin reactions in cancer patients. Cochrane Database of Systematic Reviews 2010; (5): CD008522.

[116] Das P, Cantor SB, Parker CL, Zampieri JB, Baschnagel A, Eng C, Delclos ME, Krishnan S, Janjan NA and Crane CH. Long-term quality of life after radiotherapy for the treatment of anal cancer. Cancer 2010; 116(4): 822-829.

[117] Son CH, Law E, Oh JH, Apte AP, Yang TJ, Riedel E, Wu AJ, Deasy JO and Goodman KA. Dosimetric Predictors of Radiation-Induced Vaginal Stenosis After Pelvic Radiation Therapy for Rectal and Anal Cancer. International Journal of Radiation Oncology 2015; 92(3): 548-554.

[118] Kalejaiye O and Persad R. Erectile dysfunction associated with surgery for prostate and colorectal cancer. Trends in Urology & Men's Health 2014; 5: 35–39

[119] Hassan I and Cima R. Quality of life after rectal resection and multimodality therapy. Journal of Surgical Oncology 2007; 96(8): 684–692.

[120] Bregendahl S, Emmertsen KJ, Lous J and Laurberg S. Bowel dysfunction after low anterior resection with and without neoadjuvant therapy for rectal cancer. Colorectal Disease 2013; 15(9): 1130–1139.

[121] Kasparek MS, Hassan I, Cima R, Larson DR, Gullerud RE and Wolff BG. Long term quality of life and sexual and urinary function after abdominoperineal resection for distal rectal cancer. Diseases of the Colon & Rectum 2012; 55(2): 147–154.

[122] Musters GD, Sloothaak DA, Roodbeen S, van Geloven AA, Bemelman WA and Tanis PJ. Perineal wound healing after abdominoperineal resection for rectal cancer: a two-centre experience in the era of intensified oncological treatment. International Journal of Colorectal Disease 2014; 29(9):1151-7.

[123] Bondeven P, Emmertsen KJ, Laurberg S and Pedersen BG. Neoadjuvant therapy abolishes the functional benefits of a larger rectal remnant, as measured by magnetic resonance imaging after restorative rectal cancer surgery. European Journal of Surgical Oncology 2015; 41(11):1493-9.

[124] Andreyev HJ, Benton BE, Lalji A, Norton C, Mohammed K, Gage H, Pennert K and Lindsay JO. Algorithm-based management of patients with gastrointestinal symptoms in patients after pelvic radiation treatment (ORBIT): A randomised controlled trial. The Lancet 2013; 382: 2084–2092.

[125] Provencher S, Oehler C, Lavertu S, Jolicoeur M, Fortin B and Donath D. Quality of life and tumor control after short split-course chemoradiation for anal canal carcinoma. Radiation Oncology 2010; 5: 41.

[126] Adams E, Boulton MG, Horne A, Rose PQ, Durrant L, Collingwood M, Oskrochi R, Davidson SE and Watson EK. The effects of pelvic radiotherapy on cancer survivors: Symptom profile, psychological morbidity and quality of life. Clinical Oncology 2014; 26: 10–17.

[127] Knowles G, Haigh R, McLean C, Phillips HA, Dunlop MG and Din FVN. Long term effect of surgery and radiotherapy for colorectal cancer on defecatory function and quality of life. European Journal of Oncology Nursing 2013; 17(5): 570-577.

[128] Bruheim K, Guren MG, Skovlund E, Hjermstad MJ, Dahl O, Frykholm G, Carlsen E and Tveit KM. Late side effects and quality of life after radiotherapy for rectal cancer. International Journal of Radiation Oncology Biology and Physics 2010; 76(4): 1005–1011.

---

[129] de Bree E, van Ruth S, Dewit LG and Zoetmulder FA. High risk of colostomy with primary radiotherapy for anal cancer. Annals of Surgical Oncology 2007; 14(1); 100–108.

[130] Aggarwal A, Duke S and Glynne-Jones R. Anal cancer: Are we making progress? Current Oncology Reports 2013; 15(2): 170–181.

[131] James R, Wan S, Glynne-Jones R, Sebag-Montefiore D, Kadalayil L, Northover J, Cunningham D, Meadows H, Ledermann J and National Cancer Research Institute (NCRI) ACT II Trial Management Group. A randomised trial of chemoradiation using mitomycin or cisplatin, with or without maintenance cisplatin/5FU in squamous cell carcinoma of the anus (ACT II). Journal of Clinical Oncology 2009; 27(18).

[132] Bentzen AG, Guren MG, Vonen B, Wanderås EH, Frykholm G, Wilsgaard T, Dahl O and Balteskard L. Faecal incontinence after chemoradiotherapy in anal cancer survivors: long-term results of a national cohort. Radiotherapy Oncology 2013;108(1):55-60.

[133] Fakhrian K, Sauer T, Dinkel A, Klemm S, Schuster T and Molls M. Chronic adverse events and quality of life after radio chemotherapy in anal cancer patients. Strahlentherapie und Onkologie 2013; 189: 486–494.

[134] Welzel G, Hagele V, Wenz F and Mai SK. Quality of life outcomes in patients with anal cancer after combination radio chemotherapy. Strahlentherapie und Onkologie 2010; 3: 175–182.

[135] Das P, Cantor SB, Parker CL, Zampieri JB, Baschnagel A, Eng C, Delclos ME, Krishnan S and Janjan NA, Crane CH. Long term quality of life after radiotherapy for the treatment of anal cancer. Cancer 2010; 116(4): 822–829.

[136] Mustian KM, Griggs JJ, Morrow GR, McTiernan A, Roscoe JA, Bole CW, Atkins JN and Issell BF. Exercise and side effects among 749 patients during and after treatment for cancer: A University of Rochester Cancer Center Community Clinical Oncology Program Study. Supportive Care in Cancer 2006; 14(7): 732–741.

[137] Morrow GR. Cancer-related fatigue: Causes, consequences, and management. The Oncologist 2007; 12(1): 1–3.

[138] Small W Jr and Kachnic L. Postradiotherapy pelvic fractures: Cause for concern or opportunity for future research? Journal of the American Medical Association 2005; 294(20): 2635–2637.

[139] Doyen J, Benezery K, Follana P, Ortholan C, Gerard JP, Hannoun Levi JM, Gal J and Francois E. Predictive factors for early and late local toxicities in anal cancer treated by radiotherapy in combination with or without chemotherapy. Diseases of the Colon & Rectum 2013; 56(10): 1125–1133.

[140] Margalit DN, Mamon HJ, Ancukiewicz M, Kobayashi W, Ryan DP, Blaszkowsky LS, Clark J, Willett CG and Hong TS. Tolerability of combined modality therapy for rectal cancer in elderly patients aged 75 years and older. International Journal of Radiation Oncology Biology and Physics 2011; 81: 735–741.

[141] Pasetto LM, Friso ML, Pucciarelli S, Basso U, Falci C, Bortolami A, Toppan P, Agostini M, Rugge M, Serpentini S, Nitti D and Monfardini S. Rectal cancer neoadjuvant treatment in elderly patients. Anticancer Research 2006; 26(5B): 3913–3923.

[142] Mariotto AB, Rowland JH, Ries LA, Scoppa S and Feuer EJ. Multiple cancer prevalence: A growing challenge in long-term survivorship. Cancer Epidemiology Biomarkers Prev 2007; 16: 566–571.

---

[143] Berrington de Gonzalez A, Curtis RE, Kry SF, Gilbert E, Lamart S, Berg CD, Stovall M and Ron E. Proportion of second cancers attributable to radiotherapy treatment in adults: A cohort study in the US SEER cancer registries. Lancet Oncology 2011; 12(4): 353–360.

[144] Muirhead R, Adams RA, Gilbert DC, Glynne-Jones R, Harrison M, Sebag-Montefiore D and Hawkins MA. Anal cancer: Developing an Intensity-modulated radiotherapy solution for ACT2 fractionation. Clinical Oncology 2014; 26(11): 720–721.

[145] Jansen L, Koch L, Brenner H and Arndt V. Quality of life among long-term (5 years) colorectal cancer survivors–systematic review. European Journal of Cancer 2010; 46: 2879–2888.

[146] Sodergre SC ,Vassiliou V and Dennis K. Systematic review of the quality of life issues associated with anal cancer and its treatment with radio chemotherapy. Supportive Care in Cancer 2015; 23(12):3613-3623.

[147] The Christie NHS Foundation Trust. CTCAE/LENT SOMA questionnaires. 2015. http://www.christie.nhs.uk/our-standards/clinical-outcomes/clinical-oncology-scoring-treatment-effects/ctcaelent-soma-questionnaires.aspx, accessed October 2015.

[148] Svedlund J, Sjödin I and Dotevall G. GSRS – a clinical rating scale for gastrointestinal symptoms in patients with irritable bowel syndrome and peptic ulcer disease. Digestive Diseases and Sciences 1988; 33(2): 129–134.

[149] Temple LK, Bacik J, Savatta SG, Gottesman L, Paty PB, Weiser MR, Guillem JG, Minsky BD, Kalman M, Thaler HT, Schrag D and Wong WD. The development of a validated instrument to evaluate bowel function after sphincter-preserving surgery for rectal cancer. Diseases of the Colon and Rectum 2005; 48(7): 1353–1365.

[150] Emmertsen KJ and Laurberg S. Low anterior resection syndrome score: Development and validation of a symptom-based scoring system for bowel dysfunction after low anterior resection for rectal cancer. Annals of Surgery 2012; 255: 922–928.

[151] Glaser A. A new approach. Health Service Journal (Supplement April 2011). http://www.ncsi.org.uk/wp-content/uploads/HSJ_survivorship_supplement.pdf, accessed October 2015.

[152] Kock SM, Rietveld MP, Govaert B, van Gemart WG and Baeten CG. Retrograde colonic irrigation for faecal incontinence after low anterior resection. International Journal Colorectal Disease 2009; 24: 1019–1022.

[153] Burch J. Management of stoma complications. Nursing Times 2011; 107(45): 17–20.

[154] Pittman J, Kozell K and Gray M. Should WOC nurses measure health-related quality of life in patients undergoing intestinal ostomy surgery? Journal of Wound Ostomy Continence Nursing 2009; 36(3): 254–265.

[155] Ito N, Ishiguro M, Uno M, Kato S, Shimizu S, Obata R, Tanaka M, Makoto K, Nagano M, Sugihara K and Kenichi K. Prospective longitudinal evaluation of quality of life in patients with permanent colostomy after curative resection for rectal cancer: A preliminary study. Journal of Wound Ostomy Continence Nursing 2012; 39(2): 172–177.

[156] Tekkis PP, Cornish JA, Remzi FH, Tilney HS, Strong SA, Church JM, Lavery IC and Fazio VW. Measuring sexual and urinary outcomes in women after rectal cancer excision. Diseases of Colon and Rectum 2009; 52(1): 46–54.

---

[157] Milbury K, Cohen L, Jenkins R, Skibber JM and Schover LR. The association between psychosocial and medical factors with long-term sexual dysfunction after treatment for colorectal cancer. Supportive Care in Cancer 2013; 21: 793–802.

[158] Annon JS. 1974. The behavioural treatment of sexual problems. Enabling Systems: Honolulu, HI.

[159]Holmes L, Miles T, Punt L, Golby S, Kent E, Smith L. Guidance on long-term consequences of treatment for gynaecological cancer: Part 1 pelvic radiotherapy. 2014. Pages 22-23. http://www.macmillan.org.uk/Documents/AboutUs/Health_professionals/MAC14942_GYNAE_GUIDE_PRINT.pdf, accessed October 2015.

[160] White ID. Sexual Difficulties after Pelvic Radiotherapy: Improving Clinical Management.
Clinical Oncology 2015; 27(11): 647 – 655.

[161] http://www.ncsi.org.uk/wp-content/uploads/Inter-Best-Practice-Guide-Vaginal-Dilators-July-2012.pdf. The NFGON website is being updated and this will be available on there some time in October (info. via Tracie Miles).

[162] The Hospital Anxiety and Depression Scale. R Philip Snaith. Biomed Central. 2003. http://www.biomedcentral.com/content/pdf/1477-7525-1-29.pdf, accessed October 2015.

[163] National Institute for Clinical Excellence. Guidance on cancer services: Improving supportive and palliative care for adults with cancer. 2004, page 78. https://www.nice.org.uk/guidance/csgsp/evidence/supportive-and-palliative-care-the-manual-2, accessed October 2015.

[164] Newell SA, Sanson-Fisher RW and Savolainen NJ. Systematic review of psychological therapies for cancer patients: Overview and recommendations for future research. Journal of the National Cancer Institute 2002; 94(8): 558-584.

[165] NHS England. Cancer patient experience survey 2014: National report. September 2014. https://www.quality-health.co.uk/resources/surveys/national-cancer-experience-survey/2014-national-cancer-patient-experience-survey/2014-national-cancer-patient-experience-survey-national-reports/688-2013-national-cancer-patient-experience-survey-national-report-pdf/file, accessed October 2015.

[166] Corrao G, Bagnardi V, Zambon A and La Vecchia C. A meta-analysis of alcohol consumption and the risk of 15 diseases. Preventive Medicine 2004; 38(5): 613–619.

[167] Meyerhardt JA, Giovannucci EL, Ogino S, Kirkner GJ, Chan AT, Willett W and Fuchs CS. Physical Activity and Male Colorectal Cancer Survival. Arch Intern Med 2009; 169(22): 2102-2108.

[168] Vrieling A, and Kampman E. The role of body mass index, physical activity, and diet in colorectal cancer recurrence and survival: a review of the literature. The American Journal of Clinical Nutrition 2010; 92(3): 471-490.

[169] Campbell PT, Patel AV, Newton CC, Jacobs EJ and Gapstur SM. Associations of recreational physical activity and leisure time spent sitting with colorectal cancer survival. Journal of Clinical Oncology 2013; 31(7): 876-885.

[170] Cramer H, Lauche R, Klose P, Dobos G and Langhorst J. A systematic review and meta-analysis of exercise interventions for colorectal cancer patients. European Journal of Cancer Care 2014; 23: 3–14.

---

[171] Department of Health. Living with and beyond cancer: Taking action to improve outcomes. 2013. https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/181054/9333-TSO-2900664-NCSI_Report_FINAL.pdf, accessed October 2015.