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Management of diet in gastrointestinal cancer

Clare Shaw [iD]
Biomedical Research Centre at the Royal Marsden and Institute of Cancer Research, Fulham Road, London SW3 6JJ, UK

Nutrition and gastrointestinal cancer are inextricably linked. The metabolic effects of cancer along with changes in dietary intake, the development of cancer cachexia and the presence of sarcopenia can influence changes in body composition. These have a negative impact on quality of life and tolerance to cancer treatment. Treatment for cancer presents some significant nutritional challenges as nutrition impact symptoms may develop, be exacerbated by treatment and may contribute to a worsening in nutritional status. Nutrition screening and assessment should be an integral part of holistic patient care. The provision of appropriate, evidence-based dietary advice should occur before, during and after cancer treatment. Appropriate and timely methods of nutritional support across the spectrum of gastrointestinal cancer are needed to ensure that people are adequately supported during courses of treatment that can span weeks and months. These can range from standard approaches of supplementing oral intake to complex interventions such as managing high output intestinal stomas. The gastrointestinal tract is particularly susceptible to impact from systemic anti-cancer treatments and radiotherapy. Gastrointestinal late effects of cancer treatment are now recognised to present particular challenges in terms of both medical and nutritional management. These late effects have a significant impact on the individual and their quality of life in addition to implications for the health service. Dietary intake following cancer treatment has an impact on quality of life and future research may demonstrate its influence on the risk of recurrence of gastrointestinal cancer.

Gastrointestinal cancer: Nutrition support: Disease-related malnutrition: Nutrition impact symptoms

Gastrointestinal cancers

The term gastrointestinal cancer is used collectively to refer to cancers of the digestive tract and includes oesophageal, liver, gastric, gallbladder and biliary tract, pancreatic, gastrointestinal stromal tumours, small bowel, colorectal and anal cancers. Colorectal cancer is the most common being the fourth most common cancer in the UK accounting for 42 000 new cases every year, 12 % of all new cancers. Some gastrointestinal cancers, for example, gall bladder cancer are rare and account for 1000 new cases in the UK every year, accounting for less than 1 % of all new cancers. Diet and lifestyle plays a role in the aetiology of gastrointestinal cancers with increased body weight and lack of physical activity increasing risk. Specific components of diet also play a role, for example red and processed meat and alcohol increasing the risk of colorectal cancer whilst dairy foods and dietary fibre are protective[1].

Survival rates vary considerably between diagnoses with the best survival in colorectal cancer and anal cancer. In these diagnoses, 5 year survival is 54 and 57 % respectively for all stages of cancer. If cancer is diagnosed at an early stage then survival rates are higher, for example, 5 year survival for stage 1 colorectal cancer is 98 % and for stage 4 is 44 %. Oesophageal and pancreatic cancer patients have the worst outcomes with 12–13 and 1 % respectively being predicted to survive their disease for 10 years or more[2].

Early detection is therefore paramount in improving outcomes for people with cancer. Planned treatment pathways will vary depending on the stage of the disease with surgery being used more often in early stage disease.

Gastrointestinal cancer may be detected either by routine screening, for example, in the case of colorectal cancer or due to the presentation of local or systemic symptoms resulting in the person presenting to their general practitioner or to emergency healthcare. Unintentional weight loss, dysphagia, anorexia, early satiety and changes in bowel habits may be presenting features of the disease along with other less-specific symptoms including pain, fatigue or anaemia. In the UK, some of these may be identified as red-flag symptoms necessitating an urgent referral for suspected cancer under the 'two week' rule.

Treatment plans are formulated following appropriate investigations which allow the extent of the disease to be assessed. A multi-disciplinary team recommends the most appropriate treatment plan based on the staging and assessment which will either be potentially curative or aimed at extending life if the disease is deemed to not be curable. Treatments used are often multi-modal and may include a combination of systemic anti-cancer therapy (SACT), radiotherapy, surgery and more recently targeted treatments in the form of immunotherapy. An individualised treatment plan is developed and discussed with the person based on the knowledge of the most effective treatment, an assessment of the extent of the disease, co-morbidities and performance status (PS). In the UK, the recommendations for treatment are described in guidance produced by the National Institute for Health and Care Excellence[3].

Impact of gastrointestinal cancer on nutritional status

People with gastrointestinal cancer have a high rate of malnutrition compared to other types of cancers[4]. Upper gastrointestinal cancers pose the highest risk to the development of malnutrition and studies have identified that 22 % may be severely malnourished and 63 % being moderately malnourished or at risk of malnutrition. Lower gastrointestinal cancers pose a lower risk with 10–17 % being severely malnourished and 25–60 % being moderately malnourished or at risk of malnutrition[5].

The presence of cancer may influence nutritional status through a number of mechanisms. These can be due to changes in dietary intake due to a lack of appetite, physical obstruction of the gastrointestinal tract causing dysphagia or early satiety, changes in taste perception and the effect of the tumour on bowel symptoms. Psychological distress and anxiety are also instrumental in influencing food intake[6]. The resulting impact on dietary intake may be an overall reduction in food intake or an alteration in the habitual intake, both of which can influence the overall quantity of diet consumed or the quality of the diet. Additional symptoms such as gastrointestinal bleeding may influence particular nutrient status, for example iron, folate or vitamin B_{12}[7].

Changes in physical activity because of symptoms, such as fatigue, in addition to metabolic changes facilitated through inflammatory pathways, can impact body composition causing loss of lean muscle and adipose[8]. The resulting syndromes of cachexia and sarcopenia and their impact on the patient, tolerance to treatment and clinical outcomes are discussed in more detail.

Identification of the presence of disease-related malnutrition or the risk of malnutrition should initially be through the use of thorough and systematic nutrition screening. Nutrition screening is mandated by the National Institute for Health and Care Excellence and should be used for all people with a cancer diagnosis as early as possible[9]. It should be undertaken during the process of investigations, particularly if the person is presenting with nutrition impact symptoms or unintentional weight loss. A nutrition screening tool that has been validated in cancer should be used as these have been demonstrated to have better sensitivity than generic tools[10,11].

Identifying this early is crucial to ensure that they can be referred for appropriate advice and support from a registered dietitian as required[4,12]. Often referrals to a dietitian are late in the treatment pathway making optimal management of dietary intake more challenging[13]. Nutrition impact symptoms are a significant barrier to dietary intake and patients often experience more than one symptom. In a cohort of patients referred for dietary advice, of which half were gastrointestinal or biliary cancer patients, 70 % had two nutritional barriers. The most common cited were anorexia, nausea and early satiety[13]. An assessment by the dietitian as to whether the patient would have benefited from an earlier referral identified that referrals should have occurred earlier in nearly half of cases.

Cancer cachexia

Cancer cachexia is a syndrome characterised by weight loss, loss of muscle and fat mass. It contributes to impaired function, decreased physical performance, decreased tolerance to cancer treatment and poorer survival[14]. The contributory factors are reduced dietary intake, weight loss and metabolic changes which create a proinflammatory environment that may drive an increased energy expenditure[15,16]. Systemic inflammation is further exacerbated by proinflammatory cytokines produced by the tumour. Tumour-derived cytokines including IL-1, IL-6 and TNF-α act as signals resulting in the disruption of metabolism of carbohydrate, fat and protein[17].
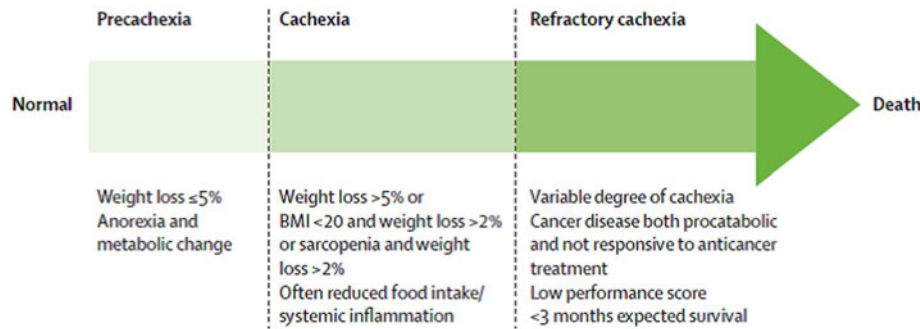
Fig. 1. Stages of cancer cachexia[16].

A consensus view on the definition of cachexia was published by Professor Ken Fearon and this identified that there are potential three stages of cachexia, that is precachexia, cachexia and refractory cachexia[16] (Fig. 1). Each stage is defined by varying degrees of weight loss, anorexia and metabolic changes which include reduced albumin and raised markers of systemic inflammation, for example C-reactive protein. There is no universal consensus on the definition of cancer cachexia and more recent studies aiming to classify cancer cachexia have used a scoring system using additional assessments including weight loss, a screening questionnaire for sarcopenia (SARC-F), appetite loss and abnormal biochemistry[14,18].

Documentation of PS is common in cancer care. It is a score that estimates the patient's ability to perform certain activities of daily living[19]. People who have a worse PS and limited functional capacity tend to have more difficulty tolerating rigorous cancer treatments and have less favourable outcomes than those with a better PS. Formal assessment and categorising of cancer cachexia, which is also associated with poorer outcomes, is rare in the clinical setting.

Sarcopenia

The definition of sarcopenia is low muscle strength, low muscle quantity or quality and low physical performance[20]. Sarcopenia is part of the ageing process and has been well categorised in older people and its presence increases the risk of falls, fractures, physical disability and mortality[8]. Studies have recognised that sarcopenia may begin earlier in life and there is overlap between the physiological changes that occur in cancer cachexia and sarcopenia[21].

The European Working Group on Sarcopenia in Older People recommends the use of SARC-F questionnaire to elicit self-reports from patients on indicators that are characteristic of sarcopenia[20]. The self-report questionnaire asks about limitations in strength, walking ability, rising from a chair, stair climbing and experience with falls. Additional tests such as hand grip strength, chair stand test may be used to assess strength and muscle mass may be assessed using dual-energy X-ray absorptiometry, bioelectrical impedance analysis, whole body MRI or lumbar muscle cross-sectional area by computed tomography. Tests for physical performance may include gait speed and the timed-up-and-go test.

Impact of cachexia and sarcopenia on clinical outcomes

Cachexia and sarcopenia have a negative clinical impact on outcomes in cancer[22]. A systematic grading system of percentage of involuntary weight loss and BMI developed by Martin et al. demonstrated that both of these factors predicted survival independently of conventional prognostic factors including cancer site, stage and PS[23]. Observational studies that have linked unintentional weight loss with poorer outcomes during SACT have suggested that this may be due to reduced dose of drugs which is based on body weight and surface area estimations and increase toxicity of drugs requiring breaks in treatment[24]. The consequences of cancer cachexia are both clinical and financial. They include reduced immune competence with increased risk of infections, psychosocial stress, lower quality of life, treatment toxicity and greater risk of mortality[17]. Financial implications include higher costs of care and increased length of hospital stay[17].

The presence of sarcopenia has been shown to confer poorer outcomes in both surgical gastrointestinal cancer patients and those receiving SACT[25–27]. Reduced muscle mass, as measured by total psoas area from cross-sectional imaging, was identified as an independent risk factor for mortality following pancreatic resection for adenocarcinoma[25]. Studies of the impact of sarcopenia in different cancer diagnoses have indicated varying results. Some have indicated that the loss of muscle mass influences tolerance to SACT with low muscle mass, in people with normal or increased body weight, increases the risk of toxicity often resulting in dose reduction of drugs[28,29]. Other studies have suggested that myosteatosis, fatty infiltration of muscle, defined as attenuated mean skeletal muscle Hounsfield units observed on computed tomography scanning, has a greater bearing on survival rather than reduced muscle mass alone[26]. These observational studies have raised important questions as to whether interventions can reverse or prevent such changes and what effect this may have on clinical outcomes.

Management of cachexia by drugs or nutrients has yet to produce effective solutions[30]. Approaches have

included appetite stimulants such as progestins, corticosteroids and cannabinoids, drugs and nutrients to influence body weight and the inflammatory response in cachexia including non-steroidal anti-inflammatory drugs and fish oils high in *n*-3 fatty acids along with nutrients such as specific amino acids aimed at increasing fat-free mass.

Diet following diagnosis of cancer

Optimisation of nutritional status before, during and after cancer treatment is recommended with the aim of improving tolerance to treatment and improving quality of life[30]. The dietary advice or suitable nutritional support will vary according to the patient, their nutritional status, nutrition impact symptoms, planned treatment, toxicity of treatment, co-morbidities and PS. These factors should be assessed at the beginning of treatment and at regular intervals through the treatment pathway to ensure that nutrition impact symptoms are well managed and nutritional needs addressed accordingly.

Prehabilitation

Prehabilitation is the optimisation of the individual through diet, exercise, symptom management, medicines management and optimal management of co-morbidities prior to cancer treatment. It requires expert screening and intervention along with appropriate support to enable people to change their behaviour with respect to diet and exercise[31]. Early studies have demonstrated that this approach confers benefit in some patients in terms of improvements in post-operative body composition, more rapid recovery following surgery and an improved quality of life[32–35]. Pooled data from three prehabilitation trials in colorectal cancer patients detected an improvement in 5-year disease-free survival in those with stage 3 disease[36]. The author of the present paper calls for further trials to confirm this which is also supported by publication of principles and guidance for prehabilitation within the management and support of people with cancer[32]. A systematic review of any prehabilitation, nutrition only or nutrition with exercise, significantly shortened length of hospital stay by 2 d after colorectal surgery[37]. Currently there are varying definitions of what constitutes a prehabilitation intervention; however, the recent review by Gillis *et al.* suggested that it should be at a minimum defined by its nutritional and exercise components with nutrition adding complementary and functional benefits for the colorectal patient[37].

Dietary advice and nutritional support during treatment

The importance of identifying the risk of disease-related malnutrition has been identified in European guidance[17,30]. Regular screening through treatment should feed into a robust system that gives the person access to an appropriate nutritional assessment and management plan. A full nutritional assessment should be carried out by a registered dietitian with the relevant expertise in oncology. This should include a full assessment of weight,

height, weight history, measures of body composition and energy expenditure, nutrition impact symptoms including appetite, biochemical parameters including cancer-related systemic inflammation such as C-reactive protein and albumin and physical function[30]. Additional factors which may impact the advice given include psychosocial factors, co-morbidities and anticipated treatment. An important role of the registered dietitian may be to address questions about nutrition and dispel some of the myths that arise from testimonials and opinions, particularly those voiced on social media. Such dietary regimens may include changes in macronutrient intake, for example restriction of sugar intake, or promotion of individual foods or dietary supplements with the aim of specifically influencing the growth of cancer. These dietary changes have no proven efficacy and may increase the risk of malnutrition through the restriction of macronutrient or micronutrient intake[30]. Their use should be discussed along with the use of any dietary supplements that can potentially interact with cancer treatment.

The optimal time for initiating nutrition support has yet to be defined, however, the consensus view is that this should occur prior to malnutrition developing and ideally should be in the pre-cachexia stage[16,23].

In pre-cachexia and cachexia nutritional support aims to lower or alleviate the burden of cachexia by the provision of adequate nutrients. European Society for Clinical Nutrition and Metabolism guidelines recommend the measurement of resting energy expenditure through the use of indirect calorimetry for all cancer patients[17]. In clinical practice, this may not be possible and in the absence of this measurement nutritional requirements can be estimated as 105–126 kJ/kg/d with 1·2–1·5 g protein/kg/d[17] as a target.

Dietary advice is individualised to take into account personal preferences, nutrition impact symptoms, avoidance of foods which confer a high risk of food borne pathogens and ability to cook and shop whilst experiencing symptoms such as fatigue. Attention should be given to individual symptoms that are influencing food intake, particularly dysphagia, anorexia, taste changes and mucositis. Dietary advice encompasses food and fluid choice, fortification of food, meal pattern, snacks and advice to help with symptom management. Oral nutritional supplements may be used to help meet requirements when dietary advice alone is ineffective. Nutritional supplementation has been demonstrated to be effective at improving dietary intake and body weight when used in conjunction with dietary counselling in malnourished patients, as described in a systematic review published by Baldwin and Weekes[38]. Individualised dietary advice during radiotherapy treatment for colorectal cancer was demonstrated to have a positive effect on late radiation toxicity and mortality in a group of normally nourished colorectal patients[39].

Artificial nutrition support

Artificial nutrition support may be considered when estimated requirements are unable to be met with dietary intake alone. In practice, for those people receiving

SACT, it is likely that their dietary intake will be highly variable on a daily basis due to the side effects of treatment resulting in short-term fluctuations in nutritional status. Overall an aim to resume dietary intake and regain any lost weight prior to the next course of SACT would be optimal. Consideration of artificial nutrition support should be made when a person has a deterioration in nutritional status despite dietary advice and oral nutritional supplements or where it is anticipated that they will be unable to meet requirements. The use of nutritional support have been shown to improve body weight and energy intake but not survival[30]. European guidance does not recommend the use of routine artificial nutrition support for people undergoing SACT or radiotherapy[30]. In the case of surgery when it is anticipated that dietary intake will not resume within a period of up to 5 d then appropriate nutritional support should be planned and implemented to prevent a deterioration in the nutritional status. Enteral nutrition should be instigated as the first choice with parenteral nutrition being used when the gastrointestinal tract is not accessible or in cases of intestinal failure[12,30].

Refractory cachexia

The term refractory cachexia is used to characterise patients with a low PS, who are not responsive to anti-cancer treatments, and have an expected survival time of less than 3 months[16,18].

The use of artificial nutrition support in advanced gastrointestinal cancer can be controversial. If SACT is being offered to the patient, even though the intention of treatment is palliative rather than curative, then ongoing screening and assessment of nutrition should be provided as part of holistic care. If nutritional status deteriorates then this should be discussed with the patient and within the multi-disciplinary setting to ascertain whether artificial nutritional support is acceptable and will be thought to be beneficial[40]. As artificial nutrition support is a medical intervention it therefore requires an indication for achieving a treatment goal and the informed consent of the competent patient[40]. Cancer cachexia may progress with advancing disease to become refractory cachexia[16]. It is in this advanced state that the provision of nutrition is unable to reverse the changes in body composition despite the provision of adequate energy, protein and micronutrients.

Nutrient ingestion and digestion

Gastrointestinal cancer may have a significant impact on the ingestion and digestion of nutrients in the diet. Of particular influence are the upper gastrointestinal cancers where oesophageal and gastric cancer may impact the ability to eat and drink. This is managed with the use of texture modification and fluids to ensure nutritional adequacy of the diet. Artificial nutrition support may be required if nutritional status has deteriorated or nutritional requirements cannot be met through oral intake. Gastrointestinal cancers or adhesions from previous surgery may influence gastrointestinal function. Malignant bowel obstruction has a profound effect on the ability to eat, drink and digest nutrients. Management depends on the site of the obstruction, potential treatments including surgery, stenting and SACT[41]. Adequate nutrition continues to be a goal of treatment and may require the use of parenteral nutrition if the gastrointestinal tract is not functioning. A deterioration in nutritional status is associated with prolonged hospitalisation, reduced tolerance to treatment and poor overall survival[41].

Pancreatic cancer can be a cause of steatorrhoea or diarrhoea, abdominal pain, bloating and weight loss through the systemic effects on reduced appetite in addition to the specific influence on pancreatic exocrine function. Digestion requires pancreatic stimulation, synthesis and release of pancreatic enzymes and the synchronisation of secretions to mix with ingested food[42]. The presence of cancer in the pancreas may disrupt the delivery of pancreatic enzymes into the lumen of the gut. Alternatively, surgery to the upper gastrointestinal tract may influence small intestinal function resulting in poor synchronisation of enzymes and food.

Nutrient absorption

Some types of gastrointestinal cancer can influence nutrient absorption necessitating specific medical or nutritional support. Nutrients necessary for the formation of erythrocytes are subject to high losses, for example, when bleeding occurs within the gastrointestinal tract. Absorption of iron may be reduced when gastric acid is suppressed following partial gastrectomy or through the use of acid suppressing drugs[7,43,44]. Vitamin B_{12} absorption may be influenced by loss of intrinsic factor due to the presence of disease or removal of the stomach as part of the treatment of gastric cancer[45,46]. Removal of any part of the small intestine or formation of a stoma, for example, an ileostomy may influence the ability to absorb macronutrients, electrolytes, fluids and trace elements[47]. This can be due to loss of total surface area of the gastrointestinal tract that is available for absorption or the effect on a specific site of the gut such as the terminal ileum responsible for the absorption of vitamin B_{12} and the reabsorption of bile acids or may be due to increased losses through the stoma site. Optimal nutritional and fluid management requires a multi-professional team approach including gastroenterology and dietetics along with an assessment of the residual part of functioning bowel[48]. Continued SACT, immunotherapy or radiotherapy may further exacerbate nutritional losses through toxicities affecting the integrity of the gut or gut motility.

Dietary management of gastrointestinal toxicity of cancer treatment has been a subject of debate for many years. Transient malabsorption of specific nutrients such as lactose as a result of chemotherapy was identified in the 1990s yet no intervention studies have confirmed that its restriction is effective at influencing symptoms[49,50]. Pelvic radiotherapy causes damage to non-

cancer gastrointestinal mucosa and has an effect on secretory and absorptive functions[51,52]. A review of dietary interventions to manage symptoms highlighted weak evidence for some dietary changes including elemental, low or modified fat and low lactose interventions[53]. The use of probiotics was more promising with four out of five studies suggesting that some symptoms benefit from their use although variations in the strength and strains and study methodologies make firm recommendations difficult. It is also important that there are additional data on the safety of probiotic use in people receiving SACT and immunotherapy. Higher intakes of dietary fibre intake during pelvic radiotherapy may impact the severity of acute and long-term symptoms[54]. The introduction of immunotherapy has created a different spectrum of toxicities with colitis being a significant feature which impacts dietary intake[55]. No specific dietary interventions are known to be effective for these and the medical management is often the use of corticosteroids increasing the risk of steroid induced diabetes. Initial recommendations based on professional consensus suggest some dietary modifications in the initial stages to assist in symptom management, however, these have not been tested in the clinical setting[55]. There is much interest in the link between the gut microbiome and the efficacy of immunotherapies in cancer treatment[56]. The underlying mechanisms of interactions are poorly understood but may, in the future, provide a means of influencing the response to treatment.

Diet after treatment for gastrointestinal cancer

People who have completed treatment for cancer have significant health concerns compared to the general population[57]. This is generally centred on management of symptoms following treatment including fatigue, insomnia, anxiety and concern about the risk of recurrence. Health and well-being events aim to provide information for people to help them manage symptoms, consider lifestyle behaviours including diet and physical activity and manage psychological aspects of living with a diagnosis of cancer. Diet may continue to be a focus through management of malnutrition, symptom management or being considered along with lifestyle with the aim of influencing recurrence. Intervention studies to date in people following treatment for gastrointestinal cancer have failed to demonstrate that changes to body composition, dietary intake or physical activity can influence the risk of recurrence or overall survival[58]. Observational studies have suggested that body increased waist circumference, higher BMI and low adherence to the World Cancer Research Fund; Dietary Guidelines for Primary Prevention are associated with poorer global health status in people following treatment for colorectal cancer[59,60]. Ongoing dietary intervention studies aim to provide stronger guidance for the optimal lifestyle, including dietary changes that should be adopted at the end of treatment. Advice should be tailored to the individual depending on their diagnosis, stage of disease, any future long-term treatment, nutritional status and growing evidence base.

Conclusion

Diet has an integral role in the development and management of gastrointestinal cancer. Its role in aetiology is potentially through specific dietary components such as dietary fibre, dairy products, red and processed meat and alcohol or the overall influence on body composition, body weight and obesity.

Following diagnosis of cancer, dietary intake, along with metabolic changes can contribute to the development of cancer cachexia and sarcopenia. These changes can influence body composition with accelerated loss of body weight, muscle mass and changes in physical function. Such changes can negatively impact PS, tolerance to cancer treatment and quality of life. European and UK recommendations highlight the importance of nutrition screening about the time of diagnosis, especially for people who are experiencing nutrition impact symptoms and weight loss. Once nutrition risk has been identified then a full nutrition assessment from a registered dietitian with a nutrition care plan should be developed alongside medical management and planned cancer treatment. Increasingly the optimisation of people through diet and exercise, known as prehabilitation, is recommended before cancer treatment commences although the evidence base to demonstrate improved outcomes needs to be strengthened. Treatment for gastrointestinal cancer can have a major impact on dietary intake and absorption of nutrients and requires appropriate nutritional support alongside optimal symptom management.

Appropriate individualised lifestyle advice on diet and exercise at the end of treatment should be offered to optimise health or to assist in the management of gastrointestinal late effects of treatment.

Conflict of Interest

None.

Authorship

The author had sole responsibility for all aspects of preparation of this paper.

References

1. World Cancer Research Fund and American Institute for Cancer Research (2018) Diet, Nutrition, Physical Activity and Cancer: A Global Perspective. https://www.wcrf.org/dietandcancer.
2. Cancer Research UK (2010–2011) Oesophageal Cancer Survival. https://www.cancerresearchuk.org/health-professional/cancer-statistics/statistics-by-cancer-type/oesophageal-cancer#heading-Two.
3. National Institute for Health and Care Excellence (2020) NICE Guidance. https://www.nice.org.uk/guidance.
4. Bozzetti F (2009) Screening the nutritional status in oncology: a preliminary report on 1,000 outpatients. *Support Care Cancer* **17**, 279–284.
5. Burden ST, Hill J, Shaffer JL *et al.* (2010) Nutritional status of preoperative colorectal cancer patients. *J Hum Nutr Diet* **23**, 402–407.
6. Wheelwright SJ, Hopkinson JB, Darlington AS *et al.* (2017) Development of the EORTC QLQ-CAX24, A questionnaire for cancer patients With cachexia. *J Pain Symptom Manage* **53**, 232–242.
7. Stein J, Connor S, Virgin G *et al.* (2016) Anemia and iron deficiency in gastrointestinal and liver conditions. *World J Gastroenterol* **22**, 7908–7925.
8. Cruz-Jentoft AJ, Bahat G, Bauer J *et al.* (2019) Sarcopenia: revised European consensus on definition and diagnosis. *Age Ageing* **48**, 601.
9. National Institute for Health and Care Excellence (2012) Quality statement 1: screening for the risk of malnutrition. https://www.nice.org.uk/guidance/qs24/chapter/Quality-statement-1-Screening-for-the-risk-of-malnutrition.
10. Zhang X, Pang L, Sharma SV *et al.* (2019) The validity of three malnutrition screening markers among older patients with cancer. *BMJ Support Palliat Care*. [Epublication ahead of print version]
11. Shaw C, Fleuret C, Pickard JM *et al.* (2015) Comparison of a novel, simple nutrition screening tool for adult oncology inpatients and the Malnutrition Screening Tool (MST) against the Patient-Generated Subjective Global Assessment (PG-SGA). *Support Care Cancer* **23**, 47–54.
12. National Institute for Clinical Excellence (2012) Nutrition Support in Adults. http://pathways.nice.org.uk/pathways/nutrition-support-in-adults#content=view-info%3Aintroduction-source.
13. Lorton CM, Griffin O, Higgins K *et al.* (2019) Late referral of cancer patients with malnutrition to dietitians: a prospective study of clinical practice. *Support Care Cancer*. **28**, 2351–2360.
14. Martin L, Senesse P, Gioulbasanis I *et al.* (2015) Diagnostic criteria for the classification of cancer-associated weight loss. *J Clin Oncol* **33**, 90–99.
15. Dunne RF, Loh KP, Williams GR *et al.* (2019) Cachexia and sarcopenia in older adults with cancer: a comprehensive review. *Cancers (Basel)* **11** [Epublication 25 November 2019].
16. Fearon K, Strasser F, Anker SD *et al.* (2011) Definition and classification of cancer cachexia: an international consensus. *Lancet Oncol* **12**, 489–495.
17. Arends J, Baracos V, Bertz H *et al.* (2017) ESPEN expert group recommendations for action against cancer-related malnutrition. *Clin Nutr* **36**, 1187–1196.
18. Zhou T, Wang B, Liu H *et al.* (2018) Development and validation of a clinically applicable score to classify cachexia stages in advanced cancer patients. *J Cachexia Sarcopenia Muscle* **9**, 306–314.
19. West H (2015) Performance status in patients with cancer. https://jamanetwork.com/journals/jamaoncology/fullarticle/2432463 (accessed February 2020).
20. Cruz-Jentoft AJ, Bahat G, Bauer J *et al.* (2019) Sarcopenia: revised European consensus on definition and diagnosis. *Age Ageing* **48**, 16–31.
21. Ryan AM, Power DG, Daly L *et al.* (2016) Cancer-associated malnutrition, cachexia and sarcopenia: the skeleton in the hospital closet 40 years later. *Proc Nutr Soc* **75**, 199–211.
22. Naumann P, Eberlein J, Farnia B *et al.* (2019) Cachectic body composition and inflammatory markers portend a poor prognosis in patients with locally advanced pancreatic cancer treated with chemoradiation. *Cancers (Basel)* **11**. [Epublication 26 October 2019]
23. Martin L, Senesse P, Gioulbasanis I *et al.* (2015) Diagnostic criteria for the classification of cancer-associated weight loss. *J Clin Oncol* **33**, 90–99.
24. Andreyev HJN, Norman AR, Oates J *et al.* (1998) Why do patients with weight loss have a worse outcome when undergoing chemotherapy for gastrointestinal malignancies? *Eur J Cancer* **34**, 503–509.
25. Peng P, Hyder O, Firoozmand A *et al.* (2012) Impact of sarcopenia on outcomes following resection of pancreatic adenocarcinoma. *J Gastrointest Surg* **16**, 1478–1486.
26. Rollins KE, Tewari N, Ackner A *et al.* (2016) The impact of sarcopenia and myosteatosis on outcomes of unresectable pancreatic cancer or distal cholangiocarcinoma. *Clin Nutr* **35**, 1103–1109.
27. Tan BH, Brammer K, Randhawa N *et al.* (2015) Sarcopenia is associated with toxicity in patients undergoing neo-adjuvant chemotherapy for oesophago-gastric cancer. *Eur J Surg Oncol* **41**, 333–338.
28. Prado CMM, Lieffers JR, McCargar LJ *et al.* (2008) Prevalence and clinical implications of sarcopenic obesity in patients with solid tumours of the respiratory and gastrointestinal tracts: a population-based study. *Lancet Oncol* **9**, 629–635.
29. van den Berg M, Kok DE, Posthuma L *et al.* (2018) Body composition is associated with risk of toxicity-induced modifications of treatment in women with stage I–IIIB breast cancer receiving chemotherapy. *Breast Cancer Res Treat* **173**, 475–481.
30. Arends J, Bachmann P, Baracos V *et al.* (2017) ESPEN Guidelines on nutrition in cancer patients. *Clin Nutr* **36**, 11–48.
31. Ferreira V, Agnihotram RV, Bergdahl A *et al.* (2018) Maximizing patient adherence to prehabilitation: what do the patients say? *Support Care Cancer* **26**, 2717–2723.
32. Macmillan Cancer Support. RCoA, NIHR Cancer and Nutrition Collaboration (2019) Principles and guidance for prehabilitation within the management and support of people with cancer. https://www.macmillan.org.uk/assets/prehabilitation-guidance-for-people-with-cancer.pdf.
33. Silver JK (2015) Cancer prehabilitation and its role in improving health outcomes and reducing health care costs. *Semin Oncol Nurs* **31**, 13–30.
34. Silver JK & Baima J (2013) Cancer prehabilitation: an opportunity to decrease treatment-related morbidity, increase cancer treatment options, and improve physical and psychological health outcomes. *Am J Phys Med Rehabil* **92**, 715–727.
35. Gillis C, Fenton TR, Sajobi TT *et al.* (2019) Trimodal prehabilitation for colorectal surgery attenuates post-surgical losses in lean body mass: a pooled analysis of randomized controlled trials. *Clin Nutr* **38**, 1053–1060.

36. Trepanier M, Minnella EM, Paradis T *et al.* (2019) Improved disease-free survival after prehabilitation for colorectal cancer surgery. *Ann Surg* **270**, 493–501.

37. Gillis C, Buhler K, Bresee L *et al.* (2018) Effects of nutritional prehabilitation, with and without exercise, on outcomes of patients who undergo colorectal surgery: a systematic review and meta-analysis. *Gastroenterology* **155**, 391–410.

38. Baldwin C & Weekes CE (2012) Dietary counselling with or without oral nutritional supplements in the management of malnourished patients: a systematic review and meta-analysis of randomised controlled trials. *J Hum Nutr Diet* **25**, 411–426.

39. Ravasco P, Monteiro-Grillo I & Camilo M (2012) Individualized nutrition intervention is of major benefit to colorectal cancer patients: long-term follow-up of a randomized controlled trial of nutritional therapy. *Am J Clin Nutr* **96**, 1346–1353.

40. Druml C, Ballmer PE, Druml W *et al.* (2016) ESPEN Guideline on ethical aspects of artificial nutrition and hydration. *Clin Nutr* **35**, 545–556.

41. Franke AJ, Iqbal A, Starr JS *et al.* (2017) Management of malignant bowel obstruction associated with GI cancers. *J Oncol Pract* **13**, 426–434.

42. Nikfarjam M, Wilson JS & Smith RC (2017) Diagnosis and management of pancreatic exocrine insufficiency. *Med J Aust* **207**, 161–165.

43. Kim DJ & Kim W (2016) Laparoscopy-assisted proximal gastrectomy with double tract anastomosis is beneficial for vitamin B12 and iron absorption. *Anticancer Res* **36**, 4753–4758.

44. Lam JR, Schneider JL, Quesenberry CP *et al.* (2017) Proton pump inhibitor and histamine-2 receptor antagonist use and iron deficiency. *Gastroenterology* **152**, 821–829. e821.

45. Kornerup LS, Hvas CL, Abild CB *et al.* (2019) Early changes in vitamin B12 uptake and biomarker status following Roux-en-Y gastric bypass and sleeve gastrectomy. *Clin Nutr* **38**, 906–911.

46. Dawson DW, Sawers AH & Sharma RK (1984) Malabsorption of protein bound vitamin B12. *Br Med J (Clin Res Ed)* **288**, 675–678.

47. Pironi L, Arends J, Bozzetti F *et al.* (2016) ESPEN Guidelines on chronic intestinal failure in adults. *Clin Nutr* **35**, 247–307.

48. Mountford CG, Manas DM & Thompson NP (2014) A practical approach to the management of high-output stoma. *Frontline Gastroenterol* **5**, 203–207.

49. Parnes HL, Fung E & Schiffer CA (1994) Chemotherapy-induced lactose intolerance in adults. *Cancer* **74**, 1629–1633.

50. Andreyev J, Ross P, Donnellan C *et al.* (2014) Guidance on the management of diarrhoea during cancer chemotherapy. *Lancet Oncol* **15**, e447–e460.

51. Wedlake LJ, Shaw C, Whelan K *et al.* (2013) Systematic review: the efficacy of nutritional interventions to counteract acute gastrointestinal toxicity during therapeutic pelvic radiotherapy. *Aliment Pharmacol Ther* **37**, 1046–1056.

52. Andreyev J (2007) Gastrointestinal symptoms after pelvic radiotherapy: a new understanding to improve management of symptomatic patients. *Lancet Oncol* **8**, 1007–1017.

53. Wedlake LJ (2018) Nutritional strategies to prevent gastrointestinal toxicity during pelvic radiotherapy. *Proc Nutr Soc* **77**, 357–368.

54. Wedlake L, Shaw C, McNair H *et al.* (2017) Randomized controlled trial of dietary fiber for the prevention of radiation-induced gastrointestinal toxicity during pelvic radiotherapy. *Am J Clin Nutr* **106**, 849–857.

55. Haanen J, Carbonnel F, Robert C *et al.* (2017) Management of toxicities from immunotherapy: ESMO clinical practice guidelines for diagnosis, treatment and follow-up. *Ann Oncol* **28**, iv119–iv142.

56. Helmink BA, Khan MAW, Hermann A *et al.* (2019) The microbiome, cancer, and cancer therapy. *Nat Med* **25**, 377–388.

57. Tan SY, Turner J, Kerin-Ayres K *et al.* (2019) Health concerns of cancer survivors after primary anti-cancer treatment. *Support Care Cancer* **27**, 3739–3747.

58. Aubrey V, Hon Y, Shaw C *et al.* (2019) Healthy eating interventions in adults living with and beyond colorectal cancer: a systematic review. *J Hum Nutr Diet* **32**, 501–511.

59. Vissers PAJ, Martucci RB, Mols F *et al.* (2017) The impact of body mass index and waist circumference on health-related quality of life among colorectal cancer survivors: results from the PROFILES registry. *Nutr Cancer* **69**, 1177–1184.

60. van Veen MR, Mols F, Bours MJL *et al.* (2019) Adherence to the World Cancer Research Fund/American Institute for Cancer Research recommendations for cancer prevention is associated with better health-related quality of life among long-term colorectal cancer survivors: results of the PROFILES registry. *Support Care Cancer* **27**, 4565–4574.