OXFORD
Collaborative Research

BJS, 2024, znae223
https://doi.org/10.1093/bjs/znae223
Original Article

Association of Upper Gastrointestinal Surgery of Great Britain and Ireland (AUGIS)/perioperative quality initiative (POQI) consensus statement on prehabilitation in oesophagogastric surgery

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Abstract

Background: Prehabilitation is safe, feasible and may improve a range of outcomes in patients with oesophago-gastric cancer (OGC). Recent studies have suggested the potential of prehabilitation to improve body composition, sarcopenia and physical fitness, reduce surgical complications and improve quality of life. Despite this, prehabilitation services are not offered throughout all OGC centres in the UK. Where prehabilitation is offered, delivery and definitions vary significantly, as do funding sources and access.

Methods: A professional association endorsed series of consensus meetings were conducted using a modified Delphi process developed by the Peri-Operative Quality Initiative (POQI) to identify and refine consensus statements relating to the development and delivery of prehabilitation services for OGC patients. Participants from a variety of disciplines were identified based on a track record of published studies in the field of prehabilitation and/or practice experience encompassing prehabilitation of OGC patients. Approval from the POQI board was obtained and independent supervision provided by POQI.

Results: A total of 20 statements were developed and agreed by 26 participants over a preliminary meeting and 2 semi-structured formal POQI meetings. Ten research themes were identified. In the case of one statement, consensus was not reached and the statement was recorded and developed into a research theme. A strong recommendation was made for the majority of the consensus statements (17 of 20).

Discussion: Consensus statements encompassing the interventions and outcomes of prehabilitation services in oesophago-gastric cancer surgery have been developed to inform the implementation of programmes.

Introduction

Prehabilitation can be described as the process of enhancing the functional capacity of an individual to enable them to withstand a stressful event[1,2]. A more cancer-specific definition is: 'A process on the cancer continuum of care that occurs between the time of cancer diagnosis and the beginning of acute treatment and includes physical and psychological assessments that establish a baseline functional level, identify impairments, and provide interventions that promote physical and psychological health to reduce the incidence and/or severity of future impairments.'[2]

Prehabilitation usually incorporates a multimodal approach[3] and three stages: screening, assessment and intervention[4]. Screening identifies those at need of in-depth assessment.

Received: May 07, 2024. **Revised:** August 11, 2024. **Accepted:** August 16, 2024

Assessment defines in detail needs, resources and abilities to inform subsequent interventions. Interventions can be universal (applied to everyone); targeted, to specific requirements which are disease- or patient-specific; or specialist, for those with chronic, severe and complex needs[5].

A range of interventions make up prehabilitation. Physical activity is always present, dietary and psychological support are often present, other interventions such as smoking and alcohol cessation may also be considered. All components act synergistically to improve outcomes.

Prehabilitation is safe and improves a variety of patient outcomes in oesophago-gastric cancer (OGC)[6–8]. Despite this, prehabilitation services are not offered throughout all OGC centres in the UK[4]. Where prehabilitation is offered, there are variations in the nature of interventions, implementation, delivery, access and funding sources[9]. Current curative treatment pathways for OGC patients present an opportunity to deliver effective, evidence-based prehabilitation interventions from diagnosis through neoadjuvant treatment and prior to surgery[10,11].

An association (AUGIS—Association of Upper Gastrointestinal Surgery)-endorsed series of meetings were conducted using a modified Delphi process as developed by the Peri-Operative Quality Initiative (POQI). POQI is an international multidisciplinary non-profit organization that prepares consensus conferences on clinical topics related to perioperative medicine and surgery. Each POQI conference assembles a collaborative, multidisciplinary group of diverse national and/or international experts to develop consensus-based recommendations. The aim was to produce guidance statements, based on current evidence and expert opinion to inform the development and delivery of prehabilitation services for OGC patients and identify future research questions.

Methods

A modified Delphi method was employed, designed to garner the collective knowledge of the participants to answer clinically important questions on prehabilitation during treatment for OGC. Healthcare professionals were recruited based on their expertise in prehabilitation and perioperative management of patients undergoing surgery for oesophageal and gastric cancer and were divided into two groups, each with a clinical chair and a representative from POQI as a moderator. One group focused on the outcomes (outcomes group) of prehabilitation and the other focused on the specific interventions that should be included in a prehabilitation programme (interventions group). Before the conference, a systematic review of prehabilitation during cancer treatment (accepted for publication separately in the *Journal of Surgical Oncology*) incorporating OGC and non-OGC studies, regardless of findings (positive or negative) was conducted (search terms:"exercise"[Mesh] OR "Exercise*"[tiab] OR "physical activity*"[tiab] OR "physical training"[tiab] OR "physical exercise*"[tiab] OR "sport*"[tiab]) AND ("Neoadjuvant Therapy"[Mesh] OR "cancer treatment*"[tiab] OR "chemo"[tiab] OR "chemotherapeutic*"[tiab] OR "chemotherap*"[tiab] OR "cancer therapy*"[tiab]) limited to RCT and observational studies (OS)). This formed the basis of the data presented to participants. A national survey of current OGC prehabilitation practice and combined data from four prospective UK prehabilitation trials was also presented[9].

The POQI conferences were held virtually using an online platform (MS Teams). A preliminary meeting was arranged to introduce the process, expand the group to include a full range of OGC multidisciplinary professionals and to agree a longlist of statements. At the first one-hour plenary session of the conference, draft consensus statements were presented. For each statement, data were presented to support or refute the statement and categorized according to the strength of evidence (*Table S1*) and whether the data were OGC-specific, non-OGC or based on combined UK collaborative data[9].

The POQI group then split into the outcomes and interventions subgroups for a one-hour discussion. In the subsequent plenary session, each group summarized their discussions and modifications to the consensus statements were presented to the whole group, with further refinements made.[10] After the first conference, the outcomes and interventions working groups further refined the statements before a second conference. This followed the same format as the first. At the end of the second conference, refined and graded POQI statements were either accepted by consensus or rejected if consensus could not be reached. In addition a series of 10 research questions were derived and agreed at the end of the second conference.

Groups assigned strength of evidence underlying recommendations using a modified GRADE structure in keeping with previous AUGIS/POQI guidance[12]. The strength of evidence was graded A (High) to D (Very Low) and the strength of recommendation was either 'Strong' or 'Weak' for or against (*Table S1*).

Results

Consensus statements

Consensus Statement 1:

A multimodal prehabilitation programme is recommended to improve neoadjuvant chemotherapy completion rates.

Exercise assessment and intervention Grade: B (Moderate), Strength: Strong

Nutritional assessment and intervention Grade: C (Low), Strength: Strong

Psychological assessment and intervention Grade: D (Very Low), Strength: Weak

There is strong evidence that exercise can improve chemotherapy completion rates. Allen *et al.*[7] in a randomized trial of exercise during neoadjuvant chemotherapy (NAC) compared exercise, nutritional and psychological support with usual care in 54 patients reporting a NAC completion rate of 75% in the exercise group compared to just 46% in the control group ($P = 0.036$). The PIC trial, a randomized trial of resistance training (RT) and sensorimotor training (SMT) during chemotherapy[13], demonstrated more patients reaching a clinically relevant relative dose intensity (RDI) in the exercise groups compared to usual care (94% *versus* 76%; $P = 0.032$).

The group felt that the statement needed to be separated into the component parts of multimodal prehabilitation, as although the evidence to support this statement is strongly supported by RCTs, most of these studies were small and did not include psychological or nutritional support as part of the experimental arm.

Consensus Statement 2:

A multimodal prehabilitation programme is recommended to optimize the body composition of patients undergoing neoadjuvant chemotherapy.

Grade: B (Moderate), Strength: Strong

Many studies have used BMI as a measured outcome in prehabilitation. In a feasibility study Grabenbauer *et al.*[14] reported that median BMI ($P = 0.001$) and median fat mass ($P = 0.001$) decreased at 3 months with a home aerobic training (AT) programme. The OptiTrain trial[15] compared a 16-week high intensity interval training (HIIT) programme in addition to either AT or RT with usual care (UC) during chemotherapy in 240 women. At 12 months BMI was reduced in both the AT ($P < 0.001$) and RT ($P < 0.021$) groups compared to UC.

However, BMI remains a problematic outcome measure. Patients with OGC frequently present with malnutrition and weight loss despite oesophageal adenocarcinoma being a disease associated with obesity[16]. Therefore, within the OGC surgical patient population, the desired outcome could be weight gain, stability or reduction depending on the individual patient. Reversal of sarcopenia may be more important than weight per se[17,18].

Better measures of body composition exist and have been employed in prehabilitation studies in OGC. Zylstra *et al.*[8] in the PRE-EMPT trial demonstrated that fat-free mass index was improved in the prehabilitation group ($P = 0.026$). This concurred with the randomized trial by Lin *et al.*[19] that reported a reduction in mean body fat percentage in the exercise arm ($P = 0.002$). Stuecher *et al.*[20] randomized 44 patients receiving chemotherapy for gastrointestinal cancer to AT or UC. They reported lean body mass improved over 12 weeks in the intervention group ($P = 0.02$).

Consensus Statement 3:

A multimodal prehabilitation programme is recommended to optimize muscle strength.
Grade: C (Low), Strength: Weak

Allen *et al.*[7] reported a reduction in muscle mass loss ($P = 0.049$) with improved hand grip strength in the intervention group ($P = 0.016$), but only in those without sarcopenia at baseline. Halliday *et al.*[21] reported skeletal muscle area (SMA) at midpoint of the third lumbar vertebra ($P = 0.039$) and skeletal muscle index ($P = 0.05$) fell less in the intervention group. Hand grip strength was also increased in the Optitrain study ($P < 0.001$)[15].

Lin *et al.*[19] reported a significant increase in skeletal muscle mass in their exercise group ($P = 0.008$) and a corresponding increase in upper ($P = 0.037$) and lower ($P = 0.025$) limb strength. The PIC trial[13] reported an improved quadriceps strength in adherent exercisers ($P < 0.001$). The e-CuidateChemo study[22] reported abdominal, back and lower body strength all improved in the exercise groups (all $P < 0.001$).

Taken together, it was felt that the statement should reflect an optimization rather than an increase in muscle strength, as prehabilitation appears to mitigate the decline seen in those that do not exercise.

Consensus Statement 4:

A multimodal prehabilitation programme is recommended to optimize physical fitness.
Grade: B (Moderate), Strength: Strong

Allen *et al.*[7] reported an attenuated decrease in VO_2Max in the intervention group *versus* control (mean change in the exercise group −0.4 *versus* controls −2.5 ml/kg/min; $P = 0.022$) but no intervention effect was discovered for the trials primary end point, anaerobic threshold. Christensen *et al.*[34] prevented a fall in VO_2Max in OGC patients who exercised during chemotherapy (25.23 ml/kg/min pre-NAC *versus* 26.62 ml/kg/min post-NAC).

The BEAUTY study[23] reported improved VO_2Max in the exercise group (+1.9 ml/kg/min, $P = 0.018$) as did a feasibility study by Grabenbauer *et al.*[14] at 3 months ($P = 0.005$) and at 12 months ($P = 0.003$). The e-CuidateChemo[22] study in breast cancer showed improved 6 min walked test (6MWT) (+15.42 m, $P = 0.015$) in exercised individuals.

Consensus Statement 5:

A multimodal prehabilitation programme is recommended to optimize postoperative quality of life.
Grade: C (Low), Strength: Weak

Lin *et al.*[19] and Müller *et al.*[13] used the EORTC QL-C30 questionnaire, both revealing significant improvements in the exercise group.[24] Allen *et al.* also reported a significant improvement in global quality of life (QoL), particularly at 6 weeks post-surgery (EORTC QL-C30 global health score $P = 0.001$)[7]. In the BEAUTY trial[23] FACT-B total score at 24 weeks was improved by 7.4 points compared to baseline ($P = 0.002$) and at 12 weeks ($P = 0.001$). Overall, a lack of patient numbers in OGC-specific trials was noted and so it was felt that this conclusion might change with publications from larger trials.

Consensus Statement 6:

A multimodal prehabilitation programme is recommended to reduce surgical complication rates.
Grade: B (Moderate), Strength: Strong

A systematic review by Tukanova *et al.*[25] demonstrated a reduction in patients with Clavien Dindo (CD) grade 3 or higher complications. However, this included studies where the intervention was perioperative and where inspiratory muscle training was utilized rather than a multimodal prehabilitation programme. The PREPARE trial[26], an OGC-specific study, demonstrated a reduction in postoperative pneumonia from 66% to 26% ($P < 0.001$). Combined data from four UK OGC prehabilitation trials also demonstrated a reduction in CD ≥3 complications (19% *versus* 34%; $P = 0.038$)[9]. In colorectal cancer, the PREHAB trial[27] recently published a reduction of 50% in the rate of severe complications (Comprehensive Complication Index > 20) with prehabilitation.

Consensus Statement 7:

A multimodal prehabilitation programme is recommended to shorten postoperative length of stay.
Grade: C (Low), Strength: Weak

Tukanova *et al.*[25] demonstrated a reduction in length of stay (1.74 days) as did the PREPARE trial[26] (13 days down to 10 days). The group noted that with enhanced recovery (ERAS) programmes now in widespread use, deviations from a planned length of stay (as determined by ERAS protocols) were arguably a better parameter, more often reflective of complications.

Consensus Statement 8:

A multimodal prehabilitation programme is recommended to improve response to neoadjuvant therapy.
Grade: D (Very Low), Strength: Weak

Zylstra *et al.*[8] assessed regression in the primary tumour using the Mandard tumour regression grading (TRG) demonstrating more responders (TRG1–2) in the exercise arm (Exercise 7/21 *versus* 1/19 Control, $P = 0.044$). A similar result was observed in a colorectal study[28], following chemoradiotherapy and surgery (OR 8.5, 95% c.i. 1.4 to 51.5, $P = 0.02$). Subsequent to the POQI conference, Sanft *et al*[29] demonstrated improved histological tumour regression in a randomized trial of breast cancer patients (complete response 53% *versus* 28%; $P = 0.037$).

Consensus Statement 9:

A multimodal prehabilitation programme is recommended to improve survival.
Consensus not reached: Research Question

One study, in colorectal cancer[30], has shown improved survival after prehabilitation; however, the study was limited by the fact that data were pooled from three prehabilitation trials (two RCTs, one cohort). An analysis of patients who declined to participate or dropped out of the PRE-EMPT study showed significantly worse survival in the non-participant group compared to both intervention and control arms[31]. The group felt that there was evidence for improvement in outcomes associated with overall survival but not enough evidence to directly support the statement at present. Since the conference, however, Lavery *et al.*[32], in a large database study from the United States, showed that exercise was associated with a 25% reduction in all-cause mortality compared with non-exercise after a cancer diagnosis (HR, 0.75; 95% c.i., 0.70 to 0.80; $P \leq 0.05$).

Consensus Statement 10:

A multimodal prehabilitation programme is recommended from diagnosis through to surgery.
Grade: C (Low), Strength: Strong

Numerous studies have demonstrated the feasibility of delivering multimodal prehabilitation during all stages of treatment from diagnosis through to surgery, incorporating the neoadjuvant treatment period[14,24,33,34]. To maximize the potential benefits, the group felt unanimously that it was important to start the intervention as early as possible in the patient pathway.

Consensus Statement 11:

Nutritional assessment and intervention from a dedicated oesophago-gastric specialist dietitian is recommended for all patients as part of a multimodal prehabilitation programme.
Grade: C (Low), Strength: Strong

Patients with OGC are at significant risk of malnutrition due to dysphagia and also cancer cachexia[35,36]. This unintentional weight loss can be reduced by early expert nutritional intervention[37].

Since 2018, NICE have recommended all patients undergoing curative OGC treatment should be offered nutritional assessment and specialist dietetic support before, during and after surgery. It is now a quality indicator in national audits.

Consensus Statement 12:

Smoking cessation is recommended for patients as part of a multimodal prehabilitation programme.
Grade B (Moderate), Strength: Strong

A meta-analysis of 6 RCTs and 15 OS demonstrated a relative risk reduction of 41% ($P = 0.01$) for prevention of postoperative complications after surgery[38]. Each week of cessation increased the magnitude of effect by 19%. Trials of at least 4 weeks' smoking cessation had a significantly larger treatment effect than shorter trials ($P = 0.04$). A retrospective study of 2469 patients undergoing surgery for gastric cancer demonstrated an increased risk of complications among smokers (OR 1.51, $P < 0.001$)[39]. In this study, the rate of pulmonary complications was higher in those who had stopped smoking for less than 4 weeks (10.0% *versus* 3.1% if >4 weeks; $P = 0.019$).

The group felt that specific interventions for smoking cessation such as nicotine replacement therapy (NRT) were beyond the remit of this study. However, it was acknowledged that there was good evidence that NRT improves preoperative smoking cessation[40], but the effect of NRT on surgical and oncological outcomes remains unknown.

A Cochrane review of three RCTs investigated the effect of alcohol cessation on postoperative complications, concluding that it reduced the risk of surgical complications (risk ratio 0.62, 95% c.i. 0.40 to 0.96). It was felt unclear as to how applicable this was to the OGC patient population and so the group stopped short of making a recommendation.

Consensus Statement 13:

Specialist psychological assessment and intervention with a focus on preoperative need from a qualified psychologist is recommended to selected patients as part of a multimodal prehabilitation programme.
Grade: D (Very Low), Strength: Weak

Since 2004, NICE have recommended a four-step model of professional psychological assessment and support[41] for patients with cancer. Steps 1–2 can be delivered by professionals with some training in assessment psychological support and should screen patients that might require further intervention. The majority (65%) of patients will be suitable for this level. Some (25%) will require more targeted interventions delivered by accredited individuals such as therapists and counsellors (Level 3). Finally, 10% will require the support of professionals such as clinical psychologists trained to manage complex psychological health needs such as co-existing psychopathologies that may be exacerbated by a cancer diagnosis and its treatment. A Cochrane review of psychological preparation and postoperative outcomes in general surgery demonstrated a potential improvement in postoperative pain, length of stay and quality of life[42]. Estimates indicate that having professional psychological services embedded within adult cancer services can save up to 20% of healthcare utilization costs[43].

The consensus group felt that the evidence for psychological interventions in OGC surgery was of low quality and heterogeneous, hence the weak recommendation that follows existing NICE guidance. Further OGC cohort–specific research was recommended.

Consensus Statement 14:

Physical activity is recommended to target the WHO criteria.
Grade: A (High), Strength: Strong

The updated WHO guidelines on physical activity provide clear, evidence-based recommendations for physical activity for adults from 18 to 64 years and 65 years and above[44]. The group felt that these recommendations were applicable to OGC patients and should be accepted in full.

Consensus Statement 15:

Prescribed exercise with monitoring is recommended to improve aerobic capacity and whole-body strength. The prescription should be clearly defined in terms of frequency, intensity, time, type and progression.
Grade: A (High), Strength: Strong

The main principles of physical training are well established including specificity, overload, progression, initial values, reversibility and diminishing returns[45]. There are few data to support one aerobic exercise modality over another. The FITT principles (frequency, intensity, time, type) have guided exercise prescription for more than 25 years[46]. Aerobic training was felt to be an important component of exercise programmes and has recently been endorsed by the American Heart Association not only to improve fitness but also because of clinically beneficial effects on cardiovascular disease[47]. There was strong consensus that exercise should be monitored to allow for response assessment and facilitate adaptive patient-specific targets.

Consensus Statement 16:

It is recommended that exercise programmes are prescribed by a professional qualified in exercise prescription with relevant experience in cancer care.
Grade: C (Low), Strength: Strong

Prehabilitation exercise programmes are prescribed and delivered by a variety of professionals. In UK practice, the majority are delivered by NHS physiotherapists[7,48]. The group recognized that units may employ professionals of different backgrounds to deliver the intervention but there was strong consensus that the prescriber (supervising the programme) should have the necessary skillset and relevant experience in cancer care.

Consensus Statement 17:

It is recommended that, where exercise programmes are delivered in-person, the setting should be quality assured, safe, have appropriate facilities and level of supervision.
Grade: C (Low), Strength: Strong

Published trials have delivered exercise programmes in hospitals, gyms, at home and at a variety of other locations[7,22,33,34]. The group felt that the specific location was less important than its quality and safety, the level of supervision and monitoring of an individuals' progress. Although the evidence was considered weak, the group felt that it was consistently in favour of a supervised intervention regardless of the specific location[49,50]. Remote programmes delivered at home have been successfully delivered, particularly during the COVID-19 pandemic[51]. Although these are clearly less likely to utilize specialist exercise equipment, it would be incumbent on the patient to ensure their own suitable environment for the planned activity.

Consensus Statement 18:

Regular professional contact is recommended, at least weekly, as part of a prehabilitation programme.
Grade: C (Low), Strength: Weak

There is limited evidence to support the level and frequency of professional supervision. However, where supervised programmes have been compared to unsupervised, there has been a clear benefit for supervision[49,50]. The group felt that at least weekly contact should be recommended, whether this interaction is remote or in-person[52].

Consensus Statement 19:

Needs-based individualization of prehabilitation programmes is recommended.
Grade: C (Low), Strength: Strong

Generic 'one-size-fits-all' prehabilitation programmes are inflexible and represent a potential barrier to patient engagement. The group noted that cancer services deal with a wide range of patients, each with their own complex needs. These include individuals' physical limitations, exercise history and psychosocial background, including the availability of exercise facilities. The evidence for tailored programmes is hampered by trial protocols necessitating a homogeneous intervention in the pursuit of experimental rigour. However, given the broad agreement that prehabilitation now be adopted as a standard of care (Statement 21), the group felt that the need for such homogeneity should make way for the (potentially more successful) needs-based personalization of programmes.

Consensus Statement 20:

a) A validated baseline assessment of aerobic capacity, strength, nutrition and psychology is recommended to inform prehabilitation prescription.Aerobic capacity and strength. Grade: B (Moderate), Strength: StrongNutritional assessment and intervention. Grade: C (Low), Strength: StrongPsychological assessment and intervention. Grade: D (Very Low), Strength: Weak

b) Monitoring of the response to prehabilitation, which may include repeat of the baseline assessment, is recommended to refine prehabilitation prescription.Grade: C (Low), Strength: Strong

A variety of baseline and monitoring assessments exist. The national survey identified 50% of units using cardiopulmonary exercise testing (CPET) at baseline with most (80% of these, 40% total) also using CPET to measure response. Although a recognized gold standard, CPET was acknowledged to be more time-consuming and expensive than alternatives (6MWT, Sit2stand) that may be assessed in a clinic environment. Although validated in cancer patients, these assessments lack the same granularity of data afforded by CPET. The role of wearable devices was felt to be of interest, but these have yet to be fully established.

Consensus Statement 21:

Multimodal prehabilitation is recommended as a standard of care.
Grade: B (Moderate), Strength: Strong

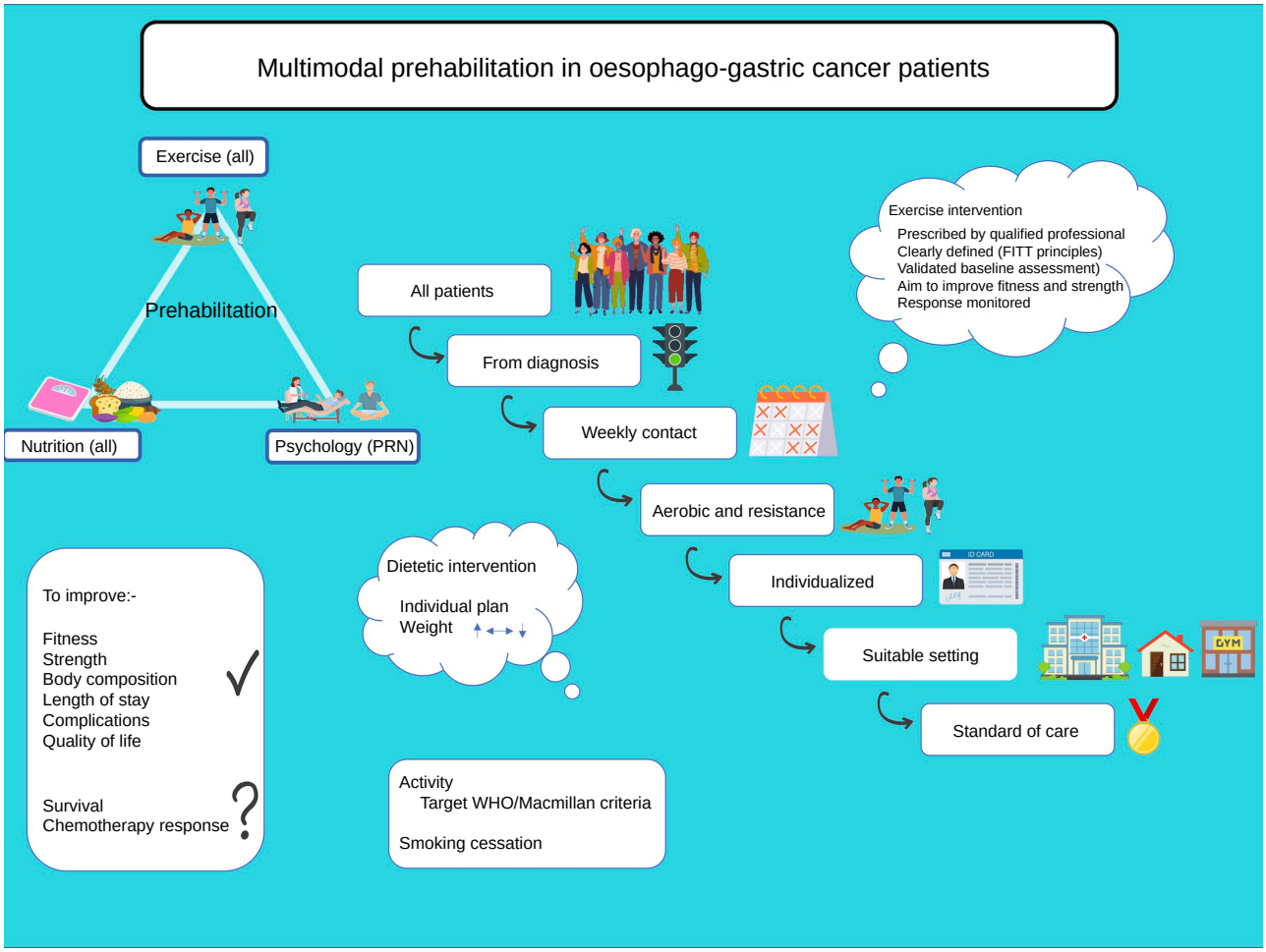

Fig. 1 Infographic: multimodal prehabilitation in oesophagogastric cancer patients

Taken together, the weight of evidence and expert consensus in support of prehabilitation was such that it should no longer be confined to individual centres to promote prehabilitation in OGC patients. The group recommended that prehabilitation should be considered as a standard of care for patients with OGC on a surgical pathway.

Having reached consensus on the above statements, a series of 10 research questions were developed by the groups and agreed (*Table 1*) with the objective of informing future research and funding.

Discussion

This multidisciplinary, society-endorsed, modified Delphi process conducted *via* a series of POQI conferences has gained consensus agreement on 20 statements related to prehabilitation in patients undergoing surgery for OGC. Multimodal prehabilitation incorporates exercise, nutrition and psychological components and should now be considered standard of care in OGC surgical patients. Outcomes that can be improved by prehabilitation and the key components of intervention have been agreed and areas for future research have been identified (*Table 1*). This represents a benchmark within UK OGC prehabilitation practice whereby the core components of these services have been established, summarised in our infographic (*Fig. 1*).

Several methodological issues merit further discussion. The modified Delphi process using POQI conferences is a well-established method for gaining consensus. The multidisciplinary group represented a wide range of professionals with expertise in the prehabilitation of patients with OGC. It is acknowledged that enthusiasts are more likely to exhibit bias in support of a given intervention.

As part of the process, the group was presented with contemporaneous data in the form of a systematic review of the prehabilitation literature, a national survey of UK prehabilitation practice in OGC and combined data from four prospective UK prehabilitation trials. Limitations in the strength of the data were acknowledged, with many studies relatively small. Trials from other cancer groups were included as many of the interventions and outcomes of interest were considered applicable to all cancer patients. Careful consideration was given before providing strong recommendations with a weak evidence base, as moderated by the clinical and POQI co-chairs. As with any Delphi process, the statements represent the consensus views of an expert group of participants and not the scientific community as a whole. In a rapidly developing field, it is acknowledged that the statements will require updating as new evidence emerges, particularly the results of some ongoing large multicentre randomized trials such as WES-FIT and SAFE-FIT[51,53]. Although the field of prehabilitation has gained substantial research interest in recent years, a significant degree of heterogeneity exists within programmes across the UK. The presented statements represent a much-needed move towards greater evidence-based standardization and will provide

Table 1 Research questions

Research questions	
What type of exercise interventions should be prescribed?	A 'gold standard' exercise prescription is yet to emerge. Whereas all agree that physical activity should meet the WHO criteria and strongly support, in principle, the use of aerobic and strength training it was also acknowledged that different exercise programmes may suit different patient populations. Trials thus far have incorporated inspiratory muscle training[26], aerobic training[8], resistance training[9], high-intensity interval training (HIIT)[35], sensorimotor training[14] and increasing step count[34] as well as combinations thereof, all under the umbrella of 'exercise interventions'. Very little is known with regards to the thresholds at which to train patients and few comparisons between the different training modalities. Clarification and validation are required to inform future programmes.
What type of nutrition intervention should be prescribed (mode/intensity/frequency/duration)?	Although there is a clear association between malnutrition and poorer outcomes in OGC[37,38], many unknowns still exist, including which markers of nutritional status most correlate with clinical outcomes, how best to deliver perioperative nutritional supplementation and how to balance achieving improved body composition in a frequently overweight population alongside malnutrition in patients receiving cancer treatment.
What type of psychological intervention should be prescribed (mode/intensity/frequency/duration)?	Psychological support to cancer patients should follow NICE guidelines and the four-step approach. However, there is a lack of evidence to support the delivery of these services and the evidence that does exist supports the cost-effectiveness of psychological interventions for 'cancer care' rather than for OGC patients specifically[44]. Clarification and validation in this patient group, specifically regarding whether the intervention is selective or universal and to what degree patients in lower-risk groups for psychological morbidity rates may benefit from input will help to inform future programmes and funding.
How do the three prehabilitation pillars interact?	The three pillars of prehabilitation—that is, exercise, nutrition and psychosocial support[54]—are often discussed as a combination in trials and prehabilitation programmes. Some researchers have been able to quantify the combined effects compared to a unimodal programme[55]. However, designing tailored prehabilitation programmes that not only optimize the three pillars individually but also explore the interaction between them will be important.
What are the underlying mechanisms behind altered response to chemotherapy in the tumour microenvironment (such as T-cell function) and the effects of exercise on these mechanisms?	There is growing evidence to suggest that exercise has a role in modulating various pro- and anticancer activities within the tumour microenvironment[56] from modulating hypoxia and oxidative stress to improving cytotoxic T-cell mobility[57]. Trials have shown a reduction in circulating pro-inflammatory cytokine biomarkers and a corresponding increase in anti-inflammatory biomarkers in exercised groups undergoing chemotherapy[58]. In OGC, one trial demonstrated cytotoxic T-lymphocyte levels were significantly higher in exercised individuals and IL6 rises were attenuated[9]. In the same trial there were more responders to chemotherapy in the exercise group[31]. Future research should investigate these findings and explore the underlying basic science with the potential to include exercise as an anticancer treatment in its own right.
What is the effect of prehabilitation on short- and long-term survival?	Most studies to date have stopped short of being able to definitively demonstrate an effect on oncological and/or survival outcomes. This has largely been due to the limited size of published studies, which have often been in the feasibility or pilot phase. Larger trials are required to confirm whether there is a clear survival benefit.
What are the cost implications of a prehabilitation service?	Within a financially restrained national health service, the costs and cost benefits for prehabilitation remain poorly quantified, largely owing to the significant variations in the components of these programmes between centres. Certain outcome measures reported in trials, for example blood analysis of inflammatory/immunological markers, can be expensive and fall into the remit of future research rather than being required in all patients. Many of the outcomes highlighted as having an established evidence base such as a reduction in surgical complications or hospital length of stay would be surrogate markers of reduced cost. High-quality health economic analysis would be crucial to securing managerial support for the introduction or further development of prehabilitation programmes.
What are the benefits of prehabilitation in non-surgically managed cancer patients?	The expert consensus saw no reason to exclude non-surgically managed patients from prehabilitation in OGC and, indeed, Macmillan guidelines clearly state that prehabilitation should be accessible to all patients. However, studies so far have focused on the presurgical optimization of patients and the resource requirements to expand prehabilitation programmes to patients in a metastatic setting would be significant. It was felt that this should be addressed in future studies to generate an evidence base in palliative OGC patients.
Should interventions be delivered face to face or is remote prehabilitation sufficient?	Modern technology, the Internet and the experience of the COVID-19 pandemic have heralded a more innovative approach to patient interactions, and particularly a greater acceptance of remote communication. Non–face-to-face encounters are feasible and have certain advantages in terms of limiting time and travel requirements. However, it has not yet been shown whether the effectiveness of delivering complex interventions remotely is equivalent to a more traditional face-to-face model.

(continued)

Table 1 (continued)

Research questions	
Should patients be screened for prehabilitation interventions or should prehabilitation be delivered to all?	The greatest magnitude of effect for exercise intervention is seen in patients with the lowest functional baseline[45,55]. It therefore follows that these patients, who pose the highest risk for surgery, should be a focus within a system that has limited resources. However, modern anticancer therapy is an 'aggregation of marginal gains' pertaining to numerous potential beneficial outcomes that work on a continuous scale. Denying patients with higher functional baselines access to an outcome-changing exercise intervention based on screening would be considered, by many, clinically and ethically inappropriate. Therefore, within a resource-limited system, the extent to which screening should be employed remains unclear. It is acknowledged that certain aspects of the intervention such as psychology may be more suitable for a more selective, screening-based approach. Moves towards personalized care may allow different models of prehabilitation to be administered to different patients according to their individual characteristics, needs and wishes.

IL6, interleukin 6; OGC, oesophago-gastric cancer.

a framework for centres looking to establish prehabilitation services.

A range of outcomes that can be improved by prehabilitation gained strong support. Other outcomes such as length of stay, quality of life and chemotherapy response gained support, albeit weaker based on limited available evidence. Taken together, the group felt that although further studies may improve the quality of the literature in support of the intervention, the evidence convincingly endorsed broad outcome improvements with prehabilitation.

Funding and manpower were identified as significant barriers to implementing prehabilitation in the national survey. Although health economic analyses were not specifically addressed, being highlighted as an area in need of further research, this is clearly a vital factor in the pursuit of more widespread adoption of these services. Some outcomes that were supported, such as reduced complications and length of stay could attract savings to balance the costs.

There was strong consensus that prehabilitation should be considered multimodal, incorporating exercise and nutritional input for all patients and selective psychological input based on a screening assessment. The national survey highlighted that only 50% of units had access to psychological support and hence resource limitations also guided this recommendation[9]. Guidance on the specifics of nutritional interventions in OGC was being conducted by another society-endorsed working group and so a number of dietary issues were deliberately avoided to prevent repetition.

The key principles agreed were that prehabilitation programmes should be supervised, in locations that are suitable in terms of safety and facilities. It was not felt appropriate for the guidance to be more prescriptive, as each centre would have its own factors to consider and few data exist to support one setting over another.

There was strong consensus that exercise be distinguished from activity, being prescribed by a healthcare professional experienced in the prescription of exercise in cancer patients. The group stopped short of stipulating the professional background of the prescriber. The exercise prescription was recommended to reflect the widely acknowledged FITT principles and incorporate a baseline and response assessment.

Whereas CPET was considered the gold standard assessment modality, providing quantifiable and reproduceable metrics of cardiorespiratory function, it was also acknowledged to be more resource-intensive than alternatives. Aerobic and resistance training were recommended to optimize aerobic capacity and whole-body strength, although the type of aerobic training was not stipulated due to a lack of evidence. Weekly contact was recommended given evidence of improved compliance with regular professional contact[52].

The principle of personalized programmes gained strong support based on an individual patient's specific needs while acknowledging that this tailored approach would limit the scientific comparison of interventions by introducing heterogeneity. Prospective research studies should address specific hypotheses in order to refine aspects of prehabilitation interventions that afford the greatest benefit.

In conclusion, prehabilitation should be routinely delivered to patients undergoing surgery for OGC courtesy of a strong evidence base across a range of outcome measures. Core component recommendations of the intervention have been identified and areas for future research to refine specific uncertainties highlighted. Improving the consistency of prehabilitation programmes nationally and lending support to clinical teams in justifying managerial investment in prehabilitation remains an important agenda with a clear pathway to patient benefit.

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Funding

The authors have no funding to declare.

Acknowledgements

R. C. W. and S. B. Joint first authors.

Disclosures

The authors declare no conflict of interest.

Supplementary material

Supplementary material is available at *BJS* online.

Data availability

PowerPoint presentations used in the POQI conferences are available on request. No other relevant data were produced for this project.

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