

**Nutrition Care Needs and
Multidisciplinary Rehabilitation in
Upper GI Cancer Survivors**

**A Thesis Submitted toward the Degree of
Doctor of Philosophy**

by

Fatemeh Sadeghi

Supervisors

Professor Juliette Hussey

Dr Suzanne Doyle

**Submitted to the Trinity College Dublin, the
University of Dublin**

2025

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Declaration

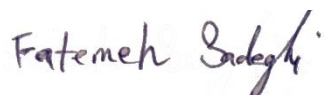
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Fatemeh Sadeghi



Date of submission

28/07/2025

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List of Abbreviations

AC	Adenocarcinoma
AI	Adequate Intake
AICR	American Institute for Cancer Research
ASCO	American Society of Clinical Oncology
ASM	Appendicular Skeletal Muscle Mass
aUPFs	Adapted Ultra-Processed Foods
BIA	Bioelectrical Impedance Analysis
BMI	Body Mass Index
CI	Confidence Interval
CPET	Cardiopulmonary Exercise Test
CT	Computed Tomography
CT	Chemotherapy
DIFA	Definitive Intervention and Feasibility Awards
DRVs	Dietary Reference Values
EFSA	European Food Safety Authority
EORTC-QLQ	European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire
ESPEN	European Society for Clinical Nutrition and Metabolism
EWGSOP	European Working Group on Sarcopenia in Older People
FFMI	Fat Free Mass Index
FFM	Fat Free Mass
FM	Fat Mass
FMI	Fat Mass Index
GAC	Gastric Adenocarcinoma
GI	Gastrointestinal
GLIM	Global Leadership Initiative on Malnutrition
GORD	Gastro-Oesophageal Reflux Disease

GSRS Gastrointestinal Symptom Rating Scale
 HADS Hospital Anxiety and Depression Scale
 HGD High Grade Dysplasia
 HGS Hand Grip Strength
 HPV Human Papillomavirus
 HRB Health Research Board
 HRQOL Health-Related Quality of Life
 INDI Irish Nutrition and Dietetic Institute
 IOM Institute of Medicine
 IPAQ-SF International Physical Activity Questionnaire Short Form
 MASCC Multinational Association of Supportive Care in Cancer
 MCID Minimal Clinically Important Difference
 MD Mean Difference
 MET Metabolic Equivalents
 MST Malnutrition Screening Tool
 NCO National Cancer Organisations
 NCCP National Cancer Care Programme
 NIS Nutrition Impact Symptoms
 OGD Oesophagogastro-Duodenoscopy
 ONS Oral Nutritional Supplements
 PAL Physical Activity Level
 PG-SGA Patient-Generated Subjective Global Assessment Tool
 PIL Participant Information Leaflet
 PRI Population Reference Intake
 PROMs Patient Reported Outcome Measures
 PROs Patient Reported Outcomes
 PRISMA Preferred Reporting Items for Systematic Reviews and Meta-Analyses

ReStOre Rehabilitation Strategies Following Oesophagogastric Cancer

RI	Reference Intake Range
RT	Radiation Therapy
SCC	Squamous Cell Carcinoma
SD	Standard Deviation
SJH	St James's Hospital
SMM	Skeletal Muscle Mass
SNAQ	Simplified Nutritional Appetite Questionnaire
SPPB	Short Physical Performance Battery
TCI	Thresholds for Clinical Importance
TILDA	The Irish Longitudinal Study on Ageing
TSJCI	Trinity St James's Cancer Institute
TUH	Tallaght University Hospital
UGI	Upper Gastrointestinal
UWL	Unintentional Weight Loss
WCRF	World Cancer Research Fund

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Adaptations to PhD research plan in response to COVID-19 pandemic

This PhD programme started in March 2020 to primarily investigate the effects of the ReStOre II (Rehabilitation Strategies following Oesophago-gastric Cancer) programme on nutrition outcomes. The ReStOre II programme is a multidisciplinary research study with core components of nutrition and exercise, which aims to improve overall physical functioning and quality of life in patients following UGI cancer treatment.

Unfortunately, the initial research plan was significantly impacted by the COVID-19 pandemic. In March 2020, COVID-19 was first declared as a global pandemic by the World Health Organisation. On March 27th, Ireland went into the first full lockdown, and five waves of COVID-19 followed. Each wave brought tight restrictions on movement that significantly affected the progress of this PhD project, particularly as it prevented the ReStOre II trial from starting as per the planned timeline in April 2020. Recruitment for the ReStOre II study was postponed until March 2022, and as of August 2024, recruitment has just finished. Hence, the initial research plan for this PhD pivoted to include a pilot study to examine the feasibility of remote delivery of the ReStOre II programme during COVID-19, namely the ReStOre@home study.

Additional observational studies were included in the PhD plan to investigate nutrition and supportive care needs in UGI cancer survivors. However, COVID-19 also impacted the design and recruitment of these studies. Therefore, several modifications and adaptations were made during this PhD programme to overcome these challenges and complications.

Key modifications that have been made in the present PhD plans are as follows:

- A pilot clinical trial was conducted to examine the feasibility of virtual delivery of a multidisciplinary rehabilitation (ReStOre@Home)
- Due to limitations in recruiting participants, both online and paper-based versions of the cross-sectional survey were designed (Chapter 3).

Additional challenges encountered during the present thesis:

- As COVID restrictions lifted, few UGI cancer survivors attended the UGI clinic for in-person appointments, and most surveillance visits continued remotely. Also, high refusal rates were observed when attempting to recruit participants for the survey at the UGI clinic. These challenges subsequently limited recruitment from the UGI clinic.
- Amendments to introduce recruitment via postal survey required additional approval from the ethics committee, which delayed the completion of the study (Chapter 3).
- Implementing further infection control and safety measures at in-person assessments limited the number of assessments completed per day, ultimately prolonging study procedures (Chapter 5).

Summary

Treatment side effects significantly affect the nutritional status and quality of life of upper gastrointestinal (UGI) cancer survivors. There are limited data on the unmet nutrition needs of UGI cancer survivors in Ireland. This information is needed when developing specialised survivorship care plans. Multidisciplinary care models are often recommended to address the diverse needs of cancer survivors, yet their effectiveness in UGI cancer patients requires further examination.

This PhD thesis aimed to address these knowledge gaps through five studies. Three of these studies focused on quantitative and qualitative exploration of the nutrition and supportive care needs of UGI cancer survivors. A systematic review assessed the effectiveness of multidisciplinary rehabilitation for this population. Finally, a pilot study examined the feasibility and practicality of remote delivery of nutritional interventions within a multidisciplinary rehabilitation programme.

The findings from these studies observed persistent malnutrition, gastrointestinal symptoms, psychological distress, and impaired quality of life in UGI cancer survivors. Survivors and their carers reported several unmet nutrition care needs and expressed a desire for greater dietetic input and personalised, practical nutrition advice throughout survivorship. These deficits must be considered in developing survivorship care plans for UGI cancer survivors. Additionally, the findings of the present thesis indicated a need for further high-quality studies which report a core outcome set to allow conclusions on the effectiveness of multidisciplinary interventions in UGI cancer survivors. Finally, this thesis demonstrates that remote delivery of nutritional interventions is acceptable and feasible;

however, the effectiveness of this model of care needs to be examined in future studies.

Lay Abstract

During the last decades, the number of people diagnosed with upper gastrointestinal (UGI) cancers, such as oesophageal (gullet) and stomach cancer, increased in Ireland. Fortunately, with early diagnosis and advances in treatment, more people are surviving these cancers. However, survivors often experience different side effects after cancer treatment, which can impact their ability to eat and absorb food and impair their quality of life. Nevertheless, little is known about the challenges that survivors face beyond treatment in Ireland and which type of care is required to meet their needs.

In this thesis, five studies were completed to answer these questions. In the first two studies, a survey and 1:1 interviews, people diagnosed with UGI cancer were asked about their symptoms, quality of life, psychological status, and need for additional nutrition care. The findings of this study suggested that malnutrition and gastrointestinal discomfort remain an issue in survivors of UGI cancer. Impaired quality of life and psychological distress were also observed in this group of cancer survivors. Furthermore, survivors spoke of the need for clear, practical, and timely nutritional information, extensive input during the acute phase of recovery, increased follow-up throughout survivorship, support groups, and resources for caregivers.

In the third study, nutritional status, muscle mass and dietary intake of disease-free UGI cancer survivors participating in a rehabilitation study were evaluated. Results of this study showed that one in three of those UGI cancer survivors was malnourished, and one in eight had low muscle mass and strength. It was also

observed that they had a poor-quality diet that did not comply with recommendations for cancer prevention.

In the fourth study, available scientific evidence was reviewed to see if care programmes with core components of nutrition and exercise can improve food intake, physical function, and quality of life in UGI cancer survivors. The results of this study showed that little information is available about the effectiveness of nutrition and exercise in improving these factors in UGI cancer survivors, and further studies are required to answer this question.

In the fifth study, the practicality of remote delivery of a nutrition intervention to UGI cancer survivors was investigated. The findings demonstrated that this approach is practical and acceptable for participants. Further studies are needed to see if this approach can be as effective as in-person nutrition interventions.

Overall, studies completed in this thesis demonstrated that UGI cancer survivors are not returning to their normal lives after treatment. The findings of the present thesis highlighted the urgent need for tailored survivorship care programmes to address these survivors' unique needs. Additionally, further research is essential to determine the most effective survivorship care plans to meet the long-term needs of UGI cancer survivors.

Aims and Objectives of the Thesis

The overall aims of this PhD programme were to:

- Comprehensively investigate the nutrition and supportive care needs of UGI cancer survivors in Ireland.
- Review the current evidence regarding multidisciplinary intervention in UGI cancer survivors and examine the feasibility of a remote nutritional intervention within a telehealth multidisciplinary rehabilitation programme in UGI cancer.

As described below, five parallel studies were conducted to answer the research questions of the present thesis.

Chapter 3. Nutrition and Supportive Care Needs in UGI Cancer Survivors- An Anonymous Survey

Research Questions:

- What is the nutritional and psychological status and quality of life of UGI cancer survivors in Ireland?
- Do UGI cancer survivors have ongoing nutrition care needs?

Chapter 4. Nutrition Care Needs in UGI Cancer Survivors- A Qualitative Study

Research Questions:

- How do UGI cancer survivors perceive the nutrition care they receive in survivorship?
- What are the unmet nutrition and supportive care needs of survivors?
- What are the unmet nutrition and supportive care needs of carers?

Chapter 5. Nutritional Status, Sarcopenia and Dietary Intake in UGI Cancer Survivors-A Cross-Sectional Study

Research Questions:

- What is the prevalence of malnutrition and sarcopenia in disease-free UGI cancer survivors?
- Do UGI cancer survivors meet their dietary requirements?
- Do UGI cancer survivors adhere to dietary guidance for cancer prevention?

Chapter 6. The Effectiveness of Nutrition Interventions Combined with Exercise in Upper Gastrointestinal Cancers- A Systematic Review

Research Questions:

- Can multidisciplinary interventions with a core component of nutrition and exercise improve nutritional status and physical function in UGI cancers?

Chapter 7. Feasibility, Practicality and Outcomes of a Nutritional Intervention within a Telehealth Rehabilitative Programme in UGI Cancer Survivors: Results from ReStOre@Home Feasibility Study

Research Questions:

- Is virtual delivery of a nutritional intervention within a multidisciplinary rehabilitation feasible and practical in UGI cancer survivors?
- Does virtual delivery of a nutritional intervention have the potential to improve nutritional intake and status?

Dissemination of Research

First Author Published Papers:

- Sadeghi, F.; Mockler, D.; Guinan, E.M.; Hussey, J.; Doyle, S.L. The Effectiveness of Nutrition Interventions Combined with Exercise in Upper Gastrointestinal Cancers: A Systematic Review. *Nutrients* 2021, 13, 2842. <https://doi.org/10.3390/nu13082842>

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Non-Peer Reviewed Publications:

- Nutrition and exercise interventions in upper gastrointestinal cancers, knowledge gaps and direction for future studies. Fatemeh Sadeghi, David Mockler, Emer M Guinan, Juliette Hussey, Suzanne L Doyle. *Professional Nutrition & Dietetic Review*. Volume 6 Issue - 4 - Winter 2021.
- Multidisciplinary Rehabilitation in Upper Gastrointestinal Cancer Survivors – The ReStOre programme. Fatemeh Sadeghi, Linda O'Neill, Emer Guinan, Louise Brennan, Laura Smyth, et al. *Professional Nutrition & Dietetic Review*. Volume 7 Issue - 2 - Summer 2022.

Poster Presentations:

The Irish Nutrition and Dietetic Institute (INDI) Symposium 2021,

Online

- Fatemeh Sadeghi, David Mockler, Emer M Guinan, Juliette Hussey, Suzanne Doyle. The effectiveness of nutrition interventions combined with exercise in improving muscle wasting and quality of life in upper gastrointestinal cancer survivors: a systematic review.

The Irish Nutrition and Dietetic Institute (INDI) Symposium 2022,

Online

- Fatemeh Sadeghi, Louise Brennan, Laura Smyth, Linda O'Neill, Claire Timon, et al. Feasibility of an online rehabilitation programme in oesophagogastric cancer survivors.

The Irish Nutrition and Dietetic Institute (INDI) Symposium 2024,

Dublin

- Fatemeh Sadeghi, Juliette Hussey, Suzanne L Doyle. Nutritional status and unmet needs in oesophagogastric cancer survivors.

Chapter 1 Introduction

This chapter provides background information on UGI cancers, from definition, epidemiology, and pathogenesis, to diagnosis and treatment. It reviews the connection between UGI cancers and nutrition in prevention and treatment. Furthermore, it describes available evidence regarding nutrition in patients with UGI cancers and suggests future research in this area. In this chapter, the studies included in the present thesis and their objectives will be introduced.

1.1 UGI Cancer: Definition and Epidemiology

Upper gastrointestinal (UGI) cancer refers to cancers of the oesophagus, stomach, small intestine, liver, bile duct, gall bladder, and pancreas [1]. UGI cancers are among the most common cancers worldwide [2]. In 2020, UGI cancers accounted for more than three million new cases of cancer globally [3]. UGI cancers account for 26% of global cancer incidence and 35% of cancer-related deaths [4].

The present thesis mainly focuses on two common types of UGI cancer, namely oesophageal and gastric cancer. Global prevalence of oesophageal cancer has increased in recent decades, with 0.961 million cases diagnosed in 2019 and 0.54 million related deaths in 2020 [5, 6]. Despite declines in gastric cancer incidence in most regions, it remains a public health issue as the fifth most common cancer worldwide [7, 8]. Gastric cancer incidences reached >1.2 million cases in 2019, with associated mortality in >950,000 patients [9].

Cancer is the most common cause of death in Ireland and was responsible for 28% of all deaths in Ireland in 2021 [10]. Oesophageal and gastric cancer were among the 10 most common causes of cancer death during 2019-2021 (6th and 10th respectively) in Ireland [10]. The incidence of oesophageal cancer increased from 300 cases in 1994 to 532 cases in 2021, indicating an incidence rate of 8.37 per 100,000 population in 1994 and 10.62 in 2021 [10]. Despite an overall increased number of gastric cancer cases from 1994 to 2021 (484 to 577), gastric cancer incidence rates decreased in Ireland from 13.50 cases per 100,000 population in 1994 to 11.51 in 2021 [10].

1.2 Pathogenesis and Risk Factors

Squamous cell carcinoma (SCC) and adenocarcinoma (AC) are the most common types of oesophageal carcinoma, with SCC accounting for the majority of cases globally [6]. Squamous cells of the oesophagus mucosa are where SCC initiates, and it mainly affects the cervical oesophagus or upper and middle thoracic oesophagus[6]. AC often occurs in the lower oesophagus and originates from the gland cells[6]. Gastro-oesophageal reflux disease (GORD) may cause pre-malignant tissue changes, known as Barrett's oesophagus, which may progress to oesophageal adenocarcinoma [6]. AC develops in the gastroesophageal junction, where the oesophagus joins the stomach and, based on the location of their nuclei and whether extended toward the oesophagus or stomach, is classified as oesophageal or gastric cancer [6, 8]. Gastric adenocarcinoma is the most common histological type of gastric cancer types, while SCC of the stomach is a rare condition [11, 12]. Gastric cancers can be classified using different systems, such as the Lauren classification, which is widely used [13]. Lauren classifies gastric cancer into intestinal and diffuse types [13]. Intestinal types are commonly found in the proximal part (fundus) of the stomach and are associated with better prognosis [13, 14]. Diffuse-type tumours are described as poorly differentiated infiltrating lesions and are more prevalent in younger patients [14].

Several modifiable risk factors are associated with oesophageal cancer, with geographical variations depending on the dietary habits and financial status of countries [15]. While alcohol intake, smoking, low dietary intake of fruits and vegetables, obesity and gastroesophageal reflux disorder are suggested to be common risk factors of oesophageal cancer in affluent countries, drinking hot beverages, opioid use, poor oral health and poor nutritional status are reported as additional risk factors in developing counties [15-18].

Additionally, involvement of human papillomavirus (HPV) infection has been reported to increase the risk of oesophageal SCC [16, 19, 20]. Modifiable risk factors of gastric cancer include obesity, reflux, smoking, salt-preserved food, low dietary intake of vitamin A and C, consumption of salt-preserved food and products containing N-nitroso compounds and H. pylori infection [8, 21]. Additionally, food safety-related issues, such as insufficient refrigeration and contaminated drinking water, are linked to a higher risk of gastric cancer [21].

1.3 Diagnosis

Difficulty in swallowing (dysphagia) is the most common clinical presentation of oesophageal cancer, which limits dietary intake [16, 22]. Therefore, patients often report unintentional weight loss at diagnosis. Also, patients may complain of reflux, heartburn and chest pain[16]. However, these are somewhat non-specific to oesophageal cancer and are similar to symptoms of GORD [16]. Painful swallow (odynophagia), frequent nausea and vomiting, anaemia, appetite loss (anorexia), and gastrointestinal bleeding are other symptoms of oesophageal cancer [16, 23]. Similar to oesophageal cancer, unexplained weight loss, dysphagia, abdominal pain, nausea and anorexia are common presenting symptoms for gastric cancers [21, 24]. Early satiety and indigestion are also often reported in gastric cancer patients [21, 24].

Endoscopic examination is offered to patients presenting with suspicious symptoms of UGI cancers, and an oesophagogastroduodenoscopy (OGD) is the standard diagnostic procedure [21, 24]. During endoscopy, direct biopsies of oesophageal or gastric lesions are taken to determine the histological type and stage of the tumour [16, 21, 24]. In addition to OGD, a computed

tomography (CT) scan of the thorax and abdomen is performed to obtain information on metastases [16, 21, 24]. These investigations determine whether curative or palliative care is appropriate for patients[24].

1.4 Treatment

Surgical resection is still the primary curative treatment for UGI cancers [24], supplemented by either or both neoadjuvant/adjuvant chemotherapy and radiation therapy to achieve better treatment outcomes [16]. Neoadjuvant chemoradiotherapy followed by surgery is the standard treatment for patients diagnosed with locally advanced operable tumours [25-27]. This strategy reduces tumour size and improves treatment outcomes and overall survival [27, 28]. While surgery remains the cornerstone of curative therapy in UGI cancers, post-operative chemoradiotherapy is often provided to reduce the risk of the cancer recurrence, particularly for patients who have residual disease or are high risk for recurrence [29].

1.5 Surgical Resection: Procedure and Side Effects

1.5.1 Oesophagectomy

Oesophagectomy is the curative surgery for oesophageal cancer, which involves the removal of all or part of the oesophagus. Oesophagectomy is followed by GI reconstruction to restore gastrointestinal continuity [30]. As presented in Figure 1-1, reconstruction commonly involves using the stomach, jejunum, or colon to replace the resected oesophagus [30, 31].

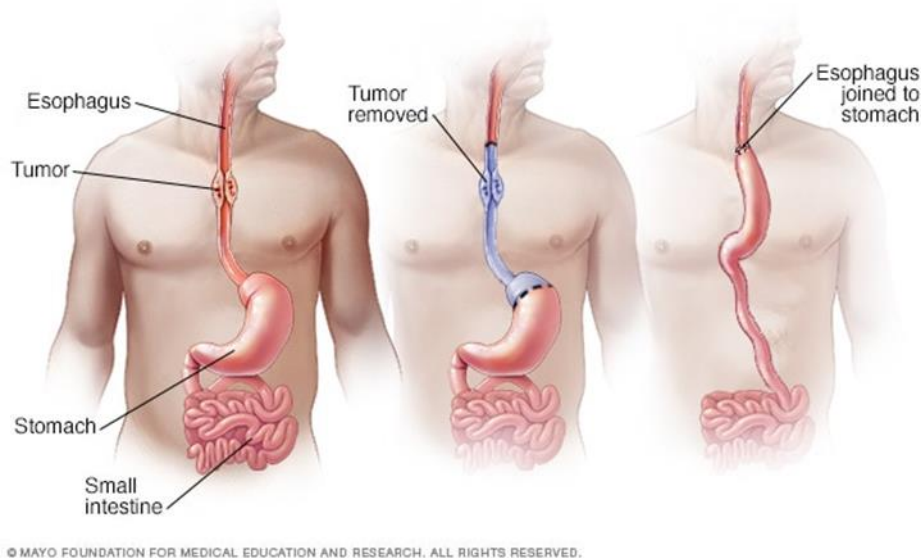


Figure 1-1. Oesophagectomy

1.5.2 Gastrectomy

Gastrectomy is the main treatment for resectable gastric tumours, as presented in Figure 1-2. Gastrectomy involves the removal of either part (partial gastrectomy) or all of the stomach (total gastrectomy), depending on the location of the tumour. Following reconstruction of the digestive tract, the oesophagus or remaining stomach will be anastomosed to the jejunum [30].

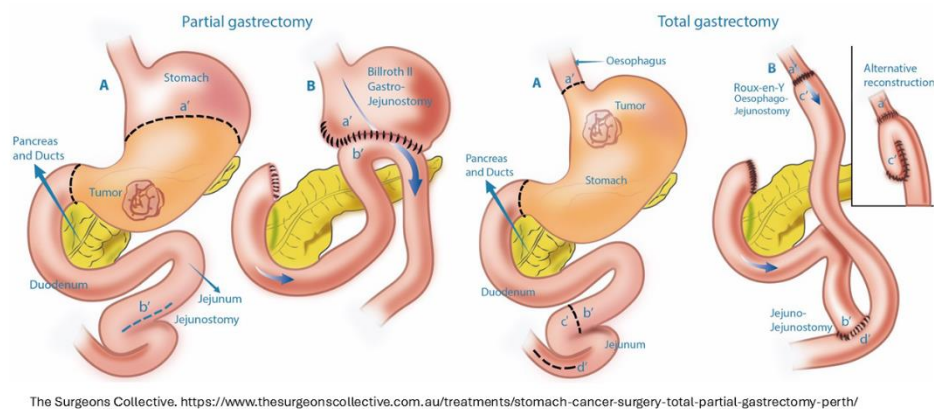


Figure 1-2. Gastrectomy

1.5.3 Side Effects of UGI Cancer Surgery

Despite advancements in surgical techniques, UGI cancer surgery is associated with significant short and long-term side effects.

Postoperative short-term complications include pneumonia, atrial dysrhythmia, anastomotic leak, conduit necrosis, chyle leaks, recurrent nerve injury, jejunostomy tube complications and bowel obstruction. These postoperative complications often require acute treatment, which involves extended hospital admission, readmissions and additional surgeries [30, 32]. Additionally, postoperative physiological changes in the GI tract can impair GI function and lead to long-term persistent side effects [30].

The vagal nerves, as part of the parasympathetic nervous system, play a crucial role in regulating gastric, intestinal, and pancreatic functions through a complex interaction between the brain and digestive system [33, 34]. Due to the high likelihood of lymph node metastasis in oesophageal cancer, vagotomy may be performed to ensure a thorough lymph node dissection [35, 36]. However, vagotomy can lead to delayed gastric emptying in the gastric conduit, resulting in early satiety, reduced appetite, weight loss, and an increased risk of reflux [30]. Additionally, vagotomy can impair pancreatic secretions and bile salt absorption, leading to diarrhoea following UGI cancer surgeries [30].

Anastomotic stricture, a common complication following oesophagectomy, is typically caused by scar tissue contraction and can lead to symptoms such as dysphagia, regurgitation, and reflux [30, 37]. Dysphagia can reduce food intake and lead to weight loss and malnutrition [38].

Dumping syndrome is another potential complication following UGI surgery, characterised by abnormal GI motility with rapid movement of food from the stomach into the small intestine [39]. While the pathophysiology of dumping syndrome remains unclear, it is thought to result from alterations in GI anatomy and function, such as reduced stomach capacity, vagotomy, gastric

denervation, and changes in gastrointestinal regulation following UGI surgeries [30, 39]. Dumping syndrome is classified into early and late forms based on the timing of symptom onset after eating. Early dumping occurs within 30 minutes of a meal due to rapid fluid shifts and excessive gastrointestinal hormone release as hypertonic gastric contents enter the small intestine. Early dumping presents with palpitations, abdominal cramps, diarrhoea, and nausea. Late dumping occurs 2–3 hours after eating and is marked by hypoglycaemic symptoms such as dizziness, lethargy, cold sweats, and hunger [30, 40].

Total gastrectomy leads to the loss of parietal cells and intrinsic factor, resulting in vitamin B₁₂ deficiency that can progress to pernicious anaemia [30]. Additionally, alterations in the gastrointestinal tract disrupt the absorption of iron and calcium, increasing the risk of iron deficiency anaemia and osteoporosis [30, 41]. Additionally, loss of the gastric pacemaker cells can also lead to delayed gastric emptying and its associated complications [30].

Overall, the physiological alterations post UGI surgical treatment have a significant impact on GI function, which subsequently can negatively impact the nutritional status, quality of life and survival of UGI cancer survivors [30].

1.6 Nutrition and UGI Cancer

1.6.1 Weight Loss, Malnutrition and Body Composition

Nutrition is a major point of discussion in cancer prevention and treatment[42]. Oesophageal and gastric cancers, in particular, are strongly linked with nutrition in terms of prevention, treatment, and survival. As described earlier in the section 1.2, several nutritional factors increase the risk of UGI cancer. Furthermore, poor

nutritional status has been associated with chemotherapy and radiotherapy toxicity, treatment discontinuation, and poor treatment outcome and prognosis in UGI cancer patients [43, 44].

As mentioned in section 1.4, the curative treatment for oesophageal and gastric cancer often involves a combination of surgical resection and either neoadjuvant or adjuvant chemotherapy and/or radiotherapy [45, 46]. While surgery is the cornerstone of treatment for resectable tumours, significant changes in the GI structure and function following oncology resection of the gastrointestinal tract can bring about several side effects, such as eating and swallowing difficulties, anorexia, reflux, nausea, vomiting, diarrhoea, dietary restrictions and malabsorption for survivors [46-49]. Thus, these nutrition-impact symptoms (NIS) are highly prevalent in UGI cancer survivors [50-52]. NIS impede oral intake and lead to inadequate energy and protein intake, contributing to unintentional weight loss [53, 54].

Unintentional weight loss is one of the major complications in UGI cancers, negatively impacting body composition, physical function, fatigue and quality of life [55, 56]. A European multicentre study in oesophageal cancer (LASER) reported ongoing weight loss in 10.4% of disease-free survivors of at least one year [57]. Another study reports persistent weight loss in 25% of long-term survivors at a median of 65.5 months post-surgery [58]. Kiyama et al. reported that after total gastrectomy, over half of patients fail to regain their pre-surgical weight [59]. This unintentional weight loss is a concern as it is a key indicator of malnutrition [60].

Malnutrition is associated with poor prognosis and survival and is thought to contribute to 10–20% of cancer patients' deaths [61-63]. Malnutrition can worsen cancer-related fatigue and frailty, limit patients' physical function and reduce their quality of life [64-

66]. Malnutrition may also be linked with psychological stress in cancer survivors [67]. Alongside malnutrition, sarcopenia, which is defined as low skeletal muscle mass accompanied by either low muscle strength or low muscle performance, is highly prevalent after UGI surgeries [68, 69]. Several possible reasons are suggested to explain the altered and abnormal body composition observed in UGI cancer survivors. Firstly, the oesophageal or gastric tumour itself may be associated with hypermetabolism and cachexia [69, 70]. Secondly, the reduced nutritional intake and malabsorption, which is associated with diagnosis, treatment and surgery, may play an important role in unintentional weight loss and muscle wasting [69, 70]. Thirdly, inactivity and poor muscle engagement following treatment could further decrease muscle mass, strength, and function [69, 70]. This can perpetuate a vicious cycle whereby reduced muscle mass and strength lead to reduced activity and further muscle loss, functional disability, and poor quality of life [71, 72]. Sarcopenia is a predictor of postoperative complications and poor survival in UGI cancer [73, 74].

Several studies have examined the prevalence of postoperative malnutrition and changes in body composition in UGI cancer survivors [53, 75, 76]. Results of these studies indicated that malnutrition and muscle wasting remain serious issues following surgical resection, even in long-term disease-free survivors [53, 76]. Despite this, the long-term nutritional consequences of surgery are often overlooked in cancer care [77]. Active and extended nutritional assessment and intervention should be considered after surgical treatment of oesophageal cancer for early detection and management of malnutrition [78]. However, there is a significant lack of data in Ireland regarding the prevalence and extent of postoperative malnutrition and sarcopenia in UGI cancer survivors. Collecting this data is essential for planning survivorship care tailored

specifically to the needs of UGI cancer survivors. Thus, Chapter 5 of the present study aimed to examine the prevalence of malnutrition and sarcopenia in a cohort of UGI cancer survivors.

1.6.2 Dietary Adequacy Following Surgery for UGI Cancers

As described in section 1.6.1, UGI cancer survivors often suffer from NIS, which can result in inadequate dietary intake. However, only a small number of studies to date have evaluated dietary intake in oesophageal and gastric cancer survivors [53, 79-83]. A study by Ryan et al. reported that at discharge from the hospital, patients met 70% and 65% of their energy and protein requirements, respectively [79]. Haverkort et al. reported that at 12 months post-oesophagectomy, 76% and 93% of the patients met their energy and protein requirements, respectively [82]. In the Ludwig et al. study, 78% of patients were able to meet or exceed their daily energy requirements at a mean of 34±22 months after oesophagectomy [80]. In a study by Grace et al., 42% of oesophagogastric cancer survivors were meeting their estimated energy requirement at 12 months post-surgery [84]. While the percentage of participants meeting their energy and protein requirements can be impacted by calculating nutritional requirements using different methods and assessing patients at various time points post-surgery, all results indicated suboptimal intake of energy and protein post-treatment [53, 79-82].

Inadequate intake of micronutrients has also been reported in previous studies. The study conducted by Haverkort et al. reported insufficient intake of folic acid, vitamin D, copper, calcium and vitamin B₁ following oesophagectomy [82]. Also, Baker et al. reported

inadequate intake of selenium, zinc, magnesium and vitamin A after oesophagectomy and total gastrectomy [81].

To date, no study has examined the nutritional adequacy of UGI cancer survivors in Ireland. Thus, the study in Chapter 5 aimed to assess nutrient intake and dietary quality in a cohort of UGI cancer survivors. The result of this study can inform the nutritional interventions required in this cohort of cancer survivors.

1.7 UGI Cancer Survivorship

Advances in cancer diagnosis and treatment have led to higher survival rates. Recent data reports that at the end of 2021, approximately 215,000 cancer survivors were alive in Ireland, which indicates that 1 in 23 Irish adults is a cancer survivor [10]. The Irish National Cancer Registry reported significant improvements in the 5-year net survival of oesophageal and gastric cancer. According to its latest annual report published in 2023, 5-year net survival of oesophageal and gastric cancer increased by 11.6% and 14.5%, respectively, between 1998 and 2018 [10]. At the end of 2021, 1651 individuals diagnosed with oesophageal cancer and 2571 diagnosed with gastric cancer were still alive in Ireland [10].

Cancer survivorship begins at the time of diagnosis and continues throughout life and includes those currently living with cancer and who are cancer-free [85]. Despite substantial improvement in survival rate, cancer survivors often do not return to their pre-diagnosis health and suffer from long-term treatment side effects such as malnutrition, impaired physical function, and psychological problems [76, 86, 87]. These complications can impair the quality of life in survivorship [76, 86, 87]. Long-term impairment of quality of life after treatment of oesophageal cancer may persist even 10 years after surgery [88]. Thus, ongoing care and long-term

follow-up are required to address the side effects of UGI cancer treatment on survivors' physical and psychosocial needs and improve their overall quality of life [89].

Survivorship care is defined as the provision of healthcare services tailored specifically for individuals who have survived cancer or are living with cancer until the end of life [90]. The US Institute of Medicine (IOM) outlined key elements of survivorship care as (1) preventing cancer recurrence, new cancers, and late effects of treatments; (2) monitoring for recurrence, new cancers, and physical or psychological impacts; (3) addressing treatment-related issues, including symptom relief and practical support; and (4) ensuring coordination between cancer specialists and primary care providers to meet all the survivor's needs [91].

Current survivorship care is predominantly consultant-led and focused on monitoring for cancer recurrence, leaving many of the survivors' needs unaddressed as it inadequately responds to the broader medical and psychosocial consequences of cancer and its treatment [92]. Additionally, with growing numbers of cancer survivors, consultant-led care models are becoming unsustainable due to the shortage of healthcare professionals to meet the demand [92]. Hence, the traditional model of follow-up care led by oncologists needs to be restructured to meet the unmet needs and demands of the growing population of post-treatment cancer survivors [93]. While several countries, like the United States, Canada, and the UK, have established national guidelines for survivorship care, there are no specific international guidelines for survivorship care [94-97].

The importance of developing and promoting effective survivorship care pathways in Ireland has been emphasised in the Third National Cancer Strategy [98]. Recommendation 41 of the Ireland National Cancer Strategy 2017-2026 highlighted the

requirement to conduct a National Cancer Survivorship Needs Assessment to ascertain the most suitable model of survivorship care in Ireland [98]. Subsequently, the National Cancer Survivorship Needs Assessment was completed to review services available to cancer survivors and their unmet needs in Ireland [85]. Results of this need assessment were reported in 2019 and showed that most cancer survivorship care is provided through follow-up clinics in acute settings and largely focuses on monitoring for cancer recurrence [93]. Hence, it often overlooks or fails to fully address the broader physical and psychological needs of survivors [93]. The assessment of cancer survivors' unmet needs showed that many cancer survivors had unmet care needs, including management of physical complications (pain, fatigue, and sleep disturbances), psychological burden, access to support services, and information deficits [99]. Additionally, some cancer-specific needs were identified, including management of urinary incontinence and erectile dysfunction in men with prostate cancer, bowel dysfunction in colorectal cancer survivors and eating difficulties in head and neck cancer survivors [99].

Data from the National Cancer Survivorship Needs Assessment highlighted the necessity for improved survivorship care to meet cancer survivors' complex and dynamic needs, which subsequently led to the proposal of the ALLIES model of cancer survivorship care, which is presented in Figure 1-3. The ALLIES survivorship care plan aims to improve the quality of life for cancer survivors, facilitate the transition from active treatment to survivorship, and ensure a coordinated approach to cancer care [85].

Despite increased efforts in developing national models of care for survivorship, there remains a significant lack of research on the needs of UGI cancer survivors [99]. Additionally, as survivorship needs and their associated burdens are likely impacted by

deprivation status, more information is needed on how unmet needs relate to survivors' socio-demographic characteristics to tailor services to individual needs [99].

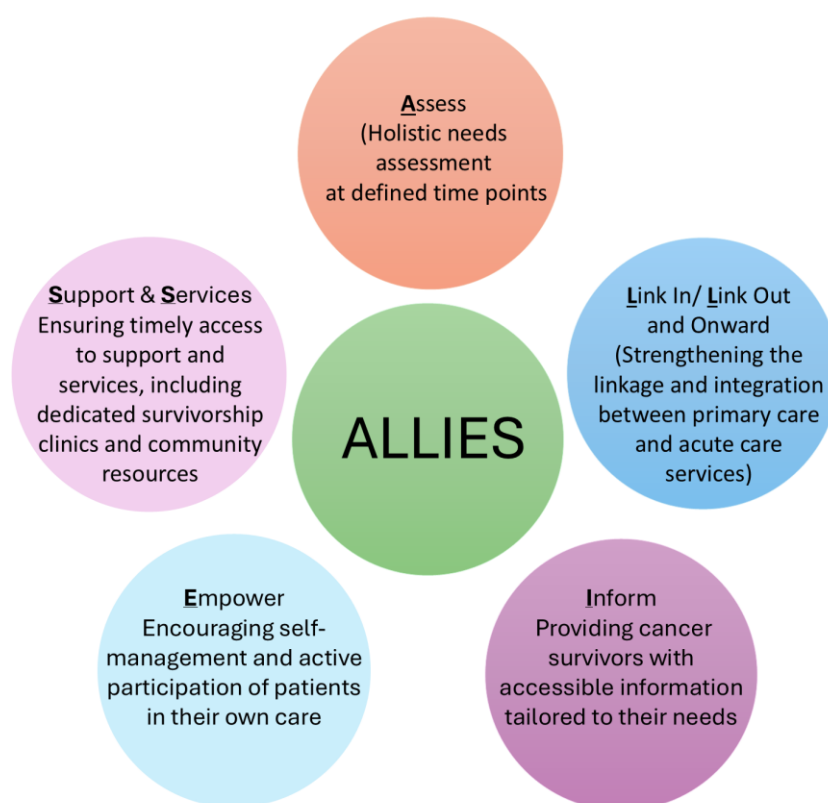


Figure 1-3. ALLIES model of cancer survivorship care

Obtaining data on the survivorship needs of UGI cancer survivors and identifying subgroups who are most at risk is an essential first step in creating effective survivorship care services [99]. Thus, in Chapter 3 and 4 of the present thesis, the unmet supportive care needs of UGI cancer survivors in Ireland were quantitatively and qualitatively assessed, which can provide useful insights into the survivorship needs of this cohort of cancer survivors.

1.8 Nutrition Care Needs in UGI Cancer Survivors

As discussed in section 1.6, UGI cancer survivors often experience severe complications following treatment. Thus, they require a specific survivorship care programme tailored to their unique medical, nutritional, physical and psychosocial needs [99, 100]. Nutrition should be considered an essential part of survivorship care in UGI cancers due to the high prevalence and severity of nutritional complications in survivors and the benefits of nutritional intervention in symptom management and improving nutritional status, physical function, fatigue, and quality of life [101-105]. However, understanding the prevalence and extent of nutritional complications, along with exploring patients' insights and preferences regarding nutrition care, is crucial for developing and delivering effective survivorship care [92].

To date, there is limited evidence available regarding the unmet nutrition needs of survivors of rarer or more aggressive types of cancer in Ireland, as the majority of survivorship research is focused on the most common cancers such as breast, prostate and colorectal [99]. Despite some similarities in complications and unmet needs in cancer survivors, some complications are cancer-specific (i.e., swallowing difficulties and dumping syndrome in UGI cancer) [99]. Therefore, the unmet needs of cancer survivors vary due to the distinct challenges they face post-treatment [99]. Thus, further studies are needed to achieve a more detailed and in-depth understanding of UGI survivors' care needs, identify the support needed for managing their symptoms, and determine the optimum dietetic strategies to meet these needs. Hence, the qualitative study described in Chapter 4 aimed to investigate the UGI cancer survivors' experience with nutrition care in Ireland and their unmet nutrition care needs following UGI cancer diagnosis by a qualitative approach.

Caregivers and family members play a crucial role in supporting patients throughout cancer treatment, from co decision-making to managing side effects and daily living [106-108]. However, providing care to a loved one with cancer can be distressing and disrupt carers' careers and daily routines [106]. Three Irish and UK-based studies reported carers strain and psychological distress in carers of oesophageal cancer survivors [109-111]. Carers are challenged by new roles and responsibilities such as preparing special meals, monitoring food intake and weight change, contributing to caregiver burden [109, 112]. Thus, understanding carers' insights and experiences of nutrition care may inform the optimum design of supportive nutrition care services to address complex survivorship needs to meet the needs of both survivors and their caregivers [113]. Hence, carers of UGI cancer survivors were also recruited in the qualitative study in Chapter 4 to investigate their experience and unmet needs, particularly regarding nutrition care in survivorship in Ireland.

1.9 Clinical Guideline and Nutrition Care Pathway for UGI Patients

Several national and international guidelines provide recommendations for nutrition in cancer [114-117]. They frequently recommend early malnutrition screening and assessment at diagnosis and provide guidance on nutritional interventions in the pre and postoperative period, during neoadjuvant and adjuvant therapy, and for management of treatment side effects. Also, several specialised clinical guidelines are available for the treatment and management of UGI cancers [118-122]. These guidelines emphasise the importance of integrating nutrition care as a critical component of comprehensive cancer care and recommend timely and

individualised nutritional care [118-122]. They also provide guidance on nutritional interventions for UGI cancer patients, from treatment to survivorship and palliative care [118-122]. All guidelines stress the importance of ongoing, individualised follow-ups with dietitians but often leave the frequencies or extent of follow-ups to clinical judgment and the patient's condition.

In Ireland, the National Clinical Guideline No. 19, developed by the National Cancer Control Programme (NCCP), primarily focuses on the diagnosis, staging, and treatment of patients with oesophageal or oesophagogastric junction (OGJ) cancer [123]. This guideline is intended for healthcare professionals involved in UGI cancer care, ensuring standardised and evidence-based practices to improve patient outcomes [123]. This guideline recommends early referral to a specialist dietitian for all patients as good clinical practice [123]. It suggests the use of the enhanced recovery after surgery (ERAS) programme for patients with oesophageal or oesophagogastric junction cancer and indicates the high-quality evidence for early enteral nutrition (vs. late and parenteral) as part of ERAS [123]. However, this guideline does not provide details on specific dietary interventions or protocols, focusing instead on the importance of involving dietitians in the multidisciplinary care team [123]. While this guideline emphasises the importance of a multidisciplinary approach in managing patients, including ongoing assessment of patient needs throughout their illness, it does not outline specific recommendations for survivorship care [123].

1.10 Multidisciplinary Rehabilitation in UGI Survivorship

As previously noted in section 1.6, curative surgery for UGI cancer is accompanied by physical and nutritional impairment, which

can reduce the quality of life and survival [88]. Published data have demonstrated numerous benefits of nutrition care and physical activity for cancer survivors. These include improved physical function and quality of life, reduced side effects and treatment toxicity, symptom management, and supporting survivors to return to pre-treatment health and physical status [124-128]. Therefore, it is suggested that combined nutrition and exercise intervention may have synergic effects in improving outcomes in survivors and offer a more comprehensive and holistic approach to rehabilitation [129]. UGI cancer survivors, in particular, require such holistic care to address their complex survivorship needs [130].

Multidisciplinary rehabilitation has been the centre of attention in cancer survivorship due to its potential to address the complex and distinct needs of cancer survivors [131]. However, despite this growing interest, data on the effectiveness of multidisciplinary programmes in UGI cancer survivors, particularly those centred around nutrition and exercise, remain limited and inconsistent [132-135]. Thus, a systematic review was conducted to evaluate the current evidence in this area. This systematic review, described in Chapter 6 of this thesis, aimed to summarise the available data, identify knowledge gaps, highlight limitations in previous studies, and ultimately suggest directions for future research on multidisciplinary rehabilitation in UGI cancer survivors [136].

1.10.1 Multidisciplinary Rehabilitation for UGI Cancer Survivors in Ireland - The ReStOre Programme

The ReStOre programme, a multidisciplinary rehabilitation programme designed by the Exercise Oncology Research Group for UGI cancer survivors, consisted of 12 weeks of supervised and home-

based exercise, individual dietetic counselling and group education [137]. The ReStOre programme demonstrated high feasibility and acceptability among oesophageal cancer survivors [137]. This feasibility study also reported clinically significant improvements in functional performance and QOL in oesophageal cancer survivors [137]. Learnings from this pilot study led to the incorporation of a resistance training component into the intervention to counteract the effects of sarcopenia in UGI cancer survivors [137]. The effectiveness of this modified version of the ReStOre programme was subsequently tested in a randomised controlled trial (RCT), which showed improved cardiorespiratory fitness in disease-free survivors post-oesophagogastric cancer surgery [132]. Importantly, despite increased exercise participation, the ReStOre programme did not lead to weight or muscle loss, emphasising the benefits of a rehabilitation approach that integrates exercise with personalised dietary guidance [132].

Subsequently, in order to address the limitations and methodological weaknesses of previous rehabilitation studies, the ReStOre II study was designed to further evaluate the effectiveness of multidisciplinary rehabilitation in a large cohort of UGI cancer survivors [138]. However, as previously noted, recruitment for the study was delayed by two years due to the COVID-19 restrictions. In response to the COVID-19 pandemic, the Exercise Oncology Research Group developed and conducted the ReStOre@Home study, a remotely delivered version of ReStOre II [139, 140]. Telehealth is a new mode of delivery in nutrition care; thus, the feasibility, practicality, and potential challenges of delivering these interventions to UGI cancer survivors must be explored [141-145]. The implementation of the remote nutritional intervention within the ReStOre@Home study was examined and described in Chapter 7 of the present thesis.

1.11 Overall Thesis Aim

Collectively, the studies completed during the present PhD programme aimed to examine in depth the nutritional challenges facing UGI cancer survivors and also explore nutrition interventions to target those challenges.

The nutritional status and nutrition care needs of UGI cancer survivors and their carers were investigated to achieve a better understanding of UGI cancer survivorship challenges and survivors' unmet needs. The current evidence regarding the effectiveness of multidisciplinary intervention in addressing survivorship recovery in UGI cancers was critically evaluated. Finally, the feasibility and challenges of delivering remote nutritional interventions within a multidisciplinary rehabilitation programme and its potential to improve nutritional status and complications was explored. The overall research questions of this thesis and how they were addressed are illustrated in Figure 1-4.

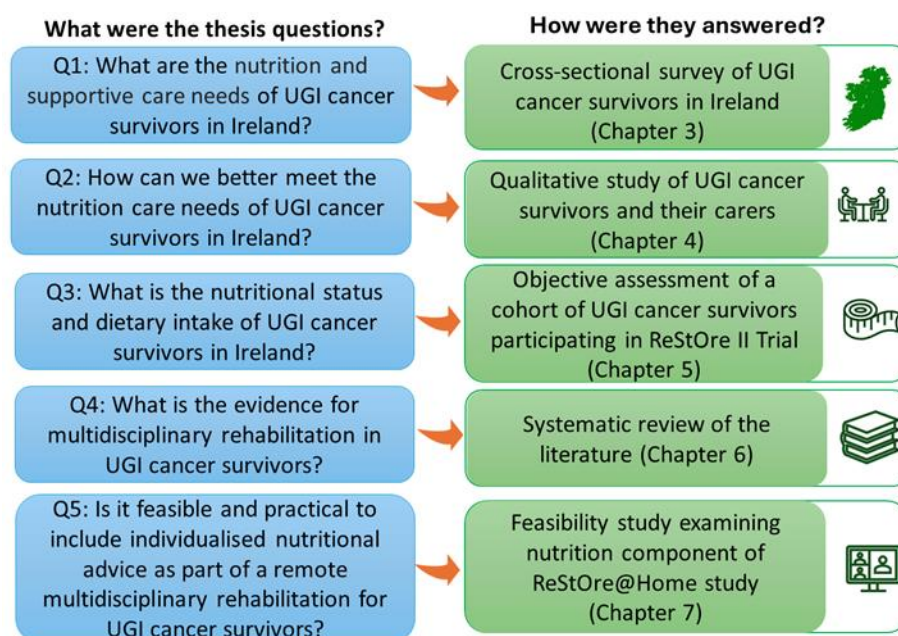


Figure 1-4. Research questions of this thesis

Chapter 2 Methodology and Investigator's Contributions

This chapter provides a comprehensive overview of the methodologies used in conducting research studies within this thesis. However, specific details of the methods used in each study are described in relevant chapters. The present chapter aims to describe the process of designing studies, obtaining ethical approvals, recruitment, data collection, nutritional and functional assessments, statistical analysis, and information on funding of studies. Also, details of my contribution as the lead investigator in the included studies are described in the present chapter.

2.1 Investigator's Contribution

In the studies described in Chapter 3, Chapter 4, and Chapter 6, I conducted all elements of the research and composed the final thesis.

I contributed to conducting the ReStOre@Home study, Chapter 7, as a member of the Exercise Oncology Research Group. I was involved in participant screening and recruitment. I provided the dietetic intervention to participants throughout the ReStOre@Home study, collected dietary intake data, and conducted anthropometric and body composition assessments. I was responsible for data entry and analysis of dietetic outcomes. Also, I contributed as an author in preparing research papers and conference posters derived from this study.

It should be noted that data used in the cross-sectional study in Chapter 5 were initially collected as part of a large clinical trial, the ReStOre II study, designed by the Exercise Oncology Research Group. In this study, I was involved in participant screening and recruitment by screening the database of the UGI Cancer Registry at St James's Hospital, seeking clinical clearance, posting participant information leaflets (PILs) and study invitations, and following up and scheduling assessment visits. Also, I was responsible for collecting dietary intake data and anthropometric assessments, sharing this task with two other research assistants (Ms Sanela Begic and Ms Fiona Murphy) within the Exercise Oncology Research Group. I completed all data entry and analysis and described the results in Chapter 5. These research studies were conducted between March 2020 and March 2024.

2.2 Ethical Approvals

Ethical approval was obtained from St James's Hospital/Tallaght University Hospital Joint Research Ethics Committee and Trinity Faculty of Health Sciences Research Ethics Committee prior to conducting studies. Ethical approval letters are included in Appendix I. All studies were conducted in accordance with the Declaration of Helsinki (1964) and its later amendments.

2.3 Informed Consent

Written informed consent was obtained from individuals who participated in the qualitative interviews (Chapter 4), cross-sectional study (Chapter 5, sub-study of ReStOre II [138]), and ReStOre@Home (Chapter 7). Participants in the anonymous survey (Chapter 3) were asked to provide consent by agreeing with two statements of consent at the beginning of the survey questionnaires, which indicated that they had read and understood the participant information leaflet (PIL) and consent to participate in this anonymous survey. Of note, the online survey setting has been modified at Qualtrics not to record any IP address or respondent's location to ensure the anonymity of participants.

All participants were provided with a copy of the PIL describing details of the research study they were invited to participate in, as well as relevant contact information for researchers and data protection officer. Copies of the PILs are included in the appendices. For studies in Chapter 4, Chapter 5, and Chapter 7, a reflection period of seven days was considered after posting the study invitations to eligible participants before a follow-up telephone call to obtain initial verbal consent. In all cases, participants were advised that participating in research is entirely voluntary and a

decision not to consent would have no adverse consequences or affect future medical treatment. Participants were advised that consent could be withdrawn at any time except after completing the anonymous survey, as respondents' data were not identifiable. A copy of the signed consent form was provided to study participants.

2.4 Data Management

Research data was collected and stored pseudonymously for studies in Chapter 4, Chapter 5, Chapter 7, and anonymously for Chapter 3. Personal and identifiable information, if collected (for the purpose of contacting individuals), were pseudonymised, and key codes were stored in paper format in a locked cabinet and access restricted room in the Trinity Centre for Health Sciences; only the research team involved in the studies could access these data. Electronic pseudonymised data keys were also stored onto password-protected Microsoft Word documents as a backup to the paper data keys. Pseudonymised interview recordings and transcriptions were stored onto password-protected audio files and Microsoft Word documents. Quantitative data were stored onto a password-protected Microsoft Excel file. All electronic data were stored on a password-protected encrypted Trinity laptop. Backups were stored to TCD OneDrive password-protected files and onto a password-protected hard drive stored in a locked room at the Trinity Centre for Health Sciences site. Consent forms, key codes and any other data in paper formats were stored in a locked cabinet in an access-restricted room in the Trinity Centre for Health Sciences, and only investigators could access it.

2.5 Study Design

Five separate studies were completed to achieve the objectives of this thesis. This included three cross sectional studies, presented in Chapter 3, Chapter 4 and Chapter 5, a systematic review in Chapter 6 and a single arm feasibility study described in Chapter 7. The scientific process and rationale for designing each study are described in the relevant chapters. It should be noted that the ReStOre II and ReStOre@Home studies were designed by the Exercise Oncology Research Group [138, 146].

2.6 Assessments

A variety of quantitative and qualitative assessments were carried out across the studies in this thesis. This section describes the procedures for completing assessments. The frequency and schedule of individual assessment components in the different studies are described in their respective chapters.

2.6.1 Anthropometric Measurements

2.6.1.1 Weight and Height

Weight and height were measured following standard procedures[147] using a SECA digital medical scale and stadiometer. Study participants were asked to remove footwear, headgear, heavy clothing such as coats and jackets and any heavy objects from pockets. Height and weight were recorded to the nearest 0.1kg/0.1cm.

2.6.1.2 Body Mass Index

Body mass index (BMI) was calculated by dividing weight in kg by height in metres squared. WHO classification was used to interpret the calculated BMI as presented below in Table 2-1.

$$\text{BMI} = \text{Weight}(\text{kg}) \div \text{Height}^2(\text{m})$$

Table 2-1. BMI classification

BMI	Nutritional status
Below 18.5	Underweight
18.5–24.9	Normal weight
25.0–29.9	Overweight (Pre-obesity)
30.0–34.9	Obesity class I
35.0–39.9	Obesity class II
Above 40	Obesity class III

2.6.1.3 Waist Circumference

Waist circumference was measured using a non-stretch flexible tape placed over a light layer of clothing. Participants were asked to wrap the tape around their waist, and then the assessor positioned the tape at the midpoint of the last rib and the top of the hip bone (iliac crest), horizontally across the back and front and parallel with the floor. Participants were asked to breathe normally, and the measurements were noted after normal expiration to the nearest 0.1cm. Waist measurements were completed in duplicate, and the average was used for data analysis.

2.6.1.4 Mid-Upper Arm Circumference

Mid-upper arm circumference was measured using a non-stretch flexible tape. Participants were asked to stand and flex the left arm to 90 degrees at the elbow. The midpoint of the arm (midpoint between the lateral acromion and distal olecranon) was identified. Then, participants were asked to relax their arms, and the measurement was taken in duplicate and recorded at the nearest

0.1cm. The average of two recorded measurements was used in data analysis.

2.6.2 Body Composition Analysis

Bioelectrical Impedance Analysis (BIA) was used to assess body composition. BIA measures body composition by determining the individual's resistance to a weak electric current, allowing for the estimation of fat mass (FM) and fat-free mass (FFM) through empirically derived equations [148, 149]. BIA is commonly used in oncology research as a non-invasive, rapid and cost-effective technique for objective assessment of body composition[148]. BIA is widely used for estimating body composition and is a recommended tool for assessing low muscle mass phenotypic criterion within the Global Leadership Initiative on Malnutrition (GLIM) criteria for the diagnosis of malnutrition [150, 151]. BIA is also an appropriate and reliable technique for evaluating body composition in oncology [148]. Measurements obtained through BIA have demonstrated significant clinical importance in preoperative risk assessment and serve as a prognostic tool for cancer survivors [148]. BIA-derived low muscle volume has been shown to be an important prognostic marker for patients undergoing oesophagectomy [152]. However, BIA has certain limitations which need to be acknowledged. Its accuracy can be influenced by factors such as hydration status, recent food intake, physical activity, and limb length; potentially introducing variability in measurements[148]. Moreover, BIA provides indirect estimates of body composition, compared to computed tomography (CT) and magnetic resonance imaging (MRI) which offer precise imaging and can directly assess muscle and adipose tissue distribution[153, 154]. Nonetheless, these methods are often expensive, not routinely conducted, and may expose patients to radiation (as in the case of CT), which makes them difficult to access[148].

BIA was selected to assess body composition in the present thesis due to its accessibility, ease of use, and minimal burden on participants. Furthermore, as discussed above, it is considered an appropriate method for evaluating body composition in oncology as BIA-derived measurements have demonstrated significant clinical value, in patients with cancer.

BIA was performed using the SECA mBCA 515 (Seca, Hamburg, Germany). Participants were screened for contraindication to BIA, including electronic implants (pacemaker/implantable cardioverter defibrillator) and metallic joint replacements, e.g., total hip and total knee replacement. Participants were asked to empty pockets and remove heavy clothing, footwear (shoes, socks, tights), and jewellery. Then, participants were instructed to step on the SECA mBCA, positioning their feet to touch metal electrodes on the base of the machine and stand still until their weight was calculated. Participants were then asked to hold the pair of hand electrodes as instructed by assessors and stand still until the BIA analysis was complete (usually about 10-15 seconds). After completing the BIA analysis, participant's date of birth, gender, ethnicity, and physical activity level (PAL) as per SECA mBCA instruction were inputted to assign BIA measurements to participants. The BIA report included the following measures; body weight, BMI, fat mass, fat-free mass, % fat mass, % fat-free mass, segmental skeletal muscle, skeletal muscle index, hydration (total, intracellular and extracellular) and phase angle.

2.6.3 Functional Assessments

2.6.3.1 Hand Grip Strength

Hand Grip Strength (HGS) is widely used for assessing muscle strength and is a reliable test for assessing physical function and predicting postoperative complications and survival in cancer

patients [155-157]. Hand-grip strength is an inexpensive, quick, and highly predictive tool for assessing both mortality and morbidity in oesophageal cancer [157, 158]. The Global Leadership Initiative on Malnutrition (GLIM) recommends using HGS for evaluating muscle function as an essential component of nutritional and functional assessments in patients [151].

However, it should be noted that HGS captures upper limb strength only and may not represent total body muscle strength[159, 160]. Despite this, HGS remains a low-cost, accessible tool with strong predictive value in gastrointestinal (GI) cancers [161].

HGS of the dominant hand was measured using a Jamar digital dynamometer. Participants were asked to remain in a sitting position in a chair without armrests, with elbow at 90 degrees. HGS was measured three times, allowing one minute rest between attempts. The highest value of three measurements, recorded in kilograms, was considered for data analysis.

2.6.3.2 Short Physical Performance Battery

Physical performance was assessed using the Short Physical Performance Battery (SPPB), which is a reliable and valid measure of physical functioning in cancer survivors [162, 163]. Clinicians are advised to consider using the SPPB to assess physical function in older cancer survivors because of its high reliability [163]. Changes in SPPB scores could predict survival rates, functional decline, mortality, and treatment-related complications among cancer survivors [164]. SPPB is an objective test which includes three lower extremities tests: gait speed, sit to stand and standing balance test. Each test is scored out of four, with a total score ranging from 0 to 12. Higher scores indicate better physical functioning [162]. To perform this test, participants were asked to stand with their feet together in the side-by-side, semi-

tandem, and tandem positions for 10 seconds to determine balance. To assess gait speed, participants were asked to walk a 4-meter course. For repeated chair stands test, participants were timed to rise from a chair and return to the seated position 5 times without using their arms. A copy of test instructions and scoring is included in Appendix IV.

As noted above, SPPB primarily assesses lower extremity performance and may overlook upper body strength or other functional domains. To address these limitations, the SPPB was combined with HGS measurement in the present thesis to provide a more comprehensive evaluation of overall physical function and muscle strength.

2.6.4 Dietary Intake and Assessment of Malnutrition Risk

2.6.4.1 Dietary Recall

Dietary intake was assessed by collecting three 24-hour food recalls using the Foodbook24 tool [165]. Foodbook24 is a web-based tool used for collecting 24-hour dietary recall data. It has been developed for the Irish adult population, and its validity and user acceptability have been demonstrated in previous studies [165]. A registered dietitian trained participants in using the Foodbook24 tool to self-record their 24-hour dietary recall. In some instances, the dietitian inputted the details directly while interviewing the participant. It has been observed that these two methods are comparable in terms of nutrient and food intake data derived from these methods [166]. The 24-hour dietary intake was logged in the Foodbook24 tool, and the mean dietary intake was calculated using Foodbook24 output.

While 24-hour recall is widely used to collect dietary intake data in clinical and research settings, it is also subject to several limitations, including recall bias, underreporting or overreporting, interviewer bias, and day-to-day variability in intake which can compromise the accuracy of collected data[167]. To address these, three non-consecutive 24-hour recalls were collected to better capture usual intake. Moreover, the Foodbook24 tool was used to facilitate standardise data entry and minimise interviewer bias[168, 169].

2.6.4.2 Simplified Nutritional Appetite Questionnaire

The Simplified Nutritional Appetite Questionnaire (SNAQ) has been shown to predict weight loss in community-dwelling adults and can be used as a malnutrition screening tool in cancer patients [170, 171]. SNAQ is a short, self-administered questionnaire including four questions about appetite, satiety, food taste, and number of meals per day [170]. Total SNAQ scores range from 4 to 20, and a score ≤ 14 predicts malnutrition and unintentional weight loss within 6 months [170]. The SNAQ was used in Chapter 5 and Chapter 7 for identifying the risk of malnutrition.

It should be noted that, the subjective nature of the SNAQ may introduce various forms of bias due to inter- and intra-individual variability in the perception of sensory factors such as appetite, food taste, and satiety[172, 173]. Additionally, SNAQ does not assess actual intake and cannot be substituted for a full nutritional assessment. To address these limitations, SNAQ was used in conjunction with other clinically relevant measures in this thesis, including anthropometric measurements, body composition, dietary intake, and GI symptoms to allow a more holistic and accurate assessment of nutritional status and malnutrition risk.

2.6.4.3 Malnutrition Screening Tool

The Malnutrition Screening Tool (MST) was used to assess participants' malnutrition risk in the Nutrition Care Needs Survey (Chapter 3) [174]. MST has been reported as a validated tool for predicting malnutrition risk in oncology [175, 176]. MST is an easy and rapid screening tool which includes two questions, examining unintentional weight loss and reduced appetite and nutritional intake. A score of 2 or higher suggests a risk of malnutrition [174].

The MST is a useful and valid malnutrition screening tool and offers practical advantages such as simplicity and rapid administration[174]. However, it should be acknowledged that MST is a screening tool to identify patients who require a full nutritional assessment and is not intended to diagnose malnutrition[177].

2.6.5 Quality of Life and Symptom Assessment

2.6.5.1 European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire

Quality of life was assessed using the European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC-QLQ-C30 version 3.0). The EORTC QLQ-C30 is a reliable and valid tool designed to assess health-related quality of life in patients with cancer [178]. This tool includes 30 questions and consists of five functional domains (physical, role, cognitive, emotional, and social), eight symptom domains (fatigue, pain, nausea/vomiting, constipation, diarrhoea, insomnia, dyspnoea, and appetite loss), as well as global health/quality-of-life and financial impact [178]. To score the EORTCQLQ-C30, the average of the items included in each domain was calculated as a raw score. Raw scores were standardised using a linear transformation as per the developer's manual to calculate final scores, which ranged from 0 to 100 [179]. In functional

domains, a higher score indicates greater function, whereas in symptom domains, a higher score is indicative of a higher symptom burden [179]. A higher score in the global health status scale represents a better quality of life [179]. A minimal clinically important difference (MCID) of ≥ 10 points was considered to determine clinically meaningful differences in EORTC QLQ-C30 scores compared to the general population [180, 181]. Also, the thresholds for clinical importance (TCI) were considered to identify clinically important symptoms [182].

Despite its demonstrated validity, reliability, and widespread use in oncology, the EORTC QLQ-C30, like many HRQoL measures, does not account for broader determinants of patients' quality of life such as personality, socioeconomic status, educational background, or the availability of formal and informal support [183]. Nevertheless, it was selected for the present thesis due to its practical applicability in assessing multidimensional quality of life among cancer survivors.

2.6.5.2 Hospital Anxiety and Depression Scale

The Hospital Anxiety and Depression Scale (HADS) questionnaire was used to evaluate anxiety and depression in participants in the Nutrition Care Needs Survey (Chapter 3) [184]. HADS has been reported to be a valid tool for assessing anxiety disorders and depression [185] and can accurately screen for psychosocial distress in cancer patients [186]. HADS is a 14-item questionnaire containing seven questions related to anxiety and seven questions related to depression [185]. A HADS score of ≥ 11 indicates definite cases of anxiety or depression, scores between 8 and 10 suggest a probable case, and if the score is ≤ 7 , the respondent does not have anxiety or depression.

Despite the validity and reliability of the HADS, it is also important to recognise that self-reported psychological distress may not always indicate the clinical presence of anxiety or depressive disorders. A false positive may be due to acute stress reactions, and a false negative could be due to social desirability bias, and under-reporting of psychological distress[187].

The HADS was used in the studies in this thesis as a screening tool to identify individuals who may be at risk and warrant further psychological evaluation. Given the limited number of studies assessing the psychological status of cancer survivors, the use of a valid and widely recognized tool like HADS can serve as an important first step in recognising unmet psychosocial needs and informing holistic survivorship care.

2.6.5.3 Gastrointestinal Symptoms

Gastrointestinal symptoms were measured using the Gastrointestinal Symptom Rating Scale (GSRS), a 15-item questionnaire representing five domains assessing reflux, abdominal pain, indigestion, diarrhoea and constipation. Completing the GSRS takes approximately 3-5 minutes and asks respondents to recall symptom severity during the last week. It employs a Likert-type scale with seven graded points, where 1 indicates the absence of problematic symptoms, while 7 shows highly problematic symptoms. Consequently, higher GSRS scores indicate more severe and problematic gastrointestinal symptoms. The reliability and validity of the GSRS as a self-administered tool is well documented, and normative values for the general population are available [188-192].

However, despite these strengths, the GSRS is not without limitations as like other subjective tools, its reliance on self-reporting

and a 1-week recall period may introduce recall bias or fail to reflect symptom variability over time[193]. Nonetheless, the GSRS was used in studies in the present thesis due to its practicality, low respondent burden and ability to capture a broad range of core gastrointestinal symptoms relevant to UGI cancer survivors.

AstraZeneca, who possesses and licenses the GSRS, were consulted to seek advice on GSRS scoring and to deal with missing items, as some participants left some questions blank. Therefore, following AstraZeneca instruction, the mean value for the items in each dimension was calculated to score the GSRS, and in the event of missing data, if the missing data were less than 50% of the item scores within a dimension, the missing items were imputed using the mean score of the non-missing item scores. However, if more than 50% of the item scores were missing, no imputation was performed, and the dimension score was excluded from the analysis. Of note, the licence agreement for using the GSRS questionnaire in the Nutrition Care Needs Survey (Chapter 3) has been formally executed between FS and AstraZeneca company. The Licence Agreement is included in Appendix V.

2.6.6 Physical Activity

The International Physical Activity Questionnaire Short form (IPAQ-SF) was used to measure physical activity, which evaluates physical activity in metabolic equivalents (MET) over the last seven days [194]. IPAQ-SF is a validated questionnaire to monitor self-reported physical activity levels in adults [194]. The IPAQ has been shown to be a valid and reliable tool for measuring physical activity in studies conducted across 20 different countries [195]. It is also the most frequently used and recommended physical activity questionnaire for assessing moderate-to-vigorous physical activity in adult populations within the EU [196]. The self-administered version

of this questionnaire was used in the present thesis, comprising 7 questions that record physical activity in four different intensity levels, including:

1. Vigorous physical activities such as heavy lifting, digging, aerobics, or fast bicycling.
2. Moderate physical activities such as carrying light loads or bicycling at a regular pace.
3. Walking
4. Sitting

The IPAQ-SF score was calculated by multiplying the minutes, days, and MET values of each level of physical activity. The following MET levels were used for each level of physical activity as per the developers' scoring protocol.

- Walking = 3.3 METs
- Moderate Intensity = 4.0 METs
- Vigorous Intensity = 8.0 METs

IPAQ-SF scores were classified to different physical activity levels as below:

- Low physical activity was defined as having a physical activity level of less than 600 MET minutes/week.
- Moderate physical activity was defined as activities achieving a minimum of at least 600 MET-minutes/week.
- High physical activity was defined as achieving over 3000 MET-minutes/week.

While the IPAQ-SF is not without limitations including susceptibility to recall and social desirability biases, the decision to use the IPAQ-SF in the present thesis was based on its practicality and low respondent burden, especially as physical activity was not the

primary outcome in the included studies in the present thesis[197, 198].

2.7 Qualitative Interviews

A qualitative approach was taken to understand UGI cancer survivors' and carers' experience of nutrition care during cancer treatment and their unmet nutritional care needs. The research dietitian (FS) collected qualitative data by semi-structured individual interviews. The interview draft was adopted from similar previous studies, which explored several topics, including survivors' experience of provided nutrition care, their nutritional challenges and complications, and their unmet nutrition care needs. Interviews were audio-recorded and transcribed verbatim for data analysis. Braun and Clarke's 6 stage approach was used for thematic analysis of collected data. FS and SD analysed all transcripts following an agreed process using nVivo 12 (QSR International, Australia).

2.8 Statistical Analysis

Statistical analysis was performed using IBM SPSS software (Version 29.0), employing relevant statistical tests. A descriptive analysis of measured outcomes and patient characteristics was completed. The normality of data was checked by Kolmogorov–Smirnov and the Shapiro–Wilk test before data analysis to select parametric or non-parametric tests. Further details of specific tests used are described in relevant chapters.

Chapter 3 Nutrition and Supportive Care Needs in UGI Cancer Survivors- An Anonymous Survey

This chapter details a cross-sectional survey conducted to assess the malnutrition risk, psychological status, and quality of life of UGI cancer survivors in Ireland. This study also investigated differences in malnutrition risk across various demographic groups. Furthermore, the present study explored patients' perspectives on weight loss, extended nutrition care, and need for nutrition information.

3.1 Introduction

As described earlier in sections 1.6 and 1.7, despite advances in cancer treatment, which have resulted in higher survivorship rates, many survivors face long-term or late side-effects. Among these, nutrition impact symptoms (NIS) and malnutrition are particularly prevalent in upper gastrointestinal (UGI) cancer survivors, significantly impairing their quality of life. Understanding the long-term effects of cancer treatment is crucial for developing and delivering tailored survivorship care [199]. Further exploration of the symptom burden associated with UGI cancers is necessary to inform the design of such care [99].

In Ireland, whilst a number of studies have reported on impaired physical function, reduced health-related quality of life (HRQOL), high malnutrition risk, and persistent NIS in UGI cancer survivors, these studies have focused exclusively on disease-free survivors [127, 200-203]. A study by Donohoe et al. found that long-term survivors of oesophagectomy experienced significantly reduced global health status compared to both the general population and pre-treatment cancer patients [203], while Gannon et al. observed no differences in global health status between disease-free oesophageal cancer survivors and case-matched non-cancer controls [202]. Nonetheless, in the Gannon study, oesophageal cancer survivors had significantly lower physical and role functioning scores and higher symptom burden for the fatigue and diarrhoea domains compared to healthy controls [202]. A prospective study by Guinan et al. observed significant deficits in multiple domains of HRQOL, including global health status, physical functioning and role functioning at one month post oesophagectomy, with role functioning remaining impaired at six months post-surgery [201]. Also, in Guinan's study, a significant

symptom burden of fatigue, pain, dyspnoea, nausea and vomiting, appetite loss, and diarrhoea was observed at one month post-surgery with fatigue and dyspnoea persisting at six months post oesophagectomy [201]. Two studies by Murphy et al. and Bennett et al. presented data from a pilot nutrition and survivorship clinic for oesophageal cancer [127, 200]. In the study by Bennett et al., malnutrition remained prevalent among oesophageal cancer survivors at 12 months post-oesophagectomy [200]. Similarly, NIS persisted throughout the postoperative period, with 36% of patients reporting more than two bothersome symptoms at 12 months post-oesophagectomy, respectively [200]. Additionally, the prevalence of malabsorption and dumping syndrome significantly increased over time [200]. In the study by Murphy et al., early satiety, fatigue, and appetite loss were prevalent at six months postoperatively, with early satiety and fatigue remaining among the most severe symptoms at one year post-operatively [127]. Additionally, in the study by Murphy et al., impaired HRQOL was significantly associated with several symptoms, including fatigue, pain, discomfort while eating, dumping syndrome, and early satiety [127]. In Murphy's study, global health status improved at one year compared to six months post-surgery. However, in these studies, patients received tailored dietitian-led survivorship care, potentially influencing their results due to the benefits of attending this clinic [127, 200]. Thus, there is a need for further research into the symptom burden experienced by UGI cancer survivors in Ireland receiving routine available care.

The psychosocial and emotional burden associated with UGI cancer treatment is substantial [204]. Previous studies have indicated that UGI cancer patients experience significant psychological distress, beginning at diagnosis and persisting for up to four years after treatment completion [205, 206]. Depression and anxiety can lead to noncompliance with treatment and negatively impact survival [207,

208]. Furthermore, psychological symptoms are often associated with malnutrition and a reduced quality of life in cancer patients [209, 210]. Despite these findings, most research has primarily concentrated on impaired physical function and NIS, leaving the psychological impact on UGI cancer survivors in Ireland unexplored [99, 204].

Some studies have shown that demographic factors, such as gender, education level, and employment status, are associated with malnutrition in cancer survivors [211-215]. Living arrangements may further influence malnutrition risk, as living alone might limit meal preparation and adversely affect nutritional status [216]. Investigating sociodemographic factors associated with an increased risk of malnutrition can help identify nutritionally at-risk patients and provide them with timely and targeted nutrition care [214, 217].

Given the importance of managing malnutrition in UGI cancer survivors, it is crucial to examine survivors' attitudes toward weight loss, nutrition care, and dietary information. Understanding patients' perspectives can guide the development of patient-centred care, enhancing adherence to nutritional interventions and improving overall nutritional outcomes [218, 219].

In summary, while adverse and long-lasting effects of UGI cancers on nutritional and psychological status and quality of life have been reported in several studies, there is a scarcity of such data concerning UGI cancer survivors in Ireland [53, 99, 220, 221]. National data are required to inform the required services for improving outcomes for UGI cancer survivors in Ireland. Therefore, the present study aimed to:

- Assess the risk of malnutrition, GI symptoms, psychological distress, and quality of life in UGI cancer survivors.

- Investigate variations in malnutrition risk across different demographic factors.
- Explore survivors' views on unintentional weight loss and the need for ongoing nutrition care and dietary information.

3.2 Methods

3.2.1 Inclusion and Exclusion Criteria

Adults aged 18 and older with a history of oesophageal or gastric cancer who could provide informed consent and were fluent in English were invited to complete the survey questionnaires.

3.2.2 Recruitment

The present study coincided with the COVID-19 pandemic, which limited recruitment. Therefore, several recruitment pathways were adopted. Recruitment ran from September 2021 to May 2022.

3.2.2.1 Recruiting for Online Survey

Participants were recruited by inviting them to complete an online survey as access to clinics was limited due to infection control protocols at that time. The study was advertised through charity partners, the Irish Cancer Society and the Oesophageal Cancer Fund, as well as virtual social networks (Twitter, Facebook, Instagram) to identify interested participants. A virtual poster and an animation clip were used to introduce and advertise the survey. A link to the online survey was included in the advertisement, as well as a link to the PIL. Contact details of the research team were provided in the advertisement to allow participants to call/email investigators and request more information about the project or assistance in

completing the questionnaires. The PIL and the study poster are included in Appendix II.

3.2.2.2 Recruiting at UGI Clinic

When COVID-19 restrictions for attending UGI clinics were lifted, patients were invited to complete a paper-based version of the survey. Potentially eligible patients attending the outpatient UGI cancer clinic at St James's Hospital were informed about the study while awaiting their appointment and received a copy of the PIL and survey. If they decided to participate, they were asked to leave the completed survey at the clinic office. A stamped addressed envelope was also provided to patients to enable them to complete the survey at home and return it to the researcher.

3.2.2.3 Recruiting for Postal Survey

An amendment was submitted to the SJH/TUH joint ethics committee and approved prior to utilising this recruitment method. This amendment allowed the UGI clinic patient database and GDPR-compliant research mailing list to be used to access patients' postal addresses. All the patients listed in this GDPR-compliant research mailing list have already consented to be contacted for research purposes. A simple random sampling method was used to select patients from the mailing list by using a random number generator. The PIL and survey were posted to these potential participants, and a stamped addressed envelope was also provided to allow the return of the completed survey.

3.2.3 Ethical Approval

Ethical approval was sought from the St James's Hospital/Tallaght University Hospital Joint Ethics Committee (Project ID:0247).

3.2.4 Survey Components

The survey consisted of five sections and incorporated a number of validated questionnaires. In section one, demographic data, along with data on employment status, living arrangements, education level, and type of medical insurance, were collected. In addition, relevant clinical details of cancer diagnosis and treatment were ascertained. In section two, nutritional status was assessed using the Malnutrition Screening Tool (MST) [174]. Additionally, a set of questions investigated survivors' concerns regarding weight loss, whether they sought dietetic advice through their cancer journey, and if they thought they would benefit from more contact with a dietitian. Participants were also asked what type of nutritional information or advice they required, if any. Relevant literature was reviewed to guide the design of these additional questions [113, 222-224]. An external UGI dietitian (AMM) was also consulted in designing these questions addressing nutritional issues specific to UGI patients and their care needs during survivorship. In section three, quality of life was measured by the European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC-QLQ-C30) [178]. Section four explored GI symptom burden using the Gastrointestinal Symptom Rating Scale (GSRS) [188]. Finally, in section five, psychological well-being was assessed using the Hospital Anxiety and Depression Scale (HADS) questionnaire [184]. The developed questionnaire was then discussed and reviewed by members of the Exercise Oncology Research Group to ensure its alignment with the research objectives. Lastly, the research team reviewed the wording and readability of the questions, and final modifications were made to improve clarity and comprehension. A copy of the survey questionnaire is attached in Appendix VI.

3.2.5 Statistical Analysis

Statistical analysis was performed using SPSS software (Version 29). Descriptive analysis was used to present mean and standard deviation (SD) for continuous data and frequency and percentage for categorical data. The Kolmogorov–Smirnov test was used for assessing the normal distribution of data. Chi-square and Mann-Whitney U tests were used to compare differences in the prevalence of malnutrition risk and MST score across demographic variables. A one sample T-test was used to determine statistically significant differences between sample and reference values for GSRS.

3.3 Results

The recruitment process and response rate are presented in Figure 3-1. Of the 200 posted survey packets, 106 patients (53%) returned the survey. Overall, one hundred and nineteen (119) survey responses were received from all three recruitment pathways. Five responses were excluded from the analysis due to the following reasons:

- One participant returned a questionnaire belonging to another research study.
- Two returned blank questionnaires.
- Two surveys completed at the UGI clinic were excluded as patients had no confirmed diagnosis of UGI cancer.

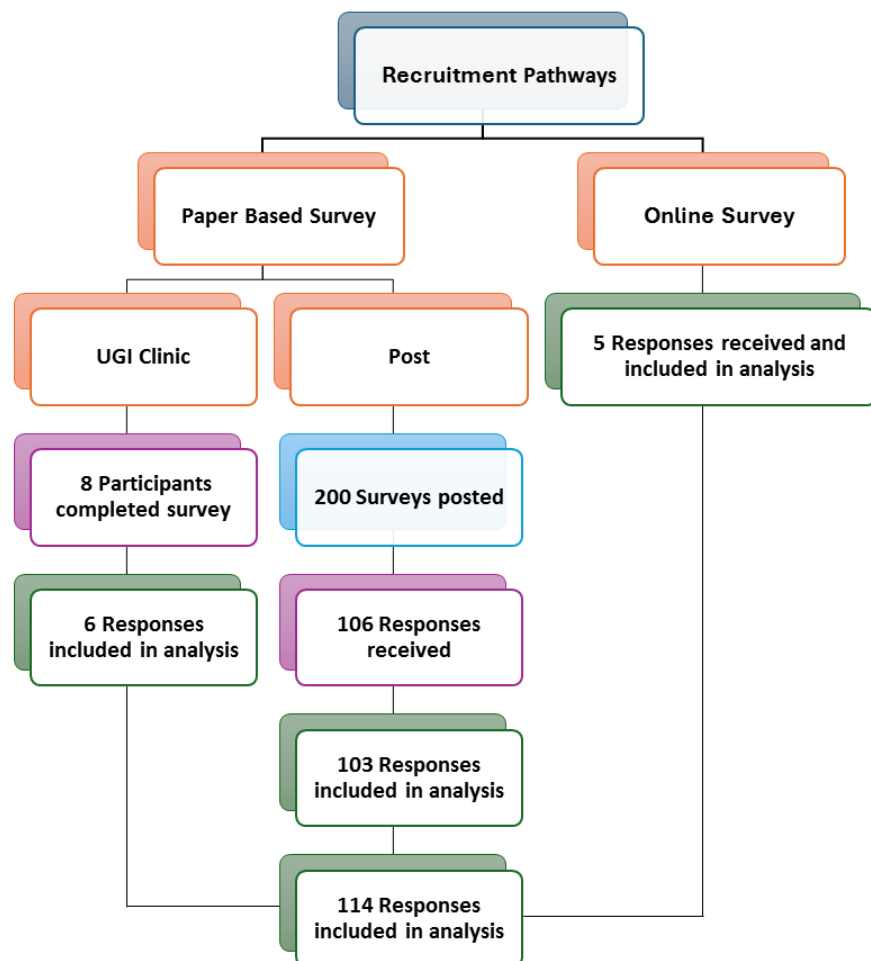


Figure 3-1. Recruitment process flowchart

Participants' demographic characteristics are presented in Table 3-1. One hundred and fourteen participants are included in the data analysis. The majority of participants were male (72, 63%). The mean age was 70.36 ± 9.19 (41-88), and the majority were aged over 65 years (n=82, 71.9%). Less than 20% were living alone (21, 18.4%). Over 65% were retired, and less than 15% were in full-time employment. Over 30% had private health insurance, and less than 35% of participants had third-level education.

Table 3-1. Participants' demographic characteristics (n=114)

	n (%)
Age (Mean $\pm$SD, Range)	70.36 $\pm$ 9.19, 41-88 –
Gender	Female
	42 (36.8)
	Male
	72 (63.1)
Living Arrangement	Living with others
	93(81.6)
	Living alone
	21 (18.4)
Employment Status	Retired
	78 (66.6)
	Employed Full time
	17 (14.9)
	Employed Part-Time
	6 (5.2)
	On sick leave
	5(4.3)
	Homemaker
	4 (3.5)
	Unemployed
	3 (2.6)
	Self-employed and on disability payment
	1 (0.8)
Ethnicity	Irish
	107 (93.8)
	Other White backgrounds
	7 (6.1)
Health Insurance	Medical Card
	59 (51.7)
	Private health insurance
	38 (33.3)
	GP visit Card
	10 (8.7)
	None
	6 (5.2)
	Other
	1(0.8)
Education	Primary school
	19 (16.6)
	Post-primary school
	54 (47.3)
	Diploma
	20 (17.5)
	Bachelor's degree
	13 (11.4)
	Master's degree
	6 (5.2)
	Prefer not to answer
	2 (1.7)

Participants' clinical details are summarised in Table 3-2. The majority of participants were oesophageal cancer survivors (75.4%).

Almost all participants underwent curative surgery (99%), and 42% were no longer receiving cancer treatments at the time of the study. More than 70% of participants were 2 years post diagnosis.

Table 3-2. Participant's clinical details

		n (%)
Cancer Diagnosis, (n=114)	Oesophageal Cancer	86 (75.4)
	Gastric Cancer	28 (24.5)
Cancer History, (n=114)	History of previous cancers	8 (7.01)
Time from Diagnosis (months) mean $\pm$SD, (n=108)	mean $\pm$ SD: 44.76 $\pm$ 34.18 Range: 2-270	-
	Less than 6 months	2 (1.9)
	6-12 months	10 (9.3)
	12-24 months	17 (15.7)
	>2-5 years	54 (50)
	>5 years	25 (23.1)
Cancer Treatment, (n=114)	Surgery only	43 (37.7)
	Chemotherapy only	1 (0.87)
	Surgery+ Chemotherapy	51 (44.7)
	Surgery+ Radiotherapy	2 (1.75)
	Surgery +Chemotherapy+ Radiotherapy	16 (14.03)
	Surgery +Chemotherapy+ Radiotherapy +Immunotherapy	1 (0.87)
	No longer receiving treatment	48 (42.1)
	On a break from cancer treatment	4 (3.5)

As presented in Table 3-3, one-third of the participants were identified as at risk of malnutrition, and >35% reported ongoing nutrition-related symptoms and complications. Reflux, diarrhoea, dumping syndrome and swallowing difficulty were the most commonly reported GI complications. Eighty-eight respondents provided information about their supplement intake. Among them, over 19% were consuming oral nutrition supplements (ONS), and >5% were on enteral feeding. Forty-three (48.8%) reported vitamin and/or mineral supplement intake, and just over 3% followed a special diet (modified texture diet, gluten-free diet).

Table 3-3. Participant's nutritional status screened by the malnutrition screening tool (MST) (n=114)

Nutritional status		n (%)
MST Score (Mean± SD)	1.11±1.51	-
Risk of Malnutrition	Low	79 (69.29)
	Medium	21(18.42)
	High	14(12.28)
Ongoing Nutritional Symptoms	Yes	42(36.84)
	No	72(63.15)
Nutritional Supplement Intake	Oral Nutritional supplement (ONS)	17 (19.31)
	Multivitamin	43 (48.8)
	Single vitamin ¹	16 (18.18)
	Minerals ²	13 (14.72)
	Other ³	9 (10.22)
	Unknown Nutritional supplement	7 (7.95)
	None	12 (13.63)
Special Diet	Modified texture diet	2(2.27)
	Gluten-free	1(1.13)
Nutrition Support	Tube feeding	5 (5.68)

¹ Vitamin C, D, B₁, B₁₂. ² Calcium, Iron, Magnesium, Zinc. ³ Yogurt drinks, Plant protein powder, Fish oil, Cod liver oil, Probiotics, Turmeric.

As presented in Table 3-4, study subjects scored significantly higher on all five domains of GSRS compared to the general population, which highlights the higher prevalence and severity of gastrointestinal complications in UGI cancer survivors.

Table 3-4. Gastrointestinal symptoms rating scale scores

GSRS domains score	Sample			Reference value, general population [192]	P-Value
	n	Mean Score (SD)	CI	Mean Score	
Abdominal Pain Syndrome (score range 1-7)	109	1.85 (1.01)	1.65, 2.04	1.56	0.004
Reflux Syndrome (score range 1-7)	108	2.05 (1.41)	1.78, 2.32	1.39	<0.001
Diarrhoea syndrome (score range 1-7)	113	2.40 (1.59)	2.11, 2.70	1.38	<0.001
Indigestion Syndrome (score range 1-7)	111	2.15 (1.24)	1.91, 2.38	1.78	0.002
Constipation Syndrome (score range 1-7)	113	1.93 (1.23)	1.70, 2.16	1.55	0.001
Total score	108	2.06 (1.02)	1.86, 2.25	1.53	<0.001

One sample T-test was used to determine statistically significant differences between groups.

Table 3-5 summarises the EORTC QLQ-C30 quality of life data. Compared to the general population and considering minimal clinically important difference (MCID) of ≥ 10 points [180, 181], respondents reported impaired physical and social functioning. Additionally, a high symptom burden was observed, particularly for nausea and vomiting, dyspnoea, appetite loss, constipation, diarrhoea, and financial difficulties. Notably, 31.7% of respondents had a global health status score below 66.1, indicating impaired quality of life [200, 225]. Also, considering thresholds for clinical importance (TCI) of EORTC scores, physical function, nausea and vomiting, dyspnoea, and diarrhoea may require clinical attention in this cohort of UGI cancer survivors [182].

Conversely, respondents' scores for global health status were higher than reference values for oesophageal and gastric cancer.

Also, they reported lower symptom severity for fatigue, pain, appetite loss, and constipation compared to reference values for oesophageal and gastric cancer.

Compared to reference values for all cancer survivors, similar scores for functional and symptom domains were observed except for pain and diarrhoea, which were more severe in respondents.

Table 3-6 presents the results of the HADS questionnaire. The study respondents had lower anxiety scores compared to the normative value for the general population but scored higher on the depression scale. As shown in Figure 3-2, >25% were identified with anxiety or borderline anxiety, and >22% of respondents' depression scale scores indicated the prevalence of depression or borderline depression.

Table 3-5.Participants' quality of life (EORTC QLQ-C30)

	Scale	Sample	Reference Values[226]			
		Mean (SD)	All Cancers, all stages	Oesophageal cancer, all stages	Gastric cancer, all stages	General population
Global Health Status / QoL	QoL (n=107)	66.27(24.21)	61.3 (24.2)	55.6 (24.1)	53.1 (26.5)	71.2(22.4)
Functional Scales¹	Physical Functioning (n=111)	79.50(20.80)	76.7 (23.2)	77.3 (23.9)	79.6 (21.8)	89.8(16.2)
	Role functioning (n=112)	77.67(28.61)	70.5 (32.8)	69.0 (33.5)	58.7 (37.4)	84.7(25.4)
	Emotional Functioning (n=111)	78.3(26.61)	71.4 (24.2)	70.6 (24.2)	68.8 (25.4)	76.3(22.8)
	Cognitive Functioning (n=111)	79.27(20.25)	82.6 (21.9)	83.3 (21.5)	80.1(23.7)	86.1(20)
	Social Functioning (n=111)	74.62(26.57)	75.0 (29.1)	75.6(28)	66.8 (33.3)	87.5(22.9)
Symptom Scales²	Fatigue(n=111)	31.83(21.25)	34.6 (27.8)	36.6 (26.6)	44.5 (31.2)	24.1(24)
	Nausea and vomiting(n=112)	13.24(20.88)	9.1 (19)	16.8 (23.3)	18.8 (27.4)	3.7(11.7)
	Pain(n=111)	15.76(22.90)	27.0 (29.9)	26.5 (27)	31.4(31.7)	20.9 (27.6)
	Dyspnoea (n=112)	19.94(27.01)	21.0 (28.4)	19.2 (27.3)	20.9 (29.7)	11.8(22.8)
	Insomnia(n=111)	27.92(31.63)	28.9 (31.9)	29.8 (32.8)	31.7 (33.6)	21.8(29.7)
	Appetite Loss(n=111)	22.52(32.46)	21.1(31.3)	33.7 (37.4)	37.6 (38.3)	6.7(18.3)
	Constipation(n=112)	14.88(24.02)	17.5 (28.4)	25.5 (31.1)	26.4 (33.6)	6.7(18.4)
	Diarrhoea (n=110)	23.63(29.03)	9.0 (20.3)	7.3 (18.9)	15.9 (27.6)	7.0 (18)
	Financial Difficulties(n=110)	17.57(26.60)	16.3 (28.1)	15.4 (27.7)	12.6 (26.4)	9.5 (23.3)

QoL, Quality of Life, SD, Standard Deviation. EORTC, European Organisation for Research and Treatment of Cancer. ¹ The Score ranges from 0 to 100; a higher score represents a better quality of life or a higher level of functioning. ² The Score ranges from 0 to 100, and a higher score represents more severe symptoms

Table 3-6.Hospital anxiety depression scale

	Sample Mean (SD) (n=112)	Normative Value (General Population) Mean (SD)[227]
Anxiety Scale	5.26 (4.48)	6.14 (3.76)
Depression Scale	4.72 (3.81)	3.68 (3.07)
Total Score	9.98 (7.70)	9.82 (5.98)

Scoring: 0-7 = Normal, 8-10 = Borderline abnormal (borderline case), 11-21 = Abnormal (case)

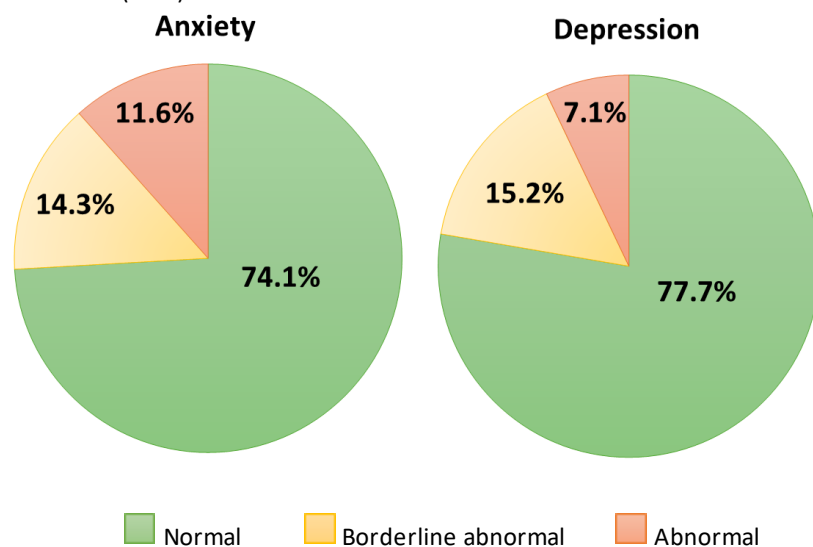


Figure 3-2.Hospital anxiety depression scale score

MST score and malnutrition risk amongst respondents are summarised in Table 3-7. There was no statistical difference in mean MST score and risk of malnutrition between different sociodemographic factors. However, higher MST scores and a greater proportion of participants at risk of malnutrition were noted among those living alone (42.9% vs 27.9%), those not in employment (31.4% vs 16.2%), and those with public health insurance (38.3% vs 24.5%), compared to their respective counterparts. Further analysis of socioeconomic indicators showed that compared to those with private health insurance, medical card holders had a higher mean MST score (1.25 ± 1.52 vs 0.92 ± 1.046) and a higher proportion at risk of malnutrition (36.3 % vs 24.5%) although these differences were not statistically significant.

Table 3-7.Malnutrition risk and demographics

Demographic characteristics		MST score Mean (SD)	P-Value ¹	At risk of malnutrition n (%)	P-Value ²
Gender	Female (n=42)	0.97(1.27)	0.81	12 (28.5)	0.83
	Male (n=72)	1.19 (1.64)		23 (31.9)	
Living Arrangement	Alone (n=21)	1.48 (1.63)	0.20	9 (42.85)	0.19
	Living with others (n=93)	1.03 (1.48)		26 (27.95)	
Employment Status	Employed (n=24)	0.79(1.31)	0.31	4 (16.16)	0.13
	Not employed (n=90)	1.20(1.55)		31(34.4)	
Ethnicity	Irish (n=107)	1.12(1.50)	0.73	34 (31.77)	0.43
	Non-Irish (n=7)	1(1.82)		1 (14.28)	
Health Insurance	Public (n=47)	1.36 (1.63)	0.13	18 (38.29)	0.34
	Private (n=61)	0.92 (1.41)		15 (24.5)	
Education	Third level education (n=39)	1.26(1.56)	0.32	13 (33.33)	0.66
	No Third level education (n=73)	1.03(1.49)		21 (28.76)	

¹ Mann-Whitney Test used to determine statistically significant differences between groups. ² Chi-Square test used to determine significant differences between groups

Collected data on respondents' nutrition care needs are presented in Table 3-8. More than half of respondents were concerned about weight loss to some extent. Almost one-third (29.8%) of respondents reported weight loss, of which >75% reported that they were concerned about weight loss. Although approximately 60% of respondents had sought dietetic advice, >50% agreed they would benefit from further contact with a dietitian. Similarly, nearly 60% of respondents expressed interest in additional information on nutrition. The most commonly reported subjects of interest for nutritional information were symptom management, recipes and meal plans, supplements, healthy eating and portion sizes.

Table 3-8. Participants reported nutrition care needs

Nutrition care needs	n (%)
Concern about weight loss (n=110)	
Not concerned at all	51 (46.3)
A bit concerned	31 (28.18)
Moderately concerned	18 (16.36)
Severely concerned	10 (9.09)
Sought advice from a dietitian (n=109)	
Yes	63 (57.7)
No	46 (42.2)
Time point of receiving dietetic advice (n=70)	
Before treatment	12 (17.14)
During treatment	25 (35.71)
After treatment	46 (65.7)
Would benefit from further dietitian contact (n=111)	
Yes	58 (52.25)
No	53 (47.74)
Expression of interest in nutrition information (n=111)	
Interested	64 (57.65)
Not interested	47 (42.34)
Nutrition information topics (n=111)	
Managing symptoms	41 (35.9)
Recipes and meal plans	26 (22.80)
Supplement	26 (22.8)
Healthy eating	25 (21.9)
Portion size	22 (19.29)
Weight loss	17 (14.91)
Swallowing difficulty	14 (12.28)
Appetite loss	10 (8.77)
Obesity	4 (3.50)
Tube feeding	1 (0.87)

3.4 Discussion

The present study explored the risk of malnutrition and the severity of GI symptoms in UGI cancer survivors, along with their quality of life and psychological well-being. It also investigated survivors' perceptions of weight loss, ongoing nutritional care, and nutrition information needs. The findings indicated that malnutrition and GI symptoms remain prevalent among UGI cancer survivors. The results of the present study showed impaired quality of life and the presence of psychological distress among UGI cancer survivors. Additionally, the majority of UGI cancer survivors had a positive attitude towards further dietary support and a strong interest in receiving additional nutritional information.

3.4.1 Malnutrition

In the present study, one in three participants was found to be at risk of malnutrition. Evidence shows patients undergoing surgery for UGI cancer are at higher risk of malnutrition compared to other cancer patients [228, 229]. The prevalence of malnutrition in UGI cancers ranges from 22% to 85%, depending on factors such as the stage of cancer, cancer treatment, and survivorship phase [228, 230-232]. Some studies have suggested a lower malnutrition risk and reduction in the pace of weight loss at 12+ months post-surgery [233, 234]. This is notable, as the results in the present study may be influenced by the fact that over 73% of respondents were survivors of more than two years.

In the present study, no significant differences in MST scores or malnutrition risk were observed between groups stratified by sociodemographic variables, including gender, ethnicity, living arrangement, education level, employment status, and healthcare

access. However, descriptive trends suggested that participants living alone, those not in employment, and those with a medical card had higher MST scores and a greater proportion of them were at risk of malnutrition. While these differences did not reach statistical significance, they may indicate underlying socio-economic disparities in nutritional vulnerability among UGI cancer survivors.

In a previous study by Wang et al., survivors who were employed had better nutritional status post-gastrectomy [214]. This may be because gastric cancer patients with poor nutritional status often experience reduced strength and energy, making it challenging for them to maintain employment [214]. However, no significant difference between nutritional status and employment was observed in the present study. This could be attributed to the fact that over 65% of participants in the present study were retired, potentially diminishing the relevance of employment status as a factor influencing nutritional outcomes. With respect to gender differences and nutritional risk, the evidence in the literature is conflicting [214, 231]. Wang et al. reported better nutritional status in females post-gastrectomy [214]. However, in the Wang study, the gender difference in nutritional status may be due to different disease severity, as 21.8% of men had stage III gastric cancer compared to 7.9% of women [214]. Conversely, in a study by Cao et al., female oesophageal cancer survivors had a higher incidence of malnutrition and greater weight loss; however, following logistic regression analysis, gender was not identified as a risk factor for malnutrition [231]. Several factors, such as lower dietary intake and higher prevalence of nutritional insufficiencies in women compared to men, have been reported in previous studies and may contribute to higher malnutrition risk in women [231, 235]. Further longitudinal studies, with greater numbers of both males and females, would be required

to determine if gender influences malnutrition risk in UGI cancer survivors.

Overall, data on demographic and social determinants of malnutrition in UGI cancer survivors are scarce and inconsistent. Some studies have found that low socioeconomic status (SES) may be linked to a higher risk of malnutrition in cancer patients [214, 217, 236, 237]. However, data on SES were not collected in the present study due to the complexity of SES indicators and challenges with using household income to examine SES [238]. It is also important to consider that medical card eligibility in Ireland may be influenced by cancer diagnosis, potentially confounding its utility as an independent SES marker. Future research is required to investigate the impact of SES on malnutrition risk in cancer survivors in Ireland. Such data will be valuable in designing targeted interventions for those at the highest risk of malnutrition.

3.4.2 Unintentional Weight Loss

Although unintentional weight loss (UWL) is frequently reported in UGI cancers, information on patient's subjective experience and perception of weight loss is limited [239]. In the current study, almost one-third (29.8%) of respondents reported weight loss, comparable with 34.9% reported from a study with participants with mixed cancer diagnoses [239]. A national survey by O'Sullivan et al. reported a higher prevalence of weight loss in a mixed cohort of cancer survivors, with 44% of participants experiencing weight loss [222]. In the present study, nearly 80% of respondents who experienced weight loss expressed concern about it, compared to 42% of participants in the study by O'Sullivan et al. The lower rate of concerns about UWL in the O'Sullivan study may be attributed to the recruitment of a mixed cohort of cancer survivors, with over 50% being breast cancer survivors. For breast cancer

survivors, being overweight or obese is often a risk factor for overall survival, which may reduce the level of concern about weight loss [240]. In contrast, for patients with UGI cancers, overweight or obesity can be a protective factor for overall survival, and UWL is a significant risk factor for poor overall survival [240]. Additionally, as noted earlier, UWL is highly prevalent in UGI cancer; hence, it remains a key concern for many patients, their caregivers, and the healthcare team throughout their cancer treatment [53, 241, 242]. The higher rate of concern about weight loss in the present study may be a reflection of the acute awareness that UGI patients have regarding weight loss and its implications. It may suggest that there is a higher psychological burden of UWL in UGI cancer survivors.

3.4.3 Nutrition Care and Information Needs

The present study also obtained respondents' perceptions of nutrition care and information needs. The findings indicate that approximately 60% of respondents sought advice from a dietitian at some stage of their cancer treatment. Based on a national survey conducted by O'Sullivan, patients with GI cancers were most likely to see a dietitian during their cancer journey compared to other cancer types (71.8%) [222]. In the present study, over 50% of respondents had a positive view of further dietetic input and expressed interest in receiving additional nutritional information. These findings are consistent with previous studies, highlighting the unmet need for nutrition information among cancer survivors [222, 243-245]. Despite understanding the important role of nutrition in cancer recovery and their strong interest in receiving nutritional information, many still lack access to the information they need [222, 243-245]. However, accessing reliable, evidence-based information can be challenging due to the current staffing shortages in dietetic services across Ireland [246].

3.4.4 Gastrointestinal Symptoms

The results of the present study indicate the persistence of GI symptoms in UGI cancer survivors, as respondents scored higher in all domains of GSRS compared to the general population. A similar study reported long-term persistence of GI disturbance, including early satiety, regurgitation, and heartburn for more than five years after oesophagectomy [247]. Reflux, diarrhoea, dumping syndrome and swallowing difficulty were the most commonly reported symptoms in the current study, in line with other studies reporting reflux, abdominal pain, indigestion, and diarrhoea as the most troublesome symptoms after UGI cancer treatment [233, 248]. Aligned with previous studies, the findings of the present study further supported the need for tailored interventions to address the burden of NIS in UGI cancer survivors.

3.4.5 Quality of Life

The adverse impact of UGI cancers on health-related quality of life (HRQOL) is well documented [249-251]. Results of the present study indicate impairment of physical and social function in UGI cancer survivors. Additionally, a high symptom burden, particularly for nausea and vomiting, dyspnoea, appetite loss, constipation, and diarrhoea were observed in participants. Long-lasting and possible lifelong impairment of quality of life and persistence of symptoms following UGI cancers have been observed in previous studies [252-255]. The findings of the present study further indicate the persistence of nutrition impact symptoms post UGI cancer, which may affect HRQOL. The results of the present study demonstrated impaired quality of life in 31.7% of respondents, comparable to a previous study, which reported impaired quality of life in 26% of oesophageal cancer survivors between 5 and 10 years post

operatively [253]. Interestingly, an Irish study by Bennett et al. reported impaired quality of life in 20% and 14.3% of the patients attending a nutrition survivorship clinic at 6 and 12 months post oesophagectomy, respectively [200]. This may highlight the benefits of nutrition care in symptom management and improving the quality of life of UGI cancer survivors.

In the present study, participants exhibited a higher global health status score, lower symptom severity for fatigue, pain, appetite loss, and constipation and higher severity of diarrhoea compared to reference values for patients diagnosed with oesophageal and gastric cancer. These differences can be attributed to the differences in patient profiles in these cohorts. The reference EORTC scores reflect baseline data collected from untreated oesophageal and gastric cancer patients, while the majority of respondents in this study were >2 years post-diagnosis, and almost all participants underwent curative surgery. It can explain some of the observed results, as it has been reported that HRQOL recovers 3-5 years after surgery [256, 257]. Nevertheless, it has also been suggested that improved quality of life in survivorship might be due to adaptation and acceptance of a new normal post treatment, which might impact internal standards and values regarding HRQOL [258].

Incorporating regular monitoring of HRQOL into standard care can provide valuable insights into how cancer and its treatment affect patients' overall well-being, helping to track treatment toxicity and effectiveness and assisting clinicians in delivering personalised care tailored to each patient's needs and preferences [259]. However, further research is warranted to examine current practices in Ireland and to identify potential challenges and the necessary infrastructure required for integrating HRQOL monitoring into routine clinical

practice, ensuring it becomes a practical and effective part of patient care.

3.4.6 Psychological Status

Higher rates of anxiety are reported in cancer survivors compared to the general population [260]. The prevalence of anxiety and depression in patients with cancer varies in different studies and ranges from <10% to 30% [261]. Several factors, such as type and stage of cancer and cancer treatment, may impact patients' psychological status and explain the variability in the prevalence of anxiety and depression reported in studies [262, 263]. In the present study, 25.9% and 22.3% of patients scored above the cut-off for a possible-probable anxiety and depression disorder, respectively. This result was similar to a previous study, which observed that 24% of patients reported depression at a median of 45 months following diagnosis of oesophageal cancer [206]. Furthermore, a longitudinal study including both oesophageal and gastro-oesophageal junction cancer patients reported anxiety and depression rates of 24% and 27%, respectively, at 12 months post-diagnosis [205]. In another longitudinal study that assessed psychological distress after oesophageal cancer surgery, the prevalence of anxiety was 33% prior to surgery, 28% at 6 months, and 37% at 12 months. It also reported that prior to surgery, 20% of patients reported depression, which increased to 27% at 6 months and 32% at 12-month follow-up [264].

It is important to note that cultural factors, differences in access to mental health services, and social support may impact rates of psychological complications reported in studies from different countries [265, 266]. Thus, it is important to consider the psychological morbidity in the general Irish population when interpreting the results of the present study. In the present study, 11.6% of respondents had a HADS-anxiety score of ≥ 11 and 7.1% had

a HADS-depression score of ≥ 11 , indicating moderate to severe depression and anxiety. According to the Mental Health Association of Ireland (2001), the prevalence of moderate to severe anxiety and depression in the Irish population using HADS was 13% and 4%, respectively [267]. Although the rate of anxiety in the Mental Health Association report was similar to the findings of the present study, compared to recent data from The Irish Longitudinal Study on Ageing (TILDA), a higher score of anxiety was observed in the present study, considering a minimal clinically important difference (MCID) of two points (5.26 ± 4.48 versus 3.14 ± 3.12) [268, 269]. Moreover, in the present study, 22.3% of UGI cancer survivors were categorised as borderline or clinically depressed compared to 11% of those aged 65 years and over in an Irish study by McGee et al. [270]. Of note, in the present study, six (5.35%) participants had both HADS-D and HADS-A ≥ 11 , compared to 3.4% of participants in an Irish study of a mixed cohort of oncology patients [271]. The findings of the present study have demonstrated higher psychological morbidity in UGI cancer survivors compared to the general population, which highlights the importance of incorporating targeted psychological support into UGI cancer survivorship care plans.

As noted earlier in section 3.1, psychological complications can limit treatment adherence, which not only impacts patients' survival but also has the potential to dilute data on the effectiveness of interventions and underestimate the efficacy of therapies [208]. Symptoms of depression and anxiety have been linked to poor adherence to dietary recommendations [272]. Additionally, depression may impair patients' capacity to understand and process information regarding prognoses [207]. Incorporating psychological assessment into standard cancer care and survivorship may provide more accurate information on the prevalence of psychological morbidities and psychological consequences of cancer [208]. It also

may facilitate access to required services for those affected, which subsequently may improve treatment adherence, quality of life and survival [208].

3.5 Strengths and Limitations

To the best of our knowledge, this cross-sectional survey is the first study in Ireland investigating UGI cancer survivors' nutrition and supportive care needs. In the present study, the respondents' demographic was reflective of the age and gender profile of UGI cancer survivors in Ireland, which may improve the reliability of the findings in representing survivorship and nutrition care needs in this cohort of cancer survivors. In the present study, 72% of survivors were over 65 years old, which is comparable to the age profile at diagnosis according to national data. Also, the majority of participants were male, which is reflective of the higher incidence of these cancer types in men, as over 60% of new cases are male [10]. Moreover, using validated tools to examine the risk of malnutrition (MST), GI symptoms (GSRS), QOL (EORTC-30), and psychological status (HADS) is another strength of this study.

However, the results of the present study should be interpreted with caution, considering the following limitations. The findings reflected data from patients who responded to the survey; thus, the possibility of non-response bias may limit the generalisation of findings to the broader population of UGI cancer survivors. There may also be an element of responder bias in that those with a particular concern regarding their nutritional status or ongoing symptoms were more likely to complete the survey.

The medical history data collected in the present study were self-reported, which may introduce the potential for errors such as recall bias and inaccurate reporting [273]. Also, detailed information

on the type of surgery, treatment and prognosis would be beneficial in determining factors that might affect survivors' needs. This information was not collected in the present study due to limited and inconsistent evidence on the accuracy of self-reported medical history and surgical procedures [274-276]. Another rationale was to minimise the number of questions, as survey length can reduce response rate, engagement, and accuracy of responses [277].

It also should be noted that in the present study, a clinically relevant proportion of participants had a HADS score greater than 7 in the depression subscale (22.3%), indicating possible or probable depression. This may impact perception of GI symptoms, quality of life and nutrition care needs[278]. Thus, considering mental health status as a potential confounding factor in the interpretation of findings of the present study should be acknowledged.

3.6 Future Direction

The nutrition assessment in this study was self-completed, and although MST is reported to be a suitable tool for detecting cancer cachexia in patients diagnosed with cancer, the application of a single screening tool might not be an optimal diagnostic method for detecting malnutrition and evaluating nutritional status in cancer survivors [279, 280]. Therefore, in Chapter 5, a comprehensive nutritional assessment was performed using a malnutrition screening tool along with anthropometric measurements, body composition, dietary intake, and physical function to investigate the prevalence of malnutrition and sarcopenia in a cohort of UGI cancer survivors.

Previous studies have reported the association between psychological morbidity and risk of malnutrition [67, 281, 282]. Also, an interaction between GI symptoms and psychological status is observed both in the general population and UGI cancer survivors

[283, 284]. However, causality or directionality cannot be inferred from the present study, and further research is warranted to understand the complex interplay between mental health, QOL, nutrition impact symptoms and malnutrition. In addition, due to poor prognosis and higher prevalence of UGI cancers in those over 65 years old, long-term follow-up studies are rare [252]. Future research should seek to follow participants in a longitudinal study to investigate the type and extent of supportive care needs at different stages post-treatment.

It should be noted that the online version of this survey struggled to recruit participants despite repeated advertisements through various social media platforms. This may be due to the demographic profile of UGI cancer survivors, as the majority of diagnosed cases are >65 years of age, which may have lower digital literacy [285]. Also, it was reported that in 2019, 33% of the Irish population aged between 65 and 74 had never accessed the internet, and nearly half of individuals aged 64–75 never used the internet [286, 287]. These factors should be considered while designing future studies in this cohort of cancer survivors.

There are limited data describing patients' insights and perceptions of unmet nutrition care needs in UGI cancer survivorship. Understanding the unique concerns and information needs of UGI cancer survivors would be helpful in guiding tailored supportive care programmes to address these unmet needs. Accordingly, a qualitative study capturing survivors' and their carers' insights was completed and reported in Chapter 4.

3.7 Conclusion

Results of the present study indicated a high risk of malnutrition, persistent GI complications, impaired quality of life, and psychological burden in UGI cancer survivors. The findings highlighted ongoing challenges in the long-term recovery of UGI cancers and the need for continued monitoring of outcomes and providing supportive care for survivors.

Chapter 4 Nutrition Care Needs in UGI Cancer Survivors- A Qualitative Study

This chapter presents a qualitative study that explored the experiences of UGI cancer survivors and their caregivers with nutrition care during and beyond cancer treatment. It also explored their nutrition-related challenges and unmet nutrition care needs in survivorship.

4.1 Introduction

As discussed earlier in section 1.6, nutritional complications are highly prevalent in UGI cancer patients and can negatively impact their quality of life. Given the significant relationship between nutrition and cancer, nutrition care should be considered an essential part of cancer treatment at all stages [288]. Several guidelines and position papers describe optimal nutrition care pathways and interventions to improve treatment outcomes in cancer survivors [289]. They often include regular nutrition screening and assessment, preoperative and postoperative nutrition support, and delivering nutrition care within a multidisciplinary team [289]. However, there is a gap in current evidence-based guidelines for nutrition care in managing the long-term symptoms and malnutrition experienced by UGI cancer survivors [289].

Several studies have also investigated cancer survivors' and healthcare professionals' awareness of nutritional considerations in cancer, their insight into the role of nutrition in cancer care and the practicality of implementing these nutritional guidelines in clinical practices [290-293]. It has been found that despite positive attitudes toward nutrition, the integration of nutrition into oncology care has been hindered by the lack of resources, motivation, and knowledge [290, 292, 293]. In a study by Keaver et al., cancer survivors considered nutrition as a means of empowerment, allowing them to take control over an aspect of their care [290]. However, they were vulnerable to misinformation as evidence-based guidance was not always available [290]. Interestingly, when dietetic services were available, sometimes they were underutilised, partly because patients were overwhelmed by numerous appointments and found it difficult to add additional appointments for nutrition input [290]. The

lack of collaboration between oncologists and clinical nutritionists may be another reason for the limited integration of nutrition care into patient care [291]. Also, oncologists' knowledge and ability to identify patients who are at risk of malnutrition is essential to advocate for and provide nutrition care [292].

As recommended by the Multinational Association of Supportive Care in Cancer (MASCC) and the American Society of Clinical Oncology (ASCO), survivorship care should be person-centred and tailored to the survivors and their caregivers' preferences and needs [294, 295]. Gaining insight into survivors' experience of nutrition care services and their preferences can guide the development of tailored nutrition resources and services to address patients' and their carers' needs post-treatment [296]. Previous research in Ireland showed that cancer survivors consider nutrition an important part of cancer care and are interested in receiving nutritional information from trusted sources [297-299].

As discussed in section 1.8, caregivers play a crucial role in supporting cancer patients. They often are burdened with significant psychological distress and challenged by their new role and its responsibilities [107]. Therefore, understanding their experiences with nutrition care can help tailor support services to better meet the needs of both survivors and their caregivers.

Thus, this study aimed to investigate the availability of nutrition services and whether existing resources meet the nutrition care needs of patients and their carers. The present study aimed to expand current knowledge and awareness of survivors' unmet nutrition care needs. In the present study, qualitative methods were applied to bring the UGI cancer survivors' voices into our studies of survivorship care.

4.2 Methods

4.2.1 Eligibility

Adults over 18 years who were diagnosed with oesophageal or stomach cancer or their caregivers or family members were eligible to take part in the present study. Fluency in English was necessary to be eligible for the current study. Participants had to be Irish residents, with treatment completed in Ireland.

4.2.2 Ethical Approval

Ethical approval was sought from the Faculty of Health Sciences Ethics Committee at Trinity College Dublin. (Reference number: 2111010).

4.2.3 Recruitment

Recruitment for this study took place between April 2022 and January 2024 by voluntary sampling. The qualitative study was advertised through charity partners; the Irish Cancer Society and the Oesophageal Cancer Fund social media accounts. The study was advertised online in virtual social networks (LinkedIn, Facebook, Instagram), to identify interested participants. Additionally, in collaboration with the UGI clinic, a newsletter was prepared to introduce ongoing studies on oesophageal and gastric cancer. A section of the newsletter was devoted to the interview study, which introduced and advertised the study to potential participants. Contact details of the research dietitian (FS) were provided in the advertisement to offer participants the opportunity to call/email the investigator and request more details about the project or register their interest in taking part in the interviews. The newsletter was posted to UGI clinic patients on behalf of SJH UGI clinic.

4.2.4 Data Collection

Individuals were invited to take part in a semi-structured telephone interview. In addition to qualitative data, primary quantitative data regarding demographics, cancer diagnosis and treatment were also collected at the start of the interview. All interviews were conducted by a research dietitian (FS). The interview guide was adapted from a similar study on cancer survivors [113]. The interview script is included in Appendix VIII. Survivors and carers were asked about the availability of nutrition care during cancer treatment and recovery. They were also asked about nutritional challenges they faced during and post-cancer treatment and their coping strategies. Participants were asked about their experiences with nutrition care, and their recommendations for improving nutrition care were also explored.

The interviews were audio recorded and transcribed verbatim by FS. All identifiable data (names of participants, family members, clinical sites and medical team members) were removed from transcriptions prior to analysis.

4.2.5 Data Analysis

Descriptive statistics were used to summarise participants' characteristics. The interview transcript was analysed using Braun and Clarke's 6-stage approach to thematic analysis [300]. NVivo 12 software (QSR International, Australia) was used to code the interview transcripts. The analysis started with familiarisation with data by reading and rereading each transcript and noting initial impressions. Then, initial codes were generated by reviewing and analysing all individual transcripts. All quotes and phrases which captured or expressed the same or similar meaning and concept were set under relevant codes. In the next step, codes were grouped into

initial themes relating to research aims. Interview quotes, codes, and themes were independently reviewed and analysed by two researchers (FS and SD). FS and SD met and reviewed the preliminary analysis and completed a joint coding, which involved merging or removing codes to reach consensus on core themes and subthemes relating to the research question.

4.3 Results

Initially, 19 individuals expressed interest in taking part in interviews. However, seven participants did not complete the interviews due to the following reasons:

1. Two individuals (one survivor and one caregiver) did not meet the inclusion criteria as the cancer treatment was completed outside Ireland, and they were not Irish residents.
2. Five individuals didn't progress to enrolment as they did not respond to the researchers' phone calls and emails after initial expression of interest and receiving PIL.

Consequently, twelve interviews were completed and analysed in the present study. The average length of interviews was 46 minutes, ranging from 19 to 98 minutes. The final sample consisted of nine oesophageal and gastric cancer survivors and three family members of oesophageal cancer survivors. Participant characteristics are presented in Table 4-1. Participants received treatment and nutrition care from seven different hospitals located in the East (4), West (2), and South (1) of Ireland.

Following data analysis, three main themes and six subthemes were identified, as shown in Table 4-2.

Table 4-1. Characteristics of cancer survivors and family members participating in interviews (n=12)

	Participant Code	Age	Sex	Cancer Diagnosis	Time since surgery (months)
1	P1	76	M	Oesophageal	108
2	P2	56	M	Oesophageal	24
3	P3	63	M	Oesophageal	24
4	P4	34	M	Oesophageal	23
5	P5	51	F	Gastric	24
6	P6	71	M	Oesophageal	62
7	P7 ¹	60	F	Oesophageal	62
8	P8	62	F	Gastric	15
9	P9	58	M	Oesophageal	112
10	P10 ¹	50	F	Oesophageal	NA ²
11	P11	70	M	Oesophageal/Gastric	87/20
12	P12 ¹	55	M	Oesophageal	NA ²

¹ Interviewed family member, age and gender represent the interviewee's age and gender. ² The patient did not undergo surgical resection.

Table 4-2. Themes and subthemes

Theme	Subthemes	Codes
Nutrition related challenges and complications	Gastrointestinal related complications	Gastrointestinal symptoms
		Barriers to ONS compliance
	Impact on individuals' daily life	Meal preparation and altered meal plans
		Limited food choices
		Disturbed daily and social life
Experiences with dietetic service	Access and effectiveness	Accessibility of dietetic service
		Effectiveness of dietitian visits
		Continuation and frequency of dietetic follow-up
		Reiterating dietary advice
	Information needs	Tailored and practical dietary advice
		What to expect post-treatment
		Additional educational material and methods
Coping strategies	Practical strategies	Dietary modifications
		Accepting new normal
		Support for meal preparation
		Consideration for eating out
	Peer and external support	Peer support
		Support for carers

ONS, Oral Nutritional Supplement.

4.3.1 Nutrition-Related Challenges and Complications

Participants reported various nutrition-related challenges. These included complications associated with gastrointestinal (GI) symptoms and challenges impacting individuals' dietary habits, normal routine, and social life.

4.3.1.1 Gastrointestinal related Complications

Participants reported ongoing and long-lasting nutrition-related and GI symptoms from the start of their cancer journey and diagnosis through to survivorship. Diarrhoea, swallowing difficulty, and dumping syndrome were frequently reported symptoms.

"The only problem that I had, food-wise, I suppose, was every two or three weeks, I was getting bad runs of diarrhoea." [P3]

"I still have very loose bowels at the moment." [P6]

"Any type of chunky food will get caught. At a couple of times, I ended up in A&E but through dilation, it improved." [P9]

"If I eat something, half a glass of wine or a glass of water or anything after, it seems to push the food down too quickly, and I dump, dumping syndrome." [P11]

Participants also highlighted challenges for compliance with oral nutritional supplements (ONS). Taste fatigue, GI disturbance, prolonged and repetitive consumption of ONS, and a dislike of taste and texture were reported as factors that limit compliance with the ONS regimen.

"I kind of eased off the (ONS drink name) because you kind of get sick of the same flavours." [P2]

"You have to buy a box of 30. You have the same flavour. You just get tired of it." [P10]

"I think she was on it for so long. She just got sick of it. It was boring." [P12]

"I couldn't tolerate them because of its sugar." [P4]

"She'd (dietitian) given me some protein drinks, and they weren't really agreeing with me." [P5]

"I refuse to eat it (ONS) because they would make me gag." [P8]

"They cater very much towards fruit, hmm, and I think maybe if they could have more savoury ones." [P10]

"Supplements were very heavily tasted, although there were maybe fruit flavours, it was, it was still heavy creamy." [P11]

4.3.1.2 Impact on Individuals' Daily Life

Nutritional challenges and complications impacted survivors' daily routine and social life post-treatment. Several participants

highlighted the challenges associated with meal preparation and altered meal plans. Participants noted meal preparation as a time-consuming and effortful task due to altered dietary patterns post-treatment, which interfered with everyday life, work and leisure time. Also, the significant burden on caregivers in relation to meal preparation was reported.

"It's just you feel as if you're eating all the time or preparing food, oh that's tough I have to say." [P2]

"I find that my whole thinking every day revolves around, a lot of it, revolves around, you know, what am I going to eat next or what time will I eat." [P4]

"Keeping up that routine is kind of challenging for you on the weekend or when you're on holiday." [P2]

You can't sit down on the hour every two hours and have your lovely, prepared meal like it just doesn't work in everyday life, you know, especially if you're working." [P4]

"It's very hard when you consistently put food on the table, and somebody looks at it and then they go and get sick. As a partner, you're trying to second guess all the time. What will I cook? Will it? Will it appeal?" [P7]

Participants also reported limited food choices post-surgery due to fear of post-prandial complications or prioritising low-volume and high-calorie food choices to prevent weight loss.

“This is the same thing again is all. It looks so boring when you write it all down..... That’s just become so unusual to sit down to, you know, a salad. Normally, if I go out to my dinner and put salad on the side of the plate, somebody else will eat it because I’m not interested in using up that space for the salad.” [P2]

“No carbs, limit fruit and veg for nearly a year, very little, it’s all very different and hard to get your head around it.” [P5]

“I always like prawns and mussels and things like that, and I’m afraid to eat them now.” [P6]

Nutritional challenges and complications impacted survivors’ social life post-treatment. Participants discussed their concerns about socialising and dining with others due to GI disturbance and their special dietary requirements. They also noted the unpredictability of nutrition-related symptoms and how this impacted their daily routine as well as planning for leisure activities and socialising.

“You know the thing is, I don’t drink, so going out for a meal used to be our social thing. You know, its suddenly going out for a meal, it’s a bit of, a bit of an issue.” [P2]

"We didn't eat out, and then we did, but very much just together, never, never back with friends." [P7]

"We didn't go out, and she wouldn't go out. She was quite sick. She lost a lot of weight, and she didn't, she didn't really, she didn't feel like going out either." [P12]

"I would have loved to have gone out and had a few glasses of wine and, you know, a bit of fun and all that there for it. Now life is much more serious, and you know?" [P5]

"You'd be avoiding travelling like that if you couldn't get to the bathroom fast enough." [P3]

"You know he always has to be close to a loo, and he might very frequently, you know, throw up after eating." [P7]

"Every day is unpredictable. You can't plan. You cannot make a plan. We would never know, say next Friday we're doing this, it will depend, and at lunchtime, on Friday or in the middle of the afternoon, we might say, are we gonna do this?" [P7]

Some participants reported a lack of awareness and an unwillingness of hospitality staff to accommodate the dietary restrictions of UGI cancer survivors, which limited dining out and socialising around food.

"Actually, restaurants, most of are not very good. If you say to them, hey, I can't eat a lot, so please just give me half a

portion. I'm happy to pay for the whole dish. I'm not asking for a reduction in price. But just for food wastage or whatever, just give me a very small portion. Uhm, restaurants don't like that. They don't, they don't take that, and they always assume that you just want to pay less. It it's a challenge.” [P7]

“If I asked for the children's menu because it would be smaller, they wouldn't give it to me because I'm an adult, like very few places would accommodate.” [P8]

Also, participants voiced the psychological burden associated with special dietary considerations and symptoms as a barrier to social eating.

“You know, anxiety that something will happen could happen, that he could choke, that he might choke.” [P10]

“It is embarrassing going out with other people, and their having a three-course meal and here's me stuck with the main course.” [P9]

4.3.2 Experiences with Dietetic Service

4.3.2.1 Access and Effectiveness

The majority of participants reported a high degree of accessibility to dietetic services, particularly after surgical resection. Providing dietetic care simultaneously with cancer surveillance visits and remote dietetic services facilitated access to nutrition care.

“I used to e-mail them (dietitians and nurses); nothing was ever a panic. I'd e-mail them, and they get back in touch with

me within a few days..... It was made so easy. I wouldn't be shy about sending an e-mail to say If I had a problem." [P2]

"I have their (dietitians) number, and if I had any problems, I could always give a ring if I wanted to..... when I went up to see the consultant, I was meeting the dietitians the same day as she was checking weight and all that like and saying how I was.... doing like" [P3]

"They're (clinical team including dietitians) always there if I ever had a worry or a query, an e-mail or a call, and they're straight back to me." [P4]

"I have the dietitian's number on my phone. I just ring her. I can just ring her anytime I want." [P5]

"I had her (dietitian) number, and I had her two numbers, and she was contactable anytime I want to see her." [P8]

"The dietitian was available any time when you went for an appointment, and we had a phone number, we could ring."
[P10]

"Every time I visit the hospital to see the surgeon, which was maybe once, once a month for the first few months and then once every three months after that, I would see the dietitian

.... If I needed a dietitian, all I had to do was ring and make an appointment.” [P11]

The majority of participants reported positive feedback on their dietetic visits and found sessions helpful in answering their questions and concerns.

“The dietitians, they were very good, they were very attentive.” [P2]

“I was in contact with a dietitian up in the hospital. She was very good, and she put me in contact with my area dietitian then who, I’ve spoke on the phone two or three times, you know, she was very helpful too.” [P4]

“We were talking through where he (survivor) was with food or what he was doing, where we were going, those kinds of things, those kinds of meetings were very useful for me.” [P7]

“Every question was answered, and we were also given additional information to take home.” [P10]

However, when asked about the adequacy of dietitian contacts, participants expressed a need for additional contact with dietitians during the early stages of post-surgery. They also stated a need for extended survivorship care and contact with dietitians to manage the long-term and late effects of surgical resection.

“The only thing...that I was a little disappointed in because they the (hospital name) dietitians, they never get to find out

how things went for you.....Perhaps if they do a bit more over those six-monthly checks.” [P2]

“If it had been the case where they followed up, maybe more often, as I said for the month or two months afterwards, it probably would have helped me a little bit more.” [P4]

“I think if there was a way that you could have almost a weekly check-in with a dietitian, whether it's over the phone or in the hospital for the first three months, maybe even for the first six weeks, that maybe would have made a phenomenal difference.” [P7]

“It (dietitian visits) came to an end after a year, I felt this should continue for longer..... I just feel like you're on your own after a certain amount of time, you know.” [P9]

4.3.2.2 Information Needs

Despite positive feedback on the benefits of dietitian visits, participants discussed unmet information needs. Participants noted the necessity for personalised, tailored dietary advice to improve symptom self-management.

“The only thing that I didn't have was, the only thing I was ever a little bit unsure of was how acceptable my weight was. Because I had an idea of what I was, I knew I was going to lose weight, but I was never sure at what point, you know, do I get in touch?” [P2]

"It's not like a one leaflet fits all or one-size-fits-all. If it could be kind of tailored to suit the type of surgery that the person had, you know, it might benefit individuals better in, in my own opinion." [P4]

"Everybody's different, you know, it's different for everyone. One size doesn't fit all.....practical things that you can go out and buy in the shop like the protein yoghurts and fortified milk." [P5]

"They talk about having snacks and things like that, you know. Well, what exactly is a snack?" [P6]

"The advice was always very much the same. You know, just try, have high calorie-dense food, and you know that just wasn't appealing." [P7]

"You can't always go on what the leaflets tell you because everyday in my situation it's a different day.... even though we had the same diagnosis, but each cancer is different." [P8]

Participants expressed that they received limited information on nutritional challenges and common complications post-treatment. This information was deemed essential to facilitate adopting dietary modifications post-treatment. Participants also reported that this information may provide insight for recognising common versus major complications post-surgery, which might require clinicians' input.

"It would have been nice to have a little bit more support, a little bit more information about what to expect." [P1]

"Just generally (know) what will happen after the surgery. How you will tolerate foods, what kind of food and drinks you'll be able to have." [P4]

"Receiving a little bit more clear information about the biology and how your body has changed and what's the reason that you need to do this modification in your diet after the surgery.... you know what is normal and what isn't." [P5]

"Possibly if I had had those recipe books at the beginning, I might have been practising some of those recipes, trying to see what they would look like taste like. You know, we might have been talking a little bit more about how the schedule would need to change after his surgery." [P7]

"I didn't receive any information about swallowing or choking. This was, this was a new experience for me, I believe that if there were, you know, if it's common that people choke after gastrectomy and the oesophagostomy, then there should be some information there to indicate... at least give the patient an idea of what's ahead of them." [P11]

"I suppose just knowing what was ahead because it was, it was difficult to deal with it as it was happening, you know."

But if you knew what was ahead of you....., it would help to pre-arm you.....and could help.” [P12]

When asked for feedback on information received (i.e., written information, books, leaflets, etc.), participants suggested additional educational material and methods such as videos, trusted online resources and online forums to allow live interactions between survivors and dietitians.

“Maybe a few short little videos made that would back up the leaflets. if you could visually see the person with the stomach cramps, maybe run into the toilet, you know, different things like that, you kind of know what is ahead of you because sometimes reading it, it doesn't have the same impact actually.” [P4]

“YouTube videos and how to, you know, on recipes, easy recipes to make yourself in the in the early days.” [P5]

“If there was a website or a web, you know, someplace I could log into that would have that information just all in one place. I tend to be a bit messy, and I pick things up and put them down and forget where I put them.” [P6]

“I do think what might have worked, what would work, would be some sort of a forum that includes dietitians that is optional for people to call in to if they're struggling with food or struggling with recipes, are struggling with taste that people could maybe share, share what works or what doesn't work.” [P7]

Reflecting on received nutrition information and care, participants highlighted the benefits of continuous education and reiteration of dietary recommendations to improve compliance. It also was noted that complications at the acute phase post-surgery might limit the absorption and retention of dietary information. Therefore, repeated self-education and reminders from dietitians were suggested to improve adherence to dietary advice.

"I just started reading through that (leaflet) again, you just remember things about chewing everything to the very last bit." [P2]

".... like the dietitians, and that would have, I suppose, reinforced a lot of the stuff that you had been told earlier on, like." [P3]

"I tend to forget things quite quickly, whereas a book, you can go back and look where it is." [P5]

"You know, I was very ill at that stage very, very ill, and I found it very hard to take everything that was coming at me on board....it was a lot for me to take on board, you know. So, I tended to, you know, I picked up some of it and then I would try and look it up on the internet." [P6]

"You would read something and go, I really do need to implement these smaller meals and more often because you kind of keep falling back into this view of I'm OK again, so I'm

normal again, so.... I think your brain goes back to what it used to be.” [P7]

4.3.3 Coping Strategies

When participants were asked about how they managed their GI symptoms and complications, several coping strategies to deal with post-treatment complications were described. It included practical and suggested strategies, peer support, and additional support for family members and caregivers.

4.3.3.1 Practical Strategies

Following dietary recommendations and modifying food choices were attempted to prevent and manage complications. Eating small frequent meals, avoiding drinking at mealtime, avoiding certain food items, and safe swallow strategies were often reported to reduce nutritional complications.

“Certain items which I have trouble with, mushrooms, for example, unless they have been cut very, very, very small otherwise, they regurgitate.” [P1]

“I don't drink anything when I'm eating now.” [P2]

“If there is extra fat or if they're extra heavy, you might not eat as much.” [P4]

“Maybe 20% of my diet is carbs, and then I try, and I have 50% protein.” [P5]

"I've cut down a lot on white bread, and I keep well away from spicy type (of food)." [P6]

"I have to be very careful; like anything with sugar, like chocolate, I can eat, but like jellies and things like that, I have to avoid candy sweets and things like that." [P8]

"(The) amount of food I can eat at each meal is small amount and often, like a main meal divided...., you see, broken to two or three meals." [P9]

"We exchanged rice for plenty of mashed potato and fish and sauces and stews. So, it wasn't getting stuck in the oesophagus." [P10]

"I can't take a piece of meat, chew it up and swallow it. I have to chew it and chew it, chew it and chew it until I am very sure that pieces are very small, and then I can swallow it without problems." [P11]

Acceptance was highlighted as a key strategy for adapting to changes and new life post-treatment.

"You just adapt. Just over time, you know, it's just the new normal, and it's OK." [P5]

"I think you come out the other side of this, and you learn to adapt, and you learn to live differently or live in a way that works." [P7]

"I've learned to live with them. I accept that my eating is not the way it was before my treatment." [P9]

"We've made it the norm that that's the way it is. So, at this stage, it's just accepted, you know." [P10]

"I don't believe I'll, I'll ever be able to, to get back to where I used to be. I've come to terms with that." [P11]

Availing of support from family and caregivers for meal preparation and purchasing ready meals was suggested to improve food access and nutritional adequacy post-treatment. It also may reduce the burden on survivors.

"If you get somebody to cook for you, ... would be great. It's a big help.....the pre-prepared meals, something like that, that might help somebody." [P2]

"Supply of ready meals might be a good idea..... on the weeks where the food is in the fridge, they work better than the week where you're trying to decide day-to-day what will we have today." [P7]

Participants also discussed their strategies for limiting the impact of treatment on their social life by considering changes in their social dining habits. These included requesting smaller portions or one-course meals and adjusting the type, time and duration of social dining.

"If I go to a restaurant, I'll ask for the children's menu.... we'll have a child size menu and I'll; I'll pace myself so there's a small amount in the evening rather than a full-blown meal, it's like I have two starters rather than a starter and a meal." [P1]

"You might go out, and you just have a starter instead of a whole meal.... I say no, no, I want this starter, but at the main course time." [P2]

"I wouldn't have something like soup for a starter or something like that because it's so filling." [P3]

"So, we now if we're meeting friends, we just go for an early bird in a very kind of concise short window of time and it's great. We can catch up with friends again, but. But it's not too long, and it's early so that he can cope with that.... we tend now to eat out differently and to eat out maybe just order one course." [P7]

"I would always order the main course. I would never have the starter or the dessert because I just cannot eat that amount of food." [P9]

"We would look at the menu very carefully and choose very carefully. Umm, go for a light fish, not a steak." [P10]

4.3.3.2 Peers' and External Support

When asked about insights or experiences of attending support groups, some participants described the benefits of joining support groups, such as peer learning and emotional support for coping with the side effects of treatment. However, availability and access to support groups varied depending on geographical location and type of cancer. Establishing virtual support groups was also suggested to improve access to peer support.

"In one of those support meetings, some other fella said that he had the same problem. But he takes the (medication name) before he goes to bed, and I started doing that, and it has changed my life." [P3]

"You could actually talk to others that were in the same boat, or you could discuss, you know, how you are getting on with your food intake or what works for you and then you know what works for someone else.... what people are able to eat or hints or tips that others might have." [P4]

"It would be good if there was a support group in Ireland for stomach cancer survivors.... I'd love to talk to somebody been through the same journey as me. So, like that would have really helped." [P5]

"Probably WhatsApp group, which may be backed up with a possibility of an online meeting every now and again, or even a, you know, the group get together at some stage." [P6]

"You might hear other people asking questions. You might realise that you're not alone, that this, this, this particular thing is impacting more than you, and you might pick up, you know, from other people's questions, you might pick up better tips or better advice." [P7]

"People could share, you know, any fears that they're having, whether it's patient or carer or a mix of both, that it would definitely be open to both. I sometimes think you don't know what you want to ask until you hear somebody else ask it, and then you go, Oh my God, that's a great piece of information. You know, and that's why I think the forum is better than a one-to-one." [P7]

"Even manage to connect with somebody who is also a carer that could be a support. Because as a carer on this journey, you're very alone." [P7]

"It (support group) does help because, like, you know you're not the only one." [P8]

"You learn like not everyone has the same side effects. Some of them do, and some of them have some. It's always interesting to hear the stories and these similarities.....you're not the only one who's on this type of diet, and it's nice to see that." [P9]

“Just to share stories or share what care at different stages that other people are going through that you might need in the future.” [P10]

Participants also highlighted the lack of information on available resources for caregivers and family members. Introducing available resources at an appropriate time was suggested to support caregivers.

“A little bit more information for carers in general in terms of what resources are there for them at the beginning would be really, really a good thing.... I think to know that there were some more resources that were just there, you could have availed of them if you'd known. I think all of that just a little bit earlier on would make a huge difference for the, for the people who are part of the support network of the patient.” [P7]

“You don't realise until things go bad that you need support. In the good times, you go fine, don't need, everything's fine, grand you know, and things go bad, you go. Oh, my goodness. Where do I turn? Who do I turn to?” [P10]

4.4 Discussion

This study explored for the first time the experiences of UGI cancer survivors and their caregivers regarding dietetic services in Ireland, the nutritional challenges they face post-treatment, and their preferences for receiving nutritional care. Four key findings emerged:

1. UGI cancer survivors continue to experience long-term effects that significantly impact their daily and social lives.

2. Although dietetic services are available during the acute recovery phase, there is a clear need for more intensive support during this period and extended follow-up care.
3. There are several unmet needs, including limited information on post-treatment complications, lack of practical and personalised dietary advice, lack of innovative and interactive education tools, and the necessity for repeated education.
4. Survivors suggested several strategies to manage the adverse effects of treatment, including dietary modifications, acceptance, peer support, and additional resources to assist both survivors and their caregivers.

4.4.1 Persistent GI Disturbance

In the present study, participants reported persistent GI disturbance, which they attempted to manage with dietary and lifestyle modifications. This finding was in line with a previous study which reported the implementation of dietary modifications by cancer survivors to limit nutrition impact symptoms (NIS) [301]. Participants also spoke of accepting and adopting a “new normal” as another coping strategy, which is a common theme in the literature exploring patients’ experiences after UGI cancers [109, 241, 302]. Whilst some level of adaptation is to be expected, it must be considered that some of these symptoms do not need to be simply tolerated and may, in fact, persist as a result of inadequate dietetic support and follow-up. Aligned with previous studies, the results of the present study demonstrated that persistent and unpredictable NIS were associated with emotional distress and anxiety in social situations involving eating [303, 304]. Long-lasting NIS beyond the acute phase of survivorship can impact cancer survivors’ physical, emotional, and social function [241, 305]. Post-operative follow-up has traditionally focussed on tumour recurrence and survival, but

given the significant and long-lasting burden of GI symptoms in UGI cancer survivors, there is an increasing need to monitor and address GI symptoms and complications to enhance survivors' quality of life [306].

4.4.2 Accessibility and Effectiveness of Dietetic Services

The majority of participants in the present study acknowledged the helpfulness of dietitian input and reported that dietetic services were generally accessible. This finding is consistent with a national survey which reported positive views regarding the role of nutrition in cancer care, high ratings of the helpfulness of dietetic input in cancer survivors, and greater access to dietetic services in UGI cancers [222, 297]. However, the need for repeated dietary education, extended dietetic reviews and follow-ups, frequent contact with dietitians in the acute phase post-discharge, and practical and timely information was highlighted in the present study. Limited dietary follow-up led participants to seek dietary advice from other sources, which may be complicated by the difficulty in identifying reliable information sources [307]. Previous studies have suggested that frequent exposure to nutritional information can lead to dietary modifications and highlighted the need for repeated nutritional education to address cancer survivors' dynamic needs [308, 309]. Regular contact with a dietitian has also been shown to improve self-confidence in symptom management and lead to positive behavioural changes in gastrointestinal cancer survivors[310, 311].

It was noteworthy that participants reported receiving limited information and guidance about common postoperative complications and symptoms. This aligns with findings from Bennett

et al., where oesophageal cancer survivors reported a lack of information about what to expect throughout cancer treatment and survivorship and highlighted the importance of this information to empower patients and their families to prepare for challenges during the cancer journey [312]. Preoperative nutritional consultation has been shown to positively impact weight loss, oral intake, and reduce readmissions due to tube-feeding-related complications in oesophageal cancer survivors[311, 313]. Thus, providing information on treatment and its associated side effects should be considered in standard care to prepare patients and their caregivers for managing potential symptoms and improving overall treatment adherence.

4.4.3 Resource Limitations and Alternative Approaches

As noted above, the findings of the present study highlight a significant need for intensive dietetic input with pre-operative education, frequent support during the acute post-operative recovery, and extended dietetic follow-up into long-term survivorship. However, resource limitations can impact the frequency and continuity of contact with dietitians [310, 314]. This is particularly relevant in the current Irish context, where oncology dietetic services are severely under-resourced [222, 246]. In 2019, the Irish Nutrition & Dietetic Institute (INDI) reported to the National Cancer Control Programme (NCCP) that the dietitian-to-patient ratio was far below the desirable level of 1:120, with only one dietitian per 4,500 cancer survivors in Ireland [222, 246, 315]. In light of resource limitations, dietetic service providers should consider various approaches to care delivery. Alternative approaches to improve care delivery, such as telephone consultations, virtual group education, and online forums and dedicated websites, were suggested by participants. Respondents also suggested access to online interactive information sources and visual education material to enhance the effectiveness

of nutritional education. Interactive forums have been recommended as cost-effective strategies to deliver nutrition care amidst a stretched dietetic service and have previously been reported as the preferred method for receiving nutritional information and support by Irish cancer survivors [299, 316].

4.4.4 Reviewing Standard Dietary Advice

The standard dietary advice provided to UGI cancer survivors should also be reviewed in light of the findings of this study. For example, oral nutritional supplements (ONS) remain the cornerstone of dietary advice for poor appetite and malnutrition [114, 117, 317]. However, it was evident in this study that they were poorly tolerated and complied with, which will negate their benefit. Factors affecting adherence to ONS in cancer patients include changes in taste and smell, swallowing difficulty, GI disturbance, palatability, and prolonged ONS consumption [318]. Several strategies are recommended to improve ONS compliance, including considering sensory changes in cancer in designing ONS products, optimising ONS texture and flavour profiles, and providing ONS products based on individual preference [318, 319]. However, these strategies can only be effective as part of a framework where there is regular dietetic contact with survivors and caregivers throughout treatment and survivorship to adapt a personalised care plan.

Participants also emphasised the need for personalised and practical dietary advice. Receiving generic dietary advice and a lack of practicality were reported in previous studies involving Irish and international cancer survivors [298, 299, 307, 320]. Practical, individualised dietary guidance that considers the real-life challenges of meal preparation is essential for ensuring better nutritional outcomes for UGI cancer survivors. In a study by Wang et al., difficulty in meal preparation was reported as a predictor of poor nutritional

status in gastric cancer survivors [214]. In the current study, survivors and their caregivers highlighted the burden of meal preparation and the lack of practical dietary advice and information to help manage this challenge. To address this issue, participants in the current study suggested that caregiver assistance with meal preparation and access to ready-made meals could help reduce the burden. Similarly, previous studies suggested that formal and informal support, ready meals, and food delivery services can support meal preparation and prevent dietary inadequacy [113, 321]. Therefore, it is recommended that post-treatment dietary advice be individualised, with particular attention given to meal preparation challenges to ensure effective nutritional care.

4.4.5 Peer Support

Access to support networks has an important role in coping with psychological challenges in cancer survivors [320]. In this study, participants highlighted limited access to peer support and emphasised the benefits of such support. In line with the participants' views, information, emotional support, and transferring knowledge and experience are suggested as benefits of peer support in cancer [304, 322]. However, it is important to consider the potential challenges in developing support groups, including the negative impact of observing the deterioration of peers' health, diverse information needs, group dynamics, leadership and sustainability [304, 322].

4.4.6 Support for Carers

Participants also stressed the importance of timely access to information about available services and support for caregivers. Caring for a loved one with UGI cancer is stressful and restrictive and often can change caregivers' daily routines [107]. Indeed, the adverse

impact of cancer treatment has been shown to affect carers' social life and their relationships [323]. Therefore, it is essential to consider caregivers' needs and implement strategies to prepare caregivers for supporting cancer survivors and also addressing their needs [107, 324]. Providing a list of available psychosocial support and other resources at the time of diagnosis is recommended to better support patients and their caregivers throughout the cancer journey [91]. A recent systematic review of studies on carers' experience of supporting UGI cancer survivors indicated the benefits of social, psychological, and practical resources on mediating carers' burden [112]. Providing caregivers with psychoeducational programmes, skills training interventions, and therapeutic counselling has been shown to significantly reduce caregiver burden, enhance their coping abilities, boost their self-efficacy, and improve various aspects of their quality of life [325].

4.5 Strength and Limitations

The present study focused on UGI cancer survivors who received treatment and resided in the Republic of Ireland, representing current unmet nutrition care needs in the Irish health system (Health Service Executive). Also, participants in the present study completed their treatment in seven different hospitals located in various regions in Ireland. This can reduce the bias associated with differences in care received and capture common unmet needs in UGI cancer survivors in Ireland. The majority of participants were >2 years post-treatment, which allowed investigation of nutrition care needs in long-term survivorship. Furthermore, the semi-structured design of interviews and the completion of all interviews by a single researcher ensured consistency in data collection. Moreover, the interviews were completed by phone at the survivors' convenience

while in their own environment, perhaps creating a more comfortable situation for reflecting on their survivorship challenges [326]. Also, by collecting qualitative information through individual interviews, the impact of peers on respondents delivering expected and stereotypical answers can be reduced [327].

The following limitations need to be taken into account when evaluating the findings of the present study. Firstly, study participants were not blinded to the research question; therefore, there is a possibility that survivors who completed the interview had a strong positive interest in nutrition or had more profound nutrition-related complications. Other limitations include the possibility of recall bias in long-term survivors, and social desirability bias, which may impact the findings of the present study [320, 328].

4.6 Conclusion

To our knowledge, the present study was the first to obtain UGI cancer survivors' and their carers' experience of nutrition care and their insight on current gaps and optimum nutrition care in Ireland. The findings highlighted the need for more dietitian support pre-operatively, during the acute recovery phase and extending into long-term survivorship. Additionally, the present study highlighted the importance of offering timely, personalised, and practical dietary information to survivors and their caregivers. Furthermore, the findings highlight the need for peer support and additional resources to help survivors, and their caregivers effectively manage the long-term effects of cancer. This information can guide the development of tailored nutrition care programmes for UGI cancer survivors in Ireland.

Chapter 5 Nutritional Status, Sarcopenia and Dietary Intake in UGI Cancer Survivors-A Cross- Sectional Study

This chapter describes a cross-sectional study that objectively investigated the prevalence of malnutrition and sarcopenia in a sample of UGI cancer survivors enrolled in a clinical trial examining multidisciplinary rehabilitation (ReStOre II study). It also examined nutritional adequacy and dietary habits in this cohort.

5.1 Introduction

As described earlier in 1.6, inadequate dietary intake, unintentional weight loss, and malnutrition are prevalent and significant concerns in patients with UGI cancers. Approximately 80% of these patients may experience clinically significant (>10%) weight loss and have the highest malnutrition rates (40% to 80%) among all tumour groups [229, 329-331]. Previous Irish and international studies have highlighted the persistence of malnutrition among UGI cancer survivors, with approximately 30% remaining malnourished or at risk of malnutrition after treatment [75, 200, 233, 332].

Unintentional weight loss and malnutrition are often accompanied by sarcopenia, which results in impaired muscle function and strength [333]. UGI cancer survivors are at high risk of developing sarcopenia due to the malignancy itself and the side effects of treatment [66, 70]. Several studies have reported an association between sarcopenia and reduced survival in cancer patients [334-336]. The risk of sarcopenia may remain high after the completion of treatment due to long-term and ongoing treatment-related complications [337]. However, despite its significance, few studies have evaluated the prevalence of sarcopenia in UGI cancers following surgery. A previous study by Mayanagi et al. found that 59% of patients experienced a continued reduction in skeletal muscle mass from diagnosis to four months post-oesophagectomy [338]. In Mayanagi's study, skeletal muscle wasting was an independent prognostic factor for worse overall and recurrence-free survival [338]. Another study by Kudou et al. found that 30% of disease-free survivors developed sarcopenia at 6 months post curative surgery for oesophagogastric cancer, and this group had a higher recurrence rate compared with patients who did not develop sarcopenia [339]. The

results of these two studies suggested that post-operative muscle wasting and sarcopenia may be a stronger prognostic factor for poor overall survival than pretreatment sarcopenia status [338, 339]. Previous Irish data have also indicated an increased prevalence of sarcopenia and muscle loss following surgery [76, 340]. A study by Elliott et al. reported that 35% of survivors had sarcopenia one year after undergoing oesophagectomy [340]. Similarly, a study by Heneghan et al. demonstrated a significant reduction in skeletal muscle index between 18 and 24 months after oesophageal and gastric cancer surgery [76].

Malnutrition and sarcopenia are not only associated with poor prognosis and reduced survival rates but also impair quality of life and physical function [334-336, 339, 341]. Thus, timely diagnosis and treatment of malnutrition and sarcopenia are crucial for improving outcomes for cancer survivors [342]. However, there is a notable lack of data on the prevalence and severity of malnutrition and sarcopenia in long-term, disease-free UGI cancer survivors in Ireland. This information is essential for developing a tailored, cancer-specific survivorship care plan.

Although arresting unintentional weight loss and reducing symptom burden have been the primary targets of nutritional interventions in cancer, the growing population of long-term cancer survivors demands a broader focus on long-term health outcomes [343]. Previous studies have reported increasing numbers of cancer survivors living with chronic medical conditions like hypertension, diabetes, and obesity [344, 345]. A higher prevalence of these comorbidities was observed in UGI cancers compared to other cancer types [346, 347]. Management of these comorbidities, whether they have been present before cancer diagnosis or developed after, can be challenging [348, 349]. Lifestyle modifications such as diet,

smoking, alcohol consumption and physical activity may be beneficial in the management of chronic comorbidities as well as contributing to improved cancer survival and reducing recurrence [350, 351]. Despite the recognised benefits of these lifestyle modifications, there is a lack of specific guidelines for cancer survivors on preventing recurrence; therefore, cancer survivors are advised to follow the general recommendations for cancer prevention, such as those published by the World Cancer Research Fund (WCRF) and the American Institute for Cancer Research (AICR) [352]. The WCRF/AICR scoring system assesses adherence to eight of the ten cancer prevention recommendations from their third expert report published in 2018. These recommendations aim to promote a healthy diet and physical activity for cancer prevention [352]. In several studies, greater adherence to WCRF/AICR recommendations was associated with reduced risk of cancer diagnosis and mortality [350, 351]. However, research on the adherence of UGI cancer survivors to these recommendations, especially post-surgical treatment, is scarce [233].

Overall, the present study aimed to address the aforementioned knowledge gaps. Hence, in a cohort of UGI cancer survivors enrolled in a trial examining multidisciplinary rehabilitation, the following were assessed:

- The prevalence of malnutrition and sarcopenia
- Dietary intake and adequacy
- Compliance with cancer prevention guidelines

The findings of the present study may help to identify nutritional interventions required to improve long-term outcomes in UGI cancer survivorship.

5.2 Methods

The assessments and data collection presented in this chapter were carried out as part of the baseline assessments of the ReStOre II study [138]. The data represent nutrition-related assessments collected between March 2022 and March 2023. Ethical approval for the ReStOre II study was sought from the Tallaght University Hospital (TUH)/ St James's Hospital (SJH) Joint Ethics Committee[138].

5.2.1 Eligibility

Cancer survivors with a histologically confirmed diagnosis of cancer of the oesophagus or stomach who had undergone surgery with curative intent were eligible to participate. Participants were required to complete their cancer treatment (surgery $\pm$ adjuvant therapy) at least three months prior to enrolment without any ongoing severe postoperative morbidity, evidence of active or recurrent disease or medical disapproval to participate [138].

5.2.2 Recruitment

Participants were recruited for the ReStOre II study as per the study protocol [138]. The patient database in St James's Hospital (National Centre for Oesophageal and Gastric Cancer) was screened to identify eligible participants. A list of eligible participants was sent to the clinical team requesting clinical clearance to be invited to participate in the ReStOre II study. Following this, a copy of the PIL and an invitation letter were sent to suitable participants. After seven days of reflection, a follow-up telephone call was made. Initial verbal consent was obtained over the phone, and an in-person baseline assessment was scheduled at the Wellcome Trust HRB Clinical Research Facility at St James's Hospital, Dublin, Ireland. Written informed consent was obtained before starting assessments.

5.2.3 Outcome Measures

5.2.3.1 Demographics and Medical History

Demographic data and medical history were collected from participants' electronic medical records. These included age, gender, cancer diagnosis and treatment, past medical history and comorbidities.

5.2.3.2 Anthropometric Measurement and Body Composition

Anthropometric measurements, including height, weight, waist circumference and mid-arm circumference, were completed as described previously in Chapter 2, section 2.6.1. Body composition was assessed by BIA as described in Chapter 2, section 2.6.2.

5.2.3.3 Muscle Strength and Physical Function

Hand grip strength was measured using a Jamar grip strength dynamometer per standard guidelines described in Chapter 2, section 2.6.3.1. Physical function was assessed using the short physical performance battery (SPPB) test as described in Chapter 2, section 2.6.3.2.

5.2.3.4 Dietary Intake

Dietary intake was recorded by 24-hour food recall using the Foodbook24 tool [165], which converted food intake to nutrient intake. The dietary intake data were compared to dietary reference values (DRVs) from European Food Safety Authority (EFSA) guidelines [353].

5.2.3.5 Adherence to WCRF/AICR Recommendations

Adherence to cancer prevention recommendations was assessed by scoring 24-hour food recalls according to the WCRF/AICR scoring

system [354, 355]. In the present study, adherence to 7 recommendations (breastfeeding excluded) was assessed, and a breakdown of scoring is presented in Table 5-1. In the present study, it was necessary to modify the scoring of the red and processed meat component. Since 24-hour recalls were obtained, daily intake of red and processed meat was used to score this component instead of weekly consumption of red and processed meat. Therefore, daily intake of 71g/day of red meat (500g/7 days) and 3-14g/day of processed meat (21g-100g/7 days) were considered as cut-off points for scoring this recommendation. A list of items considered as processed meat is included in Appendix IX. Adapted ultra-processed foods (aUPFs) were considered under the fast food and processed food category. These foods were adapted from the NOVA classification system, excluding ultra-processed foods and drink products that were already addressed elsewhere in the score, such as sugar-sweetened drinks and red and processed meat. A list of food and beverages considered as aUPF is presented in Appendix X. Grams of red and processed meat, fruits and vegetables consumed as composite dishes were also calculated using the standardised recipes in the Food Standards Agency recipes database and were added to amounts consumed as single food items to calculate the total amount consumed [356]. It should be noted that to access the Food Standards Agency standard recipes database, an End User Licence agreement was signed between the UK Data Service and the research dietitian (FS). The list of recipes used and food components disaggregated from recipes is included in Appendix XI. However, the percentage of the components is not reported due to End User Licence terms and conditions.

Table 5-1. Breakdown of the 2018 WCRF/AICR score[354]

2018 WCRF/AICR Recommendations	Operationalisation of Recommendations	Score
1. Be a healthy weight	BMI (kg/m ²)	
	18.5–24.9	0.5
	25–29.9	0.25
	<18.5 or ≥30	0
	Waist circumference (cm (in.))	
	Men: <94 (<37) Women: <80 (<31.5)	0.5
	Men: 94–<102 (37–<40) Women: 80–<88 (31.5–<35)	0.25
	Men: ≥102 (≥40) Women: ≥88 (≥35)	0
2. Be physically active	Total moderate-vigorous physical activity (minute/week)	
	≥150	1
	75–<150	0.5
	<75	0
3. Eat a diet rich in whole grains, vegetables, fruit and beans	Fruits and vegetables (g/day)	
	≥400	0.5
	200–<400	0.25
	<200	0
	Total fibre (g/day)	
	≥30	0.5
	15–<30	0.25
	<15	0
4. Limit consumption of “fast foods” and other processed foods high in fat, starches or sugars	Per cent of total kcal from ultra-processed foods (aUPFs)	
	Tertile 1	1
	Tertile 2	0.5
	Tertile 3	0
5. Limit consumption of red and processed meat	Total red meat (g/week) and processed meat (g/week):	
	Red meat <500 and processed meat <21	1
	Red meat <500 and processed meat 21–<100	0.5
	Red meat >500 or processed meat ≥100	0
6. Limit consumption of sugar-sweetened drinks	Total sugar-sweetened drinks (g/day):	
	0	1
	>0–≤250	0.5
	>250	0
7. Limit alcohol consumption	Total ethanol (g/day)	
	0	1
	>0–≤28 (2 drinks) males and ≤14 (1 drink) females	0.5
	>28 (2 drinks) males and >14 (1 drink) females	0
Total Score Range		0–7

5.2.3.6 Malnutrition

The Simplified Nutritional Assessment Questionnaire (SNAQ) was used for malnutrition screening and identifying the risk of malnutrition. Global Leadership Initiative on Malnutrition (GLIM) criteria were used for malnutrition diagnosis [357]. Phenotypic and etiologic criteria used for the diagnosis of malnutrition are summarised in Table 5-2. According to the GLIM criteria, at least one phenotypic and one etiologic criterion should be met to confirm malnutrition diagnosis.

Table 5-2. Phenotypic and etiologic criteria for the diagnosis of malnutrition [357]

Phenotypic Criteria			Etiologic Criteria	
Weight loss (%)	Low body mass index (kg/m ²)	Reduced muscle mass	Reduced food intake or assimilation	Inflammation
>5% within the past six months, or >10% beyond six months	<20 if <70 years, or <22 if >70 years	Reduced by validated body composition measuring techniques	Any chronic GI condition that adversely impacts food assimilation or absorption)	Acute disease/injury or chronic disease-related

Body composition was assessed by BIA, and a fat-free mass index (FFMI) cut-off of <17kg/m² and <15kg/m² indicated reduced muscle mass for men and women, respectively [357]. Dietary intake data obtained from the 24-hour recalls were used to determine reduced food intake. A cut-off of ≤50% of minimum energy requirements was considered as an indication of reduced food intake [357], considering 25kcal/kg body weight as the minimum energy requirement [114]. Self-reported chronic diarrhoea, dysphagia, nausea, vomiting, and oesophageal strictures were considered as indicators of reduced food assimilation or absorption. The presence of conditions associated with mild to moderate inflammation,

including heart failure, chronic obstructive pulmonary disease, asthma, Crohn's disease, coeliac disease, rheumatoid arthritis, diabetes, metabolic syndrome, chronic kidney disease, mild/moderate pancreatitis, were considered as chronic/disease-related inflammation [358]. These data were extracted from electronic patient records.

5.2.3.7 Sarcopenia

The European Working Group on Sarcopenia in Older People (EWGSOP) developed a practical clinical definition and diagnostic criteria for age-related sarcopenia [359]. The operational definition of sarcopenia is presented in Table 5-3 and Figure 5-1 below. Probable sarcopenia was identified by Criterion 1, and the diagnosis was confirmed by additional documentation of Criterion 2. If Criterion 1, 2 and 3 are all met, sarcopenia was considered severe [359].

Table 5-3.2018 EWGSOP operational definition of sarcopenia [359]

Criteria	Definition
Criterion 1	Low muscle strength
Criterion 2	Low muscle quantity or quality
Criterion 3	Low physical performance

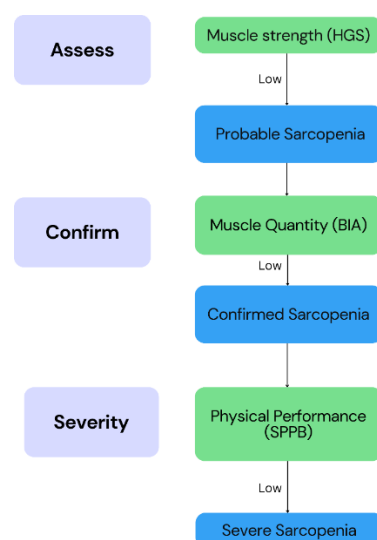


Figure 5-1. EWGSOP2 algorithm for sarcopenia diagnosis and quantifying severity[359]

In the present study, HGS was used to examine criterion 1, with cut-offs of HGS <16kg for women and HGS <27kg for men, indicating low muscle strength [359]. Appendicular skeletal muscle mass (ASM) was used to define low muscle quantity, and cut-offs of ASM <15kg for women and ASM <20kg for men were considered low muscle quantity [359]. ASM was calculated by the sum of total arms and legs skeletal muscle mass measured by BIA. The Short Physical Performance Battery (SPPB) was used for the identification of low physical performance, and an SPPB ≤ 8 was considered an indicator of poor physical performance [359].

5.2.4 Statistical Analysis

Statistical analysis was performed using SPSS software (Version 29). A Shapiro-Wilk test was used to assess normal data distribution. Descriptive analysis was used to present frequencies (number and per cent) of ordinal and categorical variables. Continuous data are presented as mean and standard deviation (SD). A one-sample t-test was used to compare means. A P-value of 0.05 or less was considered statistically significant.

5.3 Results

5.3.1 Demographics

Baseline data from the first 43 participants of the ReStOre II study were analysed. The majority of participants were male (70%) with oesophageal cancer (72%), and 28 subjects (65%) were over 65 years old. The mean time from surgery was 46 months; over 75% were >12 months post-surgery, and 67% were >2 years post-surgery. Participants' demographic characteristics and medical history are summarised in Table 5-4.

Table 5-4.Participants' demographic characteristics and background medical history (n=43)

Characteristics		Value
Age (Years,) Mean (SD; range)		68.02 (9.25; 44-86)
Sex, n (%)	Male	30 (69.8)
	Female	13 (30.2)
Cancer type, n (%)	Oesophageal	31 (72)
	Gastric	12 (28)
Tumour type, n (%)	Adenocarcinoma	35 (81)
	Squamous cell carcinoma	6 (14)
	Associated Barrett's (High-grade dysplasia, HGD)	2 (5)
Time since surgery in months, Mean (SD; range)		46.03 (39.35; 3.5-145)
Underwent neoadjuvant treatment, n (%)		26 (60.5)
Underwent surgical resection, n (%)		43 (100)
Surgical procedure, n (%)	2 stage oesophagectomy	21 (48.8)
	3 stage oesophagectomy	6 (13.9)
	Total gastrectomy	12 (27.9)
	Subtotal gastrectomy	4 (9.3)
Underwent adjuvant treatment, n (%)		10 (23)
Smoking, n (%)	Never	19 (44.2)
	Ex-Smoker	24 (55.8)
Alcohol, n (%)	Yes	29 (67.4)
	No	14 (32.5)
Gastroesophageal reflux disease (%)	Yes	21 (48.8)
	No	22 (51.2)

5.3.2 Nutritional Status

As presented in Table 5-5, according to WHO BMI cut-offs, the majority of participants (79%) were classified as healthy weight or overweight, with only 7% underweight.

Table 5-5.Anthropometric measurements (n=43)

Anthropometric Measure	Mean (SD)
Waist Circumference (cm)*	89.95 (13.57)
Mid arm circumference (cm)*	28.08 (3.08)
Weight kg	70.96 (16.22)
BMI kg/m ²	25.25(4.64)
n (%)	
Underweight (<18.5 kg/m ²)	3 (7)
Healthy weight (18.5-24.9 kg/m ²)	17 (39.5)
Overweight (25-29.9 kg/m ²)	17(39.5)
Obese (> 30 kg/m ²)	6 (14)

* Data available on 40 participants

A SNAQ score was available for 42 participants. The mean SNAQ score was 14.21 (SD 2.59), and 21 individuals (50%) had a SNAQ score ≤ 14 , indicating a high risk of malnutrition. Data were available for 38 participants to confirm malnutrition based on GLIM criteria, of which 12 (31.57%) participants had confirmed malnutrition based on GLIM criteria.

Table 5-6. Malnutrition diagnosis according to GLIM (n=43)

GLIM criterion		Participants fulfilling the criterion n (%)
Phenotypic	Low BMI	8 (21.05)
	Significant weight loss	2 (5.26)
	Reduced muscle mass	10 (26.31)
Etiologic	Disease burden/inflammatory condition	6 (15.78)
	Food intake $\leq 50\%$, n (%)	0 (0)
	Presence of symptoms of reduced food assimilation/absorption	25 (65.78)
Diagnosis of malnutrition		12 (31.57)

5.3.3 Sarcopenia and Physical Performance

Grip strength was available in 42 participants, and 10 (23.8%) had probable sarcopenia based on HGS. BIA data were available for 8 out of 10 participants who were identified with probable sarcopenia, of which five (62.5%) had low muscle quantity. Data were available for 40 participants for sarcopenia diagnosis according to the EWGSOP2 algorithm. Subsequently, 5 (12.5%) of participants were diagnosed with sarcopenia, and none were identified as having severe sarcopenia. Only 1 participant had a SPPB ≤ 8 , indicating poor physical performance. The number of participants meeting each criterion is presented in Table 5-7.

Table 5-7. The number of participants meeting EWGSOP2 criteria.

Criteria	Definition	Cut off	n (%)
Criterion 1	Low muscle strength (n=42)	HGS<16 Women HGS<27 Men	10 (23.8)
Criterion 2	Low muscle quantity or quality (n=34)	ASM<15 Women ASM<20 Men	9 (26.47)
Criterion 3	Low physical performance (n=43)	SPPB≤ 8	1(2.32)

5.3.4 Dietary Intake

The dietary intake of macro and micronutrients is presented in Table 5-8. Mean energy intake was 30.34 ± 9.40 kcal per kg body weight (range 13.42-55.39kcal/kgBW), and mean protein intake was 1.2 ± 0.37 gram per kg body weight (range 0.4-2.11g/kgBW). Over 70% of participants were meeting their minimum energy and protein requirements. Less than 10% of participants were meeting recommended fibre intakes.

Regarding the macronutrient composition of the diet, 16 participants (37%) consumed less than 45% of their daily energy intake from carbohydrates. For fat intake, 26 participants (60%) derived more than 35% of their energy from fat, while one participant consumed less than 20% of their energy from fat.

The mean ethanol intake was 9.05 g/day. However, based on 24hr dietary recall data, 26 participants (60.5%) consumed no alcohol, and a further 6 (14%) consumed less than 5 g/day. When restricting the analysis to participants who had any alcohol intake >0 g/day (n=17), the mean ethanol intake was substantially higher at approximately 22.8 g/day. Self-reported drinking habits indicated that 14 survivors (32.6%) identified as fully abstinent, 8 (18.6%) as occasional or social drinkers, 2 (4.7%) as former heavy drinkers attempting to reduce intake following diagnosis, and 1 (2.3%) as a continuing heavy drinker.

Also, <5% of participants had adequate vitamin D intake. Additionally, inadequate intakes of vitamin E, folate, magnesium, copper, zinc and potassium were noted, with <50% of participants meeting requirements for these nutrients. Over 60% of participants had >2g sodium intake per day.

Table 5-8. Participant's dietary intake and adequacy (n=43)

	Study sample	Dietary Reference Values (DRVs)	Meeting requirements n (%)
Energy & Macronutrients, Mean (SD)			
Energy (kcal)	2066.58 (551.20)	25kcal/kg	31 (72.1)
Protein (g)	83.55 (26.38)	1g/kg	32 (74.4)
Protein (% energy)	16.49 (5.02)		
Carbohydrate(g)	240.10 (61.48)		
Carbohydrate (% energy)	46.97(7.04)	45-60% energy intake (RI)	27 (62.79)
Fat(g)	86.74 (31.78)		
Fat (% energy)	37.72 (7.80)		
Sugars(g)	98.40 (43.93)		
Starch(g)	137.05 (35.64)		
Dietary fibre(g)	17.61 (5.38)	25 g/day (AI)	4 (9.3)
Alcohol(g)	9.05 (28.23)		
Vitamins, Mean (SD)			
Retinol (µg)	1203.60 (599.60)		
Carotene(µg)	2519.76 (2576.57)		
Vitamin D(µg)	6.49 (4.37)	15 µg/day (AI)	2 (4.7)
Vitamin E (mg)	15.90 (10.22)	13 mg/day male/11 mg/day female (AI)	21 (48.8)
Vitamin B ₁ (mg)	2.68 (2.05)	0.1 mg/MJ	42 (97.6)
Vitamin B ₂ (mg)	2.69 (1.47)	1.6 mg/day (PRI)	31 (72.1)
Niacin(mg)	35.01 (12.91)	1.6 mg NE/MJ	43 (100)
Vitamin B ₆ (mg)	3.50 (3.79)	1.7 mg/day male/1.6 mg/day female (PRI)	35 (81.4)
Vitamin B ₁₂ (µg)	6.73 (8.81)	4 µg/day (AI)	31 (71.2)
Folate(µg)	373.77 (181.57)	330 µg DFE/ day (PRI)	21 (48.8)
Biotin(µg)	73.46 (49.62)	40 µg/day (AI)	26 (60.5)
Pantothenic acid(mg)	9.48 (5.04)	5 mg/day (AI)	35 (81.4)
Vitamin C (mg)	165.67 (191.66)	110 mg/day male/95 mg/day female (PRI)	24 (55.8)

Table 5-8.Participant's dietary intake and adequacy (n=43). (Continued)

	Study sample	Dietary Reference Values (DRVs)	Meeting requirements n (%)
Minerals, Mean (SD)			
Calcium(mg)	1017.95 (340.16)	950 mg/day (PRI)	25 (58.1)
Magnesium (mg)	341.12 (115.59)	350mg male/300gram female (AI)	18 (41.8)
Phosphorus(mg)	1383.21 (363.31)	550 mg/day (AI)	43 (100)
Iron(mg)	19.35 (17.69)	11mg/day (PRI)	35 (81.4)
Copper(mg)	1.34 (0.50)	1.6 mg/day male/1.3mg/day female (AI)	11 (25.58)
Zinc(mg)	12.51 (4.96)	12.9mg male/10.1 mg female (PRI)	21 (48.83)
Potassium(mg)	3233.85 (954.96)	3500 mg/day (AI)	17 (39.5)
Sodium(mg)	2276.80 (665.78)	Under 2g/day	16 (37.2)
Manganese(mg)	8.10 (13.69)	3mg/day (AI)	35 (81.4)

DRVs: Dietary Reference Values, Kcal: Kilocalorie, Kg: kilogram, g: Gram, AI: Adequate Intake, RI: Reference Intake range, µg: Microgram, mg: Milligram, MJ: Megajoule, PRI: Population Reference Intake. Energy and protein requirements are considered according to ESPEN guidelines in cancer[114].Dietary reference values according to European Food Safety Authority (EFSA) guidelines[353]. Vitamin B₁ and Niacin requirements were calculated based on EFSA guidelines as 0.1 mg and 1.6 mg per MJ energy requirements, respectively. Zinc requirement depends on levels of phytate intake; due to a lack of data on phytate intake, the mean of zinc requirements based on four levels of phytate intake is calculated and considered as DRV.

All participants were independent in grocery shopping and meal preparation, and 37 participants (86%) reported that they accessed informal support (partner, family) for the same if required.

5.3.5 Gastrointestinal Symptoms

As presented in Table 5-9, gastrointestinal symptoms remain an issue for UGI cancer survivors, with average scores for all domains higher in the study sample compared to normative values from the general population. Data collected during the nutritional assessment indicated that survivors frequently complained of GI symptoms, as more than 50% reported ongoing diarrhoea and more than 40%

reported still suffering from reflux. Nausea and bloating were the next most frequently reported nutrition impact symptom, reported by 23% of participants.

Table 5-9. Participants' gastrointestinal symptoms

GSRS	n	Mean Score (SD)	Reference value Mean Score (CI)[192]	P Value
Diarrhoea syndrome (score range 1-7)	42	2.50(1.23)	1.38 (1.35, 1.41)	<0.01
Indigestion syndrome (score range 1-7)	42	2.23(1.08)	1.78 (1.75,1.82)	0.01
Constipation syndrome (score range 1-7)	42	1.85(0.93)	1.55 (1.51, 1.58)	0.04
Abdominal pain syndrome (score range 1-7)	41	1.95(0.75)	1.56 (1.53,1.59)	<0.01
Reflux syndrome (score range 1-7)	42	1.82(1.06)	1.39 (1.36,1.43)	0.01

One sample T-test was used to determine statistically significant differences between groups.

5.3.6 Adherence to Cancer Prevention Recommendations

Participant adherence to individual components of WCRF/AICR recommendations is presented in Table 5-10. Participants achieved an average score of 3.53 out of 7 (range 1.5-5.75). Less than half of survivors met the BMI goal, while 60% met the waist circumference threshold. Participants reported an average of 146.55 minutes of physical activity per week; however, only 30% of participants achieved the maximum score for this recommendation. Approximately 60% of participants fully adhered to recommendations for limiting sugar-sweetened drinks and alcohol.

Fibre intake had the lowest adherence, with no participants achieving the maximum score. Fruit and vegetables, red and processed meat and processed foods also had low scores, with only 10%, 17.5% and 22.5% of participants achieving the maximum score for these components, respectively. Participants reported a mean

daily intake of 40g of red meat, 27g of processed meat and 236g of fruit and vegetables. The mean intake of calories from processed foods was 26.40% of total energy.

Table 5-10. Participants' adherence to cancer prevention recommendations using the WCRF/AICR scoring system (n=40).

Component	Mean (SD)	Score	n (%)
BMI	0.30 (0.19)	0	8 (20)
		0.25	15 (37.5)
		0.5	17 (42.5)
Waist circumference	0.32 (0.22)	0	12 (30)
		0.25	4 (10)
		0.5	24 (60)
Fibre	0.16 (0.12)	0	14 (35)
		0.25	26 (65)
		0.5	0
Fruit and vegetable	0.16 (0.16)	0	18 (45)
		0.25	18 (45)
		0.5	4 (10)
Processed foods	0.50 (0.33)	0	9 (22.5)
		0.5	22 (55)
		1	9 (22.5)
Sugar-sweetened drinks	0.68 (0.41)	0	9 (22.5)
		0.5	7 (17.5)
		1	24 (60)
Alcohol	0.73 (0.33)	0	4 (10)
		0.5	13 (32.5)
		1	23 (57.5)
Red and processed meat	0.22 (0.39)	0	29 (72.5)
		0.5	4 (10)
		1	7 (17.5)
Physical Activity	0.42 (0.43)	0	18 (45)
		0.5	10 (25)
		1	12 (30)
Total WCRF score	3.53 (0.98)		

Data available on 40 participants for calculation of the WCRF/AICR score

5.4 Discussion

5.4.1 Malnutrition

In the present study, based on GLIM criteria, one in three participants was malnourished, while only one in fourteen was classified as underweight according to BMI. However, when applying the GLIM criteria, in addition to low BMI, other factors such as

unintentional weight loss, reduced muscle mass, reduced food intake or assimilation, presence of inflammation or a disease state that increases nutritional needs or impairs nutrient utilisation are considered to allow a more comprehensive assessment of malnutrition. This finding highlights the limitations of using BMI as the sole indicator of malnutrition in UGI cancer survivors, as malnutrition risk can be masked when relying exclusively on BMI [360]. This underscores the importance of adopting more comprehensive criteria for identifying malnutrition, such as GLIM, which go beyond BMI to identify malnutrition in UGI cancer survivors [360].

Malnutrition is highly prevalent in UGI cancer survivors and could affect as many as 90% of patients [361, 362]. Several factors, including reduced dietary intake, GI disturbance, change in gut hormones, and altered metabolism, are suggested as potential underlying causes of malnutrition in UGI cancer survivors [362-364]. The findings of the present study highlighted that malnutrition is a long-term and persistent issue post-treatment of UGI cancers, as while over 75% of participants were >12 months post-surgery at the time of assessment, over 30% were malnourished. The prevalence of malnutrition in the present study is comparable to the recent national data reporting risk of malnutrition in 33.8% of hospital patients, highlighting the considerable and ongoing nutritional vulnerability of community-dwelling UGI cancer survivors[365]. Several studies that have investigated malnutrition in long-term UGI cancer survivorship have observed similar results compared to the present study [75, 200, 332]. A previous study by Ouattara et al. showed that malnutrition (defined by weight loss of at least 15% of the pre-treatment body weight) affected 25% of survivors at one year post oesophagectomy [75]. A prospective study that assessed survivors' nutritional status using the Patient-Generated Subjective

Global Assessment tool (PG-SGA) found that 27% of UGI cancer survivors had severe malnutrition six months post-surgery [332]. In the study by Bennett et al., nutritional risk index (NRI) was used for malnutrition diagnosis, which showed that 29.7% of participants were malnourished at 12 months post oesophagectomy [200]. In a recent Irish study, SNAQ scores indicated that 27.5% of long-term UGI cancer survivors, with an average time since surgery of 28.8 months, were at risk of malnutrition [233]. Additionally, several studies that collected data pre and post-operatively have reported exacerbation of malnutrition in UGI cancer survivorship. In a study by Ryu et al., 80% of patients were malnourished at 6 months post-gastrectomy compared to 31% at admission, according to the subjective global assessment [366]. Similarly, a study by Fujiya et al. reported that at 12 months post-gastrectomy, 30.9% of patients were malnourished, increasing from 13.0% preoperatively [105]. Despite differences in malnutrition screening tools and diagnostic criteria used in previous studies, the consistent findings across studies highlight the long-term nature of malnutrition in this population. These findings underscore the critical need for ongoing nutritional monitoring and intervention in survivorship. Integrating comprehensive and standardised nutritional assessments into survivorship care plans will be crucial in reducing the risk of malnutrition and its related complications in UGI cancer survivors.

5.4.2 Sarcopenia

In the present study, one in eight (12.5%) participants were sarcopenic. As noted earlier in section 5.1, sarcopenia is associated with impaired physical function, quality of life and shorter survival. However, data on post-treatment changes in body composition, muscle mass and strength are scarce [53, 127, 340, 367]. It is also important to consider the possibility of reverse causality in

interpreting these findings. Higher rates of sarcopenia observed in patients with disease recurrence may reflect the effects of cancer progression, rather than being a cause of recurrence. This complicates the interpretation of associations between sarcopenia and clinical outcomes and underscores the need for prospective, longitudinal studies to better understand the directionality and underlying mechanisms of this relationship[368, 369].

A previous study by Elliott et al. reported an increased prevalence of sarcopenia, from 6.9% at diagnosis to 21.1% preoperatively and 34.7% at one year post oesophagectomy, indicating ongoing muscle loss in oesophageal cancer survivors [340]. In a study by Shiomi et al., surgery-induced sarcopenia developed in 14.8% of oesophageal cancer survivors within 6 months post-surgery [367]. A study by Murphy et al. observed probable sarcopenia in 29.7% of oesophageal cancer survivors at 12 months post-surgery [127]. In line with the findings of the present study, the results of these studies indicate a persistence of sarcopenia in UGI cancer survivors. Therefore, repeated screening and assessments during different phases of the cancer journey are recommended for timely detection and management of cancer-related sarcopenia [370, 371].

5.4.3 Nutritional Adequacy

The profound impact of surgical treatments for UGI malignancy on survivors' nutritional status in acute recovery is well established [53, 372]. However, data on the effects of cancer and treatment on nutritional status and dietary intake in long term survivorship are scarce [233]. Although inadequate oral intake is suggested as one of the underlying causes of malnutrition in UGI cancer, few studies have assessed dietary intake in UGI cancer survivors [53]. In the present study, >25% of participants had suboptimal energy and protein intake. Also, the results indicated

suboptimal intakes of several micronutrients, with less than half of participants meeting their vitamin D, vitamin E, folate, magnesium, copper, zinc and potassium requirements. Other studies that assessed dietary intake data in UGI cancer survivors also indicated dietary inadequacy [80, 83, 233, 373]. A previous study by Ludwig et al. observed inadequate energy intake in 22% of patients post-oesophagectomy without a gastric emptying procedure [80]. Similarly, in a study by Haverkort et al., inadequate energy and protein intake were observed in 24% and 7% of survivors, respectively, at 12 months post oesophagectomy with gastric tube reconstruction [373]. Furthermore, less than 10% of the patients had an adequate intake of all micronutrients [373]. In a longitudinal study by Grace et al., 58% of UGI survivors were not meeting their energy requirement, and 10% had inadequate protein intake one year post oesophagectomy [83]. Different inclusion criteria and surgical procedures, methods for estimating energy and protein requirements, cut-off points for defining suboptimal intake, standard nutrition care provided, and time points of dietary intake assessment may impact the nutritional adequacy rate reported in different studies, making direct comparisons difficult.

Of note, in the present study, 14% of participants were still under the care of a dietitian, as in St James's Hospital, all UGI cancer survivors receive routine nutritional assessment and intervention (if indicated) up to 12 months post-surgery as standard care. Additionally, patients who required further follow-up with a dietitian due to malnutrition and post-surgical complications, i.e., oesophageal stricture, malabsorption, etc., receive nutrition care beyond 12 months. This structured approach to dietetic care may have contributed to the relatively favourable outcomes observed in this study as nearly 70% of participants did not meet the criteria for malnutrition, and nearly three-quarters were meeting their energy

and protein requirements suggesting that targeted nutrition support may have been effective in mitigating nutritional inadequacy and reducing malnutrition risk. However, notwithstanding this level of nutrition care, over 25% still were not meeting their energy and protein requirements, and less than half met the recommended intake for several micronutrients. In line with previous studies, the results of the present study indicated inadequate nutritional intake in long term survivorship. There is a clear need for evidence-based and practical nutrition care to address persistent nutritional inadequacy in UGI cancer survivorship [374].

5.4.4 Gastrointestinal Symptoms

The results of the present study indicated that GI disturbance remains an issue for disease-free UGI cancer survivors, as participants frequently reported persistent symptoms such as diarrhoea and reflux, with over 50% reporting ongoing diarrhoea. Additionally, participants in the present study had higher GSRS scores compared to the general population, indicating a greater symptom burden in UGI cancer survivors. A previous study by van Erning et al. reported similar results with the persistence of gastrointestinal symptoms in 38.9% and 33.7% of patients at 9-12 months post oesophagectomy and gastrectomy, respectively [375]. A study by Bennett et al. reported an increase in dumping syndrome and malabsorption with time post oesophagostomy [200]. Similarly, 75% of disease-free oesophageal cancer survivors recruited from 20 European centres (LASER study) experienced ongoing GI symptoms more than one year after surgery [57]. These long-lasting complications may contribute to cancer-related malnutrition [83, 376]. Persistent GI symptoms are also associated with poor quality of life in survivors [375], and as discussed by the participants in the qualitative study in Chapter 4, it negatively impacts UGI cancer survivors' daily and social lives.

Evidence-based and personalised interventions targeting symptom management are recommended to reduce symptom burden and improve cancer survivors' nutritional status and quality of life [92]. Also, models of care supporting self-management of symptoms are suggested to improve survivorship care in cancer [92].

5.4.5 Adherence to Cancer Prevention Recommendations

In the present study, UGI cancer survivors reported poor adherence to WCRF/AICR recommendations, with a mean score of 3.53 out of 7. These results were in line with previous studies reporting poor adherence to lifestyle modification in cancer survivors [377, 378]. With more people living longer with and beyond cancer, there is a need to consider steps to reduce the risk of cancer recurrence and secondary morbidity in survivorship [92, 379]. Indeed, according to the US Institute of Medicine (IOM), prevention of new and recurrent cancer is one of the essential components of survivorship care [92]. Lifestyle modification, such as compliance with the WCRF/AICR cancer prevention recommendations, may be associated with reduced risk of cancer recurrence, metabolic syndrome, and mortality in cancer survivors [351, 380, 381]. Also, cancer diagnosis and treatment have been suggested as a “teachable moment”, as survivors are highly motivated for lifestyle modifications to improve quality of life and survival [379]. However, several studies reported no difference between cancer survivors and people without cancer diagnosis in terms of compliance with lifestyle modification such as consuming a healthy diet, physical activity and weight management [382-385]. In the present study, compliance with different components of the WCRF/AICR recommendations varied, with recommendations relating to fibre, fruit and vegetables, red and processed meat and processed foods intake being poorly

adhered to. A recent similar study in UGI cancer survivors showed similar results to the present study as observed suboptimal intake of fibre, fruit and vegetables and high intake of meat and meat products [233]. However, it should be noted that whilst fibre and fruit and vegetable intake were below recommendations, they were comparable to the general Irish population [386]. Similarly, levels of processed meat were comparable with data from the general Irish population, but participants consumed lower levels of red meat in the current study [387]. In the present study, 26.40% of daily calories consumed came from UPFs. This is lower than the general population consumption based on a study on household availability of ultra-processed foods, which reported that 46% of calories in Irish shopping baskets came from ultra-processed foods [388]. On the other hand, approximately 60% of participants fully adhered to the recommendation for limiting sugar-sweetened drinks and alcohol. This may be associated with strict dietary advice against alcohol and sugar-sweetened drink consumption postoperatively to prevent exacerbation of GI symptoms [389-391]. Notably, 60.5% of participants in the present study reported no alcohol consumption based on the 24-hour dietary recall data. This was consistent with findings from a previous study reporting that over 60% of gastric cancer survivors were not current drinkers [392]. However, when restricting the analysis to participants who reported alcohol intake, the mean ethanol consumption was substantially higher (22.8 g/day). This underscores the importance of distinguishing between drinkers and non-drinkers when interpreting averages of alcohol consumption, as cohort-wide figures may underestimate actual intake among consumers.

Considering the long-lasting GI complications in UGI cancer survivors, adherence to recommendations on fibre and fruit and vegetable intake might be challenging in this cohort of cancer

survivors [233]. Also, UGI cancer survivors are often provided with food fortification advice for weight loss prevention, which might conflict with some of the WCRF/AICR recommendations [389]. Additionally, some studies reported variation in adherence to WCRF/AICR recommendations by sociodemographic factors [393]. Age, gender and education level can impact adherence to WCRF/AICR recommendations [394, 395]. Moreover, other factors such as fatigue, stress, poor appetite, change in taste, food craving, family and social support, and cost of healthy eating may impact the adherence to recommendations in survivorship [223, 396, 397]. Further research to identify barriers and factors associated with adherence to cancer prevention recommendations in UGI cancer survivors may inform the optimum nutritional intervention to support UGI cancer survivors in adopting lifestyle modification.

Collectively, the results of the present study indicated that UGI survivors consume similar foods to the general Irish population. Hence, public health interventions focused on increasing awareness and compliance with cancer prevention recommendations are required to improve compliance in both the general population and cancer survivors in Ireland.

5.5 Strength and Limitations

This study has several strengths. Validated tools and methods for nutritional assessment and measuring physical activity and functional status were used, and standard criteria for diagnosing malnutrition and sarcopenia were applied. The use of FoodBook24, which includes images of portion sizes, assisted with the accuracy of dietary recalls.

However, due to the small sample size and the fact that the study only recruited disease-free survivors who were interested in

multidisciplinary rehabilitation, the results of this study should be interpreted with caution, and the results may not be generalisable to all UGI cancer survivors. Additionally, survival and mortality bias should be acknowledged. It should be considered that there is a possibility that individuals who were more severely malnourished, had inadequate dietary intake, had sarcopenia, or engaged in unhealthy behaviours such as smoking and excessive alcohol consumption may not survive long enough or were not well enough to be eligible to participate in the present study. These factors may have led to an underestimation of the burden of malnutrition, sarcopenia, and lifestyle-related risk factors in the broader UGI cancer survivor population.

Lastly, the cross-sectional design of the present study limits the ability to assess changes over time and causal relationships between nutritional status, sarcopenia, and survivorship outcomes. Future research employing longitudinal approaches and larger, more diverse cohorts of UGI cancer survivors is warranted to better understand these dynamics and to develop targeted interventions.

5.6 Conclusion

The findings of this study highlighted the persistent and unresolved nutrition-related challenges faced by UGI cancer survivors. The present study showed that malnutrition and sarcopenia remain significant concerns in survivorship care, with one in three participants being malnourished and one in eight diagnosed with sarcopenia. Additionally, many survivors continued to experience NIS, with over 50% reporting persistent diarrhoea. The present study also found that more than 25% of disease-free survivors were failing to meet their dietary requirements and reported poor adherence to cancer prevention guidelines. The results

of the present study underscore the need for continued nutritional care and personalised interventions to address these persistent issues and improve long-term survivorship outcomes. Further studies should examine effective interventions for optimising nutrition intake, managing GI symptoms and promoting healthy lifestyles in UGI cancer survivors [398].

The American Society of Clinical Oncology's Survivorship Care Compendium has outlined multidisciplinary survivorship care as a suggested model of care for cancer survivors [96]. However, data on the effectiveness of these interventions in UGI cancer survivors are lacking. A systematic review of the literature has been conducted to review the impacts of multidisciplinary intervention in improving outcomes in UGI cancer survivors and is discussed in Chapter 6.

Chapter 6 The Effectiveness of Nutrition Interventions Combined with Exercise in Upper Gastrointestinal Cancers- A Systematic Review

This chapter describes a systematic review investigating the effectiveness of multidisciplinary interventions with core nutrition and exercise components in UGI cancer survivors. The present study reviewed current evidence, limitations of previous studies, and knowledge gaps that need to be explored by future studies.

Published Work List

All figures, tables, and sections in this chapter have been previously published (Sadeghi et al., The Effectiveness of Nutrition Interventions Combined with Exercise in Upper Gastrointestinal Cancers: A Systematic Review); please see Appendix XII.

6.1 Introduction

As discussed previously in Chapter 1, Chapter 3, Chapter 4 and Chapter 5, UGI cancer treatments are often accompanied by adverse effects on patients' nutritional status and physical function [101, 201, 399-401]. Due to the tumour location and the unique influences of curative surgery on a patient's dietary intake, patients with UGI cancer are at a greater risk of malnutrition and its related complications [84, 402, 403]. Cachexia and muscle loss are one of the main complications that hinder cancer treatment and survival [101]. Muscle wasting is accompanied by reduced physical function, fatigue, chemotherapy toxicity, lower quality of life and a higher rate of postoperative complications [86, 340, 404, 405]. As the survival rates for UGI cancer continue to improve, the long-term nutritional and physical status of UGI cancer survivors requires further attention. There is a need to offer effective care plans to prevent muscle wasting and sarcopenia and optimise nutritional and functional status in UGI cancer patients, which subsequently would improve treatment outcomes and enhance survivors' quality of life.

Multimodal interventions consisting of nutrition and exercise prescription have been reported to favourably change health-related outcomes in cancer patients, such as fatigue, quality of life and functional capacity [406, 407]. As both nutrition and exercise positively affect muscle loss, combining nutrition and exercise may further improve muscle protein synthesis and increase muscle mass [129]. However, it should be mentioned that the impact of combined nutritional care with physical exercise specifically on body composition, is not clear yet [132, 408-412]. Thus, the present systematic review of combined nutritional and exercise interventions in UGI cancer patients aims to determine whether these

interventions are an effective approach for preserving muscle mass. In addition, these care programmes need to be evaluated to define optimal intervention design and optimal timepoint for delivery within the cancer trajectory, i.e., prehabilitation or rehabilitation. Moreover, patients' acceptance and adherence to these programmes needs to be reviewed, as the effectiveness and acceptance of nutritional and exercises interventions may be different in patients with UGI cancer compared to other cancer types, owing to the impact of surgery on food intake and postoperative complications such as food intolerance and malabsorption.

To the best of our knowledge, this is the first systematic review to research the effectiveness of combined nutritional and exercise interventions on muscle wasting and quality of life in UGI cancer survivors.

The primary objective of this systematic review was to evaluate the effectiveness of nutritional interventions combined with exercise in improving outcomes in UGI cancer patients. Specifically, it assessed whether these types of interventions, as compared to usual/standard care, can significantly prevent or reverse muscle wasting and functional decline, improve health-related quality of life, and decrease treatment complications. Moreover, this systematic review aimed to discover the acceptability of these interventions in patients diagnosed with UGI cancer.

6.2 Methods

6.2.1 Study Registration

This study is registered with the PROSPERO database (registration number: CRD42021239675) and has been reported

using the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) checklist [413].

6.2.2 Study Eligibility Criteria

The following criteria were considered for selecting eligible studies:

6.2.2.1 Study Designs

All types of randomised clinical trials (RCTs), excluding feasibility and pilot studies, were included. Cross-sectional, cohort, case-control, and case report studies were excluded. Although review and systematic review articles were excluded, reference lists and citations of relevant reviews were screened to locate additional relevant studies.

6.2.2.2 Publication Type

Original studies published in peer-reviewed journals and reported in English were considered eligible.

6.2.2.3 Participants

Studies that recruited adults (aged ≥ 18 y) diagnosed with UGI cancer, namely oesophageal cancer, gastric cancer, hepatic cancer, pancreatic cancer, and cancer of the biliary system, were included, excluding studies that enrolled patients receiving interventions as part of a palliative care plan.

6.2.2.4 Intervention

Studies investigating the effects of multidisciplinary care programmes combining nutritional and exercise intervention were included. Studies that provided any type of nutritional and exercise intervention were included. No limitation on delivery mode,

minimum or maximum intervention period, follow-up, or type of setting in which studies were conducted was applied.

6.2.2.5 Comparators

Studies that considered standard or usual care provided to patients as the control group were included.

6.2.2.6 Outcomes

The following outcomes were analysed and graded in the present systematic review if reported in the included studies.

- Body composition (fat mass, fat-free mass, muscle mass) and anthropometric measurements (weight, BMI, waist/hip circumference, triceps skinfold)
- Health-Related Quality of Life (HRQOL)
- Functional outcomes (handgrip strength, exercise capacity and physical activity level)
- Dietary Intake
- Post-operative complications

6.2.3 Search Strategy and Information Sources

A comprehensive literature search was conducted to identify all relevant studies. Electronic databases, including MEDLINE, EMBASE, Web of Science, Cochrane Library, and CINHALL, were searched up to August 26th, 2020.

The specialised search strategy was designed by the subject librarian (David Mockler, Trinity College Dublin) with no limitations on the type of studies, language, study design, time frame, etc. The full search strategy is included in Appendix XIII. The search result that was achieved through this search strategy was reviewed by the

research dietitian (FS) to confirm that an acceptable portion of relevant studies had been retrieved by using it.

6.2.4 Data Management

All search results were imported to Covidence systematic review software (Veritas Health Innovation, Melbourne, Australia. Available at www.covidence.org) to facilitate the review process. Duplicates were excluded, and multiple reports from one study were collated.

6.2.5 Selection Process

FS and SD independently screened the titles and abstracts. Subsequently, FS and SD reviewed full texts independently to identify studies that met the inclusion criteria. Reasons for exclusion of the ineligible studies were recorded. Any disagreements in screening and full-text review were resolved through discussion.

6.2.6 Data Collection

FS performed data extraction independently. Extracted data included; study title, publication date, correspondent author's name and contact, study design, setting or location, sample size, participant details including age, gender, cancer type and treatment, intervention design including details of the nutrition and exercise components, mode of delivery, duration of intervention, comparators, adherence rate to intervention, withdrawal rate, adverse events, and reported outcomes (body composition and anthropometric measurements, quality of life, physical functioning, post-operation complications).

6.2.7 Risk of Bias in Individual Studies

The revised Cochrane Risk of Bias tool (RoB2) was used to determine the risk of bias [414]. FS and SD independently assessed the risk of bias for each included study. Disagreements were resolved by discussion.

6.2.8 Measuring the Intervention Effect

Extracted continuous data are presented as mean difference (MD) and standard deviation (SD) or parameter estimate (β) and confidence interval (CI). For dichotomous data (such as adverse events, complications, etc.), the treatment effect is reported as number and percentage.

6.2.9 Data Synthesis

A meta-analysis was not appropriate due to the heterogeneity of studies and a high degree of variance in interventions, study period and measured outcomes observed in the included studies. A narrative summary of results has been provided instead.

6.3 Results

A total of 4780 articles were identified. After removing duplicates and screening titles and abstracts, 148 articles were selected for full-text review, of which 5 studies met the inclusion criteria [132, 133, 135, 407, 415]. A detailed record of the selection process and PRISMA flow diagram is presented in Figure 6-1.

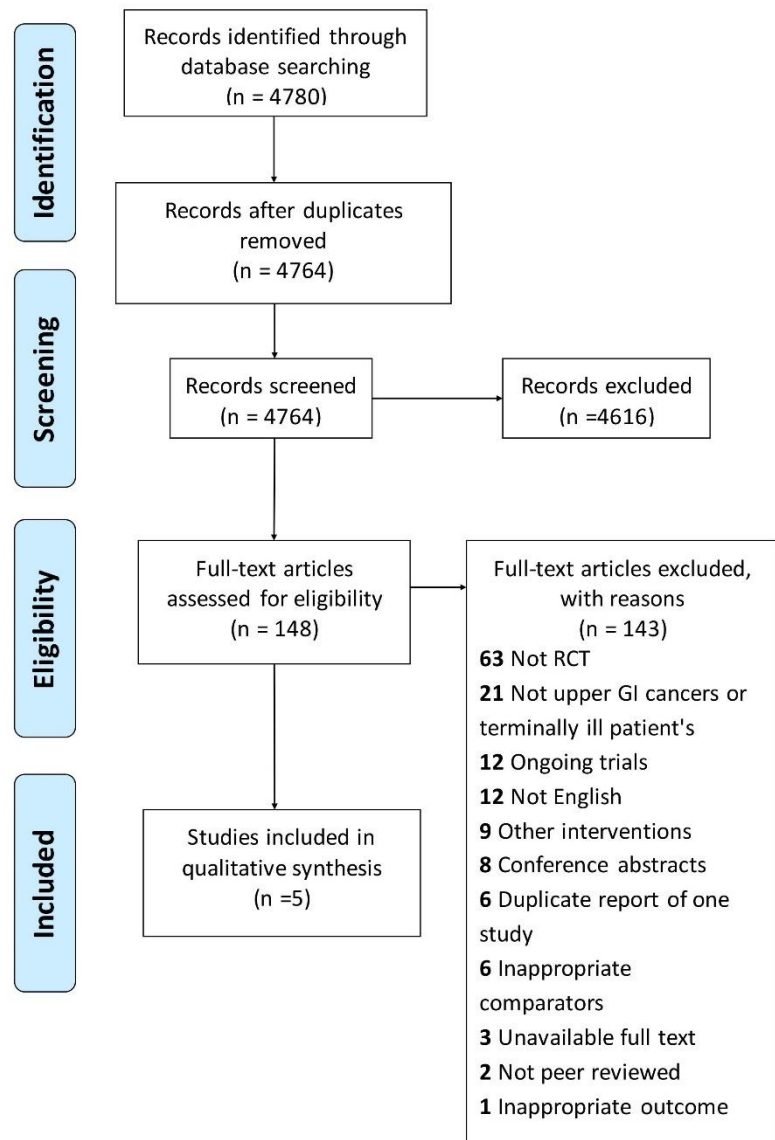


Figure 6-1. PRISMA flow diagram

This figure has been published in the paper Sadeghi, F., et al., 2021, please see Appendix XII.

An overview of the included studies has been summarised in Table 6-1. High variation in intervention design and standard care was observed in included studies, and a detailed description of the interventions is provided in Table 6-2.

With regards to sample size calculation, four of the included studies conducted a power calculation (80% power) to estimate the minimum required sample size [133, 135, 407, 416]. One of the studies failed to conduct a power calculation before starting the trial, although post hoc analysis showed a power of 83-100% for primary outcomes except for lean muscle mass, for which 48% power was indicated to detect group differences [415]. Reported recruitment rates ranged from 40.3% to 96%, and the dropout rates ranged from a minimum of 5% to a maximum of 25%. The adherence rate ranged from 32% to 94%. None of the studies reported major adverse events related to the intervention. A summary of the results is presented in Table 6-3 and a visual overview of changes in the outcomes across the five included studies is provided in Figure 6-2. The result of the risk of bias assessment is shown in Figure 6-3.

Table 6-1. Overview of included studies (n=5)

Author, Year	O'Neill et al, 2018	Yu-Juan Xu et al, 2015	Yu-Ling Chang et al, 2020	Minnella et al, 2018	Ausania et al, 2019
Country	Ireland	Taiwan	Taiwan	Canada	Spain
Cancer type	Oesophagogastric	Oesophageal	Oesophageal	Oesophagogastric	Pancreaticoduodenal
Timepoint of Intervention	Rehab (6mo- 5 yr. post-treatment)	During neoadjuvant chemoradiotherapy	Rehab (Immediately after surgery)	Prehab	Prehab
Participant No (Randomised)	43 (Intervention =21, Control=22)	59 (Intervention=30, Control=29)	88 (Intervention=44, Control=44)	68 (intervention=34, control =34)	40 (intervention=18, Control=22)
Participants' Sex (%Male)	81%	92.9%	90.9%	74.5%	55%
Participants' Age	Intervention: 67.19 ±7.49 Control: 64.14 ± 10.46	Intervention: 58.1 ±9.6 Control: 61.1 ±9.0	Intervention: 56 ±8.9 Control: 56 ±10.0	Intervention: 67.3 ±7.4 Control: 68.0 ±11.6	Intervention: 66.1 (38-80) Control: 65.7 (38-81)
Recruitment rate	40.3%	92%	94.6%	60.1%	96%
Dropout rate	9.3%	5.1%	9.1%	25%	16%
Adherence	Supervised exercise: 94 ±12% Unsupervised exercise: 78 ±27	Nutritional sessions: 100% Walking sessions: 68% (32%–100%). Target maximal heart rate was achieved in 71% 54% completed more than 80% of walking sessions	NR	63%	NR
Adverse event	None	NR	NR	None	NR

Abbreviations: NR Not reported. This table has been published in the paper Sadeghi, F. et al., 2021; please see Appendix XII.

Table 6-2. Description of interventions in included studies (n=5)

Author, Year	O'Neill et al, 2018	Yu-Juan Xu et al, 2015	Yu-Ling Chang et al, 2020
Exercise component	14 Supervised aerobic training sessions (treadmill walking, stationary cycling, cross-training) 14 Supervised resistance training sessions (free weights, horizontal leg press) 37 unsupervised home-based aerobic sessions (walking or stationary cycling) 10 unsupervised resistance training sessions (using TheraBand)	Nurse-supervised walking three times per week 5-minute warm-up (ankle circles, leg swings, pelvic loops, arm circles), 20 minutes of hallway ambulation at the patient's own pace before or after radiotherapy intensity of 60%	Home-based walking at a moderate intensity level after meals, 3–5 days per week for 30 minutes, or a total of 150 minutes per week Desired heart rate reserve percentage: 55–65%.
Nutrition component	Nutritional assessment 1:1 Dietary counselling Personalised nutritional advice Number of sessions depended on the patients' status	Weekly dietetic consult (weight and intake assessment, advice on eating and feeding difficulties, food or formula selection, skills for modifying food texture, and oral care before and after eating)	E-books containing dietary guidance and advice
Other components	7 group education sessions delivered by surgeon, dietitian, physiotherapist, occupational therapist, and psychotherapist specialised in mindfulness	None	e-books (exercises, symptom management and psychological advice) Online nurse support to answer survivors' questions An online discussion group referring patients to appropriate medical professionals for an in-person visit if needed
Control	Standard care	Standard care (Nutritional and self-care advice from nurses)	Standard care (Conventional postoperative feeding, wound care, and regular postoperative rehabilitation exercises)
Duration	12 weeks	4-5 weeks	12 weeks

Abbreviations: ERAS enhanced recovery after surgery, IQR interquartile range, BS blood sugar. This table has been published in the paper Sadeghi, F. et al., 2021; please see Appendix XII.

Table 6-2. Description of interventions in included studies (n=5) (Continued)

Author, Year	Minnella et al, 2018	Ausania et al, 2019
Exercise component	Home-based aerobic exercise (brisk walking, jogging, or cycling) 3 days per week, 30 minutes each day (including 5-minute warm-up and 5-minute cooldown) Strengthening activity: 3 sets of 8 to 12 repetitions for 8 muscle groups using TheraBand, 1 day/week, 30 minutes (including 5-minute flexibility and 5-minute stretching) a weekly telephone call by a kinesiologist	5 sessions (60 minutes each) high-intensity endurance training performed on a cycle-ergometer stationary bicycle, 10 minutes of warm-up cycling, 20 minutes of muscle toning exercise, 20 minutes of aerobic exercise, and 10 minutes of cool-down. Unsupervised home-based functional exercises and breathing exercises
Nutrition component	Nutritional assessment and consult Whey protein supplement if required. Weekly phone call by a dietitian	Nutritional assessment Nutritional support (liquid oral nutrition supplements and vitamin supplements.) Total parenteral nutrition if required. Follow-up in the outpatient clinic
Other components	None	Metformin or insulin if required for BS control. Blood glucose monitor to check glucose level at home. Pancreatic enzyme replacement therapy
Control	Standard care (perioperative care according to the ERAS Society Guideline protocol, + Nutritional counselling session	Standard care (nutritional counselling, physical activity recommendation and advice on smoking cessation and, if indicated pancreatic enzyme supplementation, dietitian referral, preoperative biliary drainage)
Duration	Median 36 days (IQR, 17-73)	Median 12.6 days (Minimum 7 days was planned in the intervention)

This table has been published in the paper Sadeghi, F. et al., 2021; please see Appendix XII.

Table 6-3. Summary of results (n=5)

Author, Year	Relevant outcome measure	Results
O'Neill et al, 2018	Cardiorespiratory fitness (CPET, VO₂ Peak) * HRQOL (EORTC-QLQ-C30) Body composition & anthropometric measurements (BIA, weight, height, waist and midarm circumference) Physical activity level (ActiGraph GT3X) Dietary intake (24hrs food recall)	Significant improvement in cardiorespiratory fitness post-intervention (VO₂ Peak:22.20±4.35 versus 21.41±4.49, P=0.000) and 3 months post-intervention (VO₂ Peak 21.75±4.27 versus 20.74±4.65, P=0.001) No significant changes in HRQOL, except cognitive function higher in the control group following the intervention [100.00± 16.67 compared to 83.33 ±16.67, P=0.031] No changes in anthropometric measurements and body composition except higher mid-arm circumference in the intervention group at post-intervention assessment (28.35 ±4.70 compared to 28.55 ±5.57, P=0.019) No changes in PAL Not reported
Yu-Juan Xu et al, 2015	Functional capacity (6MWT, HGS) * Body composition & anthropometric measurements (BIA, weight) * Treatment tolerance (chemotherapy or radiotherapy interruption, unplanned hospital admission, grade > 2 neutropenia, fever> 38.5°C, Intravenous nutritional support Wheelchair use	100 meters less decline in walk distance (P=0.012); 3kg less decrease in hand-grip strength (P=0.002) Non-significant reduction in muscle mass loss (1.3kg, P=0.057) Significant reduction in weight loss (2.7kg, P<0.001) No differences in chemotherapy/radiotherapy interruption, unplanned hospital admissions Neutropenia and fever Lower rates of parenteral nutrition support (3.6% compared to 50%, P<0.001) Lower rate of wheelchair use (0% compared to 32.1%, (P<0.01)

CPET Cardiopulmonary Exercise Testing, VO₂ Peak highest value of oxygen uptake, HRQOL Health-Related Quality Of Life, EORTC-QLQ-C30 The European Organisation for Research and Treatment of Cancer Quality of Life questionnaire-Cancer, BIA Bioelectrical Impedance Analysis, 6 MWT Six-Minute Walk Test, HGS Hand Grip Strength, VO₂ max Maximum rate of oxygen uptake, EORTC QLQ-OES18 EORTC oesophageal cancer-specific questionnaire, BMI Body Mass Index, CDC Clavien-Dindo classification, CCI Comprehensive Complication Index, FEV₁ forced expiratory volume in one second, FVC forced expiratory volume, O₂ sat oxygen saturation, 10 MWT 10 Meter Walk Test, HS Hospital Stay, DGE delayed gastric emptying. * Primary outcome/s of the study. This table has been published in the paper Sadeghi, F. et al., 2021; please see Appendix XII. *Primary outcome/s of the study.

Table 6-3. Summary of results (n=5) (Continued)

Author, Year	Relevant outcome measure	Results
Yu-Ling Chang et al, 2020	Exercise capacity (CPET (VO ₂ max), 6MWT) HRQOL (EORTC-QLQ-C30 & EORTC QLQ-OES18) * Albumin Daily steps (smart bracelet) BMI	Higher maximal oxygen consumption (β =2.61, 95% CI 1.54, 3.69, P <0.001), effect size=0.97, Greater distance on the six-minute walking test (β =83.30, 95% CI 52.60,113.99, P <0.001), effect size=0.36 Significantly better HRQOL at different time points following discharge. Physical (1 & 3 months), role (1, 3, & 6 months), emotional (1 month), social (3 months) and global health (3 months), insomnia (1 & 3 months) and nausea/vomiting (3 & 6 months). Improvement in oesophageal cancer-specific symptoms, dry mouth (1 month), dysphagia (3 months), loss of taste (1 & 6 months) Higher levels of albumin at 3 months after discharge (β =0.32, 95% CI 0.09, 0.54, P <0.01), minimal effect size Data not reported No changes in BMI
Minnella et al, 2018	Functional capacity (6MWT) * Post-operative morbidity (CDC &CCI), length of hospital stay, 30-day hospital visit, readmission rate, death, adherence to planned neoadjuvant therapy	Improvement in functional capacity before (mean [SD] 6MWD change, 36.9 [51.4] vs -22.8 [52.5] m; P <0.001) and after surgery (mean [SD] 6MWD change, 15.4 [65.6] vs -81.8 [87.0] m; P <0.001). No differences were observed in post-operative outcomes
Ausania et al, 2019	Cardiopulmonary status (FEV 1, FVC, O ₂ sat%) Functional capacity (10MWT &HGS) Post-operative complications (CDC)*, pancreatic leak, HS, readmission, DGE	Improvement respiratory function in the intervention group compared to baseline, changes in FVC (l, median) =0.6, FEV 1(l, median) =0.48, O ₂ sat% =0.3 Improvement in functional capacity in the intervention group compared to baseline 10-meter walk test (1.2 sec), HGS (left hand=5.9, right hand=4.8) No differences in post-op complications, hospital stay, or readmission between the intervention and control group, significantly lower DGE, 5.6% vs 40.9% in the standard care group (P =0.01)



	O'Neill et al, 2018	Yu-Juan Xu et al, 2015	Yu-Ling Chang et al, 2020	Minnella et al, 2018	Ausania et al, 2019
Cardiorespiratory fitness	Significant improvement	Not assessed	Significant improvement	Not assessed	Not assessed
Cardiopulmonary status	Not assessed	Not assessed	Not assessed	Not assessed	Improvement (significance unclear)
HRQOL	Mixed result	Not assessed	Significant improvement	Not assessed	Not assessed
Body composition	No significant change	No significant change	Not assessed	Not assessed	Not assessed
Anthropometric measurements	Mixed result	Significant improvement	No significant change	Not assessed	Not assessed
Physical activity	No significant change	Not assessed	Not reported	Not assessed	Not assessed
Functional capacity	Not assessed	Significant improvement	Significant improvement	Significant improvement	Improvement (significance unclear)
Dietary intake	Not reported	Not reported	Not assessed	Not reported	Not reported
Treatment tolerance	Not assessed	No significant change	Not assessed	Not assessed	Not assessed
Rate of parenteral nutritional	Not assessed	Significant improvement	Not assessed	Not assessed	Not assessed
Wheelchair use	Not assessed	Significant improvement	Not assessed	Not assessed	Not assessed
Albumin	Not assessed	Not assessed	Significant improvement	Not assessed	Not assessed
Post-operative complications	Not assessed	Not assessed	Not assessed	No significant change	Mixed result

Figure 6-2. Visual summary of outcome measures reported in the included studies

		Risk of bias domains					
		D1	D2	D3	D4	D5	Overall
Study	O'Neill et al, 2018						
	Yu-Juan Xu et al, 2015						
	Yu-Ling Chang et al, 2020						
	Minnella et al, 2018						
	Ausania et al, 2019						
		Domains: D1: Bias arising from the randomization process. D2: Bias due to deviations from intended intervention. D3: Bias due to missing outcome data. D4: Bias in measurement of the outcome. D5: Bias in selection of the reported result.					Judgement  High  Some concerns  Low

Figure 6-3.Risk of bias assessment.

Risk of Bias completed using the revised Cochrane Risk of Bias tool (RoB2). This figure has been published in the paper Sadeghi, F. et al., 2021; please see Appendix XII.

6.3.1 Health-Related Quality of Life

The effects of combined nutrition interventions with physical training in improving health-related quality of life (HRQOL) were investigated in only two studies with inconsistent results [132, 133]. Both studies used the European Organisation for the Research and Treatment of Cancer-Core Quality of Life Questionnaire (EORTC-QLQ-C30) for measuring changes in HRQOL and the oesophageal cancer-specific quality of life questionnaire (EORTC QLQ-OES18) was additionally used by Yu-Ling Chang [132, 133]. O'Neill et al. examined the effect of a 12-week multidisciplinary rehabilitation programme in a cohort of oesophagogastric cancer survivors in which they did not observe any significant improvements in HRQOL following the intervention. Of note, a significantly higher score in cognitive function was reported in the control group [$F(1, 38)=4.992$, $P=0.031$, η^2 (eta squared)=0.12] following intervention [132]. In the second study by Yu-Ling Chang et al., delivering a 12-week nurse-led exercise and health education informatics programme resulted in a significant improvement in HRQOL [133]. In this study, significant improvement

in functioning scales, global health status, and symptom domains were reported in both the control and intervention groups ($P < 0.01$ to $P < 0.001$) and there were significant differences between groups regarding HRQOL domain scores at varied time points. For instance, in the intervention group, a significant improvement was observed in functional domain at 1 month ($\beta = 10.02$, 95% CI 3.46, 16.58, $P < 0.01$) and 3 months ($\beta = 10.25$, 95% CI 1.55, 18.93, $P < 0.05$) after discharge; while the role functioning score was significantly higher at all three time points (1 month: $\beta = 11.68$, 95% CI 0.90, 22.47, $P < 0.05$, 3 months: $\beta = 14.03$, 95% CI 2.43, 25.64, $P < 0.05$, 6 months: $\beta = 16.12$, 95% CI 4.21, 28.03, $P < 0.01$). Significant improvements in emotional functioning were observed at 1-month post-discharge ($\beta = 8.91$, 95% CI 2.67, 15.15, $P < 0.01$) and in social functioning at 3 months after discharge ($\beta = 9.25$, 95% CI 0.20, 18.29, $P < 0.05$). Global QOL showed a greater improvement in the intervention group 3 months following hospital discharge ($\beta = 10.71$, 95% CI 2.48, 19.94, $P < 0.05$). Regarding symptom domains, following GEE analysis, lower scores for insomnia at 1 and 3 months post-discharge ($\beta = -14.50$, 95% CI -22.91, -6.09, $P < 0.01$; and $\beta = -12.81$, 95% CI -2.74, -0.89, $P < 0.05$, respectively) were reported in the intervention group. Calculated scores for nausea and vomiting were also lower in the intervention compared to control groups at 3 and 6 months following discharge from hospital ($\beta = -12.62$, CI -20.48, -4.79, $P < 0.01$; and $\beta = -11.67$, 95% CI -20.77, -2.57, $P < 0.05$, respectively) [29]. Analysis of oesophageal cancer-specific quality of life scores (QOL-OES-18) showed lower scores for dry mouth ($\beta = -8.68$, 95% CI -16.86, -0.50, $P < 0.05$) at the one-month post-discharge assessment; similarly, there were lower scores for dysphagia at 3 months ($\beta = -12.56$, 95% CI -21.34, -3.76, $P < 0.01$) and at one and six months following discharge for loss of taste ($\beta = -8.30$, 95% CI -14.41, -2.19, $P < 0.01$; and $\beta = -13.66$, 95% CI -22.40, -4.93,

P<0.01 respectively) in the intervention group versus the control [133].

6.3.2 Body Composition and Muscle Mass

Body composition, muscle mass or anthropometric measurements were measured outcomes in three studies [132, 133, 415]. Body composition was measured by bioelectrical impedance analysis (BIA) in studies by O'Neill and Yu-Juan Xu, and no significant differences in muscle mass were detected following the intervention [132, 415]. There were inconclusive results regarding changes in anthropometric measurements. O'Neill et al. reported higher mid-arm circumference in the intervention group at the post-intervention assessment (28.35 ± 4.70 compared to 28.55 ± 5.57 , $P=0.019$) and no changes in other anthropometric measurements of weight, BMI, and waist circumference. This was similar to the results of the Yu-Ling Chang study, which reported no changes in body mass index. However, Yu-Juan Xu reported significantly less weight loss (2.7 kg, $P<0.001$) following the intervention [132, 133, 415].

6.3.3 Physical Function and Cardiorespiratory Fitness

Functional capacity and cardiorespiratory fitness outcomes were examined in all five included studies [132, 133, 135, 407, 415]. Cardiorespiratory fitness was assessed in two studies by cardiopulmonary exercise test (CPET) and both RCTs reported significant improvement in cardiorespiratory fitness following the rehabilitative intervention [132, 133]. In the ReStOre study by O'Neill et al., the intervention group had a higher VO_{2Peak} compared to the control group (22.20 ± 4.35 versus 21.41 ± 4.49 , $P=0.000$) post-intervention as well as at 3 months post-intervention assessment (VO_{2Peak} 21.75 ± 4.27 versus 20.74 ± 4.65 , $P=0.001$) [132]. In the trial by Yu-Ling Chang et al., the intervention group had a significantly higher

VO_{2max} value post intervention ($\beta=2.61$, 95% CI 1.54, 3.69, $P<0.001$) [133].

Three studies examined changes in functional capacity by 6-minute walk test (6MWT), and a significant improvement was observed in all three studies post intervention [133, 407, 415]. Yu-Juan Xu et al. reported less decline in 6MWT walk distance following a walk and eat intervention during neoadjuvant chemoradiotherapy, compared to control ($-18\pm75\text{m}$ vs -118 ± 160.5 ; group difference: 100m, adjusted $P=0.012$) [415]. Likewise, a significantly improved 6MWT was observed ($\beta= 83.30$, 95% CI 52.60, 113.99, $P<0.001$) following a rehabilitation intervention by Yu-Ling Chang et al. [133]. Moreover, another prehabilitation study showed improvement in walking distance both before surgery (mean[SD] 6MWD change, 36.9 [51.4] vs -22.8 [52.5] m; $P<0.001$) and after surgery in the intervention group versus control (mean [SD] 6MWD change, 15.4 [65.6] vs -81.8 [87.0] m; $P<0.001$) [407].

Two studies measured hand-grip strength and both reported improvements following a multidisciplinary intervention. Yu-Juan Xu et al. observed a 3kg less decrease in hand-grip strength in the intervention group ($-1.1\pm2.5\text{kg}$ vs $-4.1\pm4.0\text{kg}$, $P=0.002$), and Ausania reported an increase of 4.8kg and 5.9kg in right and left-hand grip strength following prehabilitation, although this outcome was measured only in the intervention group [135, 415].

6.3.4 Dietary Intake

None of the included studies reported dietary intake data. Although O'Neill et al included dietary assessment in the intervention, dietary intake data were not reported in the study results [416]. Likewise, Ausania and Minnella assessed nutritional intake and dietary habits before the intervention but no data

regarding dietary intake were included in the results of these studies [135, 407]. Similarly, Yu-Juan Xu reported evaluation of dietary intake during weekly nutritional counselling sessions, yet no dietary intake data were presented in this study [415].

6.3.5 Post-Operative Complications/Other Outcomes

Three studies looked at complications post-surgery, and all reported no significant differences in number or severity of complications, hospital stay and readmission in the intervention group compared to standard care [135, 407, 415]. However, Yu-Juan Xu et al. observed lower rates of parenteral nutrition support (3.6% compared to 50%, $P < 0.001$) as well as a lower rate of wheelchair use (0% compared to 32.1%, ($P < 0.01$)) in the intervention group [415]. Also, Yu-Ling Chang reported that the intervention group had significantly higher levels of albumin at 3 months post-discharge ($\beta = 0.32$, 95% CI 0.09, 0.54, $P < 0.01$) compared to the usual care group [133].

6.4 Discussion

This systematic review described the effectiveness of multidisciplinary programmes, whose core component was nutritional and exercise interventions, in improving outcomes in patients diagnosed with UGI cancers. Nutritional interventions were mainly individual consults alone or along with prescribing oral nutritional supplements to ensure energy and protein requirements were met. It's noteworthy that the rationale behind prescribing nutritional supplement or parenteral nutrition were not explained in the Ausania et al. and Minnella et al. studies. This lack of details regarding delivered intervention may complicate interpretation of reported results in these studies [135, 407].

Considering the results of reviewed studies, interventions incorporating nutrition and exercise appear to be safe and acceptable in patients diagnosed with UGI cancer, with a higher compliance rate with supervised interventions [132, 415]. However, only three studies reported compliance with the intervention, of which a single study reported adherence to nutrition counselling sessions [132, 407, 415]. O'Neill et al. did not report adherence to dietetic consults and education sessions and Minnella et al. reported overall compliance with prehab intervention rather than specifying adherence to exercise and nutrition components separately [132, 407]. Lack of sufficient data regarding adherence rate in some of the reviewed studies makes it difficult to understand whether non-significant findings were due to ineffectiveness of the interventions or lack of compliance with the intervention. Additionally, reporting adherence to different components of a multidisciplinary intervention is important as it might help design acceptable and practical multimodal interventions. Moreover, it would be worthwhile to further examine factors that may play a role in patients' enrolment and completion of these interventions, such as participants' nutritional and psychological status, physical function, fatigue and weakness at baseline; transportation difficulties, and familial and professional commitments [417, 418]. Acquiring more data on underlying reasons for non-participation, withdrawal, and non-compliance is essential in order to design convenient, acceptable, and practical interventions.

Regarding physical functioning, the promising effects of combined nutritional interventions with physical training on functional and cardiorespiratory outcomes have been reported in several studies [419, 420]. Included studies in this systematic review showed consistent results regarding improvements in patients' physical function following multimodal interventions with core

nutrition and exercise components. Whilst the reported functional outcomes varied among different studies, CPET and 6MWT demonstrated improvement following the intervention [132, 133, 407, 415]. This improvement in physical performance is important as higher physical performance and functioning have been associated with improved quality of life, treatment response, and prognosis in cancer patients in several studies [421-423]. However, further high-quality studies are needed to confirm the positive effects of multidisciplinary interventions on physical functioning due to the limitations of the included studies.

The present systematic review showed that changes in body composition following multimodal interventions in UGI cancer patients has been understudied and the limited available evidence showed mixed results. As mentioned previously, muscle wasting is associated with impaired quality of life and reduced survival following cancer treatments [424]. However, the optimal care which can effectively counteract cancer-associated cachexia has not yet been defined [424]. Cachexia and muscle wasting has received much attention in the scientific literature in recent years, but there remains limited evidence regarding the effectiveness of combined nutritional and exercise interventions in improving impaired body composition [425, 426]. It is acknowledged that meeting patients' protein and energy requirements is crucial to maintain muscle mass during cancer treatment and recovery, and exercise interventions may be effective in preventing and reversing muscle wasting [427-429]. It is worthy of note that, although four of the included studies assessed dietary intake at some time point of the study, none of them reported dietary intake data [132, 135, 407, 415]. This could be considered as one of the factors which resulted in a high risk of bias in the reviewed studies as lack of dietary intake data makes it difficult to examine whether nutritional adequacy had been achieved by these interventions.

Dietary intake assessment is crucial to ensure whether adequate protein and energy intake has been supported during multidisciplinary interventions. This is even more important in UGI cancer survivors as they experience severe reductions in their dietary intake and impaired food tolerance following surgeries[84].

The increased survival rate of patients diagnosed with cancer is accompanied by an acknowledgement of the need to ensure good quality of life. Cancer can negatively impact quality of life and improved HRQOL may be associated with lower mortality and recurrence [430]. In the present review, changes in patients' quality of life was assessed in two studies with inconsistent results. Assessing changes in HRQOL during and beyond cancer, and following interventions, can assist researchers to have a better understanding of the effects of treatment on patients' physical, mental, and emotional status [431].

The multidisciplinary interventions reviewed here failed to show any beneficial effects on post-operation complications and hospital stay. Although contradictory results were reported in other non-RCT studies, with a lower mortality rate and severity of complications or shorter hospital stay following a multidisciplinary prehabilitation programme [432, 433]. However, their small sample size and methodological limitations may limit their power to examine these outcomes properly. Optimisation of patients' nutritional and physical status before the surgery has been recommended for improving post-operative outcomes [434]. More high-quality research studies are needed to identify the most effective prehabilitation and/or rehabilitation interventions based on cancer site and type of surgery to improve operative outcomes.

Although this systematic review aimed to examine the optimal timepoint for delivery of multidisciplinary interventions

within the cancer trajectory, the high risk of bias in the reviewed studies along with the high degree of variance regarding design and delivery of the intervention and measured outcomes, prevented a clear conclusion on this issue. The limited studies which examined the effectiveness of prehabilitation versus rehabilitation in cancer reported inconsistent results from observing no significant differences in functional walking capacity to better responses to prehabilitation compared with rehabilitation [435, 436]. Therefore, the optimal timepoint for providing multidisciplinary care programmes is yet to be determined and requires further research.

It should be acknowledged that the present systematic review has several limitations. First, although a comprehensive search was conducted to locate all relevant studies, some studies, including non-peer reviewed, may be missed. Secondly, a considerable number of ongoing trials were identified (12 relevant ongoing trials listed in Appendix XIV) and, when contacted, the authors of these studies reported that they were still ongoing, stalled due to the COVID-19 pandemic, or in pre-publishing stages [437]. The results of these studies may be helpful in yielding a more explicit conclusion.

Also, it is important to note that the study by Ausania et al. focused on pancreaticoduodenal cancers, which are clinically distinct from gastric and oesophageal cancers. However, its inclusion was considered appropriate as these malignancies share similar postoperative challenges, particularly regarding gastrointestinal symptoms and dietary adaptation.

Moreover, it should be mentioned that the standard care varied significantly across different settings and in most settings, control groups were provided with standard care consisting of some nutrition and/or exercise prehabilitation or rehabilitation care, which may be considered a confounding factor to observe the significant

positive effects of these interventions on postoperative complications as well as nutritional status and quality of life. Furthermore, the importance of reporting details of standard care needs to be highlighted as it may complicate the interpretation of results. For instance, it's unclear whether the lack of significant changes in body composition, HRQOL and PA in the O'Neill study was due to the high quality of standard care as the details of standard care were not discussed [132].

On account of scarce evidence, variance and heterogeneity of studies in terms of intervention design, duration of study and follow-up, the time point of intervention delivery, and measured outcomes, etc., it was not possible to perform metanalysis and/or draw a firm conclusion on the effectiveness of these interventions on measured outcomes.

Adding to this, as indicated in Table 6-3, the primary outcome varied significantly across included studies which may limit meaningful comparisons across studies and evidence synthesis. Moreover, as primary outcomes are the basis of conducting power and sample size calculations, some studies may not be adequately powered to detect the group differences for a specific outcome of interest in this systematic review. For instance, the Yu-Juan Xu et al study has a low power (48%) for detecting group differences in lean muscle mass [415].

Finally, as the results of the risk of bias assessment indicated, more high quality and well-designed RCTs are required to draw more robust judgment on the effectiveness of these multidisciplinary interventions, specifically on body composition and quality of life. Some key points need to be considered to reduce the risk of bias in future studies including considering blinded assessment and analysis, dietary intake assessment and reporting dietary intake data to ensure

nutritional adequacy, providing greater details of delivered intervention such as the rationale behind prescribing nutrition support or supplements, providing greater details regarding adherence to different components of the intervention, and describing details of standard/control care.

6.5 Conclusion

Limited evidence is available on the effectiveness of multimodal interventions, with a core component of nutrition and exercise, in improving outcomes in UGI cancer patients. Although studies demonstrated improvements in physical function and exercise capacity, the evidence regarding positive changes in muscle mass and quality of life was scarce and conflicting. In conclusion, due to the poor quality of limited available evidence, further high-quality studies are warranted to examine the effectiveness of multidisciplinary care programmes in improving outcomes in UGI cancers with a focus on improving body composition and quality of life in these patients. Considering a core outcome set for measuring the clinical effectiveness of multidisciplinary supportive care programmes may improve the consistency and quality of future investigations [438]. Moreover, it may facilitate more meaningful comparisons across studies and support evidence synthesis.

Chapter 7 Feasibility, Practicality and Outcomes of a Nutritional Intervention within a Telehealth Rehabilitative Programme in UGI Cancer Survivors: Results from ReStOre@Home Feasibility Study

In this chapter the practicality and challenges of remote delivery of a nutrition intervention within the ReStOre@Home programme is explored. The impact of this feasibility study on nutritional outcomes was also evaluated to determine whether the remote delivery of this multidisciplinary rehabilitation programme could potentially reduce the burden of nutrition impact symptoms (NIS), improve nutritional status and dietary intake, and increase compliance with cancer prevention recommendations.

7.1 Introduction

Supportive nutrition care is vital to target malnutrition and its related comorbidities in UGI cancer patients [101]. As noted earlier in Chapter 6, combining nutrition and exercise interventions may offer greater benefits in improving muscle strength and function for cancer survivors [131, 439, 440]. While multidisciplinary rehabilitation programmes that integrate nutrition and exercise have shown promising results in enhancing cardiorespiratory fitness and functional capacity, there is a lack of high-quality research on the effectiveness of these programmes in UGI cancer survivors, particularly regarding their impact on nutritional status and body composition [136]. This highlights the need for further investigation in this area.

ReStOre II, a 12-week multidisciplinary intervention incorporating exercise training, dietetic counselling, and education, has been developed to investigate the effects of this multimodal approach in UGI cancer survivors [441]. However, the commencement of this study was delayed due to the COVID-19 pandemic, as group sessions posed a high risk of infection, particularly for UGI cancer survivors who had recently completed treatment and were especially susceptible to viral transmission [140]. Whilst the COVID-19 pandemic placed significant strain on healthcare services and stalled many clinical trials [442, 443], it accelerated the use of telehealth and e-health [444]. Telehealth refers to the use of digital information and communication technologies for the remote delivery of healthcare services [445]. Telehealth can be delivered through various communication channels, including video calls, phone calls, text messages, email, etc. [445]. During the COVID-19 pandemic, telemedicine emerged as a revolutionary method facilitating safe healthcare delivery [446].

The COVID-19 pandemic also led to a transition from in-person to remote or hybrid visits in clinical trials, enabling the continuation of research studies [447, 448].

Thus, in response to the COVID-19 pandemic, an adapted version of ReStOre II was designed to examine the feasibility of virtual delivery of this rehabilitation programme [139]. However, adopting an online version of ReStOre II, presents challenges as it should replicate all aspects of the in-person programme, which was designed to meet the complex needs of UGI cancer survivors, including group sessions, individual consultations and peer support [140]. Thus, the feasibility, practicality and challenges in telehealth delivery of ReStOre II needed to be examined.

The feasibility of ReStOre@Home was established by determining the recruitment rate, adherence rate, acceptability of the programme, and retention rate [140]. This present chapter focused on the nutrition intervention within the ReStOre@Home programme and the nutrition outcomes. Specifically, it aimed to assess the following:

- The feasibility and acceptability of the nutrition intervention
- The impact of the programme on body composition
- The impact of the programme on nutrition impact symptoms
- The impact of the programme on dietary adequacy

7.2 Methods

The ReStOre@Home study took place between July and October 2021. Ethical approval was sought from the Tallaght University Hospital (TUH)/St James's Hospital (SJH) joint Ethics

Committee. The present study was conducted in accordance with the Declaration of Helsinki (1964) and its later amendments. Data presented in this chapter were collected as part of baseline and post intervention assessments of ReStOre@Home study [140].

7.2.1 Eligibility

Cancer survivors who had a histologically confirmed diagnosis of oesophageal or gastric cancer and underwent curative surgery were eligible to participate in the ReStOre@Home study. Participants were required to have completed their cancer treatment (surgery±adjuvant therapy) at least three months prior to enrolment. Additionally, access to home broadband was necessary to be eligible for recruitment [139].

7.2.2 Recruitment

Participants were recruited to the ReStOre@Home study as outlined in the study protocol [139]. The patient database in St James's Hospital (National Centre for Oesophageal and Gastric Cancer) was screened to identify eligible participants. A list of eligible participants was sent to the clinical team requesting clinical clearance to be invited to participate in the ReStOre@Home study. Following this, a copy of the PIL and an invitation letter were sent to suitable participants. After seven days of reflection, a follow-up telephone call was made. Initial verbal consent was obtained over the phone, and an in-person baseline assessment was scheduled at the Wellcome Trust HRB Clinical Research Facility at St James's Hospital, Dublin, Ireland. Written informed consent was obtained before starting assessments.

7.2.3 Anthropometric, Functional, and Dietary Outcome Measures

Assessments were completed at baseline (T0) and post-intervention (T1). Weight, body mass index (BMI), body composition (bioimpedance analysis (BIA)), and waist and mid-upper arm circumference (MAUC) were measured as previously described in section 2.6 [140]. Functional status was determined using hand grip strength (HGS), leg press and short physical performance battery (SPPB) [140].

Dietary intake was assessed by 24-hour food recall using the Foodbook24 tool [165]. Foodbook24 is a web-based, self-administered tool developed for assessing dietary intake in the Irish population [165]. Participants were asked to record their dietary intake on three non-consecutive days using the Foodbook24 tool. Participants' nutrient intake was compared with the European Food Safety Authority's (EFSA) nutritional recommendations [353]. The energy requirements of participants were calculated as per ESPEN guidelines for clinical nutrition in cancer [449].

A registered dietitian (FS) trained participants to use the Foodbook24 tool and assisted participants in inputting their first recall. This was completed remotely by a video call and facilitated by sharing the researcher's screen. Afterwards, participants were provided with access to log in to the Foodbook24 system to record the subsequent 24-hour recalls.

Compliance with cancer prevention recommendations was assessed using the WCRF/AICR score. The score was modified to a maximum of 6, excluding the physical activity and breastfeeding recommendation [450].

The Gastrointestinal Symptom Rating Scale (GSRS) was used to assess gastrointestinal (GI) symptoms[188]. The Simplified Nutritional Appetite Questionnaire (SNAQ) was used to assess malnutrition risk [451].

7.2.4 Intervention

The 12-week ReStOre@Home programme consisted of exercise (aerobic and resistance training), 1:1 dietary counselling and group education sessions delivered virtually using the Salaso platform. ReStOre@Home intervention components and schedule are shown in Figure 7-1 and described in detail elsewhere [140].

Week	1	2	3	4	5	6	7	8	9	10	11	12
Independent walking sessions	 	 	 	 	 	 	 	 	 	 		
Video call check in meeting with physiotherapist												
Video call resistance training session												
Independent resistance training session												
Video call with dietitian												
Video call group education session												

Figure 7-1.ReStOre@Home 12-week intervention. (This figure has been published by Brennan L. et al.2022.)

7.2.5 The Nutrition Intervention

The nutrition component of the ReStOre@Home programme included dietary assessment, individual dietary counselling, and two group education sessions on nutrition in cancer survivorship. Personalised dietetic counselling sessions were delivered via video calls. Participants were due to receive a minimum of fortnightly sessions, but this was personalised based on their requirements and nutritional status. The dietary intervention aimed to (I) reduce the burden of GI symptoms by improving self-management, (II) optimise

nutritional intake, ensuring adequate energy, protein, and micronutrient intake, and (III) prevent unintentional weight and/or muscle loss.

In the 1:1 dietetic sessions, the baseline assessment results were shared and discussed with participants at their first nutrition counselling session, and collaborative nutritional goals for the programme were agreed upon. Participants reported weight changes, dietary intake, and symptoms during each session, and the study dietitian (FS) provided nutritional advice based on the participant's progress towards the agreed-upon goals. The dietary advice was tailored but often included guidance on following a high protein, high energy diet, food fortification, dietary strategies to minimise postprandial complications, and self-management of GI symptoms. Oral nutritional supplements were recommended if dietary intake was deemed inadequate [114].

In the first group education session, common dietary complications and GI symptoms after surgery and strategies to minimise the side effects were discussed. The WCRF recommendations for cancer prevention and survivorship were discussed at the second group education session [352].

7.2.6 Statistical Analyses

Statistical analyses were performed using SPSS 29 (SPSS Inc., Chicago, IL, USA). Data presented as mean (standard deviation). Normal distribution of variables was examined by the Shapiro–Wilk test. Normally distributed data were analysed using a paired t-test and nonparametric data were analysed using the Wilcoxon Signed Rank test. A p-value of <0.05 was considered statistically significant.

7.3 Results

7.3.1 Participant Characteristics

Twelve oesophagogastric cancer survivors (age 65.42 ± 7.24 years) were recruited. The participants' characteristics are presented in Table 7-1. The majority of participants were male ($n=11$) and diagnosed with adenocarcinoma of the oesophagus ($n=9$), with a mean time from surgery of 10.8 months. Most participants were classed in either a healthy weight ($n=5$) or overweight ($n=5$) BMI category.

Table 7-1. Demographic characteristics of participants ($n=12$)

Characteristics		Value
Age (Years,) Mean (SD; range)		65.24 (7.24; 53-76)
Sex, n (%)	Male	11 (92)
	Female	1 (8)
Cancer type n (%)	Oesophageal	10 (83)
	Gastric and lung	1 (8)
	Oesophagogastric junction	1 (8)
Time since surgery Mean (SD; range)		10.8 (3.9; 5–17)
Underwent neoadjuvant treatment, n (%)		7 (58)
Underwent adjuvant treatment, n (%)		4 (33)
BMI kg/m^2 , Mean (SD)		25.6 (4.31)
Underweight ($<18.5 \text{ kg/m}^2$), n (%)		1 (8)
Healthy weight ($18.5\text{-}24.9 \text{ kg/m}^2$), n (%)		5 (42)
Overweight ($25\text{-}29.9 \text{ kg/m}^2$), n (%)		5 (42)
Obese ($>30 \text{ kg/m}^2$), n (%)		1 (8)
Ability to prepare food, n (%)		12 (100)
Access to help in food preparation, n (%)		11 (92)

Three participants withdrew from the study and did not complete the post intervention assessments. Results presented from this point forward reflect the participants' who completed the programme ($n = 9$).

7.3.2 Delivery and Feasibility of the Nutrition Intervention

The dietary component of the rehabilitation program included a planned total of seven individual counselling sessions per participant. However, the number of individual dietary counselling sessions was personalised according to participants' nutritional status and nutrition care needs and ranged from 4-7 sessions (mean 6.22). The initial session lasted approximately one hour, while subsequent sessions were 30 minutes each. The mean attendance rate for dietary counselling sessions was 90%. Reasons for non-attendance included participants' difficulty logging in to the call, work commitments, being on holiday, and forgetting planned dietetic consult sessions. During the intervention period, a total of 50 dietary counselling sessions were completed. Of these, 6 were converted from video call to phone call due to session rescheduling (2 sessions, participants forgot to log in to the planned video call), microphone issues (1 session), and poor internet connection (3 sessions). In all video calls, both the participant and the dietitian had cameras turned on, and no participants requested or expressed a preference to have the cameras turned off.

Additionally, two group nutrition education sessions were delivered via video call, each lasting one hour. Each session began with a 20-minute presentation by the research dietitian, followed by group discussion on the session topic. During the group discussion participants asked questions about nutritional information presented and also shared their experiences regarding symptom management and dietary modifications. All participants communicated with each other using microphones and had their cameras turned on and no alternative preferences, such as using the chat box for interacting with others, were requested.

7.3.3 Anthropometric Measurements and Body Composition

Changes in anthropometric measures and HGS are shown in Table 7-2. No significant changes were observed in body composition and anthropometric measures pre to post-intervention. At baseline, three participants (33%) had low HGS (<27 kg for men and <16 kg for women), which indicated probable sarcopenia, compared to post-intervention, which reduced to one participant (11%).

Table 7-2. Anthropometric measurements pre- and post-intervention (n=9)

Measure	T0 Mean (SD)	T1 Mean (SD)	P value
Weight (kg)	74.46 (13.59)	72.45 (14.12)	0.064
BMI (kg/m ²)	25.60 (4.31)	24.83 (4.42)	0.063
Waist Circumference (cm)	95.25 (12.22)	93.97 (13.59)	0.324
Mid-upper arm Circumference (cm)	28.83 (2.82)	28.51 (2.74)	0.416
HGS -Right(kg)	31.02 (10.15)	33.94 (9.35)	0.169
HGS -Left(kg)	29.2 (12.4)	30.77 (9.90)	0.601
Fat Mass (kg)	19.92 (10.91)	18.40 (11.32)	0.081
Fat Mass (%)	24.88 (8.77)	23.38 (9.33)	0.096
Fat Free Mass (kg)	55.45 (3.91)	55.73 (3.50)	0.507
Fat Mass Index (kg/m ²)	6.60 (3.33)	6.23 (3.69)	0.207
Fat-Free Mass Index (kg/m ²)	18.65 (1.70)	18.76 (1.67)	0.219
Skeletal Muscle Mass (kg)	27.28 (2.28)	26.96 (2.35)	0.166

7.3.4 Malnutrition, Gastrointestinal Symptoms and Dietary Intake

The SNAQ score increased from 13.56±3.20 at baseline to 14.56±3.35 following intervention. The number of participants at risk of malnutrition reduced after intervention as 55% (n=5) had an SNAQ score of 14 or less at baseline versus 33% (n=3) post-intervention.

As presented in Table 7-3, compared to the general population, participants in the present study had higher GSRS scores at both baseline and post-intervention. Following the intervention, mean GSRS scores for abdominal pain, reflux and diarrhoea were reduced; however, scores for constipation and indigestion slightly increased. Overall, no significant changes in the GSRS score and its subscales were observed compared to the baseline.

Table 7-3. Gastrointestinal symptoms and nutritional status pre- and post-intervention (n=9)

Measure	T0 Mean Score (SD)	T1 Mean Score (SD)	Reference value, general population[4 52] Mean Score	P value
GSRS¹				
Abdominal pain (score range 1-7)	2.37 (1.56)	2.25 (1.46)	1.56	0.52
Reflux syndrome (score range 1-7)	2.05 (1.48)	1.88 (1.43)	1.39	0.43
Diarrhoea syndrome (score range 1-7)	2.70 (1.51)	2.66 (1.62)	1.38	0.94
Indigestion syndrome (score range 1-7)	2.63 (1.45)	2.80 (1.65)	1.78	0.419
Constipation syndrome (score range 1-7)	1.59 (0.61)	1.66 (0.74)	1.55	0.81
SNAQ²				
Total score (score range 4-20)	13.56 (3.20)	14.56 (3.35)		0.067
SNAQ ≤14, n (%)	5 (56%)	3 (33%)		-

¹ Scores are calculated by taking the mean of the items completed within an individual scale, with higher scores indicating greater symptom severity; ² SNAQ score ≤14 indicates a significant risk of at least 5% weight loss within six months.

Dietary intake of key nutrients, often sub-optimal in UGI cancer survivors, is reported in Table 7-4. The intake of all macro and micronutrients is available in Appendix XV. Total protein intake increased following the intervention (71.99±25.57g vs 106.06±42.83 g). Also, there was an increase in the number of participants meeting a minimum daily protein intake of 1g/kg body weight following intervention (77% (n=7) versus 44% (n=4)). Similarly, total energy intake was increased (1610 kcal vs 1909 kcal). At baseline, on

average, participants met 86% of their energy requirements, increasing to 108% post-intervention. The increased energy intake was reflected in the increases in protein, carbohydrate, and fat intake following intervention.

Regarding the macronutrient composition of diet, at baseline 4 participants (44%) consumed less than 45% of their daily energy intake from carbohydrates, with none exceeding 60%. This pattern remained unchanged after the intervention. Regarding fat intake, 4 participants (44%) consumed more than 35% of their energy from fat at baseline, which increased to 6 participants (66%) after the intervention.

Dietary intake of vitamin D, retinol, vitamin E, folate, iron, and calcium increased following intervention and intake of B₁₂ remained unchanged. The number of participants meeting their dietary requirements of fibre, retinol, vitamin E, folate, calcium, and iron increased post-intervention. At baseline, three participants took a multivitamin/mineral supplement, which increased to four post-intervention.

Regarding compliance with WCRF/AICR recommendations, the mean WCRF/AICR score increased following intervention, from 2.83 ± 0.96 at baseline to 3.16 ± 0.72 post-intervention. As presented in Table 7-5, adherence to recommendations on healthy weight, consuming a plant-based diet, and limiting fast food consumption improved, while this remained unchanged for red and processed meat and alcohol intake. Whilst reported intakes of plant-based foods increased at T1, it remained the recommendation with the lowest adherence score. None of the participants achieved the maximum score at baseline or post-intervention. This was followed by the recommendation to limit fast and ultra-processed foods, with a mean score of 0.33 at baseline and 0.44 post-intervention.

Table 7-4. Dietary intake pre- and post-intervention (n=9)

Nutrient	T0 Mean (SD)	T1 Mean (SD)	Δ Mean (SD)	P value	DRV	T0 % meeting requirement	T1 % meeting requirement
Energy & Macronutrients							
Energy (Kcal)	1610.62 (589.39)	1909.47 (757.71)	298.84 (913.35)	0.80	25-30 kcal/kg/day (ESPEN)[101]	44%	66%
Protein (g)	71.99 (25.57)	106.06 (42.83)	34.07 (50.49)	0.08	1-1.5 gr/kg bw (ESPEN)[101]	44%	77%
Protein (% energy)	18.52(5.57)	27.52 (20.98)	8.99 (20.55)	-			
Carbohydrate (g)	180.83 (68.36)	206.38 (71.40)	25.55 (99.98)	0.95			
Carbohydrate (% energy)	45.18 (6.72)	45.06 (7.10)	-0.12 (7.26)	-	45-60% energy intake (RI)	55%	55%
Fat (g)	62.08 (25.38)	81.31 (42.85)	19.23 (47.86)	0.82			
Fat (% energy)	34.9 (7.64)	36.38 (7.71)	1.47 (10.05)	-	20-35% energy intake	55%	33%
Fibre (g)	12.35 (4.9)	16.39 (7.12)	4.03 (9.30)	0.68	25g/day (AI)	0%	11%

DRV: Dietary Reference Values, Kcal: Kilocalorie, Kg: Kilogram, g: Gram, bw: body weight, RI: Reference Intake, AI: Adequate Intake, µg: Microgram, PRI: Population Reference Intake, mg: Miligram, DFE: Dietary Folate Equivalents. Energy and protein requirements are considered according to ESPEN guidelines in cancer. Dietary reference values according to European Food Safety Authority (EFSA) guidelines. Zinc requirement depends on levels of phytate intake; due to a lack of data on phytate intake, the mean of zinc requirements based on four levels of phytate intake is calculated and considered as DRV.

Table 7-4.Dietary intake pre- and post-intervention (n=9).(Continued)

Nutrient	T0 Mean (SD)	T1 Mean (SD)	P value	Δ Mean (SD)	DRV	T0 % meeting requirement	T1 % meeting requirement
Vitamins and Minerals							
Vitamin (µg) D	2.85 (3.10)	6.11 (4.02)	0.67	3.26 (4.66)	15 µg /day (AI)	0%	0%
Retinol (µg)	504.75 (506.66)	952.15 (638.17)	0.08	447.39 (999.9)	650 µg /day (F), 750 µg /day (M), PRI	22%	44%
Vitamin E (mg)	9.51 (6.60)	13.09 (8.29)	0.59	3.58 (12.49)	11mg/day (F)-13 mg/day(M)	22%	44%
Vitamin B ₁₂ (µg)	4.30 (3.37)	4.79 (3.05)	0.31	0.48 (3.59)	4 µg /day (AI)	44%	44%
Folate (µg)	178.05 (110.64)	320.04 (176.27)	0.10	141.99 (256.24)	330 µg DFE/ Day (PRI)	11%	44%
Iron (mg)	13.19 (11.59)	15.18 (6.89)	0.44	1.99 (15.43)	11 mg/day (PRI)	33%	66%
Calcium(mg)	739.92 (361.08)	909.92 (442.41)	0.37	170 (633.96)	950 mg/day (PRI)	11%	33%
Zinc (mg)	10.27 (8.27)	12.05 (5.11)	0.31	1.78 (10.90)	12.9mg male/10.1 mg female (PRI)	22%	44%

Table 7-5. Adherence to WCRF/AICR recommendations pre- and post-intervention (n=9)

2018 WCRF/AICR Cancer Prevention Recommendations		Maximum potential score	T0 Score Mean (SD)	T1 Score Mean (SD)
1. Be a healthy weight	BMI	0.5	0.27 (0.19)	0.33 (0.21)
	Waist circumferences	0.5	0.27(0.23)	0.30 (0.20)
2. Eat a diet rich in whole grains, vegetables, fruits, and beans	Fruits and vegetables	0.5	0.08 (0.12)	0.22 (0.15)
	Fibre	0.5	0.08 (0.12)	0.13 (0.13)
3. Limit consumption of "fast foods" and other processed foods high in fat, starches, or sugars		1	0.33 (0.43)	0.44 (0.46)
4. Limit consumption of red and processed meat		1	0.5 (0.5)	0.5 (0.5)
5. Limit consumption of sugar-sweetened drinks		1	0.55 (0.46)	0.5 (0.5)
6. Limit alcohol consumption		1	0.72 (0.26)	0.72 (0.26)
Total score		6	2.83 (0.96)	3.16 (0.72)

7.4 Discussion

The present study explored the feasibility and practicality of delivering a remote nutritional intervention within the ReStOre@Home programme. It also assessed the potential impact of this intervention on improving the nutritional outcomes measures. The findings indicated that the remote delivery of the nutrition intervention of ReStOre@Home is both feasible and practical. However, it is important to consider that the personalised approach of delivering up to seven dietary counselling sessions was appropriate for the present study's context. However, in real-world clinical settings, providing this number of sessions may not be feasible due to limited resources and staff capacity. Future clinical implementations could consider adjusting the model by increasing the interval between sessions, reducing the total number of

sessions, or incorporating alternative delivery approaches such as group counselling to maintain intervention effectiveness and sustainability. Participants showed improvements in dietary intake and adherence to cancer prevention recommendations, although GI symptoms remained unchanged. Importantly, muscle mass was preserved along with increased physical activity and possible higher energy expenditure, likely due to the programme's effectiveness in ensuring dietary adequacy. However, the significance of these improvements cannot be conclusively determined, as this pilot single-arm feasibility study was not powered to detect significant changes in outcome measures.

7.4.1 Impact on Malnutrition, Gastrointestinal Symptoms and Body Weight and Composition

In the present study, malnutrition screening predicted a significant weight loss ($\geq 5\%$ of the original body weight) within the next six months for over 50% of participants at enrolment (SNAQ score of ≤ 14). Notably, only one participant was underweight according to the BMI category. As described earlier in section 5.4.1, this finding highlights the potential limitations of using BMI as the sole indicator of nutritional status [360]. Tools such as the SNAQ, which assesses factors like appetite, portion sizes and eating habits, can provide a more comprehensive view of a patient's nutritional status. Additionally, as changes in appetite and food intake may precede visible weight loss, using tools like SNAQ may allow for earlier detection of malnutrition. Thus, integrating appropriate malnutrition screening tools into routine clinical practice in oncology may lead to earlier identification of at-risk individuals and the implementation of timely interventions for malnutrition [453].

Following the intervention, 33% of participants had an SNAQ score of ≤ 14 , suggesting a potential improvement in their nutritional status. This finding is consistent with previous research, where virtual nutritional counselling was reported to improve patient-generated subjective global assessment (PG-SGA) scores in cancer patients [144]. However, due to the limited number of studies evaluating the effectiveness of telehealth in nutritional oncology and the variation in outcome measures, it is difficult to draw definitive conclusions about the effectiveness of these interventions [454, 455]. Thus, as discussed in Chapter 6, further studies and the use of a core outcome set are required to enable consistent outcome measurement and facilitate comparison between studies.

As demonstrated in Chapter 3, Chapter 4 and Chapter 5 of this present study, gastrointestinal complications remain an issue for UGI cancer survivors, with observed GSRS scores higher than the GSRS score of the general population. Gastrointestinal disturbance can compromise nutritional status by limiting dietary intake and inducing unintentional weight loss [456]. Also, higher symptom severity is reported in malnourished subjects [56]. Tailored nutritional intervention can reduce GI symptoms and improve quality of life [457]. However, in the current study, whilst some individual symptoms changed, overall GSRS scores remained unchanged post intervention. It should be highlighted that effective management of nutrition impact symptoms (NIS) may not be achieved through dietetic care alone, as medication management is also required in some cases, which extends beyond the dietitian's expertise and requires multidisciplinary intervention [458]. Additionally, poor adherence to dietary advice for managing GI symptoms can result in the persistence or worsening of symptoms, a factor that was not measured in the present study [459]. Furthermore, as discussed in Chapter 4, acceptance was identified as

a coping strategy among UGI cancer survivors. Passive acceptance, such as resignation to symptoms by perceiving them as unchangeable, and poor perception of the benefit of dietary modification may negatively impact adherence to dietary advice [460, 461].

In the present study, the ReStOre@Home programme showed promising results in preventing weight loss and muscle loss, as these remained unchanged following the intervention. Additionally, post-intervention, fewer participants were identified with probable sarcopenia, which may indicate an improvement in muscle strength. This aligns with findings from a systematic review and meta-analysis of the effectiveness of combined nutrition and exercise interventions in cancer [462]. This systematic review showed that such interventions successfully preserved body weight and lean mass, with no significant changes in either, as intended [462]. However, it was noted that only a limited number of studies measured body composition in weight maintenance interventions, which precludes meaningful interpretation of the pooled effects [462].

The effects of nutritional interventions in improving GI complications and nutritional status in UGI cancer survivors will be further examined in the ReStOre II RCT [441]. This study includes a larger sample size with greater statistical power and a control group receiving standard care, enabling assessment of the effectiveness of the nutritional interventions. Additionally, the ReStOre II study incorporates longer follow-up periods, with outcomes assessed at 3 and 12 months post-intervention, allowing for the evaluation of long-term effects, such as exacerbation of nutritional outcomes in the absence of nutritional intervention.

7.4.2 Impact on Dietary Intake

UGI cancer treatment can significantly influence dietary intake up to three years after oesophagectomy [53]. In the present study, less than 50% of participants were meeting their energy and protein requirements at baseline which correlates with the finding that over 50% were at risk of malnutrition according to the SNAQ score. In the ReStOre@Home programme, individualised nutritional counselling aimed to ensure energy and protein adequacy, which was achieved by maintained or increased dietary intake in 77% of participants following the intervention. Although the increase in energy and protein intake did not reach statistical significance, likely due to the small sample size, they represent clinically meaningful and nutritionally important changes, highlighting the positive impact of the intervention on participants' dietary intake [463].

This result was aligned with previous studies showing increased energy and protein intake following nutritional counselling in cancer patients [464-466].

The present study observed suboptimal fibre, vitamin D, retinol, vitamin E, folate and calcium intake at baseline. Following dietary intervention, the mean intake of these nutrients increased, and the number of participants meeting the recommended intake of fibre, vitamin A, vitamin E, folate, iron, and calcium increased. However, vitamin D supplementation is still required to meet dietary requirements, as is the case for the general population in Ireland [467]. There is limited evidence on the effects of nutritional intervention on micronutrient intake in UGI cancer survivors. A previous study observed a lower prevalence of fat-soluble vitamin deficiencies in oesophageal cancer survivors following the establishment of a nutrition and survivorship clinic [127]. In a study involving breast cancer survivors, telephone nutrition counselling

was used as the principal method to promote dietary modifications, which could increase the intake of folate, vitamin C, and magnesium [468].

The effectiveness of nutritional intervention on optimising nutrient intake in UGI cancer survivors will be further explored in the ReStOre II trial.

7.4.3 WCRF/AICR Recommendation

Results of the present study indicated poor compliance with WCRF/AICR recommendations in the cohort of UGI cancer survivors who participated in the ReStOre@Home study. Following intervention, some improvement in adherence was observed, namely for the recommendation to eat a plant-based diet and limit fast food consumption. However, it should be highlighted that the nutrition intervention in the ReStOre@Home programme primarily aimed to improve self-management of GI symptoms, ensure nutrition adequacy and prevent unintentional weight loss and muscle wasting. Clinical trials examining the effects of nutritional interventions in breast cancer survivors have reported improved adherence to cancer prevention recommendations following the intervention [469, 470]. However, it should be noted that these studies often focused on weight management and healthy eating [469, 470], and thus, a different problem compared to UGI cancer survivors, who often require nutritional advice for involuntary weight loss and persistent GI symptoms [63, 375]. Therefore, they may be advised to follow different nutritional advice, such as consuming high-calorie and nutrient-dense foods that can be at odds with cancer prevention recommendations [389]. Subsequently, this might limit compliance with WCRF/AICR recommendations in UGI cancer survivors. Further studies are needed to identify the barriers

to adherence to WCRF/AICR recommendations in UGI cancer survivors.

The clinical guidelines for UGI cancer recommend that nutritional interventions be individualised [118, 121, 123]. They also suggest that once patients have stabilised their weight, are no longer at immediate risk of malnutrition, and nutritional symptoms no longer impact their quality of life, the focus should shift from high-calorie diets to nutritional counselling promoting a healthy lifestyle and WCRF/AICR recommendations [118, 121, 122]. However, dietitian referral criteria are often limited to malnutrition, weight loss, and GI symptoms. Additionally, nutritional complications in UGI cancer survivors are often long-lasting, and many patients may no longer be under active surveillance by the time it is appropriate to transition from high-calorie, high-protein diets to healthy lifestyle recommendations. As a result, most survivors may not receive personalised or adequate support for implementing the WCRF/AICR recommendations.

Another observation from the present study was that the increase in WCRF/AICR score, coincided with improvements in fat mass and handgrip strength post-intervention. However, given the observational nature of the study and the absence of a control group, it is not possible to determine whether these improvements were a direct effect of the programme. Nonetheless, these findings highlight the potential for nutritional interventions to support physical recovery in this population and warrant further investigation in future controlled studies.

7.4.4 Remote Nutritional Intervention and Monitoring

In the present study, the attendance rate of 90% at dietetic sessions demonstrated the practicality and acceptability of

telehealth delivery of a nutritional intervention in UGI cancer survivors. Sessions were delivered via individual and group video calls. Videocalls have been reported to work better in building and maintaining rapport than phone calls [144]. Also, features such as screen sharing facilitate using various educational materials (i.e., assessment reports, slides, videos, websites) during sessions. This subsequently may improve the quality of nutritional consults and education [471, 472].

Using the Foodbook24 tool for collecting dietary intake data facilitated remote data collection, which reduced the time of in-person contact during baseline and post-intervention assessments, thus reducing infection risk. The dietary intake data were collected on a separate day from the in-person assessment but within 7 days. Whilst this approach was taken from a COVID-19 risk mitigation perspective, it also may also have influenced the accuracy of dietary intake data by reducing participants' burden and tiredness at time of in-person assessment. This may subsequently limit differential response bias and improve the accuracy of 24hr dietary recall data [473].

There were some key learnings from using Foodbook24 in terms of technical features to improve remote dietary intake data collection and monitoring. For instance, researchers did not have real-time access to oversee participants inputting in Foodbook24. This additional feature could be helpful in capturing errors in participants' entries (i.e. incomplete dietary recalls, errors in reported serving sizes, etc.). Also, a push notification feature is recommended to send reminders to participants to encourage the completion of all recalls in the required time frame. However, technological implications, participant burden, and limited time frame for completing baseline and post-intervention assessments

may still negatively impact the collection of multiple recalls [474]. Furthermore, it is noted that repeated dietary intake measures might influence participants' dietary intake data, for example, by improving diet by self-reflection or miss-reporting due to social desirability burden [475, 476].

7.4.5 Strength and Limitations

The present study has several strengths. For dietary data collection, Foodbook24 was used, which is an online tool developed to assess dietary intake in the Irish population based on the Irish food composition table. Foodbook24 uses a structured data collection method by including multiple passes and prompts to complete the dietary recall. It also uses images of portion size, which improves the accuracy [165]. Another strength was the application of several counselling strategies in delivering personalised dietary interventions to improve effectiveness. This included motivational interviewing, goal setting, providing different educational materials (slides, videos, recipe books, booklets), frequent contacts and follow-up sessions with the dietitian, and group education sessions. These strategies have been suggested to improve the efficacy of dietary counselling [477].

The present study also has some limitations. First, given the telehealth mode of delivery, only participants who had access to the required technology and were comfortable using it were recruited. This may bias the enrolment toward younger survivors with a higher education level living in urban areas [478-483]. This may be an influencing factor on the level of awareness of the importance of nutrition during survivorship and compliance with the dietary recommendations amongst the cohort [484, 485]. Secondly, not all participants completed all three 24-hour dietary recalls at both baseline and post-intervention. This may affect the accuracy of

dietary intake data as estimation of participants' usual dietary intake is best calculated from multiple 24-hour recalls. Finally, this feasibility study was not powered to detect statistically significant changes; observed results need to be confirmed by a randomised clinical trial; thus, it is not possible to draw definitive conclusions on the effectiveness of the intervention.

7.5 Conclusion

The present study showed that telehealth delivery of nutrition intervention is possible in UGI cancer survivors. This study has demonstrated that UGI cancer survivors are willing and able to engage in remote dietetic consultations. Incorporating a telehealth approach to dietetic consultations could expand the service provision in this cohort.

Chapter 8 Discussion

8.1 Introduction

Substantial growth in the population of cancer survivors has drawn attention to survivors' care needs [53, 486]. However, UGI cancers remain among the most aggressive cancers with a low survivorship rate [10, 487]. Therefore, UGI cancer survivors are often understudied compared to more prevalent cancers with higher survival rates [99, 488].

UGI cancer survivors often never return to normal life following the completion of their cancer treatment and face various challenges during survivorship [53]. From a nutrition perspective, UGI cancer survivors often suffer from major nutrition impact symptoms (NIS) such as appetite loss, dysphagia, early satiety, dumping syndrome, reflux, diarrhoea and abdominal cramps [50-52]. These symptoms often impede adequate oral intake, leading to unintentional weight loss, malnutrition, and muscle wasting [53, 54, 82, 489]. However, there are limited data concerning UGI cancer survivors' nutritional needs, challenges and their experience of nutritional care in Ireland [99]. Understanding these issues is crucial and can help inform the development of national survivorship care programmes to address UGI cancer survivors' nutritional needs.

Several models of care are suggested to address survivorship needs in cancer. With respect to nutritional status, UGI cancer survivors face unique challenges and require specialised multidisciplinary care programmes to manage their post-treatment complications [490]. Thus, the feasibility, acceptability, and effectiveness of these care models need to be examined in UGI cancer survivors. These data are essential for ensuring that survivorship care in UGI cancer is tailored to survivors' diagnosis,

treatments, and complications, leading to improved nutritional status and health outcomes.

8.2 Summary of Findings

The present thesis aimed to achieve two broad objectives. Firstly, it aimed to comprehensively investigate the nutrition care needs of UGI cancer survivors in Ireland, using quantitative and qualitative methods. Secondly, it set out to review the current evidence regarding multidisciplinary intervention in UGI cancer survivors and determine the feasibility of a remote nutritional intervention within a multidisciplinary rehabilitation programme in UGI cancer. Five studies were designed to achieve these objectives, and the following results were observed.

In three cross-sectional studies, the nutrition care needs, nutritional and psychological status, and quality of life of UGI cancer survivors were investigated.

- By a **national survey**, UGI cancer survivors' nutritional and psychological status, quality of life and subjective nutrition care needs were assessed. The findings indicated that more than 30% of UGI cancer survivors were at risk of malnutrition. Also, a persistence of GI disturbance in UGI cancer survivors was observed. Furthermore, the survey results demonstrated impaired quality of life and psychological distress in UGI cancer survivors compared to population norms. This study also suggested that UGI cancer survivors acknowledge the importance of nutrition in survivorship and the need for more support, with over 57% indicating a preference for further dietetic input and nutrition information.
- By a **qualitative study**, the nutrition care needs of UGI cancer survivors were further examined by interviewing

survivors and their caregivers about their current nutritional issues and the nutrition care provided to them. The findings suggested that nutrition care is accessible for UGI cancer survivors in Ireland during acute recovery. Also, UGI cancer survivors have positive views on the effectiveness of nutrition care. However, GI symptoms were persistent and troublesome. Participants reported several unmet needs regarding their nutritional care, including information needs, continuation of nutrition care, peer support, and support for caregivers. The results also described common coping strategies among UGI cancer survivors, such as dietary modifications, altered social habits, and acceptance as they adapt to a “new normal”.

- By a **cross-sectional study**, nutritional status, sarcopenia, nutritional intake, and dietary habits of a cohort of UGI cancer survivors were objectively measured. The results demonstrated that malnutrition remains an issue in disease-free UGI cancer survivors, as one in three were malnourished and one in eight were sarcopenic. Inadequate nutrient intake and poor adherence to cancer prevention guidelines were also observed in UGI cancer survivors.
- In a **systematic review**, the available evidence for the effectiveness of multidisciplinary interventions incorporating nutrition and exercise in UGI cancers was reviewed. Results of this study showed high variation in type, duration and delivery of nutrition and exercise interventions in UGI cancers. The findings of this systematic review also highlighted the variation in outcome measures and the importance of establishing a core outcome set to examine the effectiveness of these interventions and allow comparison between suggested care models.
- In a **feasibility study**, the practicality of a remote nutritional intervention within a multidisciplinary rehabilitation

programme for UGI cancer survivors was examined. This study indicated that remote nutritional intervention is practical and acceptable in UGI cancer survivors. Promising effects on nutrition-related outcomes were also observed; however, further studies are required to examine the effectiveness of this remote rehabilitation intervention.

8.3 Contribution to Knowledge

8.3.1 Nutritional Considerations in UGI Cancer Survivors

The high prevalence of malnutrition in UGI cancer survivors observed in this thesis (Chapter 3 and Chapter 5) further support and corroborate existing evidence highlighting the vulnerability of this population to nutritional deficits post treatment. The fact that the majority of participants in these studies were > 2 years post-surgery suggests that malnutrition persists in long-term survivorship. This finding underscores the importance of integrating routine nutritional assessment in survivorship care to facilitate early detection and management of malnutrition.

Building on the need for routine malnutrition screening, the findings from this thesis emphasise the inadequacy of relying solely on BMI as a marker of malnutrition in UGI cancer survivors. While BMI has been widely criticised for its inability to accurately reflect nutritional status, these limitations were particularly relevant in UGI cancer survivors in the present thesis as the majority had normal or high BMI which can obscure malnutrition diagnosis [360]. This finding highlights the importance of using validated malnutrition screening tools and diagnostic criteria such as GLIM that account for clinical symptoms beyond BMI, such as appetite changes, digestive function,

and muscle wasting to facilitate earlier detection and management of malnutrition in this vulnerable population.

In addition to the importance of considering symptoms such as appetite loss and malabsorption that may precede weight loss, the findings of the present thesis highlight the importance of non-physiological risk factors of malnutrition that may play a crucial role in nutritional inadequacy in UGI cancer survivors. UGI cancer survivors often experience physical impairment and treatment-related fatigue following surgery which can limit their ability to complete activities of daily living including meal preparation [491, 492]. Access to adequate support for meal preparation emerged as a barrier to achieving optimal nutritional intake post treatment in the qualitative study in Chapter 4. This further emphasises the importance and need for personalised interventions to maintain adequate nutrition and prevent unintentional weight loss in survivorship.

Ensuring dietary adequacy is crucial for malnutrition management in UGI cancer survivors. The data collected in Chapter 5 suggest that the majority of UGI cancer survivors were meeting their energy and protein requirements. This finding may highlight the effectiveness of current standard nutrition care in maintaining nutritional adequacy. However, the observation that >25% were failing to achieve dietary adequacy supports the need of continued and personalised nutrition care in survivorship, as requested by UGI cancer survivors in Chapter 3 and Chapter 4.

Additionally, it should be considered that although 75% of UGI cancer survivors in Chapter 5 were meeting their nutritional requirements, one-third remained malnourished and one in eight had sarcopenia. This suggests a possible discrepancy between current dietary recommendations and the specific needs of this cohort. It raises the question of whether standard nutritional

guidelines should be reviewed and potentially increased, given factors such as impaired absorption, inflammation, and altered body composition that may limit nutrient utilization in UGI cancer survivors[76, 493]. Further research, perhaps employing indirect calorimetry, is needed to evaluate whether higher or more individualised target for nutritional intake could improve outcomes.

Despite positive evidence on dietary adequacy, data collected in the present thesis showed poor diet quality in UGI cancer survivors. As discussed earlier in section 1.9, clinical guidelines indicate that once survivors are no longer losing weight or experiencing severe gastrointestinal (GI) symptoms, the focus of nutritional care should shift from food fortification and high energy high protein diets toward long-term health promotion, including adherence to cancer prevention guidelines. Based on the findings of the present thesis several factors were likely to contribute to this poor compliance. Firstly, a high burden of GI symptoms observed in UGI cancer survivors may limit adherence to dietary recommendations, such as those involving increased fibre intake. Secondly, the thesis has highlighted the lack of long-term dietary follow-up after treatment, thus once UGI cancer survivors reach a stable condition, they may not be under regular dietetic review, leading to a lack of guidance on transitioning to a preventive diet to reduce their risk of cancer recurrence and other chronic diseases. Thirdly, as reported in Chapter 4, lack of personalised dietary advice tailored to individual needs may also contribute to poor adherence to these guidelines. The findings of this thesis indicate the need for continued individualised nutrition care to address complex and evolving nutritional challenges well beyond the early recovery phase in UGI cancer.

8.3.2 Interplay Between Symptom Burden, Psychological Distress, and Quality of Life in UGI Cancer Survivors

Consistent with previous research, the findings of the present thesis indicate that cancer survivors experience higher symptom severity and psychological distress compared to the general population [233, 247, 248, 260, 261]. As discussed in Chapter 4, the qualitative findings further underscore the significant psychological burden and impaired quality of life in these survivors due to persistent GI symptoms.

One key theme that emerged from the qualitative analysis was the survivors' adoption of dietary modifications to manage their symptoms. While this strategy was commonly reported, acceptance also emerged as a critical coping mechanism for dealing with the long-term impact of UGI cancer treatment. However, although acceptance may offer psychological benefits, such as reducing emotional distress, it may also lead to resignation [460]. This resignation manifests when patients choose to live with unresolved symptoms, accepting the lasting effects of cancer treatment on their quality of life [460, 461]. The findings of this thesis suggested that this symptom resignation may partly stem from the lack of tailored, effective dietary interventions. Many survivors expressed an unmet need of long term and personalised nutrition care. This lack of personalised care may contribute to suboptimal symptom management, exacerbating the long-term impact on both their physical and mental well-being.

These findings emphasise the critical importance of providing targeted nutritional interventions for UGI cancer survivors. Such interventions should be designed to empower patients to manage

their symptoms more effectively, thereby limiting the long-term impact of cancer treatment on their overall quality of life.

8.3.3 Current Gaps in Nutrition Care and Potential of e-Health

In the present thesis UGI cancer survivors reported that dietetic services were easily accessible and available for contact during their cancer treatment and recovery. This finding was consistent with previous Irish data, which also indicated higher levels of access to dietetic services among UGI cancer survivors compared to other cancer survivors [222]. Despite a generally positive view of the accessibility of dietetic services, UGI cancer survivors voiced a clear need for more frequent contact with the dietitian as standard care, particularly during the early stages of recovery as additional tailored support was needed for adjusting to dietary changes when returning home after surgery. Additionally, there was a strong desire for additional nutritional information and continued nutrition care, indicating that existing services may not fully meet the complex, dynamic and long-term nutritional needs of survivors. While participants positively acknowledged the perceived effectiveness of dietetic services, the findings of this thesis highlighted a lack of personalised and practical nutritional guidance, experienced by those who had access to dietitian services.

Additionally, in the current study participants have suggested considering innovative educational methods and the integration of technology to improve the effectiveness of dietary education and facilitate long-term follow-up, via combinations of in-person, online, individual, and group sessions. The voice of the UGI cancer survivors has come through strongly in this research as this is the first study in Ireland that directly asked survivors how they would like their

nutrition care to be delivered. Considering their perspective is essential for developing patient-focused and effective nutrition care programmes tailored to the needs of UGI cancer survivors.

Adopting digital health solutions into dietetic consultations presents a promising avenue for improving service delivery given the well-documented dietetics staffing shortages in oncology in Ireland [246]. The ReStOre@Home study was the first to evaluate the delivery of telehealth-based nutrition care for UGI cancer survivors. The findings of this study demonstrated acceptability, feasibility and practicality of telehealth nutritional interventions for this population. Additionally, the experience from this thesis showed applying online tools like Foodbook24 can facilitate dietary data collection and analysis. Telehealth-based nutritional assessments and interventions could help bridge the gap created by resource constraints in dietetic services and ensure that survivors receive the support they need to manage their symptoms and improve their quality of life.

While telehealth can enhance access to survivorship care, especially for individuals living in remote locations, the potential challenges posed by digital literacy, particularly given the age profile of many UGI cancer survivors, and limitations in access to internet and required devices, need to be carefully considered [285-287].

8.3.4 Multidisciplinary Interventions in UGI Cancer

The systematic review of existing literature and the findings of present thesis suggested a positive impact of multidisciplinary interventions, with a core component of nutrition and exercise, in improving functional capacity, nutritional status and quality of life in UGI cancer survivors [134, 407, 416]. Despite these promising findings, the present thesis highlighted several limitations in the previous studies, such as a high risk of bias, variability in intervention

designs and outcome measurements, and selective reporting, which prevented drawing firm conclusions on effectiveness of these multidisciplinary interventions in UGI cancer survivors. The findings of the present thesis demonstrate the need for more well-designed and high quality randomised controlled trials and establishing a core outcome set to examine the effectiveness of these interventions in UGI cancer survivors. Furthermore, as the data presented in this thesis reveal significant unmet needs, including psychological distress, impaired quality of life, lack of personalised nutrition care and insufficient supportive care for both survivors and their caregivers, future multidisciplinary interventions should consider targeting these facets to effectively address the complex needs of UGI cancer survivors and their caregivers.

8.4 Recommendations for Clinical Practice

8.4.1 Routine Malnutrition Screening and Comprehensive Nutritional Assessment in UGI Cancer Care

The findings of the present thesis, aligned with other best practice guidance, recommends that nutrition care services should ensure routine malnutrition risk screening and comprehensive assessment to deliver timely personalised nutrition care in UGI cancer [101]. Malnutrition screening on hospital admission is a requirement as per The Health Information and Quality Authority (HIQA) guidelines, but screening tools are not specific for oncology and serial measures are often not performed [494, 495]. Enhancing healthcare professionals' knowledge and awareness is essential for incorporating malnutrition screening into the standard cancer care model [496]. Routine nutrition risk screening followed by a

comprehensive assessment is paramount for optimal nutrition care [497, 498]. This comprehensive assessment should include examining NIS, dietary intake, unintentional weight loss (UWL), sarcopenia and physical function, psychological distress and quality of life [498-500]. Assessments should be first completed at diagnosis, followed by systematic reassessment during cancer care, including the early recovery phase and long-term survivorship [501].

8.4.2 Extending Nutrition Care Beyond Acute Recovery in UGI Cancer

The findings of the present thesis has demonstrated an unmet need for nutrition care in UGI cancer survivors beyond acute cancer treatment into long-term survivorship to address ongoing nutritional issues. It has been demonstrated in other research that increased dietetic follow-up can improve nutritional status and outcomes [502]. Several strategies may facilitate the continuation of nutrition care, including referral to community dietitians and considering domiciliary or remote follow-up. However, it is important to note that the availability of guidelines for the nutrition care process, referral pathways, and access to community nutrition services is crucial for ensuring the continuation of care [503]. Thus, the standard nutrition care process in Ireland needs to be evaluated to identify current gaps and practical strategies for expanded survivorship care. Also, given the severe staffing crisis in dietetic oncology in Ireland, increased investment in dietetic services is required to provide timely, comprehensive care to cancer survivors [246].

8.4.3 Expanding the Use of e-Health in Nutrition Care Delivery

The application of e-health in delivering nutrition care is suggested to have the potential to overcome several barriers to delivering nutrition care, such as time and resource restraints. It could improve accessibility and continuation of care. As demonstrated in this thesis, nutrition interventions can be effectively delivered remotely or in a hybrid model. Indeed, the learnings from the feasibility study have led to the adopting of a hybrid delivery approach for future rehabilitation programmes delivered by the Exercise Oncology Research Group. Furthermore, assessment and evaluation tools can be incorporated into electronic patient records as this technology expands across Irish hospitals, allowing for easier data collection and evaluation. As a profession, dietitians should seek to embrace technology as a way to enhance practice and better monitor outcomes, for example integrating tools such as Foodbook24 into digitally recorded recalls would allow for efficient tracking of dietary quality across dietetic visits and identify areas for intervention.

8.4.4 Innovative Methods for Effective and Personalised Nutrition Education in UGI Cancer

Digital resources such as web based information can empower patients to make dietary choices and manage their cancer related symptoms [504, 505]. However, in this thesis, UGI cancer survivors and their carers reported a lack of diverse educational resources and tools for delivering nutrition information. Based on these findings, the development and implementation of innovative educational tools to improve patient engagement and the effectiveness of dietary education is recommended. Previous studies

have indicated that educational videos are flexible, accessible tools for cancer patients that can enhance their knowledge of overall health during cancer treatment and empower them, especially in resource-constrained settings [506-508].

Therefore, a recommendation of this thesis is to create a comprehensive directory of videos and animations that provide information on treatment, post-treatment changes and possible side effects, and dietary modifications for UGI cancer survivors. These resources should be made widely available through hospital websites, as well as platforms managed by the Irish Cancer Society, and the Oesophageal Cancer Fund. It should be noted that patients' feedback should be sought continuously to ensure the content remains relevant and meets the evolving needs of UGI cancer survivors.

8.4.5 Personalised Nutrition and Survivorship Care

Personalising nutrition and survivorship care is recommended to effectively address survivors' challenges post cancer treatment. The findings of this thesis demonstrate that UGI cancer survivors often are provided with general dietary advice and report a lack of a personalised nutrition care plan. It is a recommendation from this research to integrate patient-reported outcome (PROs) into nutrition assessments, to tailor the care plan to survivors' individual needs. Incorporating PRO measures can facilitate personalised care and reduce the burden on healthcare professionals and should be incorporated into clinical practice as a standard [509]. Several studies have shown that PROs more accurately capture patient symptoms compared to physician's assessment [510]. In addition, previous studies demonstrated that incorporating PROs with predefined thresholds for intervention in clinical practice leads to significant improvements in symptom management, survival and HRQOL [511-

514]. This could be attributed to the early and personalised response to patient symptoms, which helps prevent negative downstream consequences [512]. Thus, integration of UGI cancer-specific PROs such as GI symptoms, appetite, dietary intake, swallowing difficulty, weight loss, eating restrictions, and food aversions, into routine UGI cancer survivorship care, is recommended for timely and personalised nutrition and survivorship care [514-516].

8.4.6 Providing Practical Support for Cancer Survivors and Caregivers

A key finding from this thesis was that both UGI survivors and their carers require practical support. We found that the availability of assistance with meal preparation can significantly impact patients' ability to adhere to dietary recommendations. Therefore, it is a recommendation of this thesis that during nutritional assessments, clinicians should evaluate the level of support available to each patient. Where necessary, referrals should be made to services such as meal delivery programmes, shopping assistance, and home help. Integrating these support services into standard care can enhance compliance with dietary advice and improve overall patient outcomes.

Given the crucial role of caregivers in supporting survivors from the time of diagnosis and the challenges they face in adjusting to their new roles and responsibilities, it is essential to integrate caregiver-targeted interventions into the standard cancer care pathway [517]. These interventions should aim to enhance caregivers' well-being, increase their preparedness, and ultimately improve the quality of care for survivors. It is a recommendation of this thesis that education sessions for caregivers be developed and implemented as part of this approach. These sessions would provide

caregivers with a deeper understanding of the effects of cancer treatment on survivors, equip them to support survivors in making necessary dietary adjustments post-surgery, and offer valuable social support by connecting them with other caregivers facing similar challenges. Evidence from previous studies has shown that providing caregivers with similar psychoeducational and skills training interventions can reduce caregiver burden, enhance their coping abilities, and boost their self-efficacy [325]

Additionally, the findings of this thesis highlight a gap in providing timely information about available support for caregivers. To address this, it is recommended, at a minimum, to provide survivors and their caregivers with a comprehensive list of available support services at the time of diagnosis. A longer-term goal would be the establishment of an UGI cancer portal by, for example, the HSE or Irish Cancer Society, which would act as the central resource for UGI cancer survivors and their families. It could house education and details of supports available whilst also hosting forums and peer interaction, a feature that many participants discussed in the qualitative study. This proactive approach would ensure that both patients and their caregivers have access to the necessary support throughout their cancer journey.

8.4.7 Developing a Core Outcome Set for Multidisciplinary Rehabilitation in UGI Cancer Survivors

A key finding of the systematic review in this thesis that examined effectiveness of multidisciplinary rehabilitation interventions in UGI cancer survivors, was that there was considerable variation in outcome measures in existing studies, making it difficult to assess and compare the effectiveness of these

interventions. While a core outcome set has been developed to assess the clinical effectiveness of trials in oesophageal cancer, it primarily focuses on surgical outcomes such as survival, inoperability, and post-operative complications [518]. Although the core outcome set includes nutritional complications, it lacks clear definitions of these outcomes and does not provide recommendations for validated tools to assess them [518]. To address this, it is a recommendation of this thesis that a standardised core outcome set is developed to evaluate the clinical effectiveness of multidisciplinary care programmes in UGI cancer. This will enable a meaningful comparison across different care models and ensure that future research can better inform best clinical practice and improve patient care.

8.4.8 Specialised Training for Dietitians

As research in cancer survivorship continues to advance our understanding of nutritional management for cancer survivors, it is crucial that healthcare professionals, particularly dietitians, engage in ongoing professional development and training focused on the latest evidence in nutrition in oncology. It is recommended that the Irish Nutrition and Dietetic Institute (INDI) consider developing specialised courses and continuing professional development opportunities for nutrition in UGI cancers. These programmes would help dietitians to translate evidence into practice in a time-efficient manner, ultimately enhancing the quality of nutrition care provided to UGI cancer survivors.

8.5 Limitations

COVID-19 significantly impacted this thesis as this PhD commenced in March 2020 when the pandemic was first declared.

This thesis was due to examine nutritional outcomes in a randomised controlled trial of a multidisciplinary rehabilitation programme in UGI cancers (ReStOre II study), which was delayed by COVID-19 and ultimately withdrawn from this thesis plan. Also, limited access to clinical settings during the pandemic impacted the design and recruitment of additional studies included in the present thesis. These complications subsequently reduced the study sample size, which may impact the generalisation of findings for all UGI cancer survivors.

Poor prognosis and ongoing cancer-related complications might limit the engagement of certain groups of survivors in research studies and result in non-response [190]. In the present thesis, cancer survivors who are at an early-stage post diagnosis were underrepresented, and the findings may not reflect nutrition care challenges in the acute postoperative phase of survivorship. Whilst in the qualitative study (Chapter 4), efforts were made to obtain data on challenges that UGI cancer survivors faced during all stages of their cancer journey, including the acute recovery phase, to reduce this limitation, recall bias may impact the results in terms of reflecting on earlier stages of recovery. Thus, the findings presented in this thesis should be further investigated in future studies with larger sample sizes and representation from all stages of UGI survivorship.

Despite promising results regarding improved nutritional outcomes following the ReStOre@Home intervention, this feasibility study was not powered to detect statistically significant changes. Further randomised controlled trials are warranted to examine the effectiveness of remote delivery of this rehabilitation programme.

Chapter 5, the inclusion of only disease-free survivors who enrolled in a clinical trial examining the effects of a multidisciplinary rehabilitation, may limit the generalisability of findings to the broader

population of UGI cancer survivors and different stages of survivorship.

8.6 Suggestions for Future Research

8.6.1 Evaluating Screen-and-Triage Approaches for Addressing Cancer-Related Malnutrition in UGI Cancer Survivors

The findings of this thesis highlight the persistence of malnutrition as an ongoing, long-term issue among UGI cancer survivors in Ireland. Understanding the scale of malnutrition and identifying patients with the greatest need are critical steps in recognising and managing cancer-related malnutrition [403]. Thus, future research should evaluate strategies for preventing and identifying malnutrition and facilitating access to nutrition care [403]. A screen and triage approach that refers UGI cancer survivors to suitable survivorship care services is suggested to support them in meeting their survivorship care needs [519]. However, further study is required to determine the effectiveness of this model of care.

8.6.2 Exploring Patient and Public Involvement Approaches to Developing Survivorship Care Programmes

The findings of this thesis highlight several unmet nutrition care needs of UGI cancer survivors and their caregivers. Considering survivors' care needs and their personal preferences is recommended for developing patient centred survivorship care. As family members and caregivers play an essential role in survivorship, their views and unmet needs also should be considered in planning survivorship programmes.

To deliver a truly patient-centred care, it is essential to listen to and understand patients' priorities and concerns [520]. A patient and public involvement approach to the development of services is suggested to address this [521]. Going a step further, establishing an experience-based co-design approach to cancer care is recommended to enable patients and healthcare professionals to share their experiences, collaboratively identify gaps and priorities for improvement, and work together to implement these changes [522]. It is a recommendation of this thesis that future research incorporate patient and public involvement and experience-based co-design approaches into their methodologies to improve the relevance and quality of research aimed to develop and examine survivorship care programmes.

8.6.3 Further Evaluating Remote Delivery of Nutrition Interventions for UGI Cancer Survivors

The ReStOre@Home study demonstrated the feasibility of delivering multidisciplinary rehabilitation via telehealth for UGI cancer survivors. The findings have in part informed the delivery of the ReStOre II trial, which is now delivered in a hybrid format. With a larger sample size, the ReStOre II trial allows for a more comprehensive evaluation of the ReStOre protocol, particularly its impact on nutritional outcomes.

While the present thesis has demonstrated promising results regarding the practicality and acceptability of remotely delivered nutrition interventions for UGI cancer survivors, further investigation is necessary before it can be considered for broader implementation. Specifically, there is a need to explore both participant and dietitian experiences in greater detail to ensure that this approach is practical, effective and well-received.

Additionally, the comparative effectiveness of remote versus in-person nutrition interventions remains an open question. Thus, it is a recommendation that future research include randomised controlled trials to compare the effectiveness of remote versus in-person nutrition interventions for UGI cancer survivors. These studies will be essential for establishing whether remote interventions can match or surpass the effectiveness of traditional in-person care, ultimately informing future nutrition care in this cohort of cancer survivors.

8.6.4 Establishing Longitudinal Studies in UGI Cancer Survivorship

Given the increasing number of long-term UGI cancer survivors, future studies should prioritise long-term follow-up to evaluate not only survival but also complications, recovery, and quality of life over time. There is a significant lack of longitudinal data in Ireland on long-term recovery and complications in UGI cancer survivors, which is crucial for understanding their evolving needs at different stages of cancer and planning effective survivorship care. To address this gap, it is a recommendation of this thesis to establish a prospective study to track recovery, complications, and overall well-being of UGI cancer survivors in the long-term. However, the potential challenges, particularly regarding cost and feasibility are acknowledged.

To mitigate these challenges, leveraging the increasing use of electronic health records to streamline the collection and analysis of longitudinal data is recommended. Also, integration of digital health tools such as FoodBook24 into electronic health records, can facilitate data collection and analysis and should be considered in both research and clinical practice. This approach would provide a

more comprehensive understanding of survivors' health trajectories, helping to map their long-term needs more effectively and ultimately improving care and outcomes for UGI cancer survivors.

8.7 Conclusion

In conclusion, the quantitative and qualitative findings of this thesis highlight the long-term adverse effects of cancer treatment on UGI cancer survivors. Suboptimal nutritional intake, poor diet quality, gastrointestinal symptoms, psychological distress, and reduced quality of life were prevalent in this cohort of cancer survivors. Additionally, the persistence of malnutrition despite relatively healthy BMI measurements in UGI cancer survivors, emphasises the importance of applying validated malnutrition screening tools that extend beyond BMI, enabling early detection and effective management of malnutrition.

Several unmet nutritional and supportive care needs were identified, underscoring the necessity of continued, tailored survivorship care for UGI cancer survivors. These findings suggested that UGI cancer survivors face complex, multifaceted challenges across the cancer continuum, warranting further research to explore specific needs at different stages of survivorship.

Multidisciplinary care programmes are recommended to address the complex survivorship needs in UGI cancers, however the effectiveness and optimal design of these programmes requires further investigation. Finally, this thesis demonstrated the potential of e-health in delivering nutrition interventions within multidisciplinary survivorship care, which can overcome barriers such as geographic isolation and resource limitations.

To improve outcomes in UGI cancer survivors, it is imperative that patient-focused, multidisciplinary interventions are designed, delivered and evaluated. This thesis has provided critical insight into what essential nutritional care needs these programmes should address, how they could be delivered and the key outcomes that should be measured.

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Appendices

Appendix I Ethical approval letters

Appendix- Ethical approvals



Project ID: 0247

Approval Date: 9 September 2021

Submission Number: 154

Submission Title: Cancer Survivors' nutrition and supportive care needs

Submission Date: 13/05/2021 15:23

Dear Mrs Sadeghi,

On behalf of the Chair and members of the SJH/TUHL Joint Research Ethics Committee I wish to inform you that your study has received **FULL APPROVAL**. Your study can now proceed.

The following comments were made:

Title	Comment
3.2.1 What is the anticipated start date of this study?	It is understood that the anticipated start date will be amended.
3.3.4 How many participants are to be included/recruited in total from SJH?	Please confirm where the remaining 46 participants will be recruited from.
3.5.2.1 Please upload the Participant Information Leaflet	PIL (section 4): The below should read "The third section..." "The second section contains questions about your health and symptoms."
5.1.18 Survey/Questionnaire	Please align non-US spelling of "oesophagus" in printed documents (where possible to change).
5.1.24 Please upload any other relevant documents	PIL: Please rewrite the below section of the PIL: 1) Researchers have no evidence of unmet nutritional need (e.g. "...may be beneficial in learning more about cancer survivors' nutritional needs...") 2) Please briefly state why research is being undertaken. 3) State that the study may (not will) improve service/inform design of care. Section 5. Possible benefits and risks of taking part
5.1.24 Please upload any other relevant documents	Please correct errors in the advertisement poster to the following: "Volunteers are needed for..."

"Diagnosed"
"Oesophagus" (non-US spelling)
"Pancreatic"
"...if you are interested..."

The following documents were reviewed and approved:

Document Type	File Name	Date	Version
Participant Information Leaflet	PIL, 05.05.2021, online version	05/05/2021	Version I
Default	PIL, 05.05.2021, online version	05/05/2021	Version I
Default	PIL, 05.05.2021, Paper based version	05/05/2021	Version I
Default	Adversisment poster, Virtual, 05.05.2021	05/05/2021	Version I
Default	Adversisment poster, Clinics, 05.05.2021	05/05/2021	Version I
Principle Investigator C.V.	Fatemeh Sadeghi's CV 2021	05/05/2021	Version I
Survey/Questionnaire	Online questionnaire	06/05/2021	Version I
Survey/Questionnaire	Paper based survey	13/05/2021	Version I
Default	Animation Clip Link, Advertisement	13/05/2021	Version I

Please note that ethical approval for this study is only active under the following conditions:

1. Applicants must submit an annual report for ongoing projects.
2. Applicants must submit an end of study declaration/end of study report upon completion of the study.
3. All adverse events must be reported to the JREC.
4. All changes (minor and substantial) to documentation/study must be submitted to the JREC using the amendment request form and the changes must be tracked/highlighted clearly. Approval from the JREC is required before implementation of the changes.

It is the responsibility of the researcher/research team to ensure all aspects of the study are executed in compliance with the General Data Protection regulation (GDPR), Health Research Regulations and the Data Protection Act 2018.

Yours sincerely,

Ms Chita Murray

Research Ethics & Clinical Trials Manager,

SJH/TUH Joint Research Ethics Committee

The SJH/TUH Joint Research and Ethics Committee operates in compliance with and is constituted in accordance with the European Communities (Clinical Trials on Medicinal Products for Human Use) Regulations 2004 & ICH GCP guidelines.



**Tallaght
University
Hospital**
An Academic Partner of Trinity College Dublin

Ospidéal
Ollscoile
Thamhlachta



Research Office

Project ID: 0247

Dear Mrs Fatemeh Sadeghi,

Approval Date: 3 February 2022

Submission Number: 604

Submission Title: Cancer Survivors' nutrition and supportive care needs

Submission Date: 06 Jan.2022 11:55

Dear Mrs Sadeghi,

On behalf of the Chair and members of the SJH/TUHI Joint Research Ethics Committee I wish to inform you that your study has received **FULL APPROVAL**. Your study can now proceed.

The following documents were reviewed and approved:

Document Type	File Name	Date	Version
Amended Documents	0247_Participant_Information_I_caflet - 04.01.2022	04 Jan.2022	3
Participant Information Leaflet	0247_Participant_Information_I_caflet - 04.01.2022	04 Jan.2022	3

Please note that ethical approval for this study is only active under the following conditions:

- 1. Applicants must submit an annual report for ongoing projects.*
- 2. Applicants must submit an end of study declaration/end of study report upon completion of the study.*
- 3. All adverse events must be reported to the JREC.*
- 4. All changes (minor and substantial) to documentation/study must be submitted to the JREC using the amendment request form and the changes must be tracked/highlighted clearly. Approval from the JREC is required before implementation of the changes.*

It is the responsibility of the researcher/research team to ensure all aspects of the study are executed in compliance with the General Data Protection regulation (GDPR), Health Research Regulations and the Data Protection Act 2018.

Yours sincerely,

Dr Sadhbh O'Neill

Research Ethics & Clinical Trials Manager,

SJH/TUHI Joint Research Ethics Committee

The SJH/TUHI Joint Research and Ethics Committee operates in compliance with and is constituted in accordance with the European Communities (Clinical Trials on Medicinal Products for Human Use) Regulations 2004 & ICH GCP guidelines.



Coláiste na Tríonóide, Baile Átha Cliath
Trinity College Dublin
Ollscoil Átha Cliath | The University of Dublin

Fatemeh Sadeghi
Discipline of Physiotherapy, Trinity Centre for
Health Sciences, St James's Hospital,
Dublin 8.

28th March 2022

Ref: 211101
Title of Study: The nutritional challenges and nutrition care needs of upper GI cancer survivors in Ireland

Dear Fatemeh,

Further to a meeting of the Faculty of Health Sciences Ethics Committee held in March 2022. We are pleased to inform you that the above project has ethical approval to proceed.

This study has been ethically approved. We would advise you to seek review and comments on your DPIA from the DPO if required prior to study commencement'

As a researcher you must ensure that you comply with other relevant regulations, including DATA PROTECTION and HEALTH AND SAFETY.

Yours sincerely,

Prof. Jacintha O'Sullivan Chairperson
Faculty Research Ethics Committee

Dámh na nEolaithe Sláinte
Foirgneamh na Ceimice,
Coláiste na Tríonóide,
Ollscoil Átha Cliath,
Baile Átha Cliath 2, Éire.

Faculty of Health Sciences
Chemistry Building,
Trinity College Dublin,
The University of Dublin,
Dublin 2, Ireland.

www.healthsciences.tcd.ie



Coláiste na Tríonóide, Baile Átha Cliath
Trinity College Dublin
Ollscoil Átha Cliath | The University of Dublin

Fatemeh Sadeghi, Discipline of
Physiotherapy,
Trinity Centre for Health Sciences, St James's
Hospital,
Dublin 8.

25th October 2022

Ref: 211101

Title of Study: The nutritional challenges and nutrition care needs of upper GI cancer survivors in Ireland

Dear Fatemeh,

Further to a meeting of the Faculty of Health Sciences Ethics Committee held in October 2022, we are pleased to inform you that the above project (as amended with the following changes) has ethical approval to proceed.

Please give specific details of the requested amendment(s):

We would like to request extending our study to the 20th of December 2023, to be able to collect the required data. Also, we would like to submit a minor revision in the PIL (adding an additional email address: fsadeghi@tcd.ie) as well

As a researcher you must ensure that you comply with other relevant regulations, including DATA PROTECTION and HEALTH AND SAFETY.

Yours sincerely,

Prof. Jacintha O'Sullivan
Chairperson Faculty Research Ethics Committee

Dámh na nEolaíochtaí Sláinte
Foirgneamh na Ceimice,
Coláiste na Tríonóide,
Ollscoil Átha Cliath,
Baile Átha Cliath 2, Éire.

Faculty of Health Sciences
Chemistry Building,
Trinity College Dublin,
The University of Dublin,
Dublin 2, Ireland.

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Appendix II Study PIL and poster (Chapter 3)



Trinity College Dublin
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The University of Dublin

PARTICIPANT INFORMATION LEAFLET

Cancer Survivors' nutrition care needs

Principal investigator's name: Ms Fatemeh Sadeghi

Supervisors: Professor Juliette Hussey
Dr Suzanne Doyle

Consultant co-investigator's name: Dr Emer Guinan
Dr Linda O'Neill

Data Controller's/joint Controller's name/ Contact Details:
Trinity College Dublin/ St James's University Hospital

Data Processors Name/ Contact Details Not applicable

Data Handler's Name/ Contact Details: Ms Fatemeh Sadeghi
Phone number: 0896068686
Email: sadeghif@tcd.ie

Data Protection Officer's Name/ Contact Details:
Data Protection Officer, St James Hospital, dataprotection@stjames.ie

If you have any questions you or would like more information, please contact:

Ms Fatemeh Sadeghi
Research Assistant
Discipline of Physiotherapy
Trinity Centre for Health Sciences
St James's Hospital
Dublin 8
Phone: 0896068686 Email: sadeghif@tcd.ie

We would like to invite you to complete this survey which has been developed by the Exercise Oncology Research group at Trinity College Dublin. This study aims to identify cancer survivors' nutrition care needs. The results of this study will expand our knowledge and awareness of cancer survivors' nutrition care needs and the challenges they face regarding their diet and food intake. This information may help to develop effective nutritional care plans to support cancer survivors.

Before you decide whether or not you wish to take part, you should read the information provided below carefully and, if you wish, discuss it with your family, friends or GP (doctor). Take time to ask questions – don't feel rushed and don't feel under pressure to make a quick decision.

You should clearly understand the risks and benefits of taking part in this study so that you can make a decision that is right for you. This process is known as 'Informed Consent'.

You don't have to take part in this study. If you decide not to take part, it won't affect your future medical care.

You can change your mind about taking part in the study any time you like. Even if the study has started, you can still opt-out. You don't have to give us a reason. If you do opt-out, rest assured it won't affect the quality of treatment you get in the future. If you wish to opt-out, please contact Ms Fatemeh Sadeghi (Research Assistant, Discipline of Physiotherapy, Trinity Centre for Health Sciences, St James's Hospital, Dublin 8, sadeghif@tcd.ie, 0896068686) who will be able to organise this for you.

PART 1 – THE STUDY

Why is this study being done?

There is limited data on the unmet needs of cancer survivors. The purpose of this study is to evaluate patients' nutritional status, their unmet nutrition care needs, and experiences with nutrition care in Ireland. This information will expand our knowledge and awareness of cancer survivors' nutrition care needs and challenges they face regarding their diet and food intake. The results of this study may help to develop effective nutritional care plans to support cancer survivors.

Why am I being asked to take part?

As a cancer survivor, you have been invited to take part in this survey. We are aiming to involve over 200 cancer survivors in this study who have been diagnosed with gastrointestinal cancers, namely cancer of the oesophagus, stomach, pancreas, and liver.

Do I have to take part? What happens if I say no? Can I withdraw?

Participation in this study is completely **voluntary** and decision not to consent will have **no adverse consequences or affect future medical treatment**.

Consent can be withdrawn at any time. Please note as the survey is anonymous, once completed you will not be able to request access to, or deletion of, your survey results.

How will the study be carried out?

The present study will be carried out by completing an anonymous survey. This survey has 3 main sections and should take no longer than 15 minutes to complete.

The three main sections:

- The first section asks some brief questions about your background and type/s of cancer you have been diagnosed with and cancer treatment you have undergone.
- In the second section, we will ask about your nutritional status, your unmet needs, and your experiences with dietetic services.
- The third section contains questions about your health and symptoms.

There are two additional sections which are optional and contain questions about your mental health and wellbeing and gastrointestinal symptoms that you experienced during the past week.

What will happen to me if I agree to take part?

If you agree to take part in this research, you will be asked to complete the questionnaires that have been posted to you. This survey has 3 main sections and should take no longer than 15 minutes to complete. You will be asked to return the completed survey by post using the stamped addressed envelope (SAE) which has been posted to you with the questionnaires.

Are there any benefits to me or others if I take part in the study?

Although you may not benefit directly from participating in this research, the results of this study may be beneficial in learning more about cancer survivors' unmet nutritional needs, complications, and challenges in Ireland. This information may

help inform the design of effective and accessible care plans to minimize these complications.

Are there any risks to me or others if I take part in the study?

There is no risk related to participation in this study.

Will I be told the outcome of the study? Will I be told the results of any tests or investigations performed as part of this study that relate to me?

As this survey is anonymous, your data will not be identifiable, which prevents us from providing individual results to participants. But the result of this study will be published in peer-reviewed journals and reported in relevant scientific conferences.

PART 2 – DATA PROTECTION

What information about me (personal data) will be used as part of this study? Will my medical records be accessed?

This survey is completely anonymous, no personal and identifiable data will be collected or used, and your medical records will not be accessed.

PART 3 – COSTS, FUNDING & APPROVAL

Who is funding this study? Will the results study be used for commercial purposes?

This study is part of a larger project in rehabilitation funded by the Health Research Board (Grant no. HRB-DIFA-2018-009) and results will not be used for commercial purposes.

Has this study been approved by a research ethics committee?

Ethical approval has been sought from St James Hospital/ Tallaght University Hospital (SJH/TUH) Joint Research Ethics Committee, Email: ResearchEthics@tuh.ie. (Project ID: 0247, Approval date: 9 September 2021)

PART 5 – FURTHER INFORMATION

Where can I get further information?

If you have any further questions about the study or if you want to opt-out of the study, you can rest assured it won't affect the quality of treatment you get in the future.

If you need any further information now or at any time in the future, please contact:

Name: Ms Fatemeh Sadeghi

Address: Discipline of Physiotherapy, Trinity Centre for Health Sciences, St James's Hospital, Dublin 8

Phone number: 0896068686, Email: sadeghif@tcd.ie

What happens if I wish to make a complaint?

Complaints regarding this study should be directed to Professor Juliette Hussey (Email: jmhussey@tcd.ie). Complaints regarding data protection should be directed to the Data Protection Officer at St James's Hospital (dataprotection@stjames.ie).



Trinity College Dublin
Coláiste na Tríonóide, Baile Átha Cliath
The University of Dublin



VOLUNTEERS ARE NEEDED FOR AN ONLINE SURVEY



WHO IS BEING ASKED TO TAKE PART?

If you've been diagnosed with oesophageal, gastric, hepatic or pancreatic cancer, we need your help with an online survey.



WHAT IS THIS STUDY ABOUT?

We have developed an online survey to assess cancer survivors nutritional and supportive care needs. This study will expand our knowledge and awareness of cancer survivors' requirements and challenges they face, which may help to develop and deliver effective supportive care plans for them.



WHAT WILL HAPPEN TO ME IF I DECIDE TO TAKE PART?

If you are interested in taking part in the research, you will be asked to complete a survey. This online survey has 3 main sections which would take about 15 minutes to complete.



You can access the survey by clicking the provided link in the caption.



Please contact us if you need more information. Email: sadeghif@tcd.ie, Telephone: 0896068686

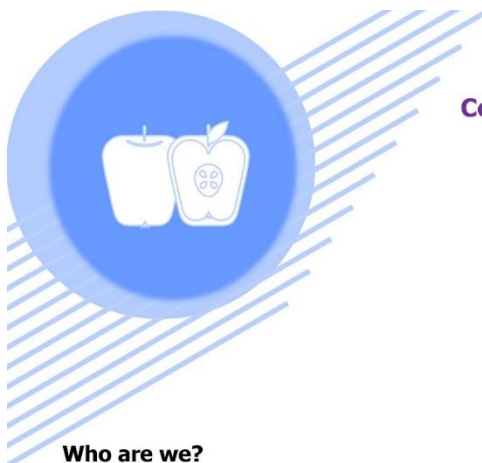
**The Nutritional Challenges
And Nutrition Care Needs
Of Upper GI Cancer
Survivors In Ireland**

We would like to invite you to participate in the present study which aims to identify upper gastrointestinal cancer survivors' nutrition care needs. The results of this study will expand our knowledge and awareness of cancer survivors' nutrition care needs and challenges they face regarding their diet and food intake. This information will help to develop effective nutritional care plans to support cancer survivors.

- ❖ Please take some time to read the following information carefully before proceeding to the survey.
- ❖ If you have any questions or would like more information, please contact:

Ms. Fatemeh Sadeghi
PhD Candidate
Discipline of Physiotherapy
Trinity Centre for Health Sciences
St James's Hospital
Dublin 8

0896068686 sadeghif@tcd.ie



Contents

In this leaflet you can find information about

- ✓ **Details of present study**
- ✓ **Data Protection**
- ✓ **Funding and Approval**
- ✓ **Future Research**
- ✓ **Further Information**

Who are we?

We are the Trinity Exercise Oncology Research Group. We are a multidisciplinary group investigating the role of exercise and nutrition in cancer care.

Why are we doing this study?

The purpose of this study is to evaluate cancer survivors' nutrition care needs, their nutritional challenges and their experiences with nutrition care in Ireland.

Why are you being asked to take part?

As a cancer survivor or family member you have been invited to take part in this study. We are inviting volunteers who have been diagnosed with gastrointestinal cancers, namely cancer of the oesophagus, stomach, pancreas, and liver in any stage of their treatment or their carers to take part in this study.

What will happen if you decide to take part?

If you agree to take part in this research, you will be asked to input your contact details in the provided link or contact the researchers to express your interest in the present study. The researchers will contact you to hold one focus group interview which will last about an hour, with you as a survivor/carer to discuss your experience and accessibility of dietetic care, your unmet needs, and nutritional challenges you have faced. The interviews will be held in the Trinity Centre for Health Sciences or remotely (Videocall/Phone call) based on your preference. Alternatively if you were not available for the focus group interview, a 20-30 minutes individual interview (in person/by phone/ video call) can be organised instead.



Possible benefits and risks of taking part

Although you may not benefit directly from participating in this research, the results of this study may be beneficial in discovering cancer survivors' unmet nutritional needs, complications, and challenges in Ireland. This information may help to inform the design of effective and accessible care plans to minimize these complications. This interview will ask you to reflect on your journey through cancer treatment and some of the challenges that you may have faced and we recognise that this may be distressing for some people. The research team have lots of experience in this area and the interview will be conducted in a manner that aims to reduce any distress. If however you wish to skip any questions, pause or stop the interview at any stage you are free to do so.

Do I have to take part? Can I withdraw

Participation in this study is entirely voluntary. You can change your mind about taking part in the study and opt out at any time before data analysis and publication of the anonymised study results. If you wish to opt out, you will be asked to fill in a withdrawal form. If you wish, you can ask for your data stored to be destroyed.

What information about me (personal data) will be used as part of this study? Who will access and use my personal data as part of this study?

Your name and contact details will be collected to organise the interview. Other personal data such as age, diagnosis and treatment will be collected as well.. Your data will only be accessible by the Exercise Oncology Research Group and all personal and identifiable data will be safely destroyed after retention period of 7 years.

Will my personal data be kept confidential?

Your privacy is important to us. We take many steps to make sure that we protect your confidentiality and keep your data safe. All personal and identifiable data will be coded and stored in password protected files and computers and in access restricted office.



What is the lawful basis to use my personal data?

We hope that this health research will improve care for those who have cancer. Our lawful basis is scientific research in the public interest. (6,1, e and 9, 2, j of the GDPR).We will also ask for patients' explicit consent as an extra measure for any health research.

What are my rights?

You are entitled to request:

- The right to access your personal information and receive a copy of it
- The right to restrict or object to the use of your personal information
- The right to object to any further use of the personal information we hold about you
- The right to have inaccurate information about you corrected or deleted
- The right to request deletion of your personal information

unless the request would make it impossible or very difficult to conduct the research.

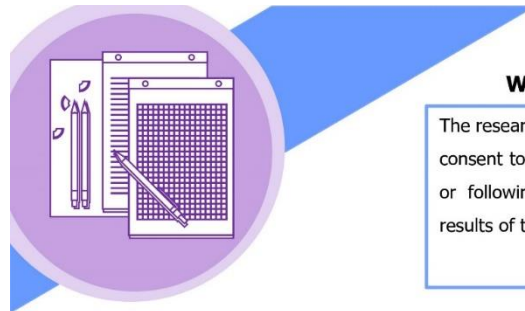
You can exercise these rights by contacting us [Ms. Fatemeh Sadeghi, Sadeghif@tcd.ie] or the Trinity College Data Protection Officer, Secretary's Office, Trinity College Dublin, Dublin 2, Ireland. Email: dataprotection@tcd.ie. Website: www.tcd.ie/privacy.

Ethical approval

Ethical approval has been sought from Trinity Faculty of Health Sciences Research Ethics Committee. Ethics approval ID: 211101

Funding

This study is part of a larger project in rehabilitation funded by the Health Research Board and results will not be used for commercial purposes.



Will I be contacted again?

The research team will only contact you again if you consent to be contacted for future research studies or following your request to be informed about results of the study or publications.

Further Information

If you have any concerns or questions, you can contact:

- Ms. Fatemeh Sadeghi, Email: Sadeghif@tcd.ie
- Professor Juliette Hussey, Email: jmhussey@tcd.ie
- Data Protection Officer, Trinity College Dublin: Data Protection Officer, Secretary's Office, Trinity College Dublin, Dublin 2, Ireland. Email: dataprotection@tcd.ie.
Website: www.tcd.ie/privacy.

Under GDPR, if you are not satisfied with how we use personal information about you, you have the right to lodge a complaint with the Office of the Data Protection Commission, 21 Fitzwilliam Square South, Dublin 2, Ireland. Website: www.dataprotection.ie.

**Thank you for taking the time to
read this information leaflet.**

**If you would like to take part in
this study, please submit your
interest and contact details here**

OR

You can contact us directly

Ms. Fatemeh Sadeghi
PhD Candidate
Exercise Oncology Research Group
Trinity Centre for Health Sciences
Dublin 8

Telephone: 0896068686 Email: sadeghif@tcd.ie

WE NEED YOUR HELP



We are looking for

Adults over 18 years who:

- Have current or previous diagnosis of oesophageal or stomach cancer
- Or
- Their family member have a current or previous diagnosis of oesophageal or stomach cancer

**Please Contact us if
you would like to
participate:**

Email:
sadeghif@ted.ie

Phone:
0896068686

What it will involve?

Participation in telephone or in person interviews to discuss your experience and access to dietetic care, unmet needs and any nutritional challenges you have faced during and after your cancer treatment.

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Appendix IV Short Physical Performance Battery

1. Balance Tests

A. Side-by-Side Stand

- Held for 10 sec ☐ 1 point
 Not held for 10 sec ☐ 0 points
 Not attempted ☐ 0 points

If 0 points, end Balance Tests

Number of seconds held if less than 10 sec:
 _____._____ Sec

If participant did not attempt test or failed, circle why:

Tried but unable	1
Participant could not hold position unassisted	2
Not attempted, you felt unsafe	3
Not attempted, participant felt unsafe	4
Participant unable to understand instructions	5
Other (specify)	6
Participant refused	7

B. Semi-Tandem Stand

- Held for 10 sec ☐ 1 point
 Not held for 10 sec ☐ 0 points
 Not attempted ☐ 0 points

If 0 points, end Balance Tests

Number of seconds held if less than 10 sec:
 _____._____ Sec

If participant did not attempt test or failed, circle why:

Tried but unable	1
Participant could not hold position unassisted	2
Not attempted, you felt unsafe	3
Not attempted, participant felt unsafe	4
Participant unable to understand instructions	5
Other (specify)	6
Participant refused	7

C. Tandem Stand

- Held for 10 sec ☐ 2 points
 Held for 3 to 9.99 sec ☐ 1 point
 Not held for < than 3 sec ☐ 0 points
 Not attempted ☐ 0 points

Number of seconds held if less than 10 sec:
 _____._____ Sec

If participant did not attempt test or failed, circle why:

Tried but unable	1
Participant could not hold position unassisted	2
Not attempted, you felt unsafe	3
Not attempted, participant felt unsafe	4
Participant unable to understand instructions	5
Other (specify)	6
Participant refused	7

D. Total Balance Tests score _____ (sum points)

Comments:

2. Gait Speed Test Scoring

Length of walk test course:

Four metres ☐

A. Time for First Gait Speed Test (sec)

1. Time for 4 metres _____._____ sec

2. If participant did not attempt test or failed, circle why:

Tried but unable	1
Participant could not walk unassisted	2
Not attempted, you felt unsafe	3
Not attempted, participant felt unsafe	4
Participant unable to understand instructions	5

Other (Specify) _____ 6
 Participant refused _____ 7
 Complete score sheet and go to chair test

3. Aids for first walk..... None ☐ Walking Stick ☐ Other ☐
 Comments:

B. Time for Second Gait Speed Test (sec)

1. Time for 4 metres _____ sec
2. If participant did not attempt test or failed, circle why:

Tried but unable	1
Participant could not walk unassisted	2
Not attempted, you felt unsafe	3
Not attempted, participant felt unsafe	4
Participant unable to understand instructions	5
Other (Specify) _____	6
Participant refused	7
- Complete score sheet and go to chair test
3. Aids for first walk..... None ☐ Walking Stick ☐ Other ☐
 What is the time for the faster of the two walks?
 Record the shorter of the two times _____ sec
 [If only 1 walk done, record that time] _____ sec

If the participant was unable to do the walk: ☐ 0 points

For 4 metre walk:

If time > 8.70 sec	☐ 1 point
If time is 6.21-8.70 sec	☐ 2 points
If time is 4.82-6.20 sec	☐ 3 points
If time is < 4.82 sec	☐ 4 points

3. Chair Stand Test

Single Chair Stand Test

	Yes	No	
A. Safe to stand without help	☐	☐	
B. Results:			
Participant stood without using arms	☐		→ Go to Repeated Chair Stand Test
Participant used arms to stand	☐		→ End test; score as 0 points
Test not completed	☐		→ End test; score as 0 points
C. If participant did not attempt test or failed, circle why:			
Tried but unable	1		
Participant could not stand unassisted	2		
Not attempted, you felt unsafe	3		
Not attempted, participant felt unsafe	4		
Participant unable to understand instructions	5		
Other (Specify)	6		
Participant refused	7		

Repeated Chair Stand Test

	Yes	No
A. Safe to stand five times	☐	☐
B. If five stands done successfully, record time in seconds. Time to complete five stands _____ sec		
C. If participant did not attempt test or failed, circle why:		
Tried but unable	1	
Participant could not stand unassisted	2	
Not attempted, you felt unsafe	3	
Not attempted, participant felt unsafe	4	
Participant unable to understand instructions	5	
Other (Specify)	6	
Participant refused	7	

Scoring the Repeated Chair Test

Unable to complete 5 chair stands or completes in > 60 sec:	☐ 0 points
If chair stand time is >16.70 sec:	☐ 1 point
If chair stand time 13.70 -16.69 sec:	☐ 2 points
If chair stand time is 11.20 -13.69 sec:	☐ 3 points
If chair stand time is <11.19 sec:	☐ 4 points

Scoring for Complete Short Physical Performance Battery

Test Scores	
Total Balance Test Score	_____ points
Gait Speed Test Score	_____ points
Chair Stand Test Score	_____ points
Total Score	_____ points (<i>sum of above points</i>)

Appendix V Licence Agreement for Gastrointestinal Symptom Rating Scale (GSRS)

Licence Agreement for Gastrointestinal Symptom Rating Scale (GSRS)

This Licence Agreement (the "**Agreement**") is made effective as of the last date written below (the "**Effective Date**") by and between

- (1) ASTRAZENECA AB, a company incorporated in Sweden under no. 556011-7482 with offices at SE-431 83 Mölndal, Sweden ("**AstraZeneca**"); and
- (2) Fatemeh Sadeghi, incorporated in Dublin, Ireland with offices at Discipline of Physiotherapy, Trinity Centre for Health Sciences, St. James's Hospital, Dublin 8, James's Street, Dublin, Ireland ("**Licensee**").

Recitals

- (A) WHEREAS, AstraZeneca is in the possession of a certain questionnaire known as the Gastrointestinal Symptom Rating Scale (the "GSRS").
- (B) WHEREAS, Licensee wishes to obtain, and AstraZeneca is willing to grant to Licensee, a right to use the GSRS solely for the Study (as defined below) on the terms and conditions set forth below.
- (C) WHEREAS, Licensee wishes to administer the GSRS via paper/electronic.

Agreement

1 Licence

- 1.1 Upon payment of the Licence Fee and for the duration of the Term (as defined below), AstraZeneca grants to Licensee and its affiliates a non-exclusive, non-assignable and non-sublicensable licence (the "**Licence**") to:
 - (a) use the GSRS worldwide in the language(s) set out in Section 1.4 below and in such other languages as agreed between the parties in writing from time to time during the Term, which shall include permission for use (to the extent necessary for the conduct of the Study) by contract research organisations and eCOA vendors engaged by the Licensee and/or its affiliate(s) to conduct the Study;
 - (b) arrange for any other reasonably required translations and validations of the GSRS be made through RWS Life Sciences, done in accordance with the process defined by AstraZeneca, as notified by RWS Life Sciences to the Licensee;
 - (c) submit copies of the GSRS and background materials (including, without limitation, documentation relating to its development, and supporting instructions and algorithms) ("**Associated Materials**") to the relevant regulatory authorities worldwide for evaluation and scientific advice on the GSRS at any time prior to, during or after the Study, as well as to use such Associated Materials for Licensee's own evaluation and review of the GSRS for use in the Study. If there are documents

that AstraZeneca does not wish to share directly with the Licensee, AstraZeneca will submit these directly to the regulatory authorities; and

- (d) keep copies of any Associated Materials and completed copies of the GSRS, together with any other relevant materials (including, without limitation, software and validation materials), and to share the same with its affiliates, contract research organisations, regulatory authorities, ethics committees and other third parties for the purposes of review and analysis of the Study data (including, without limitation, maximising Study validity and ensuring the validity of the interpretation of the Study results), archival purposes and regulatory purposes;

in each case, solely in connection with the Licensee's study, entitled Upper GI Cancer Survivors' Nutrition and Supportive Care Needs- A Cross Sectional Study (the "**Study**").

- 1.2 Except as explicitly permitted in this Section 1.2, Licensee shall not modify, publish, disclose or distribute the GSRS or part thereof or otherwise use the GSRS or part thereof for any other purpose than as set forth in Section 1.1. Licensee may reproduce and use the GSRS in a format different than the format of GSRS as provided by AstraZeneca ("**Representative Tool**") if, and only if, all of the following conditions are met for each modified formatted GSRS ("**Modified Tool**"): (i) all wording of the Representative Tool is present in the Modified Tool exactly as found and in the same order such wording is set forth in the Representative Tool; (ii) Licensee submits screenshots comprising the entire Modified Tool to AstraZeneca; and (iii) Licensee subsequently receives approval in writing from AstraZeneca to reproduce and use the Modified Tool captured in such screenshots. The Modified Tool and all other modifications to, adaptations of, improvements to, enhancements to, translations of, or other changes to the GSRS are considered Derivative Works (as defined below) of the GSRS. All uses by Licensee under the Licence shall be in compliance with all applicable laws, rules and regulations.
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- 1.4 RWS Life Sciences shall, upon receipt of the Licence Fee, provide Licensee with one electronic copy in PDF format or similar of the GSRS in the following language(s):

English (UK)

together with electronic copies in PDF format or similar of AstraZeneca's scoring instructions and the Associated Materials, all of which will be sent by e-mail to the Licensee following the Effective Date at an e-mail address provided to AstraZeneca by the Licensee in writing.

2 Licence Fee

- 2.1 Non-Commercial Use: No licence fee for hospital and university or non-industry-sponsored use.

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4 Term and Termination

- 4.1 This Agreement shall become effective on the Effective Date and shall continue in force until the completion of the Study (at which time this Agreement shall terminate automatically without further notice), unless earlier terminated in accordance with this Section 4.1 (the "**Term**"). Either party may terminate this Agreement immediately by giving written notice to the other party if the other party should commit a material breach of any of its obligations under this Agreement and fail to rectify such breach within thirty (30) days after having been given a written request for such rectification. Upon termination or expiration of this Agreement, Licensee shall cease all use of the GSRS (and any copies or Derivative Works thereof).
- 4.2 The expiration or termination of this Agreement shall be without prejudice to any rights or obligations that may have accrued prior to such expiration or termination, and shall not affect any provision which is expressly or by implication intended to come into or continue in force on or after expiration or termination, including, without limitation, Section 1.2, Section 3, and this Section 4, Section 5 and Section 6.

5 Disclaimer; Limitation of Liability

- 5.1 LICENSEE ACKNOWLEDGES AND AGREES THAT THE GSRS IS PROVIDED ON AN "AS-IS" BASIS AND THAT LICENSEE'S USE OR RELIANCE UPON THE GSRS IS AT ITS SOLE RISK AND DISCRETION. ASTRAZENECA HEREBY DISCLAIMS ANY AND ALL REPRESENTATIONS AND WARRANTIES REGARDING THE GSRS, WHETHER EXPRESS, IMPLIED OR STATUTORY, INCLUDING, WITHOUT LIMITATION, ALL IMPLIED OR STATUTORY WARRANTIES OF MERCHANTABILITY, FITNESS FOR A PARTICULAR PURPOSE AND NON-INFRINGEMENT.
- 5.2 NEITHER PARTY SHALL BE LIABLE TO THE OTHER FOR ANY SPECIAL, INDIRECT, INCIDENTAL, CONSEQUENTIAL (INCLUDING WITHOUT LIMITATION LOST PROFITS) OR PUNITIVE DAMAGES IN RELATION TO THIS AGREEMENT, REGARDLESS OF THE FORM AND BASIS OF THE ACTION AT ISSUE.

6 Miscellaneous

- 6.1 The interpretation and construction of this Agreement shall be governed by the laws of Sweden excluding any conflicts or choice of law rule or principle that might otherwise refer

construction or interpretation of this Agreement to the substantive law of another jurisdiction.

- 6.2 The parties hereby irrevocably and unconditionally consent to the exclusive jurisdiction of the Swedish courts for any action, suit or proceeding arising out of or relating to this Agreement, and agree not to commence any action, suit or proceeding related thereto except in such courts.
- 6.3 If any provision or part-provision of this Agreement is or becomes invalid, illegal or unenforceable, it shall be deemed modified to the minimum extent necessary to make it valid, legal and enforceable. If such modification is not possible, the relevant provision or part-provision shall be deleted. Any modification to or deletion of a provision or part-provision shall not affect the validity and enforceability of the rest of this Agreement.
- 6.4 This Agreement may be executed in one or more counterparts, each of which will be deemed an original and all of which will together be deemed to constitute one agreement. The Parties agree that the execution of this Agreement by industry standard electronic signature software and/or by exchanging PDF signatures will have the same legal force and effect as the exchange of original signatures.

THIS AGREEMENT IS EXECUTED by authorised representatives of the parties.

Place: East Hartford, Connecticut, USA

Place: Dublin, Ireland

Date: 11May2023

Date: 05.02.2023

Name (Print): Jenny Pyatt

Name (Print): FATEMEH SADEGHI

RWS LIFE SCIENCES ON BEHALF OF:
ASTRAZENECA AB (PUBL)

Trinity College Dublin

Jenny Pyatt

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DN: cn=Jenny Pyatt, o=RWS Group,
ou=Regulated Industries,
email=jenny.pyatt@astrazeneca.com, c=US
Date: 2023.05.11 12:15:10 GMT

Fatemeh Sadeghi

Signature

Signature

2023-05-11

4(4)

Appendix VI Survey Questionnaires (Chapter 3)



ST. JAMES'S HOSPITAL
James's Street, Dublin 8
Telephone (+353) 1 410 3000
www.sjames.ie



Cancer Survivors' nutrition care needs

We would like to invite you to complete this survey which aims to identify cancer survivors' nutrition and supportive care needs. We are specifically looking for cancer survivors diagnosed with cancer of the oesophagus, stomach, pancreas, liver, and biliary system to take part in this study.

The result of this study will expand our knowledge and awareness of cancer survivors' nutrition care needs and the challenges they face regarding their diet and food intake. This information may help to design and deliver effective nutritional care plans to support cancer survivors.

* If you agree to take part in the research, you will be asked to complete the present survey.

* This survey has 3 main sections and should take no longer than 15 minutes to complete.

* The first section asks some brief questions about your background and type/s of cancer you have been diagnosed with and the cancer treatment you have undergone.

* In the second section, we will ask about your nutritional status, your unmet needs and experiences of dietetic services.

* In the third section we will ask about your health and symptoms during the past week.

* The next two sections are optional and contain questions about your health, symptoms, feelings, and wellbeing, during the past week.

Please read provided Participant Information Leaflet before completing the survey.

Please feel free to ask any questions you may have by contacting:

Mrs Fatemeh Sadeghi
Research Assistant
Discipline of Physiotherapy
School of Medicine
Trinity College Dublin
Email: Sadeghif@tcd.ie, Tel: 0896068686

If you would like to take part in this study, please provide consent by indicating your agreement with the following statements

Please tick ✓ following two statements if you agree with.

- I confirm that I have read and understood the Information Leaflet of this survey. ☐
- I understand that participation in this anonymous survey is entirely voluntary. ☐

Please proceed to the survey questions.



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Section 1

In this section, we are interested to know more about you and your medical history. Please answer all of the questions by selecting the option that best applies to you. The information that you provide is anonymous and will remain strictly confidential.

1. Which of the following best describes your gender?

- ☐ Male
- ☐ Female
- ☐ Prefer not to answer

2. What is your date of birth?

Month Year

2. Which of the following best describes your living situation?

- ☐ Living alone
- ☐ Living with a partner
- ☐ Living with others (Children, family members, friends)

3. Which of the following best describes your employment status?

- ☐ Employed Full time
- ☐ Employed Part-Time
- ☐ On sick leave
- ☐ Homemaker
- ☐ Retired
- ☐ Unemployed
- ☐ Not currently working due to COVID-19 workplace closures

4. What best describes your ethnic origin?

- ☐ Irish
- ☐ Irish traveller
- ☐ Any other White background
- ☐ African
- ☐ Any other black background
- ☐ Chinese
- ☐ Any other Asian background
- ☐ Other (incl. mixed background)

5. What is the highest level of education you have completed?

- ☐ Primary school
- ☐ Post-primary school
- ☐ Diploma
- ☐ Bachelor's degree
- ☐ Master's degree
- ☐ Doctorate
- ☐ Prefer not to answer

6. Which of the following best describes your health insurance type?

- ☐ Medical Card
- ☐ GP visit Card
- ☐ Private health insurance
- ☐ None
- ☐ Other (Please specify) -----
- ☐ Prefer not to answer

7. Which type of cancer have you been diagnosed with?

- ☐ Oesophageal Cancer
- ☐ Gastric Cancer
- ☐ Liver cancer
- ☐ Pancreatic Cancer
- ☐ Other cancers (Please specify) -----

8. When were you first diagnosed with cancer?

.....Year Month

9. Which treatments have you received/are you receiving for your cancer? Please select all that apply

- ☐ Surgery
- ☐ Chemotherapy
- ☐ Radiation Therapy
- ☐ Other (Please specify) -----
- ☐ Diagnosed with cancer but not started treatment yet
- ☐ I am currently on a break from treatment
- ☐ I am no longer receiving any treatment for cancer



Section 2

In this section, we would like to know more about your nutritional status and any dietary symptoms you are experiencing. We would also like to know about your experience of dietetic care during and after your cancer treatment

1. Have you recently (during the past 6 months) lost weight without trying?

- ☐ Yes
- ☐ No
- ☐ Unsure

If yes, how much weight have you lost?

- ☐ 2-13 lbs
- ☐ 14-23 lbs
- ☐ 24-33 lbs
- ☐ more than 33 lbs
- ☐ Unsure

3. Have you been eating poorly because of a decreased appetite?

- ☐ No
- ☐ Yes

4. Are you concerned about losing weight unintentionally?

- ☐ A bit concerned
- ☐ Moderately concerned
- ☐ Severely concerned
- ☐ Not concerned at all

5. Are you currently experiencing nutritional symptoms/complications that you are concerned about or are bothering you?

- ☐ Yes
- ☐ No

6. If yes, what is the most troublesome nutritional symptom/ complication at the moment for you?

7. Did you seek advice from a dietitian or other health professional regarding your nutritional symptoms/complications?

- ☐ Yes
- ☐ No

If Yes, at what point of your treatment did you see a dietitian? Please select all that apply

- ☐ Before starting treatment
- ☐ During active treatment
- ☐ After completing treatment



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8. Do you think you would have benefitted from more contact with a dietitian?

- ☐ Yes
- ☐ No

If yes, for which of the following questions or issues do you feel you need more advice? Please tick all that apply.

- ☐ Healthy eating
- ☐ Managing symptoms (Nausea, constipation, diarrhoea, taste change, oral mucositis, etc.)
- ☐ Portion sizes
- ☐ Suitable recipes and meal plans
- ☐ Swallowing difficulties
- ☐ Supplements
- ☐ Artificial nutrition (Tube feeding)
- ☐ Appetite loss
- ☐ Unintentional weight loss
- ☐ Weight management, obesity
- ☐ I don't need more dietetic advice
- ☐ Other (Please specify) -----

9. Are you currently using any supplements (i.e. vitamin and minerals, high-calorie high protein powder or drinks, etc.) or following any special diets? Please tick all that apply.

- ☐ Oral Nutritional Supplements
 - ☐ Please insert the name of supplement -----
- ☐ Currently on Tube feeding
- ☐ Following a special diet (i.e. Modified texture diet such as soft or puree, weight loss/gain, healthy diet, etc.)
 - ☐ Please insert the type of diet that you are following -----

10. Which of the following best describes your overall weight change since your diagnosis?

- ☐ I lost weight approximately kg/lb since my diagnosis
- ☐ I gained weight approximately kg/lb since my diagnosis
- ☐ My weight remained unchanged
- ☐ I don't know



Section 3

In this section, we are interested to know more about you and your health. Please answer all of the questions yourself by circling the number that best applies to you. There are no "right" or "wrong" answers.

	Not at All	A Little	Quite a Bit	Very Much
1. Do you have any trouble doing strenuous activities, like carrying a heavy shopping bag or a suitcase?	1	2	3	4
2. Do you have any trouble taking a <u>long</u> walk?	1	2	3	4
3. Do you have any trouble taking a <u>short</u> walk outside of the house?	1	2	3	4
4. Do you need to stay in bed or a chair during the day?	1	2	3	4
5. Do you need help with eating, dressing, washing yourself or using the toilet?	1	2	3	4
During the past week:	Not at All	A Little	Quite a Bit	Very Much
6. Were you limited in doing either your work or other daily activities?	1	2	3	4
7. Were you limited in pursuing your hobbies or other leisure time activities?	1	2	3	4
8. Were you short of breath?	1	2	3	4
9. Have you had pain?	1	2	3	4
10. Did you need to rest?	1	2	3	4
11. Have you had trouble sleeping?	1	2	3	4
12. Have you felt weak?	1	2	3	4
13. Have you lacked appetite?	1	2	3	4
14. Have you felt nauseated?	1	2	3	4
15. Have you vomited?	1	2	3	4
16. Have you been constipated?	1	2	3	4

Please go on to the next page



During the past week:	Not at All	A Little	Quite a Bit	Very Much
17. Have you had diarrhoea?	1	2	3	4
18. Were you tired?	1	2	3	4
19. Did pain interfere with your daily activities?	1	2	3	4
20. Have you had difficulty in concentrating on things, like reading a newspaper or watching television?	1	2	3	4
21. Did you feel tense?	1	2	3	4
22. Did you worry?	1	2	3	4
23. Did you feel irritable?	1	2	3	4
24. Did you feel depressed?	1	2	3	4
25. Have you had difficulty remembering things?	1	2	3	4
26. Has your physical condition or medical treatment interfered with your <u>family</u> life?	1	2	3	4
27. Has your physical condition or medical treatment interfered with your <u>social</u> activities?	1	2	3	4
28. Has your physical condition or medical treatment caused you financial difficulties?	1	2	3	4

For the following questions please circle the number between 1 and 7 that best applies to you

29. How would you rate your overall health during the past week?

1 2 3 4 5 6 7

Very poor

Excellent

30. How would you rate your overall quality of life during the past week?

1 2 3 4 5 6 7

Very poor

Excellent



Thank you for completing the first three sections of the present survey. The next two sections of the survey are optional. We would value your help in completing the following section which will give us valuable insight into cancer survivors' mental health and gastrointestinal symptoms. This information is important to identify supportive care required by cancer survivors' in Ireland.

Section 4

This section contains some questions about gastrointestinal symptoms you may be experiencing (for example problems with your stomach or bowels). We are interested in to know how you have been feeling and what it has been like DURING THE PAST WEEK. Please tick the choice that best applies to you and your situation.

1. Have you been bothered by PAIN OR DISCOMFORT in your upper abdomen or the pit of your stomach during the past week?

☐ No discomfort at all	☐ Moderately severe discomfort
☐ Minor discomfort	☐ Severe discomfort
☐ Mild discomfort	☐ Very severe discomfort
☐ Moderate discomfort	

2. Have you been bothered by HEARTBURN during the past week? (By heartburn we mean an unpleasant stinging or burning sensation in the chest).

☐ No discomfort at all	☐ Moderately severe discomfort
☐ Minor discomfort	☐ Severe discomfort
☐ Mild discomfort	☐ Very severe discomfort
☐ Moderate discomfort	

3. Have you been bothered by ACID REFLUX during the past week? (By acid reflux we mean the sensation of regurgitating small quantities of acid or flow of sour or bitter fluid from the stomach up to the throat.)

☐ No discomfort at all	☐ Moderately severe discomfort
☐ Minor discomfort	☐ Severe discomfort
☐ Mild discomfort	☐ Very severe discomfort
☐ Moderate discomfort	

4. Have you been bothered by HUNGER PAINS in the stomach during the past week? (This hollow feeling in the stomach is associated with the need to eat between meals.)

☐ No discomfort at all	☐ Moderately severe discomfort
☐ Minor discomfort	☐ Severe discomfort
☐ Mild discomfort	☐ Very severe discomfort
☐ Moderate discomfort	



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5. Have you been bothered by NAUSEA during the past week? (By nausea we mean a feeling of wanting to throw up or vomit.)
- | | |
|--|--|
| ☐ No discomfort at all | ☐ Moderately severe discomfort |
| ☐ Minor discomfort | ☐ Severe discomfort |
| ☐ Mild discomfort | ☐ Very severe discomfort |
| ☐ Moderate discomfort | |
6. Have you been bothered by RUMBLING in your stomach during the past week? (Rumbling refers to vibrations or noise in the stomach.)
- | | |
|--|--|
| ☐ No discomfort at all | ☐ Moderately severe discomfort |
| ☐ Minor discomfort | ☐ Severe discomfort |
| ☐ Mild discomfort | ☐ Very severe discomfort |
| ☐ Moderate discomfort | |
7. Has your stomach felt BLOATED during the past week? (Feeling bloated refers to swelling often associated with a sensation of gas or air in the stomach.)
- | | |
|--|--|
| ☐ No discomfort at all | ☐ Moderately severe discomfort |
| ☐ Minor discomfort | ☐ Severe discomfort |
| ☐ Mild discomfort | ☐ Very severe discomfort |
| ☐ Moderate discomfort | |
8. Have you been bothered by BURPING during the past week? (Burping refers to bringing up air or gas from the stomach via the mouth, often associated with easing a bloated feeling.)
- | | |
|--|--|
| ☐ No discomfort at all | ☐ Moderately severe discomfort |
| ☐ Minor discomfort | ☐ Severe discomfort |
| ☐ Mild discomfort | ☐ Very severe discomfort |
| ☐ Moderate discomfort | |
9. Have you been bothered by PASSING GAS OR FLATUS during the past week? (Passing gas or flatus refers to the need to release air or gas from the bowel, often associated with easing a bloated feeling.)
- | | |
|--|--|
| ☐ No discomfort at all | ☐ Moderately severe discomfort |
| ☐ Minor discomfort | ☐ Severe discomfort |
| ☐ Mild discomfort | ☐ Very severe discomfort |
| ☐ Moderate discomfort | |
10. Have you been bothered by CONSTIPATION during the past week? (Constipation refers to a reduced ability to empty the bowels.)
- | | |
|--|--|
| ☐ No discomfort at all | ☐ Moderately severe discomfort |
| ☐ Minor discomfort | ☐ Severe discomfort |
| ☐ Mild discomfort | ☐ Very severe discomfort |
| ☐ Moderate discomfort | |



11. Have you been bothered by DIARRHOEA during the past week? (Diarrhoea refers to a too frequent emptying of the bowels.)

☐ No discomfort at all	☐ Moderately severe discomfort
☐ Minor discomfort	☐ Severe discomfort
☐ Mild discomfort	☐ Very severe discomfort
☐ Moderate discomfort	

12. Have you been bothered by LOOSE STOOLS during the past week? (If your stools (bowel motions) have been alternately hard and loose, this question only refers to the extent to which you have been bothered by the stools being loose.)

☐ No discomfort at all	☐ Moderately severe discomfort
☐ Minor discomfort	☐ Severe discomfort
☐ Mild discomfort	☐ Very severe discomfort
☐ Moderate discomfort	

13. Have you been bothered by HARD STOOLS during the past week? (If your stools (bowel motions) have been alternately hard and loose, this question only refers to the extent to which you have been bothered by the stools being hard.)

☐ No discomfort at all	☐ Moderately severe discomfort
☐ Minor discomfort	☐ Severe discomfort
☐ Mild discomfort	☐ Very severe discomfort
☐ Moderate discomfort	

14. Have you been bothered by an URGENT NEED TO HAVE A BOWEL MOVEMENT during the past week? (This urgent need to go to the toilet is often associated with a feeling that you are not in full control.)

☐ No discomfort at all	☐ Moderately severe discomfort
☐ Minor discomfort	☐ Severe discomfort
☐ Mild discomfort	☐ Very severe discomfort
☐ Moderate discomfort	

15. When going to the toilet during the past week, have you had the SENSATION OF NOT COMPLETELY EMPTYING THE BOWELS? (This feeling of incomplete emptying means that you still feel a need to pass more stool despite having exerted yourself to do so.)

☐ No discomfort at all	☐ Moderately severe discomfort
☐ Minor discomfort	☐ Severe discomfort
☐ Mild discomfort	☐ Very severe discomfort
☐ Moderate discomfort	



Section 5

In this section, we are interested to know more about your feelings and mood during the past week. Tick the box beside the reply that is closest to how you have been feeling in the past week. Don't take too long over your replies: your immediate is best.

1. I feel tense or 'wound up': ☐ Most of the time ☐ A lot of the time ☐ From time to time, occasionally ☐ Not at all	8. I feel as if I am slowed down: ☐ Nearly all the time ☐ Very often ☐ Sometimes ☐ Not at all
2. I still enjoy the things I used to enjoy: ☐ Definitely as much ☐ Not quite so much ☐ Only a little ☐ Hardly at all	9. I get a sort of frightened feeling like 'butterflies' in the stomach: ☐ Not at all ☐ Occasionally ☐ Quite Often ☐ Very Often
3. I get a sort of frightened feeling as if something awful is about to happen: ☐ Very definitely and quite badly ☐ Yes, but not too badly ☐ A little, but it doesn't worry me ☐ Not at all	10. I have lost interest in my appearance: ☐ Definitely ☐ I don't take as much care as I should ☐ I may not take quite as much care ☐ I take just as much care as ever
4. I can laugh and see the funny side of things: ☐ As much as I always could ☐ Not quite so much now ☐ Definitely not so much now ☐ Not at all	11. I feel restless as I have to be on the move: ☐ Very much indeed ☐ Quite a lot ☐ Not very much ☐ Not at all
5. Worrying thoughts go through my mind: ☐ A great deal of the time ☐ A lot of the time ☐ From time to time, but not too often ☐ Only occasionally	12. I look forward with enjoyment to things: ☐ As much as I ever did ☐ Rather less than I used to ☐ Definitely less than I used to ☐ Hardly at all
6. I feel cheerful: ☐ Not at all ☐ Not often ☐ Sometimes ☐ Most of the time	13. I get sudden feelings of panic: ☐ Very often indeed ☐ Quite often ☐ Not very often ☐ Not at all
7. I can sit at ease and feel relaxed: ☐ Definitely ☐ Usually ☐ Not Often ☐ Not at all	14. I can enjoy a good book or radio or TV program: ☐ Often ☐ Sometimes ☐ Not often ☐ Very seldom



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www.sjames.ie



Trinity College Dublin
Coláiste na Tríonóide, Baile Átha Cliath
The University of Dublin

Thank you for taking the time to complete this survey.

If you are interested in our future research studies on this topic, please contact:

Mrs Fatemeh Sadeghi

Research Assistant

Discipline of Physiotherapy

School of Medicine

Trinity College Dublin

Email: Sadeghif@tcd.ie, Tel: 0896068686

We appreciate it if you could please return the completed survey by post using the stamped addressed envelope which has been posted to you.

Appendix VII National Oesophagogastric Cancer Centre Research Newsletter

National Oesophagogastric Cancer Centre Research Newsletter

Dear Friend,

I hope you are keeping well.

We are mailing people who have been assessed by the National Oesophagogastric cancer centre in St James Hospital in recent years.

You may have been approached to take part in a number of different research studies or trials during your treatment. We thought you might like to hear about some of the studies we are undertaking and what we have found. We also wanted to share news on developments like the accreditation of the Trinity St James' Cancer Institute.

For this newsletter we are focussing on studies that have looked at quality of life in people living after oesophageal and gastric cancer treatment and research into immunotherapy.

We have also included contact information for support groups that you might find useful.

Remember, that if you have any concerns about your recovery to reach out to your Cancer Nurse Specialist for advice and support.

Wishing you well,

Claire Donohoe

Consultant surgeon

Trinity St James' Cancer Institute.

claire.donohoe@tcd.ie



Change of circumstances? Let us know!

If you do not wish to receive this mailing in future or wish to get in contact with us, please scan this QR code. It will bring you to a short form where you can leave us a message.



How to use a QR code:

- 1) Open the camera app on your smartphone
- 2) Hold it in front of the QR code you would like to scan - the app will automatically recognise it as a QR code and offer you a link to click on
- 3) Click on the link and it will take you to the website linked to the QR code.



We hope you can see that we really value your participation in research and developing our treatments. From time to time we have online meetings to discuss how to improve services or develop research projects. Taking part doesn't require any special experience or training - having experience of living with or after cancer, or caring for someone who has, brings life experience and a unique perspective to us. **If you would like to take part in future groups on research or service development, or to learn more about this role, please contact us using this form attached to above QR code.**



Cancer Survivors' Nutrition Care Needs

Recognising the large volume of cancer diagnosis and treatment undertaken in St James Hospital, the hospital and its academic partner, Trinity College Dublin have come together to form the Trinity St James's Cancer Institute. It is the first Irish cancer institute to be accredited by the Organisation of European Cancer Institutes (OECI). As a Cancer Institute, our mission is to integrate innovative and ground-breaking cancer science with compassionate, multidisciplinary, patient-focused clinical care through translation of key research findings into incremental advances in the prevention, diagnosis and treatment of cancer. It means that we benchmark our care against other leading international cancer centres. By working together across cancer types and focusing on learning with and from patients undergoing treatment through research, we hope to be able to improve care, not just within St James' Hospital but nationally.

Neo-AEGIS trial

This trial is comparing outcomes of people with oesophageal adenocarcinoma treated with either chemotherapy or chemoradiotherapy before (and after) surgery. It is lead by Prof John Reynolds. This trial was carried out here in Dublin as well as hospitals in France, Sweden, Denmark and the UK and was co-ordinated by Cancer Trials Ireland.



We are pleased to report that the trial has finished its recruitment. It has shown that there are no differences in the long-term results between the two treatment groups. Once we have assessed the outcomes of people taking part in the trial, we hope to publish the results as a report in a medical

journal.

It means that healthcare providers can choose either chemoradiotherapy or chemotherapy for their patients depending on individual patient factors since one form of treatment is not better than the other.

We would like to thank all participants for taking part and letting us understand more about treatment choices for oesophageal cancer.

Researchers at Trinity Exercise Oncology research group are conducting interviews to identify cancer survivors' nutrition care needs. The results of this study will expand our knowledge and awareness of cancer survivors' nutrition care needs and the challenges they face regarding their diet and food intake after operation. This information may help to develop effective nutritional care plans to support cancer survivors.

We are seeking to hold interviews with patients living with and beyond cancer and their family members to discuss their experience and accessibility of dietetic care, unmet needs, and nutritional challenges have faced during their cancer journey. Interviews can be done over telephone, by video call, or in person based on participants' preference

If you are interested to take part or would like more information, please contact:

Mrs Fatemeh Sadeghi

Email: sadeghif@tcd.ie, Phone: 0896068686

Priority Setting partnership

We have been asking people living with or after oesophageal cancer to tell us what the most important questions that we need to answer with research are. We got more than 280 questions, many of which were already answered by research.

We have checked all of the questions provided and have 70 questions about diagnosis, treatment and living with and after oesophageal cancer that haven't been answered by research yet.

We now need to decide the most important questions to answer with research studies. We hope to do this by discussing the questions at a meeting with patients and healthcare providers and choosing the top 10 most important questions to answer first.

If you would like to sign up to join this online meeting - please scan this code and leave your contact details:



PERCS

Personalised Exercise
Rehabilitation in
Cancer Survivorship

Personalised Exercise Rehabilitation in Cancer Survivorship (PERCS)

There is strong scientific evidence that physical activity can help improve many of the side-effects of cancer treatment and can enhance both physical and mental wellbeing. People living with and beyond cancer, particularly those additionally impacted by COVID-19, can benefit greatly from being supported to take part in physical activity.

PERCS is a project funded by the Irish Cancer Society which involves running and evaluating a new exercise-based rehabilitation triage and referral system. People who were treated for cancer during the coronavirus pandemic will be referred to a suitable exercise-based rehabilitation service with the aim to improve physical and psychosocial outcomes. The PERCS team is led by Principal Investigator Dr Emer Guinan, Clinical Lead Dr Claire Donohoe and Project Manager Dr Louise Brennan, and includes patient representatives and oncology healthcare professionals.

The PERCS project commenced in February 2022, and we are currently co-designing a webpage with patient representatives and oncology healthcare professionals. This trusted webpage will contain information about physical activity for mental and physical wellbeing in people with cancer. It will support participants being assessed in the triage and referral system, which will commence in Summer 2022.

Aoife returns to explore immunotherapy

Cancer immunotherapy is a new type of treatment which uses the patient's own immune system to fight their cancer. Dr. Aoife Kilgallon completed her PhD (studying chimeric antigen receptor (CAR) T cells) at the University of Manchester. Her new project at Trinity St James Cancer Institute will look at a type of immunotherapy known as immune checkpoint blocking agents and assess how they enable the immune system to fight cancer cells.



The ReStOre II study has recently opened at the Trinity St James's Cancer Institute. The study is testing a rehabilitation programme for people who have completed treatment for cancer of the oesophagus, stomach, pancreas or liver. In the ReStOre II study people taking part will be placed randomly into one of two groups: the intervention group or the control group. The intervention group will undertake the ReStOre rehabilitation programme, the control group will continue with their usual hospital follow-up.



The ReStOre rehabilitation programme is a 12-week programme and involves exercise, education, and advice on diet and is led by a team of health care professionals including physiotherapists, dietitians and occupational therapists. Over the next two years, up to 120 people will take part in the study. We hope that the results of the study will help inform the future care of patients recovering from cancers of the oesophagus, stomach, pancreas and liver. If you would like to receive more information about the ReStOre II study, please contact the Project Manager, Dr Linda O'Neill. Email: exerciseoncology@tcd.ie, Phone: 01 8964809/ 087 6577927

ENSURE Study

Treatment of oesophageal and gastric cancer may involve a combination of approaches, such as chemotherapy, chemoradiation and surgery, with other newer treatments such as immunotherapy expected to have a role in the future. However, following completion of treatment, the optimal follow-up strategy has not yet been established. In the ENSURE study, we sought to determine whether aspects of follow-up including routine CT scans, endoscopy, blood tests, and monitoring nutrition, made a difference to important patient outcomes including anxiety, quality of life and cancer recurrence.

The study was led by a team at St. James's Hospital, and took place across 27 centres in Ireland, Europe and North America. The study showed that follow-up plans varied widely between different countries, with some countries recommending no routine tests, and others recommending regular scans and blood tests for all patients. The majority of the centres agreed that more research was needed in this area (92%). The study then assessed the impact of an intensive follow-up plan as compared with standard follow-up. The study found that intensive follow-up was associated with increased anxiety, but similar overall quality of life. Intensive follow-up did not change cancer survival, although there was some early evidence that certain groups of people might benefit from this approach. Importantly, the study did find that monitoring nutrition (such as vitamin D, iron, folate and B12 levels) was associated with improved outcomes across all patients.

Michelle Fanning moves on

Our Senior Dietician, Michelle Fanning has moved on to a new post in Naas Hospital. We will miss her expertise and wish her well in her new endeavours!



Meet Eimear Mylod – a research scientist who has been exploring Natural killer (NK) cells our body's first line defence against cancer. Eimear has discovered that these important anti-cancer immune cells move to the fat instead of going to the tumour in cancer patients. When they are in the fat, they can either die or are altered, meaning they are less able to kill cancer cells. The movement of immune cells such as NK cells is controlled by signals from small molecules called chemokines. As part of her project Eimear has identified the signal that is guiding NK cells to the fat. She has also shown that if we block this signal, we can reduce movement towards the fat. This work is still in its infancy but Eimear and her supervisor Prof Joanne Lysaght hope that this may be an important step in understanding new treatments.



The CROSS charity supports Cancer Research of the Oesophagus and Stomach at St James's Hospital, funding education, training and vital equipment and biobanking supports for the Dept of Surgery's Translational Oncology research team. Find out more about our latest research at www.crosscharity.ie

Reactive hypoglycaemia study

After removal of the oesophagus or stomach, feeling light-headed, weak, shaky or unwell after eating can occur. We don't know how commonly this occurs. It may be caused by a low blood sugar level after a meal - a process called "Reactive hypoglycaemia".
Reactive=In response to a meal,
Hypoglycaemia=Low blood sugar

Symptoms of a low blood sugar can include light-headedness, weakness, palpitations, hunger, shakiness, anxiety, irritability, giddiness, blurred vision and confusion.

Unlike early dumping syndrome, that you can experience in the 30 minutes after a meal, a low blood sugar can catch you off guard as they can occur 1-3 hours after a meal and without the same obvious post meal pattern.

We have recently asked some people living after oesophageal surgery to wear a blood sugar monitor to assess how common it is for people to have low blood sugar levels. Although we have yet to complete the study, it looks like low blood sugar levels happen to some people after this type of surgery. Those who have taken part will receive a summary of our advice on managing low blood sugars. Here are some tips on preventing low blood sugars that you might find helpful

The advice to PREVENT low blood sugars:

1. Try not to drink while eating your meals. Wait 30 minutes after your meal before having a drink. It is okay to have a drink before your meal at this stage out from your operation).
2. Eat slowly and chew foods very well.
3. Avoid large meals and take three medium meals and 3-4 additional snacks a day.
4. Do not leave long gaps between your meals. You need to try to eat every 2-3 hours.
5. Avoid sugar in a drink, a liquid, a gel, a gum, or a syrup. Avoid the following:

- ✓ Minerals or tonics (unless diet variety)
- ✓ Cordial (unless no added sugar)
- ✓ A serving of fruit juice greater than 100mls
- ✓ Table sugar added to tea, coffee or lemon tea
- ✓ Honey added to lemon tea
- ✓ Table sugar, castor sugar, honey, treacle, maple syrup added to cereals or pancakes
- ✓ Jams and marmalade
- ✓ Glaze or icing on a cake (icing sugar and water)
- ✓ Ice lollies (frozen sugar and water)
- ✓ Jelly (sugar, water and gelatine)
- ✓ Wine gums, fruit pastilles, hard boiled sweets, toffee

We do not advise avoiding foods containing carbohydrate or sugar. In people who have lost weight before or after surgery, this is over restrictive and runs a high risk of nutrient inadequacy and further weight loss.



ARC Cancer Support Centres offer a holistic approach to people affected by cancer. Located near the major centres of excellence for cancer care in Dublin: the Mater Hospital, Beaumont Hospital, St James's Hospital and St Vincent's Hospital, clients are offered psychological, educational and practical support, complementary therapies and counselling services. All services are provided by professional staff and trained volunteers, available to anyone in Ireland and are completely free of charge. See: www.arccancersupport.



Oesophageal Cancer Fund (OCF) supports research at Trinity St James' Cancer Institute through funding vital supports like biobanking facilities, clinical trial supports (Neo-AEGIS trial) and acting as an important link between researchers and those affected by oesophageal cancer. The OCF has funded the National Barrett's Oesophagus Registry, which has registered 7,210 patients and stored biopsy samples for research from over 400. This is a unique database and collaborative network involving St James' Hospital, Mercy University Hospital Cork, Beaumont Hospital, St Vincent's University Hospital, the Mater Misericordiae University Hospital and Galway University Hospital. Find out more at www.ocf.ie

Breakthrough Cancer is an Irish medical research charity. We fund research into poor prognosis cancers, facilitate collaboration between scientists and clinicians across Ireland and internationally, and accelerate the translation of lab discoveries into new effective treatments. Investment is intended to also enhance facilities with state-of-the-art equipment and ensure that all cancer patients in Ireland can access the most up to date and effective treatment for their disease. Consultant physicians and surgeons collaborate with us across Ireland, voluntarily giving their time to research with the aim of improving the care and treatment of Irish patients. We work with dieticians, researchers and oncologists to create evidencebased cookbooks available for cancer patients who are experiencing cancer-induced weight loss. To order a free copy, visit: www.breakthroughcancerresearch.ie



The Irish Cancer Society is Ireland's national cancer charity supporting those affected by cancer with information, advice and advocacy. We are the largest voluntary funder of cancer research in Ireland, committed to improving the lives of cancer patients through research. In 2019, the public donations that make our research possible have allowed us to fund the work of over 100 talented professionals in research priority areas including prevention, early detection, better treatments, clinical trials and survivorship. In 2019 we increased our Public and Patient Involvement (PPI) in research activity, training 30 volunteers to review the PPI sections of our research applications. We would like to express our gratitude to all our researchers and PPI reviewers for their hard work and dedication to improving the lives of those affected by cancer, we very much appreciate your contributions. Please keep an eye out for more PPI reviewer opportunities in the future! For more information, visit: www.cancer.ie or call our Nurse line on 1800 20070

Appendix VIII Interview Guide (Chapter 4)

We are interested to know more about your experiences of nutrition care during your cancer journey and challenges you faced regarding your food intake, and how the nutrition care might be improved to address your needs or needs of person who you care for.

You were invited to share your experiences as a cancer survivor/carer or family member which can give us a better insight of your unmet needs to help with improving nutrition care provided to cancer survivors to meet their needs.

There are no wrong answers but rather differing points of view and experiences. So please feel free to share your thoughts. You can skip any question if you prefer not to answer it/or request to stop the interview if you wish not to continue.

I should mention that we're audio recording the session because we don't want to miss any of your comments as we can't write fast enough to record all your very helpful views and comments. You may be assured of complete confidentiality as we will not use any names in the reports and publication related to this study.

Please feel free to ask any questions before we start.

1. Can you tell us about your main challenges regarding your nutrition during your cancer journey? Prompts:

- What was the main problem, complication, or most troublesome symptoms you experienced regarding your nutrition?
- How did you deal with this?

2. If you (or the person you cared for) saw a dietitian along your cancer journey, can you tell me more about this? Prompts:

- Where did you see a dietitian?
- When did you see a dietitian? In which time point of your treatment?
- Who referred you to the dietitian or was it requested by you?
- Do you know why you were referred/ how did initial contact come about?
- How long did you wait to see a dietitian and was waiting time acceptable?

- Were your nutrition needs met during dietitian visit?
 - Were you given any written information such as booklets/brochures/information sheets? what did you think of these? Did they meet your needs?)
3. If you didn't see a dietitian along your cancer journey, did you feel you were supported with your nutrition in other ways? Prompts:
- Was there a time when you would have wanted to see a dietitian and couldn't?
 - Where did you get your advice and what did you do about your nutrition issues if you didn't see a dietitian/in addition to seeing a dietitian?
4. How did you feel about your nutrition care during your cancer journey? Prompts:
- Give examples of emotions, why you felt like this?
 - Did you get enough care at the right time?
5. Were you given information on the impact of poor nutrition at any time during your cancer journey? For example, longer recovery times etc.Prompts:
- Can you tell me more about this?
 - Did it change anything for you?
 - Who was it from?
6. Do you have any examples of when your expectations or needs around nutrition were/weren't met?
7. How can we as health professionals improve the experience for you regarding your nutrition needs during your cancer journey? Prompts:
- What could have made your experience with nutrition better/different for you during your cancer journey?
 - What changes in the service would make a difference for you?
 - If all these things were done what difference would that have made for you?
8. Do you, or did you find the side effects from your cancer treatment affected social aspects of your eating and drinking? For example, leaving the house to eat and drink, being in public with a feeding tube (if you had one), eating with others, if so, could any change make it a different experience for you?
- 9.Do you, or did you find the side effects from your cancer treatment affected emotional aspects of your eating and drinking? If so, could any changed make it a different experience for you?

10. Were there any barriers to you achieving the best nutrition that you could throughout your cancer journey?

11. Did you join any support group during your cancer journey? What was your experience regarding this and what do you think about support groups?

12. Do you have any other comments you would like to add?

Many thanks for participating in the present study, the information you provided will give us valuable insight into cancer survivors unmet nutrition care needs in Ireland. If you need to contact the research team for any support after completing this interview, please feel free to get in touch. Our contact details are on the participants information leaflet.

Appendix IX Food Items Included in the proceed meat variable for
calculating WCRF/AICR score (Chapter 5 & Chapter 7)

Food Name
Bacon rashers- fried
Bacon rashers- grilled
Black pudding, grilled
Cooked/ boiled ham
Cured meat- salami
Frankfurter
Ham slices
Sausages- fried
Sausages, grilled
Sausages, pork, chilled, fried in vegetable oil
Sliced chicken meat (processed)
White pudding, fried
White pudding, grilled

Appendix X Food items included in the aUPF variable for
calculating WCRF/AICR score (Chapter 5 & Chapter 7)

Food Name	
7up free/ sprite zero	Chocolate rich tea
All-bran type cereal, fortified	Chocolate spread
Apple juice- from concentrate	Chocolate Swiss roll- retail
Banana bread/cake	Corn cakes
Biscuits- cookies- chocolate chip- American style	Cornetto type ice-cream
Biscuits- digestive- with oats- plain	Cornflakes, unfortified
Biscuits, oat based, chocolate, half coated	Cornflakes- fortified
Blackcurrant juice drink/squash- diluted	Cranberry sauce
Black forest gateau	Cream crackers
Boiled sweets	Crunchie
Boudoir biscuit	Custard- canned and tetra pack
Bourbon creams	Custard creams biscuit
Bourbon creams biscuit	Dairy spread, e.g. Dairygold, kerrymaid
Bran flakes, fortified	Dark chocolate
Breadsticks	Diet cola
Breakfast cereal, puffed wheat, honey coated, fortified	Digestive Bisc
Brown sauce	Dressing- low fat
Bun- retail	Dressing- thousand island- regular
Cadbury miniature heroes	Drinking yoghurts, e.g. Actimel, benecol yoghurt drink
Cadbury's roses	Egg mayonnaise
Caramel biscuit	English muffin
Carrot cake-retail	Fig roll
Cereal bars	Flapjacks, retail
Cheese sauce- (packet sauce/jar)- whole milk	Fruit and fibre type cereal- fortified
Chew sweets	Fruit cake
Chickatees	Fruit gums
Chicken goujons	Full fat yoghurt- fruit
Chicken nuggets, takeaway	Gingernut biscuit
Chips- oven/microwave ready-baked	Gluten free biscuit, plain
Chips, fried, chip shop, retail	Gluten free cereal
Chips, oven/microwave ready, baked	Granola
Chocolate chip cookies	Gravy- made from granules

Food Name	
Chocolate Confectionary	Honey loop cereal, fortified
Chocolate covered bar with fruit/nut	Ice lolly
Chocolate digestive	Iceberger ice cream
Chocolate raisins	Special k type cereals
Ice-cream- vanilla	Ice-cream- flavoured
Ice-creams	Sunflower spread, e.g. Flora or other sunflower spreads
Instant noodles	Sweeteners
Jaffa cakes	Tartare sauce
Jam rings	Thin crackers
Mars bar	Toffees, mixed
Marshmallows	Jelly, made with water
Mayonnaise- regular	Kimberly Biscuit
Mikado Chocolate	Lindt Lindor chocolate
Milk chocolate	Low fat spread, e.g. Low Low, flora light
Mint sauce	Mallow cake e.g. Snowballs- chocolate teacakes
Muesli, no added sugar, unfortified	Tomato ketchup
Muesli, regular, unfortified	Tortilla crisps (e.g. Doritos)
Mustard ready made	Twister ice cream
Mustard- smooth	Twix chocolate
Penguin bar-chocolate bar	Water biscuit
Pizza, ham and pineapple, retail	Scones- plain- retail
Popcorn	Seafood sauce
Potato chips, oven ready, with batter, baked	Shortbread biscuits
Potato crisps	Snack wafer bar (pink)
Potato salad- regular- with mayonnaise	Spaghetti Bolognese (includes spaghetti/pasta component)- ready-meal
Potato waffles	
Prawn crackers	
Preserves- jam	
Preserves- marmalade	
Processed cheese, slices, plain	
Raspberry creams biscuit	
Rice cakes, covered in yoghurt / chocolate	
Rice krispies	
Rice pudding, canned	
Rich tea Biscuit	
Salted cracker e.g. Tuc- ritz	

Appendix XI List of recipes used for disaggregating red and processed meat, fruit and vegetable and aUPF consumed as composite dishes (Chapter 5 & Chapter 7)

Food Name	Food Component Disaggregated
Cauliflower cheese	Cauliflower
SOUP VEGETABLE (retail)-chilled soups - ready-meal, e.g. Cully & sully, Avonmore, Tesco finest	Vegetables
Beef goulash	Beef and Vegetables
Vegetable lasagne homemade	Vegetables
Prawn curry	Vegetables
Pasta, spaghetti, canned in tomato sauce	Vegetables
Spaghetti bolognese	Lamb and Vegetables
Homemade soups - Vegetables (no cream)	Vegetables
Baked bean in tomato sauce	Vegetables (Tomato puree)
Ham and cheese sandwich	Ham
Coleslaw	Vegetables
Lentil soup with red lentils onion toms & butter	Vegetables
Cream of tomato soup canned	Vegetables
Frankfurter with bun	Processed meat and UPF (bun-Ketchup-mustard)
Pasta with bacon and tomato	Bacon and Vegetables
Beef stew with potato	Beef and Vegetables
Steak and kidney pie	Red meat
Rice salad	Vegetables
Beet root salad	Vegetables
Burger- beef- with bun- grilled	Beef
Mushrooms- white- fried	Vegetables
Stir-fried vegetables	Vegetables
Pate, liver	Red meat-liver
Blackberries, stewed with sugar	Fruit
Pie, chicken and mushroom, single crust, homemade	Vegetables
Chicken & Vegetables pie (puff pastry), homemade	Vegetables
Fruit pie, homemade e.g. Apple pie	Fruit

Food Name	Food Component Disaggregated
Chicken stew w/ potatoes & Vegetables	Vegetables
Casserole, bean and mixed vegetable, homemade	Vegetables
Tomatoes, standard, fried in corn oil	Vegetables
Soup, lentil, canned	Vegetables
Tomato based sauces, including jars of tomato sauces for cooking	Vegetables
Sauce, tomato based, homemade	Vegetables
Minestrone soup (includes pasta)/homemade soups - stock/tomato based (no cream) / minestrone	Vegetables
Pears, canned in juice, whole contents	Fruit
Rice with vegetables	Vegetables
Mussels in tomato basil garlic, cooked	Vegetables
Pork casserole with potatoes	Vegetables
Sausage roll, retail	Processed meat
Chicken curry, homemade, korma	Vegetables
Guacamole	Vegetables
Beef/lamb in tomato-based sauce e.g. Chilli con carne, homemade	Red meat and Vegetables
Beef stir-fry, in Asian/Mexican style sauce (with/without Vegetables), homemade	Beef and Vegetables
Casserole, beef, made with cook-in sauce	Beef and Vegetables

Appendix XII Publication of The Effectiveness of Nutrition Interventions Combined with Exercise in Upper Gastrointestinal Cancers: A Systematic Review



Systematic Review

The Effectiveness of Nutrition Interventions Combined with Exercise in Upper Gastrointestinal Cancers: A Systematic Review

Fatemeh Sadeghi ¹, David Mockler ², Emer M. Guinan ³, Juliette Hussey ¹ and Suzanne L. Doyle ^{4,*}

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Abstract: Malnutrition and muscle wasting are associated with impaired physical functioning and quality of life in oncology patients. Patients diagnosed with upper gastrointestinal (GI) cancers are considered at high risk of malnutrition and impaired function. Due to continuous improvement in upper GI cancer survival rates, there has been an increased focus on multimodal interventions aimed at minimizing the adverse effects of cancer treatments and enhancing survivors' quality of life. The present study aimed to evaluate the effectiveness of combined nutritional and exercise interventions in improving muscle wasting, physical functioning, and quality of life in patients with upper GI cancer. A comprehensive search was conducted in MEDLINE, EMBASE, Web of Science, Cochrane Library, and CINAHL. Of the 4780 identified articles, 148 were selected for full-text review, of which 5 studies met the inclusion criteria. Whilst reviewed studies showed promising effects of multimodal interventions on physical functioning, no significant differences in postoperative complications and hospital stay were observed. Limited available evidence showed conflicting results regarding the effectiveness of these interventions on preserving muscle mass and improving health-related quality of life. Further studies examining the impact of nutrition and exercise interventions on upper GI patient outcomes are required and would benefit from reporting a core outcome set.

Keywords: cancer; gastrointestinal; nutrition; exercise; rehabilitation; multidisciplinary; body composition



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1. Introduction

Upper GI cancers, namely esophageal cancer, gastric cancer, hepatobiliary cancers, and pancreatic cancer, were reported to affect 3.12 million individuals (17.3% of the global cancer incidence) in 2018 [1]. Adding to this, upper GI cancers were responsible for 2.6 million deaths worldwide in 2018. The treatment for upper GI cancer includes surgery, chemotherapy, and radiotherapy. Although advances in these cancer treatments, and early cancer diagnosis, has led to higher survival rates, the treatments are accompanied by adverse effects on patients' nutritional status and physical function [2–6].

Cachexia and muscle loss are one of the main complications in cancer patients that hinder cancer treatment and survival [3]. Muscle wasting is accompanied by reduced physical function, fatigue, chemotherapy toxicity, lower quality of life, and a higher rate of postoperative complications [7–10]. Due to the tumor location and the unique influences of curative surgery on a patient's dietary intake, patients with upper GI cancer are at a greater risk of malnutrition and its related complications [11–13]. As the survival rates for upper GI cancer continue to improve, the long-term nutritional and physical status of upper GI

cancer survivors requires further attention. There is a need to offer effective care plans to prevent muscle wasting and optimize nutritional and functional status in upper GI cancer patients, which subsequently would improve treatment outcomes and enhance survivors' quality of life.

Multimodal interventions consisting of nutrition and exercise prescription have been reported to favorably change health-related outcomes in cancer patients, such as fatigue, quality of life, and functional capacity [14,15]. These multimodal interventions may play an even more significant role in older cancer patients who are at a further increased risk of suboptimal nutritional and functional status [16].

As both nutrition and exercise have positive effects on muscle loss, combining nutrition and exercise may further improve muscle protein synthesis and increase muscle mass [17]. It should be mentioned that the impact of combined nutritional care with physical exercise specifically on body composition is not clear yet [18–23]. Thus, the present systematic review of combined nutritional and exercise interventions in upper GI cancer patients aimed to determine whether these interventions are an effective approach for preserving muscle mass. In addition, these care programs need to be evaluated to define optimal intervention design and optimal timepoint for delivery within the cancer trajectory, i.e., prehabilitation or rehabilitation. Moreover, patients' acceptance and adherence to these programs need to be reviewed, as the effectiveness and acceptance of nutritional and exercises interventions may be different in patients with upper GI cancer compared to other cancer types, owing to the impact of surgery on food intake and postoperative complications, such as food intolerance and malabsorption.

To the authors' knowledge, this is the first systematic review to research the effectiveness of combined nutritional and exercise interventions on muscle wasting and quality of life in upper GI cancer survivors.

The primary objective of this systematic review was to evaluate the effectiveness of nutritional interventions combined with exercise in improving outcomes in upper GI cancer patients. Specifically, it assessed whether these types of interventions, as compared to usual/standard care, can significantly prevent or reverse muscle wasting and functional decline, improve health-related quality of life, and decrease treatment complications. Moreover, this systematic review aimed to discover the acceptability of these interventions in patients diagnosed with upper GI cancer.

2. Materials and Methods

2.1. Study Registration

This study is registered with the PROSPERO database (registration number: CRD42021239675) and has been reported using the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) checklist [24].

2.2. Study Eligibility Criteria

The following criteria were considered for selecting eligible studies.

2.3. Study Designs

All types of randomized clinical trials (RCTs), excluding feasibility and pilot studies, were included. Cross-sectional, cohort, case-control, and case report studies were excluded. Although review and systematic review articles were excluded, reference lists and citations of relevant reviews were screened for locating additional relevant studies.

2.4. Publication Type

Original studies published in peer-reviewed journals that were reported in English were considered eligible.

2.5. Participants

Studies that recruited adults (aged ≥ 18 y) diagnosed with upper GI cancer, namely esophageal cancer, gastric cancer, hepatic cancer, pancreatic cancer, and cancer of the biliary system, were included, excluding studies that enrolled patients receiving interventions as part of a palliative care plan.

2.6. Intervention

Studies investigating the effects of multidisciplinary care programs combining nutritional and exercise intervention were included. Studies that provided any types of nutritional and exercise interventions were included. No limitation on delivery mode, minimum or maximum intervention period, follow up, and type of setting that studies were conducted in was applied.

2.7. Comparators

Studies that considered standard or usual care provided to patients as the control group were included.

2.8. Outcomes

The following outcomes were analyzed and graded in the present systematic review if reported in the included studies.

- Body composition (fat mass, fat-free mass, muscle mass) and anthropometric measurements (weight, BMI, waist/hip circumference, triceps skinfold).
- Health-related quality of life (HRQOL).
- Functional outcomes (handgrip strength, exercise capacity, and physical activity level).
- Dietary intake.
- Post-operative complications.

2.9. Search Strategy and Information Sources

A comprehensive literature search was conducted to identify all published and unpublished studies. Electronic databases, including MEDLINE, EMBASE, Web of Science, Cochrane Library, and CINAHL, were searched up to 26 August 2020.

The specialized search strategy was designed by the subject librarian (DM) with no limitation on type of studies, language, study design, time frame etc. The full search strategy is included as Supplementary Materials [25]. The search result that was achieved through this search strategy was reviewed by authors (FS) to confirm that an acceptable portion of relevant studies had been retrieved by using it.

2.10. Data Management

All search results were imported to Covidence software (www.covidence.org) to facilitate the review process. Duplicates were excluded and multiple reports of one study were collated.

2.11. Selection Process

Authors SD and FS independently screened the titles and abstracts. Subsequently, SD and FS reviewed full texts independently to identify studies that met the inclusion criteria. Reasons for exclusion of the ineligible studies were recorded. Any disagreements in screening and full-text review were resolved through discussion.

2.12. Data Collection

FS performed data extraction independently. Extracted data included study title; publication date; correspondent author's name and contact; study design; setting or location; sample size; participant details, including age, gender, cancer type, and treatment; and intervention design, including details of the nutrition and exercise components, mode

of delivery, duration of intervention, comparators, adherence rate to intervention, withdrawal rate, adverse events, and reported outcomes (body composition and anthropometric measurements, quality of life, physical functioning, post-operation complications).

2.13. Risk of Bias in Individual Studies

The revised Cochrane Risk of Bias tool (RoB2) was used to determine the risk of bias [26]. SD and FS independently assessed the risk of bias for each included study. Disagreements were resolved by discussion.

2.14. Measuring the Intervention Effect

Extracted continuous data are presented as mean difference (MD) and standard deviation (SD) or parameter estimate (β) and confidence interval (CI). For dichotomous data (such as adverse events, complications, etc.), the treatment effect is reported as number and percent.

2.15. Data Synthesis

A meta-analysis was not appropriate due to the heterogeneity of studies and a high degree of variance in interventions, study period, and measured outcomes observed in the included studies. A narrative summary of the results has been provided instead.

3. Results

A total of 4780 articles were identified. After removing duplicates and screening titles and abstracts, 148 articles were selected for full-text review, of which 5 studies met the inclusion criteria [15,22,27–29]. A detailed record of the selection process and PRISMA flow diagram is presented in Figure 1. An overview of the included studies is provided in Table 1. High variation in intervention design and standard care was observed in the included studies and a detailed description of the interventions is provided in Table 2.

Table 1. Overview of the included studies.

Author, Year	O'Neill et al., 2018	Yu-Juan Xu et al., 2015	Yu-Ling Chang et al., 2020	Minnella et al., 2018	Ausania et al., 2019
Country	Ireland	Taiwan	Taiwan	Canada	Spain
Cancer type	Esophagogastric	Esophageal	Esophageal	Esophagogastric	Pancreaticoduodenal
Timepoint of Intervention	Rehab (6 mo–5 yrs. Post-treatment)	During neoadjuvant chemoradiotherapy	Rehab (Immediately after surgery)	Prehab	Prehab
Participant No (Randomized)	43 (Intervention = 21, Control = 22)	59 (Intervention = 30, Control = 29)	88 (Intervention = 44, Control = 44)	68 (intervention = 34, control = 34)	40 (intervention = 18, Control = 22)
Participants' Sex (%Male)	81%	92.9%	90.9%	74.5%	55%
Participants' Age	Intervention: 67.19 $\pm$ 7.49 Control: 64.14 $\pm$ 10.46	Intervention: 58.1 $\pm$ 9.6 Control: 61.1 $\pm$ 9.0	Intervention: 56 $\pm$ 8.9 Control: 56 $\pm$ 10.0	Intervention: 67.3 $\pm$ 7.4 Control: 68.0 $\pm$ 11.6	Intervention: 66.1 (38–80) Control: 65.7 (38–81)
Recruitment rate	40.3%	92%	94.6%	60.1%	96%
Dropout rate	9.3%	5.1%	9.1%	25%	16%
Adherence	Supervised exercise: 94 $\pm$ 12% Unsupervised exercise: 78 $\pm$ 27	Nutritional sessions: 100% Walking sessions: 68% (32%–100%). Target maximal heart rate was achieved in 71% 54% completed more than 80% of walking sessions	NR	63%	NR
Adverse event	None	NR	NR	None	NR

Abbreviations: NR Not reported.

Table 2. Description of interventions in included studies.

Author, Year	O'Neill et al., 2018	Yu-Juan Xu et al., 2015	Yu-Ling Chang et al., 2020
Exercise component	14 Supervised aerobic training (treadmill walking, stationary cycling, cross-training) 14 Supervised resistance training (free weights, horizontal leg press) 37 unsupervised home-based aerobic (walking or stationary cycling) 10 unsupervised resistance training (using TheraBand)	Nurse-supervised walking three times per week 5-min warm-up (ankle circles, leg swings, pelvic loops, arm circles), 20 min of hallway ambulation at the patient's own pace before or after radiotherapy Intensity of 60%	Home-based walking at a moderate intensity level after meals, 3–5 days per week for 30 min, or a total of 150 min per week Desired heart rate reserve percentage: 55–65%.
Nutrition component	Nutritional assessment 1:1 Dietary counselling Personalized nutritional advice Number of sessions depended on patients' status	Weekly dietetic consult (weight and intake assessment, advice on eating and feeding difficulties, food or formula selection, skills for modifying food texture, and oral care before and after eating)	E-Books containing dietary guidance and advice
Other components	7 group education sessions delivered by surgeon, dietitian, physiotherapist, occupational therapist, psychotherapist specialized in mindfulness	None	e-books (exercises, symptom management and psychological advice) Online nurse support to answer survivors' questions An online discussion group referring patients to appropriate medical professionals for an in-person visit if needed
Control	Standard care (standard clinical care as per best practice)	Standard care (nutritional and self-care advice from nurses)	Standard care (conventional postoperative feeding, wound care, and regular postoperative rehabilitation exercises)
Duration	12 W	4–5 W	12 W
Author, Year	Minnella et al., 2018		Ausania et al., 2019
Exercise component	Home-based aerobic exercise (brisk walk, jogging, or cycling) 3 days per week, 30 min each day (including 5-min warm-up and 5-min cooldown) Strengthening activity, 3 sets of 8 to 12 repetitions for 8 muscle groups using TheraBand, 1 day/week, 30 min (including 5-min flexibility and 5-min stretching) a weekly telephone call by a kinesiologist		5 sessions (60 min each) high-intensity endurance training performed on a cycle-ergometer stationary bicycle, 10 min warm-up cycling, 20 min muscle toning exercise, 20 min aerobic exercise, 10 min cool-down. Unsupervised home-based functional exercises and breathing exercises
Nutrition component	Nutritional assessment and consult Whey protein supplement if required Weekly phone call by a dietitian		Nutritional assessment Nutritional support (liquid oral nutrition supplements and vitamin supplements.) Total parenteral nutrition if required Follow-up in the outpatient clinic
Other components	None		Metformin or insulin if required for BS control Blood glucose monitor to check glucose level at home Pancreatic enzymes replacement therapy
Control	Standard care (perioperative care according to the ERAS Society Guideline protocol, + Nutritional counselling session)		Standard care (nutritional counselling, physical activity recommendation and advice on smoking cessation and if indicated pancreatic enzyme supplementation, dietitian referral, preoperative biliary drainage)
Duration	Median 36 days (IQR, 17–73)		Median 12.6 days (Minimum 7 days was planned in intervention)

Abbreviations: W weeks, ERAS enhanced recovery after surgery, IQR interquartile range, BS blood sugar.

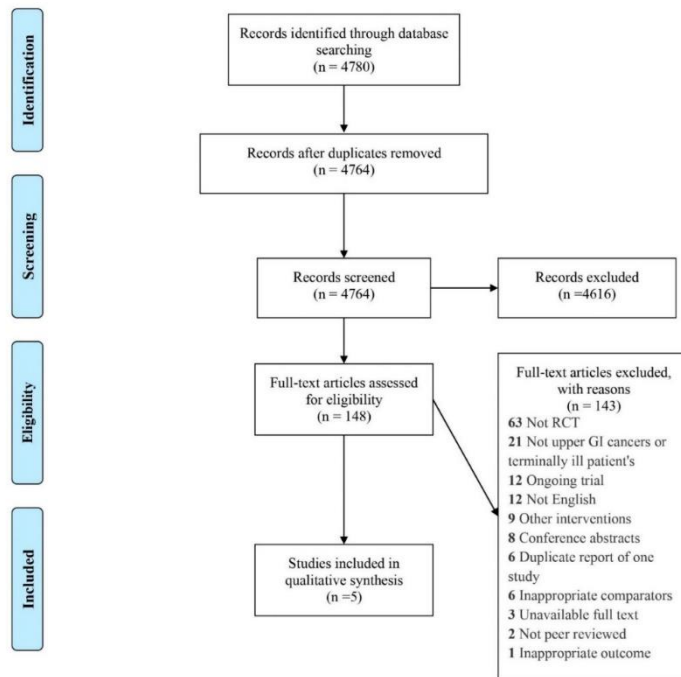


Figure 1. PRISMA flow diagram.

With regards to sample size calculation, four of the included studies conducted a power calculation (80% power) to estimate the minimum required sample size [15,22,27,29]. One of the studies failed to conduct a power calculation before starting the trial although post hoc analysis showed a power of 83–100% for the primary outcomes except lean muscle mass, for which 48% power was indicated to detect group differences [28]. Reported recruitment rates ranged from 40.3% to 96% and the dropout rates ranged from a minimum of 5% to a maximum of 25%. The adherence rate ranged from 32% to 94%. None of the studies reported major adverse events related to the intervention. A summary of the results is presented in Table 3. The result of the risk of risk bias assessment is shown in Figure 2.

Table 3. Summary of results.

Author, Year	Relevant Outcome Measure	Results
O'Neill et al., 2018	Cardiorespiratory fitness (CPET, VO2 Peak) * HRQOL (EORTC-QLQ-C30) Body composition & anthropometric measurements (BIA, weight, height, waist and midarm circumference) Physical activity level (Actigraph GT3Xp) Dietary intake (24 h food recall)	Significant improvement in cardiorespiratory fitness post-intervention (VO2 Peak: 22.20 ± 4.35 versus 21.41 ± 4.49, $p = 0.000$) and 3 months post-intervention (VO2 Peak 21.75 ± 4.27 versus 20.74 ± 4.65, $p = 0.001$) No significant changes in HRQOL, except cognitive function higher in the control group following the intervention [100.00 ± 16.67 compare to 83.33 ± 16.67, $p = 0.031$] No changes in anthropometric measurements and body composition except higher mid-arm circumference in the intervention group at post-intervention assessment (28.35 ± 4.70 compare to 28.55 ± 5.57, $p = 0.019$) No changes in PAL Not reported
Yu-Juan Xu et al., 2015	Functional capacity (6 MWT, HGS) * Body composition & anthropometric measurements (BIA, weight) * Treatment tolerance (chemotherapy or radiotherapy interruption, unplanned hospital admission, grade > 2 neutropenia, fever > 38.5 °C, intravenous nutritional support, wheelchair use)	100 m less decline in walk distance ($p = 0.012$) 3 kg less decrease in hand-grip strength ($p = 0.002$) Non-significant less muscle mass loss (1.3 kg, $p = 0.057$) Significant less weight loss (2.7 kg, $p < 0.001$) No differences in chemotherapy/radiotherapy interruption, unplanned hospital admissions, neutropenia, fever Lower rates of parenteral nutrition support (3.6% compared to 50%, $p < 0.001$) Lower rate of wheelchair uses (0% compared to 32.1%, ($p < 0.01$))
Yu-Ling Chang et al., 2020	Exercise capacity (CPET (VO2 max), 6 MWT) HRQOL (EORTC-QLQ-C30 & EORTC QLQ-OES18) * Albumin Daily steps (smart bracelet) BMI	Higher maximal oxygen consumption ($\beta = 2.61$, 95% CI 1.54, 3.69, $p < 0.001$), effect size = 0.97 Greater distance on the six-minute walking test ($\beta = 83.30$, 95% CI 52.60, 113.99, $p < 0.001$), effect size = 0.36 Significantly better HRQOL (EORTC-QLQ-C30) at different time points following discharge. Physical (1 and 3 months), role (1, 3, and 6 months), emotional (1 month), social (3 months) and global health (3 months), insomnia (1 and 3 months) and nausea/vomiting (3 and 6 months). Improvement in esophageal cancer-specific symptoms (EORTC QLQ-OES18), dry mouth (1 month), dysphagia (3 months), loss of taste (1 and 6 months) Higher levels of albumin at 3 months after discharge ($\beta = 0.32$, 95% CI 0.09, 0.54, $p < 0.01$), minimal effect size Data not reported No changes in BMI
Minnella et al., 2018	Functional capacity (6 MWT) * Post-operative morbidity (CDC & CCI), length of hospital stay, 30-day hospital visit, readmission rate, death, adherence to planned neoadjuvant therapy	Improvement in functional capacity before (mean [SD] 6 MWD change, 36.9 [51.4] vs. −22.8 [52.5] m; $p < 0.001$) and after surgery (mean [SD] 6 MWD change, 15.4 [65.6] vs. −81.8 [87.0] m; $p < 0.001$). No differences were observed in post-operative outcomes
Ausania et al., 2019	Cardiopulmonary status (FEV1, FVC, O2 sat%) Functional capacity (10 MWT & HGS) Post-operative complications (CDC) *, pancreatic leak (type B&C), DGE, HS, readmission	Improvement respiratory function in the intervention group compared to baseline, changes in FVC (l, median) = 0.6, FEV1 (l, median) = 0.48, O2 sat% = 0.3 Improvement in functional capacity in the intervention group compared to baseline 10-m walk test (1.2 s), HGS (left hand = 5.9, right hand = 4.8) No differences in post-op complications, hospital stay, readmission between intervention and control group. Significantly lower DGE, 5.6% vs. 40.9% in the standard care group ($p = 0.01$)

Abbreviations: CPET Cardiopulmonary Exercise Testing, VO2 Peak highest value of oxygen uptake, HRQOL Health-Related Quality Of Life, EORTC-QLQ-C30 The European Organization for Research and Treatment of Cancer Quality of Life questionnaire-Cancer, BIA Bioelectrical Impedance Analysis, 6 MWT Six-Minute Walk Test, HGS Hand Grip Strength, VO2 max Maximum rate of oxygen uptake, EORTC QLQ-OES18 EORTC esophageal cancer-specific questionnaire, BMI Body Mass Index, CDC Clavien-Dindo classification, CCI Comprehensive Complication Index, FEV1 forced expiratory volume in one second, FVC forced expiratory volume, O2 sat oxygen saturation, 10 MWT 10 Meter Walk Test, DGE delayed gastric emptying, HS Hospital Stay. * Primary outcome/s of the study.

Study	Risk of bias domains					Overall
	D1	D2	D3	D4	D5	
O'Neill et al, 2018						
Yu-Juan Xu et al, 2015						
Yu-Ling Chang et al, 2020						
Minnella et al, 2018						
Ausania et al, 2019						

Domains:
D1: Bias arising from the randomization process.
D2: Bias due to deviations from intended intervention.
D3: Bias due to missing outcome data.
D4: Bias in measurement of the outcome.
D5: Bias in selection of the reported result.

Judgement
 High
 Some concerns
 Low

Figure 2. Risk of bias assessment. Risk of bias completed using the revised Cochrane Risk of Bias tool (RoB2).

3.1. Health-Related Quality of Life

The effects of combined nutrition interventions with physical training in improving health-related quality of life (HRQOL) were investigated in only two studies with inconsistent results [22,29]. Both studies used the European Organization for the Research and Treatment of Cancer-Core Quality of Life Questionnaire (EORTC-QLQ-C30) for measuring changes in HRQOL and the esophageal cancer-specific quality of life questionnaire (EORTC QLQ-OES18) was additionally used by Yu-Ling Chang [22,29]. O'Neill et al. examined the effect of a 12-week multidisciplinary rehabilitation program in a cohort of esophagogastric cancer survivors in which they did not observe any significant improvements in HRQOL following the intervention. Of note, a significantly higher score in cognitive function was reported in the control group ($F(1, 38) = 4.992, p = 0.031, \eta^2 (\text{eta squared}) = 0.12$) following the intervention [22]. In the second study by Yu-Ling Chang et al., delivering a 12-week nurse-led exercise and health education informatics program resulted in a significant improvement in HRQOL [29]. In this study, significant improvement in functioning scales, global health status, and symptom domains were reported in both the control and intervention groups ($p < 0.01$ to $p < 0.001$) and there were significant differences between groups regarding HRQOL domain scores at varied time points. For instance, in the intervention group, a significant improvement was observed in the functional domain at 1 month ($\beta = 10.02, 95\% \text{ CI } 3.46, 16.58, p < 0.01$) and 3 months ($\beta = 10.25, 95\% \text{ CI } 1.55, 18.93, p < 0.05$) after discharge while the role functioning score was significantly higher at all three time points (1 month: $\beta = 11.68, 95\% \text{ CI } 0.90, 22.47, p < 0.05$; 3 months: $\beta = 14.03, 95\% \text{ CI } 2.43, 25.64, p < 0.05$; 6 months: $\beta = 16.12, 95\% \text{ CI } 4.21, 28.03, p < 0.01$) following discharge. Significant improvements in emotional functioning were observed at 1-month post-discharge ($\beta = 8.91, 95\% \text{ CI } 2.67, 15.15, p < 0.01$) and in social functioning at 3 months after discharge ($\beta = 9.25, 95\% \text{ CI } 0.20, 18.29, p < 0.05$). Global QOL showed greater improvement in the intervention group 3 months following hospital discharge ($\beta = 10.71, 95\% \text{ CI } 2.48, 19.94, p < 0.05$). Regarding symptom domains, following GEE analysis, lower scores for insomnia at 1 and 3 months post-discharge ($\beta = -14.50, 95\% \text{ CI } -22.91, -6.09, p < 0.01$; and $\beta = -12.81, 95\% \text{ CI } -2.74, -0.89, p < 0.05$, respectively) were reported in the intervention group. Calculated scores for nausea and vomiting were also lower in the intervention compared to control groups at 3 and 6 months following discharge from hospital ($\beta = -12.62, \text{ CI } -20.48, -4.79, p < 0.01$; and $\beta = -11.67, 95\% \text{ CI } -20.77, -2.57, p < 0.05$, respectively) [29]. Analysis of esophageal cancer-specific quality of life scores (QOL-OES-18) showed lower scores for dry mouth ($\beta = -8.68, 95\% \text{ CI } -16.86, -0.50, p < 0.05$) at the one-month post-discharge assessment; similarly, there were lower scores for dysphagia at 3 months ($\beta = -12.56, 95\% \text{ CI } -21.34, -3.76, p < 0.01$) and at one and six months following discharge for loss of taste ($\beta = -8.30, 95\% \text{ CI } -14.41, -2.19, p < 0.01$;

and $\beta = -13.66$, 95% CI $-2240, -4.93$, $p < 0.01$ respectively) in the intervention group versus the control [29].

3.2. Body Composition and Muscle Mass

Body composition, muscle mass, or anthropometric measurements were measured outcomes in three studies [22,28,29]. Body composition was measured by bioelectrical impedance analysis (BIA) in the studies by O'Neill and Yu-Juan Xu, and no significant differences in muscle mass were detected following the intervention [22,28]. There were inconclusive results regarding changes in anthropometric measurements. O'Neill et al. reported a higher mid-arm circumference in the intervention group at the post-intervention assessment (28.35 ± 4.70 compared to 28.55 ± 5.57 , $p = 0.019$) and no changes in other anthropometric measurements of weight, BMI, and waist circumference. This was similar to the results of the Yu-Ling Chang study that reported no changes in body mass index. However, Yu-Juan Xu reported significantly less weight loss (2.7 kg, $p < 0.001$) following the intervention [22,28,29].

3.3. Physical Function and Cardiorespiratory Fitness

Functional capacity and cardiorespiratory fitness outcomes were examined in all five included studies [15,22,27–29]. Cardiorespiratory fitness was assessed in two studies by the cardiopulmonary exercise test (CPET) and both RCTs reported significant improvement in cardiorespiratory fitness following the rehabilitative intervention [22,29]. In the ReStOre study by O'Neill et al., the intervention group had a higher $\text{VO}_{2\text{Peak}}$ compared to the control group (22.20 ± 4.35 versus 21.41 ± 4.49 , $p = 0.000$) post-intervention as well as at the 3-month post-intervention assessment ($\text{VO}_{2\text{Peak}}$ 21.75 ± 4.27 versus 20.74 ± 4.65 , $p = 0.001$) [22]. In the trial by Yu-Ling Chang et al., the intervention group had significantly higher $\text{VO}_{2\text{max}}$ value post-intervention ($\beta = 2.61$, 95% CI 1.54, 3.69, $p < 0.001$) [29].

Three studies examined changes in functional capacity by the 6-min walk test (6 MWT) and a significant improvement was observed in all of them post-intervention [15,28,29]. Yu-Juan Xu et al. reported less decline in the 6 MWT walk distance following a walk and eat intervention during neoadjuvant chemoradiotherapy, compared to control (-18 ± 75 m vs. -118 ± 160.5 ; group difference: 100 m, adjusted $p = 0.012$) [28]. Likewise, a significantly improved 6 MWT was observed ($\beta = 83.30$, 95% CI 52.60, 113.99, $p < 0.001$) following a rehabilitation intervention by Yu-Ling Chang et al. [29]. Moreover, another prehabilitation study showed an improvement in walking distance both before surgery (mean [SD] 6 MWD change, 36.9 [51.4] vs. -22.8 [52.5] m; $p < 0.001$) and after surgery in the intervention group versus control (mean [SD] 6 MWD change, 15.4 [65.6] vs. -81.8 [87.0] m; $p < 0.001$) [15].

Two studies measured hand-grip strength and both reported improvements following a multidisciplinary intervention. Yu-Juan Xu et al. observed a 3 kg less decrease in hand-grip strength in the intervention group (-1.1 ± 2.5 kg vs. -4.1 ± 4.0 kg, $p = 0.002$) and Ausania reported an increase of 4.8 and 5.9 kg in right and left-hand grip strength following prehabilitation, although this outcome was measured only in the intervention group [27,28].

3.4. Dietary Intake

None of the included studies reported dietary intake data. Although O'Neill et al. reported dietary assessment, dietary intake data were not reported in this study [22]. Likewise, Ausania and Minnella assessed nutritional intake and dietary habits before the intervention but no data regarding dietary intake was included in the results of these studies [15,27]. Similarly, Yu-Juan Xu reported an evaluation of dietary intake during weekly nutritional consult sessions, yet no dietary intake data was presented in this study [28].

3.5. Post-Op Complications/Other Outcomes

Three studies looked at complications post-surgery, and all reported no significant differences in the number or severity of complications, hospital stay, and readmission in

the intervention group compared to standard care [15,27,28]. However, Yu-Juan Xu et al. observed lower rates of parenteral nutrition support (3.6% compared to 50%, $p < 0.001$) as well as a lower rate of wheelchair use (0% compared to 32.1%, $p < 0.01$) in the intervention group [28]. Additionally, Yu-Ling Chang reported that the intervention group had significantly higher levels of albumin at 3 months post-discharge ($\beta = 0.32$, 95% CI 0.09, 0.54, $p < 0.01$) compared to the usual care group [29].

4. Discussion

This systematic review describes the effectiveness of multidisciplinary programs, whose core component was nutritional and exercise interventions, in improving outcomes in patients diagnosed with upper GI cancers. Nutritional interventions were mainly individual consults alone or along with prescribing oral nutritional supplements to ensure energy and protein requirements were met. It is noteworthy that the rationale behind prescribing nutritional supplement or support (PN) was not explained in the Ausania et al. and Minnella et al. studies. This is important as a lack of details regarding the delivered intervention may complicate interpretation of the reported results in these studies [15,27]. Exercise training included supervised and/or home-based walking and/or resistance training. Although there is growing interest in multidisciplinary care plans for cancer patients, acknowledging the potential beneficial effects of these interventions on patients' quality of life, a limited number of studies have examined the effectiveness of these interventions in upper GI cancers to date [30–32].

Considering the results of the reviewed studies, interventions incorporating nutrition and exercise appear to be safe and acceptable in patients diagnosed with upper GI cancer, with a higher rate of compliance with supervised interventions [22,28]. However, only three studies reported compliance with the intervention, of which a single study reported adherence to nutrition consult sessions [15,22,28]. O'Neil et al. did not report adherence to dietetic consult and education sessions and Minnella et al. reported overall compliance with prehab intervention rather than specifying adherence to exercise and nutrition components separately [15,22]. A lack of sufficient data regarding the adherence rate in some of the reviewed studies makes it difficult to understand whether non-significant findings were due to ineffectiveness of the interventions or lack of compliance with the intervention. Additionally, reporting adherence to different components of a multidisciplinary intervention is important as it might help design acceptable and practical multimodal interventions. Moreover, it would be worthwhile to further examine factors that may play a role in patients' enrolment and completion of these interventions, such as participants' nutritional and psychological status, physical function, fatigue and weakness at baseline, transportation difficulties, and familial and professional commitments [33,34]. Acquiring more data on the underlying reasons for non-participation, withdrawal, and non-compliance is essential to design convenient, acceptable, and practical interventions.

Regarding physical functioning, the promising effects of combined nutritional interventions with physical training on functional and cardiorespiratory outcomes have been reported in several studies [35,36]. The included studies in this systematic review showed consistent results regarding improvements in patients' physical functioning following multimodal interventions with core nutrition and exercise components. Whilst the reported functional outcomes varied among different studies, CPET and 6 MWT demonstrated an improvement following the intervention [15,22,28,29]. This improvement in physical performance is important as higher physical performance and functioning has been associated with improved quality of life, treatment response, and prognosis in cancer patients in several studies [37–39]. Although, further high-quality studies are needed to confirm the positive effects of multidisciplinary interventions on physical functioning due to the poor quality of the included studies.

The present systematic review showed that changes in body composition following multimodal interventions in upper GI cancer patients have been understudied and the limited available evidence showed mixed results. As mentioned previously, muscle

wasting is associated with impaired quality of life and reduced survival following cancer treatments [40]. However, the optimal care that can effectively counteract cancer-associated cachexia has not been defined yet [40]. Cachexia and muscle wasting have received much attention in the scientific literature in recent years, but there remains limited evidence regarding the effectiveness of combined nutritional and exercise interventions in improving impaired body composition [16,41]. It is acknowledged that meeting patients' protein and energy requirements is crucial to maintain muscle mass during cancer treatment and recovery, and exercise interventions may be effective in preventing and reversing muscle wasting [42–44]. It is worthy of note that, although four of the included studies assessed dietary intake at some time point of the study, none of them reported dietary intake data [15,22,27,28]. This could be considered as one of the factors that resulted in a high risk of bias in the reviewed studies as lack of dietary intake data makes it difficult to examine whether nutritional adequacy had been achieved by these interventions. Dietary intake assessment is crucial to ensure whether adequate protein and energy intake has been supported during multidisciplinary interventions. This is even more important in UGI cancer survivors as they experience severe reductions in their dietary intake and impaired food tolerance following surgeries [11].

The increased survival rate of patients diagnosed with cancer is accompanied by an acknowledgement of the need to ensure good quality of life. Cancer can negatively impact the quality of life and improved HRQOL may be associated with lower mortality and recurrence [45]. In the present review, changes in patients' quality of life were assessed in two studies with inconsistent results. Assessing changes in HRQOL during and beyond cancer, and following interventions can assist researchers to have a better understanding of the effects of treatment on patients' physical, mental, and emotional status [46].

The multidisciplinary interventions reviewed here failed to show any beneficial effects on post-operation complications and hospital stay. Although contradictory results were reported in other non RCT studies, with a lower mortality rate and severity of complications or shorter hospital stay following a multidisciplinary prehabilitation program [47,48], their small sample size and methodological limitations may limit their power to examine these outcomes properly. Optimization of patients' nutritional and physical status before the surgery has been recommended for improving postoperative outcomes [49]. More high-quality research studies are needed to identify the most effective prehabilitation and/or rehabilitation interventions based on cancer site and type of surgery to improve operative outcomes.

Although this systematic review aimed to examine the optimal timepoint for delivery of multidisciplinary interventions within the cancer trajectory, a high risk of bias in the reviewed studies, and a high degree of variance regarding the design and delivery of the intervention and measured outcome prevented a clear conclusion on this issue. The limited studies that examined the effectiveness of prehabilitation versus rehabilitation in cancer reported inconsistent results from observing no significant differences in functional walking capacity to better responses to prehabilitation compared with rehabilitation [50,51]. Therefore, the optimal timepoint for providing multidisciplinary care programs is yet to be known and requires further studies.

It should be acknowledged that the present systematic review has several limitations. First, although a comprehensive search was conducted to locate all relevant studies, some studies may have been missed. Secondly, a considerable number of ongoing trials were identified (12 relevant unpublished ongoing trials) and, when contacted, the authors of these studies reported that they were still ongoing, stalled due to the COVID-19 pandemic, or in pre-publishing stages [25]. The results of these studies may be helpful to yield a more explicit conclusion.

Moreover, it should be mentioned that the standard care varied significantly across different settings and in most settings, control groups were provided with standard care consisting of some nutrition and/or exercise prehabilitation or rehabilitation care, which may be considered as a confounding factor to determine the significant effects of these

interventions on postoperative complications as well as nutritional status and quality of life. Furthermore, the importance of reporting details of standard care needs to be highlighted as it may complicate the interpretation of the results. For instance, it is unclear whether the lack of significant changes in body composition, HRQOL, and PA in the O'Neill study was due to the high quality of standard care as the details of standard care were not discussed [22].

On account of scarce evidence, and the variance and heterogeneity of studies in terms of intervention design, duration of study and follow-up, the time point of intervention delivery, and measured outcomes, etc., it was impossible to perform meta-analysis and/or draw a firm conclusion on the effectiveness of these interventions on measured outcomes.

Adding to this, as indicated in Table 3, the primary outcome varied significantly across the included studies, which may limit meaningful comparisons across studies and evidence synthesis. Moreover, as primary outcomes are the basis of conducting power and sample size calculations, some studies may not be adequately powered to detect the group differences for a specific outcome of interest in this systematic review. For instance, the Yu-Juan Xu et al. study has a low power (48%) for detecting group differences in lean muscle mass [28].

Finally, as the results of the risk of bias assessment indicated, more high-quality and well-designed RCTs are required to draw more robust judgment on the effectiveness of these multidisciplinary interventions, specifically on body composition and quality of life. Some key points need to be considered to reduce the risk of bias in future studies, including considering blinded assessment and analysis, dietary intake assessment, and reporting dietary intake data to ensure nutritional adequacy, providing greater details of delivered intervention, such as the rationale behind prescribing nutrition support or supplements, providing greater details regarding adherence to different components of the intervention, and describing details of standard/control care.

5. Conclusions

Limited evidence is available on the effectiveness of multimodal interventions, with a core component of nutrition and exercise, in improving outcomes in upper GI cancer patients. Although studies showed an improvement in physical function and exercise capacity, the evidence regarding positive changes in muscle mass and quality of life was scarce and conflicting. In conclusion, due to the poor quality of limited available evidence, further high-quality studies are warranted to examine the effectiveness of multidisciplinary care programs in improving outcomes in upper GI cancers with a focus on improving the body composition and quality of life in these patients. Considering a core outcome set for measuring the clinical effectiveness of multidisciplinary supportive care programs may improve the consistency and quality of future investigations [52]. Moreover, it may facilitate more meaningful comparison across studies and support evidence synthesis.

Supplementary Materials: The following are available online at <https://www.mdpi.com/article/10.3390/nu13082842/s1>. Supplementary file: The effectiveness of nutrition interventions combined with exercise in upper gastrointestinal cancer- a systematic review [25].

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Appendix XIII Search terms systematic review (Chapter 6)

Searches were completed on 26/08/20.

Number of search result per each database:

- EMBASE - 3263
- Medline - 286
- Web of Science - 1653 Cochrane Library - 158 CINAHL – 109
- Total = 5469
- After removing deduplications = 4780

EMBASE

1. 'digestive system tumor cell line'/exp OR 'digestive system tumor'/exp
2. ((oesophag* OR esophag* OR gastroesophag*) NEAR/3 (cancer* OR neoplasm* OR tumo?r* OR adenocarcinoma* OR carcinoma*)):ab,ti
3. ((stomach OR gastric) NEAR/3 (cancer* OR neoplasm* OR tumo?r* OR adenocarcinoma* OR carcinoma*)):ab,ti
4. (('bile duct*' OR gallbladder* OR biliary OR liver OR hepato* OR hepatic) NEAR/3 (cancer* OR neoplasm* OR tumo?r* OR adenocarcinoma* OR carcinoma*)):ab,ti
5. (pancrea* NEAR/3 (cancer* OR neoplasm* OR tumo?r* OR adenocarcinoma* OR carcinoma*)):ab,ti
6. (('upper gi' OR 'upper gastrointestinal') NEAR/3 (cancer* OR neoplasm* OR tumo?r* OR adenocarcinoma* OR carcinoma*)):ab,ti
7. #1 OR #2 OR #3 OR #4 OR #5 OR #6
8. 'nutrition education'/exp OR 'diet therapy'/exp OR 'cooking'/exp OR 'nutrition'/exp OR 'enteric feeding'/exp OR 'parenteral nutrition'/exp OR 'nutritional support'/exp OR 'nutrition service'/exp OR 'cachexia'/exp
9. (Nutrition* NEAR/3 (intervention* OR therap* OR education OR support* OR treatment* OR consultation? OR consult? OR cancer* OR counsel*)):ti,ab
10. ((diet? OR dietary) NEAR/3 (intervention* OR therap* OR education OR support* OR treatment* OR consultation? OR consult? OR cancer* OR counsel* OR restrict*)):ti,ab

11. (Parenteral NEAR/3 (alimentation OR feed* OR fluid OR hyperalimentation)):ti,ab
12. (Nutrition* NEAR/3 (product* OR supplement* OR support* OR mixture)):ti,ab
13. (Diet* NEAR/3 (product* OR supplement* OR support* OR mixture)):ti,ab
14. ((Diet* OR nutrition*) NEAR/5 (educat* OR guideline*)):ti,ab
15. #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14
16. 'exercise'/exp OR 'kinesiotherapy'/exp OR 'physical activity'/exp OR 'physical activity, capacity and performance'/de OR 'training'/de OR 'endurance'/de OR 'exercise tolerance'/de OR 'physical capacity'/de OR 'sport'/exp
17. (exercis* OR isometric* or isotonic* or isokinetic*):ti,ab
18. ((resistance OR strength*) NEAR/3 train*):ti,ab
19. ((physical* or motion* or cardiopulmonary or cardiorespiratory) NEAR/3 (fit* or therap*)):ti,ab
20. (treadmill* or cross-train* or rowing or sport* OR exercise* OR "physical activit*" OR aerobic* OR run or jog* or running OR walk or walks or walking OR gym* OR yoga OR pilates OR "recreation* activit*" OR zumba or salsa* OR cycling or bicycle or bike or swim* or dance or dancer* or dances or dancing or HIIT):ti,ab
21. (circuit* NEAR/1 train*):ti,ab
22. (keep* NEAR/1 (active or fit)):ti,ab
23. #16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22
24. #7 AND #15 AND #23
25. 'conference abstract':it OR 'conference review':it OR 'editorial':it OR 'letter':it
26. #24 NOT #25

Medline (OVID)

1. exp Esophageal Neoplasms/ OR Stomach Neoplasms/ OR exp Biliary Tract Neoplasms/ or exp Liver Neoplasms/ or exp Pancreatic Neoplasms/ OR Gastrointestinal Neoplasms/
2. ((oesophag* OR esophag* OR gastroesophag*) ADJ3 (cancer* OR neoplasm* OR tumo?r* OR adenocarcinoma* OR carcinoma*)):ti,ab.
3. ((stomach OR gastric) ADJ3 (cancer* OR neoplasm* OR tumo?r* OR adenocarcinoma* OR carcinoma*)):ti,ab.
4. ((bile duct* OR gallbladder* OR biliary OR liver OR hepato* OR hepatic) ADJ3 (cancer* OR neoplasm* OR tumo?r* OR adenocarcinoma* OR carcinoma*)):ti,ab.
5. (pancrea* ADJ3 (cancer* OR neoplasm* OR tumo?r* OR adenocarcinoma* OR carcinoma*)):ti,ab.
6. ((upper gi OR upper gastrointestinal) ADJ3 (cancer* OR

- neoplasm* OR tumo?r* OR adenocarcinoma* OR carcinoma*).ti,ab.
7. or/1-6
 8. exp Nutrition Therapy/ OR Nutrition Assessment/ OR Cachexia/ OR Diet Records/ OR exp Nutrition Surveys/ OR Nutritional Status/ OR Dietetics/ OR Nutrition Policy/
 9. (Nutrition* ADJ3 (intervention* OR therap* OR education OR support* OR treatment* OR consultation? OR consult? OR cancer* OR counsel*)).ti,ab.
 10. ((diet? OR dietary) ADJ3 (intervention* OR therap* OR education OR support* OR treatment* OR consultation? OR consult? OR cancer* OR counsel* OR restrict*)).ti,ab.
 11. (Parenteral ADJ3 (alimentation OR feed* OR fluid OR hyperalimentation)).ti,ab.
 12. (Nutrition* ADJ3 (product* OR supplement* OR support* OR mixture)).ti,ab.
 13. (Diet* ADJ3 (product* OR supplement* OR support* OR mixture)).ti,ab.
 14. ((Diet* OR nutrition*) ADJ5 (educat* OR guideline* OR factor*)).ti,ab.
 15. or/8-14
 16. exp Exercise/ OR exp Exercise Therapy/ OR exp Physical Fitness/ OR exp "physical education and training"/ OR exp "Exercise Movement Techniques"/ or physical endurance/ or exercise tolerance/ OR Physical Exertion/ or exp Sports/ or Dancing/
 17. (isometric* or isotonic* or isokinetic* or exercis*).ti,ab.
 18. ((resistance OR strength) adj3 (train* OR exercise*)).ti,ab.
 19. ((physical* or motion* or cardiopulmonary or cardiorespiratory) adj3 (fit* or therap* or activit*)).ti,ab.
 20. (treadmill* or cross-train* or rowing or sport* or exercise* or physical* activit* or aerobic* or run or jog* or running or walk or walks or walking or gym* or yoga or pilates or "recreation* activit*" or zumba or salsa* or cycling or bicycle or bike or swim* or dance or dancer* or dances or dancing or physiotherapy* or physical therap*).ti,ab.
 21. (circuit* adj1 train*).ti,ab.
 22. (keep* adj1 (active or fit)).ti,ab.
 23. or/16-22
 24. 7 AND 15 AND 23

Web of Science

TS=(((oesophag* OR esophag* OR gastroesophag*) NEAR/2 (cancer* OR neoplasm* OR tumo*r* OR adenocarcinoma* OR carcinoma*)) OR ((stomach OR gastric) NEAR/2 (cancer* OR neoplasm* OR tumo*r* OR adenocarcinoma* OR carcinoma*)) OR ((“bile duct*” OR gallbladder* OR biliary OR liver OR hepato* OR

hepatic) NEAR/2 (cancer* OR neoplasm* OR tumo*r* OR adenocarcinoma* OR carcinoma*) OR (pancrea* NEAR/2 (cancer* OR neoplasm* OR tumo*r* OR adenocarcinoma* OR carcinoma*)) OR ((“upper gi” OR “upper gastrointestinal”) NEAR/2 (cancer* OR neoplasm* OR tumo*r* OR adenocarcinoma* OR carcinoma*)) AND ((Nutrition* NEAR/2 (intervention* OR therap* OR education OR support* OR treatment* OR consultation* OR consult* OR cancer* OR counsel*)) OR ((diet* OR dietary) NEAR/2 (intervention* OR therap* OR education OR support* OR treatment* OR consultation* OR consult* OR cancer* OR counsel* OR restrict*)) OR (Parenteral NEAR/2 (alimentation OR feed* OR fluid OR hyperalimentation)) OR (Nutrition* NEAR/2 (product* OR supplement* OR support* OR mixture)) OR (Diet* NEAR/2 (product* OR supplement* OR support* OR mixture)) OR ((Diet* OR nutrition*) NEAR/5 educat*)) AND ((exercis* OR isometric* OR isotonic* OR isokinetic*) OR ((resistance OR strength*) NEAR/2 train*) OR ((physical* OR motion* OR cardiopulmonary OR cardiorespiratory) NEAR/2 (fit* OR therap*)) OR (treadmill* OR cross-train* OR rowing OR sport* OR exercise* OR "physical activit*" OR aerobic* OR run OR jog* OR running OR walk OR walks OR walking OR gym* OR yoga OR pilates OR "recreation* activit*" OR zumba OR salsa* OR cycling OR bicycle OR bike OR swim* OR dance OR dancer* OR dances OR dancing OR HIIT) OR (circuit* NEAR/1 train*) OR (keep* NEAR/1 (active OR fit))))

CINAHL

1. (MH "Biliary Tract Neoplasms+") OR (MH "Liver Neoplasms+") OR (MH "Pancreatic Neoplasms+") OR (MH "Esophageal Neoplasms+") OR (MH "Stomach Neoplasms")
2. TI ((oesophag* OR esophag* OR gastroesophag*) N2 (cancer* OR neoplasm* OR tumo#r* OR adenocarcinoma* OR carcinoma*)) OR AB ((oesophag* OR esophag* OR gastroesophag*) N2 (cancer* OR neoplasm* OR tumo#r* OR adenocarcinoma* OR carcinoma*))
3. TI ((stomach OR gastric) N2 (cancer* OR neoplasm* OR tumo#r* OR adenocarcinoma* OR carcinoma*)) OR AB ((stomach OR gastric) N2 (cancer* OR neoplasm* OR tumo#r* OR adenocarcinoma* OR carcinoma*))
4. TI ((“bile duct*” OR gallbladder* OR biliary OR liver OR hepato* OR hepatic) N2 (cancer* OR neoplasm* OR tumo#r* OR adenocarcinoma* OR carcinoma*)) OR AB ((“bile duct*” OR gallbladder* OR biliary OR liver OR hepato* OR hepatic) N2 (cancer* OR neoplasm* OR tumo#r* OR adenocarcinoma* OR carcinoma*))
5. TI (pancrea* N2 (cancer* OR neoplasm* OR tumo#r* OR adenocarcinoma* OR carcinoma*)) OR AB (pancrea* N2 (cancer* OR neoplasm* OR tumo#r* OR adenocarcinoma* OR carcinoma*))
6. TI ((“upper gi” OR “upper gastrointestinal”) N2 (cancer* OR neoplasm* OR tumo#r* OR adenocarcinoma* OR carcinoma*)) OR AB ((“upper gi”

- OR "upper gastrointestinal") N2 (cancer* OR neoplasm* OR tumor* OR adenocarcinoma* OR carcinoma*))
7. S1 OR S2 OR S3 OR S4 OR S5 OR S6
 8. MH "Nutrition Education" OR MH "Nutritional Status" OR MH "Food Habits" OR MH "Diet" OR MH "Nutritional Counseling" OR MH "Nutritional Assessment" OR MH "Nutritional Requirements" OR MH "Nutritional Support" OR MH "Parenteral Nutrition" OR MH "Enteral Nutrition" OR MH "Dietary Supplements" OR MH "Cachexia"
 9. TI (Nutrition* N2 (intervention* OR therap* OR education OR support* OR treatment* OR consultation# OR consult# OR cancer* OR counsel*)) OR AB (Nutrition* N2 (intervention* OR therap* OR education OR support* OR treatment* OR consultation# OR consult# OR cancer* OR counsel*))
 10. TI ((diet# OR dietary) N2 (intervention* OR therap* OR education OR support* OR treatment* OR consultation# OR consult* OR cancer* OR counsel* OR restrict*)) OR AB ((diet# OR dietary) N2 (intervention* OR therap* OR education OR support* OR treatment* OR consultation# OR consult* OR cancer* OR counsel* OR restrict*))
 11. TI (Parenteral N2 (alimentation OR feed* OR fluid OR hyperalimentation)) OR AB (Parenteral N2 (alimentation OR feed* OR fluid OR hyperalimentation))
 12. TI (Nutrition* N2 (product* OR supplement* OR support* OR mixture)) OR AB (Nutrition* N2 (product* OR supplement* OR support* OR mixture))
 13. TI (Diet* N2 (product* OR supplement* OR support* OR mixture)) OR AB (Diet* N2 (product* OR supplement* OR support* OR mixture))
 14. TI ((Diet* OR nutrition*) N4 (educat* OR guideline* OR factor*)) OR AB ((Diet* OR nutrition*) N4 (educat* OR guideline* OR factor*))
 15. S9 OR S10 OR S11 OR S12 OR S13 OR S14 OR S15 OR S16
 16. (MH "Exercise+") OR (MH "Physical Activity") OR (MH "Physical Fitness+") OR (MH "Physical Performance") OR (MH "Sports+") OR (MH "Resistance Training") OR (MH "Therapeutic Exercise+") OR (MH "Exercise Intensity")
 17. TI (isometric* OR isotonic* OR isokinetic* OR exercis*) OR AB (isometric* OR isotonic* OR isokinetic* OR exercis*)
 18. TI ((resistance OR strength) N3 (train* OR exercis*)) OR AB ((resistance OR strength) N3 (train* OR exercis*))
 19. TI ((physical* OR motion* OR cardiopulmonary OR cardiorespiratory) N3 (fit* OR therap*)) OR AB ((physical* OR motion* OR cardiopulmonary OR cardiorespiratory) N3 (fit* OR therap*))
 20. TI (treadmill* OR cross-train* OR rowing OR sport* OR exercise* OR "physical activit*" OR aerobic* OR run OR jog* OR running OR walk OR walks OR walking OR gym* OR yoga OR pilates OR "recreation* activit*" OR zumba OR salsa* OR cycling OR bicycle OR bike OR swim* OR dance OR

dancer* or dances or dancing) OR AB (treadmill* or cross-train* or rowing or sport* OR exercise* OR "physical activit*" OR aerobic* OR run or jog* or running OR walk or walks or walking OR gym* OR yoga or pilates OR "recreation* activit*" OR zumba or salsa* OR cycling or bicycle or bike or swim* or dance or dancer* or dances or dancing)

21. TI (circuit* N1 train*) OR AB (circuit* N1 train*)
22. TI (keep* N1 (active or fit)) OR AB (keep* N1 (active or fit))
23. S16 OR S17 OR S18 OR S19 OR S20 OR S21 OR S22
24. S7 AND S15 AND S23

Cochrane Library

1. [mh "Esophageal Neoplasms"] OR [mh "Stomach Neoplasms"] OR [mh "Biliary Tract Neoplasms"] OR [mh "Liver Neoplasms"] OR [mh "Pancreatic Neoplasms"]
2. ((oesophag* OR esophag* OR gastroesophag*) NEAR/3 (cancer* OR neoplasm* OR tumo*r* OR adenocarcinoma* OR carcinoma*)):ti,ab,kw
3. ((stomach OR gastric) NEAR/3 (cancer* OR neoplasm* OR tumo*r* OR adenocarcinoma* OR carcinoma*)):ti,ab,kw
4. (("bile duct*" OR gallbladder* OR biliary OR liver OR hepato* OR hepatic) NEAR/3 (cancer* OR neoplasm* OR tumo*r* OR adenocarcinoma* OR carcinoma*)):ti,ab,kw
5. (pancrea* NEAR/3 (cancer* OR neoplasm* OR tumo*r* OR adenocarcinoma* OR carcinoma*)):ti,ab,kw
6. (("upper gi" OR "upper gastrointestinal") NEAR/3 (cancer* OR neoplasm* OR tumo*r* OR adenocarcinoma* OR carcinoma*)):ti,ab,kw
7. #1 OR #2 OR #3 OR #4 OR #5 OR #6
8. [mh "Nutrition Therapy"] OR [mh "Nutrition Assessment"] OR [mh "Cachexia"] OR [mh "Diet Records"] OR [mh "Nutrition Surveys"] OR [mh "Nutritional Status"] OR [mh "Dietetics"] OR [mh "Nutrition Policy"]
10. (Nutrition* NEAR/3 (intervention* OR therap* OR education OR support* OR treatment* OR consultation* OR consult* OR cancer* OR counsel*)):ti,ab,kw
11. ((diet* OR dietary) NEAR/3 (intervention* OR therap* OR education OR support* OR treatment* OR consultation* OR consult* OR cancer* OR counsel* OR restrict*)):ti,ab,kw
12. (Parenteral NEAR/3 (alimentation OR feed* OR fluid OR hyperalimentation)):ti,ab,kw
13. (Nutrition* NEAR/3 (product* OR supplement* OR support* OR mixture)):ti,ab,kw
14. (Diet* NEAR/3 (product* OR supplement* OR support* OR mixture)):ti,ab,kw
15. ((Diet* OR nutrition*) NEAR/5 (educat* OR guideline*)):ti,ab,kw
16. #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14

17. [mh "Exercise"] OR [mh "Exercise Therapy"] OR [mh "Physical Fitness"]
OR [mh "physical education and training"] OR [mh "Exercise Movement
Techniques"] or [mh "physical endurance"] or [mh "exercise
tolerance"] OR [mh "Physical Exertion"] or [mh "Sports"] or [mh
"Dancing"]
18. (isometric* or isotonic* or isokinetic* OR exercis*):ti,ab,kw
19. ((resistance OR strength) NEAR/3 (train* OR exercise*)):ti,ab,kw
20. ((physical* or motion* or cardiopulmonary or
cardiorespiratory) NEAR/3 (fit* or therap*)):ti,ab,kw
21. (treadmill* or cross-train* or rowing or sport* OR exercise* OR
"physical activit*" OR aerobic* OR run or jog* or running OR walk
or walks or walking OR gym* OR yoga or pilates OR "recreation*
activit*" OR zumba or salsa* OR cycling or bicycle or bike or swim*
or dance or dancer* or dances or dancing):ti,ab,kw
22. (circuit* NEAR/1 train*):ti,ab,kw
23. (keep* NEAR/1 (active or fit)):ti,ab,kw
24. #16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22
25. #7 AND #15 AND #23

Appendix XIV Details of Relevant Ongoing Clinical Trials (systematic review,Chapter 6)

Author (PI)	Title	Clinical Trial Registry	Registration ID	URL
Shinn o Naoki	Randomised trial of Exercise and Nutritional prehabilitation for Elderly Gastric Cancer patients	Japan Registry of Clinical Trials	JRCTs051190015	https://rctportal.niph.go.jp/en/detail?trial_id=jRCTs051190015
Hiroshi Miyata	Rehabilitation / nutrition intervention trial for elderly patients with oesophageal cancer	Japan Registry of Clinical Trials	JRCTs051190016	https://rctportal.niph.go.jp/en/detail?trial_id=jRCTs051190016
Sophie Allen	A randomised controlled trial to assess whether prehabilitation improves fitness in patients undergoing neoadjuvant treatment prior to oesophagogastric cancer surgery: study protocol	ClinicalTrials.gov	NCT02950324	https://pubmed.ncbi.nlm.nih.gov/30580268/
Li Yiran	A comprehensive intervention to improve quality of life in operated esophageal cancer patients: a randomised controlled trial	Chinese Clinical Trial Registry	ChiCTR1800019823	http://www.chictr.org.cn/showproj.aspx?proj=32884
Bertrand Le Roy	effect of prehabilitation in gastrooesophageal adenocarcinoma: study protocol of a multicentric, randomised, control trial—the PREHAB study	ClinicalTrials.gov	NCT02780921	https://pubmed.ncbi.nlm.nih.gov/27927660/
Yu-Juan Xu	Effects of a "Walk, Eat, & Breathe" Nursing Intervention for Patients With Esophageal Cancer	ClinicalTrials.gov	NCT02850172	https://clinicaltrials.gov/ct2/show/NCT02850172

Author (PI)	Title	Clinical Trial Registry	Registration ID	URL
Augustinas Bausys	Prehabilitation for Gastrectomy (PREFOG)	ClinicalTrials.gov	NCT04223401	https://clinicaltrials.gov/ct2/show/NCT04223401
M. Sosef	Preoperative training for patients with esophageal cancer who will undergo resection (PC-OCR II)	Netherlands Trial Register	NTR3351	https://www.trialregister.nl/trial/3200
Stefano Turi	Prehabilitation in Esophageal Surgery (PRESS)	ClinicalTrials.gov	NCT03798951	https://clinicaltrials.gov/ct2/show/NCT03798951
Makoto Yamasaki	Randomised controlled study on the efficacy of the exercise and amino acid for the elderly with esophageal squamous cell carcinoma during neoadjuvant chemotherapy	The University Hospital Medical Information Network Center	UMIN000034505	https://upload.umin.ac.jp/cgi-open-bin/ctr_e/ctrview.cgi?recptno=R000039340
Susumu Aikou	Randomised controlled trials on prevention of sarcopenia during gastric cancer surgery by exercise and nutrition intervention	The University Hospital Medical Information Network Center	UMIN000033613	https://upload.umin.ac.jp/cgi-open-bin/ctr_e/ctrview.cgi?recptno=R000038333
Linda O'Neill	Rehabilitation strategies following oesophagogastric and Hepatopancreaticobiliary cancer (ReStOre II): a protocol for a randomised controlled trial	ClinicalTrials.gov	NCT03958019	https://bmccancer.biomedcentral.com/articles/10.1186/s12885-020-06889-z

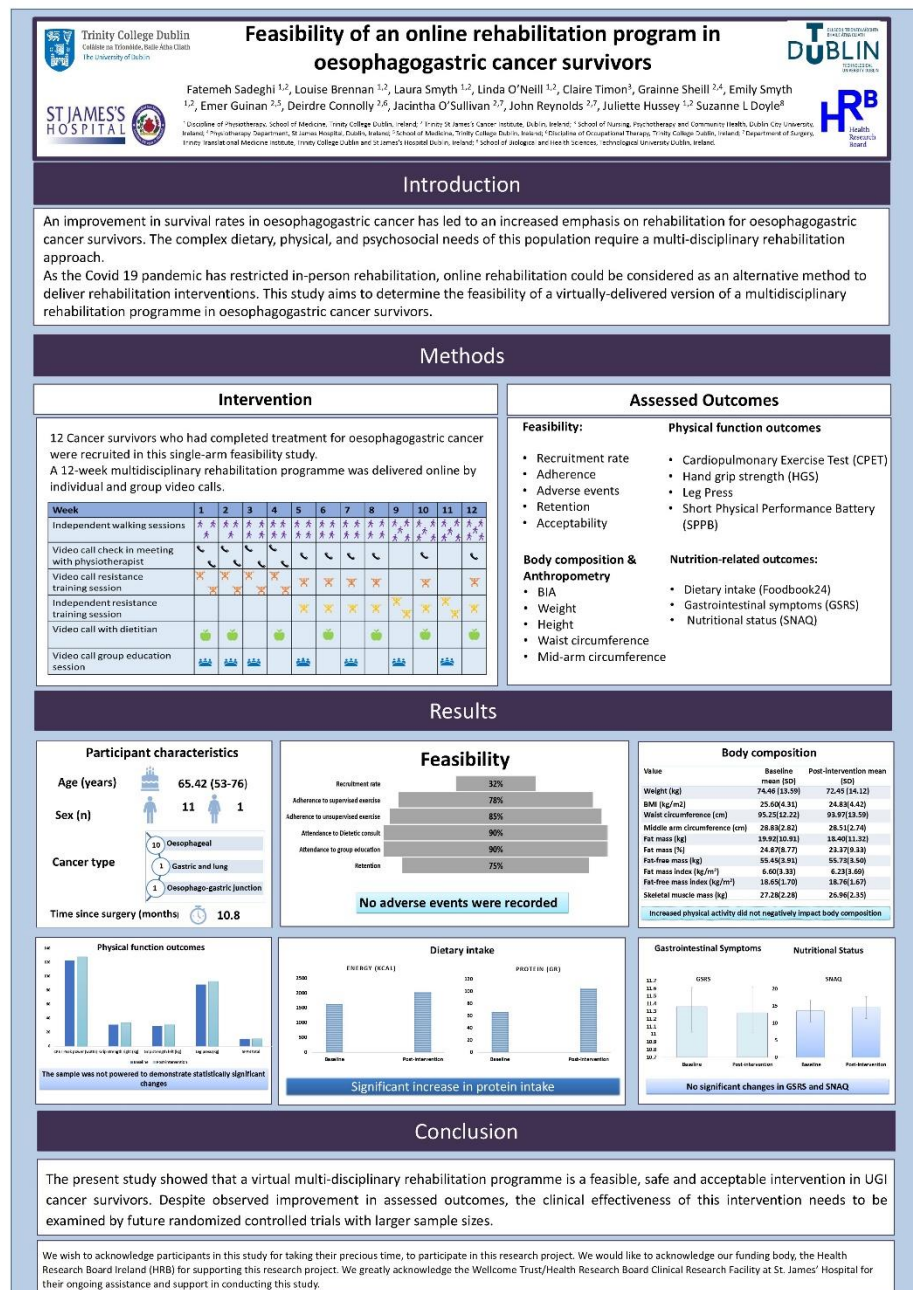
Appendix XV ReStOre@Home Participants' Dietary intake data

Nutrient	T0 Mean (SD)	T1 Mean (SD)
Energy (Kcal)	1610.62 (589.39)	1909.47 (757.71)
Protein (g)	71.99 (25.57)	106.06 (42.83)
Carbohydrate (g)	180.83 (68.36)	206.38 (71.40)
Sugar (g)	68.62 (33.43)	84.62 (47.22)
Starch (g)	110.33 (45.02)	115.65 (35.22)
Non-Starch Polysaccharides (NSP) (g)	10.37 (9.08)	12.19 (5.23)
Fat (g)	62.08 (25.38)	81.31 (42.85)
Saturated Fat (g)	22.45 (11.18)	34.83 (20.61)
Trans Fat (g)	0.93 (0.63)	1.46 (1.27)
Monounsaturated Fat (g)	22.15 (11.51)	27.26 (15.12)
Polyunsaturated Fat (g)	8.41 (2.81)	10.87 (6.07)
N3 Polyunsaturated Fat (g)	1.40 (1.53)	0.85 (0.97)
N6 Polyunsaturated Fat (g)	2.14 (1.67)	3.57 (2.90)
Alpha-Linolenic Acid (ALA) (g)	466.99 (888.17)	137.98 (254.46)
Eicosapentaenoic acid (EPA) (g)	5.12 (14.97)	5.47 (13.66)
Docosapentaenoic acid (DPA) (g)	0.02 (0.03)	0.06 (0.1)
Docosahexaenoic acid (DHA) (g)	5.96 (17.24)	9.41 (18.68)
Fibre (g)	12.35 (4.97)	16.39 (7.12)
Vitamin (µg) D	2.85 (3.10)	6.11 (4.02)
Retinol (µg)	504.75 (506.66)	952.15 (638.17)
Carotene (µg)	1110.14 (1399.92)	1217.64 (1185.72)
Vitamin E (mg)	9.51 (6.60)	13.09 (8.29)
Vitamin B1 (mg)	1.61 (1.12)	2.46 (1.30)
Vitamin B2 (mg)	1.38 (1.05)	2.37 (1.32)
Niacin (mg)	29.22 (11.23)	39.71 (14.52)

Nutrient	T0 Mean (SD)	T1 Mean (SD)
Vitamin B6 (mg)	1.98 (2.31)	2.82 (1.55)
Vitamin B12 (µg)	4.30 (3.37)	4.79 (3.05)
Folate (µg)	178.05 (110.64)	320.04 (176.27)
Biotin (µg)	43.86 (47.45)	87.64 (108.27)
Pantothenic acid (mg)	8.49 (13.93)	9.33 (4.67)
Vitamin C (mg)	64.20 (55.27)	107.19 (70.84)
Calcium (mg)	739.92 (361.08)	909.92 (442.41)
Magnesium (mg)	289.52 (209.99)	328.10 (110.04)
Phosphorus (mg)	1141.91 (404.50)	1364.64 (550.14)
Zinc (mg)	10.27 (8.27)	12.05 (5.11)
Iron (mg)	13.1 (11.59)	15.18 (6.89)
Copper (mg)	0.96 (0.65)	1.25 (0.31)
Manganese (mg)	2.80 (2.64)	19.97 (33.78)
Selenium (µg)	48.35 (36.28)	62.02 (35.90)
Iodine (µg)	200.78 (271.35)	191.13 (152.25)
Potassium (mg)	2604.20 (1309.68)	1364.64 (550.14)
Sodium (mg)	2061.81 (753.15)	2146.94 (1183.67)
Alcohol (g)	8.34 (8.94)	7.37 (8.06)

Appendix XVI Poster presentations





Introduction

- Cachexia and sarcopenia are common complications in cancer patients that hinder cancer treatment and survival and can lead to limited physical function, fatigue, chemotherapy toxicity and lower quality of life ¹⁻⁴.
- Multidisciplinary rehabilitation programmes can improve nutritional status and physical function in gastroesophageal cancer survivors⁵⁻⁷ but the impact on body composition and quality of life is not clear yet ^{8, 9-12}
- This systematic review aims to evaluate the effectiveness of combined nutritional and exercise interventions in improving muscle wasting and quality of life in patients with upper GI cancer.

Methods

Databases: MEDLINE, EMBASE, Web of Science, Cochrane Library, CINHAL

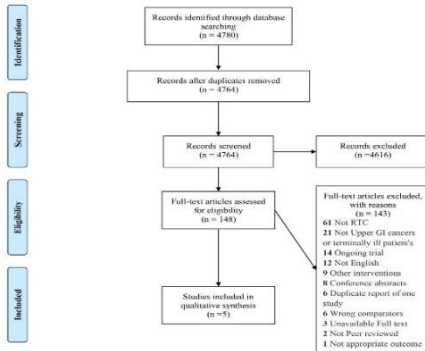
Study designs: Randomised Controlled Trials

Population: ≥ 18 yrs. & Diagnosed with upper GI cancer

Intervention: Nutrition+ Exercise

Comparator: Standard Care

Outcomes: Quality of Life, Body composition, Physical function



Results

Table 1 Overview of included studies

Author, Year	O'Neill et al., 2018	Yu-Juan Xu et al., 2015	Yu-Ling Chang et al., 2020	Minella et al., 2018	Amadua et al., 2019
Country	Ireland	Taiwan	Taiwan	Canada	Spain
Cancer type	Esophagogastric	Oesophageal	Oesophageal	Esophagogastric	Pancreaticoduodenal
Timepoint of intervention	Rehabilitation	During Neoadjuvant Chemotherapy	Rehabilitation	Prehabilitation	Prehabilitation
Sample size (n)	43 (Intervention=21, Control=22)	59 (Intervention=30, Control=29)	88 (Intervention=44, Control=44)	68 (Intervention=34, Control=34)	40 (Intervention=18, Control=22)
Sex (%Male)	81%	92.9%	90.9%	74.5%	55%
Age	Intervention: 67.19 ± 7.49 Control: 64.14 ± 10.46	Intervention: 58.1 ± 9.6 Control: 61.149 ± 9.0	Intervention: 56.1 ± 8.9 Control: 56 ± 10.0	Intervention: 67.31 ± 7.4 Control: 68.08 ± 11.6	Intervention: 66.1 (38-80) Control: 65.7 (38-81)
Recruitment rate	40.3%	92%	94.6%	60.1%	96%
Dropout rate	9.3%	5.1%	9.1%	25%	16%
Adherence	Supervised exercise: 94.12% Unsupervised exercise: 78.27	Nutritional sessions: 100% Walking sessions: 68	NR	63%	NR
Adverse event	None (musculoskeletal discomfort from a pre-existing condition in 5 participants)	NR	NR	None	NR
Exercise sessions	Supervised aerobic & resistance training Unsupervised home-based aerobic & resistance training	Nurse-supervised walking	Home-based walking	Home-based aerobic & strengthening activity Weekly phone call by a kinesiologist	Supervised high-intensity endurance training Breathing exercise
Nutrition component	Nutritional assessment 1:1 Dietary counselling Personalised nutritional advice	Dietary counselling	E-books containing dietary advice	Dietary counselling Whey protein supplement (if required) Weekly phone call by a dietitian	Nutritional counselling Nutritional support (liquid oral nutrition supplements & vitamin supplements) Total parenteral nutrition (if required) Dietetic follow-up in the outpatient clinic
Other components	Group education sessions	None	E-books (exercises, symptom management, psychological advice) Online nurse support Online discussion group	None	Metformin or Insulin (if required) Blood glucose monitor to check glucose level at home Pancreatic enzymes replacement therapy
Control	Standard Care	Standard Care	Standard Care	Standard Care	Standard Care
Duration	12 W	4-5W	12 W	Median 36 days	Median 12.6 days

Table 2 Effects of combined nutritional and exercise interventions on measured outcomes

Author, Year	O'Neill et al., 2018	Yu-Juan Xu et al., 2015	Yu-Ling Chang et al., 2020	Minella et al., 2018	Amadua et al., 2019
HRQOL	HRQOL unchanged Cognitive function higher in the control group, P<0.05	Not measured	HRQOL improved P<0.05	NR	NR
Body composition/Anthropometric measurement	Body composition unchanged Higher mid-arm circumference P<0.05	Muscle mass unchanged Less weight loss, P<0.05	BMI unchanged	NR	NR
Physical and Cardiorespiratory fitness	Higher VO _{2 max} P<0.05 PAL unchanged	Less decline in walk distance, P<0.05 Less decrease in hand-grip strength, P<0.05	Higher VO _{2 max} P<0.05 Greater walk distance P<0.05	Greater walk distance P<0.05 10 m Walk Test Dynamometer strength FVC O _{2 sat} (Not measured in the control group)	Improvement in: 10 m Walk Test Dynamometer strength FVC O _{2 sat} (Not measured in the control group)
Complications	NR	Lower rates of PN P<0.05 Lower rate of wheelchair use P<0.05 No changes in: Treatment interruption Unplanned hospital admissions Neutropenia Fever	Higher albumin P<0.05	No differences in: Complications Hospital stay Mortality ED visits Readmission rates Lower DGE, P<0.05	No differences in: Complications Hospital stay Readmission rates
Other outcomes					

Conclusion

A limited number of studies have examined the effects of combined nutritional and exercise interventions in upper GI cancers. Studies reviewed in this systematic review observed the beneficial effects of these interventions on cardiorespiratory fitness and physical functioning. Results of included studies showed that there is conflicting evidence regarding the effectiveness of these interventions on preserving muscle mass and health-related quality of life. Further studies examining the impact of nutrition and exercise interventions on upper GI patient outcomes are required and would benefit from reporting a core outcome set. This work is funded by the HRB (HRB-DIFA-2018-009).

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4. Prado CM, Baracos V, Baracos S, et al. Cachexia: A new definition. *Cancer*. 2016;119(5):914-927.
5. Prado CM, Baracos V, Baracos S, et al. Cachexia: A new definition. *Cancer*. 2016;119(5):914-927.
6. Prado CM, Baracos V, Baracos S, et al. Cachexia: A new definition. *Cancer*. 2016;119(5):914-927.
7. Prado CM, Baracos V, Baracos S, et al. Cachexia: A new definition. *Cancer*. 2016;119(5):914-927.
8. Prado CM, Baracos V, Baracos S, et al. Cachexia: A new definition. *Cancer*. 2016;119(5):914-927.
9. Prado CM, Baracos V, Baracos S, et al. Cachexia: A new definition. *Cancer*. 2016;119(5):914-927.
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11. Prado CM, Baracos V, Baracos S, et al. Cachexia: A new definition. *Cancer*. 2016;119(5):914-927.
12. Prado CM, Baracos V, Baracos S, et al. Cachexia: A new definition. *Cancer*. 2016;119(5):914-927.