TITLE:

Towards consensus of a common definition and outcomes reported in surgical prehabilitation

Chloé Fleurent-Grégoire, RD

School of Human Nutrition

McGill University, Montreal

December 11, 2023

A thesis submitted to McGill University in the partial fulfillment of the requirements of the degree of Master of Science

Abstract

Background. Surgical prehabilitation is a preoperative intervention aiming to better prepare patients to withstand the emotional and physiological stressors of surgery. Despite over two decades of research in this field, the certainty of the evidence for prehabilitation before surgery remains difficult to evaluate in part because of the lack of a universally accepted definition and the heterogeneity of reported outcomes.

Objectives. The main objectives of this thesis are to (1) identify how surgical prehabilitation is defined, and (2) systematically map what, when and how outcomes and their specific outcome assessments are reported across primary randomized controlled trials of unimodal (consisting of exercise, nutrition or cognitive/psychological training) and multimodal (two or more modalities) prehabilitation in adult patients undergoing elective surgery.

Methods. A scoping review was performed to meet both objectives. The final search was conducted in February 2023 using MEDLINE, EMBASE, PsychInfo, Web of Science, CINAHL, and Cochrane. For objective 1, a qualitative analysis was done using a method and investigator triangulation approach for summative content analysis. For objective 2, data extraction and charting were performed in duplicate and followed the International Society for Pharmacoeconomics and Outcomes Research (ISPOR) framework. Descriptive statistics (counts and frequencies) were used for the analysis of quantitative data.

Results. The review included a total of 76 trials, mostly of patients undergoing abdominal (n=26, 34%), orthopedic (n=20, 26%) and thoracic (n=14, 18%) surgeries. We consolidated the following common definition: “Prehabilitation is a process from diagnosis to surgery, consisting of one or more preoperative interventions of exercise, nutrition, anxiety-reducing strategies, and

respiratory training, that aims to enhance functional capacity and physiological reserve to allow patients to withstand surgical stressors, improve postoperative outcomes, and facilitate recovery." Fifty different outcomes were identified, measured using 184 specific outcome assessments. Observer-reported outcomes were collected in 86% of trials (n=65), reported 175 times across trials using 24 outcome assessments, with hospital length of stay being the most common. Performance outcomes were included in 80% of trials (n=61), reported 199 times across trials using 51 outcome assessments and the most reported was exercise capacity assessed with cardiopulmonary exercise testing parameters. Clinician-reported outcomes were included in 78% (n=59) of trials, reported 84 times across trials using 26 outcome assessments and the most frequent was postoperative complications using the Clavien-Dindo classification. Patient-reported outcomes were documented in 76% (n=58) of trials, reported 137 times overall using 63 outcome measurement instruments, mostly as health-related quality of life using the 36- or 12-Item Short Form Survey. Biomarker outcomes were included in 16% (n=12) of trials, reported 28 times across trials using 20 different biomarkers and C-reactive protein was the most common inflammatory marker.

Conclusion. This work has consolidated a common definition and identified frequent and meaningful outcomes for surgical prehabilitation which are the first steps towards standardization and the development of a core outcome set for future high-quality clinical trials. Harmonizing interventions and data reporting is required to enable meta-analyses of trial effects to better understand the certainty of the evidence and advance the surgical prehabilitation field.

Résumé

Contexte. La préhabilitation chirurgicale est une intervention préopératoire visant à mieux préparer les patients à supporter les facteurs de stress émotionnels et physiologiques de la chirurgie. Malgré plus de deux décennies de recherche dans ce domaine, la certitude des preuves en faveur de la préhabilitation avant la chirurgie reste difficile à évaluer en partie en raison du manque d'une définition universellement acceptée et de l'hétérogénéité des résultats rapportés.

Objectifs. Les principaux objectifs de cette thèse de maîtrise sont (1) d'identifier comment la préhabilitation chirurgicale est définie, et (2) d'identifier systématiquement quels, quand et comment les résultats ainsi que leurs évaluations spécifiques sont rapportés dans les essais contrôlés randomisés primaires portant sur la préhabilitation unimodale (composée d'exercices, de nutrition ou de formation cognitive/psychologique) et multimodale (deux modalités ou plus) chez des patients adultes subissant une chirurgie élective.

Méthodes. Une revue de la portée a été réalisée pour atteindre ces deux objectifs. La recherche finale a été effectuée en février 2023 en utilisant MEDLINE, EMBASE, PsychInfo, Web of Science, CINAHL et Cochrane. Pour le premier objectif, une analyse qualitative a été effectuée en utilisant une approche de triangulation des méthodes et une analyse de contenu sommatif. Pour le deuxième objectif, l'extraction et le classement des données ont été réalisés en double et ont suivi le cadre de *International Society for Pharmacoeconomics and Outcomes Research* (ISPOR). Des statistiques descriptives (dénombrements et fréquences) ont été utilisées pour l'analyse des données quantitatives.

Résultats. La revue a inclus un total de 76 essais, principalement chez des patients subissant des chirurgies abdominales (n=26, 34%), orthopédiques (n=20, 26%) et thoraciques (n=14, 18%).

Nous avons consolidé la définition commune suivante : "La préhabilitation est un processus allant du diagnostic à la chirurgie, consistant en une ou plusieurs interventions préopératoires comprenant des exercices, une nutrition, des stratégies de réduction de l'anxiété et un entraînement respiratoire, visant à améliorer la capacité fonctionnelle et la réserve physiologique pour permettre aux patients de supporter les facteurs de stress chirurgicaux, à améliorer les résultats postopératoires et à faciliter la récupération." Nous avons identifié cinquante résultats différents, mesurés à l'aide de 184 évaluations spécifiques des résultats. Les résultats rapportés par les observateurs ont été recueillis dans 86% des essais (n=65) et ont été signalés 175 fois dans les essais à l'aide de 24 évaluations des résultats spécifiques, la durée du séjour de l'hospitalisation étant la plus courante. Les résultats de performance ont été inclus dans 80% des essais (n=61) et ont été rapportés 199 fois à travers les essais en utilisant 51 évaluations des résultats, la capacité à l'exercice étant la plus fréquemment rapportée à l'aide des paramètres des tests d'exercice cardiopulmonaire. Les résultats rapportés par les cliniciens ont été inclus dans 78% des essais (n=59) et ont été signalés 84 fois à travers les essais en utilisant 26 évaluations des résultats, les complications postopératoires selon la classification Clavien-Dindo étant les plus fréquentes. Les résultats rapportés par les patients ont été documentés dans 76% des essais (n=58) et ont été signalés 137 fois au total en utilisant 63 instruments de mesure des résultats, principalement en ce qui concerne la qualité de vie liée à la santé à l'aide des questionnaires *36*- ou *12-Item Short Form Survey*. Les résultats des biomarqueurs ont été rapportés 28 fois dans l'ensemble des essais en utilisant 20 biomarqueurs différents, et la protéine C-réactive était le marqueur inflammatoire le plus courant.

Conclusion. Ce travail a consolidé une définition commune et identifié les résultats et leurs évaluations spécifiques fréquents et significatifs pour la préhabilitation chirurgicale. Ceci

constitue les premières étapes nécessaires vers un consensus pour guider le développement d'un ensemble de résultats de base standardisé pour les futures études cliniques de haute qualité. L'harmonisation des interventions et de la communication des données est nécessaire pour permettre des méta-analyses des effets des essais afin de mieux comprendre la certitude des preuves et faire progresser le domaine de la préhabilitation chirurgicale.

Acknowledgements

I would like to thank my supervisor, Dr. Stéphanie Chevalier, for welcoming me to her research group as a young undergraduate student to then encouraging and supporting me to pursue my graduate studies under her supervision. I have learned so much about the field of research and academia, while developing strong organizational skills during the past years. I am grateful for her incredible mentorship and guidance. I am also appreciative that Dr Chevalier has allowed me to be involved a in a unique mixed-nutrient multimodal prehabilitation trial as a research registered dietitian.

I would also like to thank my co-supervisor, Dr. Chelsia Gillis. She has brought amazing insight about the field of prehabilitation and has allowed me to grow so much and improve my critical thinking and writing skills by providing me great constructive feedback throughout my graduate studies. I am grateful for having her as a role model.

I also thank my committee member, Dr. Scheede-Bergdahl, for expertise and advice throughout my graduate program. I am also thankful for the opportunity to work in Dr. Francesco Carli's Peri-Operative Program clinic and his team. This experience has been extremely knowledgeable and rewarding.

A special thanks to my colleagues and friends, Audrey Moyen and Jade Corriveau, for fun times, great conversations, generous time and support. Thank you to my lab mates Yi Jin, Alexandra Georgalos, Didier Brassard, Claire Lawson and Aviva Rappaport for all you help and support.

Finally, I would like to thank my husband, Charlie Roy, for being by my side during this journey as well as my family for their continuous love and support.

Dedication

This MSc thesis is dedicated to my husband, Charlie Roy, and family. Your encouragements and support have made it possible for me reach my academic goals and follow my passions. I could not have done it without you.

Supervisory committee

Supervisors:

Dr. Stéphanie Chevalier, RD, PhD

Dr. Chelsia Gillis, RD, PhD

Committee Member:

Dr. Celena Scheede-Bergdahl, PhD

External Examiner:

Dr. Chantal Bémeur, DtP, PhD

Contribution of authors

Dr. Chelsia Gillis, Dr. Linda Denehy, Nicola Burgess and I have equally contributed to the study design of the first manuscript of this MSc thesis. I have written the first draft of the manuscript, then the writing of the final draft was shared between Dr. Gillis and me. The analysis of the data was conducted by Nicola Burgess and I, as we have both coded the data independently. I have created tables and figures. Finally, co-authors Dr. Daniel I. McIsaac, Dr. Stéphanie Chevalier and Dr. Francesco Carli have contributed to the editing of the manuscript and provided their expertise in the fields of prehabilitation and perioperative medicine as well as provided their guidance throughout.

For the second manuscript of this MSc thesis, I have conducted the majority of the work as the primary author. I have contributed to the study design, abstract review, study selection, data extraction and statistical analysis. I have written the manuscript and produced all figures and tables. Dr. Gillis and Dr. Denehy have co-designed the study, provided their expertise and guidance throughout in addition to editing the manuscript. Nicola Burgess and Dr. Lara Edbrooke have contributed to the data extraction and editing of the manuscript. Dr. Dominique Engel and Dr. Giuseppe Dario Testa have performed the initial search, abstract review and study selection for the purpose of a previous scoping review which we have expanded with an updated search. The co-authors Dr. Julio F. Fiore Jr., Dr. McIsaac, Dr. Chevalier, Dr. John Moore, Dr. Michael P. Grocott, Dr. Robert Copeland, Dr. Denny Levett and Dr. Celena Scheede-Bergdahl have provided their expertise in the medical, surgical outcome, and prehabilitation field, as well as reviewed and edited the manuscript. Throughout my entire academic program and writing process, Dr. Chevalier and Dr. Gillis have mentored me and provided feedback on all my work.

List of tables

List of figures

List of abbreviations

ATS – American Thoracic Society

BIA – Bioelectrical impedance analysis

CPET – Cardiopulmonary exercise testing

ClinRO – Clinician-reported outcomes

CCI – Comprehensive Complication Index

CERT – Consensus on Exercise Reporting Template

COMET – Core Outcome Measures in Effectiveness Trial

CONSORT – Consolidated Standards of Reporting of Trials

CONSORT-SPI – CONSORT Extension for Psychosocial Interventions

COS – Core outcome set

COSMIN – Consensus based Standards for the selection of health status Measurement INstruments)

ERAS – Enhanced Recovery After Surgery

FEV_1 – Forced Expiratory Volume in 1 second

FVC – Forced vital capacity

ICU – Intensive care unit

LOS – Length of stay

ObsRO – Observer-reported outcomes

MICMD – Minimally important clinical meaningful difference

MIP/MEP – Maximal inspiratory/expiratory pressure

PACU – Post-anesthesia care unit

PerfO – Performance outcomes

PICO – Population, intervention, control, and outcomes

POETTS – Perioperative Exercise Testing and Training Society

POMS – Post-Operative Morbidity Survey

PRESENT – Proper Reporting of Evidence in Sport and Exercise Nutrition Trials

PRISMA-ScR – Preferred Reporting Items for Systematic reviews and Meta-Analyses extension for Scoping Reviews

PRO – Patient-reported outcomes

QOL – Quality of Life

RCT – Randomized controlled trial

ROM – Range of motion

SF-36 – 36-item Short Form Survey

STS – Sit to Stand

TIDieR – Template for Intervention Description and Replication

TUG – Timed Up and Go

VO_2 at AT – Oxygen consumption at the anaerobic threshold

VO_2 peak – Peak oxygen

5MWT – 5-minute walking test

6MWT – 6-minute walking test

Table of Contents

1. INTRODUCTION

Each year, millions of patients across the globe will require major elective surgery with the goal of improving their disease trajectory and health outcomes (1). Surgical techniques (e.g., minimally invasive surgery) and perioperative programs (e.g., Enhanced Recovery After Surgery or ERAS) have progressed considerably over the past few decades leading to increased positive post-operative outcomes (e.g., decreased length of hospital stay). However, surgical patients are still required to withstand a substantial amount of physiological stress posing risks for morbidity and mortality after the operation (2). A portion of the risk can be attributed to factors other than those related to surgeons or health care institutions, but rather to the preoperative condition of the patients themselves. Modifiable patient-related risk factors such as medical conditions, health behaviours, functional capacity, nutritional status and physiological reserve are thought to be major contributors to poor post-operative outcomes (e.g., postoperative complications) (3).

Interventions that aim to address patient-related risk factors through exercise, respiratory, nutrition and psychological modalities, known as prehabilitation, are thought to better prepare patients for surgical stressors when compared to standard care (3). Ultimately, by improving patient's physical fitness and mental state with prehabilitation prior to surgery, postoperative recovery can be facilitated. While the prehabilitation field continues to grow across many surgical oncological and non-oncological specialties, the certainty of the evidence in regard to its effectiveness remains mostly low (4). The uncertainty of the evidence has been partially attributed to the heterogeneity of the interventions and the reported outcomes across trials. Additionally, there is currently no universally accepted definition for surgical prehabilitation. These inconsistencies and lack of consensus pose challenges when pooling data for systematic

reviews, meta-analyses and when designing prehabilitation intervention; thus, reducing the overall certainty of the effectiveness of prehabilitation on meaningful outcomes (4).

1.1 Thesis rationale

An important first step to guide consensus and achieve consistency is to have a clear understanding of how surgical prehabilitation is defined and what, when and how outcomes are reported in the current literature. To address these gaps, this research has the purpose of consolidating a common definition, and systematically mapping outcomes reported in the surgical prehabilitation literature to guide future high quality clinical trials and to inform the development of a core outcome set.

1.2 Thesis objectives

1) The first objective of this research is to identify how surgical prehabilitation is defined across primary randomized controlled trials (RCT) of unimodal (consisting of exercise, nutrition or cognitive/psychological training) and multimodal (two or more modalities) prehabilitation in adult patients undergoing elective surgery.
    1.1) To consolidate a common definition for surgical prehabilitation for future research.
2) The second objective of this research is to systematically map outcomes and specific outcome assessments reported across primary RCTs of unimodal and multimodal surgical prehabilitation.
    2.1) To identify when and how specific outcome assessments are reported across primary RCTs of unimodal and multimodal surgical prehabilitation.

1.3 Research questions

The following research questions are addressed throughout this research:

1) How is surgical prehabilitation defined in the current literature of primary RCTs of unimodal (consisting of exercise, nutrition or cognitive/psychological training) and multimodal (two or more modalities) prehabilitation lasting 7 days or more in adult patients undergoing elective surgery?
2) What is the current landscape of outcomes and specific outcome assessments across RCTs of unimodal and multimodal prehabilitation lasting 7 days or more in adult patients undergoing elective surgery? When and how are these outcomes reported?

2. LITERATURE REVIEW

2.1 The surgical stress response

Every year, it is estimated that over 320 million people across the globe will require surgery (1). Major surgeries place patients under substantial physiological stress. The stress response to surgery is proportional to the tissue trauma and is characterized by hematological, immune, neuroendocrine and metabolic changes leading, in part, to important alterations in glucose and protein metabolism (2).

The surgical stress response is initiated at the location of the surgical incision. At the trauma site, afferent nerves and cytokines produced by innate immune cells with phagocytic properties (macrophages, neutrophils and natural killer cells) trigger the activation of the hypothalamic-pituitary-adrenal axis and sympathetic nervous system which mediates the release of glucocorticoids, catecholamines, and glucagon to the circulation (5). These counter-regulatory hormones impair insulin function leading to alterations in glucose metabolism. These alterations include the increase in hepatic gluconeogenesis and glycogenolysis, the reduction in glucose uptake mainly at the skeletal muscle level (the main organ relying on insulin-mediated glucose uptake) and affect the ability of insulin to supress gluconeogenesis secondary to central insulin resistance (6). These changes in insulin and glucose metabolism contribute to the hyperglycemic response to surgery (2). Furthermore, the decrease in insulin sensitivity (i.e., the increased insulin concentration needed to achieve a half-maximal biological response) and, therefore, expected increase in intra-operative blood glucose is associated with adverse post-operative outcomes. For example, a prospective cohort study at a tertiary care hospital including 143 non- and 130 patients with diabetes undergoing cardiac surgery found that for every 20% decrease in insulin sensitivity assessed by the hyperinsulinemic-normoglycemic clamp technique, the incidence of

major complications including all-cause mortality, myocardial failure, stroke, and severe infections (severe sepsis, pneumonia requiring mechanical ventilation) more than doubled independent of the presence of diabetes before surgery (7).

Additionally, the stress response induced by surgical trauma has a catabolic effect on protein metabolism. There is a shift from equilibrium towards a net catabolism leading to whole body protein loss which is the result of the downregulation of protein synthesis and the maintenance (or upregulation during a prolonged fasted state) of protein breakdown to ensure the mobilization of substrates (amino acids) to the liver (8, 9). These changes in protein metabolism have been suggested to serve two main purposes including 1) support the production of glucose in the liver via gluconeogenesis, and 2) support the synthesis of proteins for the wounded tissues and of acute-phase plasma proteins (10). This accelerated mobilization of amino acids poses risks, especially to more vulnerable patients (e.g., older adults, sarcopenic or malnourished patients), as it results in losses in lean tissue including wasting of skeletal muscle. As an example, patients having colon cancer (n=8) lost an average of 2.3 kg of lean tissue mass measured with dual energy X-ray absorptiometry at 6 weeks post uncomplicated hemicolectomy (46.1± 3.3 kg vs 43.8±3.0 kg, $P<0.01$) (11). Using multifrequency bioimpedance analysis, similar findings were observed for absolute fat-free mass loss 4 weeks post-colorectal surgery in patient living with cancer (-1.72±0.37 kg $P=0.001$) (12). In addition to post-surgical losses of lean tissue, patients also suffer functional losses after surgery. In a cohort of older adults (n=31) undergoing minimally invasive resection for colorectal cancer, researchers demonstrated a significant sustained reduction of approximately 20% of isometric knee extension strength between baseline and 4 weeks after surgery (mean difference of 4.39 kg, $P=0.02$) (13). In fact, compared to healthy young adults, older adults are generally more susceptible to functional

decline after surgery and impaired or slower recovery to baseline levels (14). Importantly, reduced function is associated with poor clinical and functional outcomes. For example, a loss in function such as reductions in leg strength is a clinically important and significant risk factor for falls in adults over 65 years old (15). In the context of cancer, reduced skeletal muscle has been associated with reduce function. An observational study including individuals living with non-small cell cancer, reported a significant non-linear association between low skeletal muscle index (SMI) and self-reported functional deterioration (16). Individuals with initially lower SMI, below a specific breakpoint (SMI of about 42–45 cm^2/m^2 for men and 37–40 cm^2/m^2 for women), had the greatest functional decline even after adjusting for gender, age and disease stage (16). Muscle wasting in people living with cancer has also been linked to poor clinical outcomes such as chemotherapy toxicity and survival (17). The connection between structural/anatomic measure (e.g., thigh muscle mass), functional measures (e.g., leg strength) and clinical outcomes (e.g., falls) is referred to the OFF Rule ("outcomes follow function follow form" framework) (18). Impaired muscle (mass or composition), especially in more vulnerable groups, is thus a key starting point to possibly improve functional and clinical outcomes (18).

2.2 Enhanced Recovery After Surgery

To moderate the surgical stress response, minimally invasive surgery techniques and evidenced-based ERAS pathways have been developed (19). These modern perioperative interventions have led to major advances in postoperative recovery (20). The concept of ERAS, which was initially called "Fast Track Surgery", was proposed in the late 1990s by Kehlet and his research team for older high-risk patients undergoing colonic surgery (21). Fast Track Surgery was an aggressive multimodal perioperative care approach with the goal of improving post-operative outcomes for faster recovery (21, 22). Eventually, this led to formation of the

ERAS society in the early 2000s. Today, over 20 pathways and guidelines have been developed for different surgical specialties (20). These multimodal perioperative programs include minimally invasive surgery techniques (e.g., laparoscopic procedures), multimodal opioid-sparing analgesia, early mobilization and early feeding regiments and have the goal of minimizing the surgical stress response. Since the integration of the ERAS pathways in health care systems across the globe, it has translated to well-known improvements in clinical outcomes and reduction in overall health care costs. In fact, when compared to traditional standard of care settings, ERAS health centres have reported reductions of approximately one third of total postoperative complications and reductions of up to 2.5 days in length of hospital stay (23-25). Furthermore, these decreases in hospital length of stay have led to savings in healthcare between $639 and $7129 US dollars per patient across colorectal (26), major abdominal (24) and a variety of other surgical specialties (23).

2.3 Patient modifiable risk factors for surgery

While ERAS has brought tremendous advancements and improvements to the surgical field, postoperative complications remain an issue. As an example, in a surgical colorectal cohort (n=1333) of Canadian hospitals, implementation of ERAS pathways resulted in a significant reduction in the incidence of 30-day postoperative complications, from 56.9 % (95 % CI 48–65 %) pre- to 45.3 % (95 % CI 42–49 %) post-ERAS implementation (27); however, complications are still frequent despite these significant reductions. These morbidity levels are not unique to Canadian hospitals. In fact, an international cohort of minor and major elective surgeries (n=44 814) across the globe, including 474 hospitals in 19 high-, 7 middle- and 1 low-income country identified that the prevalence of postoperative morbidity ranged from 8% to 57% depending on the surgical procedure (28).

This sustained incidence of postoperative complications, despite advancements in perioperative care and surgical techniques, has prompted investigators to examine potential preoperative causes, including modifiable patient-related factors (19). This idea that the patient's preoperative status affects outcomes after surgery has been well demonstrated by a recently published large retrospective cohort (n=15 755) evaluating the relative contribution of patients, surgeons, and hospitals to postoperative complications after elective colectomy (67.6% minimally invasive; 32.4% open). Bamdad and colleagues found complications ranged from 8.7% to 30.2% and patient-related factors contributed most to the varying morbidity levels. The variance at the patient level was associated with an 8-fold increase in the development of postoperative complications when compared with the surgeon- and hospital-level variance combined (29). In fact, any preoperative condition that impairs an individual from tolerating the physiological stress of surgery (e.g., sarcopenia), impairs the immune response (e.g., malnutrition), and/or augments the catabolic response to stress (e.g., pre-existing insulin resistance) is a risk factor for poor surgical outcomes (19, 30). Given that these deviations from the "normal surgical trajectory" (31) are highly associated with the preoperative condition of the patient, there is increasing recognition of a critical need to address and optimize patient-related risk factors before surgery (19, 29). For example, a multi-centre, single-blinded, RCT assessed the effects of oral nutrition supplementation with dietary counselling before surgery in patients with colorectal cancer at nutritional risk on the development of postoperative complications (32). Burden and colleagues reported fewer infections and reductions in weight loss after surgery in those with nutrition supplements (intervention) when compared to dietary recommendations alone (control) (OR 0.341, 95%CI 0.128 to 0.909; P = 0.031) (32). Patient optimization may also include other various interventions such as medical management (e.g., pharmacological therapy

to reduce insulin resistance or improve anemia), promotion of health behaviours (e.g., drinking or smoking cessation) and enhancements of physiological reserve (e.g., increasing functional capacity, improving nutritional status) with the goal of reducing these modifiable risk factors prior to surgery (19, 33).

2.4 Surgical prehabilitation

Preoperative interventions that strengthen physiological reserve and enhance functional capacity may be a practical solution to address some patient-related risk factors. These interventions that prepare individuals before treatment are known as prehabilitation. As patients wait for their elective surgery, the preoperative period is thought to be an opportune and appropriate time to actively engage and empower patients in their care. Patients also view prehabilitation as an opportunity. A qualitative study of colorectal surgical patients (n=20) in an ERAS centre was conducted to better understand patients' perspective on surgical care. Three major themes were identified which support the argument of engaging and partnering with patients before surgery. The three main themes obtained from patient interviews in this study were: 1) passively waiting for their operation was detrimental to their physical and mental status, 2) actively preparing to address their individual needs would have been better than simply waiting, and 3) a partnership between them and the health care team would be best to support them (34).

In the cancer field, prehabilitation has commonly been described using the proposed definition by Silver and Baima published in 2013: "Cancer prehabilitation may be defined as a process on the continuum of care that occurs between the time of cancer diagnosis and the beginning of acute treatment, includes physical and psychological assessments that establish a baseline functional level, identifies impairments, and provides targeted interventions that

improve a patient's health to reduce the incidence and the severity of current and future impairments" (35). While there is no universally accepted definition for prehabilitation, other fields like colorectal surgery (36), orthopedic surgery (37), and before an anticipated intensive care unit admission (38) have used the following description: "prehabilitation is the process of enhancing functional capacity of the individual to enable him or her to withstand incoming stressor has been termed prehabilitation".

Historically, prehabilitation approaches focused on preoperative exercise therapy alone. Exercise-based prehabilitation includes aerobic exercise, resistance training or a combination of both modalities, with the goal of increasing functional capacity (often measured as peak oxygen consumption (VO_2) during an exercise tolerance test or as the distance covered during the 6 minute-walk test (6MWT)) to promote faster recovery to baseline function postoperatively (31). More recently, surgical prehabilitation interventions still include exercise therapy, but have expanded to include nutrition (39) and psychological/cognitive (40) components or a combination of these interventions as a multimodal approach (41-44). Surgical prehabilitation may be a solution to address patient-related risk factors while also complementing modern surgical practices such as ERAS pathways to achieve optimal post-operative outcomes (19).

2.5 Knowledge gaps

While there is a growing body of evidence of primary clinical trials in favour of prehabilitation before surgery and its beneficial effects on post-operative outcomes, some trials remain inconclusive. In fact, there is conflicting evidence regarding the effects of prehabilitation on clinical and functional outcomes even within the same surgical specialty. As an example, an exercise-based prehabilitation RCT in high-risk colorectal cancer patients (defined as those with a VO_2 at anaerobic threshold <11 mL/kg/min) displayed improvements in exercise capacity

before surgery led to a significant reduction in the rate of 30-day postoperative complications; 42.9% in the prehab group versus 72.9% in the control group (relative risk 0.59; 95% CI, 0.37–0.96; P=0.024) (45). Similar findings were also reported in another exercise-based prehabilitation trial in high-risk abdominal surgical patients (defined as those >70 years old and/or with an American Society of Anesthesiologists score of III/IV) as they reported a 51% reduction in postoperative complications between groups (relative risk 0.5; 95% CI, 0.3–0.8; P=0.001) (46). Furthermore, a multimodal prehabilitation (nutrition, exercise and psychological interventions) also favoured reductions in 30-day severe post-operative complications (Comprehensive Complication Index (CCI) > 20) in colorectal cancer subjects undergoing surgery (41). However, an RCT of a supervised exercise program before non- and oncological colorectal surgery did not find any differences in CCI endpoints at 30-day post-surgery when compared to the control group receiving only simple physical activity instructions (18, SD 0–43 compared to 15, SD 0–49; P=0.059) (47). Also, some trials have compared prehabilitation to rehabilitation interventions. For example, Carli and colleagues failed to demonstrate a reduction in post-operative complications in frail participants living with colorectal cancer. They conducted a similar multimodal prehabilitation program (nutrition, exercise and psychological interventions) and found no significant differences in 30-day postoperative complications measured as the adjusted mean difference of CCI score (adjusted mean difference, –3.2; 95% CI, –11.8 to 5.3; P=0.40) nor in functional exercise capacity (6MWT) at 4 weeks after surgery when compared to the rehabilitation program (adjusted mean difference, 18.5 m; 95% CI –20.2 to 57.3 m; P=0.34) (42). Interestingly, other multimodal trials have reported that clinically meaningful improvements in preoperative functional capacity in the intervention group have translated to earlier recovery of baseline function (i.e., return to baseline 6MWT) 8 weeks postoperatively

when compared to the rehabilitation group (48, 49). We must acknowledge that some of these differences across trials may be attributed to variable effects across patient populations, complications being measured differently, and that not all trials were conducted in ERAS centers and thus may have started with higher initial levels of complications.

Moreover, large systematic reviews and meta-analyses remain unable to report strong levels of certainty on the effectiveness of surgical prehabilitation for various outcomes. This is problematic as robust conclusions are needed to better target patients that may benefit from prehabilitation and are required for the implementation of these preoperative programs in health care systems. An umbrella review of 55 systematic reviews (n=1412 individual studies) of prehabilitation from 2004 to 2020 by McIsaac and colleagues supported prehabilitation's effectiveness for improving functional recovery with moderate certainty. However, the level of certainty of reductions in postoperative complications, increases in the proportion of home discharges and reductions on hospital LOS were graded as low or critically low. The uncertainty of the literature was explained by heterogeneity across interventions and diversity in reported outcomes (only 15 individual reviews could be pooled for meta-analyses due to heterogeneity), along with substantial methodological limitations of the included systematic reviews and their primary studies. The authors suggested that key priorities should be addressed to improve surgical prehabilitation evidence: 1) having a common definition, 2) finding consensus for a core outcome set, and 3) conducting additional high-quality studies (4). These recommendations have also been supported by the findings of a large scoping review (n=110 studies of prehabilitation) assessing preoperative interventions with a nutrition component (50). Additionally, a recent scoping review (n=70 RCTs of surgical prehabilitation) evaluating the quality of reporting found that trials described approximately half the checklist items recommended by methodological and

intervention reporting guidelines (CONSORT, CERT, Modified CERT, TIDieR, PRESENT, CONSORT-SPI) (51). Inadequate transparency and reporting practices most likely have contributed to methodological limitations found in systematic reviews. In fact, incomplete reporting of interventions, methods and outcomes leads to challenges when critically appraising the quality of studies (51).

The most recent systematic reviews and meta-analyses published in 2023, which were not included in McIsaac and colleagues' umbrella review, continue to acknowledge the heterogenous reporting, variability in study design and the low certainty of the evidence for prehabilitation before surgery (52, 53). Jain and colleagues (2023) conducted a review including 25 studies (n=4210 individual participants) of clinical trials and observational cohorts of abdominal surgeries and evaluated the effects of multimodal prehabilitation on surgical and functional outcomes. The authors pooled mortality, hospital LOS, postoperative complications (overall and Clavien-Dindo >2) and functional capacity assessed with the 6MWT. They were unable to pool and quantify the impact of the prehabilitation interventions on other outcomes like exercise capacity and quality of life, because of missing information and inconsistencies in the choice of outcome assessments and timeframes used in individual studies (52). A systematic review and meta-analysis by Punnoose and colleagues (2023) evaluated whether prehabilitation was associated with improved pre- and postoperative outcomes for patients undergoing various orthopedic surgical procedures across 48 RCTs (n=3570 individual participants). Authors concluded that although prehabilitation programs showed favourable statistically significant differences over usual care for pain, range of motion, and functional performance (timed up and go and stair tests), the overall certainty of the evidence was rated as low to very low (53).

While the current body of evidence for prehabilitation before surgery tends to favour its effectiveness on improving different postoperative outcomes, its poor certainty remains an issue reported across many systematic reviews and meta-analyses. These reviews have constantly reported that the heterogeneity in study design and inconsistencies in the choice of study endpoints make pooling effect estimates challenging and thus downgrade the quality of available evidence. To continue advancing the surgical care field by addressing patient-related risk factors through prehabilitation, these gaps must be addressed. Standardizing the definition of surgical prehabilitation and harmonizing reported outcomes are needed to design future high quality RCTs, better appraise the certainty of the evidence and generate robust conclusions regarding the effectiveness of prehabilitation on meaningful outcomes.

2.6 Rationale for a scoping review

An important first step to achieve consistency is to gain knowledge on how surgical prehabilitation is commonly being defined in the literature. Furthermore, having a clear understanding of what is currently being reported across trials is needed to further reduce heterogeneity and guide consensus on the selection of core outcomes for prehabilitation trials. To fill both these gaps, this MSc research project has the purpose of systematically mapping definitions and outcomes reported across RCTs of unimodal (consisting of exercise, nutrition or cognitive/psychological training) and multimodal (two or more modalities) prehabilitation lasting 7 days or more (which follows ERAS initiatives) in adult patients undergoing elective surgery. The methodological approach that best fits the purpose of this research is a scoping review.

Scoping reviews are increasingly popular in health research as the goal is to provide a general overview of how research is conducted, identify gaps or interpret issues that will inform

further research, explore and clarify key concepts and definitions and/or map the evidence of broad topics of a research field (54). Its purpose and methods differ from other common types of reviews such as meta-analyses, systematic and literature reviews. Contrary to meta-analyses and systematic reviews, scoping reviews do not intend to provide a numerical answer to a specific research question (characterized by a PICO statement) by pooling quantified data of included studies nor critically appraise the quality of the evidence (55, 56). Furthermore, scoping reviews also differ from narrative reviews as they require a structured and systematic search strategy to maximize the scope and data collected as well as reduce selection bias. While for narrative reviews, they may only include recent studies and/or limit the inclusion of studies that favors the authors perspective (56). Scoping reviews go beyond summarizing the current body and quality of evidence to a specific question as they address much broader questions and topics. The purpose and framework of a scoping review fits best with the objective of this MSc thesis as it intends to provide clarity on the broad topics of defining and reporting outcomes in the field of surgical prehabilitation.

3. METHODOLOGY

To summarize definitions and map the broad possible reported outcomes (what, how and when) of the current surgical prehabilitation literature, we conducted a scoping review using the recommended framework and best practice guidelines for reporting findings. This research used quantitative and qualitative data analysis such as descriptive statistics and summative content analysis for both manuscripts 1 and 2, and a qualitative triangulation approach for manuscript 1.

3.1 Scoping review

There are many different definitions used to define scoping reviews (54). The Canadian Institute of Health Research provides a thorough and comprehensive description of scoping research: "an exploratory project that systematically map the literature available on a topic, identifying the key concepts, theories, sources of evidence, and gaps in the research. It is often preliminary to full syntheses, undertaken when feasibility is a concern – either because the potentially relevant literature is thought to be especially vast and diverse (varying by method, theoretical orientation or discipline) or there is suspicion that not enough literature exists. These entail the systematic selection, collection and summarization of existing knowledge in a broad thematic area for the purpose of identifying where there is sufficient evidence to conduct a full synthesis or where insufficient evidence exists and further primary research is necessary" (54).

Although there is no universally accepted way of defining scoping reviews, there is consensus around its purpose and common elements to ensure its methodology is rigorous. Scoping studies aim to answer broad questions, map, summarize and disseminate the evidence using a systematic approach, identify gaps in the existing literature and/or explore an area that has not been reviewed comprehensively before (54, 57). The first proposed framework was

published in 2005 by Arksey and O'Malley (57). Since, recommendations to improve the methodological approach have been suggested by Levac, Colquhoun and O'Brien (54).

3.1.1 Scoping review framework

Following the Arksey and O'Malley framework (57) and recommendations by Levac, Colquhoun and O'Brien (54), the first five steps were used to conduct our scoping review: 1) identifying the research questions, 2) identifying relevant studies, 3) selecting studies, 4) charting the data, 5) collating, summarizing, and reporting the results, and 6) consultation (optional step, not conducted in this research).

Step 1: Identifying broad research question(s) requires the clear articulation of questions that guide the search strategy. To do so, Levac, Colquhoun and O'Brien suggest including key concepts, the target population, the health outcomes of interest or the purpose of the study to the research questions to guide an effective search strategy and the choice of inclusion criteria. The research questions for this scoping review were the following: 1) How is surgical prehabilitation defined in the current literature of primary RCTs of unimodal (consisting of exercise, nutrition or cognitive/psychological training) and multimodal (two or more modalities) prehabilitation lasting 7 days or more in adult patients undergoing elective surgery? 2) What is the current landscape of outcomes and their specific outcome assessments across RCTs of unimodal and multimodal prehabilitation lasting 7 days or more in adult patients undergoing elective surgery? When and how are these outcomes reported?

Step 2: Identifying relevant studies involves conducting the literature search, clearly defining the inclusion and exclusion criteria, and reviewing articles for study inclusion. This step was guided by the purpose of the scoping review itself and was conducted as a team. Inclusion

and exclusion criteria were established before the search strategy was developed and performed. Our research team was composed of an international and multidisciplinary group of prehabilitation health researchers and practitioners (dietitians, physiotherapist, medical doctors) to include experts on the various fields involved in prehabilitation. The search strategy was created with the assistance of an experienced librarian. General search terms were used that encompassed prehab* or pre-hab* or prerehab* or pre-rehab* or (preoperative* or pre-operative*) adj rehab*) AND randomized controlled trial (see Appendix 1 for full search). Since our objectives were to identify a common definition and map outcomes of surgical prehabilitation RCTs, we started by focusing our search to published "prehabilitation" labelled (in title, abstract or keywords) trials. Then, we included those meeting our pre-determined inclusion criteria.

Step 3: Selecting studies entails that two independent reviewers screen and select relevant abstracts to undergo full text review. The review process of each potentially eligible article was done independently. Studies were included if both reviewers agreed on study inclusion. All disagreements were discussed until consensus was reached. Studies were included in the scoping review if they met the following criteria : randomized controlled trials delivering a "prehabilitation" labelled program (in the title, keywords or abstract) before surgery for adult patients (aged ≥18 years) or met the following working definition of prehabilitation which was based on a consistent description provided in the literature (51, 58-60): A unimodal intervention consisting of exercise, nutrition or cognitive/psychological training, or a multimodal intervention that combines exercise, nutrition and/or cognitive/psychological training with or without other interventions, undertaken for seven or more days before surgery (which is a period consistent with ERAS initiatives, not prehabilitation) to optimize a patient's preoperative condition and

improve post-operative outcomes. Studies were excluded if they were narrative reviews, editorials, systematic reviews, meta-analyses, scoping reviews, pooled analyses, secondary analyses, study protocols, consensus guidelines, conference abstracts, publications not in English or French, isolated medical treatments (e.g., medication management alone) and interventions that lasted less than 7 days before surgery.

Step 4: Charting the data involves the development of data extraction form. The extraction form was developed and reviewed by the full research team and was continuously adapted throughout the data extraction process. Two independent reviewers charted the data for the first five included articles to ensure the extraction process was consistent with the research questions, and adjustments to the data extraction were made accordingly. Following these adjustments, the data for all the included clinical trials was extracted and charted. This process was performed in duplicate by three independent reviewers. All disagreements were discussed until consensus between reviewers was achieved and clarified with the senior researchers when needed. Furthermore, to help summarize complex concepts and better support and interpret quantitative data, qualitative information was also collected. Both quantitative and qualitative data were extracted from the main manuscripts as well as clearly referenced protocols and all available supplementary materials of the included trials.

Step 5: Collating, summarizing, and reporting results is the last mandatory step of the Arksey and O'Malley framework for scoping review (57). Following the recommendations by Levac, Colquhoun and O'Brien, this step was broken down to 3 portions: the analysis of the extracted data including a quantitative (descriptive statistics such as counts and frequencies) and qualitative (triangulation and summative content analysis) approaches, followed by the reporting of the results according to the research questions and objectives, and finally the interpretation of

the meaning and relevance of the findings in regards to future research (54). The conceptual framework from the International Society for Pharmacoeconomics and Outcomes Research (ISPOR) task force was used to summarize and categorize the reported outcome assessments (61). The dissemination of the findings followed the Preferred Reporting Items for Systematic reviews and Meta-Analyzes extension for Scoping Reviews (PRISMA-ScR) checklist (62) which are PRISMA reporting guidelines adapted for scoping reviews.

3.2 International Society for Pharmacoeconomics and Outcomes Research Framework

For manuscript 2, a conceptual framework from ISPOR task force was used to organize and categorize all reported outcome assessments identified across the surgical prehabilitation trials according to the five types of health-related outcomes (61).

Following the ISPOR conceptual framework, health outcomes were categorized as biomarker outcome assessments and clinical outcomes assessments which included patient-reported (PRO), clinician-reported (ClinRO), observer-reported (ObsRO), and performance (PerfO) outcomes (figure 1). Biomarkers are biochemical measures physically present in body fluids and are not subject to patient motivation or the perspective of the researcher (the rater) collecting the data. An example of biomarker outcome is a blood marker of glucose metabolism such as fasting blood glucose or glycated hemoglobin. PROs are outcomes that rely directly on the patient's response to a specific questionnaire or scale. PROs may be collected using various formats including interviews, paper or web-based forms. For this type of outcome, the patient is the rater as their responses are used directly without further interpretation. This means that the evaluation of the patient's responses by a clinician, observer or interviewer is not required. An

example of PRO is the Hospital Anxiety and Depression Scale (HADS). ClinROs are outcomes for which the appropriate health care professional is the rater. In this case, the clinician is required to apply professional expertise or judgment to the observations or is needed to interpret the patient's responses, actions or state. A specific example of ClinRO is postoperative complications which are often classified according to severity using a grading system. ObsROs are recorded by an observer (other than the patient) who does not require any specific health care professional training to appraise or record the outcome. Hospital LOS, which is often collected directly from a patient's medical chart, can be categorized as an ObsRO. PerfOs are outcomes in which patients perform a task, but no rater perspective nor clinical judgment affects the result of the assessment. The defined task or instrument used to measure the PerfO is intended to assess a meaningful functional aspect of health but may be influenced by the patient's motivation. An example of a performance measure is functional exercise capacity assessed with the 6MWT. Other outcomes (e.g., adherence) were classified as non-health-related outcomes (61).

During the data extraction step of our scoping review, individual concepts of interest for measurement and their specific outcome assessments were identified and categorized according to their type (biomarker, PRO, ClinRO, ObsRO or PerfO). The ISPOR framework defines the *concepts of interest* as what the outcome assessment intends to measure. The concept of interest represents, often in a simplified form, a meaningful aspect of the patient's health or disease state (related to feelings, function or survival). A specific *outcome assessment* is defined as the measuring tool, instrument or test providing a rating or score (categorical or continuous) that represents some aspect of the patient's health or medical status (figure 1) (61). For manuscript 2, the terms "outcome" and "measurement instrument" or "test" were used to simplify terminology.

For example, health-related quality of life (concept of interest or "outcome") can be measured using the EQ-5D questionnaire (outcome assessment or "measurement instrument").

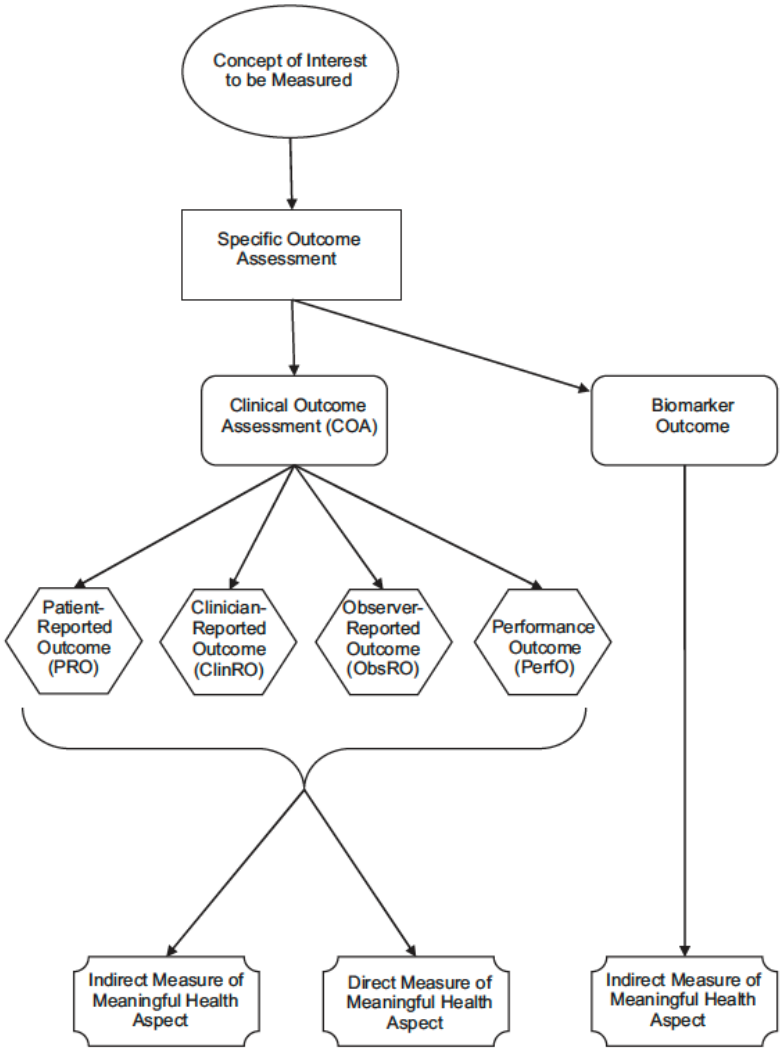

Figure 1. This figure represents the major types of specific outcomes assessments according to the ISPOR Framework: 1) clinical outcome assessments (PRO, ClinRO, OsbRO and PerfO), and 2) biomarker outcomes. These outcome assessments are selected to operationalize the measurement of the concept of interest. The concept of interest for measurement is what the outcome assessment intends to measure and is related to a meaningful aspect of health (related to feelings, function or survival) (61).

3.3 Qualitative analysis

Charting of data included quantitative and qualitative information. Therefore, analyses also included quantitative (descriptive only) and qualitative methods. The qualitative approaches used in this research were summative content analysis and triangulation to ensure trustworthiness of our findings.

3.3.1 Summative content analysis

Content analysis approaches are qualitative research methods used to analyze text. Hsieh and colleagues have defined content analysis as "a research method for the subjective interpretation of the content of textual data through the systematic classification process of coding and identifying themes or patterns" (63). These methods allow sorting of text data to understand similarities, differences, trends and associations both directly and indirectly stated in the text (64). Following Hsieh and Shannon's terminology and description for content analysis, a summative content analysis approach was applied. We used both inductive (i.e., codes were derived from keywords directly found in the text data then grouped into categories according to similar meaning) and deductive (i.e., using a predetermined framework as categories, codes were identified from keywords in the text data) summative content analysis to best answer our research questions (63).

Summative content analysis is a type of content analysis that quantifies keywords in text data. This qualitative method identifies and counts the frequency of a specific word or group of words (i.e., codes) with the goal of understanding the contextual usage of these specific words (i.e., category) (64). Codes are typically short (1-3 words) labels that describe a single concept, while categories are an organization of many codes that are related either by their content or the context of the field. Summative content analysis is suggested to be an unobtrusive and unreactive

approach, because it allows a more objective assessment of text data by identifying the most frequently used codes and categories. (64) For manuscript 1, inductive summative content analysis was performed by an independent researcher (coder) to identify common categories used to define surgical prehabilitation. This approach was also used in manuscript 2 to describe how specific outcome assessments were reported. Furthermore, a deductive summative content analysis approach was also performed in manuscript 1 to assess common codes used to define surgical prehabilitation, but according to specific framework. For the deductive summative content analysis, important pre-specified categories were used before the identification of codes which included the purpose or goal, descriptor of the intervention, intervention type, timing and target population. These categories were guided by the Template for Intervention Description and Replication (TIDieR) which is a framework used for the reporting of interventions (not specific to prehabilitation) (65). Inductive and deductive summative content analysis approaches were performed by two independent coders. Using this methodology was strategically implemented to ensure method and investigator triangulation to enhance the trustworthiness of our qualitative findings (66). Finally, the inductive approach was prioritized over the deductive approach as it was more appropriate for the final consolidation of the surgical prehabilitation definition as no exact framework currently exist for the reporting of prehabilitation intervention.

3.3.2 Ensuring trustworthiness

Quality and rigour of qualitative research is termed “trustworthiness”. This concept of trustworthiness of research findings was first proposed in 1985 by Lincoln and Guba and is comprised of *credibility*, *transferability*, *dependability*, and *confirmability* (67). For manuscript 1, specific elements were considered to ensure the trustworthiness of the consolidated definition for surgical prehabilitation (68, 69).

The first component to ensure trustworthiness is to demonstrate credibility or internal consistence (internal validity in quantitative terminology) (68) meaning that the textual evidence is consistent with the interpretation (69). To establish credibility of our qualitative results, an investigator triangulation approach was used. Investigator triangulation is the process of including two or more researchers from the study team to conduct independent analysis which provides more depth, confirms results or highlights different perspectives for the same phenomena (66). Data extraction and charting involved two independent coders, from different professional backgrounds (dietitian and physiotherapist), to ensure internal consistence.

The second component of trustworthiness is to ensure transferability (external validity or generalizability in quantitative terminology) of the qualitative findings (68). Transferability refers to whether results are transferable or valuable to other specific settings (69). Study characteristics were provided to better contextualize the findings of the proposed common definition in manuscript 1. The study characteristics included surgical specialties (abdominal, orthopedic and spinal, thoracic, cardiac, and other types), prehabilitation modalities (multimodal, exercise only, nutrition only, cognitive only) and type of population (oncological versus non-oncological surgeries).

The third component to establish trustworthiness is to address the dependability of the qualitative findings (reliability in quantitative terminology) (68). Dependability evaluates whether the process of research is logical, and the methods and decisions made by the researchers are clearly documented (69). Method triangulation which refers to the use of multiple methodological approaches for data collection was used to develop a comprehensive understanding of the text data in RCTs that defined surgical prehabilitation (66). Both inductive and deductive summative content analysis approaches were used to assess and interpret text (64).

The inductive and deductive consolidated definitions were then compared to verify conclusions were similar and dependable of each other.

The final component to improve trustworthiness of qualitative data is to ensure its confirmability (objectivity in quantitative terms) (68). Confirmability refers to the neutrality of the data interpretation and how the researchers' perspectives may influence or bias the results and interpretations (69). In this research, the confirmability was addressed by having a multidisciplinary (health researchers, dietitian, physiotherapist, medical doctor) and international (Canada, Australia, United Kingdom) team to have a diversity of perspectives. The diversity of the research team allowed for deliberation when interpreting results of manuscripts 1 and 2, and when consolidating the final surgical prehabilitation definition in manuscript 1.

4. MANUSCRIPT 1: Towards a common definition of surgical prehabilitation

Chloé Fleurent-Grégoire[1,5*], Nicola Burgess[2*], Daniel I McIsaac[3,4], Stéphanie Chevalier[1,5,6], Francesco Carli[6], Linda Denehy[7,8*], Chelsia Gillis[1,6,9*]
*First and last authors contributed equally

Affiliations:
1. School of Human Nutrition, McGill University, Montreal, Quebec, Canada
2. Department of Physiotherapy, Austin Health, Melbourne, Australia
3. Department of Anesthesiology and Pain Medicine, University of Ottawa, Ottawa, Ontario, Canada
4. Clinical Epidemiology Program, Ottawa Hospital Research Institute, Ottawa, Ontario, Canada; School of Epidemiology and Public Health, University of Ottawa, Ottawa, Ontario, Canada
5. Research Institute of the McGill University Health Centre, Montreal, Quebec, Canada
6. Department of Medicine, McGill University, Montreal, Quebec, Canada
7. Departments of Anesthesia, McGill University, Montreal, Quebec, Canada
8. Department of Physiotherapy, Melbourne School of Health Sciences, University of Melbourne, Victoria, Australia
9. Department of Health Services Research, The Peter MacCallum Cancer Centre, Victoria, Australia
10. Department of Surgery, McGill University, Montreal, QC, Canada

Corresponding author: chelsia.gillis@mcgill.ca, T: (514) 398-7905, Macdonald-Stewart Bldg MS2-045 Macdonald Campus, 21111 Lakeshore Road, Montreal, Quebec H9X 3V9

Article category: Submitted to the British Journal of Anaesthesia as an editorial article.

4.1 Summary

There is currently no universally accepted definition for surgical prehabilitation. The objectives of this scoping review are to (1) identify how surgical prehabilitation is defined across available randomized control trials and (2) suggest a common definition using a summative content analysis and triangulation approach. Our findings consolidated the following definition: "Prehabilitation is a process from diagnosis to surgery, consisting of one or more preoperative interventions of exercise, nutrition, anxiety-reducing strategies, and respiratory training, that aims to enhance functional capacity and physiological reserve to allow patients to withstand surgical stressors, improve postoperative outcomes, and facilitate recovery." A common definition is the first step towards standardization, which is needed to guide future high-quality research and advance the prehabilitation field.

4.2 Background

To our knowledge, the concept of prehabilitation was first proposed in the British Medical Journal in 1946 as a program to prepare military recruits for physical and cognitive testing (1). In the late 1990s and early 2000s, prehabilitation was introduced to the field of elective surgery as an intervention using inspiratory muscle training before lung resection (2) and before coronary artery bypass graft surgery (3). Additionally, in 2007, prehabilitation was initiated before knee arthroplasty (4) and then prior to lumbar spinal surgery (5) using exercise therapy. By 2013, prehabilitation interventions were used to support oncological surgical care pathways including colorectal (6, 7), lung (8) and oesophageal (9) cancers.

As the field of cancer prehabilitation research progressed, a definition was proposed by Silver and Baima: "Cancer prehabilitation may be defined as a process on the continuum of care that occurs between the time of cancer diagnosis and the beginning of acute treatment, includes physical and psychological assessments that establish a baseline functional level, identifies impairments, and provides targeted interventions that improve a patient's health to reduce the incidence and the severity of current and future impairments" (10). While this definition has been extensively cited (Scopus: 352) (10), a common definition for surgical prehabilitation is still missing more than 2 decades after the initial published trials. This lack of consensus is an important issue as it may partly explain the heterogeneity in interventions and outcomes across surgical prehabilitation trials as well as the difficulties in pooling data, which limits the certainty of the evidence. In fact, in a recent umbrella review of 55 systematic reviews on preoperative prehabilitation, only 15 individual reviews could be pooled for meta-analyses to measure the overall certainty of prehabilitation's efficacy on various postoperative outcomes due to heterogeneity. Despite this limitation, prehabilitation was found to improve functional recovery

after oncological surgeries with moderate certainty, while the certainty of the evidence for non-oncological surgeries was rated as low or critically low. One of the key priorities proposed to improve the quality and certainty of surgical prehabilitation evidence, is to reach a consensus around how this high-priority preoperative intervention is defined (11).

To address this gap, we conducted a scoping review with the aim of proposing a common definition for prehabilitation in the context of surgery. A clear definition will help guide future quality randomized control trials (RCTs) that are needed to generate robust conclusions regarding the effectiveness of surgical prehabilitation on meaningful outcomes.

4.3 Methods

4.3.1 Study design

The objectives of this scoping review are to (1) identify how surgical prehabilitation is defined across RCTs and (2) suggest a common definition for future research. Only primary RCTs delivering a "prehabilitation" labelled program (written as "prehabilitation" in title, abstract or keywords) prior to surgery for adult patients (aged >18 years) were included in this review. The search strategy was created with the assistance of a librarian and general search terms were used that encompassed prehab* or pre-hab* or prerehab* or pre-rehab* or (preoperative* or pre-operative*) adj rehab*) AND randomized controlled trial. A detailed description of the methodology including the search strategy, study selection and data charting has been published elsewhere (12) (Manuscript 2, Fleurent-Gregoire et al., 2023).

4.3.2 Data analysis

Study characteristics and definition components were quantified using counts and proportions. The qualitative data were analyzed by 2 independent coders using summative

content analysis which involves coding, counting and comparisons of codes, followed by an interpretation of the underlying meaning of the content (13, 14). All reported definitions were entered in the data charting sheet (using Excel, Microsoft 2010, Redmond, WA). Definition components, as words or small phrases, were identified as codes before (i.e., deductive approach) and during (i.e., inductive approach) the analysis (13). The occurrence of each identified code was tabulated (13). Investigator and method triangulation were employed to ensure the trustworthiness of the analysis: two independent coders and qualitative approaches were used to form the common definition (15). The first coder used an inductive coding strategy that prioritized the most prevalent keywords in the explicit and implicit definitions provided by study authors (13). Codes with similar meanings were grouped under an overarching category (14). The categories with 10 counts or more were included in the final inductive definition, representing the most frequently stated words of each category. The threshold of 10 counts was prespecified (arbitrarily) to denote commonalty across trials. The second coder used a deductive approach by pre-specifying important categories (purpose or goal, descriptor of the intervention, intervention type, timing and target population) guided by Template for Intervention Description and Replication (TIDieR) reporting guidelines for interventions (16). In the deductive approach, the TIDieR framework was prioritized regardless of the frequency of the individual codes. Both the inductive and deductive definitions were then compared to form a consolidated extensional (i.e., lists all things that are applicable to the defined subject) definition that represents surgical prehabilitation programs (17).

4.4 Results

4.4.1 Study characteristics

A total of 76 RCTs met the inclusion criteria (Fleurent-Gregoire et al., 2023). Trials included abdominal (n=26/76, 34%), orthopedic and spinal (n=24/76, 32%), thoracic (n=14/76, 18%), cardiac (n=7/76, 9%) and other types (n=5/76, 7%) of surgeries. Surgical prehabilitation was explicitly defined in more than half of the RCTs (n=42/76, 55%). Trials that did not report an explicit definition, provided an explicit description of the intervention such as "...maintaining good exercise capacity using aerobic and inspiratory muscle training program" (18) or "short-term HIIT program was intended to augment preoperative physiological reserves and to facilitate postoperative functional recovery" (19). More than half of the explicit definitions (n=42) were from exercise-only trials (n=22/42, 52%) and approximately one-third originated from multimodal interventions (n=15/42, 36%). Together nutrition-only and cognitive-only prehabilitation accounted for 12% (n=5/42) of the RCTs providing an explicit definition. Half of the trials with an explicit definition stemmed from the oncology literature (n=21/42). Only 14% (n=6/42) and 5% (n=2/42) of definitions were derived from RCTs of thoracic and cardiac surgical populations, respectively.

Table 1. Identified inductive and deductive categories and their most reported codes using a summative content analysis approach

Category	Total category count and frequency* (n=76)	Most reported code(s)	Code count and frequency** (n=76)
Inductive approach			
Surgical time period	74 (97)	*Preoperative*	37 (49)
Physical activity	55 (72)	*Exercise/exercise training*	25 (33)
Descriptor of prehabilitation	32 (42)	*Intervention*	16 (21)

Increase function	28 (37)	*Enhance/improve/augment functional capacity*	17 (22)
Withstand stress	20 (26)	*Withstand a stressful event/stressor of surgery*	11 (15)
Continuous (from diagnosis to treatment)	18 (24)	*Process*	12 (16)
Improve reserve	18 (24)	*Enhance/increase/optimize physiological reserve*	8 (11)
Optimize nutrition	13 (17)	*Nutrition/nutrition support*	6 (8)
Delivery modal	13 (17)	*Multimodal*	6 (8)
Improve outcomes	11 (15)	*Improve post-operative outcomes*	4 (5)
Respiratory training	10 (13)	*Pulmonary rehabilitation*	3 (4)
		Inspiratory muscle training	3 (4)
Anxiety management	10 (13)	*Anxiety-reducing strategies*	2 (3)
		Psychological intervention	2 (3)
		Reduce stress and anxiety	2 (3)
Recovery	10 (13)	*Facilitate recovery of functional capacity*	2 (3)
Rehabilitation	7 (9)	*Rehabilitation*	4 (5)
Medical optimization	5 (7)	*Optimization of medical conditions*	1 (1)
		Smoking cessation	1 (1)
		Medical support	1 (1)
		Medical management	1 (1)
		Weight loss	1 (1)
Treatment benefits	4 (5)	*Benefits/beneficial effect*	3 (4)
Attenuate deterioration	4 (5)	*Reduce patient disability*	1 (1)
		Reduce the incidence and/or severity of future impairments	1 (1)
		Ameliorate the post-surgical physiologic deterioration	1 (1)
		Prevent or attenuate functional decline	1 (1)
Behavioral support	4 (5)	*Behavioral support*	2 (3)

Education	3 (4)	*Education/education program*	3 (4)
Personalized to population	3 (4)	*For patients with lower fitness*	1 (1)
		Varies according to context and the patient's needs	1 (1)
		Older patients with frailty	1 (1)
Baseline function	2 (3)	*Establish a baseline functional level*	1 (1)
		Identify impairments	1 (1)
Cost	1 (1)	*Reduce financial burden on the health system*	1 (1)
Lifestyle modification	1 (1)	*Lifestyle modification*	1 (1)
Deductive approach			
Purpose/goal	104 (137)	*Enhance functional capacity/aerobic capacity/physical fitness*	28 (37)
		Improve post-operative outcomes	17 (22)
		Combat surgical stressors	15 (20)
Intervention type	77 (101)	*Exercise/physical activity*	42 (55)
		Nutrition	12 (16)
		Psychological	7 (9)
		Medical optimization	5 (7)
		Education	3 (4)
Timing	51 (67)	*Before surgery/preoperative*	47 (62)
Descriptor	47 (62)	*Program*	14 (18)
		Process	12 (16)
		Intervention	8 (11)
Target population	4 (5)	*Patients with lower preoperative fitness*	1 (1)
		Older patients with frailty	1 (1)
		Individualised to patients needs and context	1 (1)
		Surgical patients	1 (1)

*Total category count and frequency: number of times codes within a specific category were reported across 76 trials; **Total code count and frequency: number of times a code was reported across 76 trials; Studies may report multiple codes in one category

4.4.2 Defining surgical prehabilitation

For both inductive and deductive qualitative methods, the identified categories and predominant codes across all explicit definitions and descriptions are shown in Table 1. The findings from the inductive approach revealed 23 different categories (i.e., codes with similar content or meaning). Nearly three quarters (n=55) of trials included "physical activity" in their definition and used the codes "exercise/exercise therapy" (n=25, 33%) most often. Forty-two percent (n=32) of trials used a "descriptor of prehabilitation" category with the most prevalent code being "intervention" (n=16, 21%). The category of "increasing function" was reported in more than one-third (n=28, 37%) of trials with the code "enhance functional capacity" being the most prevalent (n=17, 22%). When using the deductive approach, similar results were observed as the codes "enhance functional capacity/aerobic capacity/physical fitness" (n=28, 37%) and "exercise" (n=42, 55%) were also the most frequent (after the code "preoperative"). Ten inductive categories were excluded from the definition as they were infrequently (< 10 counts) reported (e.g., rehabilitation, treatment benefits, cost, attenuate deterioration, education, medical management, lifestyle modification, etc.). The two qualitative approaches, produced separate definitions (Table 2). There were two discrepancies observed between the inductively and deductively derived definitions: the inductive definition did not include medical optimization nor education. The medical optimization and education categories were reported few times (n=5, 7%; n=3, 4% respectively) across the 76 trials; therefore, these uncommon codes did not meet the proposed criteria for the inductive definition. Figure 1 represents the most frequently reported codes of each category across trials using the inductive method.

Table 2. Surgical prehabilitation definitions using inductive and deductive qualitative approaches

Method	Definition
Inductive qualitative approach using most common keywords	*"Prehabilitation is a process from diagnosis to treatment that consists of a unimodal or multimodal pre-operative intervention including exercise, nutrition, anxiety-reducing strategies and/or respiratory training, and aims to enhance functional capacity and physiological reserve to allow patients to withstand surgical stressors, improve postoperative outcomes and facilitate recovery."*
Deductive qualitative approach using TIDieR checklist	*"Prehabilitation can be defined as a program delivered prior to surgery that may consist of a number of interventions including exercise therapy, nutritional optimisation, psychological strategies, respiratory training, medical optimisation, and education, and aims to enhance functional capacity and physiological reserve to allow a patient to withstand surgical stressors and improve postoperative outcomes."*
Proposed common definition	***"Prehabilitation is a process from diagnosis to surgery, consisting of one or more preoperative intervention of exercise, nutrition, anxiety-reducing strategies, and respiratory training, that aims to enhance functional capacity and physiological reserve to allow patients to withstand surgical stressors, improve post-operative outcomes, and facilitate recovery."***

TIDieR: Template for Intervention Description and Replication

4.5 Discussion

4.5.1 The need for a standardized definition

Currently, there is no standardized, universally accepted definition for surgical prehabilitation. Harmonized definitions in clinical research give rise to more robust evidence by facilitating use of consistent designs and reported outcomes, which may improve pooling of data for future meta-analysis, leading to higher levels of evidence certainty (11). In fact, scoping reviews of prehabilitation intervention (12) and outcome reporting (Manuscript 2, Fleurent-Gregoire et al., 2023) reveal significant heterogeneity, and this lack of consensus has impeded the ability to draw strong conclusions regarding the effectiveness of surgical prehabilitation (11). Ultimately, adoption of a common intervention definition, in addition to a core outcome set, could enhance the ability to develop, evaluate and implement preoperative interventions that support optimal patient recovery after surgery (11). As a first step towards standardization, this

scoping review proposes a common extensional definition of surgical prehabilitation, developed by qualitatively triangulating and synthesizing prehabilitation definitions across 76 primary RCTs.

4.5.2 Components of a common prehabilitation definition

Using both inductive and deductive approaches, we identified consistent surgical prehabilitation components across 76 trials, including timing (prior to surgery), modalities (exercise, nutrition, psychological and respiratory training) and objectives (enhancing functional capacity and physiological reserve to improve outcomes and recovery), which inform our proposed common definition. However, given the heterogeneity of the included study interventions/definitions, our proposed definition should be seen as an initial step toward the foundational work required to finalize a widely accepted definition that can be adopted internationally by the multidisciplinary and intersectoral field of prehabilitation.

We must acknowledge that uncertainty and possible controversy remains about the role of medical optimization (20, 21) and education, especially within the context of surgical prehabilitation interventions. The findings of this scoping review suggest that these components are not common interventions of prehabilitation. That said, the modalities included in our proposed definition may be enhanced by medical optimization (e.g., anemia correction), and inherently involve modality-specific education (22) (i.e., education or counselling related to anxiety management, nutrition, exercise and breathing techniques). Exclusion of "medical optimization" and broad "education" across trials of prehabilitation, and therefore our proposed definition, may reflect the distinct nature of prehabilitation modalities. For example, medical optimization (and the related concept of medical clearance) as well as preoperative education (e.g., procedure-specific logistics, expectations of surgery, carbohydrate loading, etc.) are well-

established and long standing practices, often led by internal medicine specialists, anesthesiologists or other clinicians independent of prehabilitation programming (23). Conceptually, the prehabilitation modalities included in our definition would be expected to be longitudinal, focus on activities primarily performed by patients, and are conducted with the purpose of building reserve. In contrast, surgery-specific medical optimization is most often a single encounter, focuses on testing and risk stratification, and is performed by clinicians (23). Furthermore, Enhanced Recovery After Surgery (ERAS) programs, which are evidence-based care improvement processes, already have well-established medical management procedures (e.g., preoperative cessation of smoking) embedded within the pathways (24). Similarly, procedure-specific education tends to involve a single or limited encounters, designed to provide factual information about the planned procedures (25) and is also one of the ERAS pillars (24). The infrequent reporting of education and medical management across prehabilitation trials might represent the complementarity of this intervention with existing medical optimization services, including procedure specific education, perioperative risk stratification, and medical management, to achieve optimal patient outcomes and improve patient experiences (26). It is possible that sites lacking appropriate medical optimization and education (e.g., surgery schools) were more inclined to include these components in their definition of prehabilitation. Ultimately, broad collaboration between patients, clinicians, researchers and health system leaders internationally, informed by robust knowledge synthesis, will be required to achieve a widely accepted definition.

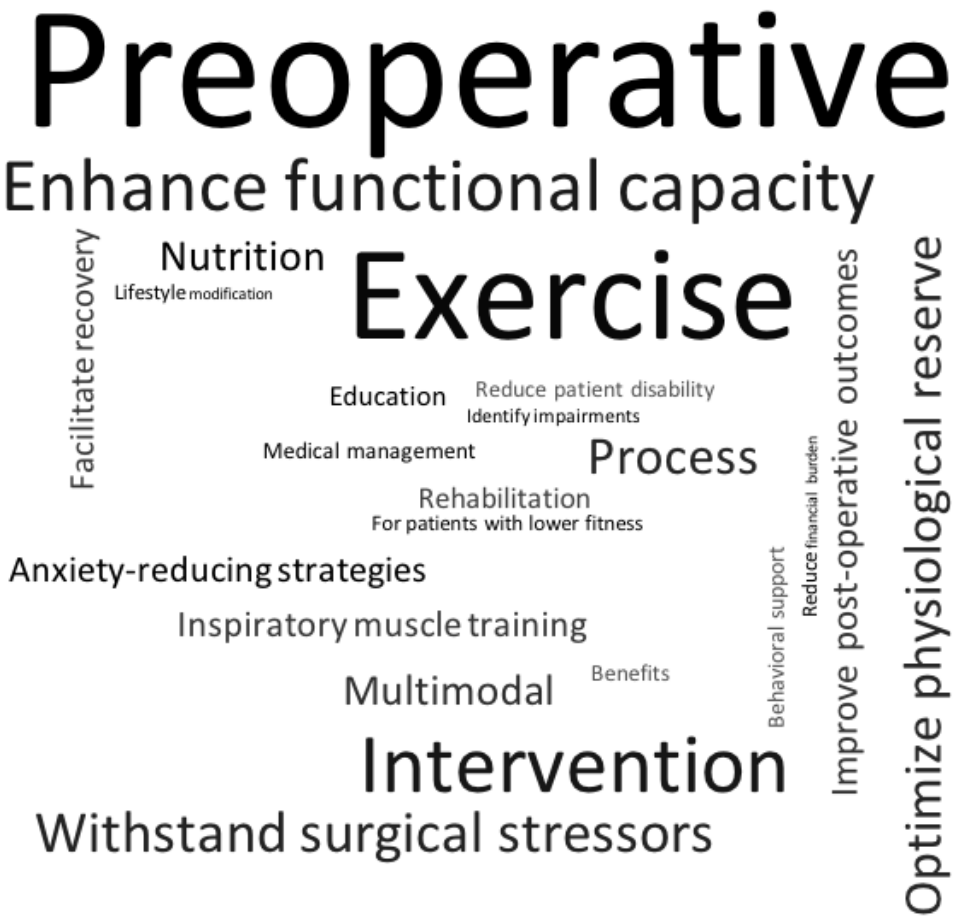

Figure 1. Word cloud using an inductive qualitative approach to define surgical prehabilitation. The scaling of each code is proportional to the number of times it was reported across all 76 trials included.

4.5.3 Limitations and future directions

The common definition produced from this scoping review is not without limitations. First, the definition has been generated using only published definitions, meaning it is limited to commonly reported components of surgical prehabilitation trials, which does not necessarily reflect validity nor consensus. Secondly, as observed in Figure 1, this definition is limited by the historical perspective of prehabilitation which has been predominantly described as "preoperative exercise" even though multimodal models in cancer and surgery have expanded beyond exercise therapy alone (27). Thirdly, the trials that reported explicit definitions (n=42, 55%) were mainly from abdominal, orthopedic and spinal specialties; therefore, this common

definition may not reflect the priorities of other surgery types. Given that the goal of this scoping review was to describe how surgical prehabilitation is currently being defined, we did not additionally consult a group of experts in the prehabilitation field for further input and consensus. We suggest that the next step is to consult international stakeholders and experts in the field to ensure the development of a comprehensive and globally accepted definition.

4.6 Conclusion

In conclusion, there are many distinctive published definitions for surgical prehabilitation. This scoping review has consolidated the available literature to suggest a common definition using a qualitative triangulation approach. The proposed common definition is the first step towards standardization, which is needed to guide future high-quality RCTs and advance the prehabilitation field.

Acknowledgements: *We would like to thank Genevieve Gore, Liaison Librarian, Schulich Library of Physical Sciences, Life Sciences, and Engineering, McGill University, for her assistance with developing and conducting the search strategy for this scoping review. We also would like to thank Dominique Engel and Giuseppe Dario Testa for conducting an important part of identifying and selecting relevant studies for this scoping review.*

Funding statement: There was no explicit funding for the development of this review.

Conflicts of interest statement: CG has received honoraria for giving educational talks sponsored by Abbott Nutrition, Nestle Nutrition and Fresenius Kabi, which were unrelated to this manuscript.

4.7 References

1. Unknown author. Prehabilitation, rehabilitation, and revocation in the Army. British Medical Journal

. 1946;1:192-7.

2. Weiner P, Man A, Weiner M, Rabner M, Waizman J, Magadle R, et al. The effect of incentive spirometry and inspiratory muscle training on pulmonary function after lung resection. The Journal of Thoracic and Cardiovascular Surgery. 1997;113(3):552-7.

3. Arthur HM, Daniels C, McKelvie R, Hirsh J, Rush B. Effect of a preoperative intervention on preoperative and postoperative outcomes in low-risk patients awaiting elective coronary artery bypass graft surgery: a randomized, controlled trial. Annals of Internal Medicine. 2000;133(4):253-62.

4. Jaggers JR, Simpson CD, Frost KL, Quesada PM, Topp RV, Swank AM, et al. Prehabilitation before knee arthroplasty increases postsurgical function: a case study. The Journal of Strength & Conditioning Research. 2007;21(2):632-4.

5. Nielsen PR, Jorgensen LD, Dahl B, Pedersen T, Tonnesen H. Prehabilitation and early rehabilitation after spinal surgery: randomized clinical trial. Clinical Rehabilitation. 2010;24(2):137-48.

6. Li C, Carli F, Lee L, Charlebois P, Stein B, Liberman AS, et al. Impact of a trimodal prehabilitation program on functional recovery after colorectal cancer surgery: a pilot study. Surgical Endoscopy. 2013;27:1072-82.

7. Mayo NE, Feldman L, Scott S, Zavorsky G, Kim DJ, Charlebois P, et al. Impact of preoperative change in physical function on postoperative recovery: argument supporting prehabilitation for colorectal surgery. Surgery. 2011;150(3):505-14.

8. Morano MT, Araújo A, S. a, Nascimento FB, da Silva GF, Mesquita R, et al. Preoperative Pulmonary Rehabilitation Versus Chest Physical Therapy in Patients Undergoing Lung Cancer Resection: A Pilot Randomized Controlled Trial. Archives of Physical Medicine & Rehabilitation. 2013;94(1):53-8.

9. Inoue J, Ono R, Makiura D, Kashiwa-Motoyama M, Miura Y, Usami M, et al. Prevention of postoperative pulmonary complications through intensive preoperative respiratory rehabilitation in patients with esophageal cancer. Diseases of the Esophagus. 2013;26(1):68-74.

10. Silver JK, Baima J. Cancer prehabilitation: an opportunity to decrease treatment-related morbidity, increase cancer treatment options, and improve physical and psychological health outcomes. American Journal of Physical Medicine & Rehabilitation. 2013;92(8):715-27.

11. McIsaac DI, Gill M, Boland L, Hutton B, Branje K, Shaw J, et al. Prehabilitation in adult patients undergoing surgery: an umbrella review of systematic reviews. British Journal of Anaesthesia. 2022;128(2):244-57.

12. Engel D, Testa G, McIsaac D, Carli F, Santa Mina D, Baldini G, et al. Reporting quality of randomized controlled trials in prehabilitation: a scoping review. Perioperative Medicine. 2023;12(1):48.

13. Hsieh H-F, Sarah. E. Shannon. Three Approaches to Qualitative Content Analysis. Qualitative Health Research. 2005;15(9):1277-88.

14. Kleinheksel AJ, Rockich-Winston N, Tawfik H, Wyatt TR. Demystifying Content Analysis. American Journal of Pharmaceutical Education. 2020;84(1):7113.

15. Carter N. BLD, DiCenso A., Blythe J., Neville A.J., editor The use of triangulation in qualitative research. Oncology Nursing Forum. 2014; 41(5):545-7

16. Hoffmann TC, Glasziou PP, Boutron I, Milne R, Perera R, Moher D, et al. Better reporting of interventions: template for intervention description and replication (TIDieR) checklist and guide. British Medical Journal. 2014;348:g1687.

17. Ostertag G. Emily Elizabeth Constance Jones. In: Zalta EN, editor. The Stanford Encyclopedia of Philosophy. Fall 2020 ed: Metaphysics Research Lab, Stanford University; 2020.

18. Satoto HH, Paramitha A, Barata SH, Sugiri, Suhartono, Wahyudati S, et al. Effect of preoperative inspiratory muscle training on right ventricular systolic function in patients after heart valve replacement surgery. Bali Medical Journal. 2021;10(1):340-6.

19. Licker M, Karenovics W, Diaper J, Fresard I, Triponez F, Ellenberger C, et al. Short-Term Preoperative High-Intensity Interval Training in Patients Awaiting Lung Cancer Surgery: A Randomized Controlled Trial. Journal of Thoracic Oncology: Official Publication of the International Association for the Study of Lung Cancer. 2017;12(2):323-33.

20. Beckerleg W, Kobewka D, Wijeysundera DN, Sood MM, McIsaac DI. Association of Preoperative Medical Consultation With Reduction in Adverse Postoperative Outcomes and Use of Processes of Care Among Residents of Ontario, Canada. JAMA Internal Medicine. 2023;183(5):470-8.

21. Wijeysundera DN, Austin PC, Beattie WS, Hux JE, Laupacis A. Outcomes and processes of care related to preoperative medical consultation. Archives of Internal Medicine. 2010;170(15):1365-74.

22. Boden I, Skinner EH, Browning L, Reeve J, Anderson L, Hill C, et al. Preoperative physiotherapy for the prevention of respiratory complications after upper abdominal surgery: pragmatic, double blinded, multicentre randomised controlled trial. British Medical Journal. 2018;360.

23. Riggs K, Segal J. What is the rationale for preoperative medical evaluations? A closer look at surgical risk and common terminology. British Journal of Anaesthesia Ltd. 2016; 117(6):681-4.

24. Ljungqvist O, Scott M, Fearon KC. Enhanced recovery after surgery: a review. JAMA Surgery. 2017;152(3):292-8.

25. Ronco M, Iona L, Fabbro C, Bulfone G, Palese A. Patient education outcomes in surgery: a systematic review from 2004 to 2010. International Journal of Evidence-Based Healthcare. 2012;10(4):309-23.

26. Gillis C, Ljungqvist O, Carli F. Prehabilitation, enhanced recovery after surgery, or both? A narrative review. British Journal Anaesthesia. 2022;128(3):434-48.

27. Macmillan Cancer Support. Principles and Guidance for Prehabilitation 2019 [Available from: https://www.macmillan.org.uk/healthcare-professionals/news-and-resources/guides/principles-and-guidance-for-prehabilitation.

Bridge Statement

Manuscript 1 has addressed the first objective of this MSc Thesis which is to identify how surgical prehabilitation is defined across primary RCT of unimodal (consisting of exercise, nutrition or cognitive/psychological training) and multimodal (two or more modalities) prehabilitation in adult patients undergoing elective surgery. It has also addressed the secondary component of the initial objective which is to consolidate a common definition for surgical prehabilitation for future research. This proposed common definition is the first step towards a universally accepted definition and harmonization of preoperative surgical interventions labelled as prehabilitation.

The following manuscript will address the second objective of this MSc Thesis which is to systematically map what, how and when outcomes and their specific outcome assessments are reported across primary RCTs of unimodal and multimodal surgical prehabilitation. This scoping review is the second step towards reducing heterogeneity which is one of the limiting factors when appraising the certainty of the prehabilitation evidence (4). In fact, understanding the current landscape of study endpoints is essential to build a set of core outcomes in a specific field of research (70). A COS for surgical prehabilitation will guide researchers when designing studies and selecting outcomes to measure and report.

5. MANUSCRIPT 2: The current landscape of reported outcomes in randomized trials of surgical prehabilitation: A scoping review

Chloé Fleurent-Grégoire[1,9], Nicola Burgess[2], Linda Denehy[3,4], Lara Edbrooke[3,4], Dominique Engel[5], Giuseppe Dario Testa[6], Julio F Fiore Jr[7], Daniel I McIsaac[8], Stéphanie Chevalier[1,9,10], John Moore[11], Michael P Grocott[12], Robert Copeland[13], Denny Levett[12], Celena Scheede-Bergdahl[14], Chelsia Gillis[1,15]

Affiliations:

1. School of Human Nutrition, McGill University, Montreal, QC, Canada
2. Department of Physiotherapy, Austin Health, Melbourne, Australia
3. Department of Physiotherapy, Melbourne School of Health Sciences, University of Melbourne, Victoria, Australia
4. Department of Health Services Research, The Peter MacCallum Cancer Centre, Victoria, Australia
5. Department of Anaesthesiology and Pain Medicine, Inselspital, Bern University Hospital, Bern, Switzerland
6. Division of Geriatric and Intensive Care Medicine, University of Florence and Azienda Ospedaliero Universitaria Careggi, Florence, Italy
7. Department of Surgery, McGill University, Montreal, QC, Canada
8. Department of Anesthesiology and Pain Medicine, University of Ottawa, Ottawa, ON, Canada; Clinical Epidemiology Program, Ottawa Hospital Research Institute, Ottawa, ON, Canada; School of Epidemiology and Public Health, University of Ottawa, Ottawa, ON, Canada.
9. Research Institute of the McGill University Health Centre, Montreal, QC, Canada
10. Department of Medicine, McGill University, Montreal, QC, Canada
11. Department of Anaesthesia, Manchester University NHS Foundation Trust, Manchester, United Kingdom
12. Perioperative and Critical Care Theme, NIHR Southampton Biomedical Research Centre, University Hospital Southampton – University of Southampton, Southampton, United Kingdom
13. Advanced Wellbeing Research Centre, Sheffield Hallam University, United Kingdom
14. Department of Kinesiology and Physical Education, McGill Research, Centre for Physical Activity & Health, McGill University, Montreal, QC, Canada
15. Departments of Anesthesia, McGill University, Montreal, QC, Canada

Corresponding author: chelsia.gillis@mcgill.ca, T: (514) 398-7905, Macdonald-Stewart Bldg MS2-045 Macdonald Campus, 21111 Lakeshore Road, Montreal, Quebec H9X 3V9

Article category: To be submitted to the British Journal of Anaesthesia, as a scoping review.

5.1 Abstract

Background: Heterogeneity of reported outcomes may impact the certainty of the evidence for surgical prehabilitation. **Objectives:** To systematically map reported outcomes and assessments tools in trials of surgical prehabilitation.

Eligibility Criteria: Randomized controlled trials (RCTs) of unimodal or multimodal prehabilitation interventions (nutrition, exercise, psychological support) lasting at least 7 days in adults undergoing elective surgery.

Methods: The final search was conducted in February 2023 using MEDLINE, EMBASE, PsychInfo, Web of Science, CINAHL, and Cochrane. Reported outcomes were classified according to the International Society for Pharmacoeconomics and Outcomes Research (ISPOR) framework.

Results: The 76 trials included patients undergoing abdominal (n=26, 34%), orthopedic (n=20, 26%) and thoracic (n=14, 18%), cardiac (n=7, 9%), spinal (n=4, 5%) and other (n=5, 7%) surgeries. Fifty different outcomes were identified, measured using 184 specific outcome assessments. Observer-reported outcomes were collected in 86% of trials (n=65), reported 175 times across trials using 24 outcome assessments, with hospital length of stay being the most common. Performance outcomes were reported in 80% of trials (n=61), reported 199 times across trials using 51 outcome assessments and the most reported was exercise capacity assessed by cardiopulmonary exercise testing. Clinician-reported outcomes were included in 78% (n=59) of trials, reported 84 times across trials using 26 outcome assessments, of which postoperative complications described using the Clavien-Dindo classification was the most frequent. Patient-reported outcomes were reported in 76% (n=58) of trials, reported 137 times overall using 63

outcome measurement instruments, with health-related quality of life using the 36- or 12-Item Short Form Survey being the most prevalent measure. Biomarker outcomes were reported in 16% of trials (n=12) for a total of 28 times across trials using 20 different biomarkers: inflammatory markers assessed with C-reactive protein was the most common.

Conclusion: There is substantial heterogeneity in the reporting of outcomes across surgical prehabilitation. The outcome assessments adopted also varied considerably. Identification of common and meaningful outcomes, and agreed outcome assessments, could inform the development of a core outcome set to harmonize outcome reporting and facilitate meta-analyses.

Keywords: pre-habilitation, pre-rehabilitation, pre-rehab, preoperative, pre-surgery, Enhanced Recovery After Surgery, clinical outcomes

5.2 Background

Every year, more than 300 million people will require surgery (1). Major surgeries put patients under substantial physiological stress. To reduce this stress response, evidenced-based Enhanced Recovery After Surgery (ERAS) pathways have been developed for more than 20 surgical specialties (2). While these advances have enhanced recovery (3-5), with some examples of significant reductions in clinical outcomes (6), postoperative complications generally remain high. This sustained incidence of complications despite the introduction of evidenced-based perioperative surgical elements has prompted investigators to examine preoperative risk of postoperative morbidity, including modifiable patient-related factors (7). A large retrospective cohort (n=15755) evaluating the relative contribution of the patient, surgeon, and hospital to postoperative clinical outcomes after elective colectomy (67.6% minimally invasive; 32.4% open) reported that *preoperative patient factors* contributed most to varying outcomes (8).

Given that deviations from the "typical surgical trajectory" (9) are highly associated with the patients preoperative status (8), there has been increasing interest in multimodal prehabilitation including preoperative exercise, psychological support and nutritional interventions (7, 10). A recent umbrella review of 55 systematic reviews of prehabilitation (n=381 individual studies) from 2004 to 2020 by McIsaac et al., supported prehabilitation's effectiveness (with moderate certainty) for improving functional recovery in patients with cancer undergoing surgery (11). Other positive effects of prehabilitation such as reductions in postoperative complications, increases in the proportion of home discharges and reductions of hospital length of stay were graded with low or critically low certainty. The poor quality of the literature was explained by substantial methodological limitations of systematic reviews and primary studies, along with heterogeneity across interventions and reported outcomes. The

authors concluded that key priorities to improve inconsistencies in prehabilitation evidence would be: 1) consensus for a core outcome set, 2) a common definition for surgical prehabilitation, and 3) additional high-quality studies (11). Heterogeneity in research reporting impedes the possibility to pool data together to support adequate meta-analyses of results, limiting the overall quality of the evidence to inform clinical practice and health care policies (12).

Before developing a core outcome set for surgical prehabilitation, an important first step to guide consensus and achieve consistency is to have a clear understanding of what is currently being reported among prehabilitation trials. To address this gap, we conducted a scoping review with the purpose of systematically mapping outcomes reported across randomized controlled trials (RCT) of unimodal (consisting of exercise, nutrition or psychological support) and multimodal (two or more modalities) prehabilitation in adult patients undergoing elective surgery.

5.3 Methods

5.3.1 Research design

To summarize and map the current prehabilitation literature, we conducted a scoping review. In contrast to a systematic review, a scoping review does not intend to critically appraise and summarize study results (related to a specific PICO question), but rather provides an overview of how research is conducted, clarifies key concepts or maps the evidence on broader topics within a specific field (13). Following the outlined framework by Arksey and O'Malley (14) and recommendations of Levac and colleagues (13), this scoping review was performed in five key phases: 1) identifying the research question, 2) identifying relevant studies, 3) selecting studies, 4) charting the data, and 5) collating, summarizing, and reporting the results. To develop

the research questions and collect the appropriate information, an international and multidisciplinary team composed of prehabilitation health researchers and practitioners was established. The reporting of our findings followed the Preferred Reporting Items for Systematic reviews and Meta-Analyses extension for Scoping Reviews (PRISMA-ScR) checklist (15).

5.3.2 Identifying the research question

The overarching objective of this scoping review was to systematically map outcomes in the surgical prehabilitation literature to inform the future development of a core outcome set to guide the conduct of future studies. Our research questions were: 1) What is the current landscape of outcomes and their specific outcome assessments across randomized controlled trials of unimodal (consisting of exercise, nutrition or psychological support) and multimodal (two or more modalities) prehabilitation lasting 7 days or more in adult patients undergoing elective surgery? 2) When and how were these specific outcome assessments reported?

5.3.3 Identifying relevant studies

Since our primary goal was to map outcomes of surgical prehabilitation RCTs, we started by focusing our search to published "prehabilitation" labelled (in title, abstract or keywords) trials, in which the participants were randomized to different groups (independent of the type and method of randomization). We included trials that met the following working definition of prehabilitation (16-19)*:* A unimodal intervention consisting of exercise, nutrition or psychological support, or a multimodal intervention that combines exercise, nutrition and/or psychological support with or without other interventions, undertaken for seven or more days before surgery (which is a period consistent with Enhanced Recovery After Surgery initiatives, not prehabilitation) to optimize a patient's preoperative condition and improve post-operative outcomes. The search strategy was created with the assistance of a librarian (GG; Appendix 1)

by following the Peer Review of Electronic Search Strategy process (20). No date restriction was set to our search strategy, therefore all studies after 1946 were included. The first search was conducted on March 25th 2022 (19), and was updated using the identical strategy with the same librarian on February 22nd 2023, using MEDLINE, EMBASE, PsychInfo, Web of Science, CINAHL, and Cochrane (GG; Appendix 1). Reference lists of all identified systematic reviews and meta-analyses of surgical prehabilitation were hand searched (DE and GDT) to include all relevant trials.

5.3.4 Study selection

Two independent reviewers used the Rayyan web-application (www.rayyan.ai, Cambridge, MA 02142, USA) (in the initial search DE and GDT, for the updated search CG and CFG) to screen titles and abstracts for inclusion. Studies were considered for full-text review if the following criteria were met: 1) studies delivering a "prehabilitation" labelled program before surgery for adult patients (aged ≥18 years) and in accordance with the above definition, and 2) were primary RCTs (including pilot and feasibility RCTs). Exclusion criteria were as follows: narrative reviews, editorials, systematic reviews, meta-analyses, scoping reviews, pooled analyses, secondary analyses, study protocols, consensus guidelines, conference abstracts, publications not in English or French, isolated medical treatments (e.g., medication management alone) and interventions conducted for less than 7 days prior to surgery. The reviewers then independently reviewed selected papers for full-text review. All disagreements were addressed by discussion until consensus was reached.

5.3.5 Charting the data

The research team collectively developed the data charting sheet (using Excel, Microsoft 2010, Redmond WA). Both quantitative and qualitative data were extracted from the main

manuscript as well as all referenced protocols and available supplementary material. Quantitative data collection included baseline study (including author, year of publication, region, surgical specialty and cancer type, specifications of the intervention, primary outcomes), patient (sex or gender, risk stratification), and care characteristics (surgical approach, ERAS). Given that surgical outcomes vary based on individual patient characteristics (e.g., malnutrition), we also charted the reporting of patient characteristics for risk assessment (21, 22).

Outcomes were classified according to the conceptual framework of the International Society for Pharmacoeconomics and Outcomes Research (ISPOR) (23). Health outcomes were categorized as biomarkers, patient-reported, clinician-reported, observer-reported, and performance outcomes (see Table 1 for definitions). For each type of outcome, individual concepts of interest for measurement and their specific outcome assessments, also referred to as outcome measurement instruments (24), were identified. The ISPOR framework defines the concept of interest for measurement as what the outcome assessment intends to measure, while the specific outcome assessment is defined as the measuring instrument providing a rating or score (categorical or continuous) that represent some aspect of the patient's medical or health status (23). The terms "outcome" for concept of interest will be used to simplify terminology going forward; "outcome assessment", "measurement instrument" or "test" will be used interchangeably to denote how the outcome was measured. As an example, health-related quality of life (concept of interest or outcome), can be measured using the EQ-5D questionnaire (specific outcome assessment or outcome measurement instrument). For each outcome, time-points were collected and categorized according to the various phases of recovery as described by Lee et al (25) and modified by Gillis, Ljungqvist, and Carli (7). The pre-admission phase of recovery was defined as the preparation period before surgery (i.e., this phase is a preparation for

postoperative recovery and is after completion of the prehabilitation intervention within a few days of surgery) (7), intermediate recovery was defined as the time from post-anesthesia care unit (PACU) discharge to discharge from hospital (i.e., within days after surgery), and late recovery described the phase from hospital discharge to return to the patient's usual function and activities (i.e., within weeks to months after surgery) (25). Qualitative data collection included verbatim descriptions of how the identified outcomes assessments were collected.

After the first eight studies were extracted, the data charting form was reviewed by the multidisciplinary team to determine whether the approach was in accordance with the research question and adjustments were made accordingly. The charting form was continuously updated during the data extraction process to collect all reported outcomes from the studies. Three reviewers (CFG, NB and LE) independently conducted data extraction, which was done in duplicate, and discrepancies were resolved by consensus discussion with senior authors (CG and LD).

Table 1. Outcome definitions and examples according to the ISPOR framework

ISPOR terminology	Definition and alternative terminology	Examples
Concept of interest for measurement	• The concept of interest for measurement represents what the outcome assessment intends to measure and is often a simplified form of a meaningful aspect of the patient's health or disease state (related to feelings, function or survival). • Alternate terminologies include "outcome" or "construct"	Health-related quality of life (concept of interest for measurement) can be measured using the EQ-5D questionnaire (outcome assessment)
Outcome assessment	• The outcome assessment is the measuring instrument providing a rating or score (categorical or continuous) that represent the concept of interest for measurement. Outcome assessment include clinical outcomes assessments and biomarkers. • Alternate terminologies include "outcome measurement instrument", "test" or "tool"	
Clinical outcome assessment	• Clinical outcome assessments include the following four types of outcomes: observer-reported, performance, patient-reported and clinician-reported outcomes.	Any observer-, patient-, clinician-reported or performance outcomes

Observer-reported outcome	• An observer-reported outcome is recorded by an observer (other than the patient) who does not require any specific health care professional training to appraise or record the outcome.	Hospital length of stay collected directly from a patient's medical chart
Performance outcome	• A performance outcome is when a patient performs a task, but no rater perspective nor clinical judgment is needed to quantify the performance. The defined task or instrument used to measure the performance outcomes is intended to assess a meaningful functional aspect of health and can be influenced by the patient's motivation.	Functional exercise capacity assessed with the 6-minute-walking test
Patient-reported outcome	• A patient-reported outcome relies directly on the patient's response (without further interpretation from a clinician, observer or interviewer) to a specific questionnaire or scale which may be collected using various formats including interviews, paper or web-based forms.	Anxiety and depression assessed using the Hospital Anxiety and Depression Scale
Clinician-reported outcome	• A clinician-reported outcome relies on the appropriate health care professional to be the rater. In this case, the clinician is required to apply professional expertise or judgment to the observation or is needed to interpret the patient's responses, actions or state.	Complications classified according the Clavien-Dindo grading system
Biomarker outcome	• A biomarker is often a biochemical measure physically present in body fluids and is not subject to patient motivation or the perspective of the researcher (the rater) collecting the data.	Blood marker of glucose metabolism such as glycated hemoglobin (HbA1c)

ISPOR: International Society for Pharmacoeconomics and Outcomes Research

5.3.6 Collating and summarizing results

Outcomes (i.e., concepts of interest) and their specific outcome assessments (i.e., tests or instruments) were categorized according to the conceptual framework of the ISPOR task force report for clinical outcome assessments (23) and according to the recovery periods described above (7, 25). Quantitative data were analyzed using descriptive statistics such as counts and frequencies. To map the current landscape of outcomes in surgical prehabilitation, type of outcomes (biomarkers, patient-reported, clinician-reported, observer-reported, and performance outcomes and non-health related outcome), specific outcomes and their assessments were counted. The total number of trials reporting a specific type of outcome were summarized as frequencies. However, given trials could have included more than one outcome assessment per

outcome (e.g., quality of life measured with EQ-5D and 36-Item Short Form Survey), the denominator for outcome assessments was reported as the number of total outcome assessments per category and per individual outcome, rather than per trial. Outcomes were also stratified per surgical specialty. To map when outcomes were reported, timeframes per outcome type and per individual outcome (trials may have used multiple time-points for one outcome) were counted. For the most prevalent outcomes, detailed qualitative descriptions were charted and analysed using summative content analysis to assess how they were reported (26). The members of the research team were consulted for the interpretation of the findings, mapping of the current state of reported outcomes, research gaps and acknowledgment for future research opportunities.

5.4 Results

5.4.1 Search results

Our search identified 1257 unique articles (Figure 1). After abstract screening, 149 articles were suitable for full-text review. A total of 79 articles were excluded because of publication type (n=36), population (n=13), study design (n=9), additional duplicates (n=17), language (n=2) and intervention type (n=2), leaving 70 articles. Hand searching produced 6 additional articles. A total of 76 articles were included in the final review (Appendix 2) (27-102).

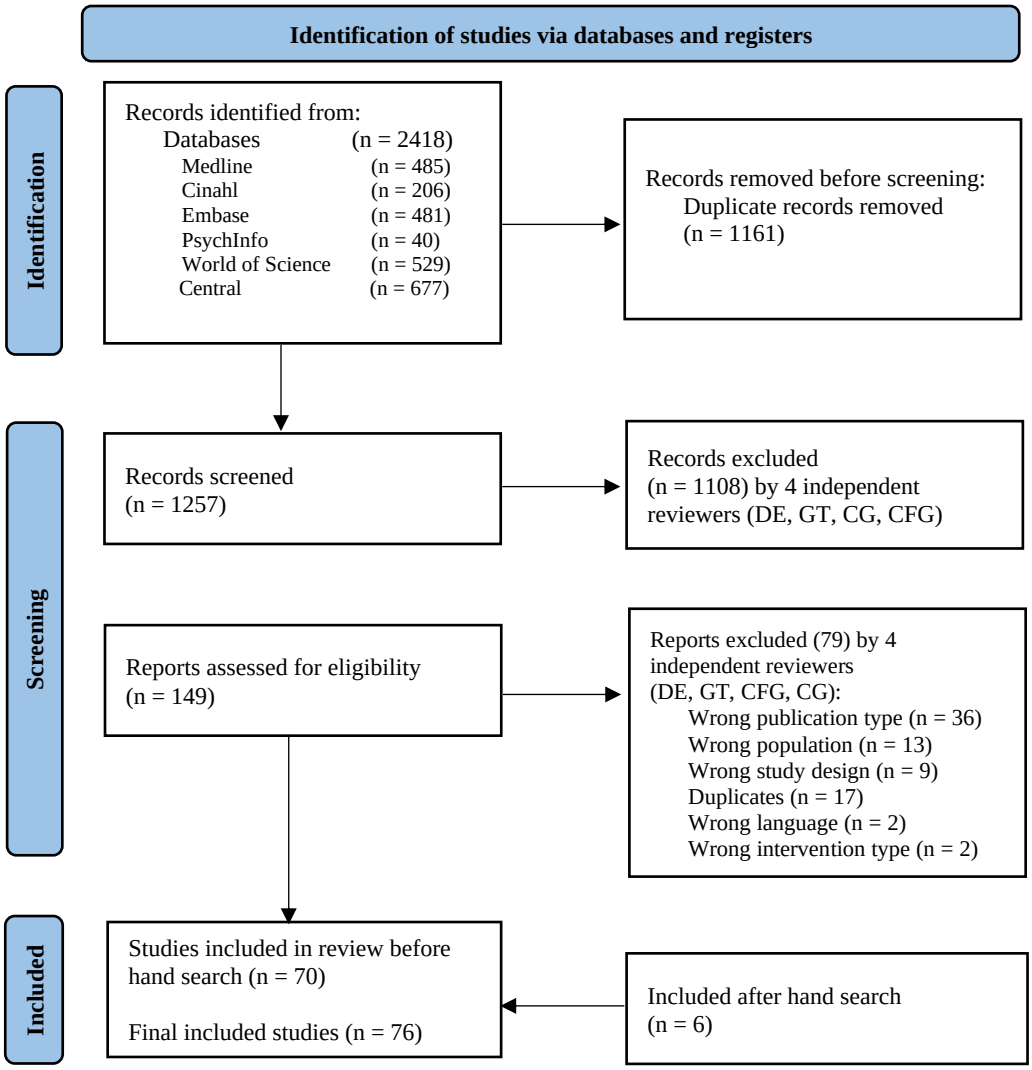

Figure 1 - PRISMA diagram flow

5.4.2 Prehabilitation study and patient characteristics

Table 2 describes study and patient characteristics. Trials (n=76) were mostly conducted in Europe (n=35, 46%) and North America (Canada n=17, 22%; United States n=9, 12%). Only one trial was conducted in multiple countries (n=1, 1%). More than half were unimodal exercise interventions (n=41, 54%) and one third were multimodal interventions (n=25, 33%). Approximately one-quarter of RCTs (n=20, 26%) specified that they were conducted in an ERAS health care center. The primary outcome was most frequently a performance outcome

(n=26, 34%) or clinician-reported outcome (n=23, 30%), and only a few used a patient-reported (n=11, 15%), observer-reported outcome (n=3, 4%) or biomarker (n=2, 3%). Six studies specified multiple primary outcomes (n=6, 8%) and some did not specify a primary outcome (n=5, 7%). The sample included patients who underwent abdominal (n=26, 34%), orthopedic (n=20, 26%), thoracic (n=14, 18%), cardiac (n=7, 9%), spinal (n=4, 5%) and other (n=5, 7%) surgeries. Of these trials, 46% were oncological-only resections (n=35) and 11% were mixed (n=8).

Almost two thirds of trials reported the surgical techniques used (e.g., minimally invasive surgery) (n=50, 66%) but few reported anesthesia techniques (e.g., general anesthesia) (n=6, 8%). To characterize the patients at baseline, more than half used at least one graded comorbidity risk assessment tool (n=39, 51%) (e.g., n=35, 46% American Society of Anesthesiologists Physical Status Classification System and/or n=12, 16% Charlson Comorbidity Index) and about one-third used a specific disease-related risk assessment tool (n=26, 34%) (e.g., n=9, 12% New York Heart Association Functional Classification or n=3, 4% ColoRectal Physiological and Operative Severity Score). Of the RCTs that included patients living with cancer (n=43), 58% reported the cancer stage (n=25/43) of their sample. Almost all trials reported the sex or gender (n=75, 98.7%) of participants (sex n=34, 45%; gender n=24, 32%; unclear n=17, 22%), but most did not explain how it was collected nor defined (n=70, 92%).

Table 2. Baseline study and patient characteristics

Characteristics	Number of trials (n=76) n (%)
Study characteristics	
Country	
Europe	35 (46)
Canada	17 (22)
United States	9 (12)
Asia	10 (13)
Australia	2 (3)
South America	1 (1)
New Zealand	1 (1)
Multiple countries	1 (1)
Study design	
Primary RCT	63 (83)
Pilot/feasibility RCT	13 (17)
Type of prehabilitation program	
Exercise only	41 (54)
Multimodal	25 (33)
Nutrition only	3 (4)
Cognitive only	3 (4)
Respiratory only	3 (4)
Pelvic floor training only	1 (1)
Primary outcome	
Performance	26 (34)
Clinician-reported	23 (30)
Patient-reported	11 (15)
Mixed	6 (8)
Unclear/not-specified	5 (7)
Observer-reported	3 (4)
Biomarker	2 (3)
Enhanced Recovery After Surgery center	
Yes	20 (26)
No	1 (1)
Not specified	55 (72)
Patient characteristics	
Population included	
Oncological surgery	35 (46)
Non-oncological Surgery	33 (43)
Mixed cohort	8 (11)
Type of surgical population	
Abdominal surgery only	26 (34)
Colorectal only	16 (21)
Urological surgery only	5 (7)
Hernia only	1 (1)
Pancreatic only	1 (1)
Hepatobiliary only	1 (1)

Mixed abdominal	2 (3)
Orthopedic surgery only	20 (26)
Thoracic surgery	14 (18)
Lung only	12 (16)
Oesophageal only	2 (3)
Cardiac surgery only	7 (9)
Spinal surgery only	4 (5)
Other	5 (7)
Mixed cohort	4 (5)
Breast only	1 (1)

5.4.3 Reported outcome assessments according to the ISPOR framework

We identified a total of 48 health and 2 non-health related outcomes (i.e., concepts of interest) across the 76 surgical prehabilitation trials. A total of 184 specific outcome assessments which included 164 clinical outcome assessments (including all assessment methods, instruments and tests) and 20 unique biomarkers were reported (Table 3 and Appendix 3).

Observer-reported outcomes

Nearly all trials reported at least one observer-reported outcome (n=65/76, 86%), which were commonly reported during the intermediate/hospital stay (n=57/65) and late phases of recovery, mostly ≤ 30 days after surgery (n=41/65). Observer-reported outcomes were reported 175 times using 24 outcome assessments (Table 3). The most frequent outcomes were hospital length of stay (LOS) (n=52/175, 30%), hospital readmissions (n=24/175, 14%) and postoperative mortality (n=23/175, 13%). Both hospital LOS and postoperative mortality were measured using 4 different approaches. Among the trials that measured LOS (n=52), 89% (n=46/52) defined LOS as the number of days from surgery to hospital discharge, while 8% (n=4/52) included total time (in days) from preoperative admission until hospital discharge after surgery, and 4% (n=2/52) also reported the cumulative hospital LOS over a 30- or 90-day period. Postoperative mortality was mostly reported independently (n=15/23, 65%) or as part of a composite score

such as grade V complication of the Clavien-Dindo classification (n=6/23, 26%). Of all observer-reported outcomes, discharge location was the most infrequently reported (n=6/175, 3%) (Appendix 3).

Table 3. Types of reported outcome assessments according to the ISPOR framework

Type of outcome assessments according to the ISPOR framework*	Total times reported across trials	Number of different outcome assessments	Number of trials reporting the outcome assessment (n=76) (n, %)	Description of timeframe according to phases of recovery**	Number of times an outcome was reported in a specific timeframe***
Performance outcome	199	51	61 (80)	Pre-admission	115
				Intermediate/hospital stay	12
				Late ≤ 30 d	34
				Late ≤ 90 d	61
				Late > 90 d	36
Observer-reported outcome	175	24	65 (86)	Pre-admission	18
				Intermediate/hospital stay	59
				Late ≤ 30 d	41
				Late >30 to ≤ 90 d	16
				Late > 90 d	5
Patient-reported outcome	137	63	58 (76)	Pre-admission	92
				Intermediate/hospital stay	10
				Late ≤ 30 d	53
				Late >30 to ≤ 90 d	106
				Late > 90 d	54
Clinician-reported outcome	84	26	59 (78)	Pre-admission	13
				Intermediate/hospital stay	22
				Late ≤ 30 d	37
				Late >30 to ≤ 90 d	18
				Late > 90 d	8
Biomarker outcome	28	20	12 (16)	Pre-admission	8
				Intermediate/hospital stay	6
				Late >30 to ≤ 90 d	2
				Late ≤ 90 d	4
				Late > 90 d	0

ISPOR: International Society for Pharmacoeconomics and Outcomes Research *Individual trials may have reported multiple outcomes within each type. **Phases of recovery: Pre-admission: preparation period before surgery (after the prehabilitation intervention); Intermediate: from after the post-anesthesia care unit to discharge from hospital; Late: from hospital discharge to return to the patient's usual function and activities. ***Trials may have collected multiple outcomes per timeframe.

Performance outcomes

At least one performance outcome was identified in 80% of RCTs (n=61/76). Of these trials (n=61), one or more performance outcomes were measured during the pre-admission recovery phase (preoperative period after the prehabilitation intervention) (n=115/61) and during the late phase of recovery, mostly within 30 to 90 days after surgery (n=61/61). In total, performance outcomes were reported 199 times using 51 specific outcome assessments (including tests) across trials (Table 3). Of all performance outcomes, exercise capacity during cardiopulmonary exercise testing (CPET) (n=43/199, 22%), strength (n=34/199, 17%), functional exercise capacity (n=33/199, 17%) and pulmonary function (n=33/199, 17%) were the most frequently reported. Ten different outcome assessments were identified to measure exercise capacity during CPET (n=43 trials). Tests were all conducted on an electromagnetically braked cycle ergometer with breath-by-breath gas exchange collected throughout an incremental load exercise protocol until volitional exhaustion. Peak oxygen (VO_2 peak) consumption was the most prevalent assessment (n=12/43, 28%), followed by peak workload (n=8/43, 19%) and oxygen consumption at the anaerobic threshold (VO_2 at AT) (n=8/43, 19%). Of the trials that measured VO_2 peak and/or VO_2 at AT, 33% (n=4/12) and 63% (n=5/8) explicitly followed the POETTS consensus, respectively (103). Thirty-eight percent (n=3/8) reported how peak workload was collected and all studies used different methods (e.g., peak workload was collected during the last 30s s up to the last 2 min of CPET) (Table 4). Nine different outcome assessments were used to describe strength (n=34), which included handgrip (n=10/34, 29%), quadriceps (n=10/34, 29%) and hamstrings strength (n=4/34, 12%). Functional exercise capacity (n=33) was most commonly measured using the 6-minute walk test (6MWT) (n=32/33, 97%), with one study using the 5-minute walk test (5MWT). Of those using the 6MWT, more than half (n=18/32, 56%) referenced or explicitly reported following the American Thoracic Society 2002 (104) or

European Respiratory Society/American Thoracic Society 2014 consensus guidelines (105). Despite reporting use of the consensus guidelines the 6MWT was conducted on different length tracks such as hallways of 10 m (n=1/32, 3%), 15 m (n=4/32, 13%), 20 m (n=3/32, 9%), and 30 m (n=2/32, 6%), as well as on an oval continuous 36 m track (n=1/32, 3%) and a treadmill (n=1/32, 3%) (Table 4). Nine different pulmonary function tests were reported with the most common being the forced vital capacity and forced expiratory volume in 1 second (both n=9/33, 27%). Gait speed (n=4/199, 2%), balance and physical function using the composite measure Short Physical Performance Battery (n=3/199, 2%) were the least reported performance outcomes (Appendix 3).

Patient-reported outcomes

At least one patient-reported outcome was included in 76% (n=58/76) of trials. Patient-reported outcomes were reported at multiple time points, including during the pre-admission recovery phase (preoperative period after the prehabilitation intervention) (n=92/58) and during the late recovery phase, mostly within 30 to 90 days after surgery (n=106/58). Of all outcome types, patient-reported outcomes were most frequently reported in the late recovery phase > 90 days after surgery (n=54/58). Patient-reported outcomes were reported a total of 137 times using 63 unique instruments (Table 3). Health-related or general quality of life, reported in 22% (n=30/137) of trials, was measured using 4 different measurement instruments including the Short Form Survey (SF-12 or SF-36) (n=20/30, 67%), EQ-5D (EQ-5D-3L or -5L) (8/30, 27%), Quality of Well Being scale (n=1/30, 3%) and 15-dimensional (n=1/30, 3%) questionnaires. Disease specific quality of life was the second most common outcome (n=23/137, 17%) and was measured with 14 different instruments which included the EORTC QLQ-C30 (n=6/23, 26%), the Functional Assessment of Cancer Therapy (all versions combined) (n=3/23, 13%) and the

Western Ontario and McMaster Universities Osteoarthritis for orthopaedic surgery (n=5/23, 22%). Anxiety and depression were measured in 15% of trials (n=21/137) using 6 different instruments including the Hospital Anxiety and Depression Scale (n=15/21, 71%) and the Patient Health Questionnaire-9 (n=2/21, 10%). Infrequent patient-reported outcomes were self-reported disability (n=8/137, 6%), patient treatment satisfaction (n=5/137, 4%), self-efficacy (n=5/137, 4%) and self-reported recovery (n=5/137, 4%) (Appendix 3).

Clinician-reported outcomes

Seventy-seven percent (n=59/76) of trials included one or more clinician-reported outcome, which were mostly reported during the intermediate/hospital stay (n=22/59) and late phase of recovery, within 30 days (n=37/59). Very few RCTs reported clinician-reported outcomes in the late phase of recovery > 90 days after surgery (n=8/59). Clinician-reported outcomes were reported 84 times overall using 26 specific outcome assessments (Table 3). Postoperative complications represented 61% of all clinician-reported outcomes (n=51/84). Almost half the trials reporting complications used the Clavien-Dindo classification (n=24/51, 47%), others used the Comprehensive Complication Index (n=8/51, 16%), and/or the Postoperative Morbidity Survey (n=2/51, 4%). Complications were stratified by graded severity (n=25/51, 49%), major/minor complications (n=9/51, 18%), surgical complications (n=6/51, 12%), medical complications (n=5/51, 10%) and/or provided frequencies of each individual complication (n=22/51, 43%) (Table 4). Twenty percent of trials (n=15/76) used at least one clinician-oriented nutrition measure such as nutritional status and/or dietary intake to describe baseline characteristics of patients or conduct a risk stratification for their intervention. However, very few reported a nutrition-related outcome post-prehabilitation (for nutritional status: n=3/84, 4%; for dietary intake: n=4/84, 5%). Time to achieve hospital discharge criteria (n=4/84, 3%),

independence and cognitive function (both n=2/84, 2%) were also reported infrequently (Appendix 3).

Table 4. Qualitative description of common outcome assessments

Outcome	Common Guidelines	Specific Outcome Assessments	Qualitative Description	Frequency per outcome assessment (n, %)
Exercise capacity by CPET (n=43)	• ATS and American College of Chest Physicians position statement (125) • Perioperative Exercise Testing and Training Society consensus guidelines (103) • MICMD $VO_{2\ peak}$: ≥10% or 1.75-2 ml/kg/min • MICMD of peak work rate: 10.5 W • MICMD VO_2 at AT: 1.15 ml/kg/min	$VO_{2\ peak}$ (n=12/43)	Defined as the average oxygen consumption over the last 20 s of peak load	4/12 (33)
			Defined as the average oxygen consumption over the last 30 s of peak load	4/12 (33)
			Defined as oxygen consumption over the last 20 to 30 s of peak load and reaching a heart rate >95% of predicted and a respiratory exchange ratio >1.1 at peak exercise	3/12 (25)
			Not defined	3/12 (25)
		Peak workload (n=8/43)	Not defined	5/8 (63)
			Defined as workload maintained for the last 30 s	1/8 (13)
			Defined as workload maintained for the last 1min	1/8 (13)
			Defined as workload maintained for the last 2min	1/8 (13)
		VO_2 at AT (n=8/43)	Defined using the three-criterion discrimination technique	5/8 (63)
			Not defined	3/8 (38)
Strength (n=34)	• No guidelines specified • Smallest worthwhile effect of 7.5 Nm for leg strength • No CID reported for handgrip	Handgrip strength (n=10/34)	Defined as maximal voluntary isometric contractions measured with a hand-held dynamometer across measurements (e.g., maximum score of 3 trials)	8/10 (80)
			Not defined	2/10 (20)
		Lower body strength (n=18/34)	Defined as maximal voluntary isometric contractions measured with a dynamometer	12/18 (67)
			Defined as 1 to 6 RM on leg extension	2/18 (11)
			Defined as 1 to 6 RM on leg press	2/18 (11)
			Defined as 1 to 6 RM on leg curl	1/18 (6)
			Conducted with load cell	1/18 (6)
Functional exercise capacity (n=33)	• ATS guidelines (104) • ERS /ATS guidelines (105) • MICMD for abdominal surgery: ≧19 m or 20 m (126)	6MWT (n=32/33)	Conducted in a 15 m hallway	4/32 (13)
			Conducted in a 20 m hallway	3/32 (9)
			Conducted in a 30 m hallway	2/32 (6)
			Conducted in a 10 m hallway	1/32 (3)
			Conducted on a treadmill	1/32 (3)
			Conducted in a 36 m oval indoor course	1/32 (3)
			Not specified	20/32 (63)

	• MICMD for thoracic surgery: between ≧14 m and ≧30 m (126, 127) • MICMD for cardiac surgery: ≧50 m (128)	5MWT (n=1/33)	Not specified	1/1 (100)
Postoperative complications (n=51)	• Clavien-Dindo classification (n=24/51) • Comprehensive Complication Index (CCI) (n=8/51) • Postoperative Morbidity Survey (n=2/51)		Listed complications individually Described severity/grading stratification (e.g., Severe complications defined as CCI score >20) Defined complications as "any deviation from the normal postoperative course" Collected and defined post-operative pulmonary complications (PPC) (e.g., Common criteria were pneumonia confirmed by new infiltrates by X-ray imaging, WBC, temperature >38.5 C and purulent sputum, atelectasis, bronchopleural fistula, pleural effusion, prolonged chest tube (>7 d), prolonged mechanical vent (>24 hrs)).	22/51 (43) 12/51(24) 5/51 (10) 4/51 (8)

CPET: Cardiorespiratory exercise testing; MICMD: minimally important clinical meaningful difference; VO_2: Oxygen consumption; AT: Anaerobic threshold; ATS: American Thoracic Society; ERS: European Respiratory Society; 6MWT: 6-minute walk test; 5MWT: 5-minute walk test

Biomarker outcomes

Of the 76 RCTs, 12 reported at least one biomarker outcome (n=12/76, 16%). Biomarkers were measured mostly during the preoperative period (after the prehabilitation intervention) (n=8/12) and during the intermediate/hospital stay phase of recovery (n=6/12). Biomarkers were reported a total of 28 times using 20 different biomarkers (Table 3). Inflammatory markers (n=11/28, 39%) were the most prevalent outcome, which was measured using 7 unique biomarkers such as C-reactive protein (n=3/11, 27%), interleukin 6 (n=2/11, 18%) and tumor necrosis factor alpha (TNFα) (n=2/11, 18%) (Appendix 3).

Non-health outcomes

Adherence to prehabilitation interventions was collected in 70% of trials (n=53/76), but only 62% (n=47/76) reported the actual adherence data in their manuscript. Finally, 8% (n=6/76) reported a cost analysis related outcome using all different assessment methods including cost of

postoperative health service utilization, cost of prehabilitation versus the cost of rehabilitation, in-hospital expenses such as daily nursing care fees, surgery-related expenses, and drug costs.

5.4.4 Reported outcomes according to surgical type

Figure 2 (and Appendix 3) illustrates reported outcomes stratified by surgical specialty including abdominal (n=26), thoracic (n=14), cardiac (n=7), orthopedic and spinal (n=24) and other (n=5) procedures. More than 80% of abdominal (n=26) and thoracic (n=14) surgeries reported at least one performance outcome, clinician-reported outcome and observer-reported outcome with the most prevalent being functional exercise capacity, postoperative complications and hospital LOS. At least one patient-reported outcome was reported in 81% of abdominal (n=21/26) and 71% of thoracic (n=10/14) surgeries, mostly as self-reported anxiety and depression and disease-specific quality of life. Almost all cardiac (n=7) prehabilitation trials included clinician-reported outcomes and observer-reported outcomes (n=6/7, 86%) of which postoperative complications, hospital LOS, intensive care unit admissions and postoperative mortality were equally as prevalent (n=4/7, 57%). In general, orthopedics and spinal surgeries (n=24) reported performance outcomes (n=19/24, 79%) as strength and range of motion (both n=10/24, 41.7%), observer-reported outcomes (n=17/24, 71%) as hospital LOS (n=10/24, 46%) and patient-reported outcomes (n=22/24, 92%) as health-related quality of life (n=12/24, 50%). Adherence was reported in most trials of abdominal procedures (n=22/26, 85%) and other surgical procedures (n=5/5, 100%). Cost analysis was infrequently reported among all surgical specialties with the highest rate being in orthopedics and spinal (n=4/24, 17%).

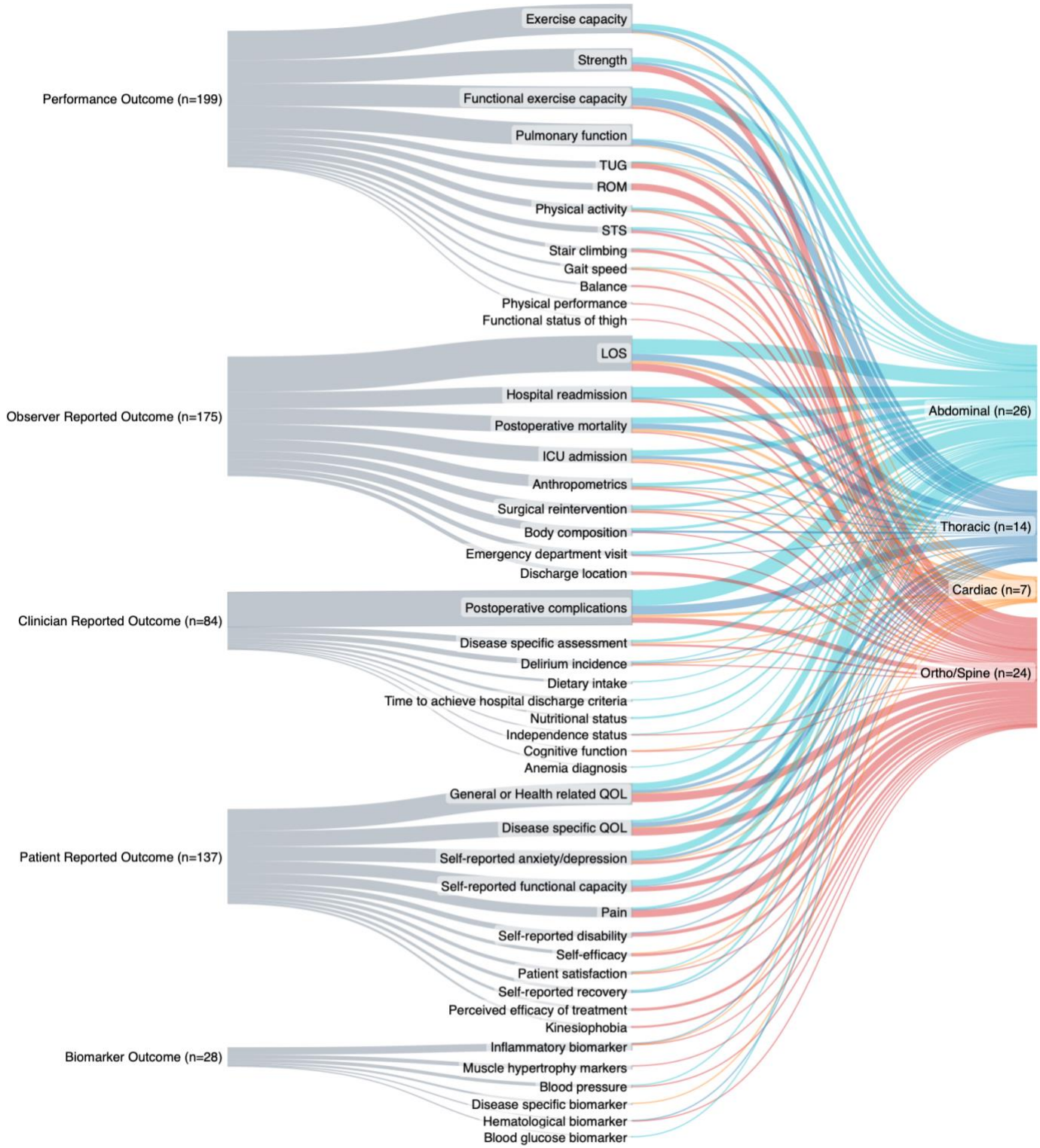

Figure 2 - Sankey Diagram describing the types of outcomes and concept of interest for measurement (outcome) per surgical type using the ISPOR framework. LOS: Length of stay; ICU: Intensive care unit; TUG: Timed Up and Go; ROM: Range of motion; STS: Sit to Stand; QOL: Quality of Life

5.5 Discussion

This scoping review of prehabilitation RCTs in adults undergoing surgery provides a comprehensive overview of all reported outcomes and the most frequently used outcome assessments (including instruments and test) across time-points. The most striking finding is the heterogeneity of outcomes used to assess the efficacy of surgical prehabilitation. Using the ISPOR framework to categorize reported outcomes (23), we identified a total of 50 different outcomes (48 health and 2 non-health related) using a total of 184 specific outcome assessments across 76 trials of surgical prehabilitation. Among all RCTs, the most common outcome was hospital LOS. Most trials (86%) reported at least one observer-reported outcome. We identified 24 different outcome assessments classified as observer-reported outcomes. Performance outcomes were reported in 80% of trials using a total of 51 different assessments tests. The most reported performance outcomes were measures of functional capacity such as exercise capacity assessed with CPET parameters and functional exercise capacity assessed with the 6MWT. Patient-reported outcomes were also prevalent across RCTs as they were reported in 76% of trials using 63 different outcome measurement instruments. The most commonly reported patient-reported outcome was generic health-related quality of life. Clinician-reported outcomes were reported in 78% of trials using 26 different outcome assessments with postoperative complications being the most reported.

Our findings indicate there is a great deal of variation in trial outcomes and lack of consistency in instruments, tests and assessment methods used to measure these outcomes. Patient-reported outcomes were the most heterogeneous as they were captured with the greatest range of instruments; we identified 2 to 14 per outcome. While use of several instruments may be necessary to capture a breadth of patient experience and outcome, measurement heterogeneity

was identified among instruments measuring the same concept of interest. For example, self-reported anxiety and depression was assessed using 6 different instruments (Hospital Anxiety Depression Scale, Patient Health Questionnaire-9, Geriatric Depression Scale, Warwick Edinburgh Mental Wellbeing Scale, Cardiac Anxiety Questionnaire, Beck Depression Inventory). These findings are not unique to prehabilitation. In fact, systematic reviews of health research/clinical trials have captured a large diversity of outcome reporting in oncological research (106), ulcerative colitis (107), cardiac arrest (108), and COVID-19 clinical studies (109). For example, a systematic review of RCTs of women living with stress related urinary incontinence found a total of 119 different outcome assessments among the 108 trials included (110). Moreover, a systematic review of patient-reported outcomes in colorectal cancer surgery (n=104 studies, including RCTs and nonrandomized studies) identified 58 different instruments (111), which is comparable to the 63 patient-reported outcomes identified in our scoping review.

Overall, the most prevalent outcome was hospital LOS, which was reported a total of 52 times. In most cases, hospital LOS was assessed as the number of days from surgery to discharge; however, some included pre-admission days and others combined the number of days patients remained in the hospital at 30- or 90-day post-operatively. Furthermore, hospital LOS may not accurately reflect how prehabilitation affects the intermediate phase of recovery from a biological nor physiological point of view (25) as it may be influenced by the institution's policies and culture, patients' expectations, and availability for postoperative support (112, 113). Readiness for (hospital) discharge, which is defined as the time from the day of surgery until the achievement of prespecified criteria (e.g., tolerance of oral intake, ability to mobilize and perform self-care) (114), may be a more appropriate index of intermediate post-operative

recovery (25, 113, 115), useful for explanatory trials, but was rarely reported in prehabilitation RCTs.

Performance outcomes measuring functional capacity were frequently reported among prehabilitation trials. These outcomes included exercise capacity (also known as aerobic capacity or exercise tolerance) assessed as VO_2 peak and/or VO_2 at anaerobic threshold (AT) during CPET and functional exercise capacity measured almost exclusively with the 6MWT. Exercise capacity (CPET parameters) and functional exercise capacity (6MWT) were predominately measured during the pre-admission phase of recovery and only functional exercise capacity was commonly measured after hospital discharge ≤ 90 day postoperatively (late phase of recovery). In our scoping review, most trials used CPET to assess changes in participants' fitness level after the prehabilitation intervention, while some used it to personalize aerobic exercise prescriptions (28, 32, 74) and a few used it as a risk assessment method (31, 84).

CPET is the gold standard for objectively measuring aerobic exercise capacity and both the VO_2peak and AT are impacted by exercise training pre-operatively (116). However, CPET requires specialist equipment and expertise and not all centres may have access to it. The 6-minute walk test may alternatively be used to evaluate the impact of therapeutic exercise interventions and does not require specialist equipment (117). Whichever measure of performance is used, it is essential that appropriate standardised methodology is used to ensure the correct interpretation and reproducibility of findings. In our review only half of the trials that reported CPET variables or used or the 6-minute walk test reported following the Perioperative Exercise Testing and Training Society consensus definitions for CPET (103) or the American Thoracic Society or European Respiratory Society guidelines for the 6MWT (104, 105). This is a concern because the method used to identify the AT may impact the reported value in a

significant and clinically meaningful way (118). Furthermore, while guidelines state that the 6MWT should be performed indoors, along a flat, straight, hard surfaced and enclosed hallway no less than 20 m long, we found that trials conducted 6MWT in hallways ranging from 10-30 m, as well as on an oval continuous track and treadmill. A crossover RCT (n=21) comparing the 6MWT conducted in a hallway versus on a treadmill, found a significant difference between the distance walked by individual participant, suggesting these surfaces are not interchangeable nor comparable (119). Moreover, 63% of trials performing the 6MWT did not provide any details on how it was measured, limiting the reader's ability to assess for measurement bias.

Altogether, our findings indicate that surgical prehabilitation trials report a wide range of outcome assessments, some of which are uncommon or non-validated, during the pre-admission, intermediate and late phases of recovery. Such heterogeneity across RCTs poses challenges to compare, contrast and combine data together to reach strong and reliable conclusions (106). A possible strategy to mitigate these challenges is the development of a core outcome set (in collaboration with patients), which is an agreed standardized minimal collection of outcomes that should be measured and reported in trials of a specific field (120). The development of a core outcome set was a key priority identified by authors of a collaborative international Delphi study identifying the top research priorities in prehabilitation (121). In addition to guiding "what" to measure and report, the selection of universally accepted and validated outcome assessments (measurements instruments, tests) and of appropriate recovery periods are crucial for mitigating the heterogeneity of "how" and "when" a given outcome is measured. The Core Outcome Measures in Effectiveness Trials (COMET) and the Consensus based Standards for the selection of health status Measurement Instruments (COSMIN) initiatives have developed guidelines on how to select relevant outcome assessments for core outcomes. These guidelines include the

following 4 steps: 1) agree on detailed constructs (outcomes) to be measured for specific population, 2) find all existing outcome assessments used for these constructs (such as our scoping review), 3) conduct a feasibility and quality assessment for the selection of outcome assessments, and 4) perform a consensus procedure for selecting core outcomes by including all relevant stakeholders (24). Developing a core outcome set with all important stakeholders, including patients, can increase consistency and facilitate the synthesis and pooling of meaningful outcomes for meta-analyses to ultimately guide clinical decision making, care guidelines, and policy (120, 122).

Finally, high-quality healthcare should be safe, effective, and improve the patient experience (123). Yet, surgical research has historically focused on clinician-oriented (e.g., LOS, complications) rather than patient-oriented outcomes (e.g., quality of life) (115). An international qualitative study on patient-defined recovery suggested that the traditional clinical outcomes important to clinicians and health care administrators are noticeably absent from patient definitions of successful recovery. Instead, patients' post-abdominal surgery value resolution of symptoms and return to daily activities (124). Our review suggests that traditional clinical outcomes continue to dominate the literature; however, in the field of surgical prehabilitation, patient-reported and performance outcomes are also quite prominent.

5.5.1 Strength and limitations

To our knowledge, this is the first scoping review to systematically map outcomes and their outcome assessments of primary RCTs of surgical prehabilitation. Having a comprehensive understanding of what, when and how outcomes are reported in the current literature is an important first step to guide consensus and achieve consistency of measurement in future research (120). All stages of the search, data extraction and charting were conducted in duplicate

by independent reviewers who followed Arksey and O'Malley's framework (14), and Levac and colleagues' recommendations (13) for performing scoping reviews. The findings of this review are reported in accordance to the PRISMA-ScR checklist (15). Furthermore, the search strategy was conducted with the assistance of an experienced academic librarian (Supplementary Material 1). However, this scoping review is not without limitations. First, given there is no universally accepted definition of prehabilitation, we included trials labelled as "prehabilitation" (in title, abstract or keywords) and met our pre-specified criteria describing prehabilitation. Secondly, we only included trials published in English and French resulting in the potential exclusion of relevant preoperative RCTs. Third, we mapped outcomes according to the ISPOR framework which involves subjective categorization. To mitigate bias, a multidisciplinary team composed of dietitians, physiotherapists, physicians and health researchers collaborated during all steps of our scoping review. Additionally, commonly used outcome assessments do not necessarily reflect consensus nor accuracy and validity of the outcome that trials intended to measure. Finally, contrary to exercise and other modalities (psychological support, respiratory), the nutrition modality was poorly reported. For instance, nutrition-related outcomes such as nutritional status, anthropometrics and body composition and dietary intake, other than for baseline measures, were infrequently reported at follow-up points making it challenging to evaluate.

5.6 Conclusion

This scoping review identified 50 different reported outcomes among surgical prehabilitation RCTs. These outcomes were measured using 184 outcome assessments (including all assessment methods, instruments, tests) across diverse time points. These results highlight the importance of identifying common, meaningful and valid outcomes for both patients and health

systems, and for developing a core outcome set to harmonize data reporting and enable meta-analyses of trial effects.

Acknowledgements: *We would like to thank Genevieve Gore, Liaison Librarian, Schulich Library of Physical Sciences, Life Sciences, and Engineering, McGill University, for her assistance with developing and conducting the search strategy for this scoping review.*

Funding statement: There was no explicit funding for the development of this review. DIM receives salary support from The Ottawa Hospital Anesthesia Alternate Funds Association, the University of Ottawa Faculty of Medicine, and Physician Services Inc. MG is supported in part by the NIHR (UK) Southampton Biomedical Research Centre and as part of the NIHR (UK) Senior Investigator Scheme.

Conflicts of interest statement: CG has received honoraria for giving educational talks sponsored by Abbott Nutrition, Nestle Nutrition and Fresenius Kabi, which were unrelated to this manuscript.

5.7 References

1. Rose J, Weiser TG, Hider P, Wilson L, Gruen RL, Bickler SW. Estimated need for surgery worldwide based on prevalence of diseases: a modelling strategy for the WHO Global Health Estimate. The Lancet Global Health. 2015;3:S13-S20.

2. Ljungqvist O, De Boer HD, Balfour A, Fawcett WJ, Lobo DN, Nelson G, et al. Opportunities and challenges for the next phase of enhanced recovery after surgery: a review. JAMA Surgery. 2021;156(8):775-84.

3. Lau CS, Chamberlain RS. Enhanced recovery after surgery programs improve patient outcomes and recovery: a meta-analysis. World Journal of Surgery. 2017;41:899-913.

4. Visioni A, Shah R, Gabriel E, Attwood K, Kukar M, Nurkin S. Enhanced Recovery After Surgery for Noncolorectal Surgery?: A Systematic Review and Meta-analysis of Major Abdominal Surgery. Annals of Surgery. 2018;267(1):57-65.

5. Zhuang C-L, Ye X-Z, Zhang X-D, Chen B-C, Yu Z. Enhanced recovery after surgery programs versus traditional care for colorectal surgery: a meta-analysis of randomized controlled trials. Diseases of the Colon & Rectum. 2013;56(5):667-78.

6. Nelson G, Kiyang LN, Crumley ET, Chuck A, Nguyen T, Faris P, et al. Implementation of Enhanced Recovery After Surgery (ERAS) across a provincial healthcare system: the ERAS Alberta colorectal surgery experience. World Journal of Surgery. 2016;40:1092-103.

7. Gillis C, Ljungqvist O, Carli F. Prehabilitation, enhanced recovery after surgery, or both? A narrative review. British Journal Anaesthesia. 2022;128(3):434-48.

8. Bamdad MC, Brown CS, Kamdar N, Weng W, Englesbe MJ, Lussiez A. Patient, surgeon, or hospital: explaining variation in outcomes after colectomy. Journal of the American College of Surgeons. 2022;234(3):300-9.

9. Carli F, Zavorsky GS. Optimizing functional exercise capacity in the elderly surgical population. Current Opinion in Clinical Nutrition & Metabolic Care. 2005;8(1):23-32.

10. Macmillan Cancer Support. Principles and Guidance for Prehabilitation 2019 [Available from: https://www.macmillan.org.uk/healthcare-professionals/news-and-resources/guides/principles-and-guidance-for-prehabilitation.

11. McIsaac DI, Gill M, Boland L, Hutton B, Branje K, Shaw J, et al. Prehabilitation in adult patients undergoing surgery: an umbrella review of systematic reviews. British Journal of Anaesthesia. 2022;128(2):244-57.

12. Hoffmann TC, Glasziou PP, Boutron I, Milne R, Perera R, Moher D, et al. Better reporting of interventions: template for intervention description and replication (TIDieR) checklist and guide. British Medical Journal. 2014;348:g1687.

13. Levac D, Colquhoun H, O'Brien KK. Scoping studies: advancing the methodology. Implement Science. 2010;5:69.

14. Arksey H, O'Malley L. Scoping studies: towards a methodological framework. International Journal of Social Research Methodology. 2005;8(1):19-32.

15. Tricco AC, Lillie E, Zarin W, O'Brien KK, Colquhoun H, Levac D, et al. PRISMA extension for scoping reviews (PRISMA-ScR): checklist and explanation. Annals of Internal Medicine. 2018;169(7):467-73.

16. Scheede-Bergdahl C, Minnella EM, Carli F. Multi-modal prehabilitation: addressing the why, when, what, how, who and where next? Anaesthesia. 2019;74 Suppl 1:20-6.

17. Luther A, Gabriel J, Watson RP, Francis NK. The Impact of Total Body Prehabilitation on Post-Operative Outcomes After Major Abdominal Surgery: A Systematic Review. World Journal of Surgery. 2018;42(9):2781-91.

18. Gillis C, Buhler K, Bresee L, Carli F, Gramlich L, Culos-Reed N, et al. Effects of Nutritional Prehabilitation, With and Without Exercise, on Outcomes of Patients Who Undergo Colorectal Surgery: A Systematic Review and Meta-analysis. Gastroenterology. 2018;155(2):391-410.e4.

19. Engel D, Testa G, McIsaac D, Carli F, Santa Mina D, Baldini G, et al. Reporting quality of randomized controlled trials in prehabilitation: a scoping review. Perioperative Medicine. 2023;12(1):48.

20. McGowan J, Sampson M, Salzwedel DM, Cogo E, Foerster V, Lefebvre C. PRESS Peer Review of Electronic Search Strategies: 2015 Guideline Statement. Journal of Clinical Epidemiology. 2016;75:40-6.

21. Ferreira V, Lawson C, Gillis C, Scheede-Bergdahl C, Chevalier S, Carli F. Malnourished lung cancer patients have poor baseline functional capacity but show greatest improvements with multimodal prehabilitation. Nutrition in Clinical Practice. 2021;36(5):1011-9.

22. Gillis C, Fenton TR, Gramlich L, Keller HH, Sajobi TT, Culos-Reed N, et al. Malnutrition modifies the response to multimodal prehabilitation: A pooled analysis of prehabilitation trials. Applied Physiology, Nutrition, and Metabolism. 2022;47(2):141-50.

23. Walton MK, Powers JH, 3rd, Hobart J, Patrick D, Marquis P, Vamvakas S, et al. Clinical Outcome Assessments: Conceptual Foundation-Report of the ISPOR Clinical Outcomes

Assessment - Emerging Good Practices for Outcomes Research Task Force. Value Health. 2015;18(6):741-52.

24. Prinsen CA, Vohra S, Rose MR, Boers M, Tugwell P, Clarke M, et al. How to select outcome measurement instruments for outcomes included in a "Core Outcome Set"–a practical guideline. Trials. 2016;17(1):1-10.

25. Lee L, Tran T, Mayo NE, Carli F, Feldman LS. What does it really mean to "recover" from an operation? Surgery. 2014;155(2):211-6.

26. Hsieh H-F, Sarah. E. Shannon. Three Approaches to Qualitative Content Analysis. Qualitative Health Research. 2005;15(9):1277-88.

27. An J, Ryu HK, Lyu SJ, Yi HJ, Lee BH. Effects of Preoperative Telerehabilitation on Muscle Strength, Range of Motion, and Functional Outcomes in Candidates for Total Knee Arthroplasty: A Single-Blind Randomized Controlled Trial. International Journal of Environmental Research & Public Health 2021;18(11):6071.

28. Argunova Y, Belik E, Gruzdeva O, Ivanov S, Pomeshkina S, Barbarash O. Effects of physical prehabilitation on the dynamics of the markers of endothelial function in patients undergoing elective coronary bypass surgery. Journal of Personalized Medicine. 2022;12(3):471.

29. Ausania F, Senra P, Melendez R, Caballeiro R, Ouvina R, Casal-Nunez E. Prehabilitation in patients undergoing pancreaticoduodenectomy: a randomized controlled trial. Revista Espanola de Enfermedades Digestivas. 2019;111(8):603-8.

30. Barberan-Garcia A, Ubre M, Roca J, Lacy AM, Burgos F, Risco R, et al. Personalised Prehabilitation in High-risk Patients Undergoing Elective Major Abdominal Surgery: A Randomized Blinded Controlled Trial. Annals of Surgery. 2018;267(1):50-6.

31. Berkel AEM, Bongers BC, Kotte H, Weltevreden P, de Jongh FHC, Eijsvogel MMM, et al. Effects of Community-based Exercise Prehabilitation for Patients Scheduled for Colorectal Surgery With High Risk for Postoperative Complications: Results of a Randomized Clinical Trial. Annals of Surgery. 2022;275(2):e299-e306.

32. Blackwell JEM, Doleman B, Boereboom CL, Morton A, Williams S, Atherton P, et al. High-intensity interval training produces a significant improvement in fitness in less than 31 days before surgery for urological cancer: a randomised control trial. Prostate Cancer & Prostatic Diseases. 2020;23(4):696-704.

33. Bousquet-Dion G, Awasthi R, Loiselle SE, Minnella EM, Agnihotram RV, Bergdahl A, et al. Evaluation of supervised multimodal prehabilitation programme in cancer patients undergoing colorectal resection: a randomized control trial. Acta Oncologica. 2018;57(6):849-59.

34. Brown K, Loprinzi PD, Brosky JA, Topp R. Prehabilitation influences exercise-related psychological constructs such as self-efficacy and outcome expectations to exercise. Journal of Strength & Conditioning Research. 2013;28(1):201-9.

35. Brown K, Topp R, Brosky JA, Lajoie AS. Prehabilitation and quality of life three months after total knee arthroplasty: a pilot study. Perceptual & Motor Skills. 2012;115(3):765-74.

36. Calatayud J, Casana J, Ezzatvar Y, Jakobsen MD, Sundstrup E, Andersen LL. High-intensity preoperative training improves physical and functional recovery in the early post-operative periods after total knee arthroplasty: a randomized controlled trial. Knee Surgery, Sports Traumatology, Arthroscopy. 2017;25(9):2864-72.

37. Carli F, Bousquet-Dion G, Awasthi R, Elsherbini N, Liberman S, Boutros M, et al. Effect of Multimodal Prehabilitation vs Postoperative Rehabilitation on 30-Day Postoperative Complications for Frail Patients Undergoing Resection of Colorectal Cancer: A Randomized Clinical Trial. JAMA Surgery. 2020;155(3):233-42.

38. Carli F, Charlebois P, Stein B, Feldman L, Zavorsky G, Kim DJ, et al. Randomized clinical trial of prehabilitation in colorectal surgery. British Journal of Surgery. 2010;97(8):1187-97.

39. Cavill S, McKenzie K, Munro A, McKeever J, Whelan L, Biggs L, et al. The effect of prehabilitation on the range of motion and functional outcomes in patients following the total knee or hip arthroplasty: A pilot randomized trial. Physiotherapy Theory & Practice. 2016;32(4):262-70.

40. Dunne DF, Jack S, Jones RP, Jones L, Lythgoe DT, Malik HZ, et al. Randomized clinical trial of prehabilitation before planned liver resection. British Journal of Surgery. 2016;103(5):504-12.

41. Ferreira V, Lawson C, Carli F, Scheede-Bergdahl C, Chevalier S. Feasibility of a novel mixed-nutrient supplement in a multimodal prehabilitation intervention for lung cancer patients awaiting surgery: A randomized controlled pilot trial. International Journal of Surgery. 2021;93:106079.

42. Ferreira V, Minnella EM, Awasthi R, Gamsa A, Ferri L, Mulder D, Sirois C, Spicer J, Schmid S, Carli F. Multimodal Prehabilitation for Lung Cancer Surgery: A Randomized Controlled Trial. Annals of Thoracic Surgery. 2021;112(5):1600-8.

43. Fulop A, Lakatos L, Susztak N, Szijarto A, Banky B. The effect of trimodal prehabilitation on the physical and psychological health of patients undergoing colorectal surgery: a randomised clinical trial. Anaesthesia. 2021;76(1):82-90.

44. Gillis C, Li C, Lee L, Awasthi R, Augustin B, Gamsa A, et al. Prehabilitation versus rehabilitation: a randomized control trial in patients undergoing colorectal resection for cancer. Anesthesiology. 2014;121(5):937-47.

45. Gillis C, Loiselle SE, Fiore JF, Jr., Awasthi R, Wykes L, Liberman AS, et al. Prehabilitation with Whey Protein Supplementation on Perioperative Functional Exercise Capacity in Patients Undergoing Colorectal Resection for Cancer: A Pilot Double-Blinded Randomized Placebo-Controlled Trial. Journal of the Academy of Nutrition & Dietetics. 2016;116(5):802-12.

46. Gloor S, Misirlic M, Frei-Lanter C, Herzog P, Muller P, Schafli-Thurnherr J, et al. Prehabilitation in patients undergoing colorectal surgery fails to confer reduction in overall morbidity: results of a single-center, blinded, randomized controlled trial. Langenbecks Archives of Surgery. 2022;407(3):897-907.

47. Granicher P, Stoggl T, Fucentese SF, Adelsberger R, Swanenburg J. Preoperative exercise in patients undergoing total knee arthroplasty: a pilot randomized controlled trial. Archives of Physiotherapy. 2020;10(1):1-11.

48. Grant LF, Cooper DJ, Conroy JL. The HAPI 'Hip Arthroscopy Pre-habilitation Intervention' study: does pre-habilitation affect outcomes in patients undergoing hip arthroscopy for femoro-acetabular impingement? Journal of Hip Preservation Surgery. 2017;4(1):85-92.

49. Gravier FE, Smondack P, Boujibar F, Prieur G, Medrinal C, Combret Y, et al. Prehabilitation sessions can be provided more frequently in a shortened regimen with similar or better efficacy in people with non-small cell lung cancer: a randomised trial. Journal of Physiotherapy. 2022;68(1):43-50.

50. Huang J, Lai Y, Zhou X, Li S, Su J, Yang M, et al. Short-term high-intensity rehabilitation in radically treated lung cancer: a three-armed randomized controlled trial. Journal of Thoracic Disease. 2017;9(7):1919-29.

51. Huang SW, Chen PH, Chou YH. Effects of a preoperative simplified home rehabilitation education program on length of stay of total knee arthroplasty patients. Orthopaedics & Traumatology, Surgery & Research. 2012;98(3):259-64.

52. Humeidan ML, Reyes JC, Mavarez-Martinez A, Roeth C, Nguyen CM, Sheridan E, et al. Effect of Cognitive Prehabilitation on the Incidence of Postoperative Delirium Among Older Adults Undergoing Major Noncardiac Surgery: The Neurobics Randomized Clinical Trial. JAMA Surgery. 2021;156(2):148-56.

53. Jahic D, Omerovic D, Tanovic AT, Dzankovic F, Campara MT. The Effect of Prehabilitation on Postoperative Outcome in Patients Following Primary Total Knee Arthroplasty. Medicinski Arhiv. 2018;72(6):439-43.

54. Jensen BT, Petersen AK, Jensen JB, Laustsen S, Borre M. Efficacy of a multiprofessional rehabilitation programme in radical cystectomy pathways: a prospective randomized controlled trial. Scandinavian Journal of Urology. 2015;49(2):133-41.

55. Kim DJ, Mayo NE, Carli F, Montgomery DL, Zavorsky GS. Responsive measures to prehabilitation in patients undergoing bowel resection surgery. Tohoku Journal of Experimental Medicine. 2009;217(2):109-15.

56. Kim S, Hsu FC, Groban L, Williamson J, Messier S. A pilot study of aquatic prehabilitation in adults with knee osteoarthritis undergoing total knee arthroplasty - short term outcome. BMC Musculoskeletal Disorders. 2021;22(1):388.

57. Lai Y, Huang J, Yang M, Su J, Liu J, Che G. Seven-day intensive preoperative rehabilitation for elderly patients with lung cancer: a randomized controlled trial. Journal of Surgical Research. 2017;209:30-6.

58. Liang MK, Bernardi K, Holihan JL, Cherla DV, Escamilla R, Lew DF, et al. Modifying Risks in Ventral Hernia Patients With Prehabilitation: A Randomized Controlled Trial. Annals of Surgery. 2018;268(4):674-80.

59. Licker M, Karenovics W, Diaper J, Fresard I, Triponez F, Ellenberger C, et al. Short-Term Preoperative High-Intensity Interval Training in Patients Awaiting Lung Cancer Surgery: A Randomized Controlled Trial. Journal of Thoracic Oncology: Official Publication of the International Association for the Study of Lung Cancer. 2017;12(2):323-33.

60. Lindback Y, Tropp H, Enthoven P, Abbott A, Oberg B. PREPARE: presurgery physiotherapy for patients with degenerative lumbar spine disorder: a randomized controlled trial. Spine Journal: Official Journal of the North American Spine Society. 2018;18(8):1347-55.

61. Liu Z, Qiu T, Pei L, Zhang Y, Xu L, Cui Y, et al. Two-week multimodal prehabilitation program improves perioperative functional capability in patients undergoing thoracoscopic lobectomy for lung cancer: a randomized controlled trial. Anesthesia & Analgesia. 2020;131(3):840-9.

62. López-Rodríguez-Arias F, Sánchez-Guillén L, Aranaz-Ostáriz V, Triguero-Cánovas D, Lario-Pérez S, Barber-Valles X, et al. Effect of home-based prehabilitation in an enhanced recovery after surgery program for patients undergoing colorectal cancer surgery during the COVID-19 pandemic. Supportive Care in Cancer. 2021;29(12):7785-91.

63. Lotzke H, Brisby H, Gutke A, Hägg O, Jakobsson M, Smeets R, et al. A person-centered prehabilitation program based on cognitive-behavioral physical therapy for patients scheduled for lumbar fusion surgery: a randomized controlled trial. Physical Therapy. 2019;99(8):1069-88.

64. Marchand A-A, Houle M, O'Shaughnessy J, Châtillon C-É, Cantin V, Descarreaux M. Effectiveness of an exercise-based prehabilitation program for patients awaiting surgery for lumbar spinal stenosis: a randomized clinical trial. Scientific Reports. 2021;11(1):11080.

65. Eil MSM, Sharifudin MA, Shokri AA, Ab Rahman S. Preoperative physiotherapy and short-term functional outcomes of primary total knee arthroplasty. Singapore Medical Journal. 2016;57(3):138.

66. Matassi F, Duerinckx J, enneucker H, Bellemans J. Range of motion after total knee arthroplasty: the effect of a preoperative home exercise program. Knee Surgery Sports Traumatology Arthroscopy. 2014;22(3):703-9.

67. McKay C, Prapavessis H, Doherty T. The effect of a prehabilitation exercise program on quadriceps strength for patients undergoing total knee arthroplasty: a randomized controlled pilot study. PM&R. 2012;4(9):647-56.

68. Minnella EM, Awasthi R, Bousquet-Dion G, Ferreira V, Austin B, Audi C, et al. Multimodal prehabilitation to enhance functional capacity following radical cystectomy: a randomized controlled trial. European Urology Focus. 2021;7(1):132-8.

69. Minnella EM, Awasthi R, Loiselle SE, Agnihotram RV, Ferri LE, Carli F. Effect of Exercise and Nutrition Prehabilitation on Functional Capacity in Esophagogastric Cancer Surgery: A Randomized Clinical Trial. JAMA Surgery. 2018;153(12):1081-9.

70. Minnella EM, Ferreira V, Awasthi R, Charlebois P, Stein B, Liberman AS, et al. Effect of two different pre-operative exercise training regimens before colorectal surgery on functional capacity: A randomised controlled trial. European Journal of Anaesthesiology. 2020;37(11):969-78.

71. Morano MT, Araújo A, S. a, Nascimento FB, da Silva GF, Mesquita R, et al. Preoperative Pulmonary Rehabilitation Versus Chest Physical Therapy in Patients Undergoing Lung Cancer Resection: A Pilot Randomized Controlled Trial. Archives of Physical Medicine & Rehabilitation. 2013;94(1):53-8.

72. Nguyen C, Boutron I, Roren A, Anract P, Beaudreuil J, Biau D, et al. Effect of Prehabilitation Before Total Knee Replacement for Knee Osteoarthritis on Functional Outcomes: A Randomized Clinical Trial. JAMA Network Open. 2022;5(3):e221462.

73. Nielsen PR, Jorgensen LD, Dahl B, Pedersen T, Tonnesen H. Prehabilitation and early rehabilitation after spinal surgery: randomized clinical trial. Clinical Rehabilitation. 2010;24(2):137-48.

74. Northgraves MJ, Arunachalam L, Madden LA, Marshall P, Hartley JE, MacFie J, et al. Feasibility of a novel exercise prehabilitation programme in patients scheduled for elective

colorectal surgery: a feasibility randomised controlled trial. Supportive Care in Cancer. 2020;28(7):3197-206.

75. O'Gara BP, Mueller A, Gasangwa DVI, Patxot M, Shaefi S, Khabbaz K, et al. Prevention of Early Postoperative Decline: A Randomized, Controlled Feasibility Trial of Perioperative Cognitive Training. Anesthesia & Analgesia. 2020;130(3):586-95.

76. Onerup A, Andersson J, Angenete E, Bock D, Borjesson M, Ehrencrona C, et al. Effect of Short-term Homebased Pre- and Postoperative Exercise on Recovery after Colorectal Cancer Surgery (PHYSSURG-C): A Randomized Clinical Trial. Annals of Surgery. 2022;275(3):448-55.

77. Peng LH, Wang WJ, Chen J, Jin JY, Min S, Qin PP. Implementation of the pre-operative rehabilitation recovery protocol and its effect on the quality of recovery after colorectal surgeries. Chinese Medical Journal. 2021;134(23):2865-73.

78. Santa Mina D, Hilton WJ, Matthew AG, Awasthi R, Bousquet-Dion G, Alibhai SMH, et al. Prehabilitation for radical prostatectomy: A multicentre randomized controlled trial. Surgical Oncology. 2018;27(2):289-98.

79. Satoto HH, Paramitha A, Barata SH, Sugiri, Suhartono, Wahyudati S, et al. Effect of preoperative inspiratory muscle training on right ventricular systolic function in patients after heart valve replacement surgery. Bali Medical Journal. 2021;10(1):340-6.

80. Sawatzky JA, Kehler DS, Ready AE, Lerner N, Boreskie S, Lamont D, et al. Prehabilitation program for elective coronary artery bypass graft surgery patients: a pilot randomized controlled study. Clinical Rehabilitation. 2014;28(7):648-57.

81. Sebio Garcia R, Yanez-Brage MI, Gimenez Moolhuyzen E, Salorio Riobo M, Lista Paz A, Borro Mate JM. Preoperative exercise training prevents functional decline after lung resection surgery: a randomized, single-blind controlled trial. Clinical Rehabilitation. 2017;31(8):1057-67.

82. Shaarani SR, O'Hare C, Quinn A, Moyna N, Moran R, O'Byrne JM. Effect of prehabilitation on the outcome of anterior cruciate ligament reconstruction. American Journal of Sports Medicine. 2013;41(9):2117-27.

83. Steinmetz C, Bjarnason-Wehrens B, Baumgarten H, Walther T, Mengden T, Walther C. Prehabilitation in patients awaiting elective coronary artery bypass graft surgery - effects on functional capacity and quality of life: a randomized controlled trial. Clinical Rehabilitation. 2020;34(10):1256-67.

84. Tenconi S, Mainini C, Rapicetta C, Braglia L, Galeone C, Cavuto S, et al. Rehabilitation for lung cancer patients undergoing surgery: results of the PUREAIR randomized trial. European Journal of Physical and Rehabilitation Medicine. 2021;57(6):1002-11.

85. Topp R, Swank AM, Quesada PM, Nyl, J, Malkani A. The effect of prehabilitation exercise on strength and functioning after total knee arthroplasty. PM&R. 2009;1(8):729-35.

86. Vagvolgyi A, Rozgonyi Z, Kerti M, Agathou G, Vadasz P, Varga J. Effectiveness of pulmonary rehabilitation and correlations in between functional parameters, extent of thoracic surgery and severity of post-operative complications: randomized clinical trial. Journal of Thoracic Disease. 2018;10(6):3519-31.

87. VE IJ-H, Wanten GJA, de Nes LCF, van den Berg MGA. Effect of a Preoperative Home-Delivered, Protein-Rich Meal Service to Improve Protein Intake in Surgical Patients: A Randomized Controlled Trial. Jpen: Journal of Parenteral & Enteral Nutrition. 2020;45(3):479-89.

88. Waller E, Rahman S, Sutton P, Allen J, Saxton J, Aziz O. Randomised controlled trial of patients undergoing prehabilitation with wearables versus standard of care before major abdominal cancer surgery (Trial Registration: NCT04047524). Colorectal disease. 2020;22:7.

89. Wang X, Che G, Liu L. A short-term high-intensive pattern of preoperative rehabilitation better suits surgical lung cancer patients. Interactive Cardiovascular and Thoracic Surgery. 2017;25(1):ivx280-037.

90. Woodfield JC, Clifford K, Wilson GA, Munro F, Baldi JC. Short-term high-intensity interval training improves fitness before surgery: A randomized clinical trial. Scandinavian Journal of Medicine & Science in Sports. 2022;28:28.

91. Yamana I, Takeno S, Hashimoto T, Maki K, Shibata R, Shiwaku H, et al. Randomized Controlled Study to Evaluate the Efficacy of a Preoperative Respiratory Rehabilitation Program to Prevent Postoperative Pulmonary Complications after Esophagectomy. Digestive Surgery. 2015;32(5):331-7.

92. Furon Y, Dang Van S, Blanchard S, Saulnier P, Baufreton C. Effects of high-intensity inspiratory muscle training on systemic inflammatory response in cardiac surgery-A randomized clinical trial. Physiotherapy Theory and Practice. 2023:1-11.

93. Franz A, Ji S, Bittersohl B, Zilkens C, Behringer M. Impact of a Six-Week Prehabilitation With Blood-Flow Restriction Training on Pre-and Postoperative Skeletal Muscle Mass and Strength in Patients Receiving Primary Total Knee Arthroplasty. Frontiers in Physiology. 2022;13:881484.

94. Heiman J, Onerup A, Wessman C, Haglind E, Olofsson Bagge R. Recovery after breast cancer surgery following recommended pre and postoperative physical activity:(PhysSURG-B) randomized clinical trial. British Journal of Surgery. 2021;108(1):32-9.

95. Milios JE, Ackland TR, Green DJ. Pelvic floor muscle training in radical prostatectomy: a randomized controlled trial of the impacts on pelvic floor muscle function and urinary incontinence. BMC Urology. 2019;19(1):1-10.

96. Rampam S, Sadiq H, Patel J, Meyer D, Uy K, Yates J, et al. Supervised preoperative walking on increasing early postoperative stamina and mobility in older adults with frailty traits: a pilot and feasibility study. Health Science Reports. 2022;5(4):e738.

97. Molenaar CJL, Minnella EM, Coca-Martinez M, Ten Cate DWG, Regis M, Awasthi R, et al. Effect of Multimodal Prehabilitation on Reducing Postoperative Complications and Enhancing Functional Capacity Following Colorectal Cancer Surgery: The PREHAB Randomized Clinical Trial. JAMA Surgery. 2023;158(6):572-81.

98. McIsaac DI, Hladkowicz E, Bryson GL, Forster AJ, Gagne S, Huang A, et al. Home-based prehabilitation with exercise to improve postoperative recovery for older adults with frailty having cancer surgery: the PREHAB randomised clinical trial. British Journal of Anaesthesia. 2022;129(1):41-8.

99. D'Lima DD, Colwell CW, Jr., Morris BA, Hardwick ME, Kozin F. The effect of preoperative exercise on total knee replacement outcomes. Clinical Orthopaedics and Related Research. 1996(326):174-82.

100. Rooks DS, Huang J, Bierbaum BE, Bolus SA, Rubano J, Connolly CE, et al. Effect of preoperative exercise on measures of functional status in men and women undergoing total hip and knee arthroplasty. Arthritis Rheumatology. 2006;55(5):700-8.

101. Beaupre LA, Lier D, Davies DM, Johnston DBC. The effect of a preoperative exercise and education program on functional recovery, health related quality of life, and health service utilization following primary total knee arthroplasty. Journal of Rheumatology. 2004;31(6):1166-73.

102. Hulzebos EH, Helders PJ, Favié NJ, De Bie RA, Brutel de la Riviere A, Van Meeteren NL. Preoperative intensive inspiratory muscle training to prevent postoperative pulmonary complications in high-risk patients undergoing CABG surgery: a randomized clinical trial. JAMA. 2006;296(15):1851-7.

103. Levett D, Jack S, Swart M, Carlisle J, Wilson J, Snowden C, et al. Perioperative cardiopulmonary exercise testing (CPET): consensus clinical guidelines on indications, organization, conduct, and physiological interpretation. British Journal of Anaesthesia. 2018;120(3):484-500.

104. American Thoracic Society Committee on Proficiency Standards for Clinical Pulmonary Function Laboratories. ATS statement: guidelines for the six-minute walk test. American Journal Respiratory Critical Care Medicine. 2002;166 (1):111-7.

105. Holland AE, Spruit MA, Troosters T, Puhan MA, Pepin V, Saey D, et al. An official European Respiratory Society/American Thoracic Society technical standard: field walking tests in chronic respiratory disease. European Respiratory Journal. 2014;44(6):1428-46.

106. Hirsch BR, Califf RM, Cheng SK, Tasneem A, Horton J, Chiswell K, et al. Characteristics of oncology clinical trials: insights from a systematic analysis of ClinicalTrials. gov. JAMA Internal Medicine. 2013;173(11):972-9.

107. Ma C, Panaccione R, Fedorak RN, Parker CE, Nguyen TM, Khanna R, et al. Heterogeneity in definitions of endpoints for clinical trials of ulcerative colitis: a systematic review for development of a core outcome set. Clinical Gastroenterology and Hepatology. 2018;16(5):637-47. e13.

108. Whitehead L, Perkins GD, Clarey A, Haywood KL. A systematic review of the outcomes reported in cardiac arrest clinical trials: the need for a core outcome set. Resuscitation. 2015;88:150-7.

109. Marshall JC, Murthy S, Diaz J, Adhikari N, Angus DC, Arabi YM, et al. A minimal common outcome measure set for COVID-19 clinical research. The Lancet Infectious Diseases. 2020;20(8):e192-e7.

110. Doumouchtsis S, Pookarnjanamorakot P, Durnea C, Zini M, Elfituri A, Haddad J, et al. A systematic review on outcome reporting in randomised controlled trials on surgical interventions for female stress urinary incontinence: a call to develop a core outcome set. BJOG: An International Journal of Obstetrics & Gynaecology. 2019;126(12):1417-22.

111. McNair A, Whistance R, Forsythe R, Rees J, Jones J, Pullyblank A, et al. Synthesis and summary of patient-reported outcome measures to inform the development of a core outcome set in colorectal cancer surgery. Colorectal Disease. 2015;17(11):O217-O29.

112. Carli F, Mayo N. Editorial I: Measuring the outcome of surgical procedures: what are the challenges? British Journal of Anaesthesia. 2001;87(4):531-3.

113. Maessen J, Dejong C, Kessels A, Von Meyenfeldt M, Group ERAS. Length of stay: an inappropriate readout of the success of enhanced recovery programs. World Journal of Surgery. 2008;32:971-5.

114. Fiore JF, Faragher IG, Bialocerkowski A, Browning L, Denehy L. Time to readiness for discharge is a valid and reliable measure of short-term recovery after colorectal surgery. World Journal of Surgery. 2013;37:2927-34.

115. Feldman LS, Lee L, Fiore Jr J. What outcomes are important in the assessment of Enhanced Recovery After Surgery (ERAS) pathways? Canadian Journal of Anesthesia. 2015;62(2):120.

116. West MA, Loughney L, Lythgoe D, Barben CP, Sripadam R, Kemp GJ, et al. Effect of prehabilitation on objectively measured physical fitness after neoadjuvant treatment in preoperative rectal cancer patients: a blinded interventional pilot study. British Journal of Anaesthesia. 2015;114(2):244-51.

117. Puente-Maestu L, Stringer W, Casaburi R. Exercise testing to evaluate therapeutic interventions in chronic respiratory diseases. BRN Reviews. 2018;4(4):274-86.

118. Beckers PJ, Possemiers NM, Van Craenenbroeck EM, Van Berendoncks AM, Wuyts K, Vrints CJ, et al. Comparison of Three Methods to Identify the Anaerobic Threshold During Maximal Exercise Testing in Patients with Chronic Heart Failure. American Journal of Physical Medicine & Rehabilitation. 2012;91(2):148-55.

119. Stevens D, Elpern E, Sharma K, Szidon P, Ankin M, Kesten S. Comparison of hallway and treadmill six-minute walk tests. American Journal of Respiratory and Critical Care Medicine. 1999;160(5):1540-3.

120. Clarke M, Williamson PR. Core outcome sets and systematic reviews. Systematic Reviews. 2016;5(1):1-4.

121. Raichurkar P, Denehy L, Solomon M, Koh C, Pillinger N, Hogan S, et al. Research Priorities in Prehabilitation for Patients Undergoing Cancer Surgery: An International Delphi Study. Annals of Surgical Oncology. 2023;30(12):7226–35.

122. Mokkink LB, Terwee CB, Patrick DL, Alonso J, Stratford PW, Knol DL, et al. The COSMIN checklist for assessing the methodological quality of studies on measurement properties of health status measurement instruments: an international Delphi study. Quality of Life Research. 2010;19(4):539-49.

123. Larson E, Sharma J, Bohren MA, Tunçalp Ö. When the patient is the expert: measuring patient experience and satisfaction with care. Bulletin of the World Health Organization. 2019;97(8):563.

124. Rajabiyazdi F, Alam R, Pal A, Montanez J, Law S, Pecorelli N, et al. Understanding the Meaning of Recovery to Patients Undergoing Abdominal Surgery. JAMA Surgery. 2021;156(8):758-65.

125. American Thoracic Society American College of Chest Physicians. American Thoracic Society/American College of Chest Physicians Statement on Cardiopulmonary exercise testing. American Journal of Respiratory and Critical Care Medicine. 2003;167(2):211-77.

126. Antonescu I, Scott S, Tran TT, Mayo NE, Feldman LS. Measuring postoperative recovery: what are clinically meaningful differences? Surgery. 2014;156(2):319-27.

127. Puhan MA, Chandra D, Mosenifar Z, Ries A, Make B, Hansel N, et al. The minimal important difference of exercise tests in severe COPD. European Respiratory Journal. 2011;37(4):784-90.

128. Perera S, Mody SH, Woodman RC, Studenski SA. Meaningful change and responsiveness in common physical performance measures in older adults. Journal of the American Geriatrics Society. 2006;54(5):743-9.

6. DISCUSSION

Surgical prehabilitation is a proactive intervention addressing patient-related modifiable risk factors before an elective operation. Initially, prehabilitation focused on exercise therapy alone, but has expanded to respiratory, functional, nutritional, cognitive and multimodal (e.g., nutrition, exercise, psychological support) interventions across many surgical specialties over the past two decades. Currently, the efficacy of surgical, multimodal prehabilitation remains mostly of low to very low certainty. The low certainty evidence can be partially explained by methodological issues in primary RCT and systematic reviews as well as the overall heterogeneity in the interventions and outcomes of interest of individual trials (4). These study limitations and inconsistencies are important issues as they may impair the ability to develop valid recommendations for patients, clinicians and health care policies. Key priorities have been identified to mitigate heterogeneity and improve the overall body of evidence which includes having a universally accepted definition, finding a consensus for a meaningful COS, and conducting additional well designed and with low risk of bias RCTs (4, 71). This MSc thesis aims to be the initial steps towards bridging these gaps and achieving consensus.

The first objective of this research was to consolidate a common definition for surgical prehabilitation. Manuscript 1 is a scoping review that explored how surgical prehabilitation was defined in primary RCTs. This review included 76 primary prehabilitation RCTs of oncological and non-oncological surgical fields. The surgical specialties of trials consisted of abdominal, orthopedic and spinal, thoracic, cardiac procedures and breast resection. More than half of the trials explicitly defined prehabilitation while others provided an implicit description. Using summative content analysis and triangulation (investigator and method) approaches to ensure the trustworthiness of our qualitative findings, the following common definition was consolidated by

our multidisciplinary research team: “Prehabilitation is a process from diagnosis to surgery, consisting of one or more preoperative intervention of exercise, nutrition, anxiety-reducing strategies, and respiratory training, that aims to enhance functional capacity and physiological reserve to allow patients to withstand surgical stressors, improve post-operative outcomes, and facilitate recovery”. This consolidated definition has allowed us to better interpret the relevance of outcomes reported in surgical prehabilitation trials (objective 2 of this MSc Thesis) and will help guide consensus for a universally accepted definition.

The second objective of this research was to evaluate what, when and how outcomes were reported in surgical prehabilitation trials as a means of understanding the current landscape to guide the development of a COS. Manuscript 2 systematically mapped all reported outcome assessments according to the ISPOR framework (ObsRO, ClinRO, PRO, PerfO, biomarker) (61) and the phases of surgical recovery (19, 72). Fifty different concepts of interest for measurement (outcomes) were identified including 48 health-related and 2 non-health-related. Furthermore, a total of 184 outcome assessments, 164 specific clinical assessments and 20 unique biomarkers, were found throughout our sample. Overall, the most frequently reported concept of interests and outcome assessments were: 1) hospital LOS measured most often as the number days from surgery to discharge, 2) post-operative complications graded according to the Clavien-Dindo classification, 3) measures of functional capacity (exercise capacity and functional exercise capacity) using the 6MWT and CPET clinical assessments (e.g., VO_2 peak) and 4) strength assessed as handgrip or quadricep strength using a dynamometer. The most common patient-oriented outcome was generic health-related quality of life measured with the 36- or 12-Item Short Form Survey. Furthermore, PROs were particularly inconsistent as they were captured with the greatest range of outcome measurement instruments; we identified 2 to 14 per individual

concept of interest. For example, self-reported anxiety and depression was assessed using 6 different measurement instruments (Hospital Anxiety Depression Scale, Patient Health Questionnaire-9, Geriatric Depression Scale, Warwick Edinburgh Mental Wellbeing Scale, Cardiac Anxiety Questionnaire, Beck Depression Inventory). Reported time points during the surgical trajectory varied tremendously across outcome assessments making it particularly difficult to group and identify overarching trends. Most outcomes reported in the pre-admission phase of surgical recovery were PerfOs and PROs, while in the intermediate phase of recovery was ObsROs, and in the late phase of recovery were ClinROs, PerfOs and PROs. Descriptions of how outcomes assessments were conducted and collected was often lacking making it difficult to discern measurement bias and were also often different from published guidelines. To support better comparison and reduce heterogeneity, these findings suggest that the minimal set of outcomes to cover in surgical prehabilitation trials going forward are: hospital LOS, postoperative complications, functional capacity, strength and health-related quality of life.

6.1 Meaningful outcomes for prehabilitation

No single trial endpoint may fully capture the effects of surgical prehabilitation on post-operative outcomes and recovery. According to our common definition, the objectives of prehabilitation prior to surgery are to 1) enhance functional capacity and 2) increase physiological reserve. While the objectives after surgery are to 1) withstand surgical stressors, 2) improve post-operative outcomes, and 3) facilitate recovery. The findings of the outcome review demonstrate that prehabilitation is commonly measured using a multidimensional approach, across different perspectives and many timeframes during the patient recovery trajectory (pre-admission, early, intermediate, late phases of recovery). In fact, out of the 76 RCTs in our sample, over 75% of trials included at least one outcome from an administrative, clinician,

patient and physical performance point of view (ObsRO n=65, 86%; PerfO n=61, 80%, ClinRO n=59, 78%; PRO n=58, 76 %). This next section will discuss meaningful outcomes for future trials that reflect the components of the consolidated common definition of surgical prehabilitation.

First, according to our consolidated common definition, functional capacity and physiological reserve should be measured before surgery. In fact, Gillis, Ljungqvist and Carli have suggested that postoperative recovery (one of the goals of prehabilitation) is not a passive process, it begins preoperatively from the diagnostic to the surgery date (19). Thus, the pre-admission phase of recovery defined as the preparation phase for postoperative recovery (measured after completion of the intervention within a few days of surgery) should assess changes in functional capacity and physiological reserve (19). Functional capacity is defined as "the ability of an individual to perform meaningful tasks" (19). The concept of interests used to reflect functional capacity of the patient were exercise capacity and functional exercise capacity (73) which were commonly assessed using the following tests: 1) peak oxygen consumption or oxygen consumption at the anaerobic threshold during a CPET on a braked cycle ergometer (73), and 2) the 6MWT (i.e., patients walk for 6 minutes and the assessor records the distance covered) conducted in a straight hospital hallway (74). These outcome assessments provide valid and reliable data to measure changes in functional capacity (75, 76). When selecting a specific outcome assessment to measure a concept of interest, practical guidelines from COSMIN indicate that both feasibility and measurement properties (e.g., content validity, internal structure, reliability, measurement error, etc.) are important aspects to consider (77). To measure functional capacity, the widespread use of the 6MWT at many timepoints during the surgical recovery trajectory may be more feasible for a hospital setting and for vulnerable surgical

patients requiring prehabilitation (e.g., malnourished or older adults). In fact, the 6MWT test does not require specialized training for the assessor nor any equipment. It also assesses submaximal levels of functional capacity which may be less burdensome to patients and more reflective of the ability to perform activities of daily living especially in older adults (76) . Finally, the 6MWT can easily be repeated after surgery to evaluate if patients recover to preoperative baseline values which is an important patient-oriented objective as ambulation represents a meaningful aspect of their health and functional recovery (78).

Secondly, measuring changes in physiological reserve from baseline to the pre-admission phase of recovery is also an important aspect according to our common definition. Physiological reserve has been described as "excess metabolic capacity that is, the ability to readily exceed normal basal metabolic function when needed to meet heightened metabolic demands" (79). In the surgical field, physiological reserve can be considered as a buffer to help the patient tolerate the stress response (19). Examples of physiological reserves are "adequate muscle mass to spare without concomitant loss in physical function or the potential cardiac output (the difference between resting and maximal values) available to overcome a stressor" (19). Thus, the body's protein "reserve" (i.e., body protein from lean tissue) is one of the aspects that contributes to physiological reserve. Patients with poor reserve related to conditions like malnutrition, which can be associated with reduced baseline muscle mass, may not be able to withstand the catabolic surgical stress response without serious functional and clinical consequences (e.g., loss of function, impair independence status) (80, 81). However, even though measuring muscle or lean mass is important for the assessment of physiological reserve (e.g., fat free mass measured with bioelectrical impedance analysis, lean tissue mass using dual-energy x-ray absorptiometry) often presents challenges such as feasibility, accessibility, cost and validity (82, 83). These challenges

may explain why proxies of muscle mass and muscle composition were infrequently reported in our scoping review when compared to cardiopulmonary reserve measured during CPET (i.e., exercise capacity) which is also a contributor to physiological reserve. Alternatively, in situations where muscle parameters cannot be readily assessed, strength which was the second most reported PerfO could be an appropriate supporting proxy of muscle function and nutritional status (80). In fact, as previously referred to the OFF rule or "outcomes follow function follow form" framework, poor function like impaired strength may already suggest alterations in structural/anatomic measure of muscle (18). Handgrip strength using a handheld Jamar dynamometer is a validated method that moderately correlates with strength for other body components while also being a powerful predictor of poor clinical outcomes (81). Furthermore, sex-specific cut-offs exist to evaluate sarcopenia and dynapenia (84). We suggest that prehabilitation trials should include measures of body composition such as lean mass or muscle, when possible, combined with handgrip strength to estimate physiological and nutritional reserve.

Moreover, our proposed definition suggests that prehabilitation aims to improve postoperative outcomes and facilitate recovery. Traditionally, clinical outcomes assessed after surgery, such as complications, are important to clinicians and health care administrators and have dominated the surgical literature. In fact, Antonescu and colleagues demonstrated that LOS and 30-day or 90-day postoperative complications remained the most reported trial endpoints published in high impact journals between 2009 and 2014 (85). These results were also confirmed by a systematic review of outcomes used for evaluating ERAS interventions (86). Our current findings corroborate these results as hospital LOS was the most reported concept of interest overall and complications were the most frequently used ClinRO. Currently, in an era

moving towards patient-centered care, researchers have advocated for the use of PROs to capture the patient's perspective on their recovery after surgery (72, 86, 87). For example, Rajabiyazdi and colleagues conducted a qualitative study to gain knowledge about the meaning of recovery for patients undergoing abdominal surgery. Interviews with patients revealed that recovery, defined as an energy-requiring process of returning to normality and wholeness (88), involved 5 overarching themes: 1) returning to habits and daily routines, 2) resolution of symptoms, 3) overcoming mental strains, 4) regaining independence, and 5) enjoying life (78). These themes suggests that meaningful outcomes for patients extend beyond traditional metrics like earlier hospital discharge or absence of complications. While there is a shift in surgery to adopt PROs, our scoping review revealed 11 different PROs assessed using as a total of 63 unique instruments suggesting there is no single relevant PRO for prehabilitation interventions. To select appropriate PRO instruments, the COSMIN checklist (77) and the International Society for Quality of Life Research provide recommendations for minimal standards including evidence for reliability, content and construct validity and responsiveness (89). However, commonly used measurement instruments in abdominal (90) and orthopedics (91) surgical trials do not follow these recommendations and have limited evidence supporting their measurement properties. As there are no specific instruments developed for the prehabilitation field, following consensus recommendations may be the best way to select meaningful PROs at each specific recovery stage (72). For instance, consensus guidelines by the American Society for Enhanced Recovery and Perioperative Quality Initiative working group advise evaluating recovery during the early and intermediate stages (24 hours after surgery to hospital discharge) using the Quality of Recovery-15 questionnaire (QoR-15) (92) because it is surgery specific and has a short recall period (93). The consensus guidelines also recommend using the World Health Organization Disability

Assessment Schedule 2.0 (WHODAS 2.0) (94) or the Patient-Reported Outcomes Measurement Information System (PROMIS) (95) for assessing the late phase of recovery (30 and 90 days after surgery, if feasible) and comparing the results with those obtained at baseline (prior to surgery). To best capture the effects of prehabilitation on postoperative outcomes and recovery, we suggest including traditional surgical outcomes as well as patient-oriented recovery metrics.

6.2 Significance and future directions

The present work is the first step towards achieving consensus in surgical prehabilitation research. The findings of this MSc thesis will guide the development of a universally accepted definition, inform the process of standardizing trial outcomes and their specific outcome assessments. The development of a COS specific to the surgical prehabilitation field has been suggested as a key priority to reduce heterogeneity while also increasing the selection of more meaningful endpoints to patients, clinicians and health institutions. Harmonizing definitions and outcomes will improve combining and comparing data in systematic reviews and meta-analyses which is crucial for generating robust conclusions to ultimately guide clinical decision-making and guidelines (77).

6.2.1 Expert consensus for a standardized definition is needed

In the context of a master's program and the available time to conduct, analyze and report findings, I led our scoping review using the five essential steps out of the total six steps described by Arksey and O'Malley's framework (57). While some argue that it should be an essential part of the scoping methodology as it may add more value and rigour to findings (54), the last and optional step of the framework is a *consultation exercise*. The purpose of conducting a consultation exercise with stakeholders as focus groups, interviews, surveys or other methods is to gain additional information, perspectives, and applicability to the scoping review (57). For

example, a scoping review on identifying key research priorities in HIV and rehabilitation included a consultation phase to their methodology by integrating a focus group and interviews with people living with HIV, health researchers, clinicians and policymakers (96). This optional step provided 6 additional research priorities, helped refine their suggested framework, improve the trustworthiness of their findings and was an opportunity for knowledge transfer to the community (96).

We consolidated a common definition for surgical prehabilitation using the most frequently used concepts described in definitions from primary literature. Even though our research group was composed of a multidisciplinary team which included expert and experienced researchers in the prehabilitation field which increases the trustworthiness of our findings, a common definition does not necessarily imply its validity. We believe that the next step to achieve a globally accepted and standardized definition is a formal consultation process such as an international Delphi survey with key stakeholders including patients, clinicians and researchers. The Delphi survey technique is a methodology that systematically gathers opinions during a multistage process, designed to transform single opinions towards group consensus on a specific question or subject among the stakeholders participating (97). The Delphi methodology with researchers, clinicians and patients has been used in health sciences to identify research priorities, including those of cancer prehabilitation (71), to develop clinical definitions (98) and to determine core outcomes to measure in clinical trials (99).

6.2.2 A core outcome set is needed

The grading of the certainty of the evidence is a crucial factor in the decision-making process of a patient's care trajectory as it is a determinant of the overall strength of recommendations in guidelines for patients, clinicians and policymakers (100). In fact, the

strength of the recommendations is defined as the extent to which we can be confident that the effect of a treatment or intervention is accurate and outweighs the potential risks (101). Poor certainty of the advantages of a particular intervention, like surgical prehabilitation, makes strong recommendations almost impossible as the disadvantages or risks (e.g., costs, side effects) may be greater than the potential benefits. The Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach is a universally adopted grading system that classifies the certainty of the evidence from high to very low. Compared to results from a single RCT, pooling data from many trials into a systematic review and meta-analysis provides more robust effect estimates to guide clinical recommendations. In fact, systematic reviews "seek to systematically search for, critically appraise and synthesize research evidence" and meta-analyses "statistically combine the data of quantitative studies to provide a more precise effect of the results and assume absence of heterogeneity" (56). Since these reviews summarize the quality and combine quantitative data of existing literature to enhance statistical power, they are often required in health research to answer a specific question with more precision and robust conclusions. However, in the prehabilitation field appraising and combining data into systematic reviews and meta-analyses remains difficult in part because of the lack of adequate reporting (51) and inconsistencies in outcomes used across individual trials leaving the overall evidence of low certainty (4, 52, 53). The current state of prehabilitation evidence makes it difficult for readers such as health professionals and policymakers to make informed decisions.

The development of a COS for surgical prehabilitation may be a practical solution to improve the level of certainty. A COS is "an agreed standardized collection of outcomes that should be measured and reported for a specific field" (101). Core outcomes in surgical prehabilitation could prompt investigators to include a set of meaningful endpoints for patients

and clinicians; therefore, all trials using the COS could contribute to useful data for future meta-analyses (99, 101). Contrary to some beliefs, a COS would not prevent researchers to investigate the effects of the interventions on other outcomes of interest nor test different or new hypotheses (101). It simply specifies a minimum of outcome that should be measured and reported. Furthermore, this can assure more transparency in final publications as authors will be required to report favourable and unfavourable results on these important outcomes which can reduce publication bias (99). Our scoping review identified 50 concepts of interest (outcomes) in 76 RCTs supporting the need for a harmonized outcome set. The Core Outcome Set-STAndards for Development (COS-STAD) project has published guidelines in 2017 that address the minimum standards for the design of a COS which include 11 practical recommendations related to three important aspects: understanding the scope of the COS, incorporating relevant stakeholders, and conducting a transparent consensus process (70). Most published health COS following these guidelines have between 10 and 12 outcomes (102-106), while few have more (up to 26) (107).

In addition to guiding "what" to measure and report in surgical prehabilitation trials, the selection of universally accepted and validated outcome assessments (e.g., measurement instruments, tests, descriptions of assessments) within the appropriate recovery timeframes are crucial for mitigating the heterogeneity of "how" and "when" outcomes are measured. In fact, we also mapped 184 different outcomes assessments which were used to measure the 48 health-related concepts of interest. The diversity in outcome assessments per each individual outcome has most likely contributed to the overall lack of consistency and difficulties in pooling data. For example, postoperative complications (n=51), which was a single outcome, were reported using the following grading systems (outcome assessments) Clavien-Dindo (n=24/51, 47%), Comprehensive Complication Index (n=8/51, 16%), Post-Operative Morbidity Survey

(n=2/51, 4%). Also, 43% (n=22/51) of the postoperative complications were also described with frequencies per individual complication using varying terminology and definitions adding to the complexity when comparing results between trials. To facilitate comparing and combining of data, complications should be defined according to consensus-based criteria specific to surgical procedure or disease, and severity evaluated according to widely recognized classification system such as Clavien-Dindo (108) or the Comprehensive Complication Index (109). Thus, the selection of appropriate and standardized outcome assessments to measure the outcomes from a COS may be warranted. Additionally, commonly used assessments methods do not necessarily reflect consensus nor validity and reliability of the outcomes trials intend to measure.

To mitigate these limitations, the COS should also suggest validated outcome assessments by using the COSMIN checklist to evaluate the methodological quality of measurement properties (77). In fact, the COMET and the COSMIN initiatives have developed guidelines on how to select outcome assessments for concepts of interest (outcomes) which includes 4 steps: 1) agree on detailed constructs to be measured for specific population (COS), 2) find all existing outcome assessments (such as our scoping review, manuscript 2), 3) conduct a quality and feasibility assessment (using the COSMIN checklist and criteria for good measurement properties), and 4) follow generic recommendations for COS (110). The fourth step suggests selecting only one measurement instrument for each outcome that achieves the minimum quality requirements (good content validity, good internal consistency if applicable). This step also suggests that the consensus procedures should be performed among all relevant stakeholders, especially patients (110).

6.3 Strengths and Limitations

6.3.1 Strengths

The major strength of this research is that our scoping review is the first to identify reported definitions and to systematically map outcome assessments of surgical prehabilitation trials. These are key priorities towards improving consistency and harmonizing measurement, therefore, advance this important field of research (4, 71). The second strength is that our research team was composed of multidisciplinary researchers and health professionals (anesthesiologist, medical doctors, physiotherapists, dietitians) from different countries (Canada, Australia, United Kingdom, Italy, Switzerland) and diverse surgical specialties (lung, oesophageal, orthopedics, spinal, colorectal, urological, hernia, pancreatic, hepatobiliary, cardiac, breast surgery) which may best represent the prehabilitation field and ensure objectivity and confirmability. In fact, as prehabilitation intervention can be composed of diverse modalities such as nutrition, exercise physiotherapy and, to some extent, medical management, it was important to include authors from all these domains. The diversity of the team brought a wide range of perspectives, informed the development of the data extraction form, and brought great depth during the analyses and interpretation phases. Also, our search strategy was developed and performed with the help of an experience librarian and used 6 different databases (111). Furthermore, data extraction of study characteristics, definitions and reported outcomes were conducted in duplicate by independent reviewers (physiotherapist and dietitian) which is not mandatory process for scoping reviews but recommended for systematic reviews (111). Furthermore, method and investigator triangulation approaches were used to analyze the qualitative text data (for manuscript 1) to ensure the trustworthiness of findings. Lastly, reporting

of our manuscripts was done in accordance with best practice guidelines for scoping reviews using the PRISMA-ScR checklist (53).

6.3.2 Limitations

This research is not without limitations. Most of the limitations are related to aspects of the design and methodology. Overall, only studies published in French or English were included in this scoping review which potentially excludes relevant trials and may lead to selection bias. Furthermore, given that there was no common definition of prehabilitation, the search strategy for identifying relevant articles focused on trials labelled as "prehabilitation" (in title, abstract or keywords) and/or that met our pre-specified criteria. These criteria were based on previous descriptions of prehabilitation used in recent review articles. The choice of inclusion criteria may have left out possible relevant RCTs.

For manuscript 1, the consolidated definition was generated using only published definitions, meaning that it was limited to commonly reported components from surgical prehabilitation trials, which does not necessarily reflect validity nor consensus between experts in the field. Also, the trials reporting an explicit and complete definition were mainly from abdominal, orthopedic and spinal specialties. Therefore, the common definition may not reflect the priorities of all and may not be transferable to other surgery types. Given that the first objective of this research was to identify and describe how surgical prehabilitation was defined, we did not conduct a consultation exercise which is an optional step for scoping reviews. Consulting a group of experts and appropriate stakeholders, such as during an international Delphi survey, is warranted and an important next step for consensus of a standard definition.

For manuscript 2, concepts of interest for measurement (outcomes) and specific outcome assessments (measurement instruments) were mapped using the ISPOR framework which involves subjective categorization. To mitigate the subjectivity when categorizing outcomes, a multidisciplinary team collaborated during all steps of the review to increase the trustworthiness of our analysis. Additionally, as the number of individual outcome assessments was strikingly high, we focused our results on the most frequently reported ones per each concept of interest. However, commonly used outcome assessments do not necessarily reflect consensus nor accuracy and validity for the concepts of interest that trials intended to measure. Therefore, further research is needed to guide de selection of appropriate outcomes assessments and instruments to measure core outcomes.

7. CONCLUSION

In conclusion, preparing patients for surgery through prehabilitation is a promising intervention. Consistency across primary clinical trials is lacking posing difficulties to evaluate the certainty of this intervention on meaningful outcomes after surgery. This research has highlighted the poor standardization in published definitions and reported outcomes across primary RCTs. Our scoping review is the first to have consolidated the available literature to suggest a common definition for surgical prehabilitation and to have systematically mapped all 50 different reported concepts of interest (outcomes) measured using 184 outcome assessments (measurements instruments). These findings are important to move towards consensus which is needed to guide future high-quality RCTs. To continue advancing the surgical prehabilitation field, a universally accepted definition by experts as well as the development of a COS including meaningful outcomes and standardized assessment methods are crucially needed for both patients and health care systems.

8. REFERENCES

1. Rose J, Weiser TG, Hider P, Wilson L, Gruen RL, Bickler SW. Estimated need for surgery worldwide based on prevalence of diseases: a modelling strategy for the WHO Global Health Estimate. The Lancet Global Health. 2015;3:S13-S20.

2. Schricker T, Lattermann R, Carli F. Physiology and Pathophysiology of ERAS. Enhanced Recovery After Surgery: A Complete Guide to Optimizing Outcomes. 2020:11-22.

3. Gillis C, Ljungqvist O, Carli F. Prehabilitation, enhanced recovery after surgery, or both? A narrative review. British Journal of Anaesthesia. 2022.

4. McIsaac DI, Gill M, Boland L, Hutton B, Branje K, Shaw J, et al. Prehabilitation in adult patients undergoing surgery: an umbrella review of systematic reviews. British Journal of Anaesthesia. 2022;128(2):244-57.

5. Cusack B, Buggy D. Anaesthesia, analgesia, and the surgical stress response. BJA Education. 2020;20(9):321.

6. Mizock BA. Alterations in fuel metabolism in critical illness: hyperglycaemia. Best Practice & Research Clinical Endocrinology & Metabolism. 2001;15(4):533-51.

7. Sato H, Carvalho G, Sato T, Lattermann R, Matsukawa T, Schricker T. The association of preoperative glycemic control, intraoperative insulin sensitivity, and outcomes after cardiac surgery. The Journal of Clinical Endocrinology & Metabolism. 2010;95(9):4338-44.

8. O'Keefe S, Sender P, James W. " Catabolic" loss of body nitrogen in response to surgery. The Lancet. 1974;304(7888):1035-8.

9. Schricker T, Meterissian S, Lattermann R, Adegoke OAJ, Marliss EB, Mazza L, et al. Anticatabolic Effects of Avoiding Preoperative Fasting by Intravenous Hypocaloric Nutrition: A Randomized Clinical Trial. Annals of Surgery. 2008;248(6):1051-9.

10. Weissman C. The metabolic response to stress: an overview and update. Anesthesiology. 1990;73(2):308-27.

11. Phillips BE, Smith K, Liptrot S, Atherton PJ, Varadhan K, Rennie MJ, et al. Effect of colon cancer and surgical resection on skeletal muscle mitochondrial enzyme activity in colon cancer patients: a pilot study. Journal of Cachexia, Sarcopenia and Muscle. 2013;4:71-7.

12. Gillis C, Fenton TR, Sajobi TT, Minnella EM, Awasthi R, Loiselle S-È, et al. Trimodal prehabilitation for colorectal surgery attenuates post-surgical losses in lean body mass: a pooled analysis of randomized controlled trials. Clinical Nutrition. 2019;38(3):1053-60.

13. Mey R, Casaña J, Díaz-Cambronero Ó, Suso-Martí L, Cuenca-Martínez F, Mazzinari G, et al. Physical and Quality of Life Changes in Elderly Patients after Laparoscopic Surgery for Colorectal Cancer-A Prospective Cohort Study. International Journal of Environmental Research and Public Health. 2022;19(22):14711.

14. Watters JM, Clancey SM, Moulton SB, Briere KM, Zhu JM. Impaired recovery of strength in older patients after major abdominal surgery. Annals of Surgery. 1993;218(3):380-90; discussion 90-3.

15. Moreland JD, Richardson JA, Goldsmith CH, Clase CM. Muscle weakness and falls in older adults: a systematic review and meta-analysis. Journal of the American Geriatrics Society. 2004;52(7):1121-9.

16. Bye A, Sjøblom B, Wentzel-Larsen T, Grønberg BH, Baracos VE, Hjermstad MJ, et al. Muscle mass and association to quality of life in non-small cell lung cancer patients. Journal of Cachexia, Sarcopenia and Muscle. 2017;8(5):759-67.

17. Jung H-W, Kim JW, Kim J-Y, Kim S-W, Yang HK, Lee JW, et al. Effect of muscle mass on toxicity and survival in patients with colon cancer undergoing adjuvant chemotherapy. Supportive Care in Cancer. 2015;23:687-94.

18. Heymsfield S, Prado CM, Gonzalez MC. Skeletal muscle-focused guideline development: hierarchical model incorporating muscle form, function, and clinical outcomes. Applied Physiology, Nutrition, and Metabolism. 2023;48(10):751-6.

19. Gillis C, Ljungqvist O, Carli F. Prehabilitation, enhanced recovery after surgery, or both? A narrative review. British Journal of Anaesthesia 2022;128(3):434-48.

20. Ljungqvist O, De Boer HD, Balfour A, Fawcett WJ, Lobo DN, Nelson G, et al. Opportunities and challenges for the next phase of enhanced recovery after surgery: a review. JAMA Surgery. 2021;156(8):775-84.

21. Bardram L, Funch-Jensen P, Jensen P, Kehlet H, Crawford M. Recovery after laparoscopic colonic surgery with epidural analgesia, and early oral nutrition and mobilisation. The Lancet. 1995;345(8952):763-4.

22. Kehlet H, Wilmore DW. Multimodal strategies to improve surgical outcome. The American Journal of Surgery. 2002;183(6):630-41.

23. Lau CS, Chamberlain RS. Enhanced recovery after surgery programs improve patient outcomes and recovery: a meta-analysis. World Journal of Surgery. 2017;41:899-913.

24. Visioni A, Shah R, Gabriel E, Attwood K, Kukar M, Nurkin S. Enhanced Recovery After Surgery for Noncolorectal Surgery?: A Systematic Review and Meta-analysis of Major Abdominal Surgery. Annals of Surgery. 2018;267(1):57-65.

25. Zhuang C-L, Ye X-Z, Zhang X-D, Chen B-C, Yu Z. Enhanced recovery after surgery programs versus traditional care for colorectal surgery: a meta-analysis of randomized controlled trials. Diseases of the Colon & Rectum. 2013;56(5):667-78.

26. Thiele RH, Rea KM, Turrentine FE, Friel CM, Hassinger TE, Goudreau BJ, et al. Standardization of care: impact of an enhanced recovery protocol on length of stay, complications, and direct costs after colorectal surgery. Journal of the American College of Surgeons. 2015;220(4):430-43.

27. Nelson G, Kiyang LN, Crumley ET, Chuck A, Nguyen T, Faris P, et al. Implementation of Enhanced Recovery After Surgery (ERAS) across a provincial healthcare system: the ERAS Alberta colorectal surgery experience. World Journal of Surgery. 2016;40:1092-103.

28. Ahmad T BR, Grigoras I, Aldecoa C, Hofer C, Hoeft A, Holt P, Fleisher LA, Buhre W, Pearse RM, Ferguson M. Global patient outcomes after elective surgery: prospective cohort study in 27 low-, middle-and high-income countries. BJA: British Journal of Anaesthesia. 2016;117(5):601-9.

29. Bamdad MC, Brown CS, Kamdar N, Weng W, Englesbe MJ, Lussiez A. Patient, surgeon, or hospital: explaining variation in outcomes after colectomy. Journal of the American College of Surgeons. 2022;234(3):300-9.

30. Gillis C, Fenton TR, Gramlich L, Keller HH, Sajobi TT, Culos-Reed N, et al. Malnutrition modifies the response to multimodal prehabilitation: A pooled analysis of prehabilitation trials. Applied Physiology, Nutrition, and Metabolism. 2022;47(2):141-50.

31. Carli F, Zavorsky GS. Optimizing functional exercise capacity in the elderly surgical population. Current Opinion in Clinical Nutrition & Metabolic Care. 2005;8(1):23-32.

32. Burden ST, Gibson DJ, Lal S, Hill J, Pilling M, Soop M, et al. Pre-operative oral nutritional supplementation with dietary advice versus dietary advice alone in weight-losing patients with colorectal cancer: single-blind randomized controlled trial. Journal of Cachexia, Sarcopenia and Muscle. 2017;8(3):437-46.

33. Gillis C, Coca-Martinez M, Santa Mina D. Tailoring prehabilitation to address the multifactorial nature of functional capacity for surgery. Journal of Human Nutrition and Dietetics. 2023;36(2):395-405.

34. Gillis C, Gill M, Gramlich L, Culos-Reed SN, Nelson G, Ljungqvist O, et al. Patients' perspectives of prehabilitation as an extension of Enhanced Recovery After Surgery protocols. Canadian Journal of Surgery. 2021;64(6):E578.

35. Silver JK, Baima J. Cancer prehabilitation: an opportunity to decrease treatment-related morbidity, increase cancer treatment options, and improve physical and psychological health outcomes. American Journal of Physical Medicine & Rehabilitation. 2013;92(8):715-27.

36. Carli F, Charlebois P, Stein B, Feldman L, Zavorsky G, Kim DJ, et al. Randomized clinical trial of prehabilitation in colorectal surgery. British Journal of Surgery. 2010;97(8):1187-97.

37. Ditmyer MM, Topp R, Pifer M. Prehabilitation in preparation for orthopaedic surgery. Orthopaedic Nursing. 2002;21(5):43-54.

38. Topp R, Ditmyer M, King K, Doherty K, Hornyak III J. The effect of bed rest and potential of prehabilitation on patients in the intensive care unit. AACN Advanced Critical Care. 2002;13(2):263-76.

39. Gillis C, Loiselle SE, Fiore JF, Jr., Awasthi R, Wykes L, Liberman AS, et al. Prehabilitation with Whey Protein Supplementation on Perioperative Functional Exercise Capacity in Patients Undergoing Colorectal Resection for Cancer: A Pilot Double-Blinded Randomized Placebo-Controlled Trial. Journal of the Academy of Nutrition & Dietetics. 2016;116(5):802-12.

40. Humeidan ML, Reyes JC, Mavarez-Martinez A, Roeth C, Nguyen CM, Sheridan E, et al. Effect of Cognitive Prehabilitation on the Incidence of Postoperative Delirium Among Older Adults Undergoing Major Noncardiac Surgery: The Neurobics Randomized Clinical Trial. JAMA Surgery. 2021;156(2):148-56.

41. Molenaar CJL, Minnella EM, Coca-Martinez M, Ten Cate DWG, Regis M, Awasthi R, et al. Effect of Multimodal Prehabilitation on Reducing Postoperative Complications and Enhancing Functional Capacity Following Colorectal Cancer Surgery: The PREHAB Randomized Clinical Trial. JAMA Surgery. 2023;158(6):572-81.

42. Carli F, Bousquet-Dion G, Awasthi R, Elsherbini N, Liberman S, Boutros M, et al. Effect of Multimodal Prehabilitation vs Postoperative Rehabilitation on 30-Day Postoperative Complications for Frail Patients Undergoing Resection of Colorectal Cancer: A Randomized Clinical Trial. JAMA Surgery. 2020;155(3):233-42.

43. Bousquet-Dion G, Awasthi R, Loiselle SE, Minnella EM, Agnihotram RV, Bergdahl A, et al. Evaluation of supervised multimodal prehabilitation programme in cancer patients undergoing colorectal resection: a randomized control trial. Acta Oncologica. 2018;57(6):849-59.

44. Minnella EM, Awasthi R, Loiselle SE, Agnihotram RV, Ferri LE, Carli F. Effect of Exercise and Nutrition Prehabilitation on Functional Capacity in Esophagogastric Cancer Surgery: A Randomized Clinical Trial. JAMA Surgery. 2018;153(12):1081-9.

45. Berkel AEM, Bongers BC, Kotte H, Weltevreden P, de Jongh FHC, Eijsvogel MMM, et al. Effects of Community-based Exercise Prehabilitation for Patients Scheduled for Colorectal Surgery With High Risk for Postoperative Complications: Results of a Randomized Clinical Trial. Annals of Surgery. 2022;275(2):e299-e306.

46. Barberan-Garcia A, Ubre M, Roca J, Lacy AM, Burgos F, Risco R, et al. Personalised Prehabilitation in High-risk Patients Undergoing Elective Major Abdominal Surgery: A Randomized Blinded Controlled Trial. Annals of Surgery. 2018;267(1):50-6.

47. Gloor S, Misirlic M, Frei-Lanter C, Herzog P, Muller P, Schafli-Thurnherr J, et al. Prehabilitation in patients undergoing colorectal surgery fails to confer reduction in overall morbidity: results of a single-center, blinded, randomized controlled trial. Langenbecks Archives of Surgery. 2022;407(3):897-907.

48. Minnella EM, Bousquet-Dion G, Awasthi R, Scheede-Bergdahl C, Carli F. Multimodal prehabilitation improves functional capacity before and after colorectal surgery for cancer: a five-year research experience. Acta oncologica. 2017;56(2):295-300.

49. Gillis C, Li C, Lee L, Awasthi R, Augustin B, Gamsa A, et al. Prehabilitation versus rehabilitation: a randomized control trial in patients undergoing colorectal resection for cancer. Anesthesiology. 2014;121(5):937-47.

50. Gillis C, Davies SJ, Carli F, Wischmeyer PE, Wootton SA, Jackson AA, et al. Current Landscape of Nutrition Within Prehabilitation Oncology Research: A Scoping Review. Frontiers in Nutrition. 2021;8:63.

51. Engel D, Testa GD, McIsaac DI, Carli F, Santa Mina D, Baldini G, et al. Reporting quality of randomized controlled trials in prehabilitation: a scoping review. Perioperative Medicine. 2023;12(1):48.

52. Jain SR, Kandarpa VL, Yaow CYL, Tan WJ, Ho LML, Sivarajah SS, et al. The Role and Effect of Multimodal Prehabilitation Before Major Abdominal Surgery: A Systemic Review and Meta-Analysis. World Journal of Surgery. 2023;47(1):86-102.

53. Punnoose A, Claydon-Mueller LS, Weiss O, Zhang J, Rushton A, Khanduja V. Prehabilitation for Patients Undergoing Orthopedic Surgery: A Systematic Review and Meta-analysis. JAMA Network Open. 2023;6(4):e238050.

54. Levac D, Colquhoun H, O'Brien KK. Scoping studies: advancing the methodology. Implementation Science. 2010;5:69.

55. Rumrill PD, Fitzgerald SM, Merchant WR. Using scoping literature reviews as a means of understanding and interpreting existing literature. Work. 2010;35(3):399-404.

56. Grant MJ, Booth A. A typology of reviews: an analysis of 14 review types and associated methodologies. Health Information & Libraries Journal. 2009;26(2):91-108.

57. Arksey H, O'Malley L. Scoping studies: towards a methodological framework. International Journal of Social Research Methodology. 2005;8(1):19-32.

58. Scheede-Bergdahl C, Minnella EM, Carli F. Multi-modal prehabilitation: addressing the why, when, what, how, who and where next? Anaesthesia. 2019;74 Suppl 1:20-6.

59. Luther A, Gabriel J, Watson RP, Francis NK. The Impact of Total Body Prehabilitation on Post-Operative Outcomes After Major Abdominal Surgery: A Systematic Review. World Journal of Surgery. 2018;42(9):2781-91.

60. Gillis C, Buhler K, Bresee L, Carli F, Gramlich L, Culos-Reed N, et al. Effects of Nutritional Prehabilitation, With and Without Exercise, on Outcomes of Patients Who Undergo Colorectal Surgery: A Systematic Review and Meta-analysis. Gastroenterology. 2018;155(2):391-410.e4.

61. Walton MK, Powers JH, 3rd, Hobart J, Patrick D, Marquis P, Vamvakas S, et al. Clinical Outcome Assessments: Conceptual Foundation-Report of the ISPOR Clinical Outcomes Assessment - Emerging Good Practices for Outcomes Research Task Force. Value Health. 2015;18(6):741-52.

62. Tricco AC, Lillie E, Zarin W, O'Brien KK, Colquhoun H, Levac D, et al. PRISMA extension for scoping reviews (PRISMA-ScR): checklist and explanation. Annals of internal medicine. 2018;169(7):467-73.

63. Hsieh H-F, Sarah. E. Shannon. . Three Approaches to Qualitative Content Analysis. Qualitative Health Research. 2005;15(9):1277-88.

64. Kleinheksel AJ, Rockich-Winston N, Tawfik H, Wyatt TR. Demystifying Content Analysis. American Journal of Pharmaceutical Education. 2020;84(1):7113.

65. Hoffmann TC, Glasziou PP, Boutron I, Milne R, Perera R, Moher D, et al. Better reporting of interventions: template for intervention description and replication (TIDieR) checklist and guide. British Medical Journal. 2014;348:g1687.

66. Carter N BLD, DiCenso A, Blythe J, Neville AJ, editor The use of triangulation in qualitative research. Oncology Nursing Forum; 2014.

67. Lincoln YS, Guba EG. Naturalistic Inquiry: sage; 1985.

68. Bengtsson M. How to plan and perform a qualitative study using content analysis. NursingPlus Open. 2016;2:8-14.

69. Noyes J BA, Hannes K, Harden A, Harris J, Lewin S, Lockwood C (editors). Critical appraisal of qualitative research: Cochrane Collaboration Qualitative Methods Group, 2011; updated August 2011 [updated September 19, 2023. Available from: http://cqrmg.cochrane.org/supplemental-handbook-guidance.

70. Kirkham JJ, Davis K, Altman DG, Blazeby JM, Clarke M, Tunis S, et al. Core outcome Set-STAndards for development: the COS-STAD recommendations. PLoS Medicine. 2017;14(11):e1002447.

71. Raichurkar P, Denehy L, Solomon M, Koh C, Pillinger N, Hogan S, et al. Research Priorities in Prehabilitation for Patients Undergoing Cancer Surgery: An International Delphi Study. Annals of Surgical Oncology. 2023;30(12):7226–35.

72. Lee L, Tran T, Mayo NE, Carli F, Feldman LS. What does it really mean to "recover" from an operation? Surgery. 2014;155(2):211-6.

73. Levett D, Jack S, Swart M, Carlisle J, Wilson J, Snowden C, et al. Perioperative cardiopulmonary exercise testing (CPET): consensus clinical guidelines on indications, organization, conduct, and physiological interpretation. British Journal of Anaesthesia. 2018;120(3):484-500.

74. American Thoracic Society Committee on Proficiency Standards for Clinical Pulmonary Function Laboratories. ATS statement: guidelines for the six-minute walk test. American Journal of Respiratory and Critical Care Medicine. 2002;166(1):111-7.

75. Singh SJ, Puhan MA, Andrianopoulos V, Hernandes NA, Mitchell KE, Hill CJ, et al. An official systematic review of the European Respiratory Society/American Thoracic Society: measurement properties of field walking tests in chronic respiratory disease. European Respiratory Journal. 2014;44(6):1447-78.

76. Rikli RE, Jones CJ. The reliability and validity of a 6-minute walk test as a measure of physical endurance in older adults. Journal of Aging and Physical Activity. 1998;6(4):363-75.

77. Mokkink LB, Terwee CB, Patrick DL, Alonso J, Stratford PW, Knol DL, et al. The COSMIN checklist for assessing the methodological quality of studies on measurement properties of health status measurement instruments: an international Delphi study. Quality of Life Research. 2010;19(4):539-49.

78. Rajabiyazdi F, Alam R, Pal A, Montanez J, Law S, Pecorelli N, et al. Understanding the Meaning of Recovery to Patients Undergoing Abdominal Surgery. JAMA Surgery. 2021;156(8):758-65.

79. Atamna H, Tenore A, Lui F, Dhahbi JM. Organ reserve, excess metabolic capacity, and aging. Biogerontology. 2018;19(2):171-84.

80. Cederholm T, Jensen G, Correia M, Gonzalez MC, Fukushima R, Higashiguchi T, et al. GLIM criteria for the diagnosis of malnutrition–A consensus report from the global clinical nutrition community. Journal of Cachexia, Sarcopenia and Muscle. 2019;10(1):207-17.

81. Cruz-Jentoft AJ, Bahat G, Bauer J, Boirie Y, Bruyère O, Cederholm T, et al. Sarcopenia: revised European consensus on definition and diagnosis. Age Ageing. 2019;48(1):16-31.

82. Prado CM, Landi F, Chew ST, Atherton PJ, Molinger J, Ruck T, et al. Advances in muscle health and nutrition: A toolkit for healthcare professionals. Clinical Nutrition. 2022(41):2244-63.

83. Prado CM, Ford KL, Gonzalez MC, Murnane LC, Gillis C, Wischmeyer PE, et al. Nascent to novel methods to evaluate malnutrition and frailty in the surgical patient. Journal of Parenteral and Enteral Nutrition. 2023;47:S54-S68.

84. Tessier AJ, Wing SS, Rahme E, Morais JA, Chevalier S. Physical function-derived cut-points for the diagnosis of sarcopenia and dynapenia from the Canadian longitudinal study on aging. Journal of Cachexia, Sarcopenia and Muscle. 2019;10(5):985-99.

85. Antonescu I, Mueller C, Fried G, Vassiliou M, Mayo N, Feldman L. Outcomes reported in high-impact surgical journals. Journal of British Surgery. 2014;101(5):582-9.

86. Neville A, Lee L, Antonescu I, Mayo N, Vassiliou M, Fried G, et al. Systematic review of outcomes used to evaluate enhanced recovery after surgery. Journal of British Surgery. 2014;101(3):159-70.

87. Feldman LS, Lee L, Fiore Jr J. What outcomes are important in the assessment of Enhanced Recovery After Surgery (ERAS) pathways? Canadian Journal of Anesthesia. 2015;62(2):120.

88. Allvin R, Berg K, Idvall E, Nilsson U. Postoperative recovery: a concept analysis. Journal of Advanced Nursing. 2007;57(5):552-8.

89. Reeve BB, Wyrwich KW, Wu AW, Velikova G, Terwee CB, Snyder CF, et al. ISOQOL recommends minimum standards for patient-reported outcome measures used in patient-centered outcomes and comparative effectiveness research. Quality of Life Research. 2013;22:1889-905.

90. Fiore Jr JF, Figueiredo S, Balvardi S, Lee L, Nauche B, Landry T, et al. How do we value postoperative recovery?: a systematic review of the measurement properties of patient-reported outcomes after abdominal surgery. Annals of Surgery. 2018;267(4):656-69.

91. Wang Y, Yin M, Zhu S, Chen X, Zhou H, Qian W. Patient-reported outcome measures used in patients undergoing total knee arthroplasty: a COSMIN systematic review. Bone & Joint Research. 2021;10(3):203-17.

92. Stark PA, Myles PS, Burke JA. Development and psychometric evaluation of a postoperative quality of recovery score: the QoR-15. Anesthesiology. 2013;118(6):1332-40.

93. Abola RE, Bennett-Guerrero E, Kent ML, Feldman LS, Fiore Jr JF, Shaw AD, et al. American Society for Enhanced Recovery and Perioperative Quality Initiative joint consensus statement on patient-reported outcomes in an enhanced recovery pathway. Anesthesia & Analgesia. 2018;126(6):1874-82.

94. Ustün TB, Chatterji S, Kostanjsek N, Rehm J, Kennedy C, Epping-Jordan J, et al. Developing the World Health Organization Disability Assessment Schedule 2.0. Bull World Health Organ. 2010;88(11):815-23.

95. Hays RD, Spritzer KL, Schalet BD, Cella D. PROMIS®-29 v2. 0 profile physical and mental health summary scores. Quality of life Research. 2018;27(7):1885-91.

96. O'Brien K, Wilkins A, Zack E, Solomon P. Scoping the field: identifying key research priorities in HIV and rehabilitation. AIDS and Behavior. 2010;14:448-58.

97. Hasson F, Keeney S, McKenna H. Research guidelines for the Delphi survey technique. Journal of Advanced Nursing. 2000;32(4):1008-15.

98. Ferguson ND, Davis AM, Slutsky AS, Stewart TE. Development of a clinical definition for acute respiratory distress syndrome using the Delphi technique. Journal of Critical Care. 2005;20(2):147-54.

99. Sinha IP, Smyth RL, Williamson PR. Using the Delphi technique to determine which outcomes to measure in clinical trials: recommendations for the future based on a systematic review of existing studies. PLoS Medicine. 2011;8(1):e1000393.

100. Guyatt GH, Oxman AD, Kunz R, Falck-Ytter Y, Vist GE, Liberati A, et al. Going from evidence to recommendations. British Medical Journal . 2008;336(7652):1049-51.

101. Clarke M, Williamson PR. Core outcome sets and systematic reviews. Systematic Reviews. 2016;5(1):1-4.

102. Jin X, Pang B, Zhang J, Liu Q, Yang Z, Feng J, et al. Core outcome set for clinical trials on coronavirus disease 2019 (COS-COVID). Engineering. 2020;6(10):1147-52.

103. McNair AG, Whistance RN, Forsythe RO, Macefield R, Rees J, Pullyblank AM, et al. Core outcomes for colorectal cancer surgery: a consensus study. PLoS Medicine. 2016;13(8):e1002071.

104. Bravington A, Obita G, Baddeley E, Johnson MJ, Murtagh FE, Currow DC, et al. Development of a Core Outcome Set for the research and assessment of inoperable malignant bowel obstruction. PloS One. 2023;18(8):e0289501.

105. Sahnan K, Tozer PJ, Adegbola SO, Lee MJ, Heywood N, McNair AG, et al. Developing a core outcome set for fistulising perianal Crohn's disease. Gut. 2019;68(2):226-38.

106. Knaapen M, Hall NJ, Moulin D, van der Lee JH, Butcher NJ, Minneci PC, et al. International core outcome set for acute simple appendicitis in children: results of a systematic review, Delphi study, and focus croups with young people. Annals of Surgery. 2022;276(6):1047.

107. Group TGRS, Lee MJ, Chapman SJ, Blackwell S, Arnott R, ten Broek RP, et al. A core outcome set for clinical studies of adhesive small bowel obstruction. Colorectal Disease. 2022;24(10):1204-10.

108. Dindo D, Demartines N, Clavien P-A. Classification of surgical complications: a new proposal with evaluation in a cohort of 6336 patients and results of a survey. Annals of Surgery. 2004;240(2):205.

109. Slankamenac K, Graf R, Barkun J, Puhan MA, Clavien P-A. The comprehensive complication index: a novel continuous scale to measure surgical morbidity. Annals of Surgery. 2013;258(1):1-7.

110. Prinsen CA, Vohra S, Rose MR, Boers M, Tugwell P, Clarke M, et al. How to select outcome measurement instruments for outcomes included in a "Core Outcome Set"–a practical guideline. Trials. 2016;17(1):1-10.

111. Shea BJ, Reeves BC, Wells G, Thuku M, Hamel C, Moran J, et al. AMSTAR 2: a critical appraisal tool for systematic reviews that include randomised or non-randomised studies of healthcare interventions, or both. British Medical Journal. 2017;358.

APPENDICES

APPENDIX 1 Literature Search

Document updated: Date: March 25, 2022 by Genevieve Gore

Database searches conducted: Date: March 22, 2022 by Genevieve Gore

Database searches peer reviewed: NA

Database searches updated: Date: by

Grey Literature searches conducted NA by

Platform	Database(s)	Database coverage dates	# Results	Search Date	Saved (account)	Remarks
Ovid	Ovid MEDLINE ALL(R)	1946 -	384	2022/03/25	gengore	*Reviews, editorials, historical articles, and records with case report in the title excluded* *Studies indexed as animal-only excluded* *Studies indexed as child-only excluded* *Limited to English or French*
Ovid	EMBASE Classic + EMBASE	1947 -	383	2022/03/25	gengore	*Excluded articles with case report/meta analysis/scoping review/systematic review) in title and the following publication types: Conference abstract/conference proceeding/"conference review"/editorial/review* *Limited to English or French*
Ovid	APA PsycInfo	1806 -	37	2022/03/25	gengore	*No exclusions given small set of results*
Web of Science	SCI-EXP, SSCI, ESCI	1900 -	420			*Reviews, conference abstracts, and editorials excluded*

EBSCOhost	CINAHL	1937 -	161	2022/03/25	NA	*Case Study, Editorial, Historical Material, Meta Analysis, Meta Synthesis, Review, Systematic Review publication types, and records with case report, meta analysis, scoping review or systematic review in the title excluded* *Studies indexed as animal-only excluded* *Limited to English or French*
Cochrane Library	CENTRAL (Trials)	Inception -	558	2022/03/22	NA	*No limits used*
JBI						Database omitted: Includes summarized and appraised evidence
Total			1943 total			

Limits or filters used:

MEDLINE search includes a combination of the Cochrane sensitive search for RTCs combined with the SIGN search for RCTs

Citation for search filter used for CINAHL:

Glanville J, Dooley G, Wisniewski S, Foxlee R, Noel-Storr A. Development of a search filter to identify reports of controlled clinical trials within CINAHL Plus. Health Information & Libraries Journal. 2019 Mar;36(1):73-90.

Original searches: [copy and paste the search strategies here]

Ovid MEDLINE(R) ALL <1946 to March 24, 2022>

Search run on March 25, 2022

1 (prehab* or pre-hab* or prerehab* or pre-rehab*).tw,kf. 1319

2 ((preoperative* or pre-operative*) adj rehab*).tw,kf. 151

3 or/1-2 1446

4 Randomized Controlled Trials as Topic/ 153780

5 randomized controlled trial/ 562420

6 Random Allocation/ 106788

7 Double Blind Method/ 170833

8 Single Blind Method/ 31741

9 clinical trial/ 534473

10 clinical trial, phase i.pt. 23481

11 clinical trial, phase ii.pt. 37481

12 clinical trial, phase iii.pt. 20254

13 clinical trial, phase iv.pt. 2301

14 controlled clinical trial.pt. 94763

15 randomized controlled trial.pt. 562420

16 multicenter study.pt. 318062

17 clinical trial.pt. 534473

18 exp Clinical Trials as topic/ 371969

19 (clinical adj trial$).tw,kf. 440698

20 ((singl$ or doubl$ or treb$ or tripl$) adj (blind$3 or mask$3)).tw,kf. 187222

21 placebos/ 35911

22 placebo$.tw,kf. 234881

23 randomi?ed.tw,kf. 719184

24 randomly.tw,kf. 379433

25 (trial or groups).ab. 2761763

26 or/4-25 4083357

27 case report.ti. 275934

28 editorial/ 599217

29 historical article/ 368034

30 systematic review/ or (scoping review or systematic review).ti. 241470

31 review.pt. 2956462

32 meta analysis/ or meta analysis.ti. 192409

33 or/27-32 4285923

34 26 not 33 3604756

35 34 not (exp animals/ not humans.sh.) 3094403

36 35 not ((exp infant/ or exp child/ or adolescent/) not exp adult/) 2836810

37 3 and 36 390

38 limit 37 to (english or french) 384

Embase Classic+Embase <1947 to 2022 March 24>

Search run on March 25, 2022

1 (prehab* or pre-hab* or prerehab* or pre-rehab*).ti,ab,kf. 2073

2 ((preoperative* or pre-operative*) adj rehab*).ti,ab,kf. 240

3 1 or 2 2280

4 "randomized controlled trial (topic)"/ 222905

5 Randomized Controlled Trial/ 703638

6 Randomization/ 93586

7 Double Blind Procedure/ 195993

8 single blind procedure/ 45621

9 placebo/ 389016

10 (random allocation or multicenter study or multicentre study or (clinical adj trial*) or ((singl* or doubl* or treb* or tripl*) adj (blind* or mask*)) or placebo* or randomi?ed or randomly).tw,kf. or (trial or groups).ab. 4990871

11 or/4-10 5281691

12 3 and 11 852

13 12 not (exp meta analysis/ or exp review/ or (case report or meta analysis or scoping review or systematic review).ti. or (conference abstract or conference proceeding or "conference review" or editorial or review).pt.) 398

14 limit 13 to (english or french) 383

APA PsycInfo <1806 to March Week 3 2022>

Search run on March 25, 2022

1 (prehab* or pre-hab* or prerehab* or pre-rehab*).ti,ab. 88

2 ((preoperative* or pre-operative*) adj rehab*).ti,ab. 5

3 1 or 2 92

4 exp randomized controlled trials/ 1156

5 clinical trials/ 12039

6 placebo/ 6205

7 treatment effectiveness evaluation/ 26555

8 exp treatment outcomes/ 131363

9 followup studies/ 12390

10 (random allocation or multicenter study or multicentre study or (clinical adj trial*) or ((singl* or doubl* or treb* or tripl*) adj (blind* or mask*)) or placebo* or randomi?ed or randomly).tw. or (trial or groups).ab. 731246

11 or/4-10 850773

12 3 and 11 37

Science Citation Expanded (SCI-EXP), Social Sciences Citation Index (SSCI), Emerging Sources Citation Index (ESCI)

Search run on March 25, 2022

420 results

(TI=(("prehab*" or "pre-hab*" or "prerehab*" or "pre-rehab*") OR (("preoperative*" or "pre-operative*") NEAR/0 "rehab*")) OR AB=(("prehab*" or "pre-hab*" or "prerehab*" or "pre-rehab*") OR (("preoperative*" or "pre-operative*") NEAR/0 "rehab*")) OR AK=(("prehab*" or "pre-hab*" or "prerehab*" or "pre-rehab*") OR (("preoperative*" or "pre-operative*") NEAR/0 "rehab*"))) AND (TS=("random allocation" OR "multicenter study" OR "multicentre study" OR (clinical NEAR/0 trial*) OR ((singl* or doubl* or treb* or tripl*) NEAR/0 (blind* or mask*)) OR placebo* OR randomi$ed OR randomly) OR AB=("trial" or "groups")) and Review Articles or Editorial Materials or Meeting Abstracts (Exclude – Document Types)

Cochrane Library

Search run on March 25, 2022 (CDT)

Search Name:

Date Run: 26/03/2022 02:39:01

Comment:

ID Search Hits

#1 (prehab* or pre next hab* or prerehab* or pre next rehab* or ((preoperative* or pre-operative*) next rehab*)):ti,ab,kw in Trials 558

CINAHL (EBSCOhost)

Search run on March 25, 2022 (CDT)

Friday, March 25, 2022 8:45:30 PM

#	Query	Limiters/Expanders	Last Run Via	Results
S10	S8 AND S9	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Plus with Full Text	161
S9	LA English OR French	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Plus with Full Text	8,026,079

S8	S7 NOT (S5 OR S6)	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Plus with Full Text	162
S7	S3 AND S4	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Plus with Full Text	199
S6	TI case report OR meta analysis OR scoping review OR systematic review	Limiters - Publication Type: Case Study, Editorial, Historical Material, Meta Analysis, Meta Synthesis, Review, Systematic Review Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Plus with Full Text	135,654
S5		Limiters - Publication Type: Case Study, Editorial, Historical Material, Meta Analysis, Meta Synthesis, Review, Systematic Review Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Plus with Full Text	1,276,321
S4	(randomized controlled trials OR MH double-blind studies OR MH single-blind studies OR MH random assignment OR MH pretest-posttest design OR MH cluster sample OR TI (randomised OR randomized) OR AB (random*) OR TI (trial) OR (MH (sample size) AND AB (assigned OR allocated OR control)) OR MH (placebos) OR PT (randomized controlled trial) OR AB (control W5 group) OR MH (crossover design) OR MH (comparative studies) OR AB (cluster W3 RCT)) NOT ((MH	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Plus with Full Text	904,609

	animals+ OR MH animal studies OR TI animal model*) NOT MH human)			
S3	S1 OR S2	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Plus with Full Text	792
S2	((preoperative* OR pre-operative*) W1 rehab*)	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Plus with Full Text	116
S1	(prehab* OR pre-hab* OR prerehab* OR pre-rehab*)	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Plus with Full Text	699

Literature Search

Document updated: Date: February 22, 2023 by Genevieve Gore

Database searches conducted: Date: March 22 & 25, 2022 by Genevieve Gore

Database searches peer reviewed: NA

Database searches updated: Date: February 22, 2023 by Genevieve Gore

Grey Literature searches conducted NA by

Platform	Database(s)	Database coverage dates	# Results	Search Date	Saved (account)	Remarks
Ovid	Ovid MEDLINE ALL(R)	1946 -	101	2023/02/22	gengore	*Reviews, editorials, historical articles, and records with case report in the title excluded* *Studies indexed as animal-only excluded* *Studies indexed as child-only excluded* *Limited to English or French* *Update limit*
Ovid	EMBASE Classic + EMBASE	1947 -	98	2023/02/22	gengore	*Excluded articles with case report/meta analysis/scoping review/systematic review) in title and the following publication types: Conference abstract/conference proceeding/"conference review"/editorial/review* *Limited to English or French* *Update limit*
Ovid	APA PsycInfo	1806 -	3	2023/02/22	gengore	*No exclusions given small set of results* *Update limit*
Web of Science	SCI-EXP, SSCI, ESCI	1900 -	109	2023/02/22	na	*Reviews, conference abstracts, and editorials excluded* *Update limit*
EBSCOhost	CINAHL	1937 -	45	2023/02/22	GG account	*Case Study, Editorial, Historical Material, Meta Analysis, Meta Synthesis, Review, Systematic Review*

						publication types, and records with case report, meta analysis, scoping review or systematic review in the title excluded *Studies indexed as animal-only excluded* *Limited to English or French* *Update limit*
Cochrane Library	CENTRAL (Trials)	Inception -	119	2023/02/22	na	*Date added to Cochrane limit used*
JBI						Database omitted: Includes summarized and appraised evidence
Total			475			

Limits or filters used:

MEDLINE search includes a combination of the Cochrane sensitive search for RTCs combined with the SIGN search for RCTs

Citation for search filter used for CINAHL:

Glanville J, Dooley G, Wisniewski S, Foxlee R, Noel-Storr A. Development of a search filter to identify reports of controlled clinical trials within CINAHL Plus. Health Information & Libraries Journal. 2019 Mar;36(1):73-90.

Original searches: [copy and paste the search strategies here]

Ovid MEDLINE(R) ALL <1946 to February 21, 2023>

1 (prehab* or pre-hab* or prerehab* or pre-rehab*).tw,kf. 1632

2 ((preoperative* or pre-operative*) adj rehab*).tw,kf. 165

3 or/1-2 1771

4 Randomized Controlled Trials as Topic/ 160538

5 randomized controlled trial/ 587215

6 Random Allocation/ 106906

7 Double Blind Method/ 174386

8 Single Blind Method/ 32503

9 clinical trial/ 537147

10 clinical trial, phase i.pt. 24627

11 clinical trial, phase ii.pt. 39298

12 clinical trial, phase iii.pt. 21410

13 clinical trial, phase iv.pt. 2386

14 controlled clinical trial.pt. 95195

15 randomized controlled trial.pt. 587215

16 multicenter study.pt. 330907

17 clinical trial.pt. 537147

18 exp Clinical Trials as topic/ 380558

19 (clinical adj trial$).tw,kf. 476812

20 ((singl$ or doubl$ or treb$ or tripl$) adj (blind$3 or mask$3)).tw,kf. 194909

21 placebos/ 35925

22 placebo$.tw,kf. 244448

23 randomi?ed.tw,kf. 769572

24 randomly.tw,kf. 403191

25 (trial or groups).ab. 2944313

26 or/4-25 4316525

27 case report.ti. 298673

28 editorial/ 637108

29 historical article/ 369088

30 systematic review/ or (scoping review or systematic review).ti. 282327

31 review.pt. 3109679

32 meta analysis/ or meta analysis.ti. 217614

33 or/27-32 4523589

34 26 not 33 3804491

35 34 not (exp animals/ not humans.sh.) 3277527

36 35 not ((exp infant/ or exp child/ or adolescent/) not exp adult/) 3004200

37 3 and 36 479

38 limit 37 to (english or french) 468

39 ("20220325" or "20220326" or "20220327" or "20220328" or "20220329" or 2022033* or 202204* or 202205* or 202206* or 202207* or 202208* or 202209* or 20221* or 2023*).dt,ez,da. 1758970

40 38 and 39 101

https://proxy.library.mcgill.ca/login?url=https://ovidsp.ovid.com/ovidweb.cgi?T=JS&NEWS=N&PAGE=main&SHAREDSEARCHID=6qIRBgjFZ3ZkM7cI3pNxsSdJMR7MGQcZQgr6O0WD59HyRyVne5GewTVzisGFCiLgl

Embase Classic+Embase <1947 to 2023 February 21>

1 (prehab* or pre-hab* or prerehab* or pre-rehab*).ti,ab,kf. 2694

2 ((preoperative* or pre-operative*) adj rehab*).ti,ab,kf. 273

3 1 or 2 2925

4 "randomized controlled trial (topic)"/ 253886

5 Randomized Controlled Trial/ 774446

6 Randomization/ 98516

7 Double Blind Procedure/ 210213

8 single blind procedure/ 50879

9 placebo/ 409933

10 (random allocation or multicenter study or multicentre study or (clinical adj trial*) or ((singl* or doubl* or treb* or tripl*) adj (blind* or mask*)) or placebo* or randomi?ed or randomly).tw,kf. or (trial or groups).ab. 5414028

11 or/4-10 5717085

12 3 and 11 1096

13 12 not (exp meta analysis/ or exp review/ or (case report or meta analysis or scoping review or systematic review).ti. or (conference abstract or conference proceeding or "conference review" or editorial or review).pt.) 507

14 limit 13 to (english or french) 489

15 limit 14 to dc=20220425-20230222 98

https://proxy.library.mcgill.ca/login?url=https://ovidsp.ovid.com/ovidweb.cgi?T=JS&NEWS=N&PAGE=main&SHAREDSEARCHID=1rzD9gqn1RRt0nm877OeXHskcrwHClk2JewF4seIoqFzT497HHmpYfS913xTri3w

APA PsycInfo <1806 to February Week 2 2023>

1 (prehab* or pre-hab* or prerehab* or pre-rehab*).ti,ab. 103

2 ((preoperative* or pre-operative*) adj rehab*).ti,ab. 5

3 1 or 2 107

4 exp randomized controlled trials/ 1385

5 clinical trials/ 12140

6 placebo/ 6418

7 treatment effectiveness evaluation/ 27502

8 exp treatment outcomes/ 135563

9 followup studies/ 12395

10 (random allocation or multicenter study or multicentre study or (clinical adj trial*) or ((singl* or doubl* or treb* or tripl*) adj (blind* or mask*)) or placebo* or randomi?ed or randomly).tw. or (trial or groups).ab. 760814

11 or/4-10 883434

12 3 and 11 40

13 limit 12 to up=20220425-20230222 3

https://proxy.library.mcgill.ca/login?url=https://ovidsp.ovid.com/ovidweb.cgi?T=JS&NEWS=N&PAGE=main&SHAREDSEARCHID=63Nuf1e5XDCNctJaBe7J7uPGgwUjyUztcYttloA1NMolXtAye5WUX1Kdeu8kY6moo

Science Citation Expanded (SCI-EXP), Social Sciences Citation Index (SSCI), Emerging Sources Citation Index (ESCI)

69 records on February 22, 2023

(TI=(("prehab*" or "pre-hab*" or "prerehab*" or "pre-rehab*") OR (("preoperative*" or "pre-operative*") NEAR/0 "rehab*")) OR AB=(("prehab*" or "pre-hab*" or "prerehab*" or "pre-rehab*") OR (("preoperative*" or "pre-operative*") NEAR/0 "rehab*")) OR AK=(("prehab*" or "pre-hab*" or "prerehab*" or "pre-rehab*") OR (("preoperative*" or "pre-operative*") NEAR/0 "rehab*"))) AND (TS=("random allocation" OR "multicenter study" OR "multicentre study" OR (clinical NEAR/0 trial*) OR ((singl* or doubl* or treb* or tripl*) NEAR/0 (blind* or mask*)) OR placebo* OR randomi$ed OR randomly) OR AB=("trial" or "groups"))

Exclude document types: Review Articles or Editorial Materials

| *Timespan: 2022-04-25 to 2023-02-22 (Index Date)*

CINAHL (EBSCOhost)

45 records on February 22, 2023

#	Query	Limiters/Expanders	Last Run Via	Results
S12	S10 AND S11	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Plus with Full Text	45
S11	EM 20220325- OR ZD "in process"	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Plus with Full Text	1,096,719

S10	S8 AND S9	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Plus with Full Text	186
S9	LA English OR French	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Plus with Full Text	8,425,119
S8	S7 NOT (S5 OR S6)	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Plus with Full Text	188
S7	S3 AND S4	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Plus with Full Text	229
S6	PT TI case report OR meta analysis OR scoping review OR systematic reviewase study" OR "editorial" OR "historical material" OR "meta analysis" OR "meta synthesis" OR "review" OR "systematic review"	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Plus with Full Text	121,752
S5	PT "case study" OR "editorial" OR "historical material" OR "meta analysis" OR "meta synthesis" OR "review" OR "systematic review"	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Plus with Full Text	1,330,836
S4	(randomized controlled trials OR MH double-blind studies OR MH single-blind studies OR MH random assignment OR MH pretest-posttest design OR MH cluster sample OR TI (randomised OR	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Plus with Full Text	956,872

	randomized) OR AB (random*) OR TI (trial) OR (MH (sample size) AND AB (assigned OR allocated OR control)) OR MH (placebos) OR PT (randomized controlled trial) OR AB (control W5 group) OR MH (crossover design) OR MH (comparative studies) OR AB (cluster W3 RCT)) NOT ((MH animals+ OR MH animal studies OR TI animal model*) NOT MH human)			
S3	S1 OR S2	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Plus with Full Text	942
S2	((preoperative* OR pre-operative*) W1 rehab*)	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Plus with Full Text	127
S1	(prehab* OR pre-hab* OR prerehab* OR pre-rehab*)	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Plus with Full Text	841

CENTRAL (Cochrane Library/Wiley)

119 results on February 22, 2023

Date Run: 22/02/2023 19:56:38

ID Search Hits

#1 (prehab* or pre next hab* or prerehab* or pre next rehab* or ((preoperative* or pre-operative*) next rehab*)):ti,ab,kw in Trials 679

Filter your results

Date added to CENTRAL database: 22/04/2022 – 22/02/2023

APPENDIX 2 Full text review

Full text review initial serach (March 2022):

1. Allen S, Brown V, Prabhu P, Rockall T, Preston S, Sultan J. Effect of prehabilitation on fitness in patients undergoing neoadjuvant treatment and oesophagogastric cancer surgery: a randomised controlled trial. Diseases of the esophagus. 2018;31:172-. **EXCLUDED – Wrong population**
2. An J, Ryu HK, Lyu SJ, Yi HJ, Lee BH. Effects of Preoperative Telerehabilitation on Muscle Strength, Range of Motion, and Functional Outcomes in Candidates for Total Knee Arthroplasty: A Single-Blind Randomized Controlled Trial. International Journal of Environmental Research & Public Health [Electronic Resource].18(11):04. **STUDY 1**
3. Argunova Y, Belik E, Gruzdeva O, Ivanov S, Pomeshkina S, Barbarash O. Effects of physical prehabilitation on the dynamics of the markers of endothelial function in patients undergoing elective coronary bypass surgery. Journal of Personalized Medicine. 2022;12(3):471. **STUDY 2**
4. Argunova YA, Zvereva TN, Pomeshkina SA, Ivanova AV, Polikutina OM, Gruzdeva OV, et al. Optimization of a Comprehensive Prehabilitation Program for Patients with Stable Coronary Artery Disease Undergoing Elective Coronary Artery Bypass Grafting. Rational Pharmacotherapy in Cardiology. 2020;16(4):508-15. **EXCLUDED – Wrong language**
5. Ausania F, Senra P, Melendez R, Caballeiro R, Ouvina R, Casal-Nunez E. Prehabilitation in patients undergoing pancreaticoduodenectomy: a randomized controlled trial. Revista Espanola de Enfermedades Digestivas. 2019;111(8):603-8. **STUDY 3**
6. Awasthi R, Minnella EM, Ferreira V, Ramanakumar AV, Scheede-Bergdahl C, Carli F. Supervised exercise training with multimodal pre-habilitation leads to earlier functional recovery following colorectal cancer resection. Acta Anaesthesiologica Scandinavica. 2019;63(4):461-7. **EXCLUDED – Wrong study design**
7. Banerjee S, Manley K, Shaw B, Kumar V, Ho ETS, Rochester M, et al. 'Prehabilitation' of patients undergoing radical cystectomy to assist recovery: results of a feasibility study. European urology, supplements. 2015;14(2):e444-. **EXCLUDED – Wrong publication type**
8. Banerjee S, Manley K, Thomas L, Shaw B, Saxton J, Mills R, et al. Preoperative exercise protocol to aid recovery of radical cystectomy: results of a feasibility study. European urology, supplements. 2013;12(6):125-6. **EXCLUDED – Wrong publication type**
9. Barassi G, Bellomo RG, Di Iulio A, Lococo A, Porreca A, Di Felice PA, et al. Preoperative Rehabilitation in Lung Cancer Patients: Yoga Approach. Advances in Experimental Medicine & Biology. 2018;1096:19-29. **EXCLUDED – Wrong population**
10. Barberan-Garcia A, Ubre M, Roca J, Lacy AM, Burgos F, Risco R, et al. Personalised Prehabilitation in High-risk Patients Undergoing Elective Major Abdominal Surgery: A Randomized Blinded Controlled Trial. Annals of Surgery. 2018;267(1):50-6. **STUDY 4**
11. Berkel AEM, Bongers BC, Kotte H, Weltevreden P, de Jongh FHC, Eijsvogel MMM, et al. Effects of Community-based Exercise Prehabilitation for Patients Scheduled for Colorectal Surgery With High Risk for Postoperative Complications: Results of a Randomized Clinical Trial. Annals of Surgery. 2022;275(2):e299-e306. **STUDY 5**
12. Bhatia C, Kayser B. Preoperative high-intensity interval training is effective and safe in deconditioned patients with lung cancer: A randomized clinical trial. Journal of Rehabilitation Medicine. 2019;51(9):712-8. **EXCLUDED – Wrong population**
13. Blackwell J, Boereboom C, Doleman B, Phillips B, Williams J, Lund J. High intensity interval training is a safe and effective way to improve fitness before surgery for cancer: a randomised control trial. British journal of surgery. 2019;106:39-. **EXCLUDED – Wrong publication type**
14. Blackwell JEM, Doleman B, Boereboom CL, Morton A, Williams S, Atherton P, et al. High-intensity interval training produces a significant improvement in fitness in less than 31 days before surgery for urological cancer: a randomised control trial. Prostate Cancer & Prostatic Diseases. 2020;23(4):696-704. **STUDY 6**
15. Bousquet-Dion G, Awasthi R, Loiselle SE, Minnella EM, Agnihotram RV, Bergdahl A, et al. Evaluation of supervised multimodal prehabilitation programme in cancer patients undergoing colorectal resection: a randomized control trial. Acta Oncologica. 2018;57(6):849-59. **STUDY 7**

16. Brosky T, Topp R, Finley M, Killian C, Pariser D, Brown K, et al. Effects of prehabilitation on early rehabilitation outcomes following total knee arthroplasty in patients with knee osteoarthritis. Physiotherapy (united kingdom). 2011;97:eS160. **EXCLUDED – Wrong publication type**
17. Brown K, Loprinzi PD, Brosky JA, Topp R. Prehabilitation influences exercise-related psychological constructs such as self-efficacy and outcome expectations to exercise. Journal of Strength & Conditioning Research. 2013;28(1):201-9. **STUDY 8**
18. Brown K, Topp R, Brosky JA, Lajoie AS. Prehabilitation and quality of life three months after total knee arthroplasty: a pilot study. Perceptual & Motor Skills. 2012;115(3):765-74. **STUDY 9**
19. Bui T, Kasvis P, Vigano A, Metrakos P, Chaudhury P, Barkun J, et al. Impact of a trimodal prehabilitation program on functional recovery after hepatobiliary and pancreatic cancer surgery: preliminary findings from a randomized controlled pilot trial. Supportive care in cancer. 2019;27(1):S240-. **EXCLUDED – Wrong publication type**
20. Calatayud J, Casana J, Ezzatvar Y, Jakobsen MD, Sundstrup E, Andersen LL. High-intensity preoperative training improves physical and functional recovery in the early post-operative periods after total knee arthroplasty: a randomized controlled trial. Knee Surgery, Sports Traumatology, Arthroscopy. 2017;25(9):2864-72. **STUDY 10**
21. Carli F, Bousquet-Dion G, Awasthi R, Elsherbini N, Liberman S, Boutros M, et al. Effect of Multimodal Prehabilitation vs Postoperative Rehabilitation on 30-Day Postoperative Complications for Frail Patients Undergoing Resection of Colorectal Cancer: A Randomized Clinical Trial. JAMA Surgery. 2020;155(3):233-42. **STUDY11**
22. Carli F, Charlebois P, Stein B, Feldman L, Zavorsky G, Kim DJ, et al. Randomized clinical trial of prehabilitation in colorectal surgery. British Journal of Surgery. 2010;97(8):1187-97. **STUDY 12**
23. Cavill S, McKenzie K, Munro A, McKeever J, Whelan L, Biggs L, et al. The effect of prehabilitation on the range of motion and functional outcomes in patients following the total knee or hip arthroplasty: A pilot randomized trial. Physiotherapy Theory & Practice. 2016;32(4):262-70. **STUDY 15**
24. Coca-Martinez M, Vitagliano M, Girsowicz EE, Obr, DI, Steinmetz OK, et al. Multimodal Prehabilitation for Peripheral Arterial Disease: results of an In-Trial Pilot Randomized Controlled Trial. Journal of vascular surgery. 2021;74(5):e426-e7. **EXCLUDED – Wrong publication type**
25. Doiron-Cadrin P, Kairy D, Vendittoli PA, Lowry V, Poitras S, Desmeules F. Feasibility and preliminary effects of a tele-prehabilitation program and an in-person prehablitation program compared to usual care for total hip or knee arthroplasty candidates: a pilot randomized controlled trial. Disability & Rehabilitation. 2020;42(7):989-98. **EXCLUDED – Wrong population**
26. Dunne D, Jones R, Lythgoe D, Malik H, Poston GJ, Jack S, et al. Prehabilitation before liver surgery. European journal of surgical oncology. 2014;40(11):S52-. **EXCLUDED – Wrong publication type**
27. Dunne DF, Jack S, Jones RP, Jones L, Lythgoe DT, Malik HZ, et al. Randomized clinical trial of prehabilitation before planned liver resection. British Journal of Surgery. 2016;103(5):504-12. **STUDY 13**
28. Edwards J, Moug S, Barry S. Does pre-habilitation, in the form of a walking programme, impact upon levels of sarcopenia (low muscle mass) in patients with rectal cancer undergoing neo-adjuvant chemoradiotherapy? Anaesthesia. 2020;75:79-. **EXCLUDED – Wrong publication type**
29. Ferreira V, Lawson C, Carli F, Scheede-Bergdahl C, Chevalier S. Feasibility of a novel mixed-nutrient supplement in a multimodal prehabilitation intervention for lung cancer patients awaiting surgery: A randomized controlled pilot trial. International Journal Of Surgery.93:106079. **STUDY 14**
30. Ferreira V, Minnella EM, Awasthi R, Gamsa A, Ferri L, Mulder D, et al. Multimodal Prehabilitation for Lung Cancer Surgery: A Randomized Controlled Trial. Annals of Thoracic Surgery.112(5):1600-8. **STUDY 16**
31. Fors M, Enthoven P, Abbott A, Oberg B. Effects of pre-surgery physiotherapy on walking ability and lower extremity strength in patients with degenerative lumbar spine disorder: Secondary outcomes of the PREPARE randomised controlled trial. BMC Musculoskeletal Disorders. 2019;20(1):468. **EXCLUDED – Wrong study design**
32. Fulop A, Lakatos L, Susztak N, Szijarto A, Banky B. The effect of trimodal prehabilitation on the physical and psychological health of patients undergoing colorectal surgery: a randomised clinical trial. Anaesthesia. 2021;76(1):82-90. **STUDY 17**
33. Garcia RS, Paz AL, Brage MIY, Moolhuyzen EG, Rioboo MS, Mate JMB. Does preoperative exercise training prevent functional decline after video-assisted thoracic surgery? European respiratory journal. 2016;48. **EXCLUDED – Wrong publication type**
34. Gillis C, Li C, Lee L, Awasthi R, Augustin B, Gamsa A, et al. Prehabilitation versus rehabilitation: a randomized control trial in patients undergoing colorectal resection for cancer. Anesthesiology. 2014;121(5):937-47. **STUDY 18**

35. Gillis C, Loiselle SE, Fiore JF, Jr., Awasthi R, Wykes L, Liberman AS, et al. Prehabilitation with Whey Protein Supplementation on Perioperative Functional Exercise Capacity in Patients Undergoing Colorectal Resection for Cancer: A Pilot Double-Blinded Randomized Placebo-Controlled Trial. Journal of the Academy of Nutrition & Dietetics. 2016;116(5):802-12. **STUDY 19**
36. Giovannini S, Coraci D, Di Caro F, Castelli L, Loreti C, Chicco A, et al. Prehabilitation and heart failure: perspective in primary outcomes, a randomized controlled trial. European Review for Medical & Pharmacological Sciences. 2021;25(21):6684-90. **EXCLUDED – Wrong population**
37. Gloor S, Misirlic M, Frei-Lanter C, Herzog P, Muller P, Schafli-Thurnherr J, et al. Prehabilitation in patients undergoing colorectal surgery fails to confer reduction in overall morbidity: results of a single-center, blinded, randomized controlled trial. Langenbecks Archives of Surgery. 2022:11. **STUDY 20**
38. Granicher P, Stoggl T, Fucentese SF, Adelsberger R, Swanenburg J. Preoperative exercise in patients undergoing total knee arthroplasty: a pilot randomized controlled trial. Archives of Physiotherapy. 2020;10:13. **STUDY 21**
39. Grant LF, Cooper DJ, Conroy JL. The HAPI 'Hip Arthroscopy Pre-habilitation Intervention' study: does pre-habilitation affect outcomes in patients undergoing hip arthroscopy for femoro-acetabular impingement? Journal of Hip Preservation Surgery. 2017;4(1):85-92. **STUDY22**
40. Gravier FE, Smondack P, Boujibar F, Prieur G, Medrinal C, Combret Y, et al. Prehabilitation sessions can be provided more frequently in a shortened regimen with similar or better efficacy in people with non-small cell lung cancer: a randomised trial. Journal of Physiotherapy. 2022;68(1):43-50. **STUDY 23**
41. Huang J, Lai Y, Zhou X, Li S, Su J, Yang M, et al. Short-term high-intensity rehabilitation in radically treated lung cancer: a three-armed randomized controlled trial. Journal of Thoracic Disease. 2017;9(7):1919-29. **STUDY 24**
42. Huang SW, Chen PH, Chou YH. Effects of a preoperative simplified home rehabilitation education program on length of stay of total knee arthroplasty patients. Orthopaedics & traumatology, surgery & research. 2012;98(3):259-64. **STUDY 25**
43. Humeidan ML, Reyes JC, Mavarez-Martinez A, Roeth C, Nguyen CM, Sheridan E, et al. Effect of Cognitive Prehabilitation on the Incidence of Postoperative Delirium Among Older Adults Undergoing Major Noncardiac Surgery: The Neurobics Randomized Clinical Trial. JAMA Surgery. 2021;156(2):148-56. **STUDY 26**
44. Jahic D, Omerovic D, Tanovic AT, Dzankovic F, Campara MT. The Effect of Prehabilitation on Postoperative Outcome in Patients Following Primary Total Knee Arthroplasty. Medicinski Arhiv. 2018;72(6):439-43. **STUDY 27**
45. Jensen BT, Jensen JB, Borre M, Laustsen S, Petersen AK. Physical prehabilitation is feasible and effective in patients with advanced bladder cancer. Cancer nursing Conference: international conference on cancer nursing, ICCN 2015 vancouver, BC canada Conference start: 20150708 conference end: 20150711 Conference publication: (varpagings). 2015;38(4):S5. **EXCLUDED – Wrong publication type**
46. Jensen BT, Borre M, Borre M, Soendergaard I, Jensen JB. One year follow up of the efficacy of physical prehabilitation in radical cystectomy pathways-secondary results from a randomized controlled trial. European urology, supplements. 2018;17(2):e1556-. **EXCLUDED – Wrong publication type**
47. Jensen BT, Laustsen S, Jensen JB, Borre M, Petersen AK. Exercise-based prehabilitation is feasible and effective in radical cystectomy pathways-secondary results from a randomized controlled trial. Journal of urology. 2016;195(4):e652-. **EXCLUDED – Wrong publication type**
48. Jensen BT. Physical prehabilitation in RC pathways session: maximising potential. Asia-pacific journal of clinical oncology. 2017;13:34-. **EXCLUDED – Wrong publication type**
49. Jensen BT, Petersen AK, Jensen JB, Laustsen S, Borre M. Efficacy of a multiprofessional rehabilitation programme in radical cystectomy pathways: a prospective randomized controlled trial. Scandinavian Journal of Urology. 2015;49(2):133-41. **STUDY 28**
50. Jensen BTJ, Krintel Petersen AKP, Jensen JB, Laustsen SL, Borre MB. Efficacy of an exercise-based rehabilitation programme in radical cystectomy pathways: a randomised controlled trial. European urology, supplements. 2014;13(1):e219-. **EXCLUDED – Wrong publication type**
51. Karenovics W, Licker M, Christodoulou M, Diaper J, Bhatia C, Bridevaux P, et al. Does short-term preoperative exercise therapy influence longterm lung functional outcome following lung cancer surgery? Interactive cardiovascular and thoracic surgery. 2016;23:i2-. **EXCLUDED – Wrong publication type**
52. Karenovics W, Licker M, Ellenberger C, Christodoulou M, Diaper J, Bhatia C, et al. Short-term preoperative exercise therapy does not improve long-term outcome after lung cancer surgery: a randomized controlled study. European Journal of Cardio-Thoracic Surgery. 2017;52(1):47-54. **EXCLUDED duplicate – Long term outcome of study of Licker et al (no.61)**

53. Kassouf W, Minnella E, Awasthi R, Ferreira V, Aprikian A, Tanguay S, et al. Prehabilitation for patients undergoing cystectomy: preliminary analysis of a single-center, randomized controlled trial. Journal of urology. 2018;199(4):e622-. **EXCLUDED – Wrong publication type**
54. Kasvis P, Bui T, Kilgour R, Carli F, Vigano A. A multimodal prehabilitation program in hepato-pancreato-biliary cancer patients awaiting surgery: preliminary results. Supportive care in cancer. 2018:S392. **EXCLUDED – Wrong publication type**
55. Kate V, Kundra P, Swaminathan N. ENHANCED RECOVERY AFTER SURGERY WITH RESPIRATORY PREHABILITATION VERSUS CONVENTIONAL PERIOPERATIVE PROTOCOL IN PATIENTS UNDERGOING ELECTIVE GASTRECTOMY– A RANDOMIZED CONTROLLED TRIAL. Gastroenterology. 2020;158(6):S-1557-S-8. **EXCLUDED – Wrong publication type**
56. Kim DJ, Mayo NE, Carli F, Montgomery DL, Zavorsky GS. Responsive measures to prehabilitation in patients undergoing bowel resection surgery. Tohoku Journal of Experimental Medicine. 2009;217(2):109-15. **STUDY 29**
57. Kim S, Hsu FC, Groban L, Williamson J, Messier S. A pilot study of aquatic prehabilitation in adults with knee osteoarthritis undergoing total knee arthroplasty - short term outcome. BMC Musculoskeletal Disorders. 2021;22(1):388. **STUDY 30**
58. Lai Y, Huang J, Yang M, Su J, Liu J, Che G. Seven-day intensive preoperative rehabilitation for elderly patients with lung cancer: a randomized controlled trial. Journal of Surgical Research. 2017;209:30-6. **STUDY 31**
59. Lawson C, Ferreira V, Carli F, Chevalier S. Effects of multimodal prehabilitation on muscle size, myosteatosis, and dietary intake of surgical patients with lung cancer - a randomized feasibility study. Applied Physiology, Nutrition, & Metabolism = Physiologie Appliquee, Nutrition et Metabolisme. 2021;46(11):1407-16. **EXCLUDED – Wrong population**
60. Liang MK, Bernardi K, Holihan JL, Cherla DV, Escamilla R, Lew DF, et al. Modifying Risks in Ventral Hernia Patients With Prehabilitation: A Randomized Controlled Trial. Annals of Surgery. 2018;268(4):674-80. **STUDY 33**
61. Licker M, Karenovics W, Diaper J, Fresard I, Triponez F, Ellenberger C, et al. Short-Term Preoperative High-Intensity Interval Training in Patients Awaiting Lung Cancer Surgery: A Randomized Controlled Trial. Journal of Thoracic Oncology: Official Publication of the International Association for the Study of Lung Cancer. 2017;12(2):323-33. **STUDY 34**
62. Ligibel JA, Dillon D, Giobbie-Hurder A, McTiernan A, Frank E, Cornwell M, et al. Impact of a Pre-Operative Exercise Intervention on Breast Cancer Proliferation and Gene Expression: Results from the Pre-Operative Health and Body (PreHAB) Study. Clinical Cancer Research. 2019;25(17):5398-406. **EXCLUDED – Wrong population**
63. Ligibel JA, Giobbie-Hurder A, Dillion D, Shockro L, Campbell N, Rhei E, et al. Impact of pre-operative exercise and mind-body interventions on patient-reported outcomes in women with newly diagnosed breast cancer. Cancer research. 2017;77(4). **EXCLUDED – Wrong publication type**
64. Ligibel JA, Giobbie-Hurder A, Shockro L, Rhei E, Troyan S, Dominici LS, et al. Impact of a pre-operative exercise intervention on Ki-67 and metabolic markers in women with early breast cancer. Journal of clinical oncology. 2016;34. **EXCLUDED – Wrong publication type**
65. Lindback Y, Tropp H, Enthoven P, Abbott A, Oberg B. PREPARE: presurgery physiotherapy for patients with degenerative lumbar spine disorder: a randomized controlled trial. Spine Journal: Official Journal of the North American Spine Society. 2018;18(8):1347-55. **STUDY 35**
66. Liu Z, Qiu T, Pei L, Zhang Y, Xu L, Cui Y, et al. Two-week multimodal prehabilitation program improves perioperative functional capability in patients undergoing thoracoscopic lobectomy for lung cancer: a randomized controlled trial. Anesthesia & Analgesia. 2020;131(3):840-9. **STUDY 36**
67. López-Rodríguez-Arias F, Sánchez-Guillén L, Aranaz-Ostáriz V, Triguero-Cánovas D, Lario-Pérez S, Barber-Valles X, et al. Effect of home-based prehabilitation in an enhanced recovery after surgery program for patients undergoing colorectal cancer surgery during the COVID-19 pandemic. Supportive Care in Cancer. 2021;29(12):7785-91. **STUDY 37**
68. Lotzke H, Brisby H, Gutke A, Hägg O, Jakobsson M, Smeets R, et al. A person-centered prehabilitation program based on cognitive-behavioral physical therapy for patients scheduled for lumbar fusion surgery: a randomized controlled trial. Physical therapy. 2019;99(8):1069-88. **STUDY 38**
69. Marchand A-A, Houle M, O'Shaughnessy J, Châtillon C-É, Cantin V, Descarreaux M. Effectiveness of an exercise-based prehabilitation program for patients awaiting surgery for lumbar spinal stenosis: a randomized clinical trial. Scientific reports. 2021;11(1):11080. **STUDY 39**

70. Marchand AA, Suitner M, O'Shaughnessy J, Chatillon CE, Cantin V, Descarreaux M. Feasibility of conducting an active exercise prehabilitation program in patients awaiting spinal stenosis surgery: a randomized pilot study. Scientific Reports. 2019;9(1):12257. **EXCLUDED – Duplicate Data used for STUDY 39**
71. Eil MSM, Sharifudin MA, Shokri AA, Ab Rahman S. Preoperative physiotherapy and short-term functional outcomes of primary total knee arthroplasty. Singapore medical journal. 2016;57(3):138. **STUDY 40**
72. Matassi F, Duerinckx J, enneucker H, Bellemans J. Range of motion after total knee arthroplasty: the effect of a preoperative home exercise program. Knee Surgery Sports Traumatology Arthroscopy. 2014;22(3):703-9. **STUDY 41**
73. McHugh G. The role of perhabilitation on the outcome of total knee arthroplasty: A randomized control trial: University College Dublin (Ireland); 2011. **EXCLUDED – Wrong publication type**
74. McKay C, Prapavessis H, Doherty T. The effect of a prehabilitation exercise program on quadriceps strength for patients undergoing total knee arthroplasty: a randomized controlled pilot study. PM&R. 2012;4(9):647-56. **STUDY 42**
75. Minnella EM, Awasthi R, Bousquet-Dion G, Ferreira V, Austin B, Audi C, et al. Multimodal prehabilitation to enhance functional capacity following radical cystectomy: a randomized controlled trial. European Urology Focus. 2021;7(1):132-8. **STUDY 43**
76. Minnella EM, Awasthi R, Loiselle SE, Agnihotram RV, Ferri LE, Carli F. Effect of Exercise and Nutrition Prehabilitation on Functional Capacity in Esophagogastric Cancer Surgery: A Randomized Clinical Trial. JAMA Surgery. 2018;153(12):1081-9. **STUDY 44**
77. Minnella EM, Awasthi R, Loiselle SE, Ramanakuma A, Ferri L, Carli F. Prehabilitation improves functional capacity in esophago-gastric cancer surgery: a randomized control trial. Canadian journal of anesthesia. 2018;65(1):S91-S2. **EXCLUDED – Wrong publication type**
78. Minnella EM, Ferreira V, Awasthi R, Charlebois P, Stein B, Liberman AS, et al. Effect of two different pre-operative exercise training regimens before colorectal surgery on functional capacity: A randomised controlled trial. European Journal of Anaesthesiology. 2020;37(11):969-78. **STUDY 45**
79. Morano MT, Araújo A, S. a, Nascimento FB, da Silva GF, Mesquita R, et al. Preoperative Pulmonary Rehabilitation Versus Chest Physical Therapy in Patients Undergoing Lung Cancer Resection: A Pilot Randomized Controlled Trial. Archives of Physical Medicine & Rehabilitation. 2013;94(1):53-8. **STUDY 46**
80. Moug S, Mutrie N, Barry S, Mackay G, Steele R, Boachie C, et al. Prehabilitation is feasible during neoadjuvant chemoradiotherapy and may minimize physical deterioration: results from the REx randomised controlled trial. British journal of cancer Conference: 2018 national cancer research institute cancer conference, NCRI 2018 United kingdom. 2018;119(1):47. **EXCLUDED – Wrong publication type**
81. Moug S, Rooney L, Mackay G, Barry S, Buchan C, Steele R, et al. Initial findings of the REx Trial: a study of the feasibility of performing pre-habilitation in patients undergoing treatment for rectal cancer. Colorectal disease. 2016;18:75-. **EXCLUDED – Wrong publication type**
82. Nguyen C, Boutron I, Roren A, Anract P, Beaudreuil J, Biau D, et al. Effect of Prehabilitation Before Total Knee Replacement for Knee Osteoarthritis on Functional Outcomes: A Randomized Clinical Trial. JAMA Network Open. 2022;5(3):e221462. **STUDY 47**
83. Nielsen PR, Jorgensen LD, Dahl B, Pedersen T, Tonnesen H. Prehabilitation and early rehabilitation after spinal surgery: randomized clinical trial. Clinical Rehabilitation. 2010;24(2):137-48. **STUDY 48**
84. Northgraves MJ, Arunachalam L, Madden LA, Marshall P, Hartley JE, MacFie J, et al. Feasibility of a novel exercise prehabilitation programme in patients scheduled for elective colorectal surgery: a feasibility randomised controlled trial. Supportive Care in Cancer. 2020;28(7):3197-206. **STUDY 49**
85. O'Gara BP, Mueller A, Gasangwa DVI, Patxot M, Shaefi S, Khabbaz K, et al. Prevention of Early Postoperative Decline: A Randomized, Controlled Feasibility Trial of Perioperative Cognitive Training. Anesthesia & Analgesia. 2020;130(3):586-95. **STUDY 50**
86. Onerup A, Andersson J, Angenete E, Bock D, Borjesson M, Ehrencrona C, et al. Effect of Short-term Homebased Pre- and Postoperative Exercise on Recovery after Colorectal Cancer Surgery (PHYSSURG-C): A Randomized Clinical Trial. Annals of Surgery. 2022;275:448-55. **STUDY 51**
87. Peng LH, Wang WJ, Chen J, Jin JY, Min S, Qin PP. Implementation of the pre-operative rehabilitation recovery protocol and its effect on the quality of recovery after colorectal surgeries. Chinese Medical Journal. 2021;134(23):2865-73. **STUDY 52**
88. Rengel KF, Mehdiratta N, Vanston SW, Archer KR, Jackson JC, Thompson JL, et al. A randomised pilot trial of combined cognitive and physical exercise prehabilitation to improve outcomes in surgical patients. British Journal of Anaesthesia. 2021;126(2):e55-e7. **EXCLUDED – Wrong publication type**

89. Reynolds SG, Baima J, Woo L, Waugh D, Sooy J, Larkin A, et al. Prehabilitation for shoulder dysfunction in breast cancer: a pilot study. PM and r. 2015;7(9):S179-S80. **EXCLUDED – Wrong publication type**
90. Santa Mina D, Hilton WJ, Matthew AG, Awasthi R, Bousquet-Dion G, Alibhai SMH, et al. Prehabilitation for radical prostatectomy: A multicentre randomized controlled trial. Surgical Oncology. 2018;27(2):289-98. **STUDY 53**
91. Satoto HH, Paramitha A, Barata SH, Sugiri, Suhartono, Wahyudati S, et al. Effect of preoperative inspiratory muscle training on right ventricular systolic function in patients after heart valve replacement surgery. Bali Medical Journal. 2021;10(1):340-6. **STUDY 55**
92. Sawatzky JA, Kehler DS, Ready AE, Lerner N, Boreskie S, Lamont D, et al. Prehabilitation program for elective coronary artery bypass graft surgery patients: a pilot randomized controlled study. Clinical Rehabilitation. 2014;28(7):648-57. **STUDY 56**
93. Sebio Garcia R, Yanez-Brage MI, Gimenez Moolhuyzen E, Salorio Riobo M, Lista Paz A, Borro Mate JM. Preoperative exercise training prevents functional decline after lung resection surgery: a randomized, single-blind controlled trial. Clinical Rehabilitation. 2017;31(8):1057-67. **STUDY 57**
94. Sell NM, Silver JK, o S, Draviam AC, Mina DS, Qadan M. Prehabilitation Telemedicine in Neoadjuvant Surgical Oncology Patients During the Novel COVID-19 Coronavirus Pandemic. Annals of Surgery. 2020;272(2):e81-e3. **EXCLUDED – Wrong publication type**
95. Shaarani SR, O'Hare C, Quinn A, Moyna N, Moran R, O'Byrne JM. Effect of prehabilitation on the outcome of anterior cruciate ligament reconstruction. American Journal of Sports Medicine. 2013;41(9):2117-27. **STUDY 58**
96. Sifuentes AMM, Flores DS, Villegas LH. Effect of pre-habilitation on quality of life and postoperative fatigue syndrome in Medico Nacional- Leon, IMSS de Leon, Guanajuato. Revista hispanoamericana de hernia. 2018;6(1):11-6. **EXCLUDED – Wrong language**
97. Steinmetz C, Bjarnason-Wehrens B, Baumgarten H, Walther T, Mengden T, Walther C. Prehabilitation in patients awaiting elective coronary artery bypass graft surgery - effects on functional capacity and quality of life: a randomized controlled trial. Clinical Rehabilitation. 2020;34(10):1256-67. **STUDY 59**
98. Swaminathan N, Kundra P, Ravi R, Kate V. ERAS protocol with respiratory prehabilitation versus conventional perioperative protocol in elective gastrectomy- a randomized controlled trial. International Journal Of Surgery. 2020;81:149-57. **EXCLUDED – Wrong study design**
99. Swank AM, Kachelman JB, Bibeau W, Quesada PM, Nyl, J, et al. Prehabilitation before total knee arthroplasty increases strength and function in older adults with severe osteoarthritis. Journal of Strength & Conditioning Research. 2011;25(2):318-25. **EXCLUDED – Wrong population**
100. Tenconi S, Galeone C, Fugazzaro S, Rapicetta C, Piro R, Formisano D. Perioperative and long-term effects of comprehensive pulmonary rehabilitation on exercise capacity, postoperative outcome and quality of life in patients undergoing lung resection: a randomized controlled trial granted by the ministry of health. Interactive cardiovascular and thoracic surgery. 2017;25:i25-. **EXCLUDED – Wrong publication type**
101. Tenconi S, Mainini C, Rapicetta C, Braglia L, Galeone C, Cavuto S, et al. Rehabilitation for lung cancer patients undergoing surgery: results of the PUREAIR randomized trial. European Journal of Physical and Rehabilitation Medicine. 2021;57(6):1002-11. **STUDY 54**
102. Topp R, Swank AM, Quesada PM, Nyl, J, Malkani A. The effect of prehabilitation exercise on strength and functioning after total knee arthroplasty. Pm & R. 2009;1(8):729-35. **STUDY 60**
103. Vagvolgyi A, Rozgonyi Z, Kerti M, Agathou G, Vadasz P, Varga J. Effectiveness of pulmonary rehabilitation and correlations in between functional parameters, extent of thoracic surgery and severity of post-operative complications: randomized clinical trial. Journal of Thoracic Disease. 2018;10(6):3519-31. **STUDY 61**
104. van Noort HHJ, Witteman BJM, Vermeulen H, Huisman-de Waal G, Hamers JPH. An outpatient nursing nutritional intervention to prehabilitate undernourished patients planned for surgery: a multicentre, cluster-randomised pilot study. Clinical nutrition (Edinburgh, Scotland). 2019. **EXCLUDED – Wrong publication type**
105. VE IJ-H, Wanten GJA, de Nes LCF, van den Berg MGA. Effect of a Preoperative Home-Delivered, Protein-Rich Meal Service to Improve Protein Intake in Surgical Patients: A Randomized Controlled Trial. Jpen: Journal of Parenteral & Enteral Nutrition. 2020;45(3):479-89. **STUDY 62**
106. Vlisides PE, Das AR, Thompson AM, Kunkler B, Zierau M, Cantley MJ, et al. Home-based Cognitive Prehabilitation in Older Surgical Patients: A Feasibility Study. Journal of Neurosurgical Anesthesiology. 2019;31(2):212-7. **EXCLUDED – Wrong study design (intervention <7days)**
107. Waller E, Rahman S, Sutton P, Allen J, Saxton J, Aziz O. Randomised controlled trial of patients undergoing prehabilitation with wearables versus standard of care before major abdominal cancer surgery (Trial Registration: NCT04047524). Colorectal disease. 2020;22:7-. **STUDY 63**

108. Waller E, Sutton P, Rahman S, Allen J, Saxton J, Aziz O. Prehabilitation with wearables versus standard of care before major abdominal cancer surgery: a randomised controlled pilot study (trial registration: NCT04047524). Surgical Endoscopy. 2021;36(2):1008-17. **EXCLUDED – Duplicate of 63**
109. Wang X, Che G, Liu L. A short-term high-intensive pattern of preoperative rehabilitation better suits surgical lung cancer patients. Interactive cardiovascular and thoracic surgery. 2017;25:i11-. **STUDY 64**
110. Weerasinghe K, Rishard M, Brabaharan S, Mohamed A. Effectiveness of face-to-face physiotherapy training and education for women who are undergoing elective caesarean section: a randomized controlled trial. Archives of Physiotherapy. 2022;12(1):4. **EXCLUDED – Wrong study design (intervention <7days)**

111. West MA, Loughney L, Lythgoe D, Barben CP, Sripadam R, Kemp GJ, et al. Effect of prehabilitation on objectively measured physical fitness after neoadjuvant treatment in preoperative rectal cancer patients: a blinded interventional pilot study. British Journal of Anaesthesia. 2015;114(2):244-51. **EXCLUDED – Wrong study design**
112. Woodfield JC, Clifford K, Wilson GA, Munro F, Baldi JC. Short-term high-intensity interval training improves fitness before surgery: A randomized clinical trial. Scandinavian Journal of Medicine & Science in Sports. 2022;28:28. **STUDY 65**
113. Yamana I, Takeno S, Hashimoto T, Maki K, Shibata R, Shiwaku H, et al. Randomized Controlled Study to Evaluate the Efficacy of a Preoperative Respiratory Rehabilitation Program to Prevent Postoperative Pulmonary Complications after Esophagectomy. Digestive Surgery. 2015;32(5):331-7. **STUDY 66**
114. Yau KWD, Underwood M, Joynt G, Lee A. Exercise prehabilitation (Prequel) for patients undergoing cardiac surgery: preliminary results. Anesthesia and analgesia. 2021;133(3):1485-6. **EXCLUDED – Wrong publication type**
115. Argunova Y, Pomeshkina SA, Kokov AN, Barbarash OL. Cardioprotective effects of exercise trainings prior to coronary artery bypass grafting. European journal of preventive cardiology. 2019;26:S37-. **EXCLUDED – Wrong publication type**
116. Argunova Y, Pomeshkina SA, Moskin EG, Sogoyan N, Barbarash OL. Effects of prehabilitation program on quality of life and adherence to therapy in patients undergoing coronary artery bypass grafting. European journal of preventive cardiology. 2019;26:S35-. **EXCLUDED – Wrong publication type**
117. Zheng Y, Huang Z, Dai L, Liu Y, Chen Y, Zhang W, et al. The Effect of Preoperative Rehabilitation Training on the Early Recovery of Joint Function after Artificial Total Knee Arthroplasty and Its Effect Evaluation. Journal of Healthcare Engineering. 2022;2022:3860991. **EXCLUDED – Wrong study design Unable to identify duration of prehab**

Full text review updated search (Februay 2023):

118. Argunova Y, Belik E, Gruzdeva O, Ivanov S, Pomeshkina S, Barbarash O. Effects of physical prehabilitation on the dynamics of the markers of endothelial function in patients undergoing elective coronary bypass surgery. Journal of Personalized Medicine. 2022;12(3):471. **EXCLUDED – Duplicate of STUDY 2**
119. Ausania F, Senra P, Melendez R, Caballeiro R, Ouvina R, Casal-Nunez E. Prehabilitation in patients undergoing pancreaticoduodenectomy: a randomized controlled trial. Revista Espanola de Enfermedades Digestivas. 2019;111(8):603-8. **EXCLUDED – Duplicate of STUDY 3**
120. Berkel AEM, Bongers BC, Kotte H, Weltevreden P, de Jongh FHC, Eijsvogel MMM, et al. Effects of Community-based Exercise Prehabilitation for Patients Scheduled for Colorectal Surgery With High Risk for Postoperative Complications: Results of a Randomized Clinical Trial. Annals of Surgery. 2022;275(2):e299-e306. **EXCLUDED – Duplicate of STUDY 5**
121. Chmelo J, Phillips AW, Greystoke A, Charman SJ, Avery L, Hallsworth K, et al. A feasibility trial of prehabilitation before oesophagogastric cancer surgery using a multi-component home-based exercise programme: the ChemoFit study. Pilot and Feasibility Studies. 2022;8(1):173. **EXCLUDED – Wrong study design**
122. Czech O, Siewierska K, Krzywińska A, Skórniak J, Maciejczyk A, Matkowski R, et al. Virtual Therapy Complementary Prehabilitation of Women Diagnosed with Breast Cancer—A Pilot Study. International Journal of Environmental Research and Public Health. 2022;20(1):722. **EXCLUDED – Wrong population**
123. de Almeida LL, Júnior AFM, da Mota Neto J, De Simoni LF, Lopes KHS, Guimarães PC, et al. Pre-Operative Scapular Rehabilitation for Arthroscopic Repair of Traumatic Rotator Cuff Tear: Results of a Randomized Clinical Trial. International Journal of Sports Physical Therapy. 2021;16(1):216. . **EXCLUDED – Wrong population**

124. Furon Y, Dang Van S, Blanchard S, Saulnier P, Baufreton C. Effects of high-intensity inspiratory muscle training on systemic inflammatory response in cardiac surgery-A randomized clinical trial. Physiotherapy Theory and Practice. 2023:1-11. **STUDY 71**
125. Franz A, Ji S, Bittersohl B, Zilkens C, Behringer M. Impact of a Six-Week Prehabilitation With Blood-Flow Restriction Training on Pre-and Postoperative Skeletal Muscle Mass and Strength in Patients Receiving Primary Total Knee Arthroplasty. Frontiers in Physiology. 2022:1057. **STUDY 72**
126. Giovannini S, Coraci D, Di Caro F, Castelli L, Loreti C, Chicco A, et al. Prehabilitation and heart failure: perspective in primary outcomes, a randomized controlled trial. European Review for Medical & Pharmacological Sciences. 2021;25(21):6684-90. **EXCLUDED – Wrong population**
127. Gloor S, Misirlic M, Frei-Lanter C, Herzog P, Muller P, Schafli-Thurnherr J, et al. Prehabilitation in patients undergoing colorectal surgery fails to confer reduction in overall morbidity: results of a single-center, blinded, randomized controlled trial. Langenbecks Archives of Surgery. 2022:11. **EXCLUDED – Duplicate of STUDY 20**
128. Haque A, Wisely N, McCollum C. Editor's Choice–The Abdominal Aortic Aneurysm Get Fit Trial: A Randomised Controlled Trial of Exercise to Improve Fitness in Patients with Abdominal Aortic Aneurysm. European Journal of Vascular and Endovascular Surgery. 2022;64(4):309-19. **EXCLUDED – Wrong population**
129. Heiman J, Onerup A, Wessman C, Haglind E, Olofsson Bagge R. Recovery after breast cancer surgery following recommended pre and postoperative physical activity:(PhysSURG-B) randomized clinical trial. British Journal of Surgery. 2021;108(1):32-9. **STUDY 73**
130. Ho C-J, Chen Y-T, Wu H-L, Huang H-T, Lin S-Y. The Effects of a Patient-Specific Integrated Education Program on Pain, Perioperative Anxiety, and Functional Recovery following Total Knee Replacement. Journal of Personalized Medicine. 2022;12(5):719. . **EXCLUDED – Wrong intervention type**
132. Juszczak A, Konecki T, Kutwin P, Roman Ł, Cichocki M, Jabłonowski Z. PD27-11 PREREHABILITATION CAN IMPROVE URINARY CONTINENCE IN PATIENTS AFTER LAPAROSCOPIC RADICAL PROSTATECTOMY. The Journal of Urology. 2022;207(Supplement 5):e497. **EXCLUDED – Wrong publication type**
133. Kasvis PV, A.; Bui, T.; Kim, H.; Hachem, Y.; Kilgour, R. D. IMPACT OF CANCER SYMPTOM BURDEN ON QUALITY OF LIFE IN PATIENTS UNDERGOING PREHABILITATION FOR LIVER RESECTION: RESULTS FROM A 12-WEEK RCT, Abstracts for MASCC/ISOO Annual Meeting 2022. Supportive Care in Cancer. 2022;30(1):1-207. **EXCLUDED – Wrong publication type**
134. Koç MA, Akyol C, Gökmen D, Aydın D, Erkek BA, Kuzu MA. Effect of prehabilitation on stoma self-care, anxiety, depression and quality of life in stoma patients: a randomized controlled trial. Diseases of the Colon & Rectum. 2022. **EXCLUDED – Wrong intervention type**
135. Kim S, Hsu FC, Groban L, Williamson J, Messier S. A pilot study of aquatic prehabilitation in adults with knee osteoarthritis undergoing total knee arthroplasty - short term outcome. BMC Musculoskeletal Disorders. 2021;22(1):388. **EXCLUDED – Duplicate of STUDY 30**
136. Labuschagne R, Roos R. Pre-operative physiotherapy for elderly patients undergoing abdominal surgery. South African Journal of Physiotherapy. 2022;78(1):9. **EXCLUDED – Wrong intervention type**
137. Ma X, Zhang Z, Peng M, Yao B, Jiang H, Ji X, et al. Face-to-Face Mentoring, Remotely Supervised Home Exercise Prehabilitation to Improve Physical Function in Patients Awaiting Kidney Transplantation: A Randomized Clinical Trial. Frontiers in Psychology. 2022;13. **EXCLUDED – Wrong population**
138. McIsaac DI, Hladkowicz E, Bryson GL, Forster AJ, Gagne S, Huang A, et al. Home-based prehabilitation with exercise to improve postoperative recovery for older adults with frailty having cancer surgery: the PREHAB randomised clinical trial. British Journal of Anaesthesia. 2022. **EXCLUDED – Duplicate of STUDY 32**
139. Milios JE, Ackland TR, Green DJ. Pelvic floor muscle training in radical prostatectomy: a randomized controlled trial of the impacts on pelvic floor muscle function and urinary incontinence. BMC urology. 2019;19(1):1-10. **STUDY 74**
140. Minnella EM, Awasthi R, Bousquet-Dion G, Ferreira V, Austin B, Audi C, et al. Multimodal prehabilitation to enhance functional capacity following radical cystectomy: a randomized controlled trial. European Urology Focus. 2021;7(1):132-8. **EXCLUDED – Duplicate of STUDY 43**
141. Nguyen C, Boutron I, Roren A, Anract P, Beaudreuil J, Biau D, et al. Effect of Prehabilitation Before Total Knee Replacement for Knee Osteoarthritis on Functional Outcomes: A Randomized Clinical Trial. JAMA Network Open. 2022;5(3):e221462. **EXCLUDED – Duplicate of STUDY 47**
142. Nowosielski K, Zębalski M, Szostek P, Szanecki W. 2022-RA-732-ESGO Prehabilitation program in ovarian cancer patients–towards more objective measurement of compliance–preliminary results. BMJ Specialist Journals; 2022. **EXCLUDED – Wrong publication type**

143. Onerup A, Andersson J, Angenete E, Bock D, Borjesson M, Ehrencrona C, et al. Effect of Short-term Homebased Pre- and Postoperative Exercise on Recovery after Colorectal Cancer Surgery (PHYSSURG-C): A Randomized Clinical Trial. Annals of Surgery. 2022;275:448-55. **EXCLUDED – Duplicate of STUDY 51**
144. Risso AM, van der Linden ML, Bailey A, Gallacher P, Gleeson N. Exploratory insights into novel prehabilitative neuromuscular exercise-conditioning in total knee arthroplasty. BMC Musculoskeletal Disorders. 2022;23(1):1-11. **EXCLUDED – Wrong population**
145. Rampam S, Sadiq H, Patel J, Meyer D, Uy K, Yates J, et al. Supervised preoperative walking on increasing early postoperative stamina and mobility in older adults with frailty traits: a pilot and feasibility study. Health Science Reports. 2022;5(4):e738. **STUDY 75**
146. Satoto HHP, A.; Baratha, S. H.; Sugiri; Wahyudati, S.; Sofia, S. N;. Right ventricular function, mechanical ventilation duration, and icu length of stay in heart valve surgery patients underwent preoperative inspiratory muscle training. Journal of the hong kong college of cardiology. 2020;28(2):82. **EXCLUDED – Wrong publication type**
147. Soler-Silva A SGL, Triguero D, Sanchis-Lopez A, Lario-Perez S, Lillo C, Lopez-Rodriguez Arias F, Sanchez-Guillen L, Oller I, Aranaz V, Alcaide MJ, Arroyo A. Abstracts from the 29th International Congress of the European Association for Endoscopic Surgery (EAES), Barcelona, Spain, 24–27 November 2021. Surgical Endoscopy. 2022;36(2):325-674. **EXCLUDED – Wrong publication type**
148. Woodfield JC, Clifford K, Wilson GA, Munro F, Baldi JC. Short-term high-intensity interval training improves fitness before surgery: A randomized clinical trial. Scandinavian Journal of Medicine & Science in Sports. 2022;28:28. **EXCLUDED – Duplicate of STUDY 65**
149. Zheng Y, Huang Z, Dai L, Liu Y, Chen Y, Zhang W, et al. The Effect of Preoperative Rehabilitation Training on the Early Recovery of Joint Function after Artificial Total Knee Arthroplasty and Its Effect Evaluation. Journal of Healthcare Engineering. 2022;2022:3860991. **EXCLUDED - Wrong study design Unable to identify duration of prehab**

Studies added by hand search:

1. McIsaac DI, Hladkowicz E, Bryson GL, Forster AJ, Gagne S, Huang A, et al. Home-based prehabilitation with exercise to improve postoperative recovery for older adults with frailty having cancer surgery: the PREHAB randomised clinical trial. British Journal of Anaesthesia. 2022. **STUDY 32**
2. D'Lima DD, Colwell CW, Jr., Morris BA, Hardwick ME, Kozin F. The effect of preoperative exercise on total knee replacement outcomes. Clin Orthop Relat Res. 1996(326):174-82. **STUDY 67**
3. Rooks DS, Huang J, Bierbaum BE, Bolus SA, Rubano J, Connolly CE, et al. Effect of preoperative exercise on measures of functional status in men and women undergoing total hip and knee arthroplasty. Arthritis Rheum. 2006;55(5):700-8. **STUDY 68**
4. Beaupre LA, Lier D, Davies DM, Johnston DBC. The effect of a preoperative exercise and education program on functional recovery, health related quality of life, and health service utilization following primary total knee arthroplasty. The Journal of rheumatology. 2004;31(6):1166-73. **STUDY 69**
5. Hulzebos EH, Helders PJ, Favié NJ, De Bie RA, Brutel de la Riviere A, Van Meeteren NL. Preoperative intensive inspiratory muscle training to prevent postoperative pulmonary complications in high-risk patients undergoing CABG surgery: a randomized clinical trial. Jama. 2006;296(15):1851-7. **STUDY 70**
6. Molenaar CJL, Minnella EM, Coca-Martinez M, Ten Cate DWG, Regis M, Awasthi R, et al. Effect of Multimodal Prehabilitation on Reducing Postoperative Complications and Enhancing Functional Capacity Following Colorectal Cancer Surgery: The PREHAB Randomized Clinical Trial. JAMA surgery. 2023. **STUDY 76**

APPENDIX 3 Supplementary tables

Table 1. Specific outcome assessments and recovery timeframes reported per concept of interest

Reported Outcomes		Specific Outcome Assessments			Timeframes	
Description of concept of interest for measurement (outcome)*	**Number of times reported as outcome across trials**	**Number of different outcome assessments**	**Most frequently used**		**Description of timeframe according to phases of recovery****	**Number per outcome**
			Description outcome assessments	**Frequency per outcome**		
Observer Reported Outcome (n=175)						
Hospital Length of Stay (LOS)	52/175 30%	4	Number of days from surgery to discharge Total number of days from preoperative admission to discharge post-op Cumulative LOS over 30 days post-op Cumulative LOS over 90 days post-op	46/52 89% 4/52 8% 1/52 2% 1/52 2%	Pre-admission Intermediate Late ≤ 30 d Late >30 to ≤ 90 d Late > 90 d	4 46 2 1 0
Hospital readmission	24/175 14%	1	Frequency of admissions	24/24 100%	Pre-admission Intermediate Late ≤ 30 d Late >30 to ≤ 90 d Late > 90 d Not specified/unclear	N/A N/A 13 2 1 9
Postoperative mortality	23/175 13%	4	Frequency alone Clavien-Dindo grade V Morbidity-Mortality Index Part of National Surgical Quality Improvement Project (NSQIP) composite outcome	15/23 65% 6/23 26% 1/23 4% 1/23 4%	Pre-admission Intermediate Late ≤ 30 d Late >30 to ≤ 90 d Late > 90 d Not specified/unclear	N/A 3 14 2 0 4

Intensive care unit admission	22/175	13%	2	Frequency of admissions Intensive care unit LOS	15/22 7/22	68% 32%	Pre-admission Intermediate Late ≤ 30 d Late >30 to ≤ 90 d Late > 90 d Not specified/unclear	N/A 1 8 0 0 10
Anthropometrics	17/175	10%	6	Weight Body Mass Index Waist circumference	7/17 6/17 2/17	41% 35% 12%	Pre-admission Intermediate Late ≤ 30 d Late >30 to ≤ 90 d Late > 90 d	8 2 2 5 4
Surgical reintervention	12/175	7%	1	Frequency of surgical reintervention	12/12	100%	Pre-admission Intermediate Late ≤ 30 d Late >30 to ≤ 90 d Late > 90 d Not specified/unclear	N/A 0 5 3 0 4
Body composition	12/175	7%	4	Fat mass (e.g., % using bioelectrical impedance analysis (BIA)) Fat free mass (e.g., % using BIA) Muscle architecture (e.g., muscle cross-sectional area using magnetic resonance imaging and/or muscle biopsy)	5/12 4/12 2/12	42% 33% 17%	Pre-admission Intermediate Late ≤ 30 d Late >30 to ≤ 90 d Late > 90 d	6 0 3 5 1
Emergency department visit	7/175	4%	1	Frequency of emergency department visits	7/7	100%	Pre-admission Intermediate Late ≤ 30 d Late >30 to ≤ 90 d Late > 90 d	N/A 0 7 0 0

Discharge location	6/175	3%	1	Frequency of discharge to home or rehabilitation	6/6	100%	Pre-admission Intermediate Late ≤ 30 d Late >30 to ≤ 90 d Late > 90 d	N/A 6 N/A N/A N/A
Performance outcomes (n=199)								
Exercise capacity using cardiorespiratory exercise testing (CPET)	43/199	22%	10	Oxygen consumption (VO_2) at peak exercise Peak work load VO_2 at the anaerobic threshold	12/43 8/43 8/43	28% 19% 19%	Pre-admission Intermediate Late ≤ 30 d Late >30 to ≤ 90 d Late > 90 d Not specified/unclear	15 0 3 1 1 2
Strength	34/199	17%	9	Handgrip strength (e.g., using handheld dynamometer) Quadricep strength (e.g., bilateral quadricep maximal voluntary isometric contractions with dynamometry) Hamstring strength (e.g., 6 repetition max leg curl)	10/34 10/34 4/34	29% 29% 12%	Pre-admission Intermediate Late ≤ 30 d Late >30 to ≤ 90 d Late > 90 d	21 1 6 13 7
Functional exercise capacity	33/199	17%	2	6-minute walk test 5-minute walk test	32/33 1/33	97% 3%	Pre-admission Intermediate Late ≤ 30 d Late >30 to ≤ 90 d Late > 90 d	28 1 14 13 8
Pulmonary function	33/199	17%	9	Forced Vital Capacity Forced Expiratory Volume in 1 second Maximal inspiratory/expiratory pressure	9/33 9/33 5/33	27% 27% 15%	Pre-admission Intermediate Late ≤ 30 d Late >30 to ≤ 90 d	12 2 3 1

							Late > 90 d	1
							Not specified/unclear	1
Timed up and go	10/199	5%	1	Timed up and go	10/10	100%	Pre-admission	8
							Intermediate	2
							Late ≤ 30 d	3
							Late >30 to ≤ 90 d	7
							Late > 90 d	5
Range of motion	10/199	5%	2	Lower body (e.g., range of motion of knee joint assessed with goniometer)	9/10	90%	Pre-admission	9
				Lumbar region (e.g., range of motion of lumbar assessed with an inclinometer)	1/10	10%	Intermediate	2
							Late ≤ 30 d	1
							Late >30 to ≤ 90 d	9
							Late > 90 d	5
Physical activity	10/199	5%	4	Accelerometer (e.g., Actigraph)	5/10	50%	Pre-admission	3
				Number of steps using a pedometer	3/10	30%	Intermediate/hospital stay	3
				Mobilization (walking distance)	1/10	10%	Late ≤ 30 d	1
				Fitbit	1/10	10%	Late >30 to ≤ 90 d	1
							Late > 90 d	3
Sit to stand	9/199	5%	3	5 x Sit to stand	3/9	33%	Pre-admission	8
				30 sec Sit to stand	3/9	33%	Intermediate	1
				60 sec Sit to stand	3/9	33%	Late ≤ 30 d	1
							Late >30 to ≤ 90 d	2
							Late > 90 d	2
Stair climbing	6/199	3%	3	Timed ascent and descent	4/6	67%	Pre-admission	5
				Steps in 60 sec	1/6	17%	Intermediate	0
				Unclear	1/6	17%	Late ≤ 30 d	1
							Late >30 to ≤ 90 d	6
							Late > 90 d	1
Gait speed	4/199	2%	3	50 feet walk	2/4	50%	Pre-admission	3

				5 m walk test	¼	25%	Intermediate	0
				10 m walk test	¼	25%	Late ≤ 30 d	0
							Late >30 to ≤ 90 d	4
							Late > 90 d	1
Balance	3/199	2%	4	Functional reach test	1/3	33%	Pre-admission	1
				One leg stand test	1/3	33%	Intermediate	0
				Fall incidence	1/3	33%	Late ≤ 30 d	0
							Late >30 to ≤ 90 d	2
							Late > 90 d	2
Physical performance	3/199	2%	1	Short Physical Performance Battery	3/3	100%	Pre-admission	1
							Intermediate	0
							Late ≤ 30 d	1
							Late >30 to ≤ 90 d	1
							Late > 90 d	0
Functional status of thigh musculature	1	1%	1	Single-leg hop test	1	100.0%	Preoperative	1
							Intermediate	0
							Late ≤ 30 d	0
							Late ≤ 90 d	1
							Late > 90 d	0
Clinician Reported Outcomes (n=84)								
Postoperative complications	51/84	61%	5	Frequency only	20/51	39%	Pre-admission	N/A
				Clavien-Dindo classification	24/51	47%	Intermediate	9
				Comprehensive Complication Index	8/51	16%	Late ≤ 30 d	28
				Postoperative Morbidity Survey	2/51	4%	Late >30 to ≤ 90 d	8
							Late > 90 d	2
							Not specified/unclear	12
Disease specific assessment	9/84	11%	7	Right or left ventricular function	2/9	22%	Pre-admission	5
				Knee Society Clinical Rating System	2/9	22%	Intermediate	4
				Delayed gastric emptying	1/9	11%	Late ≤ 30 d	2

							Late >30 to ≤ 90 d	6
							Late > 90 d	5
							Not specified/unclear	1
Delirium incidence	8/84	10%	4	Not specified	5/8	63%	Pre-admission	0
				Confusion Assessment Method (CAM)	1/8	13%	Intermediate	5
				CAM-intensive care unit	1/8	12.5%	Late ≤ 30 d	1
				Chart-Based Delirium Identification Instrument	1/8	13%	Late >30 to ≤ 90 d	0
							Late > 90 d	1
							Not specified/unclear	1
Dietary intake	4/84	5%	3	3-day food record (written diary)	2/4	50%	Pre-admission	3
				Food log in mobile app (Fitbit)	¼	25%	Intermediate	1
				Nutritional intake recorded during hospitalization	¼	25%	Late ≤ 30 d	0
							Late >30 to ≤ 90 d	0
							Late > 90 d	0
Time to achieve hospital discharge criteria	4/84	5%	1	Time to achievement to clinical milestones or pre-specified criteria for discharge	¾	75%	Pre-admission	N/A
				Unclear	¼	25%	Intermediate	4
							Late ≤ 30 d	0
							Late >30 to ≤ 90 d	0
							Late > 90 d	0
Nutritional status	3/84	4%	2	Patient-Generated Subjective Global Assessment	2/3	67%	Pre-admission	3
				Malnutrition Universal Screening Tool	1/3	33%	Intermediate	0
							Late ≤ 30 d	1
							Late >30 to ≤ 90 d	1
							Late > 90 d	0
Independence status	2/84	2%	2	Katz Index score	½	50%	Pre-admission	0
				Scoring of 4 functional tests (transfer from lying to sitting, transfer from sitting to standing,	½	50%	Intermediate	2

				walking 30 m, going up and down a flight of stairs)			Late ≤ 30 d Late >30 to ≤ 90 d Late > 90 d	0 0 0
Cognitive function	2/84	2%	1	Montreal Cognitive Assessment	2/2	100%	Pre-admission Intermediate Late ≤ 30 d Late >30 to ≤ 90 d Late > 90 d	2 1 1 2 1
Anemia diagnosis	1/84	1%	1	Not specified	N/A	N/A	Pre-admission Intermediate Late ≤ 30 d Late >30 to ≤ 90 d Late > 90 d	0 0 1 0 0
Patient Reported Outcome (n=137)								
General or health related quality of life	30/137	22%	4	12- or 36-Item Short Form Survey EQ-5D-3L or -5Linstruments 15-dimensional (15D) instrument Quality of Well Being scale	20/30 8/30 1/30 1/30	67% 27% 3% 3%	Pre-admission Intermediate Late ≤ 30 d Late >30 to ≤ 90 d Late > 90 d	6 2 11 20 14
Disease specific quality of life	23/137	17%	14	EORTC QLQ-C30 Western Ontario and McMaster Universities Osteoarthritis (WOMAC) Functional Assessment of Cancer Therapy	6/23 5/23 3/23	26% 22% 13%	Pre-admission Intermediate Late ≤ 30 d Late >30 to ≤ 90 d Late > 90 d Not specified/unclear	22 0 6 18 7 2
Self-reported anxiety and depression	21/137	15%	6	Hospital Anxiety and Depression Scale	15/21	71%	Pre-admission	19

				Patient Health Questionnaire-9	2/21	10%	Intermediate	0
				Geriatric Depression Scale	1/21	5%	Late ≤ 30 d	8
				Warwick Edinburgh Mental Wellbeing Scale	1/21	5%	Late >30 to ≤ 90 d	16
				Cardiac Anxiety Questionnaire	1/21	5%	Late > 90 d	5
				Beck Depression Inventory	1/21	5%		
Self-reported functional capacity or physical activity	18/137	13%	9	Community Healthy Activities Model Program for Seniors	8/18	44%	Pre-admission	15
				Patient Specific Functional Scale	2/18	11%	Intermediate	0
				WOMAC function subscale only	2/18	11%	Late ≤ 30 d	10
							Late >30 to ≤ 90 d	15
							Late > 90 d	5
Pain	15/137	11%	9	Visual Analogue Scale	6/15	40%	Pre-admission	12
				Numeric Rating Scale (NRS)	2/15	13%	Intermediate	3
				Brief Pain Inventory Short form	1/15	7%	Late ≤ 30 d	8
				Pain Disability Index	1/15	7%	Late >30 to ≤ 90 d	14
							Late > 90 d	10
Self-reported disability or mobility	8/137	6%	5	Oswestry Disability Index	3/8	38%	Pre-admission	6
				WHO Disability Assessment Schedule 2.0	2/8	25%	Intermediate	2
				Mobility Assessment Tool: Short Form	1/8	13%	Late ≤ 30 d	2
				Roland Moris questionnaire	1/8	13%	Late >30 to ≤ 90 d	6
				Swiss Spinal Stenosis Questionnaire	1/8	13%	Late > 90 d	4
Self-efficacy	5/137	4%	4	Self-Efficacy for Exercise scale	2/5	40%	Pre-admission	5
				Self-Efficacy Scale	1/5	20%	Intermediate	0
				Arthritis Self-efficacy Scale	1/5	20%	Late ≤ 30 d	2
				16-item Cardiac Exercise Self-Efficacy Index	1/5	20%	Late >30 to ≤ 90 d	6
							Late > 90 d	2
Patient satisfaction	5/137	4%	5	NRS	1/5	20%	Pre-admission	2
				5-point scale	1/5	20%	Intermediate	0
				New Promoter Score	1/5	20%	Late ≤ 30 d	2

				Online survey	1/5	20%	Late >30 to ≤ 90 d	0
				Questionnaire	1/5	20%	Late > 90 d	2
Self-reported recovery	5/137	4%	3	Question (“‘To what extent do you feel fully physically recovered?’’ with answering categories as “not recovered, 25%, 50%, 75%, and fully recovered”)	2/5	40%	Pre-admission	N/A
				Quality of Recovery questionnaire	2/5	40%	Intermediate	3
				Surgical Recovery Scale	1/5	20%	Late ≤ 30 d	2
							Late >30 to ≤ 90 d	2
							Late > 90 d	0
Perceived efficacy of treatment	4/137	3%	2	Patient Global Impression of Change	¾	75%	Pre-admission	2
				Outcome Expectations for Exercise scale	¼	25%	Intermediate	0
							Late ≤ 30 d	1
							Late >30 to ≤ 90 d	4
							Late > 90 d	2
Kinesiophobia	3/137	2%	2	Tampa Scale for Kinesiophobia	2/3	67%	Pre-admission	3
				Fear Avoidance Belief Questionnaire-Physical Activity	1/3	33%	Intermediate	0
							Late ≤ 30 d	1
							Late >30 to ≤ 90 d	5
							Late > 90 d	3
Biomarker Outcome (n=28)								
Inflammatory marker	11/28	40%	7	C-reactive protein (CRP)	3/11	27%	Pre-admission	2
				Interleukin 6 (IL-6)	2/11	18%	Intermediate	1
				Tumor necrosis factor Alpha (TNFα)	2/11	18%	Late ≤ 30 d	1
							Late >30 to ≤ 90 d	1
							Late > 90 d	0
Muscle hypertrophy/ atrophy	6/28	21%	6	IGF-1 (insulin-like growth factor 1)	1/6	17%	Pre-admission	1
				MuRF-1 (muscle RING-finger protein-1)	1/6	17%	Intermediate	0
				MAFbx (muscle atrophy f-box)	1/6	17%	Late ≤ 30 d	0

				MHC (myosin heavy chain) 1	1/6	17%	Late >30 to ≤ 90 d	1
				MHC Iia	1/6	17%	Late > 90 d	0
				MHC Iix mRNA	1/6	17%		
Blood pressure	5/28	18%	1	Systolic/diastolic	5/5	100.0%	Pre-admission	3
							During surgery	3
							Late ≤ 30 d	0
							Late >30 to ≤ 90 d	1
							Late > 90 d	0
Disease specific marker	3/28	11%	3	Endothelin-1 (ET-1)	1/3	33%	Preoperative	1
				Asymmetric dimethylarginine (ADMA)	1/3	33%	Intermediate	1
				estimated glomerular filtration rate (eGRF)	1/3	33%	Late ≤ 30 d	0
							Late ≤ 90 d	0
							Late > 90 d	0
Hematological marker	2/28	7%	2	Hemoglobin (Hb)	½	50%	Pre-admission	0
				White blood cells (WBC)	½	50%	During surgery	1
							Late ≤ 30 d	1
							Late >30 to ≤ 90 d	0
							Late > 90 d	0
Blood glucose marker	1/28	4%	1	glycated hemoglobin (HbA1C)	1/1	100%	Pre-admission	1
							Intermediate	0
							Late ≤ 30 d	0
							Late >30 to ≤ 90 d	1
							Late > 90 d	0

ISPOR: International Society for Pharmacoeconomics and Outcomes Research

*Studies may have reported multiple outcomes per each type of outcome according to the ISPOR Framework. The concept of interest for measurement (i.e., outcome) is the concept that the outcome assessment is intended to measure. While the specific outcome assessment is the measuring instrument or test or assessment method that provides a rating or score (categorical or continuous) that is intended to represent some aspect of the patient's medical status (61).**Phases of recovery: Pre-admission: preparation period before surgery [7]; Intermediate: from after the post-anesthesia care unit to discharge from hospital; Late: from hospital discharge to return to the patient's usual function and activities [19]

Table 2. Description of concept of interest for measurement per surgical specialty

Description of concept of interest for measurement (outcome)*	Surgical Speciality									
	Abdominal (n=26)		Thoracic (n=14)		Cardiac (n=7)		Ortho/Spine (n=24)		Other (n=5)	
Performance outcomes	**22**	**85%**	**13**	**93%**	**4**	**57%**	**19**	**79%**	**3**	**60%**
Balance	0	0%	0	0%	0	0%	3	13%	0	0%
Exercise capacity	9	35%	5	36%	1	14%	0	0%	0	0%
Functional exercise capacity	14	54%	12	86%	2	29%	3	13%	2	40%
Functional status of thigh musculature	0	0%	0	0%	0	0%	1	4%	0	0%
Gait speed	1	4%	0	0%	1	14%	2	8%	0	0%
Physical activity	3	12%	1	7%	1	14%	2	8%	2	40%
Physical Performance	0	0%	0	0%	0	0%	1	4%	2	40%
Pulmonary function	1	4%	8	57%	2	29%	0	0%	0	0%
Range of motion	0	0%	0	0%	0	0%	10	42%	0	0%
Sit to stand	3	12%	2	14%	0	0%	4	17%	0	0%
Strength	7	27%	4	29%	0	0%	10	42%	1	20%
Stair climbing	1	4%	0	0%	0	0%	5	21%	0	0%
Timed up and go	1	4%	1	7%	1	14%	7	29%	0	0%
Observer reported outcomes	**24**	**92%**	**13**	**93%**	**6**	**86%**	**17**	**71%**	**5**	**100%**
Anthropometrics	5	19%	1	7%	1	14%	3	13%	0	0%
Body composition	4	15%	2	14%	0	0%	1	4%	0	0%
Discharge location	0	0%	0	0%	0	0%	5	21%	1	20%
Emergency department visits	4	15%	2	14%	0	0%	1	4%	0	0%
Hospital length of stay	22	85%	10	71%	4	57%	11	46%	5	100%
Hospital readmission	15	58%	3	21%	1	14%	3	13%	2	40%

Intensive care unit admissions	8	31%	5	36%	4	57%	2	8%	1	20%
Postoperative mortality	9	35%	8	57%	4	57%	2	8%	0	0%
Surgical reintervention	5	19%	2	14%	1	14%	3	13%	1	20%
Clinician reported outcomes	**25**	**96%**	**13**	**93%**	**6**	**86%**	**11**	**46%**	**4**	**80%**
Anemia diagnosis	1	4%	0	0%	0	0%	0	0%	0	0%
Cognitive function	0	0%	0	0%	1	14%	1	4%	0	0%
Delirium incidence	2	8%	2	14%	1	14%	1	4%	2	40%
Dietary intake	1	4%	0	0%	0	0%	0	0%	1	20%
Disease specific assessment	4	15%	0	0%	2	29%	3	13%	0	0%
Independence status	1	4%	0	0%	0	0%	1	4%	0	0%
Nutritional status	3	12%	0	0%	0	0%	0	0%	1	20%
Postoperative complications	23	89%	13	93%	4	57%	8	33%	3	60%
Time to achieve hospital discharge criteria	2	8%	0	0%	0	0%	2	8%	0	0%
Patient reported outcomes	**21**	**81%**	**10**	**71%**	**2**	**29%**	**22**	**92%**	**3**	**60%**
Disease specific quality of life	4	15%	7	50%	1	14%	11	46%	0	0%
General or health-related quality of life	9	35%	4	29%	1	14%	12	50%	2	40%
Kinesiophobia	0	0%	0	0%	0	0%	3	13%	0	0%
Pain	3	12%	1	7%	0	0.0%	11	46%	0	0%
Patient satisfaction	1	4%	0	0%	1	14%	2	8%	1	20%
Perceived efficacy of treatment	0	0%	0	0%	0	0%	4	17%	0	0%
Self-efficacy	0	0%	0	0%	1	14%	4	17%	0	0%
Self-reported anxiety and depression	11	42%	4	27%	1	14%	4	17%	0	0.0%
Self-reported disability	0	0%	1	7%	0	0%	5	21%	1	20%
Self-reported functional capacity or physical activity	8	31%	2	14%	0	0%	7	29%	1	20%
Self-reported recovery	3	12%	1	7%	0	0%	0	0%	1	20%

Biomarker outcomes	**3**	**12%**	**2**	**14%**	**2**	**29%**	**4**	**17%**	**1**	**20%**
Blood pressure	2	8%	0	0%	0	0%	2	8%	1	20%
Disease specific biomarker	0	0%	0	0%	1	14%	0	0%	0	0%
Glucose biomarker	1	4%	0	0%	0	0%	0	0%	0	0%
Hematological biomarker	0	0%	1	7%	0	0%	1	4%	0	0%
Inflammatory biomarker	0	0%	1	7%	1	14%	1	4%	0	0%
Muscle hypertrophy/ atrophy marker	0	0%	0	0%	0	0%	1	4%	0	0%
Non-health outcomes										
Cost analysis	0	0%	1	7%	0	0%	4	17%	1	20%
Adherence	22	85%	8	57%	2	29%	10	42%	5	100%

*The concept of interest for measurement is the concept that the outcome assessment is intended to measure