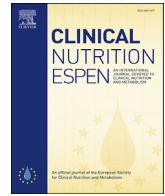




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Clinical Nutrition ESPEN

journal homepage: <http://www.clinicalnutritionespen.com>

Meta-analysis

Exploring the acceptability of and adherence to prehabilitation and rehabilitation in patients undergoing major abdominal surgery: A systematic review and meta-analysis

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ARTICLE INFO

Article history:

Received 29 July 2024

Accepted 30 July 2024

Keywords:

Prehabilitation
Abdominal surgery
Adherence
Complications
Patient perceptions

SUMMARY

Background and aims: Prehabilitation combines exercise, nutritional, and psychological interventions administered before surgery to improve patient outcomes. This comprehensive review and meta-analysis examined the feasibility, adherence, and effectiveness of prehabilitation in frail, high-risk individuals undergoing major abdominal surgery.**Methods:** We searched the Cochrane Central Register of Controlled Trials, Web of Science, MEDLINE, Embase, and Cumulative Index to Nursing & Allied Health Literature (CINAHL) databases to identify relevant studies evaluating prehabilitation programs published between 2010 and 2023, either as observational studies or randomized clinical trials (RCTs).**Results:** The 23 articles (13 RCTs and 10 observational studies) included 1849 older male and female patients aged 68.7 ± 7.2 years. Nineteen of the included studies reported on adherence to prehabilitation programmes, which was generally good (>75%) over different models, settings, and durations. Factors such as patients' desire for expedited surgery, self-assessment of fitness, personal and professional obligations, health issues, holidays, and advancement of surgery dates negatively affected adherence to prehabilitation programmes. When compared with rehabilitation or standard pre- and post-surgical care, prehabilitation was associated with a 25%, albeit not statistically significant reduction in post-operative complications, according to data from 14 studies reporting on postoperative complications (OR 0.75, 95% CI 0.48 to 1.17, $P = 0.43$; $I^2 = 65\%$). Prehabilitation has been found to improve the 6-min walk test significantly by 29.4 m (MD +29.4 m, 95% CI 5.6 to 53.3, $P = 0.02$; $I^2 = 39\%$), compared with rehabilitation or standard pre- and post-surgical care.**Conclusion:** Prehabilitation was acceptable to patients, with good adherence, and improved physical function.© 2024 The Author(s). Published by Elsevier Ltd on behalf of European Society for Clinical Nutrition and Metabolism. This is an open access article under the CC BY license (<http://creativecommons.org/licenses/by/4.0/>).

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List of abbreviations			
6MTT	6-min time trial	OR	odds ratio
6MWT	6-min walk test	PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses
ASA	American Society of Anesthesiologists	PRISMA-S	Preferred Reporting Items for Systematic Reviews and Meta-Analyses literature search extension
CI	confidence intervals	QoL	quality of life
CCI	Comprehensive Complication Index	QoR-40	Quality of Recovery Score-40
CINAHL	The Cumulative Index to Nursing and Allied Health Literature	RCT	randomized clinical trial
ERAS	Enhanced Recovery after Surgery	RevMan	Review Manager
GRADE	Grading of Recommendations, Assessment, Development, and Evaluation	RR	risk ratio
LoS	length of hospital stay	SD	standard deviation
MOOSE	Meta-analysis Of Observational Studies in Epidemiology	WHO	World Health Organization
		WMD	weighted mean difference

1. Introduction

In adult patients of any age, poor postoperative outcomes are linked to phenotypes such as low muscle mass, sarcopenia, malnutrition [1,2], low physical activity [3,4], anxiety and depression [5]. These outcomes are worse for older adults and those with frailty [6].

Frailty is defined as a unique condition of health associated with ageing and is characterised by a steady loss of the built-in reserves of several body systems [7]. After surgery, about one in five older adults who are frail report having a new disability [8–10]. Additionally, the likelihood of surgical morbidity, mortality, and institutional discharge is three-fold higher in patients with frailty [11–15].

Prehabilitation has been documented in the military literature since the 1940s where the aim was to improve the physical condition of substandard recruits [16,17]. However, despite early preoperative work in the 1950s [18] the role of prehabilitation in improving postoperative outcomes by providing preoperative exercise, nutritional optimisation and psychological support had not been studied systematically or popularised until the early 21st century [19]. Despite the theoretical advantages and attractiveness of prehabilitation, the effects on outcomes have been variable and, at times, inconclusive [20,21] mainly because of heterogeneity in patient populations, study design, prehabilitation regimens and duration of prehabilitation, and lack of adherence data. However, our recent systematic review and meta-analysis has shown that prehabilitation can significantly reduce the length of stay and decrease serious complications in frail and high-risk patients undergoing major abdominal surgery [22].

Despite the documented benefits of prehabilitation [19,21], its long-term success hinges on patient acceptability and adherence. Some patients may feel incapable of engaging in strenuous exercise, with preferences varying from home-based unsupervised programmes to supervised sessions with peers who have comparable life experiences [23–26]. “Hospital-associated, home-based” prehabilitation offers numerous advantages, such as initial advocacy, increased confidence, patient convenience, and reduced infrastructure and manpower needs, potentially lowering costs and enhancing sustainability [25]. Understanding patient perspectives is crucial for refining regimens to boost acceptability and adherence. This review expands on our recent systematic review and meta-analysis [22] by exploring previously uninvestigated areas recommended for further study (e.g. substantial variability in programmes, patient adherence, and a lack of high-quality

evidence). Building on these insights, this systematic review aimed to investigate adherence to prehabilitation in frail and high-risk patients undergoing major abdominal surgery and identify interventions that are acceptable. Additionally, we sought to assess the overall efficacy of prehabilitation.

2. Methods

2.1. Search strategy

A comprehensive search of the MEDLINE, Embase, Cochrane Central Register of Controlled Trials, Web of Science, and Cumulative Index to Nursing & Allied Health Literature (CINAHL) databases was performed to identify studies published from January 1, 2010 to July 31, 2023. This search aimed to find research evaluating the effect of prehabilitation in patients who were frail, older, and undergoing elective abdominal surgery. Due to the relatively recent use of the term prehabilitation in clinical trials, a date restriction was imposed to facilitate comparability of terms among studies. The following search terms were used: (“Prehabilitation” OR “Preoperative Exercise” OR “Perioperative Nutrition” OR “Preoperative Intervention” OR “Preoperative Exercise” OR “Psychology” OR “Counselling”) AND (“Major Surgery” OR “Colorectal” OR “Hepatobiliary” OR “pancreatic” OR “Oesophagogastric”). Further information on the search strategy is provided in the [Supplementary Table 1](#). Bibliographies of included studies and previous systematic reviews and meta-analyses were reviewed to ensure inclusion of relevant papers. Study selection, evaluation of eligibility criteria, data extraction, and statistical analyses followed the Cochrane methodology standards [27] and findings are reported in accordance with PRISMA-S (Preferred Reporting Items for Systematic Reviews and Meta-Analyses literature search extension) guidelines [28] and the Meta-analysis Of Observational Studies in Epidemiology (MOOSE) statement [29]. All co-authors participated in discussions to refine the search strategy. In accordance with the Cochrane search strategy recommendations and to further reduce the likelihood of missing relevant studies within the population of interest, the terms “frailty” and “old adults” were not applied to the search strategy [27].

2.2. Selection criteria for studies

Consideration was given to all studies on patients undergoing major abdominal surgery which consisted of elective gastrointestinal and hepatopancreaticobiliary procedures. The intervention of

interest was prehabilitation which was defined as a physical (exercise) component of the prehabilitation programme (unimodal prehabilitation), or an exercise component combined with a nutritional and/or psychological support (multimodal prehabilitation). Restrictions on exercise duration, frequency, type, or supervision (supervised or unsupervised programs) were not applied. Studies should have reported on one or more of the desired outcomes detailed in section 2.6.

2.3. Inclusion criteria

We included observational studies and randomized clinical trials (RCTs) that reported at least one relevant clinical outcome, such as the individual's adherence to the programmes, postoperative complications, or quality of life (QoL) and factors impacting QoL. To be eligible for this review, studies had to clearly define their populations as either individuals aged 60 years and older (regardless of frailty) or those younger than 60 years identified as frail. The age criterion aligns with the United Nations' definition of an "older person" to encompass high-risk patients [30]. Given the varied definitions of frailty in the literature, we did not limit our review to a single definition. Instead, we accepted studies that used different operational definitions of frailty, as outlined in Table 1. Since frailty is not exclusively age-related, individuals categorised as frail could be younger than 60 years. Our main objective was to assess the individual's adherence to the programmes to know the effectiveness of prehabilitation for individuals at high risk due to frailty or advanced age, rather than for younger, healthier individuals. The control groups in the included studies consisted of participants undergoing either rehabilitation or standard care. No language restrictions were applied in selecting the studies for this review.

2.4. Exclusion criteria

Studies focusing solely on postoperative rehabilitation, defined as interventions implemented post-surgery to aid recovery, were excluded from our review. Our study aimed to compare prehabilitation — interventions conducted before surgery to prepare patients physically and mentally — with postoperative rehabilitation or no intervention. Additionally, we excluded studies that lacked patient data, duplicates, those with restricted access to full research reports or data, review articles, editorials, letters to the editor, case reports, and conference abstracts.

2.5. Data extraction, collection and synthesis

We used the Rayyan software (<https://www.rayyan.ai>) [31] to identify duplicate papers and conduct preliminary title and abstract screening ensuring a blind and effective data extraction process. Eligible papers from the search results of all databased were then imported into the EndNote 20 programme (<https://endnote.com>) [32].

Based on review eligibility criteria, three authors (AA, PS, and DO'C) independently reviewed the listed studies for relevance. Data collection encompassed various aspects including publication details, study design, participant characteristics (such as number, age, and frailty score), surgical information, type of exercise employed, nutritional screening score, details of prehabilitation interventions (including modality, duration, frequency, and supervision), adherence rates, postoperative outcomes, QoL measurements, and factors that impacting the quality of life, attrition rate, and any pertinent comments pertaining to the reported data. Risk of bias in

the included RCTs was assessed using the Cochrane Collaboration tool RoB2 [27] within the RevMan v5.4 programme [33]. The Newcastle–Ottawa scale was used to assess risk of bias in cohort studies [34]. To assess the quality of the evidence, the Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) approach was applied [35]. The certainty of the evidence was graded as high, moderate, low, or very low, and the grading results are based on five categories (risk of bias, imprecision, inconsistency, indirectness, and publication).

2.6. End points

The acceptability of an intervention can be greatly influenced by the content, setting, and quality of treatment received, as perceived by the patient. Higher levels of adherence to applied interventions frequently suggest that patients find an intervention acceptable, which can subsequently result in improved clinical outcomes [36,37]. Therefore, the primary endpoint was the adherence of patients to the prehabilitation programmes, which was reported as a percentage. Adherence has been defined as the ratio of attended exercise sessions to the total number of planned sessions and the acceptability was reflected by the level of patients adherence. The secondary endpoints were postoperative complications (including overall postoperative complications, infections, minor/major complications, death incidences — Clavien-Dindo classification ≥ 3 [38]), QoL and factors impacting QoL, which was reported in mean loss of lean muscle mass in kg, Quality of Recovery (QoR-40) score, and 6-Minute Walk Test (6MWT) in metres. Meta-analysis was limited to severe postoperative outcomes and 6MWT.

2.7. Statistical analysis

Adherence results were pooled and represented as mean values and standard deviation (SD). Odds ratios (OR), risk ratios (RR), or weighted mean differences (WMD) with 95% confidence intervals (CI) were used to summarise dichotomous outcome measures for continuous variables. Presence of statistical heterogeneity was somewhat expected given the between-study variability in the type of surgery evaluated, number of patients per study, percentage of those malnourished or at nutritional risk in the study population, type of prehabilitation intervention used, duration of intervention, and control group selection, the presence of statistical heterogeneity was somewhat expected. Furthermore, data from single-arm trials were excluded from the analysis in order to ensure a greater degree of certainty and comparability [39]. Consequently, a random-effects meta-analysis was assumed and a quantitative synthesis of the pooled data was carried out using RevMan v5.4 software [33]. Differences were deemed statistically significant at $P < 0.05$. The I^2 statistic was used to measure heterogeneity and inconsistency between studies, and the values were interpreted in accordance with the Cochrane Handbook [40]. Heterogeneity was considered as "not important" if the I^2 value was between 0 and 40%, "moderate" if between 30 and 60%, "substantial" if between 50% and 90%, and "considerable" if between 75% and 100%.

2.8. Registration of the protocol

The protocol for this systematic review and meta-analysis was registered with the PROSPERO database: (https://www.crd.york.ac.uk/prospero/display_record.php?RecordID=496908), and the registration number assigned was CRD42024496908.

Table 1
Patient demographics in the studies included.

Study	Design	No. of participants	Age in years (median (IQR) or mean \pm SD)	Male sex (%)	Type of surgery	Type of exercise	Laparoscopic (%)	Neoadjuvant therapy (%)	Nutritional status (median (IQR) or mean \pm SD)	Definition of frailty
Barberan-Garcia et al., 2018 [43]	Double blind RCT	I = 62 C = 63	I = 71 \pm 11 C = 71 \pm 10	I = 68 C = 80	Major gastrointestinal surgery	Functional and Moderate-to-high intensity exercise	I = 79 C = 89	NS	BMI (kg/m ²): I = 21 \pm 7 C = 22 \pm 7	ASA score III/IV or Duke Activity Status Index score \leq 46
Berkel et al., 2021 [59]	2-Centers, single blinded prospective RCT	I = 28 C = 29	I = 74 \pm 7 C = 73 \pm 6	I = 57 C = 48	Colorectal cancer surgery	Resistance, and HIIT exercises	I = 82 C = 72	NS	BMI (kg/m ²): I = 29.8 \pm 4.1 C = 30.5 \pm 4.9	Patients were classified as frail based on a GFI score \geq 4.
Bojesen et al., 2022 [60]	Single-arm, prospective feasibility trial	8	80 (66–88)	50	Colorectal cancer surgery	Resistance, and HIIT exercises	NS	NS	BMI (kg/m ²): 26.18 (19.5–38.5)	Frailty was defined as having at least one positive Fried frailty criteria or a Geriatric-8 (G8) score \leq 14
Bousquet-Dion et al., 2018 [44]	Single blind RCT	I = 41 C = 39	I = 74 (67.5–78) C = 71 (54.5–74.5)	I = 81 C = 62	Colorectal cancer surgery	Resistance and personalised aerobic exercise	I = 84 C = 81	I = 14 C = 15	Albumin (g/L): I = 40 \pm 3 C = 40 \pm 3	Frailty not defined, but ASA was used to assess physical status
Bruns et al., 2019 [46]	Cohort retrospective	14	79 (74–86)	36	Colorectal cancer surgery	Resistance exercise (focusing on the movements needed to mobilise after the operation)	100	0	BMI (kg/m ²): 25 (21–28)	According to the existing Dutch guidelines, individuals are considered to meet the criteria if they have a score of 1 or higher, or an Identification of Seniors at Risk-Hospitalised patients score of 2 or higher.
Burden et al., 2017 [42]	Single blind RCT	I = 55 C = 46	I = 70.5 \pm 11.66 C = 68.9 \pm 11.49	I = 64 C = 70	Colorectal cancer surgery	No exercise	I = 68 C = 65	I = 40 C = 50	BMI (kg/m ²): I = 25.9 \pm 4.8 C = 25.5 \pm 4.54	NS
Carli et al., 2020 [52]	2-Centers, single blind RCT	I = 55 C = 55	I = 78 (72–82) C = 82 (75–84)	I = 52.7 C = 41.8	Colorectal cancer surgery	Resistance and moderate intensity aerobic exercises	I = 76.4 C = 81.2	I = 12.7 C = 11.1	BMI (kg/m ²): I = 24.9 (23.0–30.1) C = 26.4 (23.8–30.6)	Fried frailty index (1 indicates no frailty; 2–3, intermediate frailty; and 4–5, frailty)
Franssen et al., 2022 [61]	Single-arm, prospective feasibility trial	11	74 (68–78)	54.54	Colorectal cancer surgery	HIIT exercise	73	9	BMI (kg/m ²): 29.1 (24.6–33.1)	NS
Gillis et al., 2014 [41]	Single blind RCT	I = 38 C = 39	I = 65.7 \pm 13.6 C = 66 \pm 9.1	I = 55 C = 69	Colorectal cancer surgery	Resistance and personalised aerobic exercise	I = 97 C = 90	I = 26 C = 21	LBM (kg): I = 52 \pm 11 C = 56 \pm 10	Frailty not defined, but ASA was used to assess physical status
Howard et al., 2019 [47]	Cohort Prospective	I = 40 C = 76	I = 59.3 \pm 10.8 C = 58.3 \pm 13.2	I = 52 C = 50	Major gastrointestinal surgery	Walking	I = 70 C = 53	NS	BMI (kg/m ²): I = 30.2 \pm 7.7 C = 29.9 \pm 7.2	Sarcopenia was defined as a frailty index less than the median for all patients. ASA was used to assess physical status

Janssen et al., 2019 [48]	A single-center uncontrolled before-and-after trial	I = 267 C = 360	I = 77 (73–81) C = 76 (73–80)	I = 64.8 C = 62	Major gastrointestinal surgery	Resistance, aerobic, and respiratory muscle exercises	NS	NS	NS	Frailty was not clearly defined, but ASA score and CCI index to assess the physical and mental status
Karlsson et al., 2019 [49]	Feasibility RCT	I = 10 C = 11	I = 83.5 (76–85) ^a C = 74 (73–76) ^a	I = 40 C = 36	Colorectal cancer surgery	Resistance, aerobic, and respiratory muscle exercises	I = 70 C = 73	I = 10 C = 18	Albumin (g/L): I = 36 (34–38) C = 35 (32–36)	NS
López-Rodríguez-Arias et al., 2021 [55]	A prospective RCT	I = 10 C = 10	I = 66 ± 10.2 C = 66 ± 8	I = 60 C = 70	Colorectal cancer surgery	Resistance and aerobic exercises	NS	NS	NS	NS
Loughney et al., 2019 [50]	A single-center, one arm, uncontrolled before-and-after trial	32	60.5 ± 10.9	87.5	Colorectal and prostate cancer surgery	Resistance, aerobic, and HIIT exercises	NS	NS	BMI (kg/m ²): 29.7 ± 4.8	NS
Ngo-Huang et al., 2019 [51]	Single-arm, prospective feasibility trial	55	66 ± 8	52	Pancreatectomy surgery	Resistance and moderate intensity aerobic exercise	NS	NS	BMI (kg/m ²): 27.6 ± 5.3	Frailty assessment relied on Fried's criteria, evaluating weight loss, gait speed (measured by the 3-m walk test), HGS, and self-reported physical activity (captured through the International Physical Activity Questionnaire).
Northgraves et al., 2019 [53]	Feasibility RCT	I = 10 C = 11	I = 64.2 ± 10.5 C = 63.5 ± 12.5	I = 40 C = 63.6	Colorectal cancer surgery	Resistance and aerobic exercises	I = 40 C = 36.6	I = 40 C = 27.7	BMI (kg/m ²): I = 30.3 ± 4.3 C = 27.8 ± 5.7	NS
Peng et al., 2021 [54]	A prospective RCT	I = 109 C = 104	I = 63 ± 2.8 C = 62.8 ± 3.1	I = 59.6 C = 50.9	Colorectal cancer surgery	Resistance exercises only	I = 100 C = 100	0	BMI (kg/m ²): I = 22.3 ± 2.3 C = 22.6 ± 2.4	NS
Singh et al., 2018 [45]	A preliminary single arm trial	10	54.6 ± 14.1	70	Rectal cancer surgery	Resistance and personalised aerobic exercise	0	100	BMI (kg/m ²): 26.4 ± 3.8	NS
Steffens et al., 2021 [56]	Single blind RCT	I = 11 C = 11	I = 63 (48–72) C = 66 (75–84)	I = 54.5 C = 54.5	Major gastrointestinal surgery	Resistance, aerobic, and respiratory muscle exercises	NS	I = 45.5 C = 27.3	NS	NS
Taha et al., 2021 [57]	A post hoc analysis of RCT	I = 23 C = 25	I = 64.8 ± 11.5 C = 64 ± 11.9	I = 65.2 C = 48	Colorectal cancer surgery	Resistance, and HIIT exercises	I = 73.9 C = 64	NS	BMI (kg/m ²): I = 26.6 ± 3.5 C = 28 ± 5.4	NS
Tweed et al., 2021 [58]	Cohort Prospective	9	73 (70–76)	55.55	Colorectal cancer surgery	Resistance and aerobic exercises	NS	22.2	BMI (kg/m ²): 26.9 (25–32.7)	Patients were classified as frail based on a GFI score ≥4.
Waller et al., 2021 [62]	Single blind RCT	I = 11 C = 11	I = 55.5 (49.2–61.7) C = 61 (53.1–68.9)	I = 63.63 C = 36.36	Major gastrointestinal surgery	Resistance and aerobic exercises	NS	NS	BMI (kg/m ²): I = 30 (25.60–34.4) C = 27.8 (23.4–32.2)	NS
Waterland et al., 2022 [63]	Single-arm, prospective feasibility trial	50	71 (63–77)	52	Major gastrointestinal surgery	Resistance, aerobic, and respiratory muscle exercises	NS	NS	NS	NS

RCT: Randomized Clinical Trial; **SD:** Standard Deviation; **IQR:** Interquartile Range; **Op:** Operation; **QoL:** Quality of Life; **I:** intervention "Prehabilitation"; **C:** Control "Rehabilitation or Standard treatment"; **NS:** Not Stated; **BMI:** Body Mass Index; **HGS:** Hand Grip Strength; **HIIT:** High-Intensity Interval Training; **CCI:** Charlson Comorbidity Index; **GFI:** Groningen Frailty Index; **ASA:** American Society of Anesthesiologists; **QOR-40:** Quality of Recovery Score.

^a Statistically significant **P** < 0.05.

3. Results

3.1. Study selection

We identified 983 studies, of which 107 were in duplicate and consequently removed; 796 studies were unrelated to the topic after titles and abstracts were screened for inclusion (Fig. 1). Of the remaining 80 studies, 57 were excluded due to the reasons listed in Fig. 1. The list of excluded studies and rationale for the same are in Supplementary Table 2. In total, 23 studies [41–63] were included.

3.2. Study characteristics

The 23 studies included [41–63] in this review investigated acceptability and adherence to prehabilitation and rehabilitation in 1849 (1101 male) patients. The overall mean (SD) age of the patients was 68.7 ± 7.2 years. Demographic details, type of surgery, use of neoadjuvant therapy, nutritional status and frailty definition are

summarised in Table 1. Adherence was reported in 19 studies [41,42,44–50,52,53,56–63] and 14 studies [41–44,47–49,52,54–56,58,59,63] reported severe postoperative complications. QoL data were reported in 11 studies [43,45,46,50–55,62,63]. Intervention characteristics [41–63] are presented in Table 2. The definitions of nutritional status and frailty varied between the studies, indicating the necessity for standardised terminology in prehabilitation research and reflecting the variety in methodological approaches. Barberan-Garcia et al. [43], used BMI to measure nutritional health and used the American Society of Anaesthesiologists (ASA) score III/IV or a Duke Activity health Index score of ≤46 to categorise frailty. Alternatively, the Groningen Frailty Index (GFI) with a value of ≥4 was used by Berkel et al. [59] to categorise patients as frail. The Geriatric-8 (G8) score of ≤14, which indicates a more thorough evaluation of the frailty components, or at least one positive Fried frailty criterion was used by Bojesen et al. [60] to define frailty. Nutritional assessments also differed; for example, Bousquet-Dion et al. [44] used serum albumin concentrations,

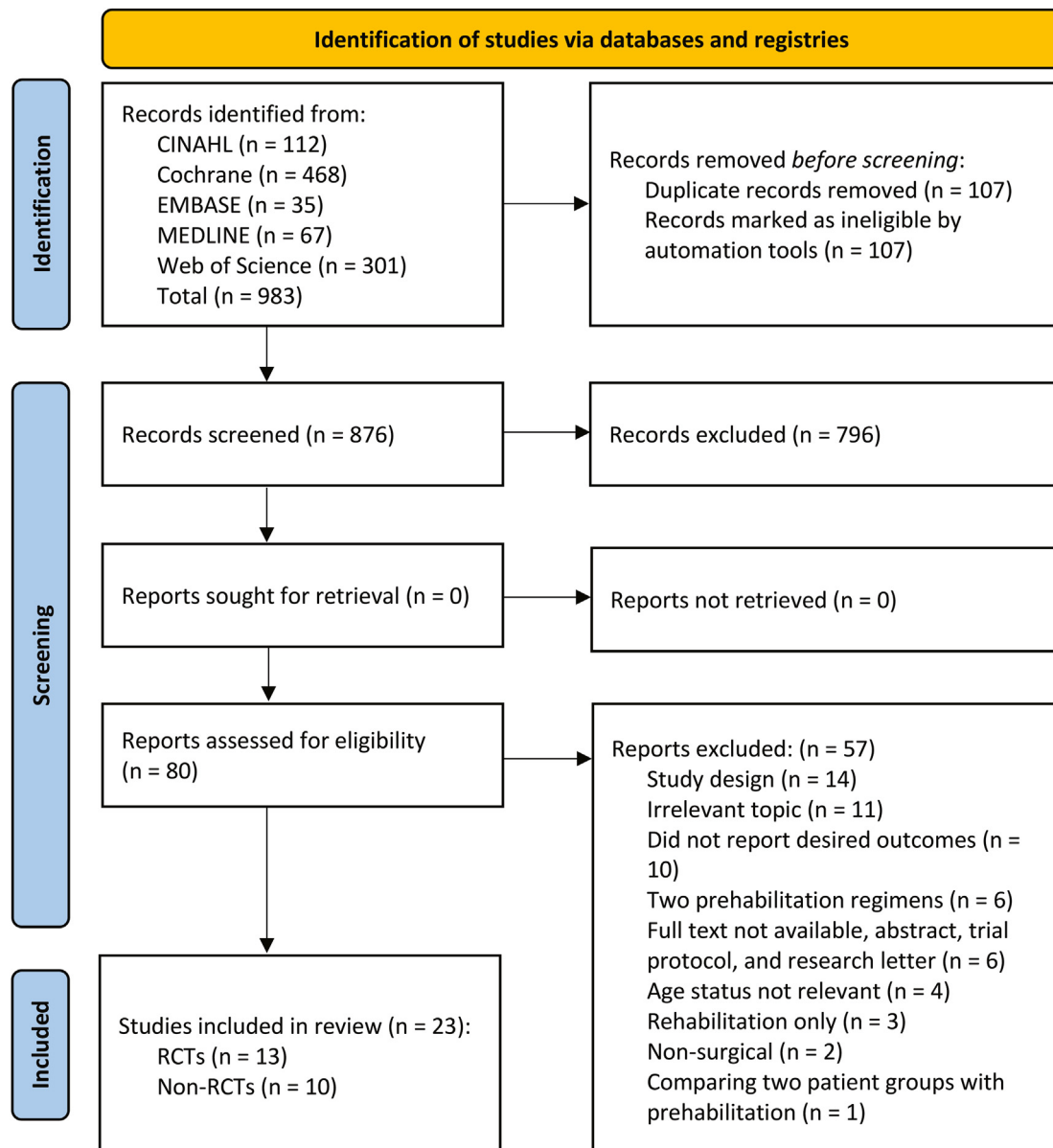


Fig. 1. PRISMA flow diagram.

Table 2

Summary of the characteristics of the studies included in this review and their clinical outcomes.

Study	Prehabilita-tion modality	Prehabilita-tion duration	Prehabilita-tion setting	Exercise frequency (session/week)	Control Group	Primary outcome	Secondary outcomes		Attrition rate for prehabilitation group ^c	Comments
						Compliance %	Post-Op outcomes Events (%)	QoL Mean ± SD		
Barberan-Garcia et al., 2018 [43]	Multi-Modal E – N - P	≥4 weeks	Supervised and home based	1-3/week	Standard preoperative care	NS	I = 19 (31%) ^a C = 39 (62%) ^a	C = 469 ± 109 I = 473 ± 91	NS	<ul style="list-style-type: none"> Overall post-Op values. QoL was reported in meters, compared with control group at pre-surgery stage of 6MWT.
Berkel et al., 2021 [59]	Uni-Modal E	3 weeks	Partially supervised	3/week	Standard preoperative care	90%	I = 12 (43%) ^b C = 21 (72%) ^b	NS	11.7%	<ul style="list-style-type: none"> The compliance percentage reflects adherence to supervised training sessions. Attrition rates reflect the missing session.
Bojesen et al., 2022 [60]	Multi-Modal E – N	≥4 weeks	Supervised	3/week	None	87%	NS	NS	13.6%	<ul style="list-style-type: none"> One arm only to investigate the feasibility. The compliance percentage represents the adherence of participants to the prescribed training sessions
Bousquet-Dion et al., 2018 [44]	Multi-Modal E – N - P	4 weeks	Supervised and home based	4-5/week	Rehabilitation	I = 99% C = 81.5%	I = 14 (38%) C = 8 (31%)	NS	2.7%	<ul style="list-style-type: none"> Compliance was calculated by the mean value derived from N and E values. Prehab compliance was taken from pre-Op period only. Rehab compliance was taken from the first 4th weeks post-Op.
Bruns et al., 2019 [46]	Multi-Modal E – N	18–32 days	Home-based	6/week	None	78.5%	NS	Baseline = 462.5 ± 82.7 Pre-surgery = 488.2 ± 93.1	24%	<ul style="list-style-type: none"> The exercise sessions were reported by average number. Compliance was calculated by the mean value derived from N and E values. QoL was reported in meters, compared with control group at pre-surgery stage of 6MWT.
Burden et al., 2017 [42]	Uni-Modal N	≥5 days	Home-based	None	Placebo	I = 74%	I = 11 (20%) ^b C = 17 (38%) ^b	NS	30.4%	<ul style="list-style-type: none"> Rehab compliance was not reported. Infection at the surgical site represents a post-operative complication.
Carli et al., 2020 [52]	Multi-Modal E – N - P	4 weeks	Supervised and home- based	1/week	Rehabilitation	I = 68% C = 14%	I = 25 (45.5%) C = 25 (45.5%)	I = 336.4 ± 121.8 C = 286.1 ± 105.1	NA	<ul style="list-style-type: none"> Compliance was reported in Mean SD. QoL was reported difference between Baseline- and pre-surgery 6MWT in meters.
Franssen et al., 2022 [61]	Multi-Modal E – N	4 weeks	Home-based	3-4/week	None	100%	NS	NS	NA	<ul style="list-style-type: none"> Age and ASA score differences existed between the groups at baseline. One arm only to investigate the feasibility. The compliance percentage represents the adherence of participants to the prescribed training sessions
Gillis et al., 2014 [41]	Multi-Modal E – N - P	4 weeks	Home-based	3/week	Rehabilitation	I = 78% C = 31%	I = 12 (32%) C = 17 (44%)	NS	26.5%	<ul style="list-style-type: none"> Prehab compliance was taken from pre-Op period only. Rehab compliance was taken from the first 4th weeks post-Op.

(continued on next page)

Table 2 (continued)

Study	Prehabilita-tion modality	Prehabilita-tion duration	Prehabilita-tion setting	Exercise frequency (session/week)	Control Group	Primary outcome	Secondary outcomes		Attrition rate for prehabilitation group ^c %	Comments
						Compliance %	Post-Op outcomes Events (%)	QoL Mean ± SD		
Howard et al., 2019 [47]	Multi-Modal E – N - P	≥2 weeks	Home-based	NS	NS	I = 70%	I = 12 (30%) C = 29 (39%)	NS	35.2%	<ul style="list-style-type: none"> Rehab compliance was not reported. Post-Op represented all complications including minor, major, and deaths. The emergency group was included in this study; however, no comparative results were analysed for this group. Significant statistical difference in ASA classification between the two patient groups in the trial. Control group compliance was not reported.
Janssen et al., 2019 [48]	Multi-Modal E – N - P	5 weeks	Home-based	NS	ERAS	73.9%	I = 109 (40.8%) C = 133 (36.9%)	NS	29.7%	<ul style="list-style-type: none"> Significant statistical difference in age between the two patient groups in the trial. Intervention group: higher comorbidity, lower baseline performance compared to standard care group. Control compliance was not reported. QoL was reported difference in the loss of lean mass between the two groups in percentage.
Karlsson et al., 2019 [49]	Multi-Modal E – N	≥2 weeks	Supervised and home-based	2–3/week	Standard preoperative care	97%	I = 6 (60%) C = 2 (18.2%)	NS	3.4%	
López-Rodríguez-Arias et al., 2021 [55]	Multi-Modal E – N - P	29 days	Home-based	≥2/week	Standard post-operative care	NS	I = 2 (20%) C = 5 (50%)	I = 1.7 ± 2.32 C = 7.1 ± 7.7	NA	<ul style="list-style-type: none"> Significant statistical difference in age between the colorectal and prostate cancer groups in the trial. QoL was reported difference between Baseline- and pre-surgery 6MTT in meters. QoL was reported difference between Baseline and pre-surgery 6MWT in meters. Post-intervention QoL was reported difference between two groups 6MWT in meters. QoL was assessed using QOR-40 to compare the physical well-being between the two groups. QoL was reported in Mean ± SD between pre- and post-operation. Volunteers included, may not a cancer or/and surgical patients. The compliance percentage reflects adherence to both supervised and home-based sessions. Adherence to the preoperative exercise sessions was (92.7%). Risk of including patient with a “good” fitness level in the Prehab group.
Loughney et al., 2019 [50]	Uni-Modal E	4 weeks	Supervised	3–5/week	None	75%	NS	Baseline = 719 ± 185 Pre-surgery = 746 ± 173	28.5%	
Ngo-Huang et al., 2019 [51]	Multi-Modal E – N	16 weeks	Home-based	2/week	None	NS	NS	Baseline = 462.5 ± 82.7 ^b Pre-surgery = 488.2 ± 93.1 ^b	NS	
Northgraves et al., 2019 [53]	Uni-Modal E	2 weeks	Supervised	3/week	Standard preoperative care	89.6%	NS	I = 473.7 ± 93 C = 460.7 ± 106	11.0%	
Peng et al., 2021 [54]	Uni-Modal E	2 weeks	Home-based	NS	Rehabilitation	NS	I = 8 (7.1%) C = 11 (10.8%)	I = 43.4 ± 5.3 ^b C = 39.2 ± 6.1 ^b	NA	
Singh et al., 2018 [45]	Uni-Modal E	10 weeks	Supervised	2/week	None	70%	NS	Pre-Op = 36.7 ± 29.2 ^b Post-Op = 21.6 ± 25.7 ^b	30%	
Steffens et al., 2021 [56]	Uni-Modal E	≥2 weeks	Supervised and home-based	5/week	Standard preoperative care	64%	I = 10 (90.9%) C = 7 (63.6%)	NS	NA	
Taha et al., 2021 [57]	Uni-Modal E	3–6 weeks	Supervised and home-based	3/week	Standard post-operative care	73%	NS	NS	NA	

Author(s) [ref]	Study Design	Duration	Supervision	Frequency	Preoperative care	Adherence (%)	Sample Size (n)	Significance	Outcome
Tweed et al., 2021 [58]	Multi-Modal E - N	4 weeks	Supervised	3/week	None	66.7%	2 (33%)	NS	One arm only to investigate the feasibility.
Waller et al., 2021 [62]	Multi-Modal E - N - P	≥2 weeks	Home-based	3/week	Standard preoperative care	84%	NS	I = 85.6 ± 100.4 ^b C = 13.2 ± 29.77 ^b	QoL was reported difference between Baseline- and pre-surgery 6MWT in meters.
Waterland et al., 2022 [63]	Multi-Modal E - N - P	2–6 weeks	Supervised and home-based	3/week	None	61%	22 (69%)	Baseline = 451 ± 103.5 Pre-surgery = 471 ± 106.4	One arm only to investigate the feasibility. The compliance percentage represents the adherence of participants to the prescribed home-based training sessions. Post-op represents the patients suffered at least one postoperative complication. QoL was reported difference between Baseline- and pre-surgery 6MWT in meters

E: Exercise; **N:** Nutrition; **P:** Psychology; **SD:** Standard Deviation; **Op:** Operation; **QoL:** Quality of Life; **I:** Intervention “Prehabilitation”; **C:** Control “Rehabilitation or Standard treatment”; **NS:** Not Stated; **NA:** Not Applicable; **6MWT:** 6-Minutes Walking Test; **6MITT:** 6-Minutes Time Trial; **6MWD:** 6-Min Walk Distance; **ERAS:** Enhance Recovery After Surgery; **ASA:** American Society of Anesthesiologists; **QOR-40:** Quality of Recovery Score.
^a Statistically significant **P** < 0.001.
^b Statistically significant **P** < 0.05.
^c The attrition rate pertains to individuals who failed to comply with the programme, did not return the leaflets, or neglected to complete and return the questionnaires.

while Carli et al. [52] used BMI in addition to the Fried frailty index, which classifies frailty according to certain criteria like inadvertent weight loss and weakened grip strength. In the study of Gillis et al. [41], physical status was evaluated using the ASA score rather than a clear definition of frailty.

3.3. Prehabilitation interventions

Prehabilitation interventions were categorised by exercise, nutritional support, psychological support, or smoking cessation. Two studies [43,44] combined aerobic and resistance exercise to reduce sedentary behaviour and enhance physical fitness. Home-based programmes were a popular option in terms of exercise treatments [41,42,46–48,59,61,62] with eight studies reporting home-based intervention involving alternating between aerobic and resistance training. Aerobic exercise encompasses activities such as walking, jogging, swimming, or cycling, which can be chosen by the individual. Resistance training is a series of exercises that target the major muscle groups. Another approach was supervised high-intensity interval training (HIIT), with the goals of improving muscular strength and aerobic capacity being the subject of studies two studies [58,60]. Furthermore, three studies [45,52,59] included a combined aerobic and resistance exercise intervention. These studies included walking, cycling, and resistance training to increase overall fitness levels.

Dietary counselling and protein supplementation were frequently the core of nutritional support treatments. To achieve dietary requirements and ensure adequate consumption of protein, three studies [41,44,60] highlighted the significance of protein supplementation. Preoperative nutritional counselling was incorporated by two studies [61,62] to optimise protein and calorie intake, customised to individual’s requirements. Control groups in these studies typically received standard care or rehabilitation. These control groups often included basic preoperative information and nutritional advice without the structured exercise or psychological interventions present in the prehabilitation groups. Supplementary Table 3 provides further details and overview of the prehabilitation interventions.

3.4. Adherence and perceptions towards prehabilitation programmes

As mentioned above, adherence to prehabilitation programmes was reported in the 19 studies [41,42,44–50,52,53,56–63], with a total of 723 patients undergoing major abdominal surgery, as a ratio of attended exercise sessions to the total number of planned sessions. The monitoring of adherence to prehabilitation interventions was performed using a variety of methods, and numerous studies utilised comparable measures. The adherence to the prescribed exercise regimen was evaluated in five studies [41,52,53,59,60] through self-reported exercise logs, as well as attendance at supervised sessions. Also, regular reviews and follow-ups were implemented to ensure and promote adherence with the prescribed exercise programme. The importance of following nutritional recommendations was investigated by monitoring adherence by keeping track of the use of oral nutritional supplements [42]. Several studies have employed pedometers, self-reported activity diaries, motivational interviews, electronic communication, and attendance records [43–45,47]. Advanced technology approaches such as internet platforms and tele-monitoring systems have been utilised by others [46,61]. Supervised sessions and direct phone conversations were used to monitor participant’s adherence [50,56–58]. In three studies [48,49,63] participant self-reports and online periodic check-ins were used to monitor and assess adherence. Participants were

required to record their exercise activities and any difficulties they encountered, which were subsequently evaluated at regular intervals by the study team.

Ten of the included studies [42,44,46,48,50,56,58,60,61,63] established an objective degree of adherence that was between 65% and 80% as a benchmark for adherence. Prehabilitation was used in seven studies [42,45,50,53,56,57,59] as a “unimodal” intervention; six of these studies [45,50,53,56,57,59] limited the intervention to “exercise”, while a single study [42] used “nutritional” prehabilitation. Within a range of 64%–90%, the patients’ overall mean (SD) adherence to unimodal prehabilitation was 76.5% ± 9.7%. Twelve studies [41,44,46–49,52,58,60–63] implemented “multimodal” prehabilitation of which seven [41,44,47,48,52,62,63] combined exercise, nutrition, and psychological prehabilitation, while the remaining five [46,49,58,60,61] combined exercise and nutrition. The overall mean (SD) adherence to multimodal prehabilitation was 80.2% ± 13.2%, with a range of 61%–100%. Adherence to the prehabilitation modality is displayed in Fig. 2 A.

Eight studies [41,42,46–48,59,61,62] used “home-based” prehabilitation, with an overall mean (SD) adherence rate of 81.1% ± 9.9% and a range of 70%–100%. Additionally, a “supervised” prehabilitation setting was used in five studies [45,50,53,58,60], with an overall mean (SD) adherence rate of 77.7% ± 10.2%, ranging from 67% to 89.6%. Six studies [44,49,52,56,57,63] using a mixed method setting “home-based with supervision” prehabilitation programme had an overall mean (SD) adherence rate of 77% ± 16.7% and an adherence range of 62%–99%. Overall mean adherence rate for each of the three prehabilitation settings utilised in the included papers is displayed in Fig. 2 B.

Prehabilitation programmes lasting one to three weeks had an overall mean (SD) adherence rate of 78% ± 12.3%, with a range of 64%–97%. The prehabilitation period varied between 1 and 3 weeks in seven trials [42,46,47,49,53,56,59]. Twelve studies [41,44,45,48,50,52,57,58,60–63] implemented prehabilitation programmes lasting more than three weeks. The overall mean (SD) patient adherence rate with these programmes was 80.4% ± 12.2%, ranging from 61% to 100%. Overall mean adherence rate in relation to duration of prehabilitation in the included papers is displayed in Fig. 2C.

Sixteen studies documented the perspectives, preferences, and feedback of patients, informing how these factors have impacted their adherence [42,44–46,48–50,53,56–63]. In terms of patient motivation and perceptions regarding prehabilitation and exercise sessions, five studies [46,48,59–61] indicated that patients felt either overwhelmed by the sessions or unmotivated, preferring to undergo surgery as soon as possible. Conversely, three studies [49,56,61] reported positive feedback from patients who felt that the exercise sessions made them stronger and more confident in moving around after surgery and in managing activities like getting in and out of hospital beds. The main reasons cited for non-adherence across studies included patients’ beliefs that they were “good enough” without the extra preparation, as well as competing work and family commitments, medical issues, holidays, and unexpected advancement in their surgery dates [45,48,50,53,57,58,62,63]. Regarding preference for the setting of exercise sessions, five studies [46,49,57,61,63] reported a preference for home-based sessions or greater motivation for home-based sessions. On the other hand, two studies [44,60] showed that patients valued supervised in-person exercise settings, while a third [59] indicated a general preference for partially supervised sessions. Patient perspectives, opinions, and feedback are presented in Table 3.

3.5. Postoperative complications

Fourteen studies [41–44,47–49,52,54–56,58,59,63], with 1628 patients reported data on postoperative complications. Ten RCTs

[41–44,49,52,54–56,59] compared the effect of prehabilitation with rehabilitation or standard care. Berkel et al. [59] and Burden et al. [42] reported a significant reduction in the number of postoperative complications in the prehabilitation group compared with the rehabilitation or standard care groups (12 and 11 vs. (21 and 17), respectively ($P < 0.05$). Also, Barberan-Garcia et al. [43] showed that prehabilitation significantly reduced the number of postoperative complications compared with standard preoperative care, (19 vs. 39, $P < 0.001$).

In two cohort studies with two arms [47,48], prehabilitation did not significantly differ from rehabilitation or standard care regarding outcomes. Similarly, within the same groups of two single-arm studies [58,63], no significant differences in outcomes were observed. Moreover, the meta-analysis comparing prehabilitation with rehabilitation or standard care for patients undergoing major abdominal surgery did not demonstrate a statistically significant reduction in the incidence of postoperative complications (OR 0.75, 95% CI 0.48 to 1.17, $P = 0.43$, Fig. 3 A). There was a notable degree of heterogeneity among the data ($I^2 = 65\%$).

3.6. Quality of recovery and factors impacting on quality of life

QoL outcomes are directly linked to the extensively validated QoR score, a key postoperative recovery measure effective up to three months post-surgery [64,65]. Peng et al. [54] demonstrated a significant improvement in the QoR-40 score (43.4 ± 5.3 vs. 39.2 ± 6.1 , $P < 0.05$) between the prehabilitation and rehabilitation groups.

3.6.1. Lean mass

The assessment of body composition, specifically lean mass, was performed in two separate studies [45,55]. Singh et al. [45] employed dual-energy X-ray absorptiometry to evaluate various parameters including total body lean mass, fat mass, and percentage of body fat. On the other hand, López-Rodríguez-Arias et al. [55] employed multifrequency bio-electrical impedance analysis. This method enabled the measurement of changes in patient weight, lean mass, and fat mass. There was no statistically significant difference when preoperative and postoperative lean mass were compared (55.7 ± 10.6 kg vs. 54.7 ± 10.5 kg, $P = 0.190$) [45]. Furthermore, when comparing the prehabilitation group with the standard care group, López-Rodríguez-Arias et al. [55] found that the decrease in the total lean mass was not statistically significant ($1.7 \pm 2.32\%$ vs $7.1 \pm 7.7\%$, $P = 0.17$).

3.6.2. 6MWT

Data on 6MWT were reported in eight studies [43,46,50–53,62,63]. Ngo-Huang et al. [51] showed an improvement in 6MWT, while a study by Loughney et al. [50] showed no significant improvement in the mean difference in 6-MWT between baseline and pre-surgery values (719 ± 185 vs. 746 ± 173 m, $P = 0.193$) and (462.5 ± 82.7 vs. 488.2 ± 93.2 m, $P < 0.05$), respectively. Also, Waller et al. [62] showed a significant performance improvement in 6MWT between prehabilitation and standard preoperative care (85.6 ± 100.4 vs. 13.2 ± 29.8 m, $P < 0.05$).

A meta-analysis of RCTs showed a significant improvement in mean pre-surgical 6MWT in prehabilitation groups compared with patients who received rehabilitation or standard care (MD +29.4 m, 95% CI 5.58 to 53.3, $P = 0.02$, $I^2 = 39\%$, Fig. 3b).

3.7. Risk of bias and quality of the evidence

With regard to the RCTs [41–44,49,52–57,59,62], nine studies [41,42,44,53–57,62] were classified as having a “high risk of bias”, and three studies [49,52,59] classified as having a “some concerns”,

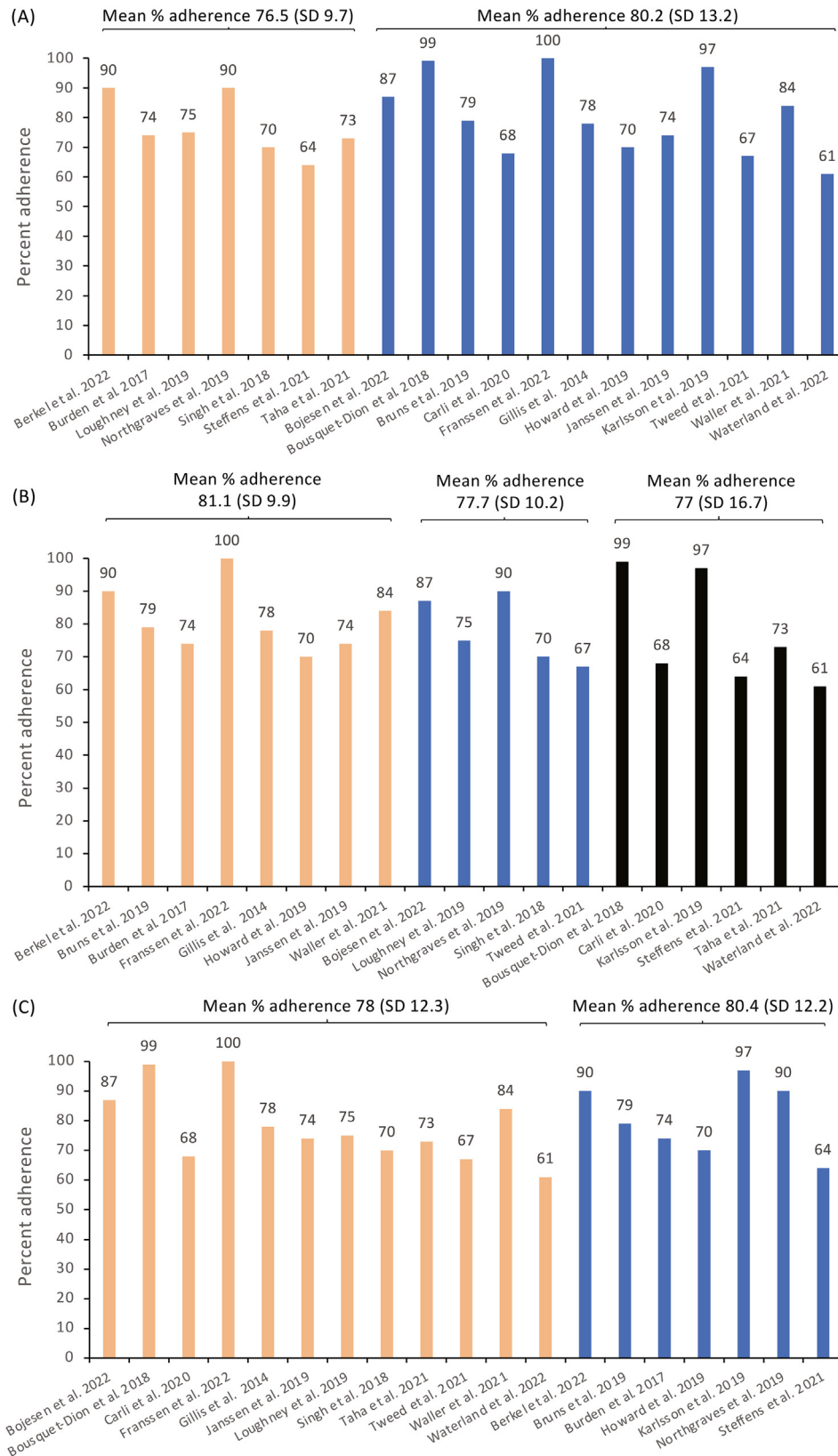


Fig. 2. (A): Reported or calculated mean percentage adherence to prehabilitation according to studies that used a unimodal (orange bars) or multimodal (blue bars) approach. (B): Reported or calculated mean percentage adherence to prehabilitation according to studies used home-based setting (orange bars), supervised setting (blue bars), and mixed approach setting (black bars). (C): Reported or calculated mean percentage adherence to prehabilitation according to studies with a duration of more than 3 weeks (orange bars), and a duration from 1 to 3 weeks (blue bars). The mean pooled percentage adherence by setting is indicated above the brackets. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

Table 3
Summary of patients' perceptions towards prehabilitation programme.

Study	Patient's perceptions/feedback/preferences
Berkel et al., 2021 [59]	<ul style="list-style-type: none"> No desire to participate in prehabilitation programme. Inability to do cycling exercise.
Bojesen et al., 2022 [60]	<ul style="list-style-type: none"> Wanted to have surgery as soon as possible. Felt overburden by extra appointments and data reporting. Difficulties with the weight-dependent dosages of protein supplements.
Bousquet-Dion et al., 2018 [44]	<ul style="list-style-type: none"> Patients appreciated supervised sessions.
Bruns et al., 2019 [46]	<ul style="list-style-type: none"> Patients appreciated supervised sessions. Felt overburden by the exercise sessions. Busy or forgot to have the exercise sessions. All patients preferred home-based programme.
Burden et al., 2017 [42]	<ul style="list-style-type: none"> Some of participants reported that they did not tolerate the supplements due to unpalatability.
Franssen et al., 2022 [61]	<ul style="list-style-type: none"> Most patients felt that home-based exercises were useful. Most patients were motivated to perform the home-based exercises. Most patients felt that home-based exercises were time-consuming. Most patients felt that weekly evaluations by telephone were beneficial to them. Most patients felt that the tele-prehabilitation programme prepared them well for the surgical treatment.
Janssen et al., 2019 [48]	<ul style="list-style-type: none"> Patients did not comply because they thought that their physical condition was good enough. Felt overburden by the exercise sessions.
Karlsson et al., 2019 [49]	<ul style="list-style-type: none"> Most patients felt that the exercises were time-consuming. Most patients were motivated and comfortable to exercise at/nearby to their homes. Most patients felt better prepared physically for their surgical treatment after the intervention.
Loughney et al., 2019 [50]	<ul style="list-style-type: none"> Reasons for non-compliance were advancement of the date of surgery, work commitments, holidays, or medical issues.
Northgraves et al., 2019 [53]	<ul style="list-style-type: none"> Reasons for non-compliance were advancement of the date of surgery, work commitments, holidays, or medical issues.
Singh et al., 2018 [45]	<ul style="list-style-type: none"> Patients reported feeling unwell as the main reason for not attending the exercise training sessions.
Steffens et al., 2021 [56]	<ul style="list-style-type: none"> It helped them manage moving, getting in and out of hospital bed. They felt stronger and more confident to move after the operation.
Taha et al., 2021 [57]	<ul style="list-style-type: none"> Reasons for non-compliance were advancement of the date of surgery, work commitments, holidays, medical issues, lack of motivation, or the weather.
Tweed et al., 2021 [58]	<ul style="list-style-type: none"> Reason for non-compliance was advancement of the date of surgery.
Waller et al., 2021 [62]	<ul style="list-style-type: none"> Reasons for non-compliance to the mindfulness intervention included participants reporting good baseline mental health, finding the App unhelpful, and only using the App when they felt they needed to, or App connection issues.
Waterland et al., 2022 [63]	<ul style="list-style-type: none"> Reasons for non-compliance to the exercise programme were fatigue, work and family commitments, medical issues, symptoms of cancer (e.g., pain), weather, boredom, or poor motivation when setbacks occurred (e.g., surgery date postponed).

while only one study [43] was rated as having a “low risk of bias”. Most of the included studies [41,42,44,53–57,62] were rated as having a “high risk” regarding the blinding of either participants or assessors. Three studies [49,52,59] were considered “unclear” with regard to allocation concealment, and another three studies [41,42,53] were considered “unclear” regarding reporting bias, while two others were classified as “unclear” for attrition rate [41] and other biases [44]. The risk of bias data for the RCTs are shown in Fig. 4.

Regarding the observational studies [45–48,50,51,58,60,61,63], five were classified as having a ‘high risk of bias’ [45,51,58,61,63], four were rated as having a ‘medium risk of bias’ [46,48,50,60], and one [47] was considered to have a ‘low risk of bias’. Because the majority of the included studies were single arm studies [45,46,50,51,58,60,61,63], they could not be evaluated in terms of comparability and the selection of the non-exposed cohort. Table 4 shows the quality assessment for the cohort studies.

In terms of quality of evidence, the certainty regarding risk of postoperative complications was downgraded to “low” due to several factors: most studies included in the meta-analysis were rated as having a “high risk” of bias, observational studies were incorporated, and there was significant heterogeneity among the studies. The analysis for the 6-MWT was similarly downgraded to a ‘very low’ level of certainty. This decision was based on the ‘high risk’ of bias in included studies, substantial heterogeneity, and the wide range of the confidence interval range (Table 5).

4. Discussion

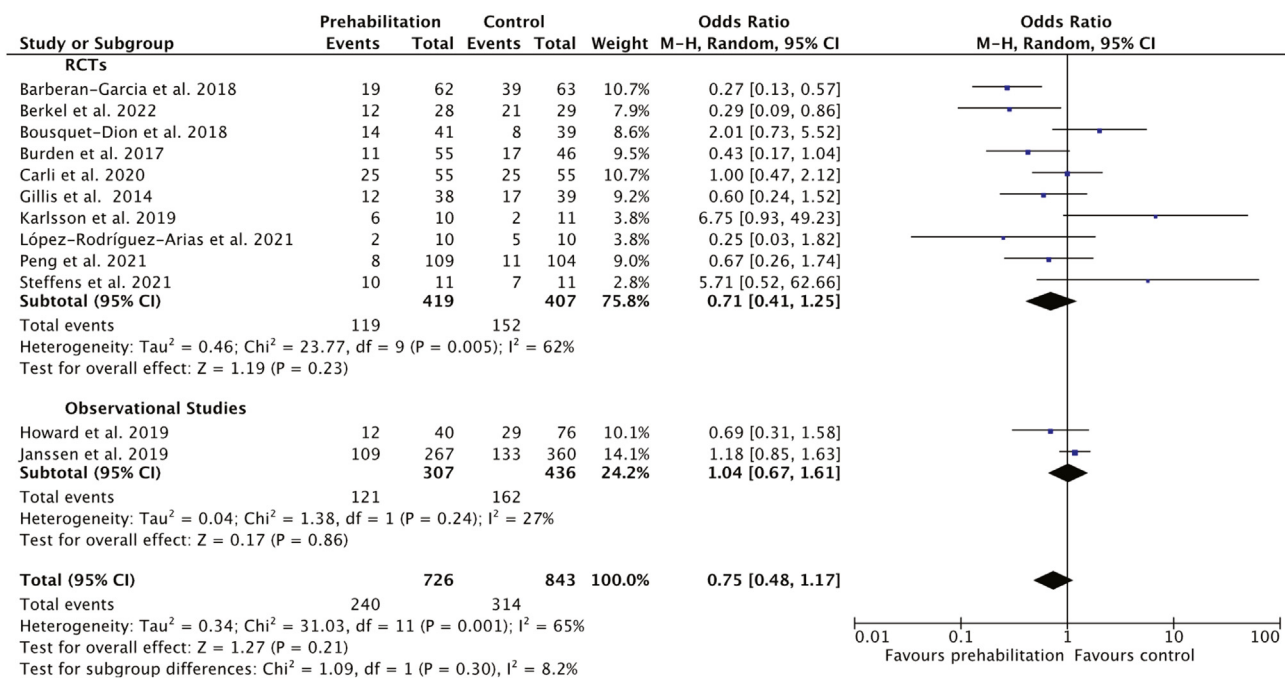
4.1. Findings of our study

This systematic review and meta-analysis of 23 studies and 1849 frail and high-risk patients undergoing major abdominal surgery

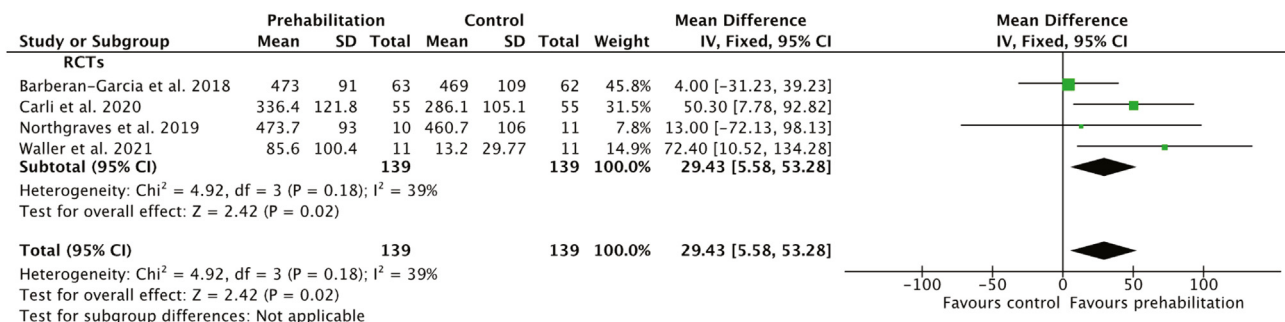
evaluated the adherence to prehabilitation and identifying interventions that are acceptable. Moreover, it assessed the overall efficacy of prehabilitation. The findings indicate that overall adherence to prehabilitation was good, with more than 75% adherence observed across a diverse range of modalities, settings, and durations among patients preparing for major abdominal surgery. There was relatively strong evidence that several factors negatively affected adherence to prehabilitation programs. These include patients' desire for expedited surgery, self-assessments of being physically fit, personal and professional obligations, health issues, holidays, and advancement of surgery dates. Studies providing patient perspectives indicated a preference for home-based exercise programs over supervised settings. Additionally, our findings, although based on low-quality evidence, suggest that prehabilitation was not associated with a significant decrease in postoperative complications when compared with rehabilitation or standard perioperative care for major abdominal surgery. Regarding QoL and the factors impacting QoL, prehabilitation has shown a statistically significant improvement in the 6MWT outcomes by 29.4 m, but this conclusion was drawn from evidence with a very low certainty level. It was also noted that patients, categorised by age or a defined frailty score, faced an increased risk of complications during treatment. The inclusion of several different abdominal surgical procedures, predominantly performed on patients with cancer, suggest that the results may be generalised to this patient group.

4.2. Factors influencing treatment adherence

Adherence to treatment is a crucial determinant that can impact the outcome [66,67]. Inadequate adherence to treatment has been observed in various healthcare fields, including physiotherapy [68–70]. The factors of intention to engage, self-motivation, self-



(A) Severe postoperative complications



(B) 6-minute walk test

Fig. 3. Forest plots of outcomes. (A) Severe complications, (B) 6-minute walk test.

efficacy, previous adherence behaviour, and social support are significant indicators of adherence to home-based physical therapies. As a result, adherence levels have been consistently high in various settings, modalities, and durations [71,72]. This led to increased total energy intake, which was associated with clinical benefits (>75%) in this systematic review. This level of adherence is comparable to that observed with pharmaceuticals [73,74]. It is important to note that the studies included herein describe both supervised and unsupervised exercise sessions. Exercise conducted in clinical settings or at home under professional supervision offer several advantages, including improved adherence and adaptability, which are particularly valuable for frail, older adults [75–77]. However, supervised sessions in clinics or hospitals can be hampered by logistical issues such as transportation availability and cost [75,77]. In addition, when therapy is offered in clinics or hospitals, the availability of transportation and the costs of transportation present significant impediments to adherence [21,26,78]. Nevertheless, this systematic review and meta-analysis showed that the overall mean adherence rates for supervised and home-based sessions were similar, at 81% and 77.6%, respectively.

Fig. 5 highlights selected factors affecting patient adherence, emphasising its critical role for the success of prehabilitation programs and overall improvement. For the analysis of postoperative data, evidence from observational studies and RCTs was examined separately, as well as in a combined analysis, to offer a more comprehensive view of the data.

4.3. Advantages of prehabilitation for postoperative outcomes

The focus of optimising perioperative care has been on reducing the surgical stress response and enhancing postoperative mobility and nutritional intake within the framework of Enhanced Recovery After Surgery (ERAS) care [79,80]. Recently, this concept has been expanded into the preoperative period, aiming to enhance patients' functional and nutritional status before undergoing surgery [81]. A 2019 systematic review and meta-analysis of 15 RCTs, involving 457 patients in the prehabilitation group and 450 patients in the control group, assessed the impact of prehabilitation on postoperative outcomes following major abdominal surgery [82]. The results indicated a significant reduction in pulmonary and overall

	Allocation concealment (selection bias)	Blinding of participants and personnel (performance bias)	Blinding of outcome assessment (detection bias)	Incomplete outcome data (attrition bias)	Selective reporting (reporting bias)	Other bias
Barberan-Garcia et al. 2018	+	+	+	+	+	+
Berkel et al. 2022	?	+	+	+	+	+
Bousquet-Dion et al. 2018	+	-	+	+	+	?
Burden et al. 2017	+	+	-	+	?	+
Carli et al. 2020	?	+	+	+	+	+
Gillis et al. 2014	+	-	+	?	?	+
Karlsson et al. 2019	?	+	+	+	+	+
López-Rodríguez-Arias et al. 2021	+	-	-	+	+	+
Northgraves et al. 2019	+	-	-	+	?	+
Peng et al. 2021	+	-	+	+	+	+
Steffens et al. 2021	+	-	+	+	+	+
Taha et al. 2021	+	-	+	+	+	+
Waller et al. 2021	+	-	+	+	+	+

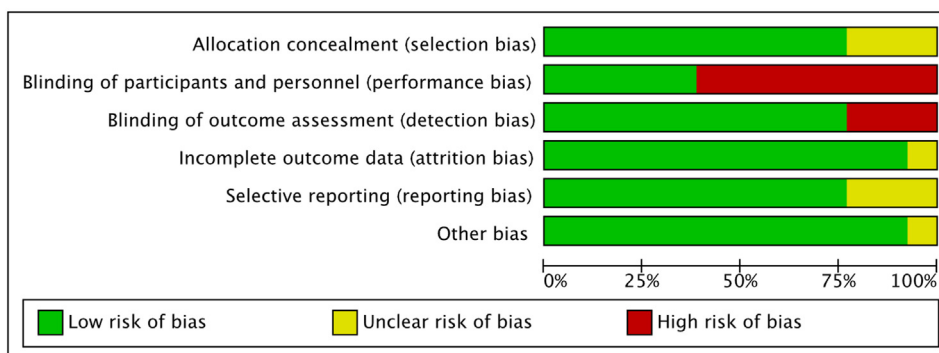


Fig. 4. Risk of bias of randomised clinical trials.

postoperative complications in the prehabilitation group (OR 0.40, 95% CI 0.23 to 0.68, $I^2 = 0%$, $P = 0.0007$; and OR 0.63, 95% CI 0.46 to 0.87, $I^2 = 34%$, $P = 0.005$, respectively) [82]. Additionally, multimodal prehabilitation was shown to improve postoperative outcomes, with a notable reduction in overall complications as

evidence by an analysis that included over 4000 patients from 13 trials and 12 observational studies (RR = 0.88, 95% CI 0.78 to 0.99, $P = 0.034$) [83]. Recently, it has been recommended that all studies in perioperative medicine, including those on prehabilitation, should be undertaken in the context of an established and well-

Table 4
Risk of bias assessment for non-RCTs studies using Newcastle Ottawa Scale tool.

Study	Risk of bias assessment			
	Selection	Comparability	Outcome/exposure	Overall score
Bojesen et al., 2022 [60]	★★	-	★★	4
Bruns et al., 2019 [46]	★★	-	★★	4
Franssen et al., 2022 [61]	★	-	★	2
Howard et al., 2019 [47]	★★★	★	★★★	7
Janssen et al., 2019 [48]	★★	★	★	4
Loughney et al., 2019 [50]	★★	-	★★	4
Ngo-Huang et al., 2019 [51]	★	-	★★	3
Singh et al., 2018 [45]	★	-	★★	3
Tweed et al., 2021 [58]	★★	-	★	3
Waterland et al., 2022 [63]	★	-	★★	3

Risk of bias.
6 or above: low risk.
4 to 5: medium risk.
1 to 3: high risk.

Table 5
Postoperative complications and 6-minute walk test.

Prehabilitation compared with placebo for patients undergoing major abdominal surgery					
Patient or population: Patients undergoing major abdominal surgery					
Setting: Surgical patients					
Intervention: Prehabilitation					
Comparison: ERAS, placebo, rehabilitation, standard preoperative care, or standard postoperative care					
Outcomes	N ^o of participants (studies) Follow-up	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with placebo	Risk difference with Prehabilitation
Postoperative complications	1569 (10 RCTs) (2 OBs)	⊕⊕○○ Low ^{a,b,c}	OR 0.75 (0.48–1.17)	372 per 1000	64 fewer per 1000 (151 fewer to 37 more)
6-min walk test	278 (4 RCTs)	⊕○○○ Very low ^{a,d,e}	–	The mean 6-MWT was 29.43 m	MD 29.43 m higher (5.58 higher to 53.28 higher)

***The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI). **ERAS:** enhanced recovery after surgery; **RCT:** randomized control trial; **OB:** observational studies; **CI:** confidence interval; **OR:** odds ratio; **MD:** mean difference. **GRADE Working Group grades of evidence High certainty:** we are very confident that the true effect lies close to that of the estimate of the effect. **Moderate certainty:** we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different. **Low certainty:** our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect. **Very low certainty:** we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

- ^a Most of the included studies were rated as high risk of bias.
- ^b Observational studies were included.
- ^c Substantial heterogeneity levels between the studies were observed, $I^2 = 65\%$.
- ^d Moderate heterogeneity levels between the studies were observed, $I^2 = 39\%$.
- ^e The result of the analysis has a wide confidence interval.

defined ERAS programme in order to determine the true benefits of the intervention [80].

4.4. Impact of prehabilitation on older adults and those with frailty

There is an inconsistent body of research on prehabilitation of older adults and patients with frailty. A recently systematic review and meta-analysis, focusing on the population undergoing major abdominal surgery, assessed the impact of prehabilitation before surgery on frail patients with colorectal cancer [84]. The prehabilitation group experienced a significantly decreased incidence of complications and shorter LOS when compared to the control group (OR, 0.48; 95% CI, 0.31 to 0.75; $P = 0.001$) and (SMD, -0.38; 95% CI, -0.50 to 0.26; $P < 0.001$), respectively [84]. In contrast to this recent evidence, our meta-analysis did not show a significant effect of prehabilitation when compared with rehabilitation or standard care on postoperative complications (OR 0.75, 95% CI 0.48 to 1.17, $P = 0.43$, Fig. 3). The nature of most included studies – primarily pilot or feasibility studies with small sample sizes intended to assess trial viability in these patient groups – and the inclusion of low-quality studies may have influenced our results. This was mainly due to insufficient follow-up time, which makes it

difficult to adequately monitor for adverse effects. Our previously published paper, which included higher quality studies with more participants, presents different outcomes, showing a significant reduction in both LoS by 1.07 days and postoperative complications by up to 44% (WMD -1.07 days, 95% CI -1.60 to -0.53 days, $P < 0.0001$, $I^2 = 19\%$) and (OR 0.56, 95% CI 0.37 to 0.82, $P < 0.004$, $I^2 = 51\%$), respectively [22].

4.5. Quality of life and functional recovery through prehabilitation

Only one study included in this systematic review reported on QoR-40 [54], which showed a significant improvement in patients who underwent prehabilitation. Furthermore, considering factors that impact QoL, there was a significant improvement in the 6MWT for patients who received prehabilitation. Future research should include QoL data.

4.6. Strength and limitations of this systematic review and meta-analysis

Our systematic review and meta-analysis aimed to assess the degree of adherence and to determine whether prehabilitation were

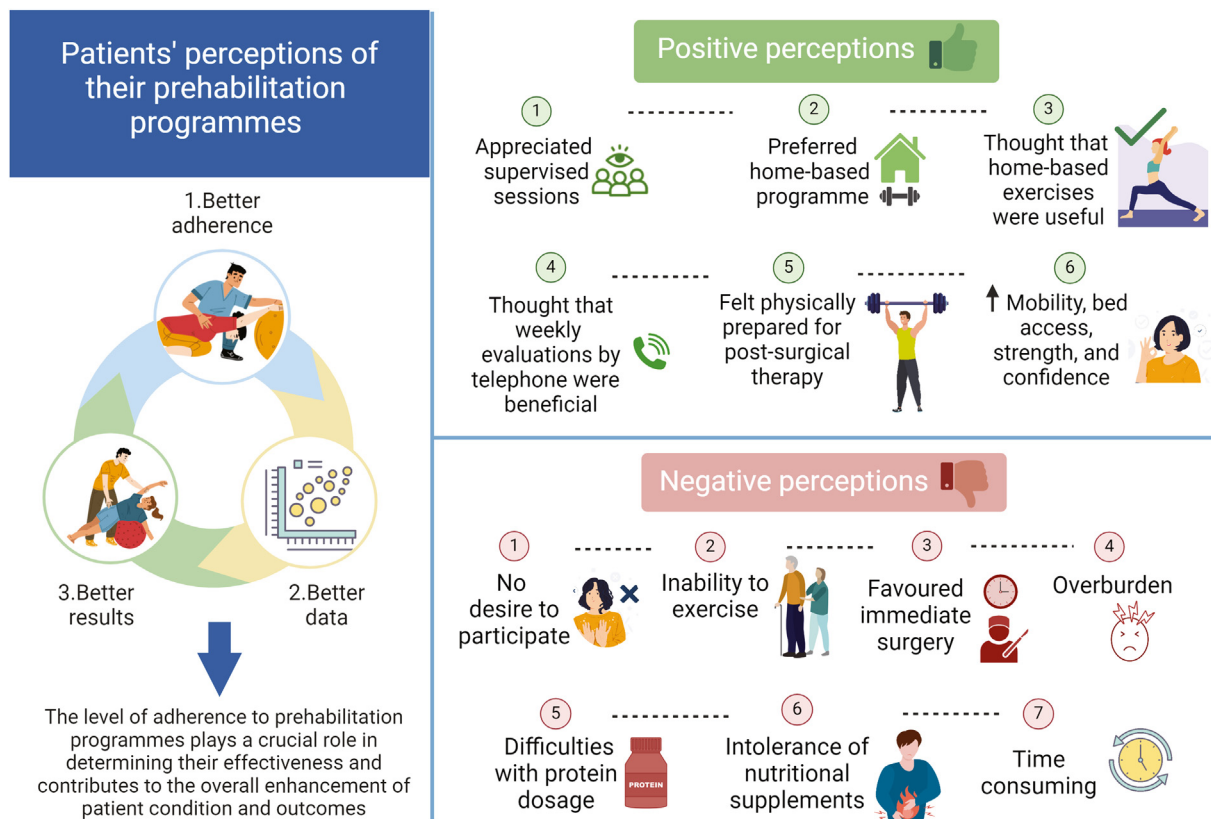


Fig. 5. Patient perceptions of prehabilitation programmes.

acceptable to high-risk and frail patients undergoing major abdominal surgery. We included all available studies (both RCTs and observational) evaluating patients' adherence to prehabilitation programmes from multiple perspectives (exercise, nutrition, and psychology) using various modalities, settings, and durations.

Although this meta-analysis has thoroughly assessed prehabilitation therapies, focusing exclusively on their use before abdominal surgery, the findings can be applied to vulnerable patients who are both frail and at high risk. However, there are several limitations that make the conclusions of this systematic review and meta-analysis less reliable. The heterogeneity between studies was high because several study designs were considered. Moreover, the majority of the included studies had a high risk of bias. The certainty of the evidence may be impacted by all of these factors. Despite that, this review has shown a good overall adherence to prehabilitation programmes (>75%), the patients' adherence was measured differently between the studies. For example, Bousquet-Dion et al. [44] implemented a combination of supervised and home-based methods in their prehabilitation programme. The level of adherence specifically measured the attendance to supervised sessions. It is also important to acknowledge that patients' preferences for their prehabilitation were reflected in the actual setting used in their study, suggesting that any unexpressed preferences to alternative settings remain unexplored. This highlights a knowledge gap regarding patient desires for different prehabilitation environments. Another limitation affecting our review is the inclusion of single-arm feasibility or pilot studies. Despite their relevance to this review, these studies are always regarded as low quality of evidence compared with RCTs, which affects the certainty of our post-operative and 6MWT analysis outcomes. Finally, the lack of detailed intervention descriptions for control groups in

many studies poses a challenge. In some cases, control groups were provided with supervised rehabilitation or physical activity guidelines, which are potentially confounding factors.

5. Conclusion

This systematic review and meta-analysis found that patients undergoing major abdominal surgery generally accepted and adhered to prehabilitation programmes. Factors negatively affecting adherence included patient desire for early surgery, perceived wellness, work and family commitments, health issues, holidays, and advancement of date for surgery. Although prehabilitation did not significantly reduce postoperative complications when compared with rehabilitation or standard perioperative care, it significantly improved the 6MWT by 29.4 m.

Ethical statement

As this was a systematic review and meta-analysis, ethical approval was not necessary.

Funding

This work was supported by the Medical Research Council [grant number MR/K00414X/1], Arthritis Research UK [grant number 19891], the National Institute for Health Research Nottingham Biomedical Research Centre [grant number NIHR203310] and the Ministry of Defence of the Czech Republic "Long Term Organization Development Plan 1011" – Clinical Disciplines II of the Military Faculty of Medicine Hradec Kralove, University of Defence, Czech Republic (Project No: DZRO-FVZ22-KLINIKA II). The

funders had no involvement in the development of the protocol, conduct or writing up of this study, or the decision to submit for publication. This work does not represent the views of the funders.

Data sharing

No original data to share. Data tables will be available upon reasonable request from AA (alyaa29@nottingham.ac.uk).

Protocol registration

The protocol for this systematic review and meta-analysis was registered with the PROSPERO database: (https://www.crd.york.ac.uk/prospero/display_record.php?RecordID=496908), and the registration number assigned was CRD42024496908.

Conference presentation

An abstract of this paper has been accepted for presentation to the Annual Congress of the European Society for Clinical Nutrition and Metabolism, Milan, September 2024 and the abstract will be published in *Clinical Nutrition ESPEN*.

Author contributions

Study design: AA, PS, CMP, DG, DNL, DO'C.
 Data collection: AA, PS, DO'C.
 Data-analysis: AA, PS.
 Data-interpretation: AA, PS, CMP, DG, DNL, DO'C.
 Writing of the manuscript: AA, PS, DNL, DO'C.
 Critical review of the manuscript: AA, PS, CMP, DG, DNL, DO'C.
 Final approval: AA, PS, CMP, DG, DNL, DO'C.
 All authors had access to the data.

Declaration of competing interests

None of the authors has a direct conflict of interest to declare. CMP has previously received honoraria and/or paid consultancy from Abbott Nutrition, Nutricia, Nestlé Health Science, Pfizer, and AMRA medical. DNL has received an unrestricted educational grant from B. Braun for unrelated work. He has also received speaker's honoraria for unrelated work from Abbott, Nestlé and Corza.

Declaration of Generative AI and AI-assisted technologies in the writing process

None used.

Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.clnesp.2024.07.1060>.

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