

1 **Exercise Prehabilitation in Elective Intra-cavity Surgery: a Role within the**
2 **ERAS Pathway? A Narrative Review**

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8 **Running heading:** Exercise Prehabilitation: a Narrative Review

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16 **Abstract**

17 The Enhanced Recovery after Surgery (ERAS) model integrates several elements of
18 perioperative care into a standardised clinical pathway for surgical patients. ERAS programmes
19 aim to reduce the rate of complications, improve surgical recovery, and limit postoperative
20 length of hospital stay (LOHS). One area of growing interest that is not currently included
21 within ERAS protocols is the use of exercise prehabilitation (PREHAB) interventions.
22 PREHAB refers to the systematic process of improving functional capacity of the patient to
23 withstand the upcoming physiological stress of surgery. A number of recent systematic reviews
24 have examined the role of PREHAB prior to elective intra-cavity surgery. However, the results
25 have been conflicting and a definitive conclusion has not been obtained. Furthermore, a
26 summary of the research area focussing exclusively on the therapeutic potential of exercise
27 prior to intra-cavity surgery is yet to be undertaken. Clarification is required to better inform
28 perioperative care and advance the research field. Therefore, this “review of reviews” provides
29 a critical overview of currently available evidence on the effect of exercise PREHAB in
30 patients undergoing i) coronary artery bypass graft surgery (CABG), ii) lung resection surgery,
31 and iii) gastrointestinal and colorectal surgery. We discuss the findings of systematic reviews
32 and meta-analyses and supplement these with recently published clinical trials. This article
33 summarises the research findings and identifies pertinent gaps in the research area that warrant
34 further investigation. Finally, studies are conceptually synthesised to discuss the feasibility of
35 PREHAB in clinical practice and its potential role within the ERAS pathway.

36 **Keywords**

37 Exercise training; Prehabilitation; Presurgical period; Intra-cavity surgery; Enhanced Recovery
38 after Surgery

39 **1. Introduction**

40 Major surgery represents a considerable stressor for older adults. The majority of surgical
41 patients are over 60 years old [1] and often present multiple comorbidities with a decreased
42 ability to cope with trauma. These age-related impairments in physiological function, coupled
43 with the raft of metabolic and hormonal perturbations that occur in response to surgery, often
44 lead to a longer convalescence for elderly patients [2]. In particular, major intra-abdominal
45 resections are associated with an in-hospital stay of up to 10-days [3] and complication rates
46 of 15-20% [4, 5].

47 The Enhanced Recovery after Surgery (ERAS) pathway was initiated in the 1990s by a group
48 of academic surgeons to improve perioperative care in these patients [6]. The ERAS model was
49 originally developed for colorectal surgery but has now been applied to almost all major
50 surgical specialities [7] and represents a paradigm shift towards a multimodal, patient-centred
51 approach to surgical care. ERAS is designed to modify the physiological and psychological
52 response to surgical trauma by integrating a range of evidence-based components into a
53 standardised clinical pathway. Ultimately, ERAS programmes aim to reduce the rate of
54 complications, improve surgical recovery, and limit postoperative length of hospital stay
55 (LOHS). Indeed, a number of recent meta-analytic reviews have reported a 30% to 50%
56 reduction in LOHS and complication rates in colorectal surgery patients receiving treatment
57 through the ERAS pathway compared to traditional perioperative care [8-12]. Furthermore,
58 this reduction has been achieved without compromising patient safety [10] and is associated
59 with lower healthcare costs [9].

60 There are 24 core elements of ERAS that are distributed along the patient pathway, as outlined
61 recently by Ljungqvist and colleagues [7]. One area that is not currently included within ERAS
62 protocols, although it is a growing field of interest, is the use of preoperative exercise or

63 prehabilitation (PREHAB) interventions. PREHAB refers to the systematic process of
64 improving functional capacity of the patient to withstand the upcoming physiological stress of
65 surgery [13]. The concept of PREHAB is contingent on the principle that patients with higher
66 levels of fitness generally exhibit reduced postoperative complications and improved clinical
67 outcomes [14]. The application of PREHAB prior to intra-abdominal and intra-thoracic surgery
68 has received considerable attention in recent years [15-19]. However, the results of existing
69 systematic reviews have been conflicting. Clarification is required to better inform
70 perioperative care and to identify pertinent gaps in the research area that warrant further
71 investigation.

72 To address this issue, a recent scoping review [20] has provided an extensive overview of the
73 PREHAB literature. The review included all types of surgery and non-exercise pulmonary
74 interventions, such as inspiratory muscle training (IMT) and incentive spirometry. Given that
75 the effectiveness of PREHAB may differ between various types of surgery and different
76 methods of preoperative therapy, a “review of reviews” that focuses exclusively on exercise
77 interventions prior to intra-cavity resection is warranted. Therefore, this review aimed to
78 evaluate the effect of exercise PREHAB on physical fitness, LOHS and postoperative
79 complications in patients undergoing elective major intra-abdominal and intra-thoracic
80 surgery.

81 **2. Process of review**

82 We conducted the literature search in PubMed (MEDLINE) and Google Scholar databases
83 from 2006 to 2016 using a combination of keywords such as prehabilitation, preoperative,
84 surgery, aerobic exercise, resistance training, physical function, abdominal, thoracic, cardiac,
85 colorectal, and lung. Keywords were also combined with the following Medical Subject
86 Headings (only relevant for search in PubMed): preoperative period, thoracic surgery,

87 colorectal surgery, exercise, and exercise therapy. Focus was on systematic reviews and meta-
88 analyses, although these were also supplemented with available individual studies. We defined
89 *PREHAB* as a structured regimen of aerobic and/or resistance training, either home-based or in
90 a supervised setting, prior to major elective intra-cavity surgery. *Intra-cavity surgery* was
91 defined as elective intra-abdominal and intra-thoracic surgery [16]. In the cases of systematic
92 reviews or meta-analyses that cited studies that included other types of surgery (e.g.
93 orthopaedic) or the predominant use of pulmonary interventions (e.g. IMT), pertinent
94 individual studies cited within the meta-analyses were reviewed independently. Finally, we
95 discuss whether the current evidence-base supports the inclusion of *PREHAB* within ERAS
96 pathways.

97 **3. PREHAB in Intra-Thoracic Surgery**

98 **3.1. Coronary Artery Bypass Graft Surgery**

99 Two well-designed meta-analyses [21, 22] have reviewed the effects of *PREHAB* in cardiac
100 patients awaiting coronary artery bypass graft (CABG) surgery. The majority of studies cited
101 within these reviews, however, exclusively involved educational interventions and/or IMT. For
102 example, Hulzebos and colleagues [21] reviewed eight randomised controlled trials (RCTs),
103 six of which only included the use of non-exercise pulmonary interventions. We identified just
104 three studies, all of which were RCTs that involved the predominant use of exercise training
105 as the *PREHAB* intervention [23-25]. In a small pilot RCT using the six minute walk test
106 (6MWT) distance as the primary outcome [23], 17 patients engaged in eight weeks of aerobic
107 exercise (walking and cycling at 85% maximal oxygen consumption [VO_{2max}]) and resistance
108 exercises (body weight and resistance bands) twice per week. Compared with control, the
109 *PREHAB* group improved 6MWT distance and 5-metre gait speed at the preoperative (6MWT:
110 136 metres; 5-metre gait speed: -1.6 sec) and 3-month postoperative (6MWT: 123 metres; 5-

111 metre gait speed: -1.2 sec) reassessments. No reduction in LOHS was found between groups
112 (PREHAB = 5.3 ± 1.0 days; CON = 5.1 ± 1.4 days), suggesting that the improvement in
113 functional capacity may not translate into favourable clinical outcomes. A lack of change in
114 LOHS was also reported following 10 weeks of combined aerobic exercise training (40 minutes
115 at 60% maximum heart rate [HR_{max}]) and mental stress reduction in 117 patients scheduled for
116 CABG and/or valve surgery (PREHAB = 6 days [range: 5 to 8]; CON = 6 days [range: 5 to 8])
117 [24]. The absence of an objective measure of physical fitness means it is unknown whether
118 PREHAB improved patients' fitness prior to surgery. Moreover, it is important to note that the
119 sample sizes for both studies were calculated in order to provide power to detect changes in
120 either objective [23] or subjective [24] measures of function, rather than clinical outcomes.

121 In the only RCT conducted with CABG patients that had LOHS as the primary outcome
122 measure, 246 patients awaiting elective surgery for CABG were randomised to receive either
123 a multi-dimensional preoperative intervention or usual care [25]. The intervention consisted of
124 30 minutes of supervised aerobic exercise (40 – 70% of VO_{2max}), in addition to a variety of
125 mobility exercises, twice weekly for approximately eight weeks (mean duration: 8.3 weeks).
126 Patients who received the PREHAB intervention spent one less day in hospital overall (95%
127 CI: 0.0 to 1.0), and 2.1 hours less time in ICU (95% CI: -1.2 to 16.0) compared to the control
128 group. The PREHAB group also displayed a greater quality of life during the waiting period
129 (measured by the SF-36), which continued up to six months after surgery. Thus, engaging in
130 PREHAB in the waiting period for CAGB surgery provided an imminent patient benefit that
131 is likely to be meaningful. Furthermore, the authors calculated the cost of PREHAB would be
132 C\$342 per day, and that an exercise test before the intervention would cost C\$240 [25]. Based
133 on the rate of one day in a Canadian hospital (C\$715), a one day reduction in LOHS would
134 provide a net cost savings of approximately C\$133 per patient per day.

135 **3.2. PREHAB in Lung Resection Surgery**

136 Overall, the quality of evidence for PREHAB in lung resection surgery is poor, with the
137 research area being dominated by RCTs with small sample sizes and single-group observational
138 trials. In a recent systematic review [19] of 10 studies consisting of 277 participants (Table 1)
139 , only four studies were RCTs, with one study being a case control study and the remaining
140 five studies were prospective cohort trials. Furthermore, only four studies included in the
141 review were considered as ‘good quality’ or above according to the Physiotherapy Evidence
142 Database (PEDro) scale. Notwithstanding the lack of high quality studies, the findings
143 indicated that PREHAB may have beneficial effects on physical fitness, which is consistent
144 with another systematic review in patients undergoing elective intra-cavity surgery [16]. The
145 authors also suggested that LOHS and complication rates may be reduced with PREHAB [19].
146 However, this conclusion was based on only two RCTs, both of which included less than 30
147 participants. In a meta-analysis of 21 studies (5 RCTs) that included 1189 patients from 2005
148 to 2013 [15], PREHAB reduced LOHS by -4.83 days (95% CI: -5.9 to -3.76) and decreased
149 the relative risk for developing postoperative complications (RR 0.45; 95% CI: 0.28 to 0.74)
150 based on pooled data from nine studies. While the meta-analysis did not quantify changes in
151 exercise capacity, several included studies reported statistically significant improvements in
152 6MWT distance and VO_{2max} , ranging from 20 metres [26] to 170 metres [27] and from 2.3
153 $mL \cdot kg^{-1} \cdot min^{-1}$ [28] to 6.3 $mL \cdot kg^{-1} \cdot min^{-1}$ [27], respectively. Furthermore, two studies also
154 demonstrated an increment in the maximal workload achieved during the cardiopulmonary
155 exercise test [29, 30].

156 Interestingly, simple walking regimens have been shown to evoke discernible benefits to
157 patients awaiting lung resection. In an RCT with LOHS as the primary outcome measurement
158 [31], 60 patients with non-small cell lung cancer (NSCLC) received either usual care, or
159 engaged in walking exercise on a treadmill three times per day for one week (intensity and
160 duration not reported) in addition to chest physiotherapy (breathing exercises and incentive

161 spirometry). The PREHAB group registered a significantly reduced LOHS in comparison
162 to the control group (5.4 ± 2.7 vs. 9.7 ± 3.1 days, respectively). Compared with baseline
163 values, the PREHAB group also significantly increased their pre-surgical walking duration
164 (18.2 ± 7.4 vs. 39.7 ± 16.2 minutes), distance (614 ± 415 vs. 991 ± 535 metres), and speed (4.0
165 ± 1.0 vs. 5.0 ± 1.1 mph), although the testing involved non-standardised procedures and the
166 change in walking capacity was measured within groups because the control group did not
167 participate in exercise testing. Nevertheless, improvements in clinical and functional outcomes
168 have also been reported following a similar four-week walking (10 – 30 minutes at 80%
169 VO_{2max} , three times per week) and IMT (10 – 30 minutes daily) intervention prior to lung
170 cancer resection [32]. Compared to patients receiving conventional chest physiotherapy
171 (breathing exercises for lung expansion), the PREHAB group increased 6MWT distance (-4.6
172 ± 20.3 vs. 50 ± 16.2 metres), reduced LOHS (12.2 ± 3.6 vs. 7.8 ± 4.8 days), had fewer days
173 with chest tubes (7.4 ± 2.6 vs. 4.5 ± 2.9 days) and exhibited less postoperative pulmonary
174 complications (7 vs. 2), respectively. Though the inclusion of IMT is likely to have augmented
175 the effects of exercise, these studies [31, 32] suggest that a short-term, simple PREHAB
176 protocol may improve pre-surgical functional capacity and can have a substantial benefit on
177 convalescence, at least in patients awaiting lung resection.

178 In the only home-based study, Coats et al. [33] investigated the effects of a 4 week PREHAB
179 intervention in NSCLC patients. The intervention included 30 minutes of aerobic exercise at
180 60-80% of peak workload and free-weight resistance exercises (1-2 sets of 10-15 repetitions
181 with 1-2 kg dumbbells) for 3-5 times per week. In contrast to several previous studies, no
182 significant improvement was found in the VO_{2max} of the 13 patients to complete the
183 intervention. The lack of supervision in Coats et al. [33] may have contributed to the difference
184 between studies; supervised programmes tend to be more effective than unsupervised
185 programmes for improving function in older adults [34]. Despite the lack of change in VO_{2max} ,

186 Coats et al. [33] reported significant and clinically meaningful improvements in the constant
187 endurance test (from 264 ± 79 seconds to 421 ± 241 seconds) and 6MWT distance (540 ± 98
188 metres to 568 ± 101 metres). Small improvements were also noted in deltoid ($\Delta 1.8 \pm 2.8$ kg),
189 triceps ($\Delta 1.3 \pm 1.8$ kg) and hamstring ($\Delta 3.4 \pm 3.7$ kg) muscle strength following PREHAB.
190 While these changes were potentially trivial, an increase in muscle strength prior to surgery
191 may play an important role in facilitating early mobilisation, which is a key component of the
192 ERAS pathway. For this reason, measures of muscle strength should be considered important
193 in future studies to assess the efficacy of PREHAB in context of ERAS.

194 In summary, there is some evidence that PREHAB can improve physical fitness prior to lung
195 resection surgery. These improvements appear to be meaningful and may translate into
196 favourable clinical outcomes. For example, studies measuring 6MWT distance reported an
197 increase of between 20 and 170 metres following PREHAB, with the majority of improvements
198 exceeding the minimal important difference previously reported in lung cancer patients (22 -
199 42 metres) [35]. In addition, Coats and colleagues [33] provided preliminary evidence that
200 PREHAB can enhance the force-generating capacity of skeletal muscle. Even so, the research
201 area is dominated by poor quality studies, mainly involving single-group observational trials
202 with small sample sizes. It is also pertinent to note that the majority of studies consisted of at
203 least five hospital-based supervised exercise sessions a week, therefore a considerable time and
204 resource (money, facility and staffing availability) burden would be placed on both the exercise
205 provider and patient in order to participate in the intervention. Older persons are more likely to
206 engage in exercise interventions that are easily accessible, do not require transport, and
207 involve no out-of-pocket costs [36].

208 **4. PREHAB in Intra-Abdominal Surgery**

209 **4.1. Gastrointestinal and Colorectal Surgery**

210 There are several published systematic reviews in the topic of PREHAB and surgery that have
211 included gastrointestinal and colorectal patients, and a further four reviews that have focused
212 solely on colorectal and/or abdominal surgery [16-18, 37]. In 2014, a meta-analysis [38]
213 suggested that no recommendation can currently be made regarding exercise training as a
214 routine intervention for colorectal cancer patients. However, this study [38] involved all stages
215 of the perioperative pathway. In the only systematic review to date specifically evaluating
216 PREHAB in patients awaiting surgery for colorectal cancer, Boereboom et al. [17] identified
217 eight studies with a total of 518 patients from 2009 to 2015, including five RCTs, two
218 prospective cohort trials and one non-randomised interventional study. Results indicated that
219 exercise PREHAB improves functional capacity, and to a lesser extent cardiorespiratory fitness
220 prior to colorectal cancer resection. 6MWT distance was the preferred primary outcome
221 measure in five of the included studies (two studies analysed the same data [39, 40]), with
222 reported improvements of between 4 metres [41] and 42 metres [42] compared with control.
223 However, there was no evidence of reduced LOHS or complications rates, and thus the
224 improvement in fitness may not translate into reduced perioperative risk or improved
225 postoperative outcomes.

226 A similar finding was reported in a systematic review by O'Doherty and colleagues [16]
227 including 10 studies from 1981 to 2011, containing 524 patients awaiting elective intra-cavity
228 surgery. Four of the studies were RCTs and six were observational. It was concluded that
229 PREHAB is effective in improving physical fitness, however, the evidence for augmented
230 postoperative clinical outcome is limited. Seven of the studies reported VO_{2max} or predicted
231 VO_{2max} as the primary outcome measure, with increases of up to $8 \text{ mL}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$ found in
232 patients undergoing gastrointestinal surgery [43]. A beneficial effect of PREHAB on objective
233 measures of cardiorespiratory performance has also been demonstrated recently by West and
234 colleagues [44] in neoadjuvant chemoradiotherapy (NACRT) patients, although a non-

235 randomised design was used and the intervention lasted six weeks, which may not be applicable
236 for colorectal surgery patients not receiving NACRT because the duration exceeds the median
237 wait time between surgical consultation and resection (~31 days) [45].

238 There appears to be a collective difficulty of converting promising results in a laboratory
239 environment into meaningful improvements in the clinical setting. This may be related to the
240 design and conduct of exercise interventions, or because all studies in this research area report
241 measures of physical fitness as the primary outcome measure and are underpowered to detect
242 differences in clinical outcomes. It has been suggested that 400 participants would be required
243 to detect a 10% reduction in the incidence of absolute postoperative complications with an
244 alpha of 0.05 and a power of 0.80 [17]; to date, these data do not currently exist.

245 In another systematic review [18] based on six RCTs (673 patients) from 1997 to 2010, the
246 authors concluded that PREHAB may be effective in enhancing physical fitness in surgical
247 patients awaiting abdominal resection. However, when considering the primary data from the
248 individual studies included within the review, no study actually reported a PREHAB-induced
249 increase in physical fitness. Of the three studies to measure physical fitness prior to surgery,
250 Kim et al. [41] and Dronkers et al. [46] failed to show changes in VO_{2max} and predicted VO_{2max} ,
251 respectively. Furthermore, Carli et al. [39] showed that the proportion of patients with an
252 improvement of ≥ 20 metres in the 6MWT was actually greater in a sham intervention group
253 compared with the PREHAB group (47% vs. 22% preoperatively, and 41% vs. 11%
254 postoperatively). Patients in the PREHAB group were instructed to cycle seven days per week
255 (20-30 min at 50% of HR_{max} , progressing by 10% each week as tolerated) and perform
256 resistance training three times per week (bodyweight and free-weight exercises until volitional
257 failure), whereas the sham intervention consisted of a recommendation to walk for 30
258 minutes every day. While task specificity (e.g. walking intervention and walking-based
259 outcome measure) and the multiple imputation of large amounts of data (i.e. due to the high

260 attrition rates) may have contributed to the results, only 16% of the PREHAB group fully
261 adhered to the protocol. Thus, patients with a low baseline fitness level may have found the
262 intensive and time-consuming design of the bike/strengthening programme intimidating or too
263 difficult. This highlights the necessity to find an appropriate balance between an exercise
264 stimulus that is sufficient to improve physical fitness, but also to maximise patient engagement
265 and safety.

266 In order to improve exercise compliance, the same research group have since conducted three
267 trimodal home-based RCTs [42, 47, 48]. In all three studies the frequency of aerobic exercise
268 was decreased from daily to three times per week, the training intensity did not exceed 50%
269 HR_{max} , and patients were allowed to choose their preferred type of exercise. The exercise
270 interventions lasted four weeks and were also appended with whey protein supplementation
271 and psychological support. The PREHAB group displayed a greater improvement in 6MWT
272 distance compared with controls in all three studies (from 29.1 metres [47] to 41.6 metres
273 [48]), which was also associated with faster postoperative recovery of 6MWT performance 8
274 weeks following resection [from 45.2 metres [48] to 85.4 metres [42]]. Compliance in the
275 preoperative period was above 75% in all three studies, suggesting that exercising at home may
276 facilitate adherence to PREHAB programmes. Indeed, home-based cardiac rehabilitation
277 programmes have tended to show greater adherence and maintenance rates than supervised
278 hospital-based programmes [49]. However, consistent with other studies investigating
279 PREHAB in abdominal surgery, no differences between PREHAB and control groups were
280 found in LOHS, 30-day complication rate, or complication severity.

281 Generally, the literature shows that PREHAB prior to colorectal resection enhances walking
282 capacity by approximately 25 to 40 metres, and can also induce small improvements
283 cardiorespiratory fitness. The promotion of walking capacity prior to surgery has led to
284 improved postoperative recovery of physical fitness, which is parallel with the objectives of

285 the ERAS pathway. However, the magnitude of change in physical fitness appears insufficient
286 or unable to translate into favourable clinical outcomes, such as reduced LOHS and
287 complication rate. The lack of multi-centred adequately powered RCTs certainly underpin, at
288 least in part, the negligible changes in perioperative outcomes. It is also conceivable that the
289 current modalities of exercise PREHAB, rather than the theory of PREHAB *per se*, also
290 contribute to the absence of improvement in outcome measures.

291 There is a distinct lack of standardised PREHAB guidelines for patients undergoing major
292 intra-abdominal and intra-thoracic surgery, ostensibly due to the conflicting findings in the
293 current literature. The majority of studies have involved generic prescriptions of moderate-
294 intensity aerobic exercise, with resistance training less frequently included within PREHAB
295 protocols. Likewise, the primary endpoint was usually a measurement of cardiorespiratory
296 fitness such as VO_{2max} or 6MWT, presumably based on the well-established relationship
297 between VO_{2max} and perioperative outcome [14]. When resistance training has been prescribed
298 in PREHAB protocols, pertinent programme design variables have largely been ignored and/or
299 not reported. Given that PREHAB is defined as the systematic process of improving functional
300 capacity of the patient to withstand surgical stress [13], and strength training has consistently
301 been shown to augment functional ability in older adults [50], further work is required to
302 investigate the therapeutic benefits of individualised resistance training programmes prior to
303 intra-cavity surgery.

304 **5. A Role for PREHAB in the ERAS Pathway?**

305 PREHAB appears to be effective for improving physical fitness prior to elective intra-cavity
306 surgery. Some studies have also reported an accelerated recovery of postoperative functional
307 capacity, which is a central tenet of ERAS pathways [7]. However, the rate of complications
308 and LOHS are also important endpoints for ERAS care, and there is limited evidence

309 suggesting that PREHAB can modify these clinical outcomes. Indeed, there appears to be a
310 collective difficulty of translating favourable changes in functional capacity into a reduction in
311 complication rates or LOHS. Furthermore, the majority of studies in the PREHAB literature
312 are included in multiple systematic reviews, meaning there are a small number of primary
313 studies and most of them are single-centred and inadequately powered to detect changes in any
314 clinical endpoint.

315 The ERAS Society have published guidelines for evidence-based perioperative care in elective
316 colonic surgery [51]. The preoperative components of the ERAS model are presented in Table
317 2. For PREHAB to be considered a worthwhile addition to the ERAS pathway, evidence is
318 required demonstrating that the benefits of presurgical exercise exceed current practice in the
319 preoperative period. Only two studies to date, both involving colorectal cancer patients, have
320 administered PREHAB in the context of ERAS. Li et al. [42] compared PREHAB to a control
321 group receiving standard ERAS care, whereas Gillis et al. [48] compared PREHAB to a group
322 undergoing exercise rehabilitation within ERAS. In agreement with the totality of literature,
323 both studies reported an increase in walking capacity following PREHAB, but there were no
324 improvements in LOHS nor complication rates when compared to a standard ERAS
325 programme [42, 48]. Further research is required directly comparing the effects of ERAS *with*
326 PREHAB versus ERAS *without* PREHAB in patients undergoing intra-cavity surgery.

327 In addition to the well-established clinical benefits, studies have shown ERAS programmes to
328 be cost-effective across a range of surgical specialities, including abdominal and thoracic
329 surgery [52, 53]. This is thought to be a consequence of shorter convalescence and reductions
330 in morbidity and complication rates [53]. In contrast, there is a paucity of data concerning the
331 cost-effectiveness of PREHAB. However, the lack of benefit to clinical outcomes suggests that,
332 currently, PREHAB may not be economically worthwhile for service providers. The adoption
333 of any new intervention in the healthcare system requires rigorous justification because of

334 major financial constraints. The absence of improvements in LOHS and complications, coupled
335 with a lack of savings, impedes the potential uptake of PREHAB into existing ERAS pathways.
336 It is unknown whether PREHAB is simply unable to improve clinical outcomes, or that
337 currently prescribed exercise interventions are insufficient to drive the necessary adaptations.
338 The exercise programmes within this body of literature are largely heterogeneous, although the
339 vast majority of studies have involved generic prescriptions of moderate-intensity aerobic
340 exercise. While these protocols have generally induced changes in aerobic fitness, a more
341 precise manipulation of training variables may improve the training stimulus and better prepare
342 the patient for the upcoming physiological stress of surgery. Therefore, future work should
343 compare the effectiveness of different training modalities and adhere to exercise trial reporting
344 guidelines (e.g. [54]) to advance our understanding of the optimal exercise PREHAB
345 characteristics and ultimately help develop consensus exercise guidelines for this patient
346 population.

347 **6. Conclusion**

348 To conclude, the current evidence-base on PREHAB for patients undergoing elective intra-
349 cavity surgery is limited by inadequately powered RCTs, single-group observational trials and
350 a lack of evidence demonstrating favourable changes in clinical endpoints. Considering these
351 drawbacks in the literature, and that only two studies have administered PREAB in the context
352 of ERAS [42, 48], this review cannot recommend that PREHAB be introduced into existing
353 ERAS pathways. Further randomised clinical trials should be powered to detect changes in
354 clinical outcomes rather than changes in physical fitness. For example, prospective studies are
355 needed to better characterise the impact of PREHAB on length of stay and complication rate.
356 In addition, the quality of prescribed exercise PREHAB interventions must be examined in
357 order to advance this research area.

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519 **Table Captions**

520 **Table 1.** Overview of the included reviews

521 **Table 2.** Preoperative components of the Enhanced Recovery After Surgery (ERAS) Pathway

Table 1. Overview of the included reviews

Authors	Type of Review	Type of Surgery	Number of studies [RCTs]	Number of patients
Pouwels et al. [19]	SR	Lung	10 [4]	277
Garcia et al. [15]	SR and meta-analysis	Lung	21 [5]	1189
Boereboom et al. [17]	SR	Colorectal	8 [5]	518
O'Doherty et al. [16]	SR	Abdominal Cardiac	10 [4]	524
Pouwels et al. [18]	SR	Abdominal	6 [6]	673

RCT- randomised controlled trial, SR- systematic review

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Table 2. Preoperative components of the Enhanced Recovery After Surgery (ERAS)

Pathway

Component	Rationale
Cessation of smoking and excessive alcohol consumption	Reduce complications
Structured preoperative information, education and counselling	Reduce fear and anxiety
Preoperative carbohydrate treatment	Reduce insulin resistance and possibly improve recovery
Not routinely using preoperative bowel preparation	Reduce dehydration, prolonged ileus and risk of anastomotic leakage
Prophylaxis against thromboembolism	Reduce thromboembolic complications
Preoperative prophylaxis against infection	Reduce rate of infections

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