

| Study (Design)                      | Risk of bias (tool + overall) |               |      | Sample size, n   | Duration prehabilitation (Baseline to surgery)  | Prehabilitation Intervention                                |  |  | Outcome  | Times measured   | Quality of life outcome – main findings                                 |  |
|-------------------------------------|-------------------------------|---------------|------|--|---|---|--|--|----------|--|---|--|
|                                     | Poor                          | Fair/Moderate | Good |  |   | Exercise  | Nutrition  | Psychologic  |          |  |   |  |
| <b>Gillis 2014</b><br><br>(RCT)     | R<br>O<br>B<br>2              | Moderate      |      | Prehab: <b>38</b><br><br>Non-prehab (rehab group): <b>39</b>   | <b>Prehab group:</b><br>24.5 days<br>IQR [20-35]<br><br><b>Non-prehab (Rehab group):</b><br>20.0 days<br>IQR [11-40]  | Unsupervised home-training                                  | Dietitian consultation<br>● Protein requirement:<br>1.2 g/kg                               | Visit by a psychologist + anxiety-reducing exercises | PRIMARY  | Functional exercise capacity (6MWT <sup>1</sup> )                          | Baseline<br><br>Prior to surgery<br><br><b>Post-surgery:</b><br>1 month | Prehabilitation did not improve QOL compared with rehabilitation.  |
|                                     |                               |               |      | QOL  | Additional outcome<br><br>SF-36 <sup>2</sup> (8 subscales & PCS <sup>3</sup> /MCS <sup>4</sup> )  | 2 months  |  |  |          |  |   |  |
| <b>Gillis 2021</b><br><br>(Cohort)  | N<br>O<br>S                   | Fair          |      | Prehab: <b>55</b><br><br><400 m: <b>28</b><br>≥400 m: <b>19</b><br><br><i>(Stratified pre-op 6MWD<sup>Felt!</sup> Bogmærke er ikke defineret.: &lt;400 m vs ≥400 m.)</i> | Median: 40 days<br>IQR [28-51]  | Weekly supervised training session                          | Personalised prescribed nutrition<br>● Protein requirement:<br>1.5 g/kg                    | Personalised coping strategies + breathing exercises | PRIMARY  | Incidence of postoperative complications within 30 days                    | Baseline<br><br>Prior to surgery<br><br><b>Post-surgery:</b><br>1 month | Prehabilitation improved QoL, particularly in patients with increased physical capacity.   |
|                                     |                               |               |      | QOL  | Additional outcome<br><br>SF-36 <sup>2</sup>  | 2 months  |  |  |          |  |   |  |
| <b>Khrykov 2014</b><br><br>(Cohort) | N<br>O<br>S                   | Fair          |      | Prehab: <b>52</b><br><br>Controls: <b>75</b>   | (Not described)<br><br>Surgery followed a 10-14-day preoperative period.  | ✗   | A comprehensive diet, containing nutritional drinks.<br>● Protein requirement:<br>1.5 g/kg | ✗  | PRIMARY  | Immediate and long-term treatment outcomes                                 | Baseline<br><br><b>Post-surgery:</b><br>Day 7                           | Significantly better early postoperative QoL, sustained during follow-up.  |
|                                     |                               |               |      | QOL  | Additional outcome<br><br>SF-36 <sup>2</sup> + EORTC QLQ-CR29 <sup>5</sup> at baseline, 7 days, and at 3, 6, 12, 24, 36 months ( <i>In controls, SF-36<sup>2</sup> only</i> ) | 3 months<br>6 months<br>12 months<br>24 months<br>36 months |  |  |          |  |   |  |
| <b>Koh 2022</b><br><br>(Cohort)     | N<br>O<br>S                   | Poor          |      | Prehab: <b>58</b><br><br>Non-prehab: <b>23</b>   | Median: 16 days<br>IQR [12.3-19.8]<br><br>Range:<br>8-35 days   | Resistance exercise + weekly physiotherapist supervision    | Dietitian consultation   | ✗  | PRI-MARY | Short-term surgical outcomes (length of stay, 30-day morbidity, mortality) | Baseline<br><br><b>Post-surgery:</b><br>1 month                         | Sustained QoL improvement from pre-surgery to 6 months in the prehabilitation group<br><br><i>(No QOL measures for controls)</i> |
|                                     |                               |               |      | QOL  | Additional outcome<br><br>EQ-5D <sup>6</sup>  | 3 months<br>6 months  |  |  |          |  |   |  |

|  |     |             |   |   |  |  |  |                |   |  |   |
|--|-----|-------------|---|---|--|--|--|----------------|---|--|---|
| <b>Li 2012</b><br><br><b>(Cohort)</b>  | NOS | <i>Good</i> | Prehab: <b>42</b><br>Non-prehab: <b>45</b>  | Median: 33 days<br>Range:<br>21-46 days | Individualised exercise program + extra cardio | Dietitian consultation<br>• Protein requirement:<br>1.2 g/kg | Visit by a psychologist + relaxation and breathing exercises       | <b>PRIMARY</b> | Functional walking capacity (6MWD <sup>1</sup> )  | Baseline<br>Prior to surgery<br><b>Post-surgery:</b><br>1 month                  | No significant difference in QoL.                         |
|  |     |             |   |   |  |  |  |                | <b>QOL</b>  | Secondary outcome<br>SF-36 <sup>2</sup>  |   |
| <b>Minella 2016</b><br><br><b>(Cohort)</b><br><i>Attention:</i> Re-analysis of Li, 2012, Gillis, 2014 and an ongoing RCT | NOS | <i>Poor</i> | Prehab: <b>106</b><br>Group B: <400 m: <b>36</b><br>Group A: ≥400 m: <b>70</b><br><i>(Stratified pre-op 6MWD<sup>3</sup>: &lt;400 m vs ≥400 m.)</i> | Approximately 30 days                   | Unsupervised home-training                     | Dietitian consultation<br>• Protein requirement:<br>1.2 g/kg | Visit by a psychologist + anxiety-reducing and breathing exercises | <b>PRIMARY</b> | 6MWD <sup>1</sup> as a measure of functional capacity reflective of activities of daily living. | Baseline<br>Prior to surgery<br><b>Post-surgery:</b><br>1 month                  | No significant QoL differences, despite functional gains. |
|  |     |             |   |   |  |  |  |                | <b>QOL</b>  | Secondary outcome<br>SF-36 <sup>2</sup><br>(PCS <sup>3</sup> /MCS <sup>4</sup> ) |   |

**Table 1** – Overview of the final included studies in the systematic review.

<sup>1</sup> 6MWD = 6-minute walk test (measures the distance that a patient can briskly walk on a flat, hard surface over a period of 6 minutes)

<sup>2</sup> SF-36 = Short Form-36 Health Survey

<sup>3</sup> PCS = Physical Component Scale (SF-36 component)

<sup>4</sup> MCS = Mental Component Scale (SF-36 component)

<sup>5</sup> EORTC QLQ-CR29 = European Organisation for Research and Treatment of Cancer – Quality of Life Questionnaire, Colorectal Cancer Module

<sup>6</sup> EQ-5D = European Quality of Life - 5 Dimensions