

## What evidence exists that describes the benefits and outcomes of a prehabilitation program for adult surgical patients?

This report aims to summarize the best available evidence regarding the benefits and outcomes of prehabilitation programs for adults undergoing surgery. This broad overview focuses on literature for prehabilitation programs for adults undergoing abdominal or thoracic surgery, although some evidence for adults undergoing other surgeries has been included where specified. This information is intended to guide clinical decision-making in refining the set-up of a prehabilitation program, taking into account four dimensions: cost savings, post-operative length of hospital stay (LoS), patient outcomes and post-operative patient quality of life (QoL).

### Key Messages:

- The theoretical framework of prehabilitation states that pre-operative interventions can improve patients' initial physiological states and help them develop a buffer of functional capacity to lessen the predictable detrimental effects of the upcoming major surgery.
- The evidence supports this theoretical framework, showing positive clinical outcomes in patients who participate in prehabilitation programs. It is important to note, however, that within the explored literature, prehabilitation programs include a variety of components, and standardized prehabilitation programs for specific adult surgical populations are only beginning to emerge.
- Overall, having a prehabilitation program is more cost-effective than cost-saving, according to the limited data found in the literature on this topic. Longitudinal studies in specific institutions offering prehabilitation programs should evaluate longer-term cost trends and the potential avoidance of specific costs.
- Evidence on LoS of surgical patients who participated in prehabilitation programs is mixed. Slightly more than half of the studies analyzed showed shorter LoS following prehabilitation, while slightly fewer studies showed that differences in LoS were not significant. However, similarly to cost, three articles mention LoS avoidance, lower risk of hospitalization or lower hospitalization rates due to fewer post-operative complications in surgical patients who participated in prehabilitation programs.
- Many types of post-operative patient outcomes are significantly improved following prehabilitation programs.
- QoL is improved post-operatively in prehabilitated surgical patients.
- The structure of prehabilitation programs in clinical settings is challenged by a number of issues, including but not limited to lack of clarity regarding which components to include (e.g. nutrition, exercise, cognitive behavioural therapy, etc.) for each surgical population, timing before surgery, intensity of exercises, program duration and patient compliance (especially when prehabilitation is administered/begun at home).

#### Who is this summary for?

This summary was requested by Antoinette DiRe, Director of Multidisciplinary Services, Adult Sites and Mental Health Mission; and responsible for the NSA/SAPA Trajectory & Dr. Francesco Carli, Anesthesiologist at the MUHC.

#### Information about this summary:

This report covers a broad collection of literature and evidence sources with a search emphasis on systematic reviews and randomized controlled trials.

#### This summary includes:

Key findings from a broad collection of very recently published literature (from 2017-2020) and evidence sources.

#### This summary does not include:

Recommendations, additional information, or detailed description of the interventions in the studies.

## 1. Background:

The idea of offering prehabilitation services at the MUHC is not new. In 2005, a prehabilitation program was conceptualized here and since 2010, prehabilitation research studies have been conducted at the MUHC on patients undergoing elective colorectal, prostate, bladder and esophageal resections for cancer. The interdisciplinary program instituted to offer this program is holistic, multimodal and includes personalized and structured exercise conditioning, nutrition therapy and relaxation strategies together with medical and pharmacological optimization.

The multimodal MUHC prehabilitation program is the only one in Québec and in Canada. Internationally, the MUHC's peri-operative program (POP) is well recognized and has organized scientific congresses, masterclasses and workshops. The unit is a centre for research, development and training. Over 40 peer-reviewed publications have been generated over the last nine years. Single and multicentre, national and international studies have been initiated. Some of the previous major findings from MUHC-led research studies on prehabilitation include the following:

- Prehabilitation programs, whether done at home or in hospital-supervised settings, are feasible, and there is around 60-90% patient compliance.
- Patients who followed a prehabilitation program displayed significantly increased physical fitness before and after various surgeries, aiding earlier recovery: 60% of prehabilitated patients returned to their baseline levels four weeks following surgery and 80% returned to their baseline levels eight weeks post-operatively, compared to only 30-40% of patients who did not participate in prehabilitation programs.
- Patients with poor baseline physical fitness are most likely to benefit from prehabilitation and improve their functional state.
- Patients at the MUHC who participated in prehabilitation programs before colorectal cancer resection were 71% less likely to experience severe complications. Economically, this saves a significant amount of money in avoided hospitalizations due to complications.
- Multimodal prehabilitation is associated with improved five-year disease-free survival in patients with stage III colorectal cancer.
- Initial findings show that prehabilitation programs for colorectal cancer patients is associated with a high probability of cost-effectiveness.

While this prehabilitation program has been part of MUHC services for many years now, one of the present aims of Multidisciplinary Services is to establish a staffed prehabilitation clinic to offer this service on a larger scale, for more adult surgical populations and with added components in its multimodal structure which could increase its effectiveness. There is also a desire to corroborate and build on the evidence found at the MUHC with evidence found in other institutions and in scientific literature. The following PICO framework was determined for this investigation:

**P (Population concerned)** = Adult patients undergoing surgery under general anesthesia

**I (Intervention)** = Prehabilitation

**C (Comparison)** = No prehabilitation

**O (Outcomes)** = Cost comparison, LoS, Patient outcomes, QoL.

### Contents:

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This rapid review presents summaries of the best available evidence for adults who participated in a prehabilitation program before undergoing major surgical procedures requiring general anaesthesia, with an emphasis on those who had colorectal, abdominal or thoracic surgery. **Four dimensions** were specifically explored and are discussed separately below: **Cost savings, post-operative LoS, patient outcomes and post-operative patient QoL**. Detailed search strategies were developed by two experienced librarians (I. Mahmoud and A. Bergeron). Sources include: Medline via Ovid SP, Embase and the Cochrane Library. The concepts were searched using both subject headings and text words (specific search terms are available upon request). The search dates were February 3rd and 17th, 2020, respectively and results were limited to within five years of publication. Initial screening and deduplication were done by the librarians, with 713 retained articles for the Evidence-Informed Decision-Making Advisor (EIDM-A) to further screen. Articles that were out of scope and studies with poor or poorly described methodology were discarded by the EIDM-A. 38 relevant articles were retained for analysis. The studies were analyzed and the report was prepared by the EIDM-A.

The retained studies that were analyzed range from 2017-present and consist mainly of systematic reviews and RCTs of moderate quality. A list of all the articles found and reviewed is available upon request ([marie-linda.boghdady@muhc.mcgill.ca](mailto:marie-linda.boghdady@muhc.mcgill.ca)).

#### **Levels of Evidence** (adapted from OHRI KTA Evidence Summary document)

Each piece of evidence presented in this summary is assigned a level.

This assignment is based on the evidence being presented and not on the claim made by the authors.

- ☀ **Platinum:** systematic reviews and meta-analysis
- ✳ **Gold:** Randomized controlled trials
- ★ **Silver:** Observational studies (non-randomized trials, case-control, time-series, cohort studies, case series, literature reviews, qualitative studies.)
- ☆ **Bronze:** Expert committee guidelines, reports or opinions, commentary or editorials.
- **Level of evidence** cannot be determined.

## **2. Summary of Findings:**

### **a. Evidence regarding cost savings and/or cost control benefits with a prehabilitation Program**

There were only two studies found which discussed this topic adequately. They both pointed to the cost-effectiveness of having a prehabilitation program in place. Note also that cost effectiveness is implied in a shorter LoS, described in the next section. It is also a more popular point of analysis than actual cost tabulation in literature.

- ✳ A 2017 cost-consequence analysis was performed using secondary data from a randomised, blinded clinical trial. The aim of this study by Barberan-Garcia et al. was to assess the midterm clinical impact and costs from a

hospital perspective of an endurance-exercise-training-based prehabilitation program in high-risk patients undergoing major digestive surgery. Health care use for the cost analysis included costs of the prehabilitation program, hospitalization and 30-day emergency room visits and hospital readmissions. Prehabilitation showed a protective effect for 30-day hospital readmissions (relative risk: 6.4; 95% confidence interval [CI]: 1.4–30.0). The mean cost of the program was €389 per patient and did not increment the total costs of the surgical process (€812; CI: 95% –878 – 2642; P=0.365). The article concludes that prehabilitation may result in health value generation. Moreover, it appears to be a protective intervention for 30-day hospital readmissions and its effects on aerobic capacity and physical activity may show sustainability at midterm. While not mentioning actual cost savings, this article shows evidence of cost effectiveness and avoidance when prehabilitation programs are present [1].

✳ A cost-utility analysis was performed alongside a 12-month clinical analysis for a randomized controlled trial of a prehabilitation program on adult patients undergoing total hip or total knee replacement surgeries. Cost information for this study by Fernandes et al. in Denmark was extracted using national registries and valued using standard tariffs for Europe. Incremental net benefit was analyzed to estimate the probability for the intervention being cost-effective for a range of threshold values. A health care sector perspective was applied. Despite including an intervention cost of €326 per patient, there was no difference in total cost between groups with prehabilitation vs. no prehabilitation intervention [€132 (95% CI –3942 to 3679)]. However, at a threshold of €40,000, pre-operative exercise was found to be cost effective at 84% probability. Therefore, they concluded that their pre-operative supervised neuromuscular exercise program for eight weeks was cost-effective for these patients [2].

#### **b. Evidence regarding post-operative LoS when a prehabilitation program is in place**

Post-operative length of stay (LoS) is the measure of the number of days the patient remains hospitalized following surgery until enough strength is gained for the patient to function independently and return home. Ten systematic reviews and seven randomized controlled trials were retained for the purposes of this review. Though the systematic reviews were well done, the studies on which they were based were of mostly moderate (and sometimes low) quality. There was also much variance in the prehabilitation interventions and the surgical populations included, rendering it difficult to achieve a standardized conclusion.

✳✳ Out of 17 included articles covering this topic, a shorter post-operative LoS was demonstrated in five systematic reviews [3] [4] [5] [6] [7], two RCTs [8] [9] and one literature review [10] (for a total of eight articles) following prehabilitation (including a systematic review by Adiamah et al. in which prehabilitation was only a special diet). Surgical patient populations included were abdominal (GI), thoracic and cardiac.

✳✳ Out of 17 included articles covering this topic, there was no significant difference found in post-operative LoS following prehabilitation in three systematic reviews [11] [12] [13] and three RCTs [14] [15] [16] (for a total of six articles). Surgical patient populations included were colorectal, abdominal (GI), pancreatic, thoracic and cardiac (excepting one systematic review that looked at surgery required for any cancer).

✳✳ Out of 17 included articles covering this topic, there was one systematic review [17] and two RCTs [1] [18] that did not demonstrate a shorter post-operative LoS following prehabilitation. However, hospitalization avoidance in the 30 days following the surgery was identified in the RCT by Barberan-Garcia et al. The protective effect of prehabilitation on 30-day hospital readmissions for a surgical GI population was reflected in the two other studies as well (for lung cancer and cardiac surgical patients).

### c. Evidence regarding patient outcomes when a prehabilitation program is in place

✿✿✿ This dimension is by far the most supported by evidence regarding prehabilitation programs. Twenty-eight articles (11 systematic reviews, 15 RCTs, one observational study and one literature review) showed a variety of significantly improved patient outcomes, including (in no particular order):

- Lower incidence of overall, composite, cardiac and pulmonary post-operative complications (cardiovascular surgery in frail patients; major abdominal, lung and cardiothoracic surgeries) [10] [8] [19] [12] [5] [9] [20] [17] [6];
- Lower levels of post-operative infectious complications (colorectal surgery) [21] [4];
- Reduced intra-operative blood loss (partial hepatectomy) [22];
- Greater pre-operative weight loss, reduced post-operative pain and decreased post-operative levels of C-reactive protein (laparoscopic Roux-en-Y gastric bypass) [23];
- Reduced delayed gastric emptying (DGE) (pancreaticoduodenectomy) [15];
- Faster return to continence and less leakage (radical prostatectomy surgery) [24];
- Increase in functional capacity (colorectal surgery, total knee arthroplasty (TKA) and total hip replacement (THR) surgery) [11] [2];
- Higher aerobic capacity and physical activity (gastrointestinal, lung and spinal decompression surgeries) [3] [1] [25] [9] [13] [20] [17];
- Enhancement of early post-operative balance and leg strength (TKA) [26] [27] [28];
- Improved six-minute walking test performance (gastrointestinal and lung surgeries, TKA and THR) [3] [29] [16] [17];
- Improved VO<sub>2</sub> and anaerobic thresholds (abdominal aortic aneurysm surgery) [30];
- Improved performance in climbing stairs (TKA and THR) [29];
- Lower pain and stiffness scores (TKA and THR) [29];
- Reduction in overall morbidity (major abdominal surgery) [19] [12].

The most frequently discussed positive patient outcome in the literature analyzed for this rapid review was the **lower incidence of post-operative pulmonary complications** following prehabilitation.

Two systematic reviews and one RCT specified that post-operative patient outcomes were not improved following prehabilitation. One systematic review mentioned that post-operative chronic pain was not prevented or reduced by prehabilitation in TKA patients [31]. This could be the case if pre-operative chronic pain remained high, even with prehabilitation. Another systematic review mentioned that a prehabilitation intervention did not produce conclusive results in an esophageal and gastric cancer surgery population; however, it noted significant heterogeneity between studies, with a variety of interventions, timelines and outcome measures reported, so that a conclusion was difficult to obtain [32]. Finally, the RCT found that exercise prehabilitation was not effective in significantly preventing peri-operative complications in bladder cancer patients undergoing cystectomy. However, this population is very specific, and perhaps adding other modalities to this prehabilitation could improve peri-operative and post-operative outcomes (the latter was not measured) [33].

Refer to the EIDM-A for the detailed articles and the particular prehabilitation interventions that resulted in the above-listed improved patient outcomes.

#### d. Evidence regarding patient QoL when a prehabilitation program is in place

✿✿✿ Some outcome measures were not clearly categorized as patient outcomes or as QoL outcomes, so there can be some overlap in results that could apply to both dimensions. That said, nine articles (three systematic reviews [19] [7] [34], five RCTs [25] [33] [24] [35] [18] and one literature review [36]) showed a somewhat significant improvement in QoL following prehabilitation and surgery. One additional systematic review also showed a slight improvement in cancer patients following prehabilitation that preceded treatment (these were not surgical patients) [37], which may prove useful for other hospital services.

How QoL was measured varied from study to study. The timeframe for QoL measurement was also not always clear (some measurements were taken up to a year after surgery). Again, this dimension was measured for various surgical populations.

### 3. Last Word

✿ A noteworthy article by Thomas et al. [38] addressed the challenges in obtaining conclusive evidence regarding the benefits of prehabilitation (patient and other outcomes), despite there being many studies in this area. The authors mention that, when studies are well done and take into account proper conditions (adequate selection and inclusion of high-risk surgical patients, providing personalized and probably multimodal (partly) supervised prehabilitation, objective monitoring of progress, measuring the incidence and impact of post-operative complications), prehabilitation effectiveness is proven.

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